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Photos top to bottom: (1) Closing Ceremony of the 8th EAHSC: Switching off the torch by Dr. Kevit Desai, PS Ministry of East African Community and Regional Development, Kenya (2) Mushema: Foetus extracted during laparotomy for omental pregnancy and (3) Shadrack: Post-Operative Supine Antero-Posterior Chest X-Ray

Comparison of Survival Outcomes between Early Breast Cancer Patients who Underwent Mastectomy and Patients Treated by Breast Conserving Therapy: A Meta Analysis

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ABSTRACT

Background: Early stage of breast cancer requires mastectomy or breast conserving therapy. However, there are disagreements regarding the outcome of these two types of therapies in term of overall survivals.
Objectives: The first aim of this meta-analysis was to assess the overall survival between patients who underwent mastectomy and those treated by breast conserving therapy. The second was to evaluate the influence of the follow up period on overall survival between the patients who benefited mastectomy and those who under went breast conservative therapy.
Methods: We systematically searched on PubMed and Cochrane library all published randomized trials comparing mastectomy with breast conserving therapy and assessing overall survival.
Results: Using dichotomous data, there was not a significant difference between mastectomy and BCT(OR:0.99; 95% CI:0.93-1.06; P:0.86). This was the same in subgroup analysis based on period of follow up. Their ORs and CI were (OR:0.97; 95% CI:0.81-1.18; P:0.79), (OR:1.01; 95% CI:0.90-1.13; P:0.87) and (OR:1.04; 95% CI:0.93-1.16; P:0.46) respectively for up to 5 years or less, between 5 and 10 years and more than 10 years of follow up. Using generic inverse variance, there was no significant difference between mastectomy and BCT, (HR:1.01; 95% CI:0.98-1.04; P:0.71). In subgroup analysis based on period of follow up, there was no significant difference between mastectomy and BCT. Their HRs, CI and P-value were (HR:1.01; 95% CI:0.951-1.07; P:0.79), (HR:0.98; 95% CI:0.92-1.04; P:0.51) and (HR:1.02; 95% CI:0.97-1.07; P:0.40) respectively for up to 5 years or less, between 5 and 10 years and more than 10 years of follow up.
Conclusion: This meta-analysis demonstrated that there was no significant difference between patients with early stage breast cancer when they are treated by mastectomy or breast consevative therapy in term of overall survival. Additionnally, the follow up period had no any influence on the both types of surgery in term of overall survival. Therefore, we suggest that breast conservative therapy or mastectomy should be discussed between the care team and the patient, taking into account the financial means available to the patient, especially in low-income countries, the benefits of the surgery and the patient's choices.

BACKGROUND

Breast cancer is one of the most common cancers worldwide. It is the leadingin female cancer in term of incidence and the second in term of mortality.[1]Patients with early stage of breast cancer undergo either mastectomy or breast conserving therapy (BCT) followed by radiation therapy with preferences for the second choose.[2] Several studies have compared the overall survival (OS) between patients treated by mastectomy with those underwent breast conserving therapy. Most of them found no significant difference between the two types of surgery regarding the overall survival but others found that the breast conserving therapy is the best and was some time advised to patients.[2-4] This was also effective in one meta-analysis performed on patients with locally advanced breast cancer after good response to neoadjuvant chemotherapy where BCT was a safe surgery for patients and had good response[5].

However, two recent meta-analyses, one using population-based studies and another randomized controlled trials concluded that mastectomy provides better OS than breast conserving surgery in women with early breast cancer.[6,7] In these meta-analyses, both considered hazard ratio estimates for overall survival and 95 % Confidence Interval (CI) as one of the inclusion criterions. Another meta-analysis performed with non-randomised studies reported that the 3 year or 5 year overall survival, was not statistically different between the BCT group and the mastectomy group.[8] For this meta-analysis, the included studies reported the outcome as dichotomous data.

It is possible to analyse time-to-event data as dichotomous data (data from each intervention arm of each study are provided in a 2 x 2 table)even

though the most appropriate way of summarising time-to-event data is to use methods of survival analysis and express the intervention effect as a hazard ratio as clarified by several studies.[9,10]

To address the divergences raised above, we conducted a meta-analysis of randomised trials using reported outcomes as dichotomous data or as hazard ratios. The objective of this meta-analysis was to comprehensively assess OS between patients with early-stage breast cancer who underwent mastectomy and those treated with breast-conserving therapy. Furthermore, it was to assess the influence of follow-up period and the effect of using dichotomous and generic inverse variances (data from each intervention group are provided as summary statistics) on OS.

METHODS
Study Selection and Data Extraction
To be included in this meta-analysis, studies should be published in English, randomized and comparing at least mastectomy with breast conserving therapy. Moreover, their outcomes should be reported in terms of overall survival (OS)and expressed either in Hazard Ratio (HR) or presented in dichotomous form.

The PubMed and Cochrane Library databases were searched for relevant papers up to 24th October 2019. The search MeSH key words were((Breast cancer) AND mastectomy) AND lumpectomy).

Study Quality and Risk of Bias Assessment
There are many tools to assess the risk of reporting biases in studies even though they have several limitations.[11,12] In this study, we adopted the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), updated on 22nd August 2019.It considers the risk of bias in the findings of any type of randomized trial and it assess the bias related to randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported result.[13]

Statistical Analysis
This study was assessed at two levels. The first was using dichotomous data and Odd Ratio (OR) with 95% confident interval(CI). The second was using life table data and Hazard Ratio(HR) with 95%CI. For the data reported as life table, they were adjusted and converted into HRs with their standard errors (SEs) by using the tool proposed by Tierney JF and his colleagues.[10] In both cases, heterogeneity among studies was significant whether $I^2 > 50\%$ with P<0.1 to 40%.[12] Review Manager (RevMan) [Computer program].Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014 was used for all statistical analyses. In both cases, we performed subgroups analysis to compare the OS in patients underwent mastectomy and those treated by BCT according to the period of follow up. The comparison was done between OS following the follow up period.

RESULTS
A total of 839 articles were identified in two online databases searched. After removing duplicates, we screened 453 articles. Only 32 abstracts were assessed after removing some papers by title. Eighteen papers

were fully evaluated. During this process, three articles were removed but simultaneously another paper was identified through references list. Finally, 16 studies[14-29] were included in the meta-analysis. Of them,14 papers were suitable for dichotomous, 6 for generic inverses variances. Four studies were common for both types of data (figure 1). All studies compared at least mastectomy with breast conserving therapy. Stage I and II were found in all studies. The follow up period varied from 1 to 30 years. Studies characteristics were resumed in table 1.

FIGURE 1: Pisma Flow Diagram
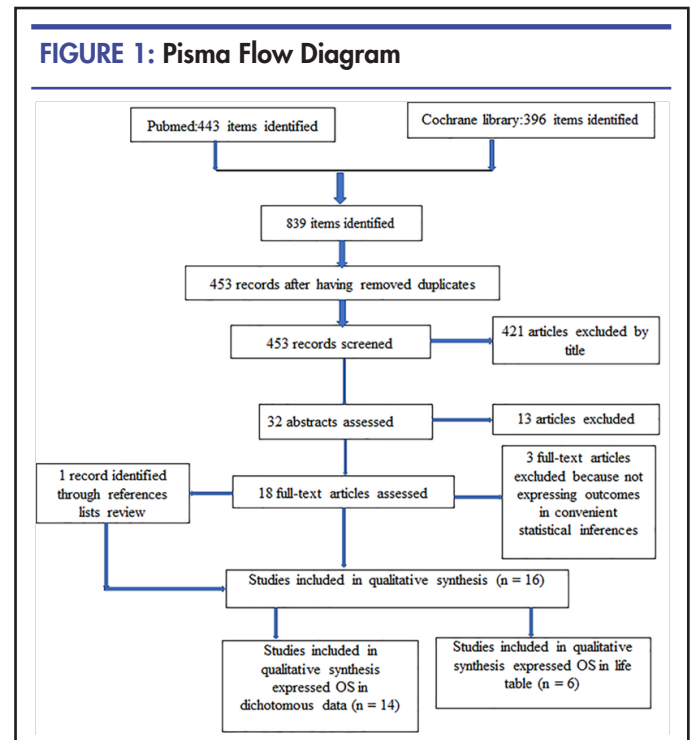
Overall Survival.
Outcome in Dichotomous Data
The OS reported as rate was available in 14 studies. In this case, it is suggested that meta-analysis should be performed using dichotomous type. Therefore, in this study, we found no significant difference between mastectomy and BCT, (OR:0.99; 95% CI:0.93-1.06; P:0.86). There was no evidence of significant heterogeneity across studies included, (I^2:0%, P:0.62), as shown in figure 2.

In subgroups analysis, there was also no significant difference according to the follow-up period, whether for less than or equal to 5 years, between 5 and 10 years or more than 10 years. Their ORs and CIs were respectively (OR:0.97; 95% CI:0.81-1.18; P:0.79), (OR:1.01; 95% CI:0.90-1.13; P:0.87) and (OR:1.04; 95% CI:0.93-1.16; P:0.46). In the three cases, there was no evidence of significant heterogeneity across studies. Their I^2 and P-value are (I^2:0%, P:0.76); (I^2:0%, P:0.97); (I^2:19%, P:0.28) respectively for up to 5 years or less, between 5 and 10 years and more than 10 years (figure 3).

Outcome in Generic Inverse Variance
The OSs reported as HRs were available in six studies. Performing meta-analysis by log (HR) with SEs, we did not find any evidence of significant difference between

TABLE 1: Studies Characteristics

Author & publication year	Interventions	Treatment after lumpectomy	Major inclusion criterion	Assessment period	Participants MT	Participants BCT
Veronesi U 1990	Classic Halsted mastectomy versus quadrantectomy, axillary dissection & radiotherapy on the ipsilateral breast	• Radiotherapy to the ipsilateral breast (50 Gy with high energy plus 10 Gy as a boost with orthovoltage) cm; N0–1	Patients (< 70 years old), tumour <2 cm, no palpable axillary nodes, Stage I: T<2	10 & 13 yrs	349	352
Fisher B 1985	Total mastectomy; segmental mastectomy alone or segmental mastectomy followed by breast radiation	• Cyclophosphamide, methotrexate, fluorouracil) • A minimum of 5000 rad	Tumour size ≤ 4cm; no palpable axillary nodes, Stage I, II (T1,2, N0,1, M0)	1,2,3,4 & 5 yrs	586	632
Litiere S 2012	Breast-conserving therapy versus modified radical mastectomy	• Whole breast radiotherapy & a tumour-bed boost (50 Gy in 5 weeks) with an additional boost dose of 25 Gy directed to the lumpectomy site	Tumours ≤ 5 cm, axillary node negative or positive disease carcinoma, Stage I or II disease	3,6,9,12,15, 18,21,24,27 & 30 yrs	420	448
Jacobson JA 1995	Breast-conservation therapy versus mastectomy	• Radiation in an isodose of 4500 to 5040 cGy to the whole breast, fractioned in 180 cGy five days per week	Clinical stage I or II (T1 or T2, which included tumours ≤ 5 cm; N0 or N1; M0) invasive carcinoma of the breast	3,6,9,12 & 15 yrs	116	121
Lee HD 1997	Modified radical mastectomy versus breast conserving therapy	• Radiotherapy (4 or 6 MeV) on the entire breast & supraclavicular fossa. Boost doses to the primary tumour site (9–15 MeV electron).	Stage I and II breast cancer with primary tumours ≤ 4 cm	6,12,18,24, 30,36,42 & 48 months	111	76
Voogd A C 2001	Breast conservation versus modified radical mastectomy	• CMF (cyclophosphamide, methotrexate, and fluorouracil) • Whole breast irradiation (within 2-6 weeks of surgery), 50 Gy and an additional booster dose to the tumour bed.	Stage I and II breast, no age limit	1,2,3,4,5, 6 7,8,9 & 10 yrs	893	879
Sarrazin D 1989	Tumorectomy and breast irradiation versus modified radical mastectomy.	• 45 Gy in 18 fractions (4 fractions of 2.5 Gy/week) over one month. A booster dose of 15 Gy in 6 fractions over 10 days	Stage I or II (T1–2 N0–1 M0) breast cancer, < 70 years old	2,4,6,8 & 10 yrs	91	88
Fisher B 1995	Total mastectomy versus lumpectomy	• Breast irradiation	Negative or positive axillary nodes & tumours ≤4 cm (stage I and II breast cancer)	2,4,6,8, 10 & 12	692	714
Simone NL 2012	Total mastectomy versus BCT	• 1,500–2,000 cGy boost to the tumour bed • Cyclophosphamide and doxorubicin	Invasive breast tumours ≤5 cm, clinically negative or positive axillary lymph nodes	5,10,15, 20,25 & 30 yrs	116	121
van Dongen JA 1992	Modified radical mastectomy versus breast conserving therapy	• Radiotherapy to the breast (50 Gy in 5 weeks and a boost with iridium implant of 25 Gy)	TNM stage I and II	2,4,6,8, 10 & 12 yrs	424	455

Continue

TABLE 1: Continued

Author & publication year	Interventions	Treatment after lumpectomy	Major inclusion criterion	Assessment period	Participants MT	Participants BCT
Fisher B 1989	Total mastectomy versus lumpectomy	• Radiation (50Gy)	Stage I, II; tumour ≤4cm, T1,2; N0, N1, M0	1,2,3,4,5,6, 7 & 8 yrs	590	629
Poggi MM 2003	Mastectomy versus Breast Conservation Therapy	• Radiation boost of 1500-2000 cGy to the tumour bed	Stage I or Stage II (T1 or T2; N0 or N1; M0)	3,6,9,12,15,18, 21,24 & 27 yrs	116	121
Lichter AS 1992	Mastectomy versus excisional biopsy (lumpectomy)	• A boost to the tumour bed using either an iridium1 implant or an electron beam for an addi- ional 1,500 to 2,000 cGy • Doxorubicin and cyclophosphamide	Stage T1 or T2, N0 or N1 invasive carcinoma of the breast	12,24,36,48,60, 72,84,96,108 &120 months	116	121
Blichert-Toft M 2008	Breast conserving surgery versus mastectomy	• Radiation (50 Gy in 25 fractions in 5 weeks) •nTumour bed received a boost dose of 10-25 Gy in 5-12 fractions •bCMF (Cyclophosphamide, Methotrexate)	Tumour ≤ 50 mm, One- sided, unifocal, <70 years old	5, 10, 15 & 20 yrs	350	381
van Dongen JA 2000	Breast-Conserving Therapy versus Mastectomy	• Radiotherapy to the breast • Booster dose of 25 Gy to (50 Gy over a 5-wee the lumpectomy site • Cyclophosphamide, methotrexate, and 5-fluorouracil	Tumours ≤5 cm	2,4,6,8,10, 12,14,16 & 18 yrsk	420	448
Fisher B 2002	Total mastectomy versus lumpectomy	• 50 Gy of radiation	Tumours ≤ 4 cm, negative or positive axillary lymph nodes (stage I or II)	4,8,12, 16 & 20 yrs	589	628

FIGURE 2: Forest Plot Comparing Mastectomy with BCT in Dichotomous Setting

Study or Subgroup	Mastectomy Events	Total	BCT Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.1.1 Mastectcomy vesus BCT: Dichotomous data						
Blichert-Toft M 1992 6y	352	429	340	430	3.6%	1.21 [0.86, 1.70]
Blichert-Toft M 2008 20a	179	364	212	367	4.9%	0.71 [0.53, 0.95]
Blichert-Toft M 2008 20y	184	364	197	367	5.0%	0.88 [0.66, 1.18]
Fisher B 1989 8y	419	590	449	629	6.8%	0.98 [0.77, 1.26]
Fisher B 1995 12a	169	692	183	714	7.2%	0.94 [0.74, 1.19]
Fisher B 1995 12b	149	589	163	628	6.3%	0.97 [0.75, 1.25]
Fisher B 1995 12c	121	494	136	515	5.2%	0.90 [0.68, 1.20]
Fisher B 2000 20y	299	589	317	628	8.3%	1.01 [0.81, 1.27]
Jacobson JA 1995 10y	87	116	93	121	1.2%	0.90 [0.50, 1.64]
Lee HD 1997 3y	104	111	72	76	0.3%	0.83 [0.23, 2.92]
Lichter AS 1992 5y	99	116	108	121	0.7%	0.70 [0.32, 1.52]
Litiere S 2012 20y	187	420	175	448	5.7%	1.25 [0.96, 1.64]
Poggi MM 2003 10y	87	116	91	121	1.2%	0.99 [0.55, 1.78]
Poggi MM 2003 15y	75	116	77	121	1.5%	1.05 [0.61, 1.78]
Poggi MM 2003 20y	76	116	64	121	1.5%	1.69 [1.00, 2.86]
Poggi MM 2003 5y	100	116	105	121	0.8%	0.95 [0.45, 2.01]
Sarrazin D 1989 10y	73	91	70	88	0.8%	1.04 [0.50, 2.17]
van Dongen JA 2000 10y	278	420	292	448	5.3%	1.05 [0.79, 1.38]
van Dongen JA 2000 13y	252	420	246	448	5.8%	1.23 [0.94, 1.61]
van Dongen JA 2000 5y	355	420	369	448	3.2%	1.17 [0.82, 1.67]
Veronesi U 1990 10y	241	349	250	352	4.0%	0.91 [0.66, 1.26]
Veronesi U 1990 13y	265	349	277	352	3.3%	0.85 [0.60, 1.22]
Voogd AC 2001 10y	598	893	589	879	10.7%	1.00 [0.82, 1.22]
Voogd AC 2001 5y	741	893	738	879	6.7%	0.93 [0.72, 1.20]
Subtotal (95% CI)		9173		9422	100.0%	0.99 [0.93, 1.06]
Total events	5490		5613			

Heterogeneity: Tau² = 0.00; Chi² = 20.29, df = 23 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.18 (P = 0.86)

Total (95% CI)		9173		9422	100.0%	0.99 [0.93, 1.06]
Total events	5490		5613			

Heterogeneity: Tau² = 0.00; Chi² = 20.29, df = 23 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.18 (P = 0.86)
Test for subgroup differences: Not applicable

0.2 0.5 1 2 5
Favours Mastectomy Favours BCT

the patients treated by mastectomy compared with those treated by BCT in term of OS, (HR:1.01; 95% CI:0.98-1.04; P:0.71).Across studies, there was no evidence of heterogeneity, (I²: 0%, P:1.00) as shown in figure 4.

In subgroups analysis, there was no any significant difference according to the follow up period. Their HRs and CI wee (HR:1.01; 95% CI:0.951-1.07; P:0.79), (HR:0.98; 95% CI:0.92-1.04; P:0.51) and (HR:1.02; 95% CI:0.97-1.07; P:0.40) respectively for up to 5 years or less, between 5 and 10 years and more than 10 years of follow up. In the three cases, there was no evidence of significant heterogeneity across studies. Their I² and P were (I²:0%, P:0.91); (I²:0%, P:0.97); (I²:0%, P:1.00) respectively for up to 5 years or less, between 5 and 10 years and more than 10 years follow up as shown in figure 5.

Risk of Bias

The most included studies had low risk of bias as assessed in figure 6 byusing the revised Cochrane risk-of-bias tool for randomised trials (RoB 2). Indeed, the red colour shows a high risk of bias and the yellow colour an intermediate risk when the green colour shows a low risk of bias, which is the case in this study.

DISCUSSION

This meta-analysis summarised the OS of breast cancer patients at early stage when they are treated by mastectomy on one hand and when they are treated bb BCT on another hand. Moreover, it assessed the influence of follow up period on OS. This meta-analysis used two methods, one very commonly used(dichotomous) and another not popular (generic inverse variance). Interestingly, both arrived at the same conclusions.

In fact, it found that using either dichotomous method or generic inverse variance, there was no any significant difference between the two types of surgery in term of OS in general and in subgroup analysis especially. However, a recent meta-analysis concluded that mastectomy was

FIGURE 3: Forest Plot Comparing Mastectomy with BCT in Follow Up Period Subgrouping

Study or Subgroup	Mastectomy Events	Total	BCT Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.2.1 Follow up ≤ 5 years						
Lichter AS 1992 5y	99	116	108	121	0.8%	0.70 [0.32, 1.52]
Lee HD 1997 3y	104	111	72	76	0.3%	0.83 [0.23, 2.92]
Voogd AC 2001 5y	741	893	738	879	7.4%	0.93 [0.72, 1.20]
Poggi MM 2003 5y	100	116	105	121	0.8%	0.95 [0.45, 2.01]
van Dongen JA 2000 5y	355	420	369	448	3.6%	1.17 [0.82, 1.67]
Subtotal (95% CI)		1656		1645	12.9%	0.97 [0.81, 1.18]
Total events	1399		1392			
Heterogeneity: Tau² = 0.00; Chi² = 1.88, df = 4 (P = 0.76); I² = 0%						
Test for overall effect: Z = 0.27 (P = 0.79)						
1.2.2 Follow up >5years but ≤ 10 years						
Jacobson JA 1995 10y	87	116	93	121	1.3%	0.90 [0.50, 1.64]
Veronesi U 1990 10y	241	349	250	352	4.4%	0.91 [0.66, 1.26]
Fisher B 1989 8y	419	590	449	629	7.6%	0.98 [0.77, 1.26]
Poggi MM 2003 10y	87	116	91	121	1.3%	0.99 [0.55, 1.78]
Voogd AC 2001 10y	598	893	589	879	11.9%	1.00 [0.82, 1.22]
Sarrazin D 1989 10y	73	91	70	88	0.9%	1.04 [0.50, 2.17]
van Dongen JA 2000 10y	278	420	292	448	5.9%	1.05 [0.79, 1.38]
Blichert-Toft M 1992 6y	352	429	340	430	4.0%	1.21 [0.86, 1.70]
Subtotal (95% CI)		3004		3068	37.3%	1.01 [0.90, 1.13]
Total events	2135		2174			
Heterogeneity: Tau² = 0.00; Chi² = 1.76, df = 7 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.17 (P = 0.87)						
1.2.3 Follow up > 10 years						
Veronesi U 1990 13y	265	349	277	352	3.7%	0.85 [0.60, 1.22]
Fisher B 1995 12c	121	494	136	515	5.8%	0.90 [0.68, 1.20]
Fisher B 1995 12a	169	692	183	714	8.0%	0.94 [0.74, 1.19]
Fisher B 1995 12b	149	589	163	628	7.0%	0.97 [0.75, 1.25]
Fisher B 2000 20y	299	589	317	628	9.2%	1.01 [0.81, 1.27]
Poggi MM 2003 15y	75	116	77	121	1.6%	1.05 [0.61, 1.78]
van Dongen JA 2000 13y	252	420	246	448	6.4%	1.23 [0.94, 1.61]
Litiere S 2012 20y	187	420	175	448	6.4%	1.25 [0.96, 1.64]
Poggi MM 2003 20y	76	116	64	121	1.7%	1.69 [1.00, 2.86]
Subtotal (95% CI)		3785		3975	49.8%	1.04 [0.93, 1.16]
Total events	1593		1638			
Heterogeneity: Tau² = 0.01; Chi² = 9.85, df = 8 (P = 0.28); I² = 19%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		8445		8688	100.0%	1.02 [0.95, 1.09]
Total events	5127		5204			
Heterogeneity: Tau² = 0.00; Chi² = 13.89, df = 21 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.55 (P = 0.58)						
Test for subgroup differences: Chi² = 0.40, df = 2 (P = 0.82), I² = 0%						

benefit compared with BCT.[7] We could thing that these disagreements are due to different methods used. In this case, this study has an advantage of having used two different methods which gave the same conclusions.

Cai X with his coleagues found that BCT was the better choice than MT for Chinese women with early-stage breast cancer even though they worked on non rendomized trials.[8] The similar results were found by Vila J and colleagues. For them, mastectomy provides better OS compared to breast conserving surgery followed by whole breast radiotherapy in early breast cancer patients aged 40 years or younger.[6] Note that they worked also on non randomised trials. At the contrary, other large population-based studies comparing breast-conserving surgery followed by radiation therapy with mastectomy supported that BCT might be good treatment in most

FIGURE 4: Forest Plot Comparing Mastectomy with BCT in Generic Inverses Variances Setting

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
2.1.1 Mastectomy vs BCT: life table data				
Blichert-Toft M 2008 10y	0.07	0.14	1.3%	1.07 [0.82, 1.41]
Blichert-Toft M 2008 15y	0.09	0.12	1.7%	1.09 [0.86, 1.38]
Blichert-Toft M 2008 20y	0.05	0.08	3.9%	1.05 [0.90, 1.23]
Blichert-Toft M 2008 5y	0	0.09	3.1%	1.00 [0.84, 1.19]
Fisher B 1985 1y	-0.2	0.18	0.8%	0.82 [0.58, 1.17]
Fisher B 1985 2y	-0.13	0.1	2.5%	0.88 [0.72, 1.07]
Fisher B 1985 3y	-0.03	0.08	3.9%	0.97 [0.83, 1.14]
Fisher B 1985 4y	-0.01	0.07	5.1%	0.99 [0.86, 1.14]
Fisher B 1985 5y	0.11	0.06	6.9%	1.12 [0.99, 1.26]
Lichter AS 1992 1y	-0.33	0.53	0.1%	0.72 [0.25, 2.03]
Lichter AS 1992 2y	0.24	0.3	0.3%	1.27 [0.71, 2.29]
Lichter AS 1992 3y	0.11	0.24	0.4%	1.12 [0.70, 1.79]
Lichter AS 1992 4y	0.04	0.19	0.7%	1.04 [0.72, 1.51]
Lichter AS 1992 5y	0.06	0.17	0.9%	1.06 [0.76, 1.48]
Lichter AS 1992 6y	0.05	0.15	1.1%	1.05 [0.78, 1.41]
Lichter AS 1992 7y	0.07	0.14	1.3%	1.07 [0.82, 1.41]
Lichter AS 1992 8y	0.05	0.14	1.3%	1.05 [0.80, 1.38]
Litiere S 2012 12y	-0.11	0.1	2.5%	0.90 [0.74, 1.09]
Litiere S 2012 15y	-0.02	0.09	3.1%	0.98 [0.82, 1.17]
Litiere S 2012 18y	0	0.08	3.9%	1.00 [0.85, 1.17]
Litiere S 2012 21y	0.01	0.08	3.9%	1.01 [0.86, 1.18]
Litiere S 2012 24y	0.04	0.07	5.1%	1.04 [0.91, 1.19]
Litiere S 2012 27y	0.04	0.07	5.1%	1.04 [0.91, 1.19]
Litiere S 2012 3y	-0.09	0.2	0.6%	0.91 [0.62, 1.35]
Litiere S 2012 6y	-0.05	0.14	1.3%	0.95 [0.72, 1.25]
Litiere S 2012 9y	-0.07	0.12	1.7%	0.93 [0.74, 1.18]
Simone NL 2012 10y	-0.01	0.27	0.3%	0.99 [0.58, 1.68]
Simone NL 2012 15y	-0.02	0.22	0.5%	0.98 [0.64, 1.51]
Simone NL 2012 20y	-0.06	0.19	0.7%	0.94 [0.65, 1.37]
Simone NL 2012 25y	0.04	0.15	1.1%	1.04 [0.78, 1.40]
Simone NL 2012 30y	0.03	0.13	1.5%	1.03 [0.80, 1.33]
Simone NL 2012 5y	0.07	0.35	0.2%	1.07 [0.54, 2.13]
van Dongen JA 1992 10y	-0.08	0.07	5.1%	0.92 [0.80, 1.06]
van Dongen JA 1992 2y	-0.12	0.23	0.5%	0.89 [0.57, 1.39]
van Dongen JA 1992 4y	0.07	0.13	1.5%	1.07 [0.83, 1.38]
van Dongen JA 1992 6y	0.06	0.09	3.1%	1.06 [0.89, 1.27]
van Dongen JA 1992 8y	-0.09	0.07	5.1%	0.91 [0.80, 1.05]
van Dongen JA 2000 10y	0	0.11	2.1%	1.00 [0.81, 1.24]
van Dongen JA 2000 12y	0.04	0.09	3.1%	1.04 [0.87, 1.24]
van Dongen JA 2000 14y	0.03	0.08	3.9%	1.03 [0.88, 1.21]
van Dongen JA 2000 16y	0.03	0.07	5.1%	1.03 [0.90, 1.18]
van Dongen JA 2000 2y	-0.18	0.29	0.3%	0.84 [0.47, 1.47]
van Dongen JA 2000 4y	-0.01	0.19	0.7%	0.99 [0.68, 1.44]
van Dongen JA 2000 6y	-0.05	0.14	1.3%	0.95 [0.72, 1.25]
van Dongen JA 2000 8y	0.06	0.12	1.7%	1.06 [0.84, 1.34]
Subtotal (95% CI)			**100.0%**	**1.01 [0.98, 1.04]**

Heterogeneity: Chi² = 17.53, df = 44 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)

Total (95% CI)			**100.0%**	**1.01 [0.98, 1.04]**

Heterogeneity: Chi² = 17.53, df = 44 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)
Test for subgroup differences: Not applicable

Favours Mastectomy   Favours BCT

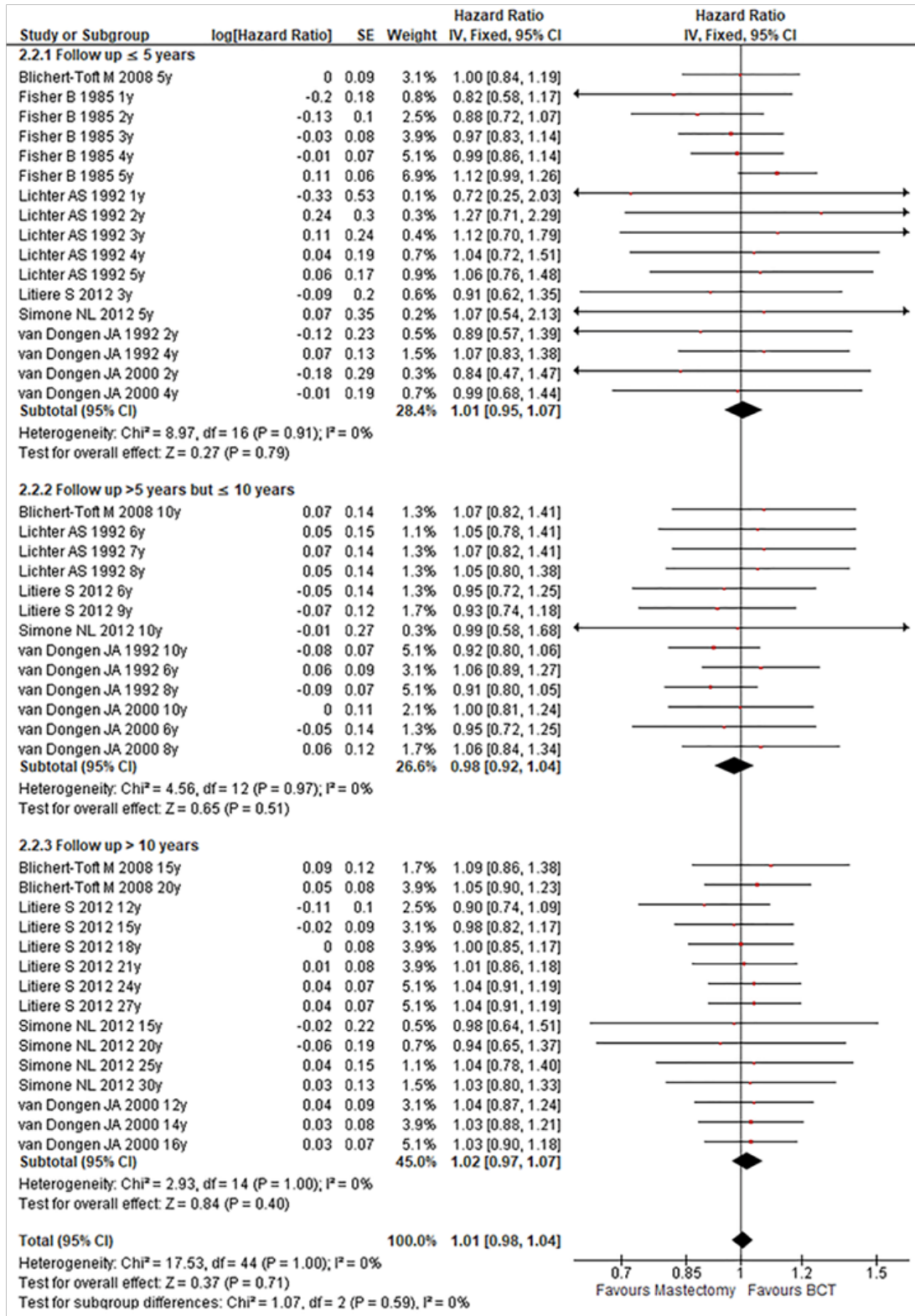**TABLE 5: Forest Plot Comparing Mastectomy with BCT in Follow Up Period Subgrouping**

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
2.2.1 Follow up ≤ 5 years				
Blichert-Toft M 2008 5y	0	0.09	3.1%	1.00 [0.84, 1.19]
Fisher B 1985 1y	-0.2	0.18	0.8%	0.82 [0.58, 1.17]
Fisher B 1985 2y	-0.13	0.1	2.5%	0.88 [0.72, 1.07]
Fisher B 1985 3y	-0.03	0.08	3.9%	0.97 [0.83, 1.14]
Fisher B 1985 4y	-0.01	0.07	5.1%	0.99 [0.86, 1.14]
Fisher B 1985 5y	0.11	0.06	6.9%	1.12 [0.99, 1.26]
Lichter AS 1992 1y	-0.33	0.53	0.1%	0.72 [0.25, 2.03]
Lichter AS 1992 2y	0.24	0.3	0.3%	1.27 [0.71, 2.29]
Lichter AS 1992 3y	0.11	0.24	0.4%	1.12 [0.70, 1.79]
Lichter AS 1992 4y	0.04	0.19	0.7%	1.04 [0.72, 1.51]
Lichter AS 1992 5y	0.06	0.17	0.9%	1.06 [0.76, 1.48]
Litiere S 2012 3y	-0.09	0.2	0.6%	0.91 [0.62, 1.35]
Simone NL 2012 5y	0.07	0.35	0.2%	1.07 [0.54, 2.13]
van Dongen JA 1992 2y	-0.12	0.23	0.5%	0.89 [0.57, 1.39]
van Dongen JA 1992 4y	0.07	0.13	1.5%	1.07 [0.83, 1.38]
van Dongen JA 2000 2y	-0.18	0.29	0.3%	0.84 [0.47, 1.47]
van Dongen JA 2000 4y	-0.01	0.19	0.7%	0.99 [0.68, 1.44]
Subtotal (95% CI)			28.4%	1.01 [0.95, 1.07]
Heterogeneity: Chi² = 8.97, df = 16 (P = 0.91); I² = 0%				
Test for overall effect: Z = 0.27 (P = 0.79)				
2.2.2 Follow up >5 years but ≤ 10 years				
Blichert-Toft M 2008 10y	0.07	0.14	1.3%	1.07 [0.82, 1.41]
Lichter AS 1992 6y	0.05	0.15	1.1%	1.05 [0.78, 1.41]
Lichter AS 1992 7y	0.07	0.14	1.3%	1.07 [0.82, 1.41]
Lichter AS 1992 8y	0.05	0.14	1.3%	1.05 [0.80, 1.38]
Litiere S 2012 6y	-0.05	0.14	1.3%	0.95 [0.72, 1.25]
Litiere S 2012 9y	-0.07	0.12	1.7%	0.93 [0.74, 1.18]
Simone NL 2012 10y	-0.01	0.27	0.3%	0.99 [0.58, 1.68]
van Dongen JA 1992 10y	-0.08	0.07	5.1%	0.92 [0.80, 1.06]
van Dongen JA 1992 6y	0.06	0.09	3.1%	1.06 [0.89, 1.27]
van Dongen JA 1992 8y	-0.09	0.07	5.1%	0.91 [0.80, 1.05]
van Dongen JA 2000 10y	0	0.11	2.1%	1.00 [0.81, 1.24]
van Dongen JA 2000 6y	-0.05	0.14	1.3%	0.95 [0.72, 1.25]
van Dongen JA 2000 8y	0.06	0.12	1.7%	1.06 [0.84, 1.34]
Subtotal (95% CI)			26.6%	0.98 [0.92, 1.04]
Heterogeneity: Chi² = 4.56, df = 12 (P = 0.97); I² = 0%				
Test for overall effect: Z = 0.65 (P = 0.51)				
2.2.3 Follow up > 10 years				
Blichert-Toft M 2008 15y	0.09	0.12	1.7%	1.09 [0.86, 1.38]
Blichert-Toft M 2008 20y	0.05	0.08	3.9%	1.05 [0.90, 1.23]
Litiere S 2012 12y	-0.11	0.1	2.5%	0.90 [0.74, 1.09]
Litiere S 2012 15y	-0.02	0.09	3.1%	0.98 [0.82, 1.17]
Litiere S 2012 18y	0	0.08	3.9%	1.00 [0.85, 1.17]
Litiere S 2012 21y	0.01	0.08	3.9%	1.01 [0.86, 1.18]
Litiere S 2012 24y	0.04	0.07	5.1%	1.04 [0.91, 1.19]
Litiere S 2012 27y	0.04	0.07	5.1%	1.04 [0.91, 1.19]
Simone NL 2012 15y	-0.02	0.22	0.5%	0.98 [0.64, 1.51]
Simone NL 2012 20y	-0.06	0.19	0.7%	0.94 [0.65, 1.37]
Simone NL 2012 25y	0.04	0.15	1.1%	1.04 [0.78, 1.40]
Simone NL 2012 30y	0.03	0.13	1.5%	1.03 [0.80, 1.33]
van Dongen JA 2000 12y	0.04	0.09	3.1%	1.04 [0.87, 1.24]
van Dongen JA 2000 14y	0.03	0.08	3.9%	1.03 [0.88, 1.21]
van Dongen JA 2000 16y	0.03	0.07	5.1%	1.03 [0.90, 1.18]
Subtotal (95% CI)			45.0%	1.02 [0.97, 1.07]
Heterogeneity: Chi² = 2.93, df = 14 (P = 1.00); I² = 0%				
Test for overall effect: Z = 0.84 (P = 0.40)				
Total (95% CI)			100.0%	1.01 [0.98, 1.04]
Heterogeneity: Chi² = 17.53, df = 44 (P = 1.00); I² = 0%				
Test for overall effect: Z = 0.37 (P = 0.71)				
Test for subgroup differences: Chi² = 1.07, df = 2 (P = 0.59), I² = 0%				

0.7 0.85 1 1.2 1.5
Favours Mastectomy Favours BCT

breast cancer patients with early stage when both treatments are available.[30,31]

Considering what said above, this study contributed to clarify this point when randomised trials are involved even though the contribution is not enough for generalization. Since there are many cancer registries world wide, several studies comparing the OS between mastectomy and BCT should be found. Nevertheless, performing a metanalysis with many non randomised studies could provide another point of view.

This study used the data generated using the tool proposed by Tierney JF with his colleagues which facilitated to incorporate time-to-event data into meta-analysis.[10] This tool was usefull because it allowed to know the log(HR) and its SEs at each level of assessment. This was not possible when used the dichotmous data. It could be evaluated in a large randomised trial to set up as software or to integrate it in the existing statistical softwares for meta-analysis.

CONCLUSION

Even thought this study had many strengths such as the use of randomised trials, combination of two different methods, it had some limitations. We may mention a small number of included studies, variabilities in different trials' protocols which could affect somehow the outcome. Therefore, further studies are still needed to strengthen this findings. Meanwhile, this study shows that there was no significant difference between patients with early stage breast cancer when they are treated by mastectomy or BCT in term of overall survivals. Additionnally, the follow up period had no any influence on the both types of treatment in term of overall survivals. We suggest that BCT or mastectomy should be discussed between the care team and the patient, taking into account the financial means available to the patient especially in low-income countries, the benefits of the surgery and the patient's preferences.

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Challenges in Diagnosis and Management of Second Trimester Omental Pregnancy in Limited Resource Settings: Case Report

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ABSTRACT

Background: Abdominal pregnancies are a rare occurrence and are associated with high maternal and perinatal mortality rates compared to intra-uterine and other ectopic pregnancies. Localization of sites of abdominal pregnancies and determining the gestational age at the time of diagnosis play a fundamental role in guiding the treatment approach and minimizing potential complications. However, the vague presentation coupled with low accuracy of ultrasound detection often leads to misdiagnosis of abdominal pregnancy, and hence delaying initiation of appropriate management. We present a case of a second trimester abdominal pregnancy detected following failure of induction for an initial diagnosis of missed abortion, and the ensuing outcome, rarely reported in limited-resource settings.

Case presentation: A 19 year old unbooked woman, gravida 2 para 1 at 17[th]week gestation age by ultrasound presented with loss of foetal movement for one week. Based on clinical assessment and referral ultrasound findings, she was initially diagnosed with missed abortion and planned for induction. Failure of induction prompted a repeat ultrasound which revealed a non-viable abdominal pregnancy. Laparotomy was done, localisation of the pregnancy at the omentum was observed and a dead foetus was extracted with the placenta left in-situ. A complication of surgical wound dehiscence with infection developed post-operatively and was managed with secondary sutures. The patient recovered and was discharged in a stable condition.

Conclusion: This case demonstrates that the diagnosis of abdominal pregnancy remains a challenge especially in settings where skilled human resources for health are few and equipment and supplies for effective and timely treatment are limited. The case sheds some light on the broader challenges in maternal and perinatal health in developing countries. Accurate pre-operative diagnosis requires a high index of suspicion, especially due to the variability of its presentation. This case emphasises the important of quality antenatal care and the need for clinicians to conduct comprehensive assessments of patients and receive training on obstetric ultrasound skills.

BACKGROUND

Abdominal pregnancies occur when there is implantation of the blastocyst in the peritoneal cavity, external to the uterine cavity and fallopian tubes. These pregnancies are rare, accounting for approximately 1% of all ectopic pregnancies,[1] and are associated with a high maternal mortality and perinatal mortality rate compared to intra-uterine and other ectopic pregnancies.[2] Estimated incidence of abdominal pregnancies has been reported to be 1 in 10,000 live births,[3] with the omentum, pouch of Douglas, pelvic side wall, spleen, bowel and liver included as potential implantation sites.[4–11]

Two mechanisms have been proposed to explain the development of abdominal pregnancies; Intra-abdominal fertilisation with primary implantation of the abdomen (primary abdominal pregnancy) and the more common mechanism of secondary implantation from an aborted tubal pregnancy, termed as secondary abdominal pregnancy.[4,5] A more useful classification of abdominal pregnancy is based on the gestation age at which it is first detected. Early abdominal pregnancies refer to those first diagnosed at or before 20 weeks while advanced abdominal pregnancies are diagnosed after 20 weeks.[12]

Factors that increase the risk of abdominal pregnancy are similar to those for any ectopic pregnancy and include previous ectopic pregnancy, tubal surgery, history of pelvic inflammatory disease, cigarette smoking, history of infertility and assisted reproductive techniques such as in vitro fertilisation and previous use of an intrauterine device.[13,14]

The clinical presentation of abdominal pregnancy is non-specific, and features vary widely owing to the different possible sites of implantation. Patients may present with nausea, vomiting, vaginal bleeding, abdominal pain, cessation of foetal movements, respi-

ratory problems, haematochezia or may even be asymptomatic. Abdominal pregnancies are usually associated with foetal death, but in very rare cases, abdominal pregnancies result in live births.[14–21]

Diagnostic evaluation of any ectopic pregnancy begins with confirmation of pregnancy in women of reproductive age presenting with vaginal bleeding, abdominal pain, or menstrual irregularities. This is followed by determining the exact location of the extra-uterine pregnancy. Ultrasound is the tool of choice in localizing the pregnancy although the accuracy of diagnosing abdominal pregnancy is as low as 50%, especially in early abdominal pregnancies.[22] However, Allibone et al[23] suggest that ultrasonography features that may support the diagnosis of abdominal pregnancy especially in the second trimester include: demonstration of a foetus in a gestational sac outside the uterus, failure to visualize the uterine wall between the foetus and urinary bladder, close proximity between the foetus and the anterior abdominal wall and localisation of the placenta outside the confines of the uterine cavity. Magnetic Resonance Imaging (MRI) may also be helpful in the localisation of abdominal pregnancies. However, its role is limited in low-resource settings.

Localisation of sites of abdominal pregnancies and determining the gestational age at diagnosis play a fundamental role in guiding the treatment approach and minimising potential complications. Surgical management by way of laparotomy remains the mainstay approach to treating second trimester abdominal pregnancies, especially if the foetus is dead as this carries a risk of infection and disseminated intravascular coagulation. The foetus is usually delivered easily, and the key issue lies in the management of the placenta. A recognised approach has been to leave the placenta in situ as attempts to remove it are associated with high risk of fatal haemorrhage. This approach however carries risk of infection and intra-abdominal abscess formation.[21,24]Postoperative methotrexate may be administered to accelerate involution.[14,21,25,26]

The vague presentation coupled with low accuracy of ultrasound detection often leads to misdiagnosis of abdominal pregnancy,[27–30] hence highlighting the need for a high index of suspicion and thorough clinical and radiological evaluation to accurately diagnose this condition. We present a case of a second trimester abdominal pregnancy detected following a failed induction for an initial diagnosis of missed abortion, and the ensuing outcome, rarely reported in limited-resource settings.

CASE PRESENTATION
A19-year-old woman, gravida 2 para 1 with no living children was referred to our institution, a regional referral hospital from a nearby health centre. She presented with loss of foetal movement that began approximately one week prior to admission. Believing this to be a transient state that would return to normal, she did not seek medical care for several days. One day prior to admission, she was attended to at a nearby health centre where an ultrasound was performed. The ultrasound report indicated an intra-uterine pregnancy at gestation age of 17 weeks, with no foetal movements or cardiac activity.

However, an image of the ultrasound was not provided. As the patient was uncertain of her last normal menstrual period, the gestation age determined by ultrasound was adopted. She was subsequently diagnosed to have a missed abortion and referred to our institution for further management.

The cessation of foetal movements was not associated with any other significant symptoms such as abdominal pain or vaginal bleeding. She had not yet booked at antenatal clinic for this pregnancy. Two years ago, she underwent a caesarean section at term. The patient had an intrauterine foetal death but the indication for the caesarean section could not be determined. The underlying cause of the intrauterine foetal death could also not be elucidated. The past medical, surgical, and gynaecological histories were otherwise unremarkable.

General examination findings on admission were essentially normal save for a slightly elevated blood pressure of 130/85mmHg. Per abdominal examination revealed a moderately distended abdomen which was non-uniform, with distension more marked in the supra-pubic region. She had a well-healed sub-umbilical midline incision (SUMI) scar. Palpation revealed no tenderness and what was assumed to be a fundal height of 18cm, corresponded with the gestational age by ultrasound. Auscultation by foetoscope did not detect any foetal heart sounds. On sterile per vaginal examination, the cervix was found to be medially positioned, firm, thick and closed.

The patient was provisionally diagnosed to have a missed abortion based on clinical findings and referral ultrasound report. Routine laboratory investigations were ordered. Full blood picture revealed microcytic hypochromic anaemia with haemoglobin level of 7.5g/dL (Table 1).Her blood group was B Rh- (negative). Initial management included oral ferrous sulphate(200mg 12-hourly) to correct anaemia as per national guidelines[31] and 400 µg misoprostol every 6 hours to manage the missed abortion as per World Health Organization (WHO) guidelines.[32] Intravenous ceftriaxone (1g 12-hourly for 24hours) and intravenous metronidazole (500mg 8-hourly for 24hours) were given for prophylaxis as per departmental protocols. On day two of admission, the patient reported to experience per vaginal bleeding. Her cervix was 3cm dilated and 60% effaced on sterile per vaginal examination. Oxytocin infusion (5IU in 500ml of Ringer's Lactate at 15 drops per minute) was added to her treatment plan as per departmental protocol.

Upon evaluation on the third day post admission, the patient still had minimal vaginal bleeding and was experiencing lower abdominal pain. There were no changes on vaginal examination, with the cervix still 3cm dilated and 60% effaced. Treatment with antibiotics, misoprostol and oxytocin was continued. Additional investigations were ordered on the fifth day post admission.A repeat haemoglobin level was 6.0g/dL; serum creatinine (2.08mmol/L) and Blood Urea Nitrogen (19.06µmol/L) were within normal limits. An ultrasound was done and reported a non-gravid and bulky uterus having thickened endometrium, free fluid in peritoneal cavity with a non-viable foetus having gestation age of 22weeks and 5 days. Consequently, the diagnosis was

TABLE 1: Full Blood Picture Report on Admission

Parameter	Result		Ref. Range	Units
White Blood Cell Count (WBC)	**7.29**		**3.50-9.50**	**10^3/µL**
Neutrophils (Neu%)	69.1		40.0-75.0	%
Lymphocytes (Lym%)	26.1		20.0-50.0	%
Monocytes (Mon%)	3.4		3.0-10.0	%
Eosinophils (Eos%)	1.3		0.4-8.0 %	
Basophils (Bas%)	0.1		0.0-1.0 %	
Absolute Neutrophil Count (Neu#)	5.04		1.80-6.30	10^3/µL
Absolute Lymphocyte Count (Lym#)	1.90		1.10-3.20	10^3/µL
Absolute Monocyte Count (Mon#)	0.25		0.10-0.60	10^3/µL
Absolute Eosinophil Count (Eos#)	0.09		0.02-0.52	10^3/µL
Absolute Basophil Count (Bas#)	0.01		0.00-0.06	10^3/µL
Red Blood Cell Count (RBC)	**4.35**		**3.80-5.10**	**10^6/µL**
Haemoglobin (HGB)	7.5	L	11.5-15.0	g/dL
Haematocrit (HCT)	26.2	L	35.0-45.0	%
Mean Corpuscular Volume (MCV)	60.2	L	82.0-100.0	fL
Mean Corpuscular Hemoglobin (MCH)	17.3	L	27.0-34.0	pg
Mean Corpuscular Hemoglobin Concentration (MCHC)	28.7	L	31.6-35.4	g/dL
Red cell Distribution Width-Coefficient of Variation (RDW-CV)	22.3	H	11.0-16.0	%
Red cell Distribution Width- Standard Deviation (RDW-SD)	48.2		35.0-56.0	fL
Platelet Count (PLT)	**321**		**125-350**	**10^3/µL**
Mean Platelet Volume (MPV)	8.5		6.5-12.0	fL
Platelet Distribution Width (PDW)	10.3		9.0-17.0	fL
Plateletcrit (PCT)	0.274		0.108-0.282	%
Platelet-Large Cell Ratio (P-LCR)	17.6		11.0-45.0	%
Platelet-Large Cell Count (P-LCC)	57		30-90	10^9/µL

one unit of blood transfusion and was scheduled for a laparotomy which was performed on the seventh day post admission.

Intra-operative findings of the laparotomy included adhesions from the previous Caesarean section for which adhesiolysis was done. The placenta was found to be implanted on the omentum which was located on the anterior abdomen and a macerated foetus was found enclosed in its membranes. The foetus was extracted and weighed 320 grams (Figure 1). The placenta and membranes were left in situ. The abdomen was closed in layers and estimated blood loss was 150milliliters. The instituted post-operative management included intravenous ceftriaxone (1g 12-hourly), intravenous gentamicin (80mg 24-hourly) and intravenous metronidazole (500mg 8-hourly) for five days for prophylaxis. Intramuscular tramadol (100mg 8-hourly) was prescribed as analgesia for 24 hours and there after she continued with oral analgesics.Oral ferrous sulphate 200mg 8-hourly was administered to correct anaemia. Additionally, she received intravenous 1L Ringer's Lactate interchangeable with Normal Saline for 24 hours, methotrexate (MTX) (50mg/m² intramuscular once daily for three days and then continued with oral methotrexate on day 5, 7, 14, 21 and 28 to reduce vascularity and promote absorption of the retained placenta. She was also transfused with an additional unit of blood.

On the second post-operative day, the patient developed a slight fever of 38.5°C. The surgical site did not have abnormal discharge, and further examination revealed nothing significant except for mild tenderness at the incision site. A repeat full blood picture on the third day post-operation showed normocytic, hypochromic anaemia with haemoglobin level of 9.0g/dL, leucocytosis of 12.33 x 10^3/uL (normal laboratory range 3.5-9.5 x 10^3/uL) with neutrophilia of 82% (normal laboratory range 40-75%) (Table 2). Her abdomen was slightly distended and tender at the incision site, with no abnormal discharge from the incision site.

On the fifth post-operative day the patient developed pus-like discharge from the incision site. By this time, she received only a single dose of methotrexate and no additional blood transfusion due to shortages at the facility. The wound was opened up to the subcutaneous layer, and a copious amount of pus was drained, and the wound was cleaned. Pus swab for culture and sensitivity could not be taken due to the patient's financial constraints. An additional diagnosis of septic gapped wound was made. She was prescribed intravenous ciprofloxacin (400mg 12-hourly), metronidazole (500mg 8-hourly) and genta-

TABLE 2: Day 3 Post-Operative Full Blood Picture Report

Parameter	Result		Ref. Range	Units
White Blood Cell Count (WBC)	**12.33**	H	**3.50-9.50**	**10^3/µL**
Neutrophils (Neu%)	82.0	H	40.0-75.0	%
Lymphocytes (Lym%)	14.4	L	20.0-50.0	%
Monocytes (Mon%)	3.1		3.0-10.0	%
Eosinophils (Eos%)	0.2	L	0.4-8.0 %	
Basophils (Bas%)	0.3		0.0-1.0 %	
Absolute Neutrophil Count (Neu#)	10.11	H	1.80-6.30	10^3/µL
Absolute Lymphocyte Count (Lym#)	1.78		1.10-3.20	10^3/µL
Absolute Monocyte Count (Mon#)	0.38		0.10-0.60	10^3/µL
Absolute Eosinophil Count (Eos#)	0.02		0.02-0.52	10^3/µL
Absolute Basophil Count (Bas#)	0.04		0.00-0.06	10^3/µL
Red Blood Cell Count (RBC)	**3.01**	L	**3.80-5.10**	**10^6/µL**
Haemoglobin (HGB)	9.0	L	11.5-15.0	g/dL
Hematocrit (HCT)	26.3	L	35.0-45.0	%
Mean Corpuscular Volume (MCV)	87.4		82.0-100.0	fL
Mean Corpuscular Hemoglobin (MCH)	30.0		27.0-34.0	pg
Mean Corpuscular Hemoglobin Concentration (MCHC)	34.3		31.6-35.4	g/dL
Red cell Distribution Width-Coefficient of Variation (RDW-CV)	13.0		11.0-16.0	%
Red cell Distribution Width-Standard Deviation (RDW-SD)	40.8		35.0-56.0	fL
Platelet Count (PLT)	**273**		**125-350**	**10^3/µL**
Mean Platelet Volume (MPV)	10.1		6.5-12.0	fL
Platelet Distribution Width (PDW)	11.6		9.0-17.0	fL
Plateletcrit (PCT)	0.275		0.108-0.282	%
Platelet-Large Cell Ratio (P-LCR)	26.4		11.0-45.0	%
Platelet-Large Cell Count (P-LCC)	72		30-90	10^9/µL

micin (160mg 24-hourly). She also received one unit of blood transfusion and continued with daily wound dressing. Her condition improved and fourteen days after the initial laparotomy she was scheduled for secondary closure of the wound. On the fifteenth post-operative day, the patient was stable and discharged with oral antibiotics and ferrous sulphate and advised to return for follow-up after two weeks.

DISCUSSION AND CONCLUSION

Clinically, abdominal pregnancy may be classified based on the gestation age at which it is first detected. Early abdominal pregnancies refer to those first diagnosed at or before 20 weeks while advanced abdominal pregnancies are diagnosed after 20 weeks.[12] The significance of an accurate gestational age is universally recognised. It aids in formulation of diagnoses, allowing comparison with different literature and determines the timing for interventions including elective deliveries.

Unfortunately, in our case, categorisation of the abdominal pregnancy could not be made as the patient could not recall her last normal menstrual period, and the ultrasound evaluations performed less than a week apart gave a discrepancy of about five weeks, initially 17 weeks and then 22 weeks. This is a clear illustration of a comm-

FIGURE 1. Foetus Extracted During Laparotomy for Omental Pregnancy

on challenge in obstetrics practice in low-resource settings where dating scans are not routinely performed[33], and women present late for first antenatal visits[34].

In our case the patient presented with a single symptom

of cessation of foetal movements. However, different case reports have documented various clinical presentations, including gastrointestinal symptoms, vaginal bleeding, respiratory problems, haematochezia or asymptomatic presentation.[14–21] This further complicates the diagnostic formulation.

Ultrasound is the imaging investigation of choice in localising the pregnancy although the accuracy of diagnosing abdominal pregnancy is as low as 50%, especially in early abdominal pregnancies.[22] There have been case reports in our review of the literature that documented a ultrasonography diagnosis of abdominal pregnancy pre-operatively as was found in our case.[14,35] Although it is not uncommon for the diagnosis to be made intra-operatively both in women who had no prior ultrasound conducted and those with a history of repeated ultrasounds.[14,15,36,37] This further supports the need for high index of suspicion among clinicians when making a diagnosis of abdominal pregnancy.

While surgical management is the mainstay for treating omental pregnancies, several approaches have been reported, particularly concerning the placenta such as resection with or without partial omentectomy, and leaving the placenta in situ with or without administration of methotrexate.[14,21] In our case, following extraction of the foetus, the placenta was left in situ and postoperative methotrexate was administered, although not as prescribed due to resource constraints. For the same reason, the patient's anaemia was not sufficiently corrected. This may have contributed to the surgical wound dehiscence and infection.

This case demonstrates the challenges in diagnosing abdominal pregnancies in resource limited settings, and sheds some light on the broader challenges in maternal and perinatal health in developing countries. Delays in initiation of antenatal care is still a prevailing public health concern in our country where only 24% of women start antenatal care before the fourth month of pregnancy and 26% do not seek antenatal care until at least the sixth month of pregnancy.[38]

Several factors contribute to this delay in the decision to seek care, including distance to health facilities, socio-cultural beliefs and lack of awareness about pregnancy complications and not knowing when pregnant women should seek help.[39] This "Type I delay" according to the "Three delays model" conceptualized by Thaddeus and Maine[40] plays a significant role in maternal mortality, especially in low-resource settings. The persistence of this and other delays to timely obstetric management calls for enhanced community awareness and sensitisation efforts, especially in hard-to-reach areas.

"Type III delay, the delay in the provision of adequate care[40] was evident in this case. Although the management of this case was successful in preventing a maternal death, there are a number of challenges that hindered effective and efficient management. These factors, exhibited in this case were shortages of essential drugs and supplies that led to the sub-optimal provision of methotrexate and blood transfusion products. Administrative barriers as exhibited by the almost week-long delay in obtaining an ultrasound and sub-optimal information in patient files e.g., absence of ultrasound images to allow verification

of imaging reports; and shortage of qualified and trained personnel that would have enabled early diagnosis and management.

In conclusion, the diagnosis of abdominal pregnancy remains a challenge in resource limited settings and requires a high index of suspicion, especially due to the variability of its presentation. This case emphasizes the need for clinicians to conduct comprehensive assessments of patients, receive capacity building training on obstetric ultrasound skills and continued advocacy for early initiation and provision of quality of antenatal care.

Ethics Approval and Consent to Participate
Ethical clearance to publish this case report was obtained from local government authorities.

Informed consent was obtained from the patient for the procedure, publication of this case report and accompanying images.

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Congenital Diaphragmatic Hernia with Gastric Volvulus and Splenic Herniation: An Unusual Delayed Presentation in a Six-Month Child

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ABSTRACT

Background: Acute gastric volvulus associated with congenital diaphragmatic hernia is an uncommon disorder in infancy and a surgical emergency.
Methods: We present a six-month female baby who presented with clinical features of intestinal obstruction. Ultrasonography of the abdomen revealed gastric volvulus. The baby underwent emergency laparotomy. Gastric volvulus with splenic herniation was encountered through a diaphragmatic hernia.
Results: The defect was corrected, the stomach and spleen were mobilized into the normal anatomical position. The baby recovered well.
Conclusion: A high index of clinical suspicion and thorough radiological assessments are necessary for this life-threatening condition along with surgical correction of the abnormalities.

BACKGROUND

Congenital Diaphragmatic Hernia (CDH) is a developmental abnormality due to the incomplete fusion and closure of the pleuroperitoneal canal during fetal development with an incidence of 0.8/10,000 to 5/10,000 births[1,2]. CDH can be diagnosed prenatally or, as is often the case, during the neonatal period. Occasionally, CDH can be missed, and children can present later in acute respiratory or gastrointestinal symptoms.[1,3]

Infants often present with respiratory distress, and presentation after infancy occurs in 5% to 10% of the affected neonates and present with respiratory distress from pleural effusion or gastrointestinal distress from intestinal obstruction. However, 1% of the cases can be asymptomatic and discovered incidentally on imaging[4]. Despite the advances in medical and surgical management of CDH the morbidity and mortality remains high.[2] Gastric volvulus associated with CDH constitutes a surgical emergency. We present a six-month-female from Tanzania with acute gastric volvulus associated with CDH who presented with features of gastrointestinal obstruction.

CASE PRESENTATION

A six-month-old female baby was referred to our tertiary centre from a regional hospital due to vomiting for four days, inability to pass stool and abdominal distention for three days. The vomiting was projectile and bilious but not stained with blood. There was no fever reported. Herbal medication was given at home with no improvement. The parents are Maasai who are the indigenous tribe, and the baby was born at term by SVD at a health centre with a birth weight of 2900 grams and received all immunisations according to local guidelines. On general examination, the patient was sick looking, not pale, acyanotic and not dyspneic. Her blood pressure was 110/60 mmHg, pulse rate 125 beats per minute, respiration rate 28 breaths per minute and saturating at 96% on room air. Body weight on admission was 8700 grams. On systemic examination, the abdomen was distended more on the left upper quadrant with traditional markings on the upper quadrants. The abdomen on palpation was tense and tender more at the epigastric region, and bowel sounds were reduced on auscultation. The rectum was empty on digital rectal examination. Heart sounds were heard normally on auscultation and lungs revealed reduced air entry more on the left lower zone.

Abdominal ultrasound (Siemens Acuson NX3, Germany) was done revealing gastric volvulus and reduced gastric peristalsis. An abdominal x-ray showed gastric air-fluid levels (Figure 1).

Her complete blood count revealed microcytic hypochromic anemia of 8.8 g/dl, raised leukocyte count of 21×10^9/L and a normal platelet count of 447×10^9/L. The serum creatinine was normal at 57 μmol/l, serum sodium 180.02 mmol/L, serum potassium 3.51 mmol/L, aspartate aminotransferase 34.02 U/l and alanine aminotransferase 13.72 U/l. Blood group was O Rhesus-positive.

The patient was given Ceftriaxone 450 mg and Metronidazole 80 mg intravenously and transfused one unit (200 milliliters) of whole blood before being taken for an emergency laparotomy. The abdomen was opened through a transverse incision, the stomach was grossly distended, the gastric antrum was rotated clockwise about 90 degrees at the level of the fundus. There was a left diaphragmatic defect of about 3 x 4 centimeters (Figure 2). The fundus and spleen were both herniated through the defect into the chest. The stomach was mobilized and rotated anticlockwise to its anatomical position. The fundus was reduced back followed by the spleen. Suctioning of fluid content from the chest was done, and the diaphragmatic defect was repaired using nylon suture in a continuous technique. The abdomen was cleaned thoroughly with warm saline and closed in layers.

FIGURE 1. An Abdominal X-Ray showing Gastric Air-Fluid Levels
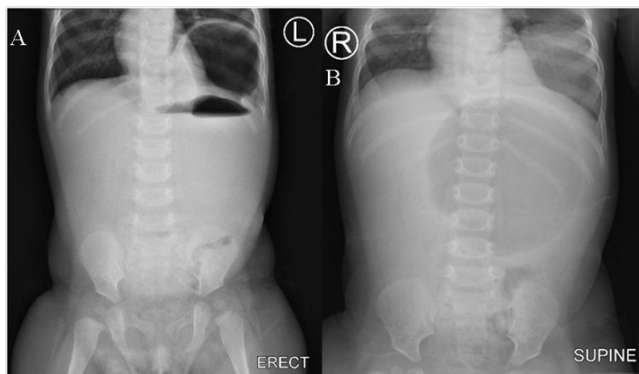
A: Erect abdomen x-ray. B: Supine abdomen x-ray. X-rays demonstrate a left congenital diaphragmatic hernia with protrusion of the stomach into the left hemithorax. Findings suggestive of bochdalek hernia.

Postoperatively, the baby was nursed in ICU for four days, transfused with 180 milliliters of whole blood and kept on intravenous Ceftriaxone 450 mg once daily and Metronidazole 80 mg eight-hourly for five days along with Paracetamol 140 mg for 24 hours. Control chest x-ray was done after 24-hours (Figure 3). Control full blood picture revealed leucocyte count of 9.71×10^9/L, hemoglobin of 16.9 g/dl and a platelet count of 200×10^9/L. The baby fared well and was discharged on day six postoperatively with Amoxicillin-Clavulanic acid syrup for five days and to return to the surgical outpatient clinic after two weeks for a review of which the baby fared well, was tolerating meals and incision had healed. After two months the bab-

y was reviewed again whereby the mother reported the baby to continue to gain weight well and reported of no complaints hence was discharged.

FIGURE 2. Image Showing Left Sided Diaphragmatic Defect
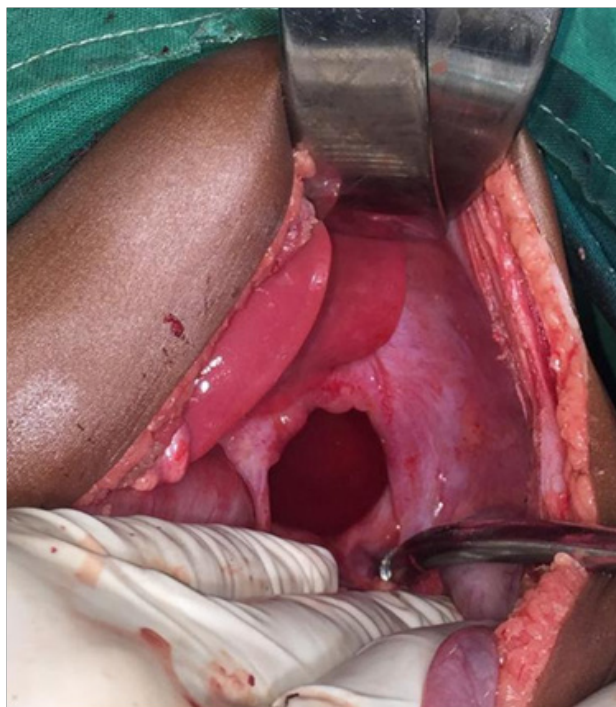
DISCUSSION

A congenital diaphragmatic hernia is a developmental defect characterized by incomplete fusion of the pleuroperitoneal canal, usually evident at birth[1,4].This defect creates a pathway for intra-abdominal structures to herniate into the thoracic cavity. It is mainly classified anatomically into three main types; posterolateral (Bochdalek) hernia which is the most common type (80-90% of cases), anterior parasternal or retrosternal (Morgagni) hernia and Central hernia[4].Our child presented with a posterolateral hernia.

A diaphragmatic defect increases the risk of gastric volvulus. However,this presentation is infrequent, with Javier et al stating that only 26 pediatric cases had been reported worldwide by 2008, and only 15 of the patients were infants[3].The risk is increased due to anomalies in any of the four ligaments (gastrocolic, gastrohepatic, gastrophrenic and gastrosplenic) inserted in the diaphragm, that hold the stomach in position[3,5,6].In patients with a defect in the diaphragm, the gastric fixation can be elongated or absent[7]. Increased subdiaphragmatic space could also increase the risk of an abnormal stomach rotation[8].

Gastric volvulus can be classified into three types, organoaxial, mesenteroaxial and combined.[9-11] Organoaxial volvulus, as seen in our case, is the most

common type seen in 60% of volvulus cases. In organoaxial volvulus, the rotation occurs along the cardio-pylorus axis due to abnormal mobility and deficient fixation at the hiatus of the stomach[12]. A diaphragmatic hernia is frequently associated with this type[13]. In mesenteroaxial volvulus, the stomach rotates around an axis between the greater and lesser curvatures. Finally, in the combined type, the stomach rotates about both axes[12]. Anomalies in the ligaments could also lead to splenic herniation as seen in the index case, although it is a rare finding in the postneonatal age[14]. Some authors report that a mobile spleen could potentially cause the volvulus by drawing the gastric fundus downwards in an erect position.[15]

FIGURE 3. Post-operative Supine Antero-Posterior Chest X-Ray

Chest x-ray, no longer shows protruding stomach in the left hemithorax. Consolidation of the anterior segment of the right upper lobe noted in keeping with pneumonia. Atelectatic bands seen in the left mid zone.

The classical triad of Borchardt which include epigastric distension, unproductive retching and inability to pass naso-gastric tube is usually described in adults, and rarely seen in neonates and infants[12,16]. Neonates usually have a typical presentation of vomiting and respiratory distress while infants present with vomiting and epigastric distentionas seen in our case.[14,17]

The diagnosis is suspected when an erect chest radiograph shows a high air-fluid level, and abdominal radiographs show increased soft tissue density in the upper abdomen[18].

Further complimentary tests are needed, such as a CT-scan or barium contrast studies, with the latter serving

to confirm the diagnosis. If the diagnosis is evident with a plain X-ray, as seen in our case, surgical management should not be delayed with further tests[1,3].

Since the diagnosis is based on a high index of suspicion, in some instances, the condition is misdiagnosed as pneumothorax, pleural effusions, hydrothorax, hydropneumothorax, bronchogenic cysts and hence subjected to inappropriate thoracocentesis[19,20].

Surgical management involves performing a laparotomy, usually as an emergency. It involves detortion of the volvulus, reduction of the herniated structure with or without resection of the necrotic segments, and repairing of the diaphragmatic defect.[3,21-23] It is recommended to fix the stomach either by gastrostomy or gastropexy, but some authors reported no fixation, with few cases or recurrences.[22,24] In our case, fixation of the stomach was not required as it was not redundant, and after reduction, it returned to its normal anatomical position.

Acute gastric volvulus with congenital diaphragmatic hernia is a surgical emergency, with mortality rates estimated up to 80% without surgical intervention[25]. Any delays in surgical intervention can lead to catastrophic complications such as acute pneumothorax, gastrothorax, splenic torsion, appendicitis, incarceration, strangulation, ischemia, perforation, peritonitis and death[26-28].

CONCLUSION

CDH with Gastric volvulus is a surgical emergency, and early diagnosis with immediate surgical intervention is required for good outcome. However many patients have limited access to specialized tertiary referral care centres, therefore diagnosis cannot be established and prompt management cannot be offered. This case report highlights the importance of thorough prenatal screening to aid multidisciplinary management plan and helps creates awareness among clinicians to have CDH as their differential diagnosis.

Ethical Consderations

Ethical approval was obtained from the Department of General Surgery, Kilimanjaro Christian Medical Centre. Written informed consent was obtained from the patient's mother for publication for this case report; additionally, accompanying images have been censored to ensure that the patient cannot be identified. A copy of the consent is available on record.

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Health Facility Readiness for Promoting Male Involvement in Family Planning Services in Tanzania: A Qualitative Study on Perspectives of Health Providers in Kibaha District

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ABSTRACT

Background: The successes and failures of health policies and programs to motivate men to develop interest in positive decision making and actions relating to reproductive and child health services (RCHs) in Tanzania are inadequately documented. Therefore, a study was done to explore the health facility readiness for motivating men to effectively participate in RCHs including Family Planning (FP) in Kibaha District.

Methods: This was a cross-sectional qualitative study undertaken in 2014 and involving in-depth interviews (IDIs) with frontline RCH providers at selected Health Facilities (HFs) and their district coordinator. Data were transcribed verbatim, coded and evaluated thematically through a narrative analysis approach.

Results: All the respondents admitted the role of men in influencing FP decisions at family and other community levels and the need for engaging them in RCHs. They all reported to have continued to note an increasing attitude and activeness of men to attend the RCH facilities available for RCHs along with their partners despite the remaining ones who still show hesitance. Family Planning interventions supported by the District Council Authority and development partners were reported to contribute in increasing the number of males coming for FP and other RCHs. Nevertheless, some shortcomings were experienced, and were reported to include some HFs providing FP services on selected week days which limit the clients who would need them any day/time; some dispensaries lacking adequate lounges or consultation room spaces for accommodating clients arriving in couples or who would be held for receiving health education in group; and the occasional stock-outs of essential FP commodities and other RCHs at some of the HFs.

Conclusions: The study reveals the pleasure frontline RCHs staff had after observing an increasing trend in male involvement in such services and the support given by the government and its allied stakeholders to make this a success. However, the prevailing deficiencies relating to HF infrastructure and FP commodity supplies need to be addressed if a universal health coverage for FP and other RCHs were to be attained as policy and program- wise advocated.

BACKGROUND

Men in developing countries play an influential role in decision making with regard to health care seeking for Reproductive and Child Health Services (RCHs), including among others, Family Planning (FP), Antenatal Care (ANC), skilled delivery and postnatal care. [1,2] Male involvement in maternal and reproductive health aspects has generally shown to improve FP, increase access to postpartum services, reduce maternal smoking and depression and reduction in infant mortality risk.[3–6] Male involvement in reproductive health issues continues to gain attention due to men's role at household/family and other social levels.[7] In spite of this recognition, the progress so far made towards engaging men in maternity care affairs such as Prevention of Mother to Child Transmission (PMTCT) of the Human Immune-Deficiency Virus (HIV), FP and other RCHs has remained low in most developing countries.[8,9]There are various factors contributing to this low male engagement and these include; long travel distance to reach a health facility (HF); inconvenient clinic hours; long waiting time at the health facility/clinic; unfriendly attitude of some health service providers; limited space to accommodate couple counselling at the HF/clinic; and financial and time costs involved in accessing the services. These glitches discourage men from participating effectively in maternal and other RCH programs.[10,11] Young men's limited use of sexual and reproductive health services has also been found to be associated with the prevailing traditions and norms leading to certain unfair beliefs and/or practices – 'stereotypes' like masculinity (e.g. perceived male status, toughness and anti-femininity). There's vast literature testifying that this experience has prevailed in Africa and numerous other communities outside Africa for a long time.[12] In those areas/communities, FP programs are previously reported to be targeting mostly women, therefore, disengaging men. Even beyond Africa, studies carried out in developed countries such as the US, reported presence of groups of people of African origin and other racial origins sharing negative per-

ception and therefore maintaining stigma against reproductive health services, especially those requiring male involvement in contraceptive use and attending RCH clinics.[12,13,19] This calls for urgent need for interventionists (reproductive and child health program officers, including planners, managers/administrators and frontline program implementers) to review their strategies and devise means aimed at promoting males' engagement in RCHs. This can be achieved through; strengthened or enhanced community/public education and sensitisation programs, strategically targeting men, including both adults and adolescent boys and the male youth.[20]

Tanzania has not lagged behind in promoting health policies, planning and intervention programs aimed at increasing male involvement or participation in RCH issues. In recognition of the role of men in influencing women's utilisation or uptake of existing reproductive health services, the ministry of health (MoH) is promoting male involvement as an integral element of the existing strategies for FP and promotion of other RCH programs/interventions. There are clear policy statements and guidelines for that, and most of these require multi-sector and multidisciplinary approaches.[3,7] Such Policy and programs/ arrangements include; the National Road Map Strategic Plan to Accelerate Reduction of Maternal, Newborn and Child Deaths 2008-2015[21], the National Adolescent Health and Development Strategy 2018[22], National Family Planning Guidelines and Standards[23], the National Strategy for Prevention of Mother-to-Child Transmission of HIV, and the Health Sector Strategic Plan IV. These documents highlight among other things, the importance of Universal Health Coverage (UHC) in relation to maternal, reproductive, adolescent and child health services.[24] Encouragingly, a number of interventions have been officially instituted for the purpose of motivating and promoting men involvement in reproductive health issues at all levels.[25,26] The encouragement of males/men to utilise some Reproductive Health commodities such as condoms could also be a catalyst for not only prevention of Sexually Transmittable Infections (STIs) like those associated with HIV[27], but also prevention of unplanned pregnancies.

In an attempt to find a basis for rationalising the present study, vast literature regarding utilisation of RCH programs in Tanzania was searched and studied. These studies did not report sufficient evidence on the extent to which the existing structures and organisation of health service delivery points support or encourage men to participate in RCHs. Based on these findings, analysis of health facilities readiness to promote male involvement in family planning services in Kibaha District, Tanzania was deemed justifiable and timely.

METHODS
Study Design
The study deployed a cross-sectional, mixed method survey study design. Data collection and analysis was conducted between April and June, 2014.

Study Setting
The study was conducted in Kibaha District, Eastern Tanzania. Kibaha District is geographically close to Dar Es Salaam Region. It forms one of the six administrative districts of Pwani Region.[33] The region is reported to be among regions with not only low FP usage coverage in Tanzania[34] but also with a decreasing trend in FP service usage.[35]

The latest National Population Census conducted in 2012 showed the Kibaha District Council to have had a total population of 75,899. Among these, women of reproductive age (15-49 years) were 19,015 whereas men aged 15 years and above were 15,598.[36] The District had a total of 24 HFs of which one was a public (government) Health Centre (HC); 23 were dispensaries (16 of them being public; 12 faith-based organisations (FBOs); 2 private/ for-profit – 'commercial'; whereas 3 were owned and run by parastatal organizations).

Study Participants and Sampling Techniques
Since the study sought to create an understanding on the extent to which the existing health service delivery points support or encourage men to participate effectively in FP and other RCH programs in Kibaha District, this information could be obtained from respondents who are dealing with provision of these services directly to male clients, as well as their superiors at health facility and district levels. The study also included Community Health Workers (CHWs) since they also deal with provision of health education and other health related services at community level according to the existing service providers' supervision and guidance policies from the National Guideline.[37]Simple Random Sampling Technique was used to identify Kibaha as the district for this study, out of the six districts forming the Pwani Region

Study participants were identified at different levels, namely; the – 'health facility', 'community' and 'district' levels. While they were purposively sampled to respond as key informants (KIs), they were reached at through a multistage sampling strategy. The selected participants were as follows: at the district level (1 district reproductive and child health coordinator – 'DRCHCo'); at health facility level (1 in-charge of RCHs, and 2 RCH staff, who were traced at Mlandizi HC, and 1 RCHs staff having been traced at the Soga Dispensary). At community level, selection involved (2 CHWs, one linked with the Soga Dispensary and another one linked with the Mlandizi HC). These form the total sample size of 8 participants.

A multistage sampling approach was employed in the selection of both the wards and health facilities (HFs) where the targeted study participants could be traced. At first, two wards were randomly selected from the available 11 wards in the district, by ensuring inclusion of the totally rural and the semi-urban ones. Focus being on facilities owned by the government (popular as 'public health facilities'), the next step was to identify facilities delivering RCHs. Randomisation was done by writing the names of the respective wards and dispensary on pieces of papers. The papers were folded and put into a box that was then shaken strongly for thorough mixing before allowing an independent person to pick the number of papers required to reveal the names of the selected study sample variable (e.g. a ward or dispensary).

The qualitative nature of the study was not oriented to presenting findings indicating statistical representativeness of the results, etc., only a depth understanding of what was considered as to whether it was important to have FP services involving men or not, how the services available were being utilised by men, modes of their delivery and the promoter or destructor factors for more policy relevant information and recommendations.

The RCH staff include those with professional skills for delivering the recommended services while CHWs were those dealing with the distribution of family planning commodities along (or concurrently) with other activities such as provision of health education and community sensitisation on various RCH related issues. The Mlandizi Health Centre was acting as a reference facility for some of the services that were not delivered at dispensary levels.

All study participants responded through answering face-to-face researcher-administered key informant interviews (KIIs) when approached individually. A working tool, namely, a KII guide was prepared in advance for this activity. The interviewers were flexible where it deemed necessary to fine-tune the questions in order to capture key information from the respondents concerned depending on their roles or positions in the health service delivery or management system and this was achieved through adoption of some probing techniques to maximise response or for additional clarity on a given study issue of interest.

Data Collection Methods

Being aware that the goal of any qualitative interview is to maximise response by generating useful and sufficient data[40], an in-depth interview (IDI) Guide was used for the collection of data through key informant interviews (KIIs) sessions. The respective IDI Guide was developed after a reasonable review of an extensive literature on the subject. The review interest was in FP program environments within the health system that could encourage or discourage male involvement in FP in Tanzania. Lessons learned from past experience in Tanzania and the outside world, especially in Africa was traced in the reviewed articles to guide the design of the themes and subsequent study questions for use in IDIs.

With the consent obtained from the study individuals who were approached, all the interviews were tape recorded, conducted at the participants' respective health facilities and district office, and took between 40 and 60 minutes. All interviews were conducted in Kiswahili, the National language which is also fluently spoken by both the study investigator and the respondents. However, flexibility was allowed, as participants were informed that they could use even English if they felt it was more convenient at some points during the interview session. Each of the main questions asked was supported by several probes that came subsequently for clarity or validation on the answer(s) given for the preceding question. Kiswahili was a language commonly used by the respondents, some of whom could be heard using English terms such as 'condoms' instead of 'mipira ya kiume', 'pills' instead of 'vidonge', and 'injection' instead of 'sindano'. Specifically, the main questions and their subsequent probes were directed to hearing stories from the respondents regarding the degree to which men (including adult and young ones) had a chance for being involved in modern FP program strategies, reasons for the observed current situation whereby questions were made on why the observed/reported to be facilitator/promoter factors or hindrances existed the way they seemed to be, to what extent or how the existing health care facilities and other FP service-related organisations provided a supportive environment for male involvement

in modern FP service affairs, and finally, what could be done to increase modern FP service coverage to men

Data Handling and Analysis

A narrative analysis approach was primarily adopted in processing the data before reaching final interpretation. Each day after the interview was carried out, the research team could sit to debrief each other based on what they had experienced in the field regarding the attitudes and responses from their study participants. This was taken as an opportunity to enlighten and remind each other on certain pertinent or important issues for improving on as the interview process continued the next day. Summaries of key points garnered from the field and as recorded in the hand-written notes were prepared and preserved for informing or updating the next stages of the data analysis. Meanwhile, the tape-recorded interviews were spared a time for undergoing transcription verbatim and this was performed after the data collection exercise was completed.

The transcripts content was analysed in regards to the study theme. To arrive at this stage, transcripts had to undergo translation from Kiswahili language to English by ensuring that the original meaning as presented by the respondents were not distorted. A codebook was prepared, with key words or phrases. Such codes were then tagged in connection with text presented as seeming to represent particular meanings meant by the respondent responding to specific questions and as they seemed to correspond to the specific themes suggested for analysis. Thus, the respective thematic framework was used by a team of analysts and each at a time looked into the data independently, interpreted it accordingly, highlighted or identified the points that seemed recurrent and key, and with an eye on possible new and unique ones that could compare or contrast the rest as presented by either the same respondent or a different one, and brought them forward for a joint go-through, discussion and deliberations on what to take, what to leave and the way-forward. Inconsistencies in the details presented out of the transcripts were repeatedly examined, and where necessary, the exercise of listening to the record tapes for ascertaining statements and making corrections, if any, was repeated. Narratives were organised in such a way that statements seeming to carry similar meanings were categorised according to the way they were falling with the respective study theme.

Charts were drafted, with headings and sub-headings to capture the theme and sub-theme of interest for a compare and contrast exercise to allow triangulation of the results. The work of each analyst could be shared across interchangeably for reading and scrutinising so as to see how it informs or validates the work of another, and this helped to reduce individual analyst's bias and enhanced data validity.[46] The final version of the transcripts translated in English was used for analysis

Two major themes emerged and these addressed the (a) Extent of male involvement in RCHs specifically FP, reasons for the observed current situation on the degree of their involvement; and (b) Health providers' views on structures and processes to support male involvement in RCHs. The latter theme had 3 sub-themes: (i) Organisation of FP services at health facility levels, focusing on service

days and waiting time; (ii) Availability and adequacy of waiting and consultation rooms to accommodate couples as indicated by the respective room having at least 2 chairs, and (iii) Availability of all FP commodities applicable for the level of health facility.

Like all qualitative studies[47,48], this stage involved going through the transcribed notes, one after another, tracing key points of interest and then comparing and contrasting the explanations/responses to particular questions or themes from different interviewees and finally reaching the decision on what to take or leave out, and what to take as general points and what to select as most important quotes for reporting.

Ethics approval and consent to participate
The study was approved by the Research and Publications Committee of Muhimbili University of Health and Allied Sciences (MUHAS) with ethical clearance number MU/PGS/SAEC/Vol. XII/3. Permission to correct data was obtained from the district and respective health facilities administration. Participants were informed about the study and were told that their participation was voluntary. To maintain confidentiality, the information collected did not include names of participants.

FINDINGS
Demographic Characteristics of Respondents
As shown in Table 1, of the 8 KIs, 4 belonged to a cadre of registered nurse midwives, the rest were; a clinical officer, a public health nurse (PHN), and 2 trained community-based distributors of FP commodities (part of CHWs). The duration of their involvement in RCHs provision ranged between 2 and 30 years.

TABLE 1: Demographic Characteristic of Respondents

Characteristic	Number
Sex	
Female	6
Male	2
Cadre	
Registered nurse/ midwives	4
Public health nurse	1
Clinical officer	1
Community health workers	2
Duration of their involvement in RCHs provision	
Less than 10 years	3
10-20 years	4
20 years and above	1

KIs' views on Male Involvement in RCHs
All KIs were of the view that male involvement in RCHs issues is very important as it increases chances for uptake of various RCHs products and associated educational and counselling interventions. Some respondents emphasised the need for men to accompany their pregnant partners for HIV screening for PMTCT program based on which they can receive health education and counselling, espe-

cially in relation to FP and other family life aspects with a positive bearing on the health of all – the mother, the baby/child and the father, for instance issues of nutrition, proper use of prescribed medicines, and appropriate birth attendance for timely and safe pregnancy and childbirth. At one dispensary, a respondent expressed when pointing to what she called 'reluctance of some men to attend Antenatal Care (ANC) clinic with their spouses in fear of being tested and found positive for HIV'. She remarked:

There are still men who hesitate to accompany their spouses to antenatal clinics when asked by their spouses as we normally advise them to do. This requires more efforts to sensitise and persuade them since they fear from being tested and proven positive for HIV. KI, from Dispensary.

Other respondents reported increasing trend of male involvement in RCH issues. As argued, a number of men visit HFs with their partners, especially for pregnancy and child health services and HFs use the opportunity to test the couple for HIV under the PMTC program. Also, there are adolescent boys who visit HFs on their own for medical consultations, with particular interest in testing their status for HIV. The latter feedback was obtained from Mlandizi HC and Soga dispensary. In such cases, the health care workers utilise the opportunity to advise such clients on sexual and reproductive health services, with emphasis on cautioning them on how to prevent unplanned pregnancies by using condoms which also protects them and their partners from HIV infection. Despite the observed increase of males showing up for ANC and other RCHs, respondents noted that, previously it was not usual to see women coming with their male partners to the RCH service clinics due to the prevailing myth or perception that attendance for such services was a female affair. Below is a statement given by one informant whose opinion or experience resembled the feedback received from informants found at almost all HFs.

"Initially it was strange to see a man accompanying his spouse, but now 5 to 6 men can be seen in this clinic per day and this makes counselling more meaningful especially when a joint decision is required" KI- 1 from Health Centre.

Responding to a subsequent probe as to why there's observed increase of male involvement in RCHs including PMTC and FP services, the feedback obtained indicated that, the combined efforts to educate and sensitise the public, along with other practical interventions initiated by the government and its development partners (DPs) to support PMTC had positively contributed to the observed difference. DPs include private agencies and non-governmental organisations (NGOs). These have worked hand in hand with the central government or the District Council to invest in money for extending consultation rooms and waiting lounges at HFs thus allowing accommodation of a larger number of clients at the same time. Therefore, the previous experience of clients having to wait for services outside the building and thus causing inconvenience could no longer be experienced. This comfort climate has convinced clients for RCHs including men. Moreover, respondents commended other efforts made by the district government authorities in cooperation with the District Council to support HFs to offer better quality of services. For example, giving men the priority, they seemed to desire for long time in relati-

on to their convincement to show up to access and use the recommended RCHs at the HF points of care that are closer to them.

These efforts included among other measures; the shortening of the clients' waiting time at the clinic by giving men first priority during consultations, strengthening community sensitisation meetings and using local community health representatives or CHWs as well as local government leaders through political meetings or local health committees as well as engaging religious leaders. These efforts were reported to be augmented or supported by the role played by mass media institutions that passed the message directly and widely to the public through various announcements, adverts and displays.

Structures and Processes to Support Male Involvement in Reproductive Health Issues.
Organisation of FP Services at Health Facility Levels
While 6 respondents claimed to have been providing health services in general and those of FP to have been delivered at almost all HFs throughout the week, one denied this experience by reporting that, there are some HFs in the district that do not deliver particular services on some days of the week for various reasons. One of the reasons reported was that, the respective service providers working at such facilities were designating some of the days each week specifically for delivering other reproductive health services particular to under-five children and pregnant women. This was testified by a respondent at a far remote based dispensary by commenting as follows:

"*We usually conduct FP clinics twice per week*" KI from Dispensary

As clarified, the few personnel working at the respective HFs found themselves too occupied with a number of duties required for the mothers and their children, both during service delivery moments and the extra-service delivery. For example, the daily filling of information in the Health Management Information System (HMIS) – Mfumo wa Taarifa za Uendeshaji Huduma za Afya 'MTUHA' registers and cleanliness.

Availability of Waiting and Consultation Rooms
Several informants commented further on the issue of 'the clients' waiting space' at the HF as one of the motivators for male's attendance for RCHs. The nature of the lounges where clients coming for services receive health education in groups, are also used as waiting place before being allowed to enter the medical or nursing consultation rooms or other places for receiving the required services. Thus, HFs that lack lounges force their clients to sit on wooden benches outside the clinic building while waiting for services. This is so inconveniencing during intense sunny or rainy days. Some of the HFs, particularly dispensaries, have no consultation rooms with capacity to accommodate all the clients attending especially when majority of such clients came in two's (as couples). This becomes a challenge on the part of frontline service providers who have to find ways for pleasingly serve such clients. One of the respondents had the following testimony:

"*Now, if a couple comes, I have to take a chair from another*

room or else I leave my seat for one of the clients and attend them while seated on the table or standing" KI-2 from Health centre.

Reports from respondents regarding waiting and service delivery space at HFs were somehow misleading. For example, respondents from either the same HF or a different one acknowledged what they reported 'availability of consultation rooms that were sufficiently equipped with chairs for meeting the needs of the staff involved directly in the provision of services and at least accommodating one client at a time. Quickly, one could think that some of the HFs were well equipped in terms of sitting tools and physical space for service delivery purposes. However, since some clients attend as couples, the issue of space shortage remains. This is because a consultation room allowing only one client at a time would not suffice for clients attending as a couple. This brings about inconveniences not only to the clients but also to the service provider who would have to operate in an already meagre-spaced consultation room. Such scenarios prompt service provision frontline staff to attend to clients in a piecemeal fashion or rotation basis. This is not only inconveniencing, but also an inconsistent trait to the guidelines suggesting couple counselling for FP and PMTCT. As a coping mechanism, one of the options the respective service providers reported to have been taking was to schedule the services in such a way that different services are provided on different days of the week. Although this seems to be an effective solution on their side, it is inconveniencing on the side of the clients since clients as they have to wait for particular days to receive particular services despite the urgency.

Waiting Time
Regarding the mechanisms used for coping with the inconvenience associated with long waiting time for services, respondents from all HFs pointed to the decision made to serve males first. It was claimed that, this decision was not made at the will and discretion of frontline service providers, but by the District Council's administration and health authorities in an effort to motivate men to show up for participating in RCHs. And as experience has shown, this move really encouraged men to participate in the recommended service programs such as FP, ANC in general and PMTCT in relation to HIV. On behalf of similar statements testifying what was attempted and achieved in relation to the latter experience, one informant made this remark:

"*We have shortened the waiting time for men who visit our facility for reproductive health services especially when they accompany their partners for PMTCT or bring their children to the under-five clinic by giving them priority for the services…..we give them services before others*" KI-1 from Health Centre.

Availability of FP Commodities
All respondents in this study reported their satisfaction with the availability/supply of FP commodities of all types, including condoms, pills, and Intrauterine Contraceptive Device (IUCD) most of the time at their workplace, although occasional stock outs of some of the commodities are sometimes experienced.In general, respondents noted that;

"For the past month, Depo-Provera has been out of stock hence those using it are forced to use other methods affecting their compliance, leading to unplanned pregnancies. This brought about complaints directed to the providers as the cause of their unplanned pregnancies". KI from dispensary

"You see, I just have samples for demonstration purposes……….. there are no Depo-Provera for the past month" KI-3,from Health Centre,

Respondents did not explicitly state reasons for the experienced commodity stock-outs and the researcher observed that respondents were adamant at speaking out the causes for the stock shortage. On further probe, respondents reported that stock shortages were due to delayed/ late distribution or supply of the commodities from the district level, partly due to either transport arrangement interruptions or delayed supply from the central Medical Stores Department in Dar Es Salaam to the District Council. Furthermore, the researcher observed that all HFs shared the same experience and that due to increasing trend of RCH services utilisation, the district health department could not project or forecast the high demand for some of the products such as those of FP.

KIs' Views on how to Improve Services to Support and encourage Men's Involvement in Family Planning Issue
Six KIs' responses, on how to make responsive FP delivery system were found to be concentrated around addressing issues mainly relating to increasing the number and sizes of consultation rooms so that they can accommodate couples showing up for health education and other services. This is so important since lack/ shortage of such rooms made HFs especially at dispensary, provide services in alternate days since available space could not accommodate all RCH clients at ago. This is an inconvenience not only to the service providers, but also to the clients who miss getting all the essential services they could have received in a single day visit to RCHs. To address this issue one respondent was of the opinion that efforts or plans are made and translated into reality by ensuring that every RCHs clinic has a waiting lounge containing a television monitor. Through this facility, clients could follow the service providers' teachings complemented with watching the demonstrations displayed on the screen with health information relating to male involvement in RCHs services.

DISCUSSION AND POLICY RELEVANCE
The present study collected useful information, reflecting the status of male involvement in RCHs and the importance of availability of well-equipped health care infrastructure and essential commodities for provision of standard FP services to the needy population in a rural district setting. It is obvious from the reports presented by KIs that Shortage of consultation rooms is a discouragement to RCH utilisation.

Apart from undermining the client's privacy during consultation moments, it also leads to disappointments to clients due to delays in seeking for services/care at the HFs. Also, disappointments can rise in a situation where clients seek for services on a particular day and yet the HFs' number of appointments are already above their capacity of personnel to attend to them within a short ti-me, thus causing long queues at the health facility.

These limitations are consistent with what is widely documented by other researchers in other parts of Tanzania[7] and elsewhere in Africa.[49] Access limitations due to long waiting time brought about by HF understaffing as well lack of waiting lounges/rooms at HF level was also reported by pregnant women attending ANC services in Mkuranga and Mufindi districts, Tanzania.[50,51] Dysfunctional or poorly equipped HFs has also been reported to be barriers to uptake of FP and other sexual and reproductive services in many other countries, within and outside of Africa.[52] To address this limitation, governments in collaboration with bilateral and multilateral agencies continuously invest more in structures, equipment, supplies and human resources.[25]

Respondents noted that male involvement in RCHs improved or enhanced the uptake of various reproductive, maternal and newborn interventions such as PMTCT and FP, as well as services delivered in programs that deal with parental engagement in childbirth and child care matters. Such improvement is supported by a number of programs run by the government in cooperation with, or exclusively run by NGOs.[55,56] This observation was due to the fact that key staff responsible for services delivery received long and short-term training on various RCH aspects which could be the reason for their positive attitude towards the campaign for involving men in the respective service programs or initiatives. In a similar way, reports from studies made in many other developing countries show that most health workers recognise and appreciate male involvement in maternal, newborn, child, adolescent, youth and adult health programs and this has in one way or another contributed to their increased motivation for delivering such services and resulting into increased male attendances.[4–6,57] Thus, health workers' recognition of the importance of male involvement in RCHs is a good indicator of positive attitude towards various interventions aimed at promoting male involvement in RCHs. These findings, therefore, suggest a need for increasing knowledge and sensitisation of health providers to increase their responsiveness in encouraging men to engage in reproductive health services.

Key Informants reported an upward trend of men visiting health facilities for various RCHs including accompanying their spouses for HIV screening to PMTCT and family planning centres. This observation might imply that the campaigns and associated interventions made so far in the district have enhanced men's awareness and knowledge about the issue. However, these strategies have not been fully investigated on, and therefore, further studies are recommended in order to verify observed results elsewhere in Tanzania.[58,59] Evidence from other studies carried out in developing countries demonstrates that, when couples and communities at large possess high health literacy, staying in an environment with proper service working infrastructures and with availability of essential supplies, such couples are likely to be motivated to seek for recommended RCH services in a timely and correct manner.[52] Also, such couples have been observed to have increased informed decision making, ownership, and responsibility which inturn lead to increased participation in PMTCT aginst HIV.[60]

There is still low male involvement in FP issues and this is expected to have negative implications on the reliability and sustainability of the apparent rise in the trend of their involvement in the study district. Thus, despite the reported observance on the increase in male involvement in RCHs in Kibaha district coupled with the high service providers' recognition of the importance of such involvement, the identified challenges might discourage potential clients to show up for the services and thus, the general public may lose trust in the existing health service system.[61] This is supported by evidence from studies carried out in other developing countries, reporting low male involvement in FP issues due to systemic/ institutional, behavioural, financial and geographical factors. Systemic/ institutional factors include; health facility building and infrastructure status, availability of essential supplies or commodities, number, skills and motivation of service providers.[4,62] Behavioural factors are attitudinal in nature and these are rooted from cultural limitations.[14,63] Financial factors are economic cost related and geographical factors are those associated with long travel distance and waiting time.[7,11,25,62,64,65]

Study Limitations
The present study, however informative it is on FP service utilisation by men in Kibaha district, the study is subject to a number of shortcomings, namely; time and financial constraints, thus, the sample size considered was very small. A sample of 8 participants raises questions relating to data saturation and representation, even though qualitative studies do not necessarily require considering large samples when compared to statistics oriented studies, observations of this study need to be tested for validity and reliability by considering a larger sample size.[48,61] The unwillingness of some respondents to disclose confidential information to the researchers was also a possible limitation to this study. There seemed a point when the participants were hesitant to disclose the reasons for the observed suboptimal coverage of men in FP and other RCHs that could be attributed to systemic deficiencies. Respondent's and Researchers' biases due to personal view or limited scope/level of understanding of the issues under this study was also a possible limitation. Different studies have noted that the place of interview/ data collection, researcher/investigator's bias, and interviewee' expectations are matter of concern since they contribute to influencing the responses from the study participants approached.[66] There was also limited focus since this study handled aspects relating to FP and RCHs differently. Most of these limitations could not be addressed given the available resources of time, human and financial nature.

CONCLUSIONS
There is no question about the role men can play if involved in FP, maternal, child and other reproductive health issues as highly recognised by the service providers interviewed in this study. Nevertheless, it suffices to appreciate that more efforts are needed to increase and sustain their involvement for betterment. The observed increase in the tendency of males to accompany their partners to RCHs clinic should be nurtured through deliberate and concerted efforts. This would involve supporting policy and guidelines for implementing the -

strategies recommended, involving of key stakeholders both at institutional and family level, and ensuring that there is sufficient supply of essential products and well-equipped health infrastructure and staffing systems, supplemented with periodic evaluation and analysis of achievements and milestones to enhance and sustain male involvement/ participation.

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Perceptions of Intrauterine Devices among Women in Tanzania

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ABSTRACT

Background: Intrauterine devices (IUD) are important for ensuring neither unplanned pregnancies, nor unsafe abortions occur as well as it helps spacing children among couples. Despite its advantages, its utilization is still inadequate. The underlying causes of low IUD use needs further exploration for a better understanding as well as appropriate handling of the gaps.

Aim of the study: To explore the perceptions regarding intrauterine devices among women aged 15 to 49 years and barriers to its utilisation in Kinondoni Municipal Council.

Methodology: The study was a community-based exploratory study adopting qualitative approach. Five wards were randomly selected in Kinondoni. Data were collected through in-depth interviews (IDIs) and focus group discussions (FGDs). Study participants were purposively sampled for both IDIs and FGDs. Ten (10) women were interviewed in IDIs from all selected wards and Thirteen FGDs were conducted. Thematic analysis was done to analyze qualitative data, into codes, sub-themes, and broader themes. Data analysis was done by using QSR NVivo version 14.

Results: The study involved 10 women aged 15 to 49 years as key informants and 13 FGDs were conducted involving two groups of women of reproductive age, five groups who ever used the method, and six groups who never used it. The study identified perceived barriers towards IUD related to cultural perspectives, negative perception, fear of side effects, individual's insecurity, perceived benefits related to baby's health and parental benefits. Challenges identified were lack of proper information that is; misinformation and misguidance from the health workers, and negative influencers which include intimacy and devices' related factors.

Conclusion: This study demonstrated that women have different perceptions regarding utilisation of IUD. Perceptions were categorized into perceived barriers and perceived benefits regarding utilization of IUD. Awareness and knowledge on importance of modern contraceptives (including IUD) should be raised. Also, healthcare workers should ensure enhancement of IUD utilization through teaching the community in a comprehensive manner.

BACKGROUND

Family planning refers to a conscious effort by a couple to limit or space the number of children through the use of contraceptive methods.[1] It is a voluntary adapted way of living and thinking by the couples based on their knowledge, attitude and responsible decisions.[2] It is noted that family planning is critical for preventing unintended pregnancies and unsafe abortions ultimately contributing to reducing maternal and child mortality.[3]

The modern methods have been demonstrated to be more scientifically compelling at forestalling unwanted pregnancies than the traditional methods.[4] Globally, in 2019, 49% of women aged 15-49 years (a total of 922 million women) were utilising some type of contraception, which is an increment from 42% (a total of 554 million women) that of 1990. Contraceptive use among women aged 15-49 years in 2019 was over 55% in 37 countries[5] despite increase of contraception use among women aged 15 to 49 years in sub-Saharan Africa from 13% in 1990 to 29% in 2019.[5]

Modern contraceptive methods include combined oral contraceptives (COCs) or "the pill", Progestogen-only pills (POPs) or "the mini-pill", Progestogen only injectables, Monthly injectables or combined injectable contraceptives (CIC), Combined contraceptive patch and combined contraceptive vaginal ring (CVR), Intrauterine device (IUD) and many others.[6]

The intrauterine methods are top tier contraceptives as they are long lasting, convenient, well-liked by users, cost-effective, unobtrusive, reversible, and have failure rates less than 1% per year for perfect and typical use and thus rivaling the efficacy of permanent tubal sterilisation.[7]

Currently, the world is addressing the population control due to proper utilization of resources. In developing countries, overpopulation has been a major concern. Though, contraception availability has been widely scaled up, there is poor acceptance of contraception methods which has been contributed to either ignorance or fear of its complication.[8] The United Nations Population Fund (UNFPA) reported that in Tanzania, the contraceptive

prevalence rate (CPR) for modern methods among currently married women (aged 15-49) is 32%. In addition, the unmet need for family planning for currently married women aged 15 to 49 is 22%.[9] Furthermore, IUD use in the general population of currently married, reproductive-aged women was quite low (about 1 percent). [10] Due to low contraceptive prevalence (32% among all women), short birth intervals have been common for example one in five births occurs within 24 months of the previous birth. [10]

The overall utilisation of long-term contraceptives as in 2019 was 18.1%, and it was reported that 3.2% of women aged 15 to 49 years used injectables, 9.1% implants, and only 1.9% utilised IUD.[11] Therefore, the underlying causes of low IUD use needs exploration for better understanding so that the issues can be appropriately addressed.

This study aimed at exploring the perception regarding IUD among women aged 15-49 years and barriers to utilisation in Kinondoni Municipal Council (MC).

METHODS
Study Design
The study adopted an exploratory design employing qualitative approach. The purpose of using this approach was to explore perception regarding IUD among women aged 15-49 years and barriers to utilization in Kinondoni MC.

Study Setting
The study was conducted at Kinondoni MC. Kinondoni was selected as a study area as it has a low proportion (1.9%) of IUD utilization among women aged 15-49 years in Dar es Salaam. [12] The Municipality has a total population of 1,775,049 and an average household size of 4.0 according to the 2012 National Census. Out of the total population, 860,802 are male and 914,247 females. [13] The study was conducted in five (5) wards at Kinondoni MC which were randomly selected.

Data Collection
A simple random sampling was used to select five wards out of 20 (Kawe, Mbezi juu, Makumbusho, Makongo and Mzimuni) in Kinondoni MC. Two streets were picked randomly from each of the selected wards. From each street, two in-depth interviews (IDIs) were conducted making a total of 10 IDIs. Before the actual data collection, the tools were pre-tested in Kunduchi ward among women of reproductive age.

Thirteen focus group discussions were conducted which included, two groups of women of reproductive age, five groups who ever used IUD, and six groups those who never used IUD. Both IDIs and FGDs involved women aged 15-49 years. FGD discussants and IDI participants were purposively sampled. With the help of local leaders, the study participants were sampled as we believed they had knowledge of the subject and could provide useful information. To facilitate FGDs, participants were separated into youth and adult groups (i.e., 18–29 and 30–49 years). Each group included 8 – 12 participants. The principle of saturation was applied where there was no new data, no new themes, and no new coding. Moreover, interview questions were structured to facilitate asking multiple participants the same questions, otherwise one would not be able to achieve data saturation, as it would be a constantly moving target. [14] Interviews were audio-recorded. A research assistant helped in taking notes. Two research assistants with a public health background were trained in the interview guide and focus group guide. They were also introduced to research ethics. The review of data collection tools was done to report any complexity of data collection and were discussed on daily basis. Interviewed women were purposively sampled from the community based on their age (15-49 years), use of modern contraceptives (current use or non-use), and residence (currently living in Kinondoni MC) to reflect the range of women living in the community.

Data Analysis
Textual data were explored using thematic analysis.[15] The principle investigator listened to the whole recording before transcribing. Then the first rough draft was transcribed. After that, the transcript was revisited and edited. The transcript was read and re-read to be familiar with entire body of data. Then, the data were organized in a meaningful and systematic way. Coding was used to reduce data into small chunks of meaning. After examining codes some of them clearly fitted together into a sub-theme. Similar sub-themes were fitted together into a broader theme that seemed to say something specific about this research question. Analysis was done by using NVivo qualitative data analysis software; QSR International Pty Ltd. Version 12, 2018.

Methodological Considerations
Several criteria are used in evaluating trustworthiness: Credibility, transferability, dependability, and confirmability.[16]In this study, the use of purposive sampling to select participants fulfilled the criteria for participation and ensured credibility. Confidentiality was encouraged and participants agreed not to share the discussion outside the group and this increased credibility. The involvement of more than one researcher in the research process ensured dependability that the interpretations emerged in data through triangulation. Description of the study context, selection criteria, data collection, analysis complemented with quotations to facilitate readers were done to assess the transferability of the findings. Before administering the instruments, there was back translation from Kiswahili to English in order to check the accuracy of translation and to meet the criterion of confirmability.

Ethical Approval
Ethical approval from the Muhimbili University of Health and Allied Sciences (MUHAS), Research Ethics Committee (REC) was granted for this study (reference number; DA.282/298/01.C/). Permission to carry out the study in Kinondoni MC was obtained from the District Medical Officer. Participants in the study were provided with informed consent after being informed about objectives and rationale of the study. Participants in the study were free to choose whether to participate in the study or not. Information collected from the participants was kept confidential, no names or any personal identity appeared in the study documents.

RESULTS

Socio-Demographic Characteristics of the Participants

The study involved 10 women aged 15 – 49 years as key informants where a half of them (50.0%) were aged 15 – 24 years. Seven participants had a primary level of education and the remaining three had secondary level of education and above. Of all participants, 8 were married, and two were not married (Table 1).

TABLE 1: Socio-demographic characteristics of the IDI participants (N=10)

Variable	Frequency (n)	Percentage (%)
Age		
15 – 24	5	50.0
25 – 34	3	30.0
35 – 49	2	20.0
Level of education		
Primary level	7	70.0
Secondary level	3	30.0
Marital status		
Married	8	80.0
Not married	2	20.0
Wards		
Kawe	2	20.0
Mbezi juu	2	20.0
Makumbusho	2	20.0
Makongo	2	20.0
Mzimuni	2	20.0

The study involved 104 women aged 15 – 49 years as FGD participants where 41.3% of them were aged 25 – 34 years. About two thirds (66.4%) had a primary level of education and the. Almost three quarters (72.1%) were married. Participants were evenly distributed by wards (Table 2).

Perceived Barriers Regarding Utilization of IUDs

The study reported numbers of barriers regarding utilisation of IUDs. These include cultural perspectives, negative perception, fear of side effects, and individual's insecurity.

Restrictive Norms and Taboos Affect IUD Decision-Making

Norms are the agreed upon expectations and rules by which a culture guides the behavior of its members in any given situation. Taboo is a prohibition of certain behavior that is so strict that violating it results in extreme disgust and even expulsion from the group or society.

Negative perceptions associated with norms and taboos have been identified as the barriers regarding utilization of IUDs in Kinondoni MC. It was reported that men as heads of families are the ones to make decisions regarding number of children and when to have a child. It has also been identified that the threat of conflict and violence discouraged women from using IUDs. Moreover, the general community has been reported to have no clear understanding regarding the use of

IUDs. One of the participants from FGD reported that: *"I always listen to what my husband suggests. These are our norms. I cannot use it without his consent. If he ever finds that I use I will be in trouble. Also, in our community, if you are found you do not have a child people might start thinking that you are infertile"* (FGD R6-non- IUD use Tandale).

TABLE 2: Socio-Demographic Characteristics of the FGD Participants (N=104)

Variable	Frequency (n)	Percentage (%)
Age		
15 – 24	39	37.5
25 – 34	43	41.3
35 – 49	22	21.2
Level of education		
Primary level	69	66.4
Secondary level	31	29.8
Illiterate	4	3.8
Marital status		
Married	75	72.1
Unmarried	29	27.9
Wards		
Kawe	21	20.2
Mbezi juu	21	20.2
Makumbusho	21	20.2
Makongo	21	20.2
Mzimuni	20	19.2

From the users' perspective, the study has identified negative perceptions characterized with misconceptions, myths and negative reactions, and number of sexual partners. The study found that some people perceive IUDs as a disturbing device during sexual intercourse. Study participants have reported that there is a lot of misleading information in the community regarding the use of IUDs. One of the FGD participants reported that:

"In short, the community, which surrounds us to be honest, we are being misled about contraception since everybody speaks his/her own. Some are saying they are causing dizziness, you will find some are saying you will be over bleeding. Therefore, everyone is having her own understanding in the street. One among ten will advise you to use family planning" (FGD R3 Tandale in IUD use).

In addition, one of the key informants reported that:
"Some are saying that IUDs, if you have the habit of having many partners, it is not allowed. This means, if you're having a husband, you're supposed to settle with him meaning you should not cheat." (IDI-06)

Fear of side effects has been identified as a barrier towards utilization of IUDs. Among the perceived side effects were PID which is the infection of one or more of the upper reproductive organs, including the uterus, fallopian tubes, and ovaries, ectopic pregnancy (a fertilized egg implants and grows outside the main cavity of the uterus), and

TABLE 3: Summary of Codes, Sub-Themes and Themes

CODE	SUB-THEME	THEME
Listen Permission Trouble Taboo Norms	Subjective norms	Perceived barriers regarding IUD
Misconceptions Myths and negative reactions	Myths and negative reactions	
Have many sexual partners Risks of PID Ectopic pregnancy Health risks	Fear of side effects	
Menstrual bleeding disturbances Ashamed Fear Scared	Individual's insecurity	
Fear of pain Better health to a baby Feeding practice	Baby's health	Perceived benefits of using IUD
Health risks Avoid unplanned pregnancy Long time Avoid health risk when using IUD	Long term method	
Family planning Support Husband supports	Family support	Acceptance of the method
No problem Accurate knowledge Good method Stays longer Economic benefits	Positive attitude	
Inaccurate Perception Husband denial Fear of pain Poor family support	Negative attitude	Disinterest to use IUD
Large male genitalia Multiple sexual partners Sex pleasure Displacement of device	Sexual factors	
Counseling Poorly informed	Being misinformed	Lack of proper information
Doctor scares	Misguidance from health workers	
No clear information Sexual pleasure Partners' disapproval Uncomfortable feeling	Intimacy factors	Negative influencers
Fears of device disappearance	Device related factors	

menstrual bleeding disturbances. One of study participants from the IDI reported that:

> "However, what friends are saying about the IUDs is that; it is interrupting the menstrual circle. This means if she was bleeding monthly, it can happen two times a week, stops, and start next week again. In addition, it can lead to pregnancies outside the uterus" (IDI-10).

Another participant reported that:
> "Am really scared of the method. I fear using the method,

> because I heard one of my friends saying it can lead to inflammation of the pelvic region"

Perceived benefits of using IUDs
The study also established perceived benefits of using intrauterine devices. The identified benefits reported by study participants were the baby's health and parental benefits. Study participants reported that the use of IUDs allows for child spacing hence gives a chance for healthy growth of child as he/she will be breastfed properly and

parents will have more time to take care of the child. One of the participants from FGD reported that:

> "Contraception is to prevent to get pregnant before the baby reaches 2 years and make a baby to grow in a good health" **(FGD-R1 Kawe in IUD use).**

Participants also reported that since IUD is a better choice for family planning as it is long-term contraceptive method, it allows parents to have more time for economic activities hence alleviating financial difficulties. A key informant reported that:

> "First, one stays for a very long time. This means it can take 3 or 5 years quite different from the injection, which is after every 3 months and you are supposed to take pills every day. So, the IUDs method is much better as I can work longer and earn more before having another pregnancy" (IDI-07).

Barriers to the Utilization of IUDs
Lack of Proper Information

Lack of proper information has been identified as among the barriers towards utilization of IUDs. This factor was found to be associated with being misinformed and poor guidance from health workers. Misinformation about IUD was found to be associated with poor counseling from the health workers regarding IUD, and misleading information among family and community members. One of the participants reported that:

> "On the side of the family members, there are those who disappointed me by saying it is not good and it might have side effects. Many disappointed me and few encouraged me. They were saying usually a woman should get her period on time and if you will not bleed on time perhaps, there will be blood clots in the stomach and later on you can get cervical problem or to get cancer (FGD-R1 Kawe not in IUD use)."

Poor guidance associated with scary information and unclear information on the use of IUD among health workers was mentioned to be the problem. Women lack counseling and adequate information from professional health workers. One the IDI participants reported that:

> "They are saying if that one stays longer, it usually gets rusty. Therefore, the Doctors in the streets are scaring us to put IUDs because each speaks her own that is why we are scared to put" (IDI-11).

Negative Influencers

Intimacy and devices' related factors were found to be negatively influencing utilization of IUDs among women aged 15-49 in Kinondoni. Intimacy factors negatively influencing IUD utilization were sexual pleasure, partners' disapproval, and uncomfortable feeling. Some of the participants reported that their husbands do not approve the issue of family planning. One of FGD participants pointed out that:

> "In short, my husband does not want me to use family planning at all. Therefore, if I will use it, you should know that I am using secretly. He does not want me to use it perhaps due to the stories, which we are hearing from outside and that is why when he is coming inside, he is strictly against that issue" (FGD-R3 Kawe not in IUD use).

Some women also reported that IUD removes sexual pleasure during sexual intercourse with their husbands.

One of the participants reported that:

> ".....we are losing sexual feelings with our husbands. This means we are not interested with them. If you are touched, it is like you're touched by the devil. This means feelings are completely cut off however, they help to do family planning" (FGD-R3 Tandale in IUD us).

As stated earlier another negative influencer was device related factors. These include fears of device disappearance and insertion procedures. The study findings report that some women tend to fear that the implant could travel throughout the body and become lost. One of the participants revealed this as she pointed out that:

> "I cannot use it due to the way it is inserted and the way it comes out and get lost and it is a challenge when removing it. It is better to use other ways only. I am scared of the implants because they are saying it is usually disappearing as well" **(FGD-R6 Mwananyamala not in IUD use).**

Some participants dislike the insertion procedure of the device. One of the participants reported that:

> "Another thing that makes people to not use the IUDs, it is how it is inserted, until you sleep so, it has many conditions" (FGD-R5 Kigogo in IUD use).

In summary, barriers to IUD utilisation are lack of information associated with misinformation from the community and misguidance from health workers; and negative influencers associated with intimacy factors and device-related factors.

DISCUSSION

The findings have answered the question exploring perception regarding IUD as they indicate perceived barriers (related to subjective norms, myths and negative reactions, fear of side effects, and individual's insecurity), and perceived benefits (baby's health and long-term method).

There are number of perceived barriers to utilization of IUD identified in the current study. The study reported that men as heads of families do not approve the use of IUD, hence women fear violence which could be the result of them using IUD. Disapproval of the method can be associated with negative perception as indicated that the general community has no clear understanding regarding the use of IUD. These finding are supported by the study done by Dyne [16] on the influence of perceptions of community norms on current contraceptive use among men and women in Ethiopia and Kenya, which reported that contraceptive use can be shaped by the interaction between the perceived community norms and an individual's own desires. The study showed use of family planning methods is influenced with community perception which is in line with study that reported negative perception lead to low utilisation of the contraceptive methods.[17] Negative perception on IUD was also observed in the study done by Gbagbo and Kayi [18] on the use and discontinuation of IUD in the Greater Accra Region of Ghana.

Fear of side effects was also reported in the current study as respondents perceived that IUD can cause PID, ectopic pregnancy, and menstrual bleeding imbalance. Similar findings that support the current study have been reported in a systematic review done by Allen et al [19] on

the interventions for pain with IUD insertion suggested that the perception of IUDs as abortifacients, risks of PID and ectopic pregnancy has led to deterred IUD use. The study done in Iran also supports the current study findings as it revealed unwillingness of women to use IUD. The study reported that women had inaccurate perception towards IUD such as fear of pain, of IUDs being larger than the genitalia, and of sexual dysfunction.[20]

The study also demonstrated perceived benefits of using IUD as pointed out by study participants. It was reported that IUD is a good method for child spacing hence supports proper healthy growth of the baby as the parents will have more time nurturing the baby. These findings are supported by the study done by Todd et al [21] on awareness and interest in IUD use among HIV-positive women in Cape Town, South Africa as it pointed that women perceived IUD having many advantages including child spacing. The finding implies that the way women or community perceive IUD determines its utilization. This has been revealed in the current study findings as they showed that those who perceived IUD as a good method were using/willing to use the method.

Lack of proper information was mentioned as one of the key challenges hindering utilisation of IUD among women. Poor guidance from health workers and misleading information from family members and community at large, were mentioned to be associated with improper information. Some of the participants heard that IUD can lead to cervical problem and even cancer. These findings are supported by the study done by Chakraborty et al[22] little is known about providers' knowledge and perceptions of the IUD in developing countries. Nepal's liberal IUD service provision policies allow the opportunity to explore provider knowledge and perceptions across cadres and sectors. This research contributes to an understanding of providers' IUD perceptions in low-resource environments, and increases evidence for IUD task-sharing and private sector involvement. Methods: A questionnaire was administered to 345 nurses and auxiliary nurse midwives (ANMs on Knowledge and perceptions of the IUD among family planning providers in Nepal as it revealed that among the barriers to utilization of IUD were lack of trained staff, limited provision of IUD services, provider bias against long-acting reversible contraception, and poor counseling skills regarding the IUD's advantages and disadvantages.

Fear of inserting a foreign device and uncomfortable feeling of using IUD were mentioned as barriers. Moreover, husbands' disapproval to any method of family planning was mentioned as a hindering factor. Similar findings were reported by Lyus et al and Harper et al on Challenges in translating evidence to practice, the provision of intrauterine contraception and use of the Mirena levonorgestrel-releasing intrauterine system and Paragard Copper-T IUD (CuT380A) IUDs in nulliparous women respectively. It was deduced that conceptual concerns and fears about having a foreign body placed inside their womb, lack of counseling and adequate information about, IUDs from healthcare providers to enable them make informed decisions, and fear of painful insertion also affected utilization.[23,24] These findings implies that the stem of these challenges is information. The community is not well informed about the method and people are misguided by the close ones and even the healthcare workers.

CONCLUSION

Hindrances to modern contraceptive use are genuine, and they discourage numerous women from utilizing family planning. To change negative perception regarding IUD, the Directorate of Policy and Planning under the Ministry of Health and other implementing partners dealing with reproductive health should strengthen campaigns to empower women such as emphasis on their education, encouraging gender balance by changing community attitude towards position/status of women in a household and in a society as a whole. Also, the campaigns to raise awareness on importance of modern contraceptives among males (husbands) should be emphasized by the Ministry of Health and other implementing partners dealing with reproductive health and should go along with those involving women. Moreover, health workers should teach the community modern contraceptives (including IUD) in a comprehensive manner aiming at enhancing acceptance and utilization of modern contraceptives.

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Role of Perioperative Intravenous Dexamethasone in Management of Post Adenotonsillectomy Morbidity: A Single Blinded Randomised Controlled Study

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ABSTRACT

Objective: To determine the role of perioperative intravenous dexamethasone in reducing post adenotonsillectomy morbidity in Dar es Salaam, Tanzania
Methods: A Prospective, randomised, placebo-controlled study was conducted at Ekenywa Specialized Hospital. Fifty patients were randomised to receive three doses of intravenous dexamethasone (13 males and 12 females) or placebo (13 males and 12 females) administered eight hourly for the first 24hours after surgery (1mg/kg). Data were analysed using statistical package for social sciences version 21 and P-value<.05 was considered to be statistically significant.
Results: Intravenous dexamethasone was found to exert significant effects in terms of reducing the severity of some observed postoperative parameters such as pain scores, post-operative nausea and vomiting (PONV), tolerance to oral fluids, discharge from hospital, postoperative hemorrhage, postoperative pain, re-admission and wound healing between the two groups of patients. In this study, dexamethasone did not significantly exert any effect on fever in the first 24 hours after surgery.
Conclusions: Intravenous dexamethasone is an effective and safe method for reducing post adenotonsillectomy morbidity.

BACKGROUND

Despite adenotonsillectomy being the commonest surgery in otorhinolaryngology practice, it is associated with significant morbidity especially if perioperative preparations are not well set in place.[1-3] Following adenotonsillectomy, surgical patients tend to adapt a new life pattern characterized by adapting pain whether at rest or during intake of foods or drinks, postoperative nausea and vomiting (PONV) thus impairing their quality of life post-surgery.[4-8] When patients experiences pain post-surgery, it tends to limit their intake of oral foods or drinks and may prolong hospital stay.[1,4,6,9-11]

To improve the quality of life during peritonsillectomy by minimising the risk of occurrence of complications, dexamethasone has been proposed to be an important perioperative medication to curb such situation.[6,7,12] There has been a variable practice globally in otorhinolaryngology pertaining the use of steroids in reduction of morbidity post adenotonsillectomy [6,7] and our country to date has no any existing standard protocol in peritonsillectomy care of patients and this created an urgent call for designing this study.

Perioperative dexamethasone has shown important effect in terms of decreasing postoperative edema at the surgical site and improving oral intake following adenotonsillectomy through its dual antiemetic and anti-inflammatory effects.[2-4,6,12]

Available studies have shown conflicting results on the role of steroids in reducing morbidity post-adenotonsillectomy.[2-4,6,7,11-13] Some studies including the one which was conducted in Switzerland where a meta-analysis of 17 trials involving use of dexamethasone for prevention of PONV in surgical patients concluded its significance in exerting antiemetic effect compared with placebo.[14]

The aim of this study was to determine the role of perioperative intravenous dexamethasone in reducing post adenotonsillectomy morbidity.

MATERIALS AND METHODS
Study Area and Population
The study was conducted at Ekenywa Specialised Hospital from January to June 2020 at the Department of Otorhinolaryngology where patients aged 2 to 18 years who were fit for adenotonsillectomy were recruited. The department of otorhinolaryngology attends about 200 outpatients on daily basis and performs an average of six elective surgeries per day

Study Design
A randomised single blinded study design was conducted to evaluate the effect of intravenous dexamethasone in managing and controlling

morbidity after adenotonsillectomy in patients aged 2 to 18 years at Ekenywa Specialised Hospital

Inclusion Criteria
Selected patients aged 2 to18 years who were fit for adenotonsillectomy were recruited after obtaining parents' or caretakers' consents.

Exclusion Criteria
Patients who had contraindications to steroids use and those with bleeding or medical disorders were excluded upon fulfilling routine pre-operative protocols for tonsillectomy/adenotonsillectomy which included history taking, thorough ear, nose and throat examination, and laboratory workup such as full blood picture, blood grouping and bleeding indices (bleeding time, prothrombin/partial thromboplastin time and international normalized ratio).

Randomisation Technique
Fifty patients between 2 and 18 years of age were randomized into intervention (n=25) or placebo (n=25). Those belonging to intervention group received three doses of intravenous dexamethasone being administered eight hourly for the first 24hours after surgery (1mg/kg). Those belonging to the control group/placebo received 5mls of normal saline.Maximum dose used was 24mg and no adverse effect of this drug was reported in this study.In our study, we administered dexamethasone 1 mg/kg, subject to a maximum dose of 8mg immediately after induction of anesthesia and the anesthetic and surgical techniques were standardized for tonsillectomy and / or adenoidectomy.

Randomization of patients commenced at the operating theatre where those belonging to the steroid arm received 1mg/kg of such drug while those assigned to placebo/saline arm received 5mls of normal saline. All the participants were blinded to treatment allocations but not investigators.

To prevent confounding effect of antiemetic drugs to surgical patients, such medication was not administered. While patients were in the wards post-surgery, trained nurses administered intravenous dexamethasone. Similar analgesics (intravenous paracetamol at 15mg/kg was administered to all surgical patients) and general anaesthetic agents (induction being done using halothane/sevoflurane and being maintained on isoflurane) were administered to cases and controls intraoperatively.

To perform tonsillectomy/adenotonsillectomy, dissection method was utilized and electrocautery was applied only when patients experienced persistent bleeding from the surgical sites intraoperatively. Patients were then kept for observation for 24hours post-surgery and thereafter discharged ready for further postoperative follow-ups scheduled on the 7,[th]14th, 21st and 28th day.

Statistical Analysis
Statistical package for social sciences (SPSS) version 21from the University of Sussex in England was utilised to analyze data. Chi-square and Fisher's exact tests were used to establish the relationship between variables in both the study and control groups. A p-value<.05 was considered to be statistically significant.

Ethical Considerations
Parents or caretakers provided written informed consent since the study participants were aged 2 to18 years. The study procedures and drug administration were explained to parents and caretakers. Ethical clearance was granted on 10th December 2019 with number Ref: *ESH/2019/05*. Study participants were not declined from receiving medical care even upon refusing from participating in the study. Confidentiality was guaranteed as no names or identifiers of the participants were collected during data collection.

RESULTS
Fisher's Exact Test
Patients in the placebo group were more likely to experience PONV, pain, fever, delayed healing of the tonsillar fossa, postoperative hemorrhage and prolonged hospital stay (Table 1). All patients receiving dexamethasone were able to tolerate 400mls of oral fluids at 8 hours after surgery whereas, none of the patients receiving the placebo could tolerate oral fluids at 8 hours postoperatively(Table 1). All patients receiving dexamethasone were able to resume to routine oral feeds earlier than their counterparts in the placebo group (Table 1). None of the patients from dexamethasone group was re-admitted signifying no any complications post adenotonsillectomy. But none in the control group completed healing on seventh postoperative day. (Table 1).

DISCUSSION
Despite adenotonsillectomy being the commonly performed procedure it is associated with postoperative morbidity. There has been no any study in our country that has tried to explore the role of intravenous dexamethasone in reducing postoperative morbidity. The aim of this study was to determine the role of perioperative intravenous dexamethasone in reducing post adenotonsillectomy morbidity at Ekenywa Specialised Hospital in Dar es Salaam, Tanzania

Adenotonsillectomy which is the commonest surgical procedure in otorhinolaryngology causes tissue injury induced acute inflammation, nerve irritation and spasm of exposed pharyngeal muscles which consequently play a role in the genesis of post adenotonsillectomy pain.[3-5,9-12]

There has been no consensus regarding the use of intravenous corticosteroids for adenotonsillectomy from the available literatures since the available studies have either ended up lacking the control group or lacking standardization for the surgical techniques and also there are conflicting ideas about the type and dose of the suitable corticosteroid, whether to use single or multiple doses and whether to use alone or as an adjuvant to other drugs.[1,2,4-6,10,11]

The main objective of this study was to find the effect of steroids on reducing the post-adenotonsillectomy morbidity (such as pain, edema,nausea and vomiting, delayed tendency of resuming to normal oral feeds). Dexamethasone was selected as an ideal perioperative steroid because it has a long half-life of 36 to 48 hours and has glucocorticoid activity.[4,6,7,10-12]
Postoperatively, those patients belonging to

TABLE 1: Comparison of Post-Adenotonsillectomy Morbidities in the Two Groups

Variables	Placebo group N=25 n (%)	Dexamethasone group N=25 n (%)	Odds ratio (95% CI)	P-value
PONV	16(64)	1(4)	0.03 (0.0-0.13)	<0.001
Pain	11(44)	3(12)	0.19 (0.06-0.54)	<0.001a
Fever	5(20)	1(4)	0.18 (0.04 – 0.95)	<0.04a
Delayed healing of the tonsillar fossa	25(100)	2(8)	0 (0.00-0.01)	<0.001
Intolerance to oral fluids post-surgery	25(100)	0(0.0)	0 (0.00-0.002)	<0.001
Delayed tendency to resume to routine oral feeds	5(20)	0(0.0)	0 (0.00-0.001)	<0.001
Re-admissions,	4(16)	0(0.0)	0 (0.00-0.001)	<0.001
Prolonged hospital stay,	1(4)	0(0.0)	0 (0.00-0.001)	<0.001
Postoperative hemorrhage,	1(4)	0(0.0)	0 (0.00-0.002)	<0.001

aFisher's Exact Test

dexamethasone group were kept on intravenous dexamethasone for the first 24 hours after surgery. The administered dose conformed with what was established in other studies where the dosage of dexamethasone, ranging from 0.15 mg/kg to 1 mg/kg with maximum doses ranging from 8 to 25 mg have been commonly used in children with safety.[7,9] In a large study involving 133 patients, Splinter and Roberts have used 0.15 mg/kg dexamethasone with good results.[15]

In our study, majority of dexamethasone treated patients did not require extra analgesics by the time they were discharged 24 hours after surgery. This indicates that dexamethasone is an effective analgesic for patients who have undergone adenotonsillectomy. This finding is in line with what was found elsewhere.[6,12] The current study reports few frequencies of PONV occurrence, thus supporting the hypothesis that intravenous dexamethasone is effective in managing and controlling the occurrence of PONV post-surgery. This finding is similar to what was found by Pappas et al who found a 40-60% decrease in the incidence of PONV after intravenous dexamethasone.[16]

The steroids administered to patients in the intervention group was effective in reducing edema post adenotonsillectomy. At the end of 24 hours after surgery, the incidence of edema of soft palate and uvula were significantly less in the dexamethasone treated patients compared to controls. The marked decrease in edema had positive impact in terms of improving oral intake of foods post-surgery due to less inflammation and pain. Such finding correlate with what was found by Steward et al in meta-analysis where children who received dexamethasone were more likely to resume soft or solid diet 24 hours post tonsillectomy while none from the control group (received saline) was able to tolerate oral feeds at 8-hours post-surgery.[17]

Findings in this study revealed that intravenous dexamethasone was not useful in controlling fever post adenotonsillectomy, a finding similar to the studies which were conducted in Kuwait and United States of America.[12,18]

In terms of duration of hospital stay post adenotonsillectomy, all patients were fit for discharge 24 hours post adenotonsillectomy and this may be due to reduced pain and inflammation and thus reduced overall morbidity. Only one patient from the placebo group had prolonged hospital stay due to severe dysphagia, fever and edema of the uvula. Such finding appears to be similar to what was found in a study that was conducted in Kuwait.[12] but different from what was established in a study that was conducted in the United States of America where there was no difference in length of hospital stay between dexamethasone and control groups.[18]

Pertaining, re-admission post adenotonsillectomy, none of the study group was re-admitted whereas four patients from the control group were re-admitted (one patient with secondary hemorrhage and three patients with severe dysphagia, fever and pain post-surgery). Such finding appears to be similar to what was established in a study which was conducted in Kuwait.[12]

During routine follow up of patients after surgery, twenty-three patients from dexamethasone group completed healing with normal tonsillar bed on seventh day postoperatively and none in the control group completed healing on seventh day postoperatively and similarly, only 20 patients from the control group completed healing after the fourteenth day postoperatively. Such similarity in terms of non-delayed wound healing following perioperative dexamethasone appear similar to what was found in a study which was conducted in Kuwait.[12] Since none in the placebo group completed healing on the seventh postoperatively, steroids have significantly

promoted healing in post-adenotonsillectomy patients.

CONCLUSION
This study has established that routine use of perioperative intravenous dexamethasone in patients undergoing adenotonsillectomy can significantly decrease the incidence of morbidity such as reduction of PONV, pain, and edema of uvula and soft palate, improves oral intake, reduces incidence of readmission, and promotes early healing of the tonsillar bed. Intravenous dexamethasone given three times daily is safe though did not show an impact in reduction of postoperative pyrexia.

Recommendations
There is an urgent need for Ekenywa hospital to establish standardized peritonsillectomy protocol of using intravenous dexamethasone due to its role in reducing morbidity post adenotonsillectomy

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Review and Assessment of Intellectual Property Policy Implementation in Tanzanian Universities and Research Institutions of Health and Sciences.

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ABSTRACT

Background: Intellectual Property Policy is one of the tools that can be used to address challenges faced by universities and research institutions in protecting and commercialising of products resulting from research activities.

Objectives: The aim of this study was to the review and assess the implementation of IP policies in universities and research institutions of health and allied sciences in Tanzania.

Methods: This study targeted universities and research institutions of health sciences in Tanzania. Data was collected through in-depth interviews and review of intellectual property policy documents.

Results: Interviewed key informants indicated sub-optimal or lack of implementation of intellectual property policies in their respective institutions. Major reasons for lack or suboptimal implementation of intellectual property policy included limited awareness on existing institutions' intellectual property policy, and in some institutions, lack of guidelines and regulations for implementation of intellectual property policy, and not knowing how and the importance of protecting and exploiting intellectual property.

Conclusion: Sub optimal and non-implementation of Intellectual Property policy in the studied institutions can be partly attributed to lack of policy guidelines and low awareness on intellectual property policy among staff members. Effective approaches for dissemination of approved Intellectual Property policy, regulations and guidelines will enhance its implementation and hence promote IP protection and commercialisation.

BACKGROUND

Recent national and international developments in intellectual property treaties, legislation, and frameworks are having profound effects on innovation systems and on how public and private research and development institutions implement their missions and how health and agricultural innovations reach the poor.[1] Research institutions and universities have assumed an expanded role in science and technologies by venturing into commercialisation activities of their institution's research and development.[2] As such, they are expected to make direct contributions to economic development and the wellbeing of society. This role requires them not only to produce but also commercialise knowledge, i.e. to use research results to create Intellectual Property (IP) and contribute to new processes and products tradable in the market.[3] However, universities and research institutions are faced with a number of challenges in generating, protecting and commercialising their IP.[4]

As the public sector devotes more of its efforts to humanitarian missions, and engages in more Product Development Partnerships in the fields of health and agriculture, there is need to critically consider the role of intellectual property in a broader innovation context. Intellectual property rights are a critical tool for fostering innovation. Managed judiciously, they balance private rights and public necessity in a manner that, overall, encourages innovation. Understanding how intellectual property fits into the much broader context of innovation and product development is important for any public sector entity.[1]

Despite efforts made by the government of Tanzanian to establish a number of Research and Development (R&D) institutions as well as training of researchers countrywide, the benefits of research have not been fully realised.[5] Evidence indicate that there is low use of IP in Tanzania and this is associated with lack of IP policy or inadequate IP guiding policies, inadequate IP knowledge and awareness, and limited capacity for IP system.[6] For effective translation of research results into intellectual assets, universities and research institutions need suitable policies that provide structure, mechanisms and frameworks for ownership, incentives, benefit sharing, collaborative research, commercialisation and management of publicly and privately sponsored research. Contribution of the Private Sector to Research and Development (R&D)

is currently limited due to weak incentives to invest in R&D, low understanding and appreciation of the financial and economic advantages of adopting new technologies, and weak multi-stakeholder platforms and partnerships.[7]

An IP policy is a formally-adopted document which clarifies the ownership of and right to use the IP resulting from the institution's own or collaborative R&D activities. IP policy sets out the rules of the institution on how to accurately identify, evaluate, protect and manage IP for its further development, usually through some form of commercialisation. IP policy provides a transparent framework for cooperation with third parties and provides guidelines on the sharing of economic benefits arising from the commercialisation of IP.[4]

Recent assessment conducted by the Ministry of Education, Science and Technology, and a pilot study conducted by Tanzania Commission for Science and Technology (COSTECH) in collaboration with National Bureau of Statistics (NBS) indicated that the use of IP system by universities of health and allied sciences, and health research institutions is very low (unpublished results). Numerous previous studies revealed that challenges associated with the low use of IP system by universities and research institutions include; limited capacity for IP system and lack of IP policies and guidelines.[8,9] The aim of this study was to review and assess implementation of IP policy in universities and research institutions of health and allied sciences in Tanzania. This study generated evidence on challenges in implementing IP policies in universities and health research institutions in Tanzania.

METHODS

The study targeted universities and research institutions of health sciences in Tanzania. Data was collected through in-depth interviews and reviews of intellectual property policy documents.

The Ministry of Health, Community Development, Gender, Elderly and Children (MOHCDGEC) through the National Institute for Medical Research (NIMR) in Tanzania was in the process of developing IP policy for the health sector. The IP policy drafting team is composed of focal personnel from 13 research institutions and universities. Hence, request to share intellectual property policy for review was sent to 13 institutions. (Table 1)

Face to face in-depth interviews were conducted using Kiswahili language with 8 key informants (Directors of research and publications) from Tanzania Food and Nutrition Centre (TFNC), Hubert Kairuki Memorial University (HKMU), University of Dar es Salaam (UDSM), Ifakara Health Institute (IHI), Kampala International University in Tanznaia (KIUT), Agha Khan University (AKU) in Tanzania, Muhimbili University of Health and Allied Sciences (MUHAS) and Open University of Tanzania (OUT). An In-Depth Interview (IDIs) guide was developed and pre-tested amongst NIMR researchers. These researchers were not included in the actual interview. In-Depth Interview (IDI) topics included; implementation of IP policy and challenges associated with protection of intellectual properties created through research activities. Trained research assistants conducted all interviews in privacy at the workplace, using the developed interview guide. The main questions in the -

guide were followed by a probing set of questions according to obtained responses. IDIs with key informants were audio-recorded and lasted between 20 and 30 minutes. The information collected was based on the principles of theoretical saturation.[10] Data was collected between April and May 2021

Data Analysis

Kvale[10] loosely guided the content analysis approach used for analysing the qualitative data. The author transcribed the audio-records verbatim and coded all transcripts on the margin of each transcript. The codes were sorted manually into categories. Quotes that were used to illustrate participants' views are reflected in this paper. Universities and research institutions were assigned codes which were used to distinguish them. This was done to ensure anonymity and to protect participants' identity.

Ethical Consideration

The study was granted ethical approval waiver from the Medical Research Coordination Committee (MRCC), Ref number NIMR/HQ/R.8a/Vol II of 2020/122 Data was collected for a needs assessment study aimed at generating information to inform IP policy developing process for universities and research institutions.

Participants Description

Two institutions responded to the request by sharing their IP policy documents through email.[11,12] Three institutions' IP policy documents[13,14,15] were accessed via internet search. Four institutions, namely; TFNC, Agha Khan University, HKMU and KIUT did not have standalone IP policy documents (Table 1). Four institutions, namely; UDOM, UDSM, KCMUco and NM-AIST have IP policy in place, however, efforts to get their policy documents did not bear fruits, and hence after several reminders, decision was made to exclude them from the study. Therefore, 5 IP policy documents were reviewed (Table 1).

RESULTS

Findings of IP Policy Documents Review

While IHI IP policy document did not have vision and mission, NIMR's IP policy vision lacked focus on safe guarding the interest of the institute and those involved in IP generation, protection and commercialisation of intellectual properties. All reviewed IP policy documents had organisational structure and procedures through which documents, publications, inventions and discoveries made in the course of research and other activities are identified, protected and are made available to the public through channels of commerce. However, NIMR and IHI IP policy documents had inadequate mechanisms for determining IP ownership.

There are variations in the way institutions set up their IP management offices. In Sokoine University of Agriculture (SUA), the Directorate of Postgraduate Studies, Research, Technology Transfer and Consultancy is responsible for managing IP matters at the University, and the Deputy Vice Chancellor (Academic) provides the oversight role in the implementation of the IP policy. For IHI, creator/inventor/scientist disclose their IP interests to the Director who reports all collected disclosures to the board of trustees. Similar set up have been observed in 3 institutions;

TABLE 1: Existing and Reviewed Intellectual Property Policy Documents, and Interviewed Institutions.

Name of Institution	IP Policy	Reviewed IP Policy	In-depth interview conducted
National Institute for Medical Research (NIMR)*	√	√	
Muhimbili University of Health and Allied Sciences (MUHAS)	√	√	√
Sokoine University of Agriculture (SUA)	√	√	
University of Dar es Salaam (UDSM) – Mbeya College of Health and Allied Sciences (MCHAS)	√		√
Ifakara Health Institute (IHI)	√	√	√
Kilimanjaro Christian Medical College (KCMco)	√		
University of Dodoma (UDOM)	√		
Hubert Kairuki Memorial University (HKMU)			√
Nelson Mandela African Institution of Science and Technology (NM-AIST)	√		
Tanzania Food and Nutrition Centre (TFNC),			√
Open University of Tanzania (OUT)	√	√	√
Aga Khan University in Tanzania (AKU)			√
Kampala International University in Tanzania (KIUT)			√
Statistics	**9/13 = 69.2%**	**5/9 = 55.5%**	**8/13 = 61.5%**

*IP policy final draft await approval

TABLE 2: Distribution of Institution's Royalty Share

	NIMR	MUHAS	IHI	OUT[a]	SUA
Administration	20%	20%	10%	-	Not stated
DRP/DRCP/DG office	20%*	15%	10%	30% or 25% or 20%	Not stated
School/Lab/Innovation hub**	10%	5%	20%	-	Not stated
Department/TT Desk***	10%	10%	10%	30% or 25% or 20%	Not stated
Total institution's share	**60%**	**50%**	**50%**	**60% or 50% or 40%**	**50%**

*The 20% is equally distributed between DRCP and administration office at NIMR Headquarters; ** School or Institute for MUHAS, Innovator's laboratory for NIMR and Innovation Hub for IHI; ***Innovator's department for NIMR and MUHAS, Technology Transfer Desk for IHI; a Division of income based on the types of intellectual property rights and the level of income. For patented inventions or discoveries with the level of income of USD 20,000 of IP royalties, University get 40%. Patented inventions with the level of income of over USD 20,000 of IP royalties, University gets50%. For other types of intellectual property rights (not patent) if IP royalty is USD 5,000, university get 40%, and if over USD 5,000, university gets50%.

TABLE 3: Emerged Categories of Intellectual Property Policy Implementation Theme

Themes	Categories
Implementation of intellectual property policy	Implementation of availablepolicies and guidelines to manage IP Performance of policies, regulations and guidelines in protection and commercialization of IP Intellectual property awareness as a barrier to IP policy implementation Willingness to adopt or improve existing IP policy

TABLE 4: Intellectual Property Policy Implementation Status and Types of Granted Intellectual Property Rights

	NIMR	MUHAS	IHI	OUT	SUA	UDSM	KIUT	AKU
Granted intellectual property rights								
Patents	0	4	0	0	11	3	0	0
Trademarks	0	0	0	0	0	0	0	0
Copyrights	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Certifications	0	0	0	0	0	0	0	0
Trade secrets	Yes	Yes	Yes	0	Yes	Yes	0	0
PBRs	NA	NA	NA	NA	3	0	NA	NA
IP Policy								
Availability	Draft	Yes	Yes	Yes	Yes	Yes	No	No
Implementation status	No	Yes	No	No	Yes	Yes	No	No

PBRs – Plant Breeders' Rights; NA – not applicable as new plant variety is not the focus of the institution.

OUT, MUHAS and NIMR. In these institutions, the IP Unit, under the Directorate of Research and Publications (DRP)/ Directorate of Research Coordination and Promotion is responsible for the day-to-day administration of IP related activities. However, the Intellectual Property Management Committee (IPMC) decides on what to protect and the modality of commercialising specific Intellectual Property Rights (IPR). For Open University of Tanzania and MUHAS, the Committee is chaired by the Director of Research and Publications. For NIMR, the Committee reports to the Director General, who is the Chairperson of the same Committee. However, in all the 3 institutions (OUT, NIMR and MUHAS), the IPMC is constituted by the Legal Officer, appointed academic members from the Schools/Institutes/Directorates/ Colleges, undergraduate and postgraduate student representatives and IP technical expert.

The rights of indigenous and traditional medicine knowledge holders have been mentioned in IHI and SUA IP policy documents. IHI and SUA considered protection of indigenous knowledge holders from any infringement of their rights, misappropriation, and misuse or exploitation of their knowledge. However, clauses of rewarding indigenous knowledge holders are only included in IHI's IP policy document.

Apart from publications of research results which are normally used to promote scientific and academic staff, there is no other non-monetary incentives mentioned in the reviewed universities' IP policy documents. Although in the NIMR IP policy draft there is mentioning of using research outputs as a major criterion for promotion of scientific staff, it is not clear on how much weight is assigned to different research outputs such as publication of research results, submitted application for IPRs, registered research products, granted patent or trademarks and commercialised IP.

While 4 IP policy documents of MUHAS, SUA, OUT and NIMR, determine institution's ownership of IP based on the significant use of the institution's resources, IHI IP policy document indicated inventor/employee ownership. However, definition of significant use of

resources varies between institutions and there is no definition of significant use in the SUA and NIMR IP policy document. For OUT, utilising of 35% of the university's resources for creation of IP is considered significant use. For MUHAS, resources use is categorised into moderate and/ or significant use. Moderate university's resource contribution includes; use of office space, library, IT services and University name. Significant university's resource contribution includes; use of University finances for IP development, protection or commercialisation; use of University's account system for grant management; engagement of University laboratory staff and use of laboratory equipment. For copyrightable materials, if the institution's contribution is considered moderate, the IP creator becomes the owner. However, the institution retains the perpetual non-exclusive and irrevocable rights to non-commercial reproduction and distribution of the copyright materials for teaching and research. The creator retains 100% ownership of the IP developed outside of the institution and without significant use of the institution's resources. Conditions for co-ownership apply in cases where IPR are obtained after the creator is no longer employed by MUHAS, provided the creation steps happened when he/she was still an employee of MUHAS. For co-owned IPR between the creator(s) and the University, the creator cannot assign or license the IPR (copyrights, patents, trademarks etc.) without the written consent of the University.

In addition to university/institution and inventor ownership, all IP policy documents recognise co-ownership. The rights of students to own IP arising from their research works is recognised by OUT, MUHAS, SUA and NIMR IP Policy documents. The student owns copyright to their scholarly work subject to royalty free license to the University/Institute to reproduce and publish. However, ownership of any other IP that the student create or discover in the course of their research is governed by the terms in the contractual agreement in cases where; (i) the student has made significant use of the University resources (such as facilities or equipment), or (ii) the student received financial support from the University or another sponsor in the form of wages, salary

, stipend or grant funds for the research, or (iii) the research is subject to materials transfer agreement, confidential disclosure agreement or other legal obligations that restricts ownership of the IP. For MUHAS and OUT IP Policy documents, in the absence of such terms, conditions for co-ownership between student and University as stipulated in the IP policy applies. IHI IP policy document is silent about student IP ownership.

While NIMR and MUHAS IP policy documents do not describe how ownership of IP created by visiting researchers will be determined. IP policy of OUT requires visiting researchers to transfer to the University any intellectual property they create in the course of their activities arising from their association with the University. Such individuals are treated as if they are part of OUT employees.

For both SUA and OUT, the rights related to intellectual property that is created during an academic visit by the employee of OUT or SUA to another university is governed by an agreement between the employee's University and such other university. If the IP Rights of the employee's University are not affected, the IP created during the visit shall belong to the other university unless otherwise provided in an agreement. Intellectual property created through commissioned work by a consultant belongs to the University/Institute, unless otherwise provided by written agreement between that person and the University/Institute or the third party. This policy is similar across all reviewed IP policy documents.

For MUHAS, SUA, OUT, IHI and NIMR, ownership of any IP that is made, discovered or created in the course of research funded by a private sponsor, the ownership is governed by the terms stipulated in the relevant agreements such as; grant or research agreement, materials transfer agreement, confidential disclosure agreement or other legal obligation affecting ownership. In addition to above mentioned agreements, NIMR IP policy document has a Memorandum of Understanding (MoU) for the same. However, the later document is not legally bound to settle ownership of created IP. In the absence of an agreement, institution ownership is claimed.

IP policy documents of IHI, NIMR, MUHAS and OUT are silent about IP ownership by non-employees who are neither visiting researchers nor students but associate with the institute/university in the creation of IP, in most cases, these are holders of traditional medicine knowledge or indigenous knowledge. SUA IP policy document require such persons to transfer to the University any intellectual property they may have created in the course of their activities arising from their association with the University. Such individuals will be treated as if they were employees of SUA.

In all the 5 institutions, intellectual property created through collaboration of two or more institutions, terms and conditions of intellectual property rights in the collaborative research contract is used to determine share of ownership.

MUHAS IP policy document explicitly described the university's position on open access, open innovation, publication and collaboration. After completion of research, data on which the research work was based is made available to other members of the university for royalty-free non-commercial use for teaching and research activities. Notwithstanding the above, members of the university have the collegial obligation to allow the owners(s) of such data a first opportunity to exploit that data for publishing. After its publication in the open literature, data on which research work is based on is made available for royalty-free non-commercial use by anyone who requests it. The data must bear the appropriate copyright marks. Exceptions to these rules are allowed only when the research is subject to; confidentiality requirements due to contractual arrangements with a sponsoring agency, delays associated with patent applications, or to university policy constraints on research involving human subjects or animals. In the case of contractual limitations, all collaborators must be made aware of, and agree in advance to such constraints. In OUT IP policy document, there are provisions for University and researcher to jointly own data generated through research activities and either party have the right to access and use the data for research purposes. Sponsors of research may own the collected data for research for purpose. Collaborators also have unrestricted access to all data obtained or collected through collaborative research activities. In spite of these provisions, entitlement to the ownership of primary data, software, and other products of research may vary, depending on the circumstances under which the research is conducted. As such, ownership of data would be specified in the contract agreement to be signed by the two or more parties.

Practice of sharing income arising from commercialisation of IP is based on the net value arrived (after deducting all applicable overheads that went into IP development, protection or commercialisation). For SUA, IHI and MUHAS, revenues accrued from commercialisation of IP are equally shared between the creator and institute or university unless legal requirements or contractual agreement dictates otherwise. However, in cases where significant or moderate institution's resources were utilised, such as use of University finances in product development, filing for patents and business incubation, the payment of royalties to MUHAS become higher than 50% as agreed between the creator(s) of IP and University. Except for SUA's IP policy document, all other reviewed IP policy documents have provisions on how the share of the institution's royalties is distributed between departments and units (Table 2).

For OUT, division of income is based on the type of Intellectual Property Rights (IPR) and the level of income. For patented inventions or discoveries with level of income of USD 20,000 of IP royalties, the inventor gets 60% and the University 40%. Patented inventions with the level of income of over USD 20,000 of IP royalties, the inventor gets 50% and the University 50%. Division of income derived from IP other than patents, for IP income of the first USD 5,000 of IP royalties, the inventor(s) get 60% and university 40%, and income of over USD 5,000 of IP royalties, the inventor(s) get 50% and university 50%. In both cases, University share is equally distributed between the inventor's department and the directorate of research and publication (Table 2).

For IHI, the apportionment due to the creators attract

eligibility of all parties including local and indigenous communities who have collaborated in one way or the other and is shared equally between parties unless provided otherwise by legal requirements and/ or contractual obligations. A community is treated as one single party unless community participation is by means of bona fide legal persons. In the absence of an agreement, multiple inventors receive equal portion of the inventors' share of net revenue. Where multiple inventors are located in different units, the unit of leading innovator will receive the total share of the net revenue. For NIMR, joint creators or inventors decide on how the 40% share is distributed among themselves.

Similar policy of assigning the IPR back to the creator in the event the institute or university is not interested in exploiting the created IP have been observed in the reviewed documents. NIMR may, in writing, allow the individual researcher to claim ownership while retaining its worldwide royalty-free licence to use the said intellectual property rights. Similarly, MUHAS assign the IPR back to the creator in writing. However, in case of successful future venture of the IP outside of MUHAS, the university receive its share of royalties as agreed between the creator and University in the IP Revenue Sharing Agreement. Vice versa, creators of IP to which MUHAS has no ownership may elect to assign IP to be managed by the university upon mutual agreement, provided that there is no conflict with the co-creators, sponsors, third party or applicable laws and regulations. For OUT, inventor(s) receive notification at least one month prior to any act or any intentional omission liable to prevent the obtainment of protection. In such cases the inventor(s) have the option to acquire related IP Rights. IP policy document of SUA have no provision regarding what happen in the event the university decides not to exploit the created IP.

FINDINGS OF KEY INFORMANT INTERVIEWS
Under the central theme of 'implementation of IP policy', 4 categories emerged (Table 3). The first category describes implementation of available policies and guidelines to manage IP. The second category underscores the performance of policies, regulations and guidelines in protection and commercialisation of IP. The third category describes how IP awareness impacts the implementation of IP policy and guidelines. The forth category addresses feasibility of improving existing IP policy or adopting a model IP policy.

Implementation of Available Policies, Regulations and Guidelines to Manage IP
This study observed that IP policy, regulations and guidelines are either lacking or inadequately implemented in universities and research institutions of health and sciences in Tanzania. This is illustrated by the following quotes from key informants:

"Legal mandate requires the institute to conduct research, but the law that established our institute have not been effectively enforced due to lack of implementation guidelines. Now, we have developed the guidelines and we have submitted the documents to relevant authorities for approval" (Male respondent from Institution 6).

"There is no means of identifying and evaluating findings with

commercialisation potential. If a student or staff invents today, or come up with an innovation, we will face some challenges as there are no guidelines on how to go about protecting and commercialising the invention" (Male respondent from Institution 8).

"Sometimes we encounter challenges when partners ask how do we protect the interest of our scientists and researchers who come up with innovations or inventions, as the policy we have is too general and does not adequately address issues of ownership" (Female respondent from Institution 2).

"I cannot say that we have specific mechanisms for identifying innovations or research with potential for commercialisation because we do not have an IP policy in place. The available research policy has been approved last year and it does not cover much on IP related issues" (Male respondent from Institution 6).

Similar to the findings from IP document reviews, key informants emphasised on the importance of having IP policy in order to safe guide institution's and staff's interests.

"Having the IP policy helps us to raise staff's and stakeholders' IP awareness and provide guidance for protection of the IP they create" (Male respondent from Institution 1).

"We live by the slogan which says "Protect before you project", that is the slogan we use to advice researchers and students to be keen in protecting their IP/ innovations" (Male respondents from Institution 3).

"When there is no IP policy, there is a possibility that the institute will be robbed off it's IP. For example, 30 years ago, we were involved in a joint program in one of the region. The program was externally funded. We developed malnutrition conceptual framework but as we speak, nobody knows that we were actively involved in developing that framework. All the credits went to the funder who claimed the ownership of the conceptual framework. May be if we had an IP policy in place, the situation would have been different" (Male respondent, Institution 6).

Intellectual Property Awareness as a Barrier to IP Policy Implementation
Inadequate implementation of IP policy is linked with lack or limited IP awareness, knowledge and capacity.
"Our IP policy is being implemented, however, more IP trainings and awareness campaigns are needed to empower our students and employees to protect their innovations and research findings" (Male respondent from Institution 3).

Most of our staff and students have limited knowledge on the applications of IP policy, so it is important to widely disseminate the policy and raise employees' and students' awareness on the existing policy (Male respondent from Institution 5).

"The policy is still at its infant stage and thus we have not encountered any challenges in its implementation. All is needed now is to continue raising awareness on the use of IP policy" (Male respondent from Institution 1).

Performance of Policies, Regulations and Guidelines in Protection and Commercialisation of IP
All key informants reported that the mission and orientation of universities and research institutions is driven by research and academic, and that social and

economic development are the priorities of such institutions.

"We do not have any research product which we have commercialised so far. We are more oriented to service provision. We use research results to inform teaching and health practices. So I would say that we have indirectly contributed to the social and economic development in this country. Improved education leads to reduced illiterate individualsand improved health practices results in improved health status and increased involvement in income generation activities and productivity" (Male respondent, Institution 4)

"Our institute's orientation is towards serving the public, and hence SMEs are being trained on preparation of various food formula and Ready to Use Therapeutic Food (RUTF). We conduct research to improve access to nutrition services to the public. We train SMEs to produce and make it easy for the public to access our products. But, the institute does not commercialise any product it creates" (Male respondent from Institution 6).

Surprisingly, certification was the most frequently mentioned type of IPR commercialisation but none of the key informants mentioned that their respective institutions had been granted certification rights for any of their research products, services or processes. Three institutions (SUA, MUHAS and UDSM) had been granted patents (Table 4). Apart from copyrights and patents, other types of IPR were not common as narrated by key informants.

"So far we have about 3 to 4 patents for our products, one of them is the herb based antimicrobial substance, and another one is the nutritional supplement which is already in the market. The other IP is in its very early stage and therefore I cannot disclose its information now" (Male respondent from Institution 1).

The University has IP policy but we have not register any of the research findings or innovation or invention for patent and other types of IPRs apart from copyrights. This is because of limited knowledge on IP protection and commercialisation, the types of research we conduct do not translate into tradable IP and limited knowledge on the use of IP policy by our students and employees" (Male respondent from Institution 5).

Having IP policy enabled us to register many of our IP for patent and copyrights. So far, 3 patents have been granted. Over 30 IPs have been submitted to BRELA for registration and application for patents and copyrights (Male respondent from Institution 1)

Willingness to Adopt or Improve Existing IP Policy

When asked if their respective institutions will be willing to adopt a model IP policy or revise their existing IP policy documents to address gaps identified by the review performed by this study, key informants responded as follows:

"We are looking forward to the operationalization of the National IP policy so that we ensure that our institution's policy is aligned it. Having a National IP policy is important as institutions will be guided to developing their IP policies that aligns with that of the nation, but for now, what you have started (NIMR), the coordination of developing a model IP policy for universities is so important" (Male respondent from Institution 1).

"Well, now that you ask me about IP policy, I think it is a good idea to have one. I will share this idea with postgraduate team and then see the possibility of developing IP policy" (Male research respondent from Institution 7).

"The move to involve universities and research institutions in developing a model IP policy is a right one, it will enable scientists and researchers to have one voice and power to stand for their rights when they create IP using own, public or private sources of funds, or create IP in collaborations and partnerships" (Female respondent from Institution 2).

"I real wish that something is done to fasten the approval of the National IP policy, this will help people, particularly those in medical schools (staff and students) know their rights for what they create" (Male respondent from Institution 8).

DISCUSSION

Intellectual property in its broadest form is the manifestation of ideas, creativity and invention in a tangible form. IP in the broad sense underpins all of the activity of a university and research institutions. However, many researchers make the assumption that intellectual property means primarily patents, and therefore think that other forms of intellectual property rights are of no direct relevance to them. The common type of IPRs used by the studied institutions is copyrights, and none of the institution used trademark for protection of the institutions' IPs. Out of 8 institutes, 5 confirmed that they used trade secrets for protection of their products or research outputs.

Trademarks are a form of IP protection that serves to distinguish the products or services of one individual, company, or organisation from the products or services of the others. A trademark can be a word, phrase, symbol, design, or a combination thereof. Trademarks can even be sounds or colours, if they are in some way distinctive, that create an immediate association in the mind of the consumer between the trademark and the good. IP protection for a trademark confers an exclusive right to use the mark in commerce. Evidence from this study indicates that trademarks are overlooked and undervalued form of intellectual property. Perhaps, research institutions and universities in Tanzania are not aware of complementing protection provided by trademarks to other forms of statutory IP protection.[1]

Advocating for one IP model may not be appropriate as there is a wide range of institutional types, with different strengths and different objectives, and ultimately different business models. However, the reviewed IP policies and the institutions' set up for management of IP did not exhibit significance differences. Thus, a strategy needs to be directed to "best fit" the objectives and/ or business model of the institution.[1]

Like public universities and research institution in Tanzania, most of the institutions in the United States of America (USA) follow the university ownership model where there is a crucial role of technology transfer office to commercialise the IP generated. Sweden has an inventor ownership model where the inventor has freedom to work on his/her patent for its commercialisation.[16] The revenue sharing mechanism could be of linear (fixed) and non-linear (variable) types. In the linear mechanism,

there would be a fixed share of revenue distribution among those who contributed in the IP generation process, whereas, in the non-linear mechanism, revenue is distributed based on milestone payments after achieving the pre-set target amount during commercialisation/marketing. Most of the European and Australian universities follow this type, and the same is being practised in Tanzania. However, there is some similarity between OUT and Boston college where revenue share of the inventor after licensing is of non-linear, step-down type, where by up to $5000 IP income, the inventor share is 100%, from $5001 to $10,000, inventor share is 85%, and from $10,001 and above, inventor share is 50% and the rest goes to the provost.[17]

Any new or revised IP policy (and IP strategy) will have to be "sold" to people both inside and outside an institution. It is important to explain *what* the policy contains and *why* the policy is designed the way it is. And perhaps staff at multiple levels should be involved in developing and revising, as needed, the IP policy. This group will be able to have extensive discussions about the role and function of intellectual property in the organisation. These discussions will be an effective mechanism for building capacity and staff support of the policy. Some of the most controversial issues can be resolved before they become an obstacle.[1]

Intellectual property is a tool to foster innovation and an instrument to achieve humanitarian objectives. Since research activities may result in tradable IP which can therefore be owned and sold, university and research communities should be encouraged to invest, based on the profit potential from research activities. IP protections can prevent access by some individuals and populations. However, there are many ways for intellectual property to be distributed. utilised and put to work for the interests of the public. Hence there is no need to either fear intellectual property or embrace it blindly, it should be managed to maximise the benefits of research for all of society, especially the poor.[1]

Policies to promote the creation and management of intellectual property by research institutions and universities in Tanzania should give first priority to advancing the mission of those institutions. This means, technology transfer should support the larger mission and not merely be seen as potential revenue sources.[1]

Limitations of the study
Relying on the empty promises made by key informants from some of the institutions that they will send their IP policy documents via email was an obstacle to this study. However, it is possible that the gaps identified in the reviewed documents do not differ with what might have been identified in the missed IP documents, because high learning institutions have more or less similar goals which are normally aligned with the IP policy goal

CONCLUSION
Sub optimal and non-implementation of IP policy in the studied institutions can be partly attributed to lack of policy guidelines and low IP policy awareness among staff members. Effective approaches for dissemination of approved IP policies and their guidelines will enhance its implementation and hence promote IP protection and commercialisation. There is also a need to put in place mechanisms for protection of rights of traditional medicine knowledge holders.

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Spatial and Spatio-Temporal Distribution of Human Respiratory Syncytial Virus, Human Parainfluenza Virus, and Human Adenoviruses Cases in Kenya 2007-2013

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ABSTRACT

Background: Human Respiratory Syncytial Virus (HRSV), Human Parainfluenza Virus (HPIV), and Human Adenovirus (HAdV) epidemics differ in geographical location, time, and virus type. Regions prone to infections can be identified using geographic information systems (GIS) and available methods for detecting spatial and time clusters. We sought to find statistically significant spatial and time clusters of HRSV, HPIV, and HAdV cases in different parts of Kenya.

Methods: To analyse retrospective data, we used a geographical information system (GIS) and the spatial scan statistic. The information was gathered from surveillance sites and aggregated at the county level in order to identify purely spatial and Spatio-temporal clusters. To detect the presence of spatial autocorrelation, the local Moran's I test was used. To detect the spatial clusters of HRSV, HPIV, and HAdV cases, we performed the purely spatial scan statistic. Furthermore, space-time clusters were identified using space-time scan statistics. Both spatial and space-time analyses were based on the discrete Poisson model with a pre-specified statistical significance levelof $p<0.05$

Results: The findings showed that HRSV, HPIV, and HAdV cases had significant autocorrelation within the study areas. Furthermore, in the Western region of the country, the three respiratory viruses had local clusters with significant positive autocorrelation ($p<0.05$). Statistically, the Western region had significant spatial clusters of HRSV, HPIV, and HAdV occurrence. Furthermore, the space-time analysis revealed that the HPIV primary cluster persisted in the Western region from 2007 to 2013. However, primary clusters of HRSV and HAdV were observed in the Coastal region in 2009-11 and 2008-09, respectively.

Conclusion: Human respiratory syncytial virus (HRSV), human parainfluenza virus (HPIV), and human adenovirus (HAdV) hotspots (clusters) occurred in Kenya's Western and Coastal regions from 2007 to 2013. The Western region appeared to be more prone to the occurrence of allthree respiratory viruses throughout the study period.Strategic mitigation should focus on these locations to prevent future clusters of HRSV, HPIV, and HAdV infections that could lead to epidemics.

BACKGROUND

Acute respiratory tract infections caused by the human respiratory syncytial virus (HRSV), human parainfluenza virus (HPIV), and human adenovirus (HAdV) account for a significant portion of the global public health burden of disease[1,2]. In 2015, HRSV incidence accounted for approximately 33.1 million of the total number of acute lower respiratory tract infections (ALRTIs) in children under the age of five years worldwide[2]. While HRSV is the most common cause of ALRTIs in children under the age of five, HPIV and HAdV also contribute to the burden of acute respiratory infections.[3,4] These tree respiratory viruses spread efficiently among humans through direct transmission such as self-inoculation, and indirect transmission such as fomites as well as droplets or aerosols[5]. In 2018, the global burden of HPIV–ALRTIs was estimated to be 29.5 million cases in children under the age of five[6]. Furthermore,

outbreaks caused by HAdV have raised public health concern, as emerging and re-emerging types have been linked to severe pneumonia in healthy children and adults[7,8] Outbreaks of these respiratory viruses occur in various locations around the world, and the timing of epidemics varies depending on population and location[9]. The variation in occurrence rates has been linked to a number of factors, including demographic, socioeconomic, and climate variables[10–12].

Several African countries have reported data indicating a significant proportion of HRSV, HPIV, and HAdV infections. Human respiratory syncytial virus (HRSV) alone had a 14.6% prevalence in people with (acute respiratory tract infections) ARTIs across the continent, indicating that the ecosystem of this continent contributes to the epidemiology of these respiratory virus infections.[13]

Despite the lack of pooled prevalence data for HPIV and HAdVs from the continent, both viruses are typically recorded through syndromic surveillance systems such as influenza-like illness (ILI) and severe acute respiratory illness (SARI) or pneumonia.[14–16] For the period 2000-2015, the proportion of ARTIs in children under the age of five years ranged from 4% to 35% of HRSV, 0.3% to 75.8% of HPIV, and 1% to 26% HAdV in Sub-Saharan Africa.[17]

Human respiratory syncytial virus (HRSV) epidemics have been reported in temperate regions during the coldest months of winter, whereas in tropical areas epidemics are mostly associated with rainy seasons[18]. However, HRSV peaks have also been recorded south of the equator during a dry season.[19] Similar to HAdV serotypes, varying seasonal peaks were observed with HPIV types (1-4), and both respiratory viruses occur throughout the year with less defined seasonality in the northern and southern hemispheres.[20,21]

Kenya, like other countries, has reported a substantial burden of disease from HRSV, HPIV, and HAdV infections. However, the identification of geographical areas prone to HRSV, HPIV, and HAdV infections, or "hotspots," in the country is lacking. These regions can be identified using geographic information systems (GIS) and the available methods for detecting spatial and space-time clusters "hotspots".[22] Techniques such as scan statistics, which combines exploratory and confirmatory capabilities, enable an unambiguous statistical assessment of spatial and spatiotemporal patterns across defined regions.[23,24]

The objective of this study was to identify statistically significant spatial and time clusters of HRSV, HPIV, and HAdV infections in Kenya at the county and regional levels. The hypothesis was that HRSV, HPIV, and HAdV infections occur in clusters with both spatial and spatio-temporal characteristics.

METHODOLOGY
Study Areas Characteristics
The research was carried out in Kenya, which is located in Eastern Africa at a latitude of -0.0236° S and a longitude of 37.9062° E[25]. Kenya's borders are 3,457 kilometers long, and it shares borders with South Sudan, Ethiopia, Somalia, Tanzania, Uganda, and the Indian Ocean.[26] The equator cuts the country in half, with roughly half of Kenya located in the northern hemisphere.

Kenya had eight provinces subdivided into 158 districts prior to the adoption of the new Kenyan constitution in 2010[27]. In 2010, the country was reorganized into 47 counties and 290 sub-counties. From 2013 onwards, this geographic boundary hierarchy was incorporated into national administration. Counties were established in accordance with the previous provinces (Figure 1), which belonged to their respective areas and populations according to the 2009 census.[28]

Kenya's coastal region (province) is divided into six counties covering an area of 79,686.1 km². The average temperature in this region is 22-30°C, and the annual rainfall ranges from 20mm to 300mm.[29] The Rift Valley region is Kenya's largest, with fourteen counties and an area of 182,505.1 Km.² The climate of the Rift Valley region is characterised by arid areas or hot desert in the

FIGURE 1: Geographical Boundaries of Kenya
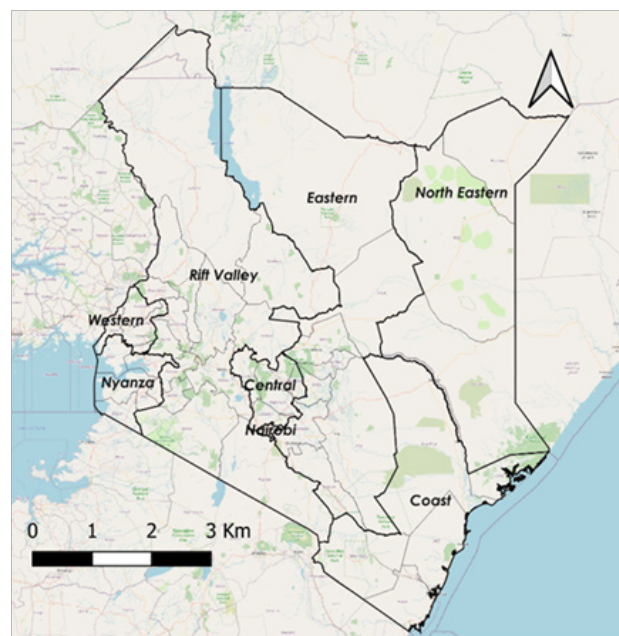
north, tropical savanna in the centre, and cooler temperate areas in the south. The average temperature ranges from 10°C to 28°C, with temperatures exceeding 40°C in the most arid areas. The rainfall ranges from 500mm to 3000mm, with the central region receiving the most.[30] With eight counties, the Eastern region has the second largest area at 140,698.6 Km². The regional characteristics range from arid in the north to semi-arid in the south, with erratic temperature and rainfall variation.[29,31,32] The North-Eastern region consists of three counties covering a total area of 127,358.5 km². The climate is more akin to that of the Eastern region, with the hottest desert or arid areas in the north and semi-arid areas that cool off toward the southeast. Both regions have sparse rainfall in the north, ranging between 250mm and 500mm per year, as well as average temperatures ranging from 20°C to 40°C. The southeastern zone, on the other hand, receives the most annual precipitation, approximately 3673 mm.[29]

Kenya's central region is made up of five counties totaling 11,449.1 km². The region experiences cooler temperatures ranging from 14°C to 28°C, as well as moderate rainfall ranging from 1016 mm to 2540 mm per year.[33] Nairobi is Kenya's capital city and the county seat, with a land area of 694.9 km². Nairobi's climate is more similar to that of the country's central region. The average temperature is around 19°C, and the average annual rainfall is 958 mm.[34] Four counties account for 7,400.4 km² of the area in the Western region. It has a climate with equatorial tropical features as well as some temperate savanna areas. This region has a mean annual rainfall of 2087mm, with the heaviest rain falling in April, and temperatures ranging

from 14°C to 36°C[29]. The Nyanza region borders the Western region; it has a land area of 12,477.1 km², six counties, and a similar climate as the Western region.

Data Sources
Cases of human respiratory syncytial virus, human parainfluenza virus, and human adenoviruses

Human respiratory syncytial virus (HRSV), parainfluenza (HPIV), and adenoviruses (HAdV) cases were identified in this study using Kenya's influenza-like illness (ILI) syndromic surveillance system. The Kenya Medical Research Institute (KEMRI) and the US Army Medical Research Directorate - Kenya (USAMRD-K) implemented the ILI surveillance system. The case datasets were collected between 2007 and 2013. Human respiratory syncytial virus (HRSV), human parainfluenza virus (HPIV), and human adenovirus (HAdV) infections were confirmed in the laboratory using assays such as polymerase chain reaction (PCR), viral culture, and immunofluorescence. The spatial coordinates of the participants' village/estate of origin was collected from the geocoded location via Earth Pro (7.3 Google LLC), recording latitude and longitude in degrees for each HRSV, HPIV, and HAdV case. In addition, the date of illness onset was recorded in months and years.

Population

The Kenya National Bureau of Statistics (KNBS) provided population data based on the 1999 and 2009 national population censuses. In the 1999 census, each district was enumerated and its population count was recorded. As a result, the following ten-year population projection from 2000 to 2010 was published as population counts per district.[35,36] The 2009 National Population Census also recorded population counts by district. Nonetheless, population projections for each district in their respective counties have been published from 2010 to 2020.[37] The population data used for this study in 2009 were the population counts from the 2009 census, not population projections; the projections were used for the inter-census years of 2007, 2008, 2010, 2011, 2012, and 2013. From the geocoded location, spatial coordinates including latitude and longitude centroid files of counties were created using the vector layer of Kenya administration boundaries.[38]

Data analysis

In the first step of the analysis, the dataset was visualised during exploratory analysis to identify obvious errors and to describe the spatial distribution of HRSV, HPIV, and HAdV cases per county. The colour symbol categories were used to indicate the pattern of a large to a small number of cases per county. A higher number of cases was represented by a darker colour, while a lower number of cases was represented by a lighter colour[22].

The second step constituted smoothing thenvisualisation. Kernel density estimation (KDE) was used for describing the spatial distribution of HRSV, HPIV, and HAdV cases in terms of the hotspots in the study area. In qGIS (V3.10.3-A Coruña), the Heatmap plugin generates a density heatmap raster from the input point of a vector layer. The density of the HRSV, HPIV, and HAdV case points is calculated based on the number of points in a location, which is the mean number of events per unit area. This allowed identifying hotspots with the use of a 10 km radius of the kernel (kernel bandwidth)[22,39]. However, from KDE it is not possible to determine the significant positive spatial autocorrelation.

In the third step, Local Moran's I test was applied to detect significant positive spatial autocorrelation from the aggregated data of HRSV, HPIV, and HAdV cases in their counties[22]. The indicators, known as "Local Indicators of Spatial Association (LISA)" were calculated as:

$$I_i = Z_i \sum_{j,j\neq i}^{n} W_{ij} Z_J \quad (1)$$

Where Z_i and Z_J are the observed values in a standardised form, and W_{ij} is a spatial weights matrix in row-standardised form. The enabled qGIS hotspots analysis plugin allowed for the execution of a local Moran's I test with a queen's cases contiguity matrix and 999 random permutations at a 5% level of significance.[40]

LISA reveals spatial clusters with values in quadrants defined as hot spots (high-high), cold spots (low-low), spatial outliers (high-low/low-high), and no significant local spatial autocorrelation.[41–44] LISA, on the other hand, does not provide spatial cluster or hotspot characteristics.

The fourth step of the analysis consisted Kulldorff's scan statistic. This was performed to account for different aspects of spatial pattern analysis.It was based on the discrete Poisson model to identify purely spatial clusters HRSV, HPIV, and HAdV cases by counties. Besides purely spatial analysis, to determine the presence of space-time clusters of HRSV, HPIV, and HAdV cases per year over the study period, space-time scan statistic was applied. It used a Space-Time Poisson model which considered the study period of 2007-2013.

To complete the fourth step of the analysis, different datasets were prepared to fit the format used in SaTScan software (SaTScan V9.6.1). A case file containing annual HRSV, HPIV, and HAdV cases per county for a study period of 2007 to 2013 was made.A coordinate file with geographic coordinates of the centroid of each county, and a population file including the projected total population per county for each year from 2007 to 2013 were also made.These datasets were prepared in order to determine whether the incidence of HRSV, HPIV, and HAdV cases was clustering in space and time retrospectively. SaTScan uses a random process to search for and identify a significantly increased risk of HRSV, HPIV, and HAdV cases exceeding the expected number within the specified spatial window.[22,4]

The analysis was based on aggregated data per county with sites that participated in the surveillance program in Kenya from 2007 to 2013. Previously, the centroid coordinate of each county was extracted from the geocoded location of Kenya administrative boundaries vector layer with the qGIS geometry tool. By the centroids algorithm, a new point layer representing the centroids of Kenya counties was generated. The features were joint with annual HRSV, HPIV, and HAdV cases for each year to the centroid of the counties. This was completed with qGIS and later converted to SaTScan format for further cluster analysis.

To identify clusters, a cylindrical window was used with

a circular geographic formbasedon each county centroid. The window moved in space and time across the study region.The spatial dimension was represented by the circular base of the cylinder with a varying radius from 0 up to the maximum value specified. The height of the cylinder constituted the temporal dimension with a time precision of 1 year. The maximum value of up to 50% of the total population at risk in space and time was considered. It was assumed that for each cylinder, HRSV, HPIV, and HAdV cases were Poisson-distributed. To assess the space-time clusters, it was assumed thatcases were randomly distributed in space and time. From the incidence of cases counted inside and outside the cylinder, the likelihood ratio was calculated for each cluster. A primary cluster was identified as the cylinder with the maximum likelihood ratio. The 999 Monte Carlo randomisations were used to obtain likelihood ratio statistics and p-values of the test. This allowed us to identify significant space-time clusters[45]. A cluster was pre-specified to be statistically significant at the 0.05 level.Sensitivity analysis was performed using different maximum scanning window sizes to test for the robustness of the clusters. Thereafter,nvisualisation of clusters was performed in qGIS to obtain the map of the clusters' locations in study regions.

Ethical approvals for this study were obtained from Kenya Medical Research Institute (KEMRI) Scientific and Ethics Review Unit (SERU) with reference number KEMRI/SERU/CVR/003/3802 and the Walter Reed Army Institute of Research (WRAIR) with reference number WRAIR#1267G.

RESULTS

From the surveillance period of 2007-2013, HRSV was reported in 13 counties (number of cases [n] =539), and HPIV and HAdV were described in 14 (n=922) and 11 (n=581) counties respectively (Figure 2).

The geographical distribution of HRSV, HPIV, and HAdV cases varied by county (Figure 3). HRSV cases were common in Kisii county (n=121) but uncommon in Meru county. Kisii county also had the highest number of HPIV cases (n=171), while Nyamira, Machakos, and Homa Bay counties had the lowest number of cases (n=1). Nairobi county had 114HAdV cases, while Kiambu county had only one.

The hotspot regions for HRSV, HPIV, and HAdVs cases were identified using a kernel density estimate (Figure 4). HRSV hotspots with a high density of cases were identified in the western and coastal regions.

Furthermore, the coastal regions were identified as a hotspot for HPIV and HAdV cases. Nonetheless, HPIV hotspots were discovered in Kenya's central (Nairobi) and western regions from 2007 to 2013. Similarly, HAdV hotspots were observed in the central (Nairobi), and western regions.

The results of spatial autocorrelation showed significant local hotspots (clusters) for HRSV, HPIV, and HAdVs (Figure 5). The 3 respiratory viruses had local clusters with significant positive autocorrelation in the western region of the country. The central (Nairobi), and coastal regions had no significant local cluster for either HRSV, HPIV, or HAdV.

FIGURE 2: Summary Statistics of HRSV, HPIV, and HAdVs Cases and Counties in Kenya (2007-2013)
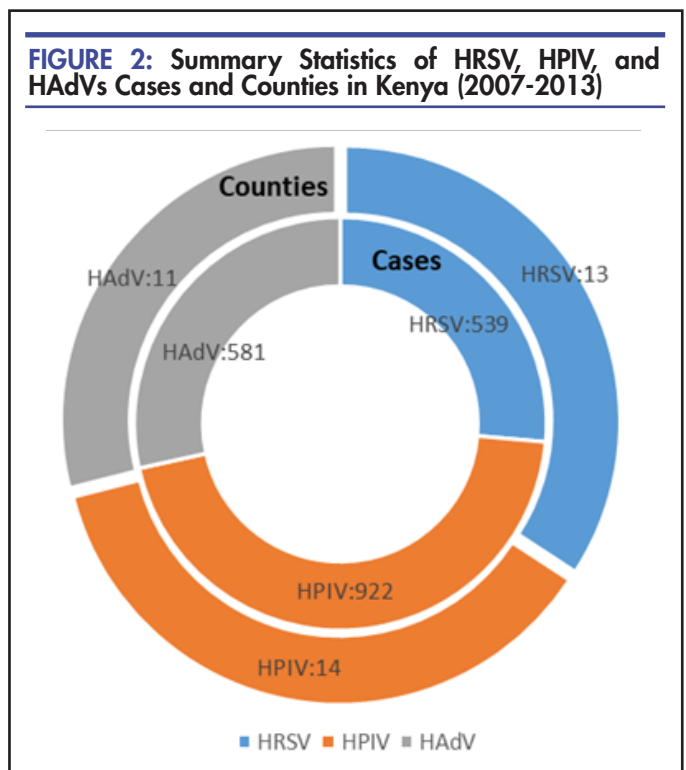
Human respiratory syncytial virus (HRSV) had a positive hotspot or cluster (high-high/HH) with a p-value (p=0.004) covering counties including Kericho, Kisumu, and other adjacent counties. Besides, the positive hotspot (high-high/HH)was noted with a p-value (p=0.02) in the adjacent area of HomaBay county. However, the observed HRSV cases (High-Low/HL or Low-High/LH) with p-value (p=0.002) were an outlier cluster in the adjacent area of the Bomet county.

Human parainfluenza virus (HPIV) positive hotspot (high-high/HH) were also observed covering the Busia, Kisumu, HomaBay, and adjacent counties with a p-value range from (p=0.002) to (p=0.04). The outlier clusters(High-Low/HL or Low-High/LH) of HPIV cases were recorded in the adjacent region with p-value varies from (p=0.002) to (p=0.03).

Human adenovirus (HAdV) positive hotspots (high-high/HH) with a p-value range from (p=0.002) to (p=0.03) were located in the same area of western regions and had outlier clusters (High-Low/HL or Low-High/LH) with (p=0.03) in the neighboring areas.

The results of the purely spatial scan statistic revealed statistically significant (P< 0.05) primary and secondary spatial clusters of HRSV, HPIV, and HAdVs occurrence (Figure 6).

HRSV cases were concentrated in a 55-kilometer radius in the western region, encompassing three major counties. Kericho, Bomet, and Kisumu counties were included, as well as an overlapping secondary cluster with an 80-kilometer radius that included Nyamira and Kisii counties. Other secondary clusters were less likely and had a radius of less than a kilometre.

FIGURE 3: Geographical distribution of (a) Human respiratory syncytial virus (HRSV); (b) Human parainfluenza (HPIV); and (c) Human adenoviruses (HAdV) cases per counties in Kenya (2007-2013)
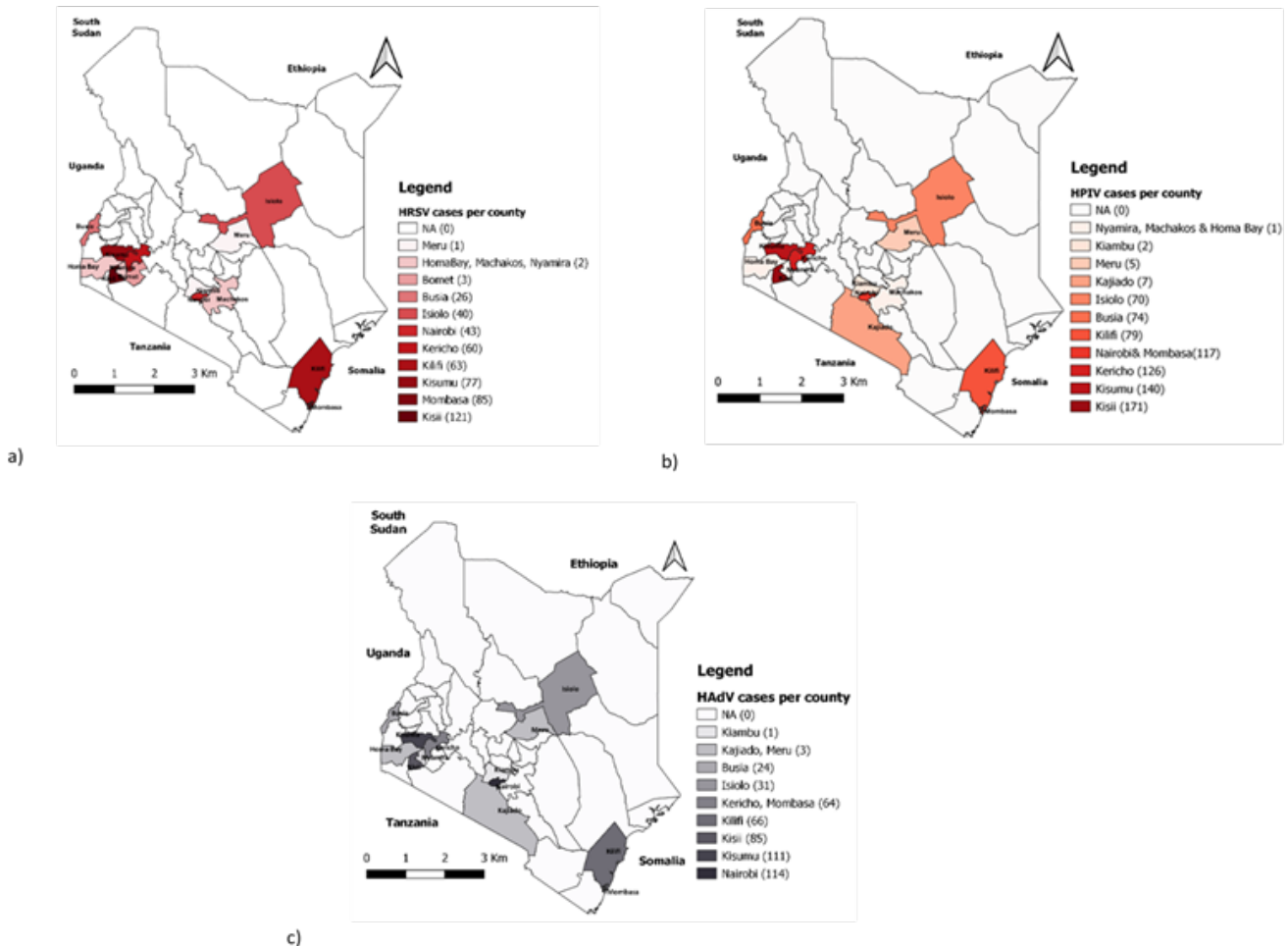
**NA=not applicable; No cases from these counties were captured at any surveillance site as part of the ILI program.

Human parainfluenza virus (HPIV) primary cluster was discovered over an 80-kilometer radius in the western region.This cluster included Kericho, Kisumu, Nyamira, and Kisii counties. Secondary clusters occurred in various regions, including the coastal area (Mombasa County) and the north eastern region (Isiolo County), with a radius of less than a Km.These secondary clusters were significantly smaller size compared to the primary cluster observed in western region.

Human adenovirus (HAdV) cases were concentrated in an 80-kilometer radius that included Kericho, Kisumu, and Kisii counties. In Isiolo County, a secondary cluster with a radius of less than one kilometre was discovered

The results of spatiotemporal cluster analysis indicated different characteristics in the spatial and temporal

distribution of HRSV, HPIV, and HAdV cases in Kenya (Figure 7).

From 2009 to 2011, the HRSV primary cluster had cases concentrated in a 93-kilometer radius at the coastal region, and it covered the main counties of Mombasa and Kilifi.A secondary cluster with an 80-kilometer radius covering Bomet, Nyamira, Kisii, Kericho, and Kisumu County was discovered in the western region.

This secondary cluster occurred from 2010 to 2011. HPIV primary cluster occurred from 2008 to 2010 with cases identified in Kericho, Kisumu, Nyamira, and Kisii County. This cluster had an 80-kilometer radius, while two secondary clusters in Mombasa and Isiolo counties had radiuses of less than a kilometre.

The primary cluster of HAdVs occurred within a

FIGURE 4: The geographical location of (a) Human respiratory syncytial virus (HRSV); (b) Human parainfluenza (HPIV); and (c) Human adenoviruses (HAdV) hotspots/clusters in Kenya (2007-2013)
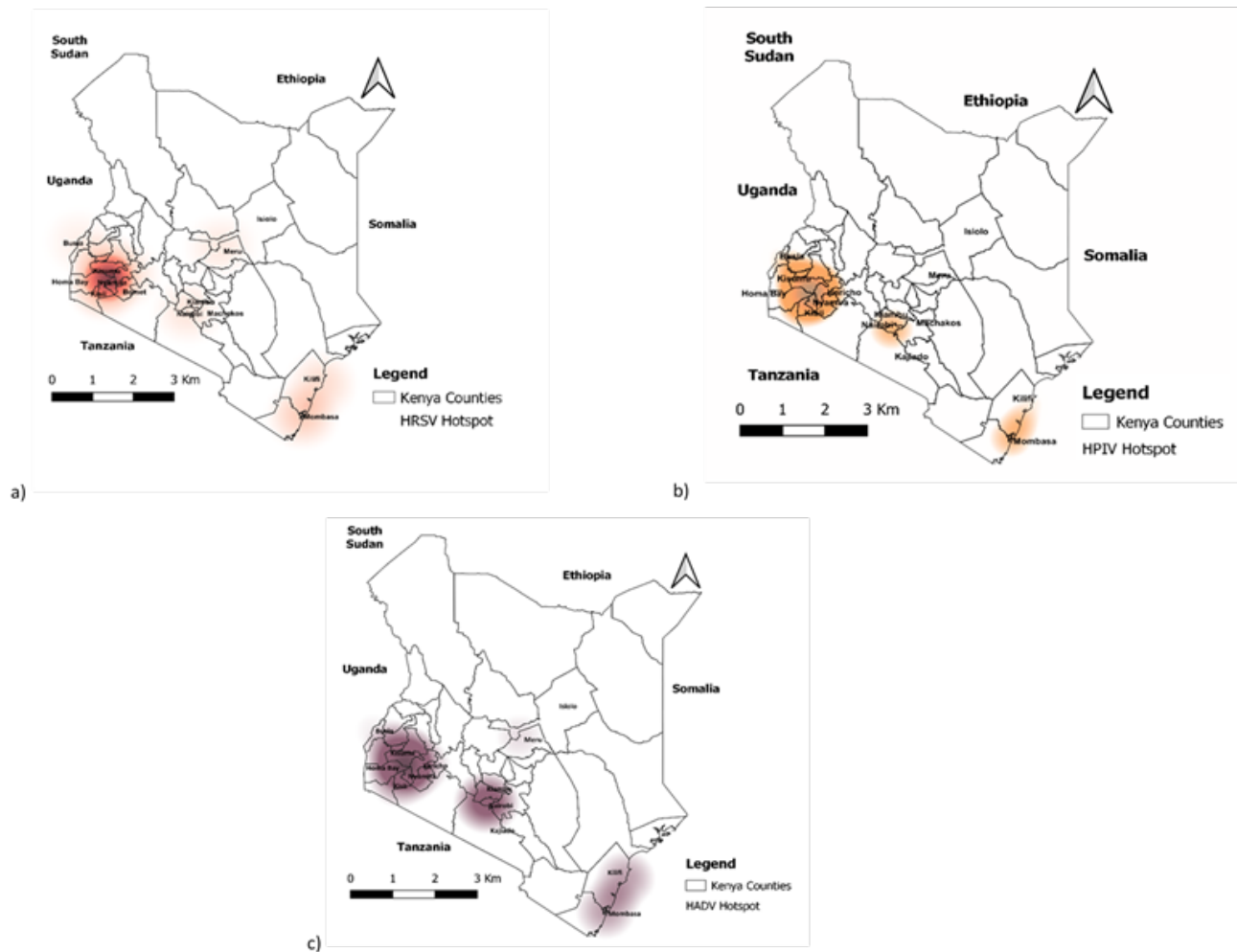
**ILI surveillance sites were located in these counties; Kilifi, Mombasa, Nairobi, Isiolo, Kisii, Kericho, Kisumu, and Busia.

93-kilometer radius of the coastal region, including Kilifi and Mombasa counties, with cases identified from 2008 to 2009. From 2007 to 2009, the western region experienced a large secondary cluster of HAdV. This secondary cluster had an 80-kilometer radius and covered Kericho, Kisumu, and Kisii counties. Another secondary cluster of HAdV with a radius of less than a kilometre was recorded in Isiolo County between 2010 and 2012.

DISCUSSION

The analysis of spatial and temporal patterns of HRSV, HPIV, and HAdV occurrence in this study provided characteristics of the influenza-like illness (ILI) distribution in Kenya from 2007 to 2013. Previous study using ILI surveillance data from the same time period reported influenza viruses causing respiratory infections. Besides that, it indicated the occurrence of other respiratory viruses in Kenya[46]. The three respiratory viruses were found at every surveillance site that participated in the influenza-like illness (ILI) surveillance programme. The surveillance sites represented Kenya's geographical regions, including Western-Nyanza, Rift Valley, Central, Eastern, and Coastal regions.

Human respiratory syncytial virus (HRSV) occurred in 13 counties, with a high number of cases in Kisii County. The Western region was identified as the major hotspot for HRSV using Kernel density estimates (KDE), which was confirmed by local spatial autocorrelation.

FIGURE 5: Geographical locations significantly associated with (a) Human respiratory syncytial virus (HRSV); (b) Human parainfluenza virus (HPIV); and (c) Human adenoviruses (HAdV) hotspots/clusters in Kenya (2007-2013)
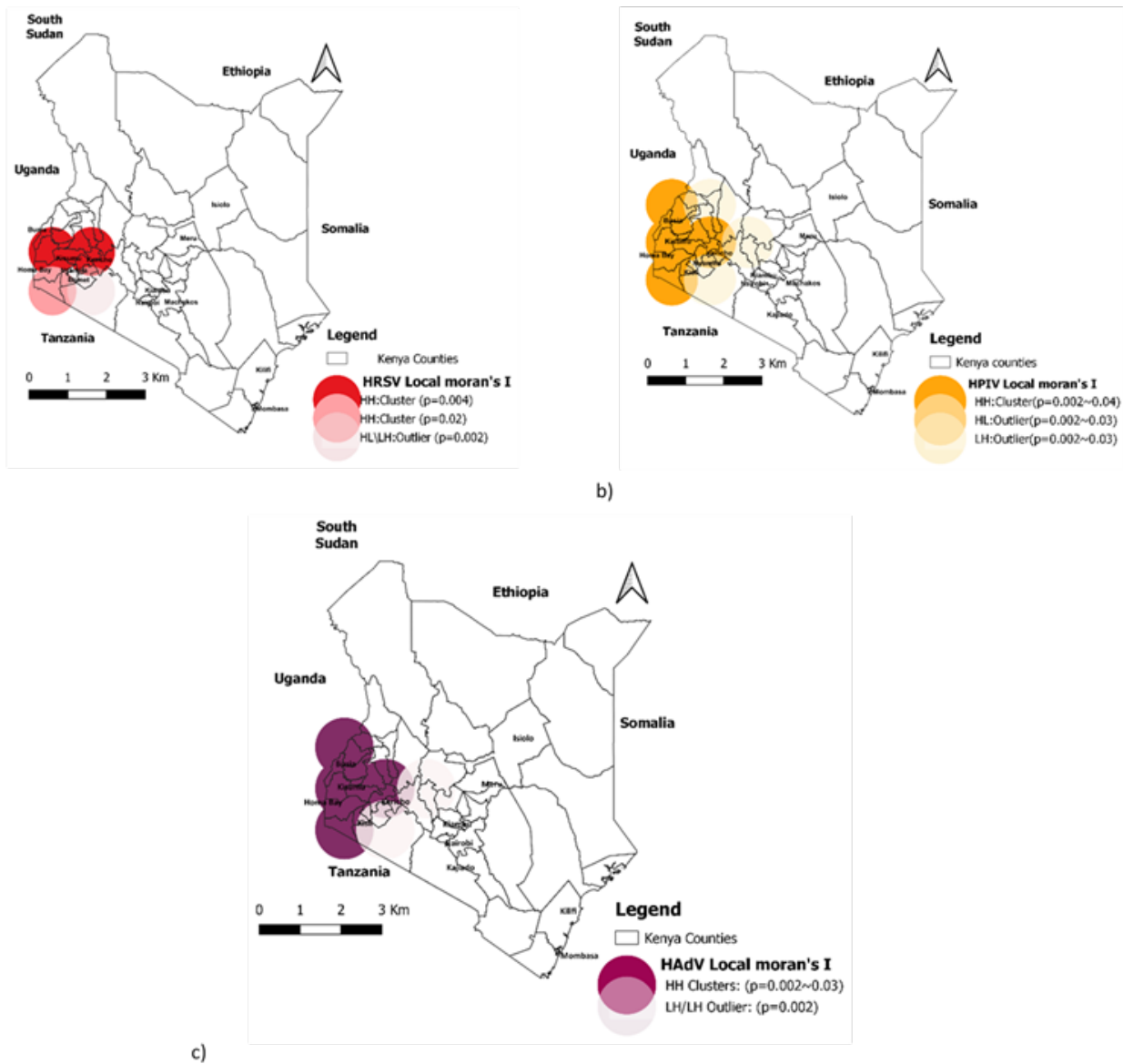
Following the statistical scan, the primary cluster in this region was purely spatial.Human respiratory syncytial virus (HRSV) clustered in the Coastal region from 2009 to 2011, according to the change in time. Not surprisingly, an HRSV hotspot was also observed in the coastal region by KDE. According to a study conducted by Nyiro et al. 2018, HRSV has been identified as one of the most common pathogens causing acute respiratory tract infections in outpatients in Kenya's coastal region.[47]

Besides the purely spatial cluster in the Western region, HRSV had primary and secondary clusters over space and time for both Western and Coastal regions respectively. The HRSV clusters could be attributed to regional population characteristics, social and climate factors. Several factors, including climate parameters, have been linked to HRSV infections in previous studies.[48,49] Rainfall and warm temperatures, which characterize the climate of the Western and Coastal regions, were the climatic conditions most commonly associated with HRSV cases.[50]

Human parainfluenza virus (HPIV) was found in 14 counties, with Kisii County having the highest number

FIGURE 6: Purely spatial clustering of (a) Human respiratory syncytial virus (HRSV); (b) Human parainfluenza (HPIV); and (c) Human adenoviruses (HAdV) cases in Kenya (2007-2013)

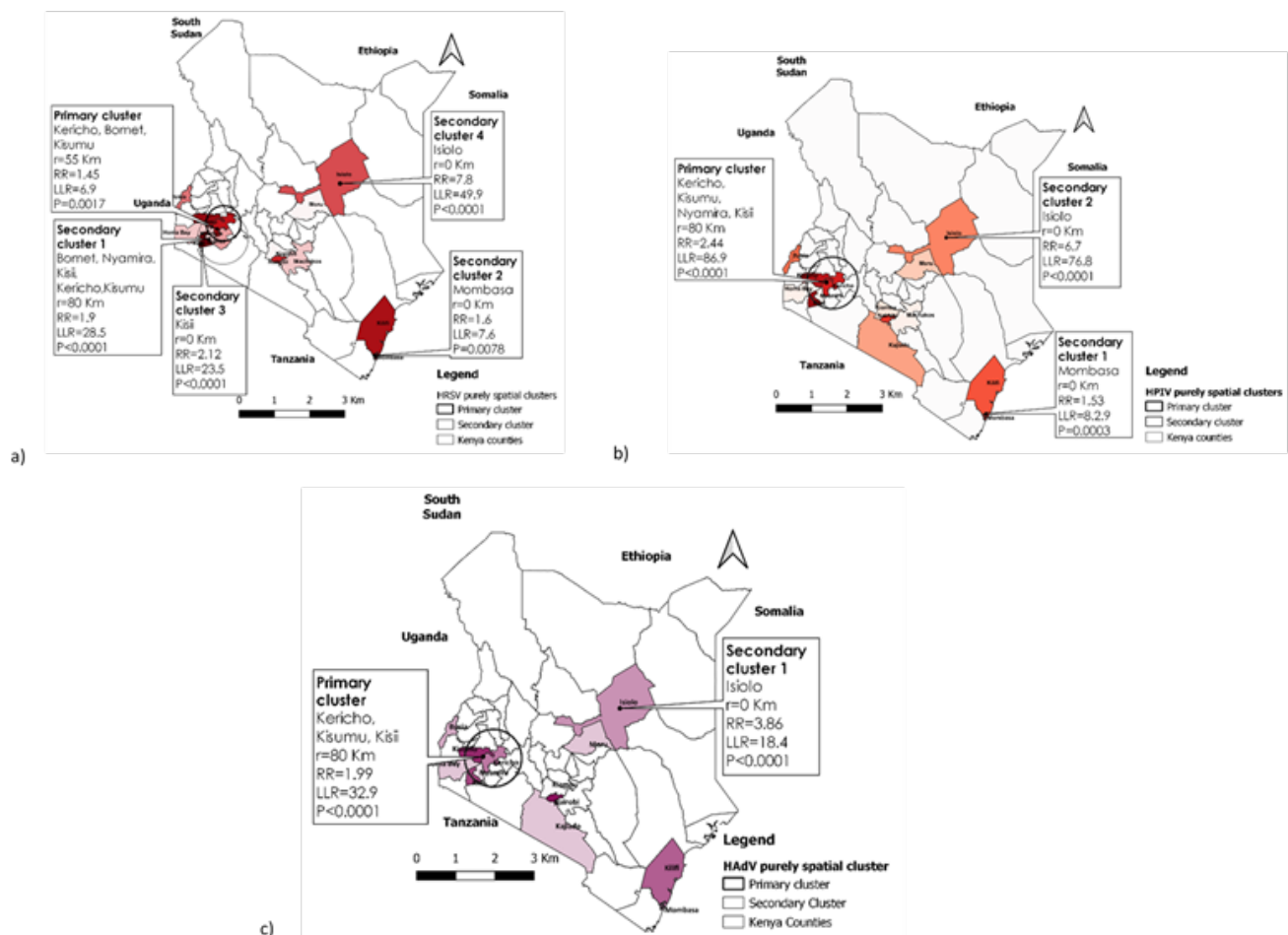of cases. Kernel Density Estimate (KDE)indicated a major HPIV hotspot in the Western region. Other HPIV hotspots, however, were identified in the coastal and central regions. The local spatial autocorrelation indicated that the Western HPIV hotspot was statistically significant. This was confirmed with the purely spatial scan statistics. The space-time analysis revealed the occurrence of the HPIV cluster in the Western region from 2008 to 2010. Unlike HRSV infections, HPIV infections had an erratic distribution with no clear seasonality in Kenya[50]. Furthermore, no significant climate parameters were associated with HPIV infections, as observed in other studies published elsewhere.[51] HPIV clusters could thus be attributed to factors other than climatic parameters.

The occurrence of HAdV was documented in 11 counties, with Nairobi County having the highest number of cases. Despite the fact that the number of HAdV cases in Nairobi was high, the major hotspot was identified

in the Western region, where several counties had a larger number of HAdVs. Other hotspots were found in the coastal and central regions. The major HAdV hotspot had a significant spatial autocorrelation with the Western region. This agreed with the HAdV primary cluster observed in the same region by the purely spatial scan statistics. However, space-time analysis indicated the HAdV primary cluster occurred in the Coastal region from 2008 to 2009. Human adenovirus (HAdV) cluster in the Western region, on the other hand, was secondary and occurred from 2007 to 2009.In Kenya, there were no seasonality patterns or climate parameters associated with HAdV infections.Only warm temperatures were suggested to have a positive influence on these infections[50]. However, other factors such as population demographics, health, and socioeconomic determinants have been linked to HAdV infections in the literature[52–54] A purely temporal analysis has previously been performed based on the same period of 2007 to 2013[50]; this study expands and augments that analysis.

FIGURE 7: Spatiotemporal clustering of (a) Human respiratory syncytial virus (RSV); (b) Human parainfluenza (PIV); and (c) Human adenoviruses (AdV) cases in Kenya (2007-2013)
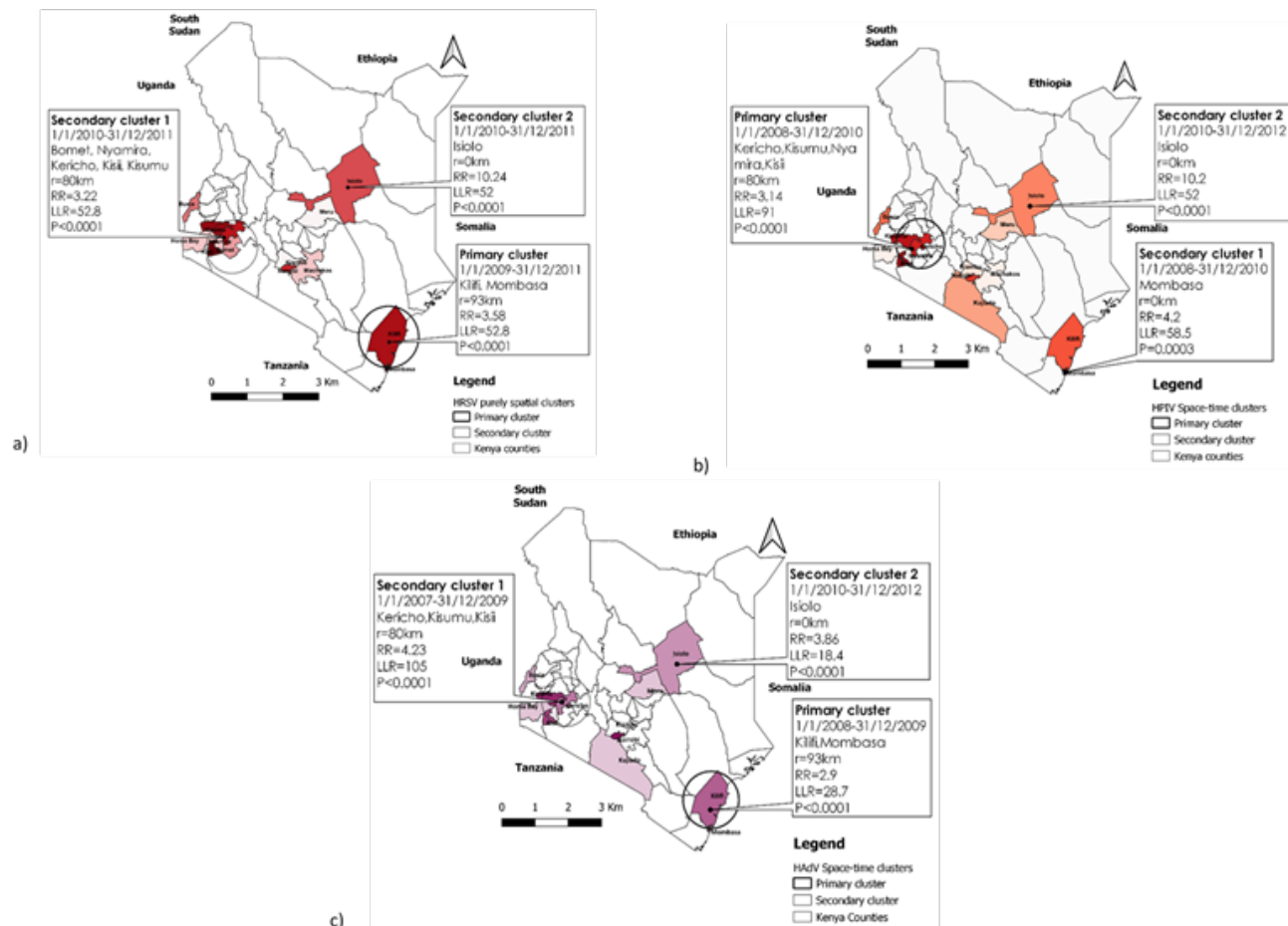
A major shortfall in this study may be due to the use of annual county population projections which are based on the inter-census data; these may not accurately count the actual population per county.[55] Also, not all county had an ILI surveillance site. Another limitation of this study could be the use of retrospective data that cannot be extrapolated to the present. The study outputs also could not be extrapolated beyond the regions without surveillance sites. Although these data-related limitations may have an impact on the study's findings, scan statistics are a well-established method for detecting disease clusters in the spatial and temporal model.[45,56–58] They are used to analyse retrospective and prospective routine data from disease surveillance programs, and the outputs can provide insights into identifying space-time clusters,which inform intervention planning and local and national public health policies.

CONCLUSION

Following the results of the study, HRSV, HPIV, and HAdV hotspots (clusters) occurred in Kenya's Western and Coastal regions between 2007 and 2013. Throughout the study period, the Western region appeared to be more prone to the occurrence of all three respiratory viruses. Furthermore, epidemiological studies should investigate the factors that influence the occurrence of clusters in these areas. Besides that, strategic mitigation should target those areas in order to prevent future clusters of HRSV, HPIV, and HAdV infections which could lead to epidemics.

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Peer Reviewed

Seroprevalence of IgG Rubella among Infants with Features Suggestive of Congenital Rubella Syndrome at a Tertiary Hospital in North Western Tanzania

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ABSTRACT

Background: Congenital Rubella Syndrome (CRS) is among the causes of infant mortality and lifelong disability due to severe birth defects. There has been an increasing number of neonates born with congenital abnormalities suggesting CRS, at the same time the rubella seroprevalence among pregnant mothers and healthy school children in the northwestern Tanzania has been noted to be alarmingly high. This study aimed to determine prevalence of rubella antibodies and associated factors among infants suspected to have CRS.

Methods: This cross-sectional study included 174 infants aged ≤ 12 months with at least one clinical features of CRS. The study was conducted between Septembers 2017and March 2018 at Bugando Medical Centre, a consultant teaching hospital in North Western Tanzania. Collection of Social demographic and other relevant information was done hand in hand with screening for clinical symptoms suggestive of CRS and Blood samples were collected. Indirect enzyme-linked immunosorbent assay (ELISA) Test were conducted on collected sera to test for specific Rubella IgM and IgG antibodies.

Results: The majority of enrolled infants were below 1 year of age; of these 83 (47.7%) were neonates and only 13.2% had received MR vaccine. Out of these, 111 (63.8%, 95%CI: 56.6-70.9) were IgG Rubella seropositive whereas none was IgM Rubella seropositive. In multivariate logistic regression analysis being neonate was the only factor that independently predicted rubella IgG seropositivity (OR 2.3; 95% CI 1.2 − 4.4; *p=0.012*)

Conclusion: A significant proportion children (<12 months) with suspected CRS are IgG seropositive which is predicted by being a neonate (0-4weeks); this indicates high maternal seroprevalence and hence extended surveillance and measures to target women of child bearing age are recommended.

BACKGROUND

Infection by Rubella virus usually causes a mild and self-limiting disease and about one half of individuals infected are asymptomatic, while symptomatic infections present with mild constitutional symptoms and rash.[1-3] However, infection in pregnant women is of public health importance due to the teratogenic effects of rubella virus resulting into Congenital Rubella Syndrome (CRS).[2,4,5]

CRS refers to variable constellations of birth defects brought by intrauterine infection with the rubella virus.[1,2,5] The risk of congenital infection and birth defects is high during the first 12 weeks of pregnancy.[6,7] Once the virus crosses the placenta and access fetal circulation, it remains in the fetal blood stream for the remainder of the pregnancy and hence neonates born with CRS can secrete the virus after birth and can infect other infants and un-vaccinated adults.[8,9]

Features of CRS include cataracts, congenital heart disease, hearing impairment, pigmentory retinopathy and glaucoma. Others include microcephaly, purpura, hepatosplenomegaly, meningoencephalitis, radiolucent bone diseases, jaundice within 24hours of birth and mental retardation.[1,10-12]

A suspected case of CRS is when an infant presents with any one or more of the mentioned symptoms whilethe probable case is when an infant presents withmore than one sign or symptom.The signs and symptoms in a probable case are grouped into major and minor categories, where presence of cataracts or congenital glaucoma,congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, OR pigmentary retinopathy are considered as major

while all the rest are minor categories. Presence of one major and any other minor sign without lab confirmation is considered as probable CRS.[6,9] Also, presence of maculopapular rash, swollen lymphnode, arthralgia andconjunctivitis during pregnancy have been found to predict rubella infection in a mother.[9–11]

There has been increased admissions of neonates with congenital abnormalities suggesting CRS at Bugando Medical Centre (BMC)[13], at the same time high seropositivity of Rubella seromarkers among pregnant women has been reported in this area.[14,15] In addition about 11% of asymptomatic under five years children in the city of Mwanza were found to have acute rubella virus infection[16], this necessitates the need to investigate infants with features suggestive of CRS. Therefore, this study aimed at establishing the magnitude and the associated factors of Rubella IgM and IgG seroprevalence among infants born with features suggestive of CRS who are seen at the Bugando Medical Centre (BMC), which is a tertiary referral hospital in North Western Tanzania.

METHODS
Study Design and Study Site
This was a hospital based cross-sectional study conductedbetween September 2017 and March 2018 at BMC, a tertiary teaching and consultant hospital in North Western Tanzania. The study participants were from paediatric wards and paediatric outpatient clinic.

Study Population
The study included all infants equal to or less than 12 months of age with at least one of the features suggesting CRS. The features included cataract(s), congenital glaucoma, congenital heart disease, pigmentory retinopathy, maculopapular rashes, hepatosplenomegaly, microcephaly, meningoencephalitis and jaundice that presented within 24 hours of birth. We excluded premature babies who had isolated Patent Ductus Arteriosus (PDA) because of high possibility of physiological occurrence.

Later on, during analysis we excluded children who missed rubella IgM, and IgG results due to insufficient blood sample.

Sample Size Estimation
The minimum Sample size of 150 was calculated using the Leslie Kish formula for cross-sectional studies (17) as follows:

$$N = \frac{Z^2\ P(1-P)}{D^2}$$

Where: Z = Score for 95% confidence interval = 1.96 ,P= Prevalence of 10.9% obtained from from Mirambo et al , D=Tolerable error = 0.05, and therefore N=0.109(1-0.109) x (1.96x1.96)/ (0.05x0.05)=148.8, however in order to attain the power to calculate for associated factors a total of 174 infants were recruited into this study.

Screening Examination
All in and outpatient attendees aged less than or equal to 12 months were evaluated by the Principal Investigator and other research assistants who were medical doctors so as to look for any sign or symptom suggestive of CRS. Screening evaluation included patients' history and through physical examination this helped to reveal presence or even history of some of the specific clinical features of CRS. Simple fundoscopy using zyrev otoscope set (USA) was done to determine those children with congenital cataract, glaucoma and or pigmentory retinopathy. Occipital Frontal Circumference (OFC) was taken for all children to rule out microcephaly and echocardiogram to find out presence of congenital heart defects.

The OFC measurement was taken using a flexible tape measure by measuring over the most prominent part on the back of the head (occiput) and just above the eyebrows (supraorbital ridges).

Echocardiogram was done by the PI using GE 2D Echo Machine- INDIAto all enrolled infants to look for presence of congenital heart defects (CHD). All echocardiography images were crosschecked by an experienced paediatric cardiologist and those who were having structural normal findings continued with other management according to BMC protocol. Those who were found to have congenital heart disease were started on medical management and those who required heart surgery were referred to Jakaya Kikwete Cardiac Institute.

Data Collection
Data was collected by the Principal Investigator with the help of the trained research assistant. Training of the research assistant and pretesting of the questionnaire were done prior to data collection, where under the observation of the PI the research assistant interviewed one parent using the questionnaire, unclear questions were corrected and the final pre tested questionnaire was formed. During actual data collection all children aged equal or less than 12 months were assessed, parents of those with one or more signs suggestive of CRS were approached and explanation of the study was given and were asked, if willing, to sign the consent. After receiving the written consent from the parentor guardian, information regarding residence, sex, age in weeks, date of birth of the enrolled infant was collected. Other information like age and relationship of a guardian, level of education, history of MR vaccination, marital status and clinical conditions was asked from the mothers and was also recorded. Presence of maculopapular rashes, hepatosplenomegally and jaundiceduring clinical assessment were evaluated and recorded. History of cataract, congenital heart disease, microcephaly, neonatal jaundice, meningoencephalitis and HIV status were also evaluated. Other information on clinical condition that we got from the mothers was any history of arthralgia, conjunctivitis, previous abortion, diabetes mellitus, prolong use of drugs, alcohol consumption, cigarette smoking and exposure to radiation or pollution.

Laboratory Procedures
Blood samples were taken by using aseptic procedure whereby approximately 2cc of blood was collected into plain vacutainer tube. Serum was separated after centrifuging by using micropipette and kept in cryovials. Sera were separated, aliquoted into vials and stored at minus 40[0]C until processing. Detection of Rubella IgG and IgM antibodies was done by using indirect enzyme immunoassay (EIA) as per manufacturer's instructions

(PISHTAZTEB DIAGNOSTICS,Iran Tehran). The PT-RUBELLA IgM-ELISA has 100% sensitivity and 99% specificity whereas PT-RUBELLA IgG ELISA has 100% sensitivity and 100% specificity. The assay was done as per manufacturer's instructions. All individuals with rubella IgG concentration ≥10 IU/ml were considered as seropositive and those with concentrations below that threshold were considered seronegative for rubella while for IgM the cut-off index lower than 0.9 was considered as negative and those greater than 1.1 were considered as positive results.

Data Management
Data were entered into a computer using Microsoft Excel 2010, cleaned and analysed using STATA version 13. Continuous variables were summarised using median (interquartile range). Logistic regression model was used to ascertain factors associated with IgG seropositivity. All factors with P value less than.20 on univariate analysis were subjected to multivariate logistic regression analysis. Crude (unadjusted) and adjusted odds ratios were calculated to quantify the strength of association between CRSseromakers and associated factors. At 95% confidence interval, P value of <.05 was considered as statistically significant.

Ethical Consideration
The study was approved by the Joint CUHAS Bugando Ethical Committee with certificate no: CREC/231/2017. The aim and importance of the study was explained to parents/caretakers before recruitment was done. All parents/caretakerswho were willing to participate in the study signed informed consent. All information regarding the patients were kept confidential throughout the study. Patients' records were kept such that their identities were not disclosed. All those who refused to participate in the study were given service and treatment regardless of their inclusion status in the study. The management of these patients was done according to the BMC Pediatric Department protocol on management of CRS.

RESULTS
During the study period 2082 (1806inpatients and 276 outpatients) infants attended and were screened for eligibility. A total of 214/2082(10.3%) infants met the study eligibility criteriaiehad at least one clinical feature suggestive of CRS. Of these, 176/214(82.2%) children were enrolled whereas 38 children were excluded for various reasons as summarised in the Figure 1. and among those eligible, 174 (81.5%) infants were included in the final analysis(Figure 1). The median age for the enrolled infants was 5.5 [1 – 24] weeks, and of the 174 analyzed only 23/174(13.2%) received the Measles Rubella (MR) vaccination, 107/174 (61.5%) had CHD and of these 63/107 (58.9%) had PDA. There were 69/174 (39.7%) infants that had history of neonatal jaundice,while 42/174 (24.1%) had hepatosplenomegaly and 30/174 (17.2%) presented with maculopapular rashes. Moreover, there were 3/174 (1.7%) children with microcephaly, 3/174 (1.7%) with meningoencephalitis and 2/174 (1.1%) with cataracts. Table 1 illustrates additional demographic and clinical features of enrolled infants.

The women whose infants were enrolledaged between 18-50 years with median age of 27 and IQR of [18 –

43]. Among them 29(16.7%) had history of abortion, 8 (4.6%) had history of arthralgia and 8 (4.6%) had history of exposure to pollutants during pregnancy.

FIGURE 1: Recruitment Flow Chart
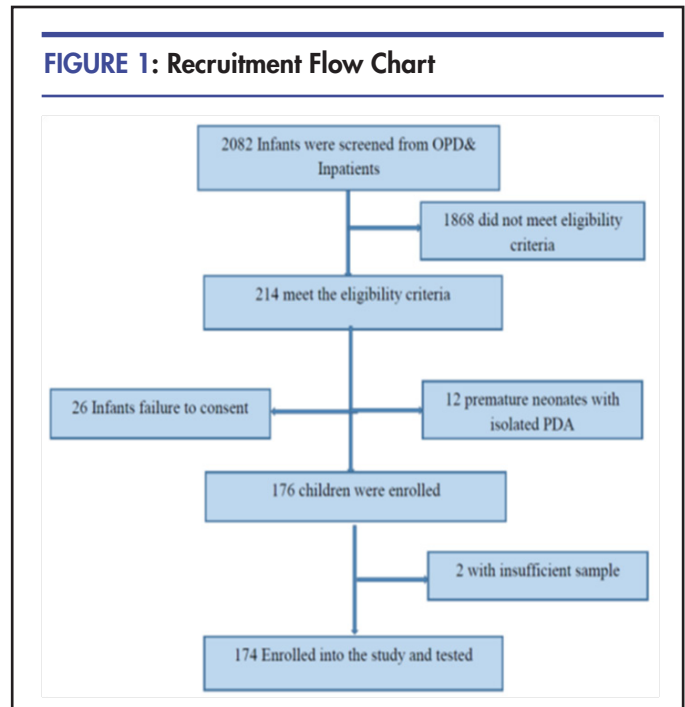
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Prevalence of Rubella Seromarkers among Infants with Clinical Features Suggesting Congenital Rubella
Among the 174 infants investigated, 111/174 (63.8%) were IgG Rubella seropositive whereas none was IgM Rubella seropositive. Out of 174 infants investigated, 26/174 (14.9%) had clinical features suggesting probable CRS (had 2 or more features suggestive of CRS). When the PDA was considered as important CHD associated with CRS the probable CRS was 15/174 (8.6%).

Factors associated with Rubella seropositivity among infants with features suggestive of CRS
On univariate analysis the factor associated significantly with Rubella seropositivity was being neonate (OR 2.3; 95% CI, 1.2 to 4.3; P=.012), whereas history of abortion in a mother had borderline significant association (OR 2.5; 95%CI, 0.9 to 6.5; P=.063. By multivariate logistic regression analysis, only being neonate independently predicted rubella IgG seropositivity (OR 2.3; 95% CI, 1.2 to 4.4; P=.012) as in Table 2

DISCUSSIONS
Prevalence of Rubella Seromarkers and Probable CRS among Infants with Suspected CRS
These findings demonstrated a high seroprevalence of Rubella among infant population (63.8%) as a proxy of

rubella seroprevalence among women of reproductive age.[6,10,11] Placental transfer of maternal IgG antibodies to the foetus is an important mechanism that provides protection to the infant.[18] The observed seroprevalence in the current study is higher than 32% and 34%, which were observed in Congo and Central African Republic, respectively.[19,20] The high prevalence in our study might be explained by inclusion of neonates whereas these two studies included children above 6 months due to the fact that maternal IgG have been found to significantly disappear from 6 months of age.[6,21] It should be noted that from neonates as the age increases, maternal IgG decrease by two fold in 4 weeks.[14,20,22] The current seroprevalence is significantly higher than 1.8 observed in Kilimanjaro.[23] The difference could be due to the assay used and population studied. The study in Kilimanjaro included asymptomatic children and they performed the ELISA from dried blood spots samples while the current study used serum. Previous studies have shown low sensitivity of dried blood spots samples in detecting Rubella specific IgG antibodies.[1]

Despite sufficient vaccination coverage in developed countries, high seroprevalence of rubella has been observed.[24] The average prevalence of IgG rubella viruses was 70% in infants up to the age of six months, whereas it was around 95% in females of childbearing age. This prevalence was significantly high compared to our study for the reasons that mothers born after vaccination programme have been seropositive hence transfer the immunity to neonates.[24]

The majority 107 (61.5%) of our study participants had congenital heart disease and of these 63 (58.9%) had PDA. This correlates with findings from a cross sectional study done in Bangladesh where among assessed children 78% had congenital heart disease and among these 47.8% had PDA.[25] The high prevalence could have been attributed to the fact that almost all these children attending to the particular institute were having cardiovascular malformations.[25] Similarly, high prevalence of congenital heart disease in CRS has been observed also in a retrospective study which evaluated the common cardiovascular malformations in CRS.[26]

Our study demonstrated that the prevalence of probable CRS by using CHD as the indicator to be 14.6%. This is higher than one found in a retrospective study done in Philippines that identified probable cases 201 out of 4339 with estimated prevalence of 4.6%.[27] The prevalence in this study was lower than ours due to the fact that being a retrospective study some clinical features might have been missed at the time of collection hence this led to the lower prevalence.

Our prevalence of probable CRS by using stringent criteria of using PDA was 8.6%. This was low compared to 20.6% found by Toizumi et al.[28] The fact that Toizumi study was done during the time of an outbreak of rubella could have led to the higher prevalence compared to ours. However, this suggests the need of investigating for CRS in infants found to have CHD.

Factors Associated with Rubella Seropositivity
By multivariate logistic regression analysis, only being neonate independently predicted rubella IgG seropositivity

(OR 2.3; 95% CI, 1.2 to 4.4; P=.012) (Table 2). Transfer of maternal IgG antibodies to the foetus is an important mechanism that provides protection to the infant.[18] Moreover, there is more evidence that placental IgG transfer depends on multiple factors such as maternal levels of total and specific IgG antibodies. Serological testing revealed that for neonates who tested positive for IgG antibodies to rubella, corresponds to the overall seropositivity rate of their mothers[29,30]. However these antibodies usually disappear in a period of 3-5months[29]. This was also noted in the in Mwanza whereby pregnant women tested for rubella antibodies had the high seroprevalence of 92.6%[14]. Similarly, in seroprevalenceassessment of rubella was reported to be 90.2% in Serbianneonates and this was found to predict the seroprevalence of rubella in their mothers.[30]

TABLE 1: Distribution of Socio Demographic and Clinical Characteristics of 174 Children with Features of Congenital Rubella Syndrome

Patients characteristics	Number (n)	Percent (%)
Age of the child		
Neonates (0-28days)	83	47.7
Young Infants(1-3months)	52	29.9
Infants(3-12months)	39	22.4
Sex of child		
Female	94	54
Male	80	46
Education of care giver		
None/incomplete	25	14.4
Primary school	81	46.5
Secondary school	43	24.7
University/ college	25	14.4
Mothers age		
18-28	96	55.2
29-39	66	37.9
40-50	12	6.9
MR vaccine		
No vaccination	151	86.8
HIV Status		
Negative	95	54.6
Positive	4	2.3
Unknown	75	43.1
Clinical signs suggestive CRS		
CHD	107	61.5
Jaundice	69	39.7
Rashes	30	17.2
Microcephaly	3	1.7
Cataract	3	1.7
Meningoencephalitis	2	1.1

In conclusion, this study found that a significant proportion of neonates (63.8%) with suspected CRS are rubella IgG seropositive. In addition, a significant proportion of infants with suspected CRS can be grouped as probable CRS. Moreover, significantly high IgGseroprevalence in neonates indicates high maternal seroprevalence. Therefore, we recommend a continuous and sustained surveillance system on CRS on infants and

TABLE 2: Factors Associated with Rubella IgG Seropositivity

Variable	Seropositive		Univariate		Multivariate	
	Yes (%)	No (%)	OR [95%CI]	Pvalue	OR [95%CI]	P value
Gender						
Female	59 (62.8)	35 (37.2)	1.0			
Male	52 (65.0)	28 (35.0)	1.1 [0.6–2.1]	0.76	1.1 [0.6–2.1]	0.739
Age of child						
Infants	50 (54.9)	41 (45.1)	1.0			
Neonates	61 (73.5)	22 (26.5)	2.3 [1.2–4 .3]	0.012	2.3 [1.2–4.4]	0.012*
Hepatosplenomegally						
No	88 (66.7)	44 (33.3)	1			
Yes	7(87.5)	1(12.5)	4.2 [0.5–34.7]	0.186	4.1[0.5 –36.6]	0.2
History of Abortion						
No	88(60.7)	57(39.3)	1.0			
Yes	23(79.3)	6(20.70	2.5 [0.9–6.5]	0.063	2.6 [1.0–6.8]	0.057

CI, confidence interval

children since the seroprevalence of CRS is still high. ThisCoordinated surveillance should involve other Units such as Ear Nose and Throat (ENT), Ophthalmology, Surgery andeven in maternity wards. In view of high proportion of neonates with rubellaseromarkers and CHD we recommend that any infant with suspected CRS should undergo cardiac evaluation by echocardiography. In addition to that these results call for revision in countries' vaccination policies, our results emphasize on the need to reconsider upper age limit for vaccination campaigns in developing countries where by screening and if possible vaccinating women in child bearing age may be cost-effective campaign to prevent CRS.

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Psychological Distress Factors among Caregivers of Children Receiving Cancer Therapy, at Muhimbili National Hospital

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ABSTRACT

Background: Psychological distress is a major problem among caregivers of patients with chronic illness such as cancer. Psychological distress in caregivers affects the provision of healthcare services.The aim of this study was to determine the magnitude and factors contributing to psychological distress among caregivers of children receiving cancer treatment at Muhimbili National Hospital.

Method: A cross sectional hospital-based study was done. Questionnaires were used to collect information on socio demographic characteristics and psychological support while Hopkins Symptoms Checklist 25 was used to determine psychological distress. The association between the socio demographic characteristics, psychological support and psychological distress was determined using logistic regression analysis (univariate and multivariate analysis) and p values of less than 0.05 were considered significant.

Results: Prevalence of psychological distress was 64(66.7%) among 96 caregivers interviewed while the proportion of psychological support was 71(74 %.) The social demographic characteristics were not associated with psychological distress. Psychological support from family member was protective against psychological distress (p=0.025, OR=0.047,CI 0.003-0.686) while other means of psychological support and self-copying mechanism to psychological distress were not associated with psychological distress.

Conclusion: The prevalence of psychological distress was high despite the high proportion of psychological support. Socio demographic characteristics had no association with psychological distress. Psychological support from family member was protective against psychological distress. Further studies are needed to assess the social cultural aspect, content and context of psychological support.

BACKGROUND

Psychological distress is a major problem among caregivers of patients with chronic illness such as diabetes, hypertension and cancer. The prevalence of psychological distress is 66% among caregivers of children with cancer while it was 65% in caregivers of spouse with cancer and 43% of caregivers of parent with cancer in the United Kingdom 2014.[1] In 2016, the prevalence of parental distress was 56.0% of parents whose children were hospitalized for cancer treatment in Lebanon [2] and in Iraq 70.5% of parents whose children have cancer were depressed.[3] In US 2013 the prevalence of psychological distress was over 50% among parents whose children had cancer and 16% had serious distress which needed immediate intervention while the national prevalence of psychological distress among population was 3%.[4] In Uganda 45% of family members of patient with cancer had anxiety and 26% had depression in 2017.[5]

In Tanzania, approximately 100 new cases of cancer are diagnosed per 100,000 populations each year.

The number of cancer patients attending specialized clinic for cancer (Ocean Road Cancer Institute) have almost doubled in 6 years from 2807 in 2006 to 5479 in 2013. [6] In Tanzania the prevalence of common mental disorder including psychological distress is 48% among patients attending traditional healer clinics, 24% among patients attending primary health care facility [7]and the characteristics of, those attending primary health care clinics (PHCs) and 6.5% among people with Asian origin living in Tanzania [8] while in the general population it is 2.5%.[9]

Psychological distress is a result of unpleasant and harmful stress that becomes too great or lasts long that may result in negative feelings or reactions. Psychological distress occurs when body copying mechanism against bad stress begins to breakdown.[10]

Caregivers of patients with cancer are at high risk of psychological distress due to financial burden of cancer treatment because cancer treatment is very expensive.[11] Psychological distress in caregivers will affect the provision of care to patients hence may aff-

ect management of the patient suffering from chronic illness such as cancer. Caring a child with chronic illness is more stressful situation than caring a healthy child.[12] Also caring a child with cancer is highly stressful situation comparing to caring a spouse and a parent with cancer.[1]

The main reasons for the distress are perception of the parents about the prognosis of cancer, child's sufferings from symptoms like severe pain, weight loss and side effects of chemotherapy like excessive vomiting. The other reasons are general knowledge on the modality of treatment like radiotherapy, chemotherapy and surgery[13], high costs of treatment and most of cancer patients have poor prognosis especially when they are at late stage.[4] The other factors for the psychological distress in caregivers of children with cancer are financial, employment status of the caregivers[2], sex of the care taker, number of hospital admissions and family support.[10]

It is important to consider psychological distress of the caregiver of the child because it is not only important for wellbeing of the caregivers but also may influence provision of service to the sick child. Thecaregivers play an important role in provision of physical and mental support to the child. Addressing the magnitude and contributing factors of psychological distress among caregivers of children with cancer in a scientific way will open eyes to the health practitioners and the community on the burden and factors associated with psychological distress among caregivers of children with cancer.

This study aimed to determine the magnitude and factors contributing to psychological distress among caregivers of children receiving cancer treatment at Muhimbili National Hospital in Dar es Salaam, Tanzania.

MATERIAL AND METHODS
Study Design
This was a hospital based cross sectionalstudy conducted for 30 days from 1st July to 30th July 2019.

Study Area
The study was conducted at Muhimbili National Hospital (MNH) in Pediatric cancer ward and clinic. MNH is also a research center and university teaching hospital located in Dar es Salaam. It has 1,500 beds capacity, 1,000-1,200 outpatients per day and 1,000-1,200 patients are admitted per week. Pediatric cancer unit has an average of 90 inpatients and 38outpatientsper week, making a total of 128 patients per week. Patients with cancer stay longer in the ward than other patients because treatment of cancer takes along duration and needs in patient care. About 300-350 new cases are admitted each year in pediatric cancer ward.[14]

Study Population
The study involved caregivers aging 18-60 years whose children were less than 18 years attending outpatient clinic or were inpatient at pediatric cancer unit at MNH and hadstarted treatment of cancer.

Dependent Variable
Dependent variable was psychological distress

Independent Variable
Independent variables were socio demographic factors;

age, sex, occupation, level of education, marital status, category of treatment, duration of cancer, longest time to stay in the hospital when admitted, number of hospital admission and living the same house. The other independent variables were type of psychological support, place of psychological support was given, number of times psychological support was given and self-copying mechanism.

Inclusion Criteria
Caregivers with children confirmed with cancer.

Exclusion Criteria
Caregivers who had experienced death of first degree relative or husband for the period of less than 6 months prior to the study and those who were on medication for mental disorders were excluded from the study because they could have psychological distress due to their situation which was not associated with the illness of their children.

Sample Size Determination
Sample size of the quantitative cross-sectional study was calculated using the following sample size calculation formula[15]. The prevalence of psychological distress was 4.8%.[16] The sample size was 73 caregivers. Adjusting to non-response rate which is 4% in similar study in Uganda[5]. The minimum sample size was 96 caregivers.

Data Collection Methods and Instruments
Caregivers were randomly selected from the clinic and in the ward. Data were collected by interview method using structured questionnaire and Hopkins Symptoms Checklist (HSCL-25) tool. Structured questionnaire was used first to collect information on demographic characteristic, social cultural factors and psychological support then HSCL-25 tool was used to determine psychological distress.

HSCL-25 has 25 items, 10 for anxiety and 15 for depression. Each item has a score from 1 to 4 indicating that whether the symptom was not at all, a little, quite a bit or extreme present, respectively. HSCL-25 score was calculated by dividing the sum of the score of individual items by the number of answered items. The score obtained can be used for determining of psychological distress. The respondent was considered has psychological distress if the middle value of HSCL-25 was ≥1.55 and the value of ≥ 1.75 was severe psychological distress which requires treatment.

The study done previously in Tanzania, shows that HSCL-25 has not only good consistency, good inter-rater reliability and test retest reliability but also valid on content, construct and discriminant methods.[18]It has a sensitivity 89% and specificity of 80% when compared toDiagnostic and Statistical Manual of Mental Disorders(DSM) IV.[19]a two-phased design included measures for health-related quality of life, perceived social support, and the HSCL-25 screen for depressive (HSCL-15 subscale It also has a sensitivity of 88% and specificity of 73% for measuring DSM III major depression.[20]

Pretest of the questionnaire was done before data collection. Data were collected by two trained research assistants using translated Kiswahili version of the questionnaire.

Data Analysis

Data were coded and entered in Statistical Product and Services Solution (SPSS) version 22 which is the property of International Business Machine (IBM) cooperation licensed 2011. Descriptive Statistics (Descriptive Analysis) was used to find the proportion of psychological distress.

Categorical variables were summarized by using proportions and quantitative variables were summarized by using measures of central tendency.

The mean, percentage, proportion and frequency were also used to summarize data from the questionnaire and HSCL-25. Data were cleaned before analysis so as to identify the incorrect and missing data. Logistic regression (univariate and multivariate analysis) were done to determine the association of independent variable and dependent variables. The *P* value of less than 0.05 was considered significant.

Ethical Consideration

Ethical approval was obtained from Muhimbili National Hospital with certificate number MNH/IRB/II/2019/018

The participation was on voluntary basis; caregivers were not given anything as a token for participating in the study. Caregivers signed consent form before participating in the study.

In case of unexpected outcomes like emotional or psychological difficulties, participants were directed to the nurse who was on duty at the clinic or in the ward for support. Caregivers were allowed to withdraw from or not to participate in thestudy and they were assured that withdrawal will not affect treatment of the patient. Confidentiality was assured to all participants

RESULTS

Demographic characteristics

A total of 96 caregivers were interviewed of whom 70(72.9%) were female. The age of the caregivers varied from 18-60 years. The majority of the cancer caregivers were peasants 39(40.6%) or self-employed 41(42.7%) while a small percentage were employed by the government 1(1%) or private sector 2(2.1%). Other demographic characteristics are shown in Table 1.

Prevalence of Psychological Distress

The prevalence of psychological distress among caregivers of children receiving cancer treatment was 64(66.7%) of the study population using HSCL-25.

Variation of psychological distress by social demographic characteristics.

The proportion of psychological distress was 48(68.6%) and 16(61.5%)among female and male caregivers, respectively. However, the difference of psychological distress according to sex of caregiver was not statically significant (OR0.733; 95% CI0.287 to1.873; *P*=.517). The proportion of psychological distress among inpatient caregivers was 42(65.6%) while it was 68.8% (22 out of 32) among outpatient caregivers. However, the difference of psychological distress according to category of treatment; either inpatient or outpatient (OR0.868; 95% CI0.350to2.152; *P*=.770) was not significant. Other results are shown in Table 2.

TABLE 1: Demographic Characteristics of the Study Population

Characteristics	Frequency (n=96)	Mean
Sex of the caretaker		
Male	26(27.1%)	
Female	70(72.9%)	
Age group of the caretaker (in years)		
18-24	11(11.5%)	
25-34	34(35.4%)	35.9 years
35-44	31(32.3%)	
45-60	20(20.8%)	
Sex of the child		
Male	53(55.2%)	
Female	43(44.8%)	
Marital status of the caretaker		
Single	9(9.4%)	
Married	73(76.0%)	
Cohabiting	4(4.2%)	
Divorced	5(5.2%)	
Widow	5(5.2%)	
Age group of the child (in years)		
< 4	36(37.5%)	
5-11	43(44.8%)	
12-14	14(14.6%)	
15-17	3(3.1%)	
Relationship with the child		
Father/Mather	79(82.3%)	
Brother/Sister	8(8.3%)	
Aunt/Uncle	3(3.1%)	
Grandmother/father	6(6.3%)	
Living the same house status		
Yes	89(92.7%)	
No	7(7.3%)	
Level of education		
Not attended school	11(11.5%)	
Primary education	62(64.6%)	
Secondary education	20(20.8%)	
University education	3(3.1%)	
Occupation		
Housewife	13(13.5%)	
Peasant	39(40.6%)	
Employed in-private sector	2(2.1%)	
Employed in-government sector	1(1.0%)	
Self employed	41(42.7%)	

Variation of Psychological Distress by Psychological Support

Caregivers were asked, if they hadreceived psychological support since their children were diagnosed with cancer. In this study, 71 (74%) of caregivers received psychological support since the time of diagnosis of their children. Among those who received psychological support 46(64.8 %%) had psychological distress (OR=1.40;95% CI=0.51to 3.80; *P* =.51) but the results were not statistically significant.

The proportion of psychological distress were higher 47(64.4%) among those patients who received counselingand those caregivers who allowed to meet with other caregivers as a way to prevent or reduce psychological distress 3(60%) but the difference was not

TABLE 2: Association Between Social Demographic Characteristics and Psychological Distress

Factors	Univariate Analysis			Multivariate Analysis		
	cOR	CI(95%)	P Value	aOR	CI(95%)	P Value
Sex of caregiver						
Male	0.733	0.287-1.873	0.517			
Female	Ref					
Category of treatment						
Inpatient	0.868	0.350-2.152	0.770			
Outpatient	Ref					
Age						
18-24	Ref					
25-34	2.000	0.494-8.069	0.331			
35-44	2.037	0.493-8.408	0.325			
45-60	1.250	0.283-5.525	0.769			
Marital						
Single	Ref					
Married	1.856	0.454-7.571	0.389			
Cohabiting	0.800	0.076-8.474	0.853			
Divorce	3,200	0.248-41.208	0.372			
Widow	0.533	0.580-4.912	0.572			
Relationship with the child						
Father/Mather	Ref					
Brother/Sister	0.463	0.107-2.003	0.303			
Aunt/Uncle	0.231	0.020-2.674	0.241			
Grandmother/father	2.316	0.257-20.865	0.454			
Living the same						
YES	Ref					
NO	0.644	0.135-3.070	0.581			
Level of education						
Not attended school	Ref					
Primary education	1.750	0.477-6.438	0.399			
Secondary education	1.548	0.345-6.942	0.568			
University education	13462	29054 0.000	0.999			
Occupation						
House wife/staying at home	Ref					
Peasant	0.711	0.186-2.724	0.619			
Employed in-private sector	0.444	0.022-9.032	0.598			
Employed in government	7179 8882 8.5	0.000 1.000				
Self employed	1.074	0.277-4.170	0.918			
Duration of diagnosis of cancer (in months)						
1-3	Ref		Ref			
4-6	0.452	0.143-1.431	0.177	0.477	0.123-1.851	0.285
7-12	0.928	0.270-3.192	0.905	1.107	0.264-4.646	0.890
13-24	0.464	0.123-1.753	0.257	0.421	0.089-1.986	0.274
Above 24	0.696	0.106-4.552	0.705	0.962	0.100-9.219	0.973
Number of admissions						
Never admitted	Ref					
1-2	2.043	0.270-15.442	0.489			
3-5	1.833	0.204-16.612	0.589			
Above 5	4.000	0.211-75.659	0.355			
Longest duration of staying in the ward when admitted(days)						
4-7	Ref		Ref			
8-14	1.667	0.074-37.728	0.748	2.036	0.086-48.208	0.660
15-30	2.778	0.367-21.029	0.323	8.417	0.323-219.212	0.200
30-60	10.00	1.260-79.339	0.029	2.540	0.125-51.427	0.544
61-150	3.667	0.619-21.730	0.152	2.425	0.117-50.055	0.566
151-210	2.738	0.565-13.267	0.211	6.201	0.212-181.428	0.289
Above 210	6.667	0.809-54.957	0.078	0.774	0.028-22.974	0.889

Abbreviations: aOR, adjusted odds ratio; cOR, cumulative odds ratio; CI, confidence interval

TABLE 3: Association Between Psychological Support and Psychological Distress

Factors	Univariate Analysis			Multivariate Analysis		
	cOR	CI(95%)	P Value	aOR	CI(95%)	P Value
Received psychological support						
YES	1.40	0.51-3.80	0.51			
NO	Ref					
Type of psychological support						
Meeting with other caregivers YES	1.22	1.19-7.83	0.83			
NO	Ref					
Counseling YES	2.00		0.001			
NO	Ref					
Place of psychological support						
Cancer Unit	Ref					
Cancer unit and other hospital	0.147	0.014-1.509	0.107	0.000	0.000	0.998
Cancer unit and home	0.442	0.058-3.374	0.431	0.302	0.038-2.40	0.258
All of them	0.221	0.019-2.587	0.229	3.780	0.127-112.467	0.442
Person who provides psychological support						
Family member YES	0.187	0.033-1.042	0.056	0.047	0.003-0.686	0.025
NO	Ref					
Friend/Neighbor YES	1.342	0.316-5.700	0.690			
NO	Ref					
Doctor/Nurse YES	0.000	0.000 1.000				
NO	Ref					
Psychologist YES	1.705	0.168-17.27	0.652			
NO	Ref					
Time taken to receive first psychological support in days						
1-3 days	Ref					
4-7 days	0.244	0.041-1.450	0.121	0.185	0.029-1.199	0.077
8-14 days	7870 2621 6.7	0.000	1.000 1797 8.8	4879	0.000	1.000
15-30 days	7870 2621 6.7	0.000	0.999 E+26	3.045	0.000	0.998
31-60 days	0.244	0.021-2.858	0.261	0.092	0.005-1.777	0.114
Above 60 days	0.974	0.083-11.43	0.984	1222 6453 9.8	0.000	0.999
Number of times psychological support						
1	Ref					
2-3	0.824	0.210-3.234	0.782			
4-7	0.714	0.179-2.843	0.633			
More than 7	0.330	0.073-1.479	0.147			
Self-coping strategy with distress						
Stay alone YES	1.079	0.422-2.759	0.84			
NO						
Sleeping YES	1.376	0.444-4.270	0.580			
NO						
Recreation YES	0.644	0.135-3.070	0.581			
NO						
Drinking alcohol YES	8205 5866 2.0	0.000	1.000			
NO						
Watching TV/Sport YES	1.525	0.152-15.26	0.720			
NO						
Talking to friends YES	1.162	0.456-2.957	0.753			
NO						
Praying YES	1.398	0.514-3.798	0.512			
NO						
Drinking water YES	2.067	0.221-19.29	0.524			
NO						

Abbreviations: aOR, adjusted odds ratio; cOR, cumulative odds ratio; CI, confidence interval

significant (OR=1.22; 95% CI=0.191to7.83; P=.83).

Psychological distress varies according to the person who provides psychological support. Caregivers who received psychological support from family member were protected against psychological distress, only 2 (38.6%) had psychological distress and the results were significant (OR=0.047;95% CI=0.003to 0.686; P=.025). However, the proportion of psychological distress among those who received psychological support from friend/neighbor was 7(70.0%)with OR=1.342; 95% CI=0.316 to 5.700; P=.69, and psychologist 3(75%) with OR=1.705; 95% CI=0.168 to17.27; P=.65 were not significant. Other results are shown in Table 3.

DISCUSION
Magnitude of psychological distress
The findings on the prevalence of psychological distress using HSCL-25 are consistent with those reported in the study done in the United Kingdom where the prevalence was 179(66.7%).[1] However, the prevalence is higher compared to that from other studies; 54(45%) in Uganda[5], 64(56.0%) in Lebanon[21] and 43(50%) in US[4] but is lower as compared with the study done in Iraq which showed prevalence of 236(70.5%).[3] The difference might be due to the fact that this study was conducted in a hospital setting which increase the risk of having psychological distress as compared to other studies which were conducted in the community.

Social demographic characteristics
Psychological distress according to sex was not statistically significant. This result is in agreement with findings reported in a cross sectional study on distress in cancer patients and their caregivers, which showed that sex of caregivers had no association with psychological distress.[22]189 pairs of cancer patients (31% gastrointestinal, 34% lung, 35% urological cancers However different studies show the association of psychological distress according to sex.,female caregivers were positive associated with psychological distress.[1,11,23,24]psychological distress, fatigue, and quality of life (QOL The difference of the finding on sex, might be due difference in culture which varies on howto handle psychological distress.

There is no association of age with psychological distress. This result is similar to that from a study on psychological distress of female caregivers and significant others.[1] Other social demographic characteristics such as marital status, relationship with the child, education level, occupation, duration of caregiving had no association with psychological distress and resemble those from a descriptive hospital based study done on caregivers of patients with schizophrenia.[25]

There is no association with other social factors such as living in the same house, number of hospital admissionsand duration of stay in the hospital and psychological distress of caregiver. However, in other studies, social demographic characteristics were associated with psychological distress; marital status, [23] duration of illness, [2,11,26,27]employment status,[11,24,28,29] number of hospital admissions,[24] relationship and bondage with the patient,[11] and education level.[11]The results of social demographic characteristics of having no association with

psychological distress among caregivers of children receiving cancer treatment at MNH may be due the fact that treatment, meals and accommodation are given for free for the whole duration oftreatment which softens the social economic burden hence making caregivers less susceptible to psychological distress.

Psychological Support
The study showed that, 71(74%) of caregivers received psychological supportand 46(64.8%) of caregivers with psychological distress received psychological support while psychological distress among caregivers with advanced cancer patients the proportion of caregivers who received psychological support was50(25%)[30]

The higher proportion of caregivers who received psychological support might be due to the fact that psychological support of the caregivers has been integrated in the management of children with cancer at MNH.

Psychological support from family member was protective against psychological distress. This result is in accordance with findings from many studies.[1,24,31] This might be due to the reason that family members know each other well in terms of strength and weakness, time used when providing psychological support and they are all concerned with the situation hence this leads to successful provisionof psychological support.

In this study, self-coping mechanisms (stay alone, sleeping, recreation, drinking alcohol, watching TV/sports, talking with friend, praying and drinking water) were not associated with psychological distress. However, in other studies, there were associations of psychological distress and spiritual supportbeing protective,[32] avoidance method being a risk,[11,33] self-directed coping strategies being risk[24] and problem solving being protective.[34] This difference of this study and other studies might be due of different culture which may affect self-copying mechanism.

Study Limitation
The study was conducted in hospital setting making caregivers being at increased risk of psychological distress as compared to community setting. The study used only one validated screening tool (HSCL-25) to determine psychological distress without assessing the clinical presentation which may cause over rating or under rating the psychological distress

CONCLUSION AND RECOMMENDATIONS
Despite claims that socio demographic characteristics and self-copying mechanism contribute to psychological distress of the caregiver; our study revealed that the only contribution to psychological distress of the caregiver was psychological support provided by the family member which was protective. Also, the study revealed that there is both high prevalence of psychological distress and proportion of caregivers who received psychological support.

Due to high prevalence of psychological distress and high proportion of caregivers who received psychological support, further studies are needed to assess the content and context of psychological support. Further studies are

also needed to assess cultural influence of psychological distress of the caregiver such as self-copying mechanism which varies across different ethnicity.

Psychological support provided by family member was protective against psychological distress while psychological support from doctor/nurse or psychologist had no association with psychological distress; studies are needed to assess the time spent by health professional on providing psychological support.

This study used quantitative methods of data collection through validated tool in assessing psychological distress; further qualitative studies are needed to assess social cultural content and context of caregiver

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Inhaler Non-Adherence, Associated Factors and Asthma Control among Asthma Patients in a Tertiary Level Hospital in Tanzania

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ABSTRACT

Background: Inhaled medications including corticosteroids are the most effective long-term controller medicines for asthma-related chronic airway inflammation. Despite this fact, 30% to 70% of the uncontrolled asthma patients report non-adherence to their inhalers. This study investigated factors affecting inhaler non-adherence among outpatient asthma patients in Muhimbili National Hospital, Dar es Salaam Tanzania and related the level of inhaler adherence to the extent of asthma control.

Methods: A cross-sectional hospital-based study was conducted among patients with bronchial asthma in the pulmonology clinic of Muhimbili National Hospital in Dar-es-salaam, Tanzania. Patients' demographic, clinical and socio-economic factors were collected using a structured questionnaire. Medication adherence was self-reported using a 10-item Test of Adherence to Inhalers (TAI) questionnaire. Adherence was gauged as good when the score was 50, intermediate (score 46-49) or poor (score ≤ 45). Asthma control was assessed using a 5-question Asthma Control Test (ACT). A score of ≥20 meant well controlled asthma while a score of ≤19 meant poorly controlled asthma. Patients' inhaler use technique was assessed using a 10-step checklist. Patient's technique was regarded correct when all the steps were performed correctly. Categorical data were summarised as proportions. Binary logistic regression was performed to identify factors associated with inhaler non-adherence. Significance level was set at p-value less than .05.

Results: A total of 385 asthma patients were enrolled in the study. Females were 206 (53.5%), 232(60.3%) were non-adherent to medications and 283(73.5%) had poorly controlled asthma. Lack of health insurance, fear of medication side effects, being too busy, having alternative medication for asthma and incorrect inhaler technique were significantly associated with non-adherence to inhalers, all p-values <.05.

Conclusion: The magnitude of inhaler non-adherence and poorly controlled asthma were very high. Promoting adherence through patients' education on asthma and its management, emphasis on patients' insurance coverage and setting aside time to care for ones' self are fundamental in optimising asthma care and treatment.

BACKGROUND

The Global initiative for asthma (GINA) defines asthma as a heterogeneous disease characterised by chronic airway inflammation. Asthma disease definition relies upon a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time in intensity, together with variable expiratory airflow limitation.[1] The long-term goals of asthma management are; to achieve good control of the symptoms, maintaining normal activity levels, minimise future risk of exacerbations, fixed airflow and limitation of side-effects from asthma medications.[2] To achieve these goals, inhaled asthma medications are preferred over oral or parental medications. Pharmacologically, two groups of inhaled medications are used. The first group comprises of reliever medications that comprise of short acting beta agonists and short acting muscarinic antagonists. The second group comprises of long-term controller or preventer medicines that

comprise of inhaled corticosteroids, long acting beta agonists, long acting muscarinic antagonists and their add-on therapies that consist of oral corticosteroids, leukotriene receptor antagonists and methylxanthines.[2] Clinically, inhaled medications reduce the severity of asthma symptoms; improve peak flow measurements and other measures of lung function. Corticosteroids specifically prevent exacerbations and possibly prevent long-term lung remodeling.[3] Despite the availability of these highly effective pharmacotherapy, non-controlled asthma is present in 70 to 95% of patients in Western Europe and the Asian-Pacific region.[4] Literature on asthma control is scarce in African countries including Tanzania despite the fact that asthma cases are on the rise in Africa. It is estimated that asthma prevalence has increased in Africa from 94.8 million in the year 2000 to 119.3 million in the year 2010.[5] In Tanzania, a 2007 study among urban and rural pupils reported a significantly higher prevalence of asthma in an urban region compared to a rural district. More pupils

(23.1%) in the urban district reported a wheeze in the past 12 months compared to 12.1% in the rural district. In the same study, self-reported asthma was found in 17.6% and 6.4% of pupils in the urban and rural districts respectively, while exercise-induced asthma was significantly higher in urban (26.3%) in rural district (2.4%).[6]

Adherence to a medication regimen is generally defined as the extent to which the amount of medication patients take corresponds with agreed recommendations from a health care provider.[7,8] Patients with persistent asthma are recommended to use preventer medicine daily throughout the year so as to keep their asthma under control.[9,10] If a patient uses his inhaler once daily instead of the recommended two doses per day, adherence is 50%, and lower than 50% if medications are taken only when symptoms are present. Typical adherence rates for prescribed medications are about 50%, being 30% to 70% among patients with asthma.[10] Medication non adherence is among the factors reported to affect asthma control in numerous previous studies.[11–13]

Inhaler non-adherence has been linked to various factors, both modifiable and non-modifiable. Non-modifiable factors are such as long duration of medication use, the use of multiple medications mostly delivered as inhalation, and the periods of symptoms remission.[2,7,9] Modifiable factors include difficulties in use of inhaler devices, misunderstanding or lack of instruction[14], complex medication regimens, dissatisfaction with healthcare professionals, medication side effects, medication costs, inappropriate expectations, poor supervision, lack of training or follow-up, and forgetfulness.[15–17] Patient's dislike of medication, fears about side effects, underestimation of disease severity and cultural or religious issues have been mentioned as contributing to non-adherence.[15–17] Socio-demographic factors linked to non-adherence to asthma medications include; lower level of education[18] and age below 50 years.[19] However, non-adherence has also been observed in advanced age[20] probably owing to memory difficulties which predispose patients to forget to take their medication. Furthermore, the elderly are often receiving treatment for other chronic health conditions thus having medication burden. Health system inadequacies may be pivotal to both poor medication adherence and asthma control. In a secondary data analysis study to explore the availability of services and level of health facilities readiness to provide management of chronic respiratory diseases and its associated factors using the 2014 to 2015 Tanzania Service Provision Assessment Survey data, it was reported that only about 10% of the facilities had high readiness to provide management of chronic respiratory diseases.[21] A similar study to explore readiness of healthcare facilities in Sub-Sahara Africa to manage chronic respiratory disease found that only one health facility in Tanzania and 5 in Sudan, attained a Chronic Lung Disease (CLD) readiness score of ≥ 50 % for CLD care.[22]

This study was conducted to investigate asthma control, inhaler non-adherence and factors affecting adherence in a Tanzanian context.

METHODS
Study Design, Site and Population

A cross-sectional hospital-based study was conducted among patients with bronchial asthma in the pulmonology clinic of Muhimbili National Hospital in Dar-es-salaam, Tanzania from September 2018 to January 2019. This site was chosen purposefully owing to its relative large number of asthma patients compared to other hospitals in Dar es Salaam. Pulmonology clinic runs once a week for public patients and daily for private patients. On average, about 20 asthma patients are attended to in the public clinic per week and 5 to 10 in the private clinic daily. In this clinic, nearly all asthma patients were on at least one Pressurised Metered Dose Inhaler (pMDI). A few patients were using powder inhalers interchangeably with pMDI depending on availability and income level. Additionally, some patients were on various oral medications for asthma such as; prednisolone, montelukast, aminophylline, antihistamines and medications for other comorbidities. Participants were eligible if they were aged 18 years or older, were outpatient, able to give informed consent and had a physician's diagnosis report positive for asthma ≥ 6 months prior to this study and had been using pMDI for asthma medications for at least 6 months.

Sample Size Estimation
Sample size was calculated using Kish and Leslie formula (1965). A minimum sample size of 385 was calculated to achieve 80% power for detecting medication adherence of at least 49.4%[23] at a significance criterion of $\alpha = 0.05$.

Study Procedures
Participants were identified consecutively and, if they met the eligibility criteria and provided consent, were enrolled until the required sample size was reached. The study screen 418 participants to obtain 385 eligible participants. Face-to-face interview-based on a structured questionnaire was conducted by trained physicians to extract patient's data including; age, gender, educational level, occupation, co-morbidity, smoking habit, health insurance coverage, medication used for asthma therapy, alternative medication for asthma apart from inhalers, duration of using inhaled medication, duration of asthma and if previously received training on pMDI use from any health personnel. Other factors that were enquired included; difficulty with medication refills, forgetfulness, fear of side effects and difficulty in inhaler use.

Assessment of Asthma Control
Asthma control was assessed using a validated Asthma Control Test (ACT)[24], a 5-questions interview-based questionnaire. The ACT is patient-centred and recalls the patient's experience of 5 items: The effect of asthma on daily functioning, Daytime and nocturnal asthma symptoms, the use of rescue medications, and patient's perception of asthma control over the previous 4 weeks. Each item includes 5 response options corresponding to a 5-point rating scale. Responses for each of the 5 items were summed to yield a score ranging from a minimum of 5 (poor control of asthma) to a maximum of 25 (complete control of asthma). The scores are categorised into 3. A score of 25 corresponds to totally controlled, 20 to 24 (well controlled) and <20 (uncontrolled). In the present study, participants who scored ≥20 were classified as well controlled while those who scored 19 and less were regarded as having poorly controlled asthma.

Assessment of Inhaler Medication Adherence

Inhaler adherence was assessed using a validated 10-item Test of Adherence to Inhalers (TAI) questionnaire.[25] The TAI questionnaire includes a patient domain that is self-administered and scored from 1 to 5 (1 = worst possible score; 5 = best possible score). The total score for the questionnaire ranges from 10 to 50. Adherence is rated as good (score: 50), intermediate (score: 46–49), or poor (score: <45)[25]. This questionnaire was administered as an interview.

Assessment of Inhaler Technique

All participants were required to demonstrate how they normally use their inhaler. To attain this, placebo pMDI was provided to each participant who was then asked to demonstrate how to use it. All demonstrated steps of the placebo pMDI use was scored against a standardised inhaler checklist.[26] The checklist composed of 10 steps derived from previously published inhaler checklist and manufacture's recommendation. Each correctly performed step was given a value of one, whereas, non-performed or incorrectly performed step was given a value of zero. The participant's technique was judged to be good if all the steps on the checklist for correct inhaler use were performed accurately and poor if any of the recommended step(s) were/ was missed out or performed inaccurately.

Ethical Approval and Consent to Participate

The Institutional Review Board of the Muhimbili University of Health and Allied Sciences gave ethical clearance for the study. The conduction of the study was in accordance to Helsinki's declaration. All participants gave an informed consent before enrolment. No participants' identifying data was collected for this study.

Data Analysis

SPSS version 23 statistical software was used for analysis of the data. Summary statistics were reported as means with standard deviations or median with interquartile range for continuous data as deemed appropriate, and frequencies with percentages for categorical data. Association between predictive variables (socio-demographic and clinical characteristics of the patients) and dependent variable (inhaler medication use classified as adherence or non-adherence) was checked using binary logistic regression. Variables with p- value ≤.20 in univariate model were included in the multivariate model. Adjustments took into account education level, occupation, possession of health insurance, inhaler affordability, fear of side effects, being too busy, forgetfulness and inhaler use technique. Significance level was set at p-value less than .05 for the multivariate model.

RESULTS

A total of 385 patients were included in the study, 206 (53.5%) were female, 213(55.3%) were married and 204 (53.0%) had attained secondary level education. Nearly half of the participants (49.1%) were self-employed. The majority (93.5%) were non- smokers. More than half of the respondents (53.8%) had healthy insurance coverage while 33.2% had at least 1 co-morbidity condition. Most of the participants (79.5%) had been diagnosed with asthma for more than 5 years and

had used inhalers for more than 2 years (55.6%) (Table 1). The median (IQR) adherence score was 44.0(42-48). The minimum score was 19 and maximum score 50. Only 153 of the 385 respondents (39.7 %) were adherent to inhalers.

Figure 1 shows the level of inhaler adherence among the participants. Good inhaler adherence was observed in 69 (17.9%) participants while 84(21.8%) had intermediate adherence and 232(60.3%) were non- adherent to inhalers.

FIGURE 1: Inhaler Adherence Levels among Asthma Patients Attending MNH Pulmonology Clinic
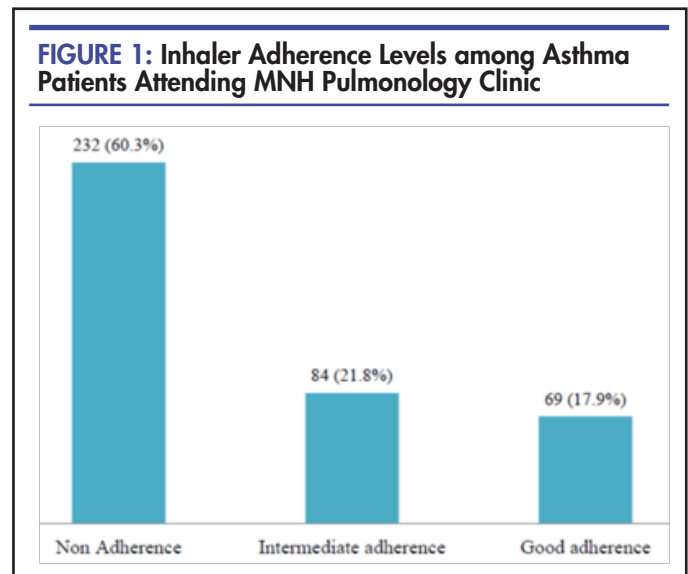
Table 2 shows the Logistic regression of factors affecting adherence to inhalers among the study participants. After controlling for other factors, the odds of inhaler non-adherence were 4 times higher among participants with no health insurance than those with health insurance, aOR (95%CI)= 4(2.1-7.8), p<.001. Respondents who had fear of side effects for inhalational medications had 8.2 times increased odds of non-adherence compared to those who had no fear, aOR (95%CI)=8.2(4.2-16), P <.01. The odds of inhaler non-adherence were about 6 times more among respondents who were too busy than those who weren't, aOR (95%CI) = 5.9 (1.5-22.4), P<.01. Participants who had alternative medications for asthma apart from inhalational medication had 2.1 times increased odds of non-adherence compared to those who had no alternative medications, aOR (95%CI)=2.1(1.6-6.2), P <.01. Patients who had incorrect inhaler technique had 12 times increased odds of non-adherence compared to those with good technique aOR(95%CI)=12.1(5.1-26.5), P<.001. Unavailability of inhalers nearby once one has been finished; unaffordability, forgetfulness and report of difficulty in use of inhalers were not associated with inhaler non-adherence.

Figure 2 shows the level of asthma control in relation to inhaler non-adherence. Using the ACT questionnaire, only 102 of the 385 participants (26.5%) had good asthma control. Significantly more patients 73(47.7%) had good asthma control among those with good or intermediate adherence to their inhalers (N=153) than among those

with poor adherence 29 (12.5%), (N=232), p<.001. Majority of patients with secondary level education (65.8%) or college/university level (100%) had insurance cover compared to those with primary level (36%) or no formal education (50%), P<.001. (Table 3)

TABLE 1: Socio-Demographic and Clinical Characteristics of Asthmatic Patients Attending MNH Pulmonology Clinic (N=385)

Character	Frequency (n)	Percent (%)
Age (years)		
18-29	138	35.8
30-39	80	20.8
40-49	72	18.7
50-59	59	15.3
≥60	36	9.4
Sex		
Male	179	46.5
Female	206	53.5
Marital status		
Single	131	34.0
Married	213	55.3
Divorced/separated	19	5.0
Widowed	22	5.7
Education level		
No formal education	6	1.5
Primary school education	143	37.6
Secondary school education	204	53.0
College/ University education	32	8.3
Occupation		
Unemployed	84	21.8
Self employed	189	49.1
Employed	66	17.1
Student	46	11.9
Smoking habit		
Former smoker	24	6.2
Current smoker	1	3.0
Never smoker	360	93.5
Possession of a health insurance		
Yes	207	53.8
No	178	46.2
Having co morbidity		
Yes	128	33.2
No	257	66.8
Duration of asthma		
≤5years	79	20.5
>5years	306	79.5
Duration of inhaler use		
≤2 years	171	44.4
>2 years	214	55.6

DISCUSSION

This study investigated inhaler adherence, asthma control and factors affecting non-adherence. The relationship between inhaler adherence and asthma control was also investigated. The study observed a high inhaler non-adherence rate of 60.3% and a low asthma control rate of 26.5%. Factors associated with poor inhaler-adherence in the studied population were; primary or lower level

FIGURE 2: Relationship between Inhaler Non-Adherence and Asthma Control among Asthma Patients Attending MNH Pulmonology Clinic
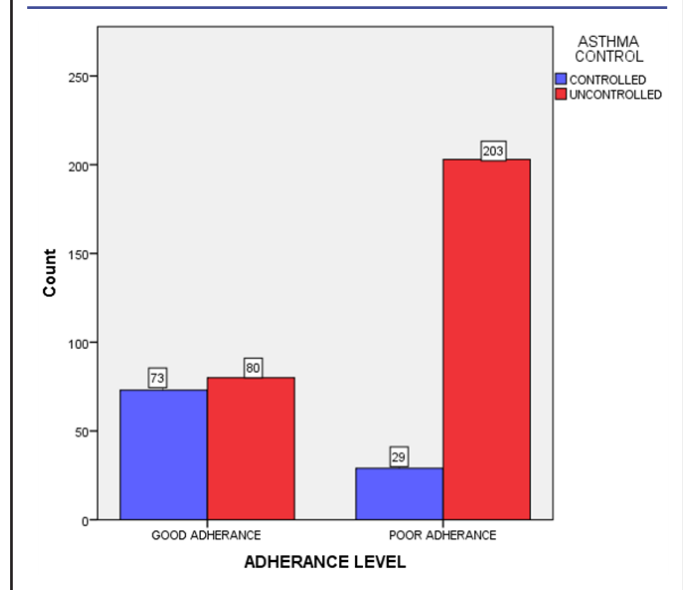
TABLE 3: Possession of insurance Cover by Level of Education among Asthma Patients in Muhimbili National Hospital, N=385

Education level	Total number	Possession of an insurance cover Yes Number(%)	P value*
No formal education	6	3(50)	
Primary level education	189	68 (36)	
Secondary level education	158	104(65.8)	
College/uniersity level	32	32(100)	< 0.001

* P value by Fisher's Exact test

education, unemployment, lack of health insurance, fear of medication side effects, being too busy or forgetful, having an alternative medication for asthma and having incorrect inhaler use technique. Most of these factors that affect inhaler adherence and thus asthma control can be modified or addressed to improve inhaler adherence and asthma control. The rate of inhaler non-adherence in the present study is comparable to previously reported adherence rates from Ethiopia (50.6%)[23], Egypt (71.7%)[27] and India (61.5%).[28] Lower rates have been reported in a systematic review conducted by Barnes et al, non-adherence to inhalers was found to range from 22% to 63%.[10]

With regards to factors affecting inhaler adherence in the present study, lack of health insurance negatively impacted inhaler adherence. This might inform on medication affordability in which case, lack of health

TABLE 2: Logistic Regression of Factors Affecting Adherence to Inhalers among Asthma Patients Attending MNH Pulmonology Clinic (N=385)

Factor	cOR	p- value	aOR	p- value
Age in years				
≤40	1		1	
>40	0.7(0.5-1.1)	0.14	0.6(0.3-1.2)	0.14
Sex				
Female	1			
Male	1.0(0.6-1,4)	0.81		
Marital status				
Married	1		1	
Single/divorced/separated	1.5(0.9-2.5)	0.08	1.6(0.8-2.9)	0.16
Education level				
Secondary or higher	1	1		
Primary or lower	1.6(1.1-2.5)	0.02	0.6(0.2-1.8)	0.39
Duration of asthma				
≤5 years	1		1	
>5 years	1.5(0.9-2.5)	0.09	2.1(0.9-4.6)	0.07
Comorbid conditions				
Yes	1			
No	0.8(0.5-1.3)	0.39		
Possession of health insurance				
Yes	1	1		
No	4.1 (2.6 – 6.4)	<0.001	4.0 (2.1 – 7.8)	<0.001
Inhaler finished and was not available nearby				
No	1			
Yes	2.2 (1.05 – 4.9)	0.037	2.6 (0.9 – 7.7)	0.072
Can't afford to buy one				
No	1			
Yes	6.3 (1.4 – 27.7)	0.014	3.2(0.48 – 1.4)	0.226
Fear of side effects				
No	1			
Yes	4.07 (2.5 – 6.4)	<0.01	8.2 (4.2 – 16)	<0.01
Use of alternative medication				
No	1		1	
Yes	2 (1.8 – 5.1)	<0.01	2.1(1.6 – 6.2)	<0.01
Inhaler technique				
Correct use	1		1	
Incorrect use	15.6(9.1-26.5)	<0.001	12.1(5.1-26.5)	<0.001

cOR=Crude odds ratio, aOR= adjusted odds ratio.

insurance translates to inability to buy medication out-of- the pocket. Results of previous studies showed that limited coverage for medications and out-of-pocket costs affect prescription initiation and consistent medication use.[23,29,30] This cost-related non-adherence had an impact to patients from minority populations with limited incomes.[23,29,30] A study conducted in Pakistan reported that 30.7% of patients were non adherent merely due to medication costs.[31]

Inhaler non-adherence among participants with low education achievements have also been reported in other similar studies.[27,31] Patients with low education achievement are more likely not to have health insurance thus predisposed to medication cost-related non-adherence, particularly in countries with no universal health insurance coverage. Furthermore, participants with low education might not be as knowledgeable about their health conditions as those with high education.

Fear of medication side effects is reported in other studies, However, this is explained to be unjustifiable since the fear does not originate from actual experience of the side effect.[23,32] A comparison study to evaluate patients' reported side effects with clinician's estimates found that patients were over reporting the side effects compared to actual prevalence reported by clinicians.[33] A meta-analysis to assess adherence-related beliefs showed that adherence to medication was influenced by the patients' beliefs and judgment about their personal need for the prescribed medication relative to their concerns about the potential adverse effects.[34] Fear of inhaler medication as well as preference to use alternative medications for asthma can also originate from lack of knowledge

about inhalers compared to other treatment options.[35]

Studies have reported that the preferred alternative drugs were oral aminophylline, salbutamol and herbal medications. Other studies have also shown an association between the use of alternative medications for asthma management and non- adherence.[7,33] This preference to alternative medication could be explained by lack of knowledge on asthma and its management as well as belief on oral medication that they are safer than inhalational medications. Most participants in this study reported that the reasons for use of alternative medications were; lack of symptoms relief with inhaler use (although this information was not systematically collected), cost of inhaler and unavailability of inhaler medication in some parties of the country.

Participants who reported to be too busy with their daily activities were non adherent to inhaler medication as compared to those who weren't too busy. In this study, nearly a half (49.1%) of the participants reported to be self-employed. With their busy schedule on daily basis in order to generate income, they turned non-adherent. Previous studies have shown that busy lives coupled with negative perceptions of medication and inhaler taking were the main reasons for forgetfulness and hence non adherence.[31,36,37]

Additionally, incorrect inhaler technique was associated with non-adherence. In this study, among the non-adherent group, majority (71.6%) demonstrated incorrect inhaler technique. Incorrect inhaler technique leads to poor drug delivery to the lungs and hence poor asthma symptoms control which may predispose a patient to non-adherence.[38] Incorrect inhaler technique seen in these patients might originate from lack of regular training on inhaler use and infrequent monitoring of its use by their physicians.

Study Limitations
The checklist used for inhaler technique assessment varies among researchers as well as inhaler manufacturer recommendations. Although the steps are more or less the same, they are not standardised. This could have magnified the error rates among study participants.

The consecutive enrolment of the participants might have introduced selection bias inclining more onto selecting those with poor inhaler adherence, thus poor asthma control.

Due to its cross-sectional design, no conclusions on causality can be drawn if non- adherence was the cause of poor asthma control or the vice versa.

CONCLUSION
Non- adherence to inhaler medication and poor asthma control were common among participants. Lack of insurance coverage significantly affected adherence to inhalers. Concurrent use of oral medications for asthma negatively affected inhaler adherence. The undue fear of inhaler medication side effects were significant. Emphasis on patients' education in asthma clinics will improve adherence level, since this will eliminate myths and undue fears about inhalers and bring about eventual attainment of optimum asthma control.

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Intestinal Parasite Infections and Associated Risk Factors among Pre-School Aged Children in Kibera Informal Settlement, Nairobi, Kenya

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ABSTRACT

Background: Infections with intestinal parasites are a major public health problem in children in developing countries like Kenya. School going children are considered at most risk and are included in school-based de-worming program. Less focus is given to pre-school children and information is scarce about intestinal parasitosis among this age group. In this study, we determined the prevalence and intensity of protozoa and helminth infections, and associated risk factors in an informal settlement.

Methods: A community based cross-sectional study was conducted from October 2016 to January 2017 among 406 children aged 2-5 years in Kibera informal settlements in Nairobi County, Kenya. Structured interviewer-administered questionnaire was used to collect sociodemographic information and data on associated factors. Stool samples were examined microscopically using formal ether concentration, iodine wet mounting, modified Ziehl-Neelsen staining, and Kato-Katz methods. Multivariable logistic regression analysis was used to identify risk factors associated with intestinal parasites.

Results: The overall prevalence of any helminth and protozoa infections was 13.1% (53/406) and 22.4% (91/406) respectively. The predominant parasites were *Giardia lamblia* (13.8%), *Ascaris lumbricoides* (11.3%), *Entamoeba histolytica/dispar* (9.4%), *Trichuris trichiura* (3.9%), *Entamoeba coli* (1.5%) and hookworm (0.2%). Prevalence of co-infection with any helminths or protozoan was 2.7%. About 10.8% (44/406) and 20.7% (84/406) children were infected with single species of helminth and protozoan parasites. All helminth infections were light, with a mean intensity of 592 egg per gram. Intensity of any protozoan infections was heavy 62.6% (57/406). Dirt floors in the household (aOR = 2.22, *p* = .046), dirty toilets (aOR = 2.33, *p*=.014), water from communal taps (aOR = 0.27, *p*=.019), parent's education level (aOR =0.27, *p*=.032) and parent's earning (aOR =3.34, *p*=.007) were factors significantly associated with intestinal parasites.

Conclusion: The study found both helminth and protozoan parasites to be prevalent among pre-school aged children in Kibera. Intervention measures including education on the improvement of hygiene and health, socio-economic conditions, sanitation, and provision of safe drinking water could reduce the prevalence of these infections.

BACKGROUND

Intestinal parasite infections (IPIs) caused by helminths and protozoa are among the most prevalent and persistent infections globally. They constitute a major public health burden worldwide, caused mostly due to faecal contamination of food and water.[1] Estimates by the World Health Organization (WHO) show that globally, 3.5 billion individuals are affected, and that approximately 450 million people suffer from these infections, with majority being children residing in developing countries.[2,3] The primary parasites responsible for IPIs are soil-transmitted helminths (STHs) including; roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*), and hookworms (*Ancylostoma duodenale* and *Necator americanus*), and pathogenic intestinal protozoa such as *Entamoeba histolytica*, *Giardia lamblia* and *Cryptosporidium* species.[2,4]

Among helminth infections, ascariasis caused by *A. lumbricoides* is the most prevalent IPIs with approximately 807 to 1,221 million infections globally. Majority of these infections occur in sub-Saharan Africa and East Asia. Hookworms and whipworms (*Trichuris trichiura*) account for 576 to 740 and 604 to 795 million infections, respectively.[4] The WHO considers STH infection as one of the Neglected Tropical Diseases (NTDs) with the greatest public health concern.[2]

Infections caused by STHs cause low mortality, however, chronic and repeated infection in children can lead to loss of appetite, vomiting, anaemia and vi-

tamin A deficiency, growth retardation, and poor mental function and cognitive development.[5,6] *A. lumbricoides* and *T. trichiura* are transmitted through the faecal-oral route, by ingestion of infective eggs from soiled hands, water, or food contaminated with human faeces. Hookworm species are transmitted transdermally, when infective larvae present in contaminated soil penetrate the skin.

With regard to intestinal protozoan infections, *G. lamblia* is the most prevalent intestinal protozoan parasite worldwide with approximately 200 million people infected.[7] *E. histolytica*, the causative agent of amoebiasis, is responsible for an estimated 40,000 to 100,000 deaths annually.[8] *Cryptosporidium* is a common opportunistic protozoan associated with diarrhoea among children, elderly, and immuno-compromised individuals.[9] Worldwide, the prevalence of cryptosporidiosis ranges from 1 to 4.5% in developed countries and 3 to 20% in developing countries.[9] The enteric protozoa pathogens; *E. histolytica*, *G. lamblia*, and *Cryptosporidium* species, are frequently associated with acute and chronic diarrhoea, malabsorption syndrome, vitamin A deficiency, stunted growth and weight loss and a higher overall risk of mortality in children.[10] Infection by *E. histolytica*, *G. lamblia*, and *Cryptosporidium* species occur by ingestion of infective cysts in food, water, or hands contaminated with faeces.

In Kenya, a developing country in Sub-Saharan Africa (SSA), the prevalence of intestinal parasitic infections poses a serious health problem among children. Presently, the Kenyan government is implementing a National school-based deworming program, aimed at reducing the disease burden associated with STHs among school-going children aged 6 to 14 years.[11] Numerous studies on Intestinal Parasites (IPs) conducted in Kenya largely focus on school-going children and use school-based surveys.[12–14] Less attention is placed on IPs in pre-school children (below 5 years) resulting in limited evidence of infection burden among this group. In view of this, an important proportion of the childhood population is excluded from existing control programs, which might lead to persistence of these infections whose long-term effects may continue to have negative health effects throughout their lives. To provide an insight on the magnitude of IPIs situation among pre-school children, this study assessed the prevalence of intestinal protozoa and helminth infections and associated risk factors among pre-school age children (2 to 5 years) in selected villages in Kibera informal settlement located in Nairobi County, Kenya.

MATERIALS AND METHODS
Study Design and Study Area
A community based cross-sectional survey was conducted among pre-school aged children in the Kibera informal settlements in Nairobi County, Kenya, between October 2016 and January 2017. Kibera is located approximately 5kms Southwest of the capital city, Nairobi. It is situated at an altitude of 1,670m above sea level and lies between latitude 36°47′0″E and longitude 1°19′0″S. Mean annual temperature and relative humidity range from 12°C to 28°C and 32% to 98%, respectively and the average annual rainfall is about 790mm.[15] Kibera occupies over 250 hectares and is the largest slum in Nairobi with an

estimated population of about 200,000 people.[16] The informal settlement are composed of 14 villages namely; Kianda, Olympic, Soweto West, Gatwekera, Raila, Karanja, Kisumu Ndogo, Makina, Kambi Muru, Mashimoni, Lindi, Laini Saba, Silanga and Soweto East.[15] Like many urban slum communities, Kibera is characterised by substandard housing conditions, overcrowding, poor sanitation and lack of safe and clean drinking water, which result to unhealthy living conditions that favour intestinal parasite transmission.[15,17,18]

Study Population and Eligibility Criteria
The study population constituted of 406 preschool children aged between 2 to 5 years residing in Kibera informal settlements. Children whose parents/guardians gave consent to participate in the study were included. Children on antiparasitic treatment, and treated recently for intestinal parasites, children who had diarrhoea at the time of stool sample collection, and whose parents/guardians did not consent to take part in the study were excluded.

Sample Size Determination and Sampling Technique
Sample size was determined using a single population proportion formula with the following assumptions: where, *n* is the sample size, *z* (1.96) is the standard deviation at a 95% Confidence Interval, *p* is the prevalence of 40.5% from a previous study among preschool children in Kibera, Nairobi[18], and *d* is the margin of error (0.05).

Thus, $n = z^2 p (1-p)/d^2$.

Then, $n = 1.96^2 * 0.405 (0.595)/0.0025 = 370$.

By considering a 10% non-response rate, the resulting sample size was 406 participants. Multi-stage sampling was used to identify study villages and households. The sampling frame included 14 villages in Kibera informal settlements. 7 out of 14 villages (first stage), were selected using a simple random sampling technique. The names of the 14 villages were written on pieces of paper which were then folded, placed in a bowl, and mixed. The blind-folded study Principal Investigator (PI) selected the desired sample by picking the required number of papers. Each village corresponding to the name chosen was then included in the sample.

In the second sampling stage, 58 households in each of the chosen villages were selected using systematic sampling procedure and these were assigned unique identifiers (i.e., village name abbreviation and household number). Taking advantage of Kenya's government program, the Community Health Strategy, which maintains updated household listings of all households with children aged 5 years and below in each village[19], 58 households in each of the chosen villages were selected from the provided lists. The study was performed with collaboration of the Community Health Workers (CHWs) that work under this program in Kibera. Every third household was picked from the list of designated households. In cases where the interviewers did not find an eligible participant in the house, they proceeded to the next house until an eligible participant was found.

Households were the basic sampling unit and only one participant per household was recruited. For households with more than one child in this age category, only one

child was considered using the lottery sampling method. 58 stool samples were obtained from enrolled children from each village (58*7), giving a total of 406 stool samples for the study.

Data Collection and Processing
Household Survey
Prior to data and stool sample collection, preliminary meetings were held with CHWs and village heads of the selected villages to explain to them the study's protocol. The data was collected using a structured questionnaire through face-to-face interviews with the children's parent or guardian. The questionnaire was prepared originally in English, translated into Swahili language and then retranslated back to English. The comparison was conducted to check for accuracy and consistency between the two versions of the questionnaire. The CHWs were trained on the questionnaire content, interview method, objectives of the study, and stool sample collection method by the PI. After the training, the study questionnaire was pre-tested on 5% of the total calculated sample size. Inconsistencies and errors identified were corrected accordingly. Questionnaires were administered by 7 CHWs. The PI prudently supervised the data collection process.

A structured questionnaire comprised of 3 parts. The first part included socio-demographic and economic characteristics of the study respondents such as age, gender, duration of residence, parent/guardian educational status, parent/guardian occupation, family income and household conditions. The second part comprised of information on environmental factors such as water source, toilet availability, toilet distance, toilet cleaning mechanisms and garbage disposal. The last part included questions regarding behavioural factors such as hand washing practice before and after using the toilet, the practice of shoe wearing, habits such as sucking the thumb, nail biting, and fingernail trimming as well as knowledge on transmission and prevention of intestinal parasite infections and history of receiving antiparasitic treatment prior to sample collection.

Collection of Stool Samples
Parents and guardians were adequately instructed on how to obtain an adequate portion of their child's stool. A single stool specimen was collected from each study participant in a clean, dry plastic container labelled with a unique identifier. Each of the specimens was checked for its quantity and labelling. Stool samples from each village were batched and transported in cool boxes by CHWs on the same day to the Centre for Clinical Research (CCR), Kenya Medical Research Institute (KEMRI) for diagnosis. Samples that could not be examined immediately were stored at 4°C and processed within a maximum of 12 hours post-collection.

Laboratory Processing and Analysis
Laboratory analysis focused on STHs (*A. lumbricoides*, *T. trichiura*, and hookworm) and protozoa (*G. lamblia*, *E. histolytica/dispar* and *Cryptosporidium* species) because they are amongst the most prevalent IPs and important contributors to global morbidity and mortality. Evidence of infection was based on the presence of protozoan cysts and oocysts and STH eggs.

Stool Sample Processing using Kato-Katz Technique
For the diagnosis of STHs, duplicate Kato-Katz thick smears were prepared from each stool sample using 41.7 mg punched plastic templates.[20] Smear were mounted on slides and covered with malachite green impregnated cellophane. The slides were examined under the microscope at a magnification of ×10. For hookworms, the slides were read within one hour of smear preparation. The smear slides were left overnight to clear for easy visualisation of other helminth eggs. The STHs eggs for each species were counted and recorded separately. The total numbers of eggs were expressed as Eggs Per Gram (EPG) of stool. The mean EPG was calculated to classify the intensity of each STH infection as light, moderate, and heavy infection according to WHO criteria[21]: for Hookworm (light infection: 1-1999 epg, moderate: 2000-3999 epg, heavy: ≥ 4000 epg). Similarly, for *A. lumbricoides* (light infection: 1-4999 epg, moderate: 5000-49999 epg, heavy: ≥ 50000 epg). Intensity of *T. trichiura* (light: 1-999 epg, moderate: 1000-9999 epg, heavy: ≥ 10000 epg).

Stool Sample Processing using Formal-Ether Concentration Technique
For diagnosis of intestinal protozoans, the remaining portion of stool specimen were concentrated by formol-ether method to increase yield of cysts, oocysts of protozoan parasites. For each specimen, about 1g of stool was transferred into 10mL of 10% formalin solution, thoroughly mixed using applicator stick and sieved through four layers of wet gauze. About 7mL of the sieved suspension was collected in a centrifuge tube. A volume of 3mL of diethyl ether was added and mixed well by shaking for about 1 minute and centrifuged at 3,000 revolutions per minute (rpm) for 1 minute.[22] The supernatant was decanted, and the sediment processed and examined using iodine wet mounting and modified Ziehl Neelsen (ZN) staining methods.

Stool sample processing using Iodine wet mount
Iodine mounts were examined to detect and determine intensities of *G. lamblia* and *E. histolytica* cysts in stool. A drop of sediment (20μl) obtained using formol ether concentration method, was placed on a slide, stained with a drop of 1% lugol's iodine, covered with a 22-by 22-mm cover slip and examined microscopically for protozoan cysts at 100× and 400× magnifications, according to WHO protocol.[22] Infection intensities was determined semi-quantitatively as; (i) negative (0 cysts in the entire sediment); (ii) rare (1-5 cysts per slide); (iii) frequent (1 cyst per observation field of x400); and (iv) very frequent (≥ 1-cyst per observation field of x400), as described by Utzinger et al.[23] Entamoeba cysts were reported as *E. histolytica/dispar*, since the two species are morphologically identical and cannot be distinguished microscopically.[24]

Stool Sample Processing using Modified ZN Staining Technique
This method was used for detection and determination of intensities of *Cryptosporidium* species oocysts in stool. Thin smears of sediments (20μl) from the concentration technique were prepared on a slide, air-dried and fixed in methanol for 2 to 3 minutes. The slides were stained with cold carbolfuchsin for about 5 to 10 minutes, decolourised

in 1% hydrochloric acid-ethanol solution for 15 to 30 seconds and thoroughly rinsed in clean tap water, then counter stained with 0.25% malachite green for 30 seconds, rinsed well in clean tap water, air-dried, and examined microscopically at 1000x magnification.[22] The intensities for *Cryptosporidium* species infection was scored semi quantitatively as: negative (0 oocysts), slight (1-5 oocysts), moderate (6-10 oocysts), severe (>10 oocysts), as described by Castro-Hermida et al.[25]

Quality Control

To ensure the quality of the investigation and results, CHWs were trained for one day on how to collect data and stool samples. Questionnaires were checked for completeness soon after the interviews. Laboratory examinations were carried out by experienced medical laboratory professionals. Stool samples were randomly selected and examined independently by experienced laboratory technologists and their respective results compared. Final decision of discordant slides was reached based on consensus and in consultation with a senior technologist.

Statistical Analysis

The observed prevalence and intensity of intestinal protozoan, and helminth infections were calculated by gender and village and 95% confidence intervals (CIs) were determined using binomial logistic regression and negative binomial regression respectively, taking into account clustering by village. Comparisons of prevalence by gender and village were performed using Fisher's exact test. The significance of the factors associated with intestinal protozoan, and helminth infections among the children was determined using a multivariable logistic regression model reporting the odds ratios at 95% CI. The choice of the model was based on the log likelihood function. The minimum adequate covariates for multivariable analysis were selected using the forward stepwise variable selection method which selected covariates with a *p-value* less than .300 in the bivariable model.[26] All statistical analysis was survey set and carried out using STATA version 12.0 (StataCorp, College Station, TX, USA).

Ethics Approval and Consent to participate

This study was reviewed and approved by the Scientific and Ethics Review Unit (SERU) of KEMRI (SERU Protocol No. 3012). Official permission to conduct field activities was obtained from the Director of Health Services, Nairobi County. Parents/guardians of the children were thoroughly briefed by CHWs about the study objectives during individual house visits, emphasising that participation was voluntary and that withdrawal from the study at any point was permitted even without reason. Signed or thumb-printed informed consent was obtained from the parents/guardians of the children before sample collection began. Data collected from each child and results of laboratory tests were kept confidential and used only for this study. The test results were returned to the parents/guardians and children found positive for pathogenic intestinal parasites were given referral letters for free treatment at the Médecins Sans Frontières (MSF) supported clinics in the Kibera informal settlement.

RESULTS

Socio-Demographic Characteristics of Study Participants

The data was collected from 406 preschool children, aged 2 to 5 years, with a mean age of 3.4 years (Standard Deviation 0.9 years) from 7 villages in the Kibera informal settlement. Information on gender was provided for 404 (99.5%) of the children and 51.7% were female. The age of the care givers of the children was between 19 and 69 years with a mean age of 29.0 years (Standard Deviation 6.2 years), the majority of the care givers (88.9%) were mothers of the children, and 6.2% were guardians. All villages were equally represented in the sample at 14.3% (Tables 1 and 2).

Prevalence and intensity of Intestinal Helminth and Protozoan Infections

The overall prevalence of intestinal helminth infection was 13.1% (95% CI: 7.6-22.6); n=53. Prevalence of *A. lumbricoides* was highest 11.3% (95% CI: 6.0-21.4); n=46, while low prevalence was recorded for *T. trichiura as* 3.9% (95% CI: 1.8-8.7); n=16, and hookworm 0.2% (95%CI: 0-1.7); n=1. Besides prevalence, the intensity of infection was estimated from the number of eggs per gram (epg) of stool. *A. lumbricoides* 577 epg, (95% CI: 179-1861), *T. trichiura* 15 epg, (95% CI: 5-47) and hookworm 1 epg, (95% CI: 0-1), all had light infections. There were no children with moderate or heavy infections. Both prevalence and mean intensity of all intestinal helminth infections were relatively high among children from Soweto East village at 31.0% (95% CI: 21.1-45.5); n=18 and 2549 epg (95% CI: 668-9722), (Table 1). Overall, 22.4% (95% CI: 15.7-32.0); n=91 of the children were infected with any protozoan parasites, with *G. lamblia* being the most prevalent at 13.8% (95% CI: 8.2-23.2); n=56, followed by *E. histolytica/dispar* 9.4% (95% CI: 6.5-13.5); n=38 and *Entamoeba coli* 1.5% (95% CI: 0.4-5.2); n=6. Infections with any protozoa were very frequent at 62.6% (95% CI: 49.9-78.6); n=57 (Table 2). The prevalence and intensity of all protozoan infections was highest among participants from Soweto West village at 43.1% (95% CI: 32.1-57.9); n=25 and 72.0% (95% CI: 56.4-91.9); n=18 (Table 2 and 3). Majority of *G. lamblia* infections were very frequent at 83.9% (71.7-98.2); n=47, while those for *E. histolytica* were rare 42.1% (95% CI: 29.5-60.1), (Table 3). In this study, co-infection was defined as simultaneous infection with different intestinal parasite species, either helminths or protozoa. The overall prevalence of co-infection with any helminth or protozoan was 2.7% (95% CI: 1.7-4.3); n=11. No child was co-infected with more than three parasite species. Single infection was more frequent with protozoa at 20.7% (95% CI: 14.0-30.5); n=84, compared to helminths at 10.8% (95% CI: 6.9-17.0); n=44 and. Highest numbers of co-infection were observed in male children 3.6% (95% CI: 1.7-7.4); n=7 compared to female children at 1.9% (95% CI: 0.7-5.1); n=4 (Table 4).

Factors Associated with Intestinal Parasitic Infections

In this study, significant factors identified as affecting prevalence of IPs were dirt floors in the household, dirty toilets, water from communal taps, parent's education level and parent's earning (*p<.05*). Whereas, factors such as drainage and flooding, gender, parent/guardian marital status, hand washing habit, consistency of wearing shoes,

TABLE 1: Prevalence (%) and Mean Intensity (Epg) of Intestinal Helminth Infections

	n (%) [N=406]	Any helminths Prevalence % (95%CI); n	Any helminths Mean intensity [epg] [95%CI]	Hookworm Prevalence % (95%CI); n	Hookworm Mean intensity [epg] [95%CI]	Ascaris lumbricoide Prevalence % (95%CI); n	Ascaris lumbricoide Mean intensity [epg] [95%CI]	Trichuris trichiura Prevalence % (95%CI); n	Trichuris trichiura Mean intensity [epg] [95%CI]
Overall	406 (100%)	13.1 % (7.6-22.6); n=53	592 (186-1880)	0.2% (0-1.7); n=1	1 (0-1)	11.3% (6.0-21.4); n=46	577 (179-1861)	3.9% (1.8-8.7); n=16	15 (5-47)
Village									
Kambi-Muru	58 (14.3%)	15.5% (8.5-28.3); n=9	32(6-167)	0	0	15.5% (8.5-28.3); n=9	32(6-167)	0	0
Lindi	58 (14.3%)	17.2% (9.8-30.3); n=9	948 (142-6337)	0	0	15.5% (8.5-28.3); n=9	883(117-6690)	5.2% (1.7-15.6); n=3	65(2-1906)
Silanga	58 (14.3%)	12.1% (6.0-24.2); n=7	383 (39-3741)	0	0	6.9% (2.7-17.8); n=4	373(16-8777)	5.2% (1.7-15.6); n=3	10(1-189)
Soweto East	58 (14.3%)	31.0% (21.1-45.5); n=18	2549 (668-9722)	1.7% (0.2-12.0); n=1	1 (0-115)	29.3% (19.7-43.7); n=17	2523 (623-10146)	12.1% (6.0-24.2); n=3	24(4-160)
Soweto West	58 (14.3%)	8.6% (3.7-19.9); n=5	88 (7-1122)	0	0	6.9% (2.7-17.8); n=4	85 (5-1547)	3.4% (0.9-13.5); n=2	3(0-80)
Kianda	58 (14.3%)	1.7% (0.2-12.0); n=1	7 (0-1784)	0	0	0	0	1.7% (0.2-12.0); n=1	7(0-1784)
Laini Saba	58 (14.3%)	5.2% (1.7-15.6); n=3	138 (4-4717)	0	0	5.2% (1.7-15.6); n=3	138 (4-4716)	0	0
Gender									
Male	195(48.3%)	11.3 % (7.6-16.7); n=22	413 (113-1512)	0.5%; (0.1-3.6); n=1	0 (0-35)	10.3% (6.8-15.5); n=20	402 (102-1584)	4.1% (2.1-8.1); n=8	11(2-70)
Female	209(51.7%)	14.4% (10.3-20.0); n=30	760 (249-2315)	0	0	12.0% (8.3-17.3); n=25	739 (214-2559)	3.8% (1.9-7.6); n=8	20(3-145)

N= total sample size, n= total number of individuals, CI = confidence interval and epg = eggs per gram

TABLE 2: Prevalence (%) of Protozoan Infections

	n (%) [N=406]	Any protozoa % (95%CI); n	Entamoeba histolytica % (95%CI); n	Entamoeba coli % (95%CI); n	Giardia lamblia % (95%CI); n
Overall	406 (100%)	22.4% (15.7-32.0); n=91	9.4% (6.5-13.5); n=38	1.5% (0.4-5.2); n=6	13.8% (8.2-23.2); n=56
Village					
Kambi-Muru	58 (14.3%)	24.1% (15.3-38.1); n=14	12.1% (6.0-24.2); n=7	0	12.1% (6.0-24.2); n=7
Lindi	58 (14.3%)	20.7% (12.5-34.2); n=12	0	0	20.7% (12.5-34.2); n=12
Silanga	58 (14.3%)	27.6% (18.2-41.9); n=16	10.3% (4.8-22.1); n=6	1.7% (0.2-12.0); n=1	19.0% (11.1-32.3); n=11
Soweto East	58 (14.3%)	12.1% (6.0-24.2); n=7	10.3% (4.8-22.1); n=6	0	1.7% (0.2-12.0); n=1
Soweto West	58 (14.3%)	43.1% (32.1-57.9); n=25	13.8% (7.2-26.2); n=8	1.7% (0.2-12.0); n=1	29.3% (19.7-43.7); n=17
Kianda	58 (14.3%)	12.1% (6.0-24.2); n=7	6.9% (2.7-17.8); n=4	0	5.2% (1.7-15.6); n=3
Laini Saba	58 (14.3%)	17.2% (9.8-30.3); n=10	12.1% (6.0-24.2); n=7	6.9% (2.7-17.8); n=4	8.6% (3.7-19.9); n=5
Gender					
Male	195 (48.3%)	21.5% (16.5-28.2); n=42	10.3% (6.8-15.5); n=20	2.1% (0.8-5.4); n=4	12.3% (8.5-17.9); n=24
Female	209 (51.7%)	23.4% (18.4-30.0); n=49	8.6% (5.5-13.4); n=18	1.0% (0.2-3.8); n=2	15.3% (11.1-21.1); n=32

N= total sample size, n= total number of individuals, CI = confidence interval

TABLE 3: Prevalence (%) of Intensity Of Protozoan Infections

	Any protozoa % (95%CI); n			Entamoeba histolytica % (95%CI); n			Entamoeba coli % (95%CI); n			Giardia lamblia % (95%CI); n		
	Rare	Frequent	Very frequent	Rare	Frequent	Very frequent	Rare	Frequent	Very frequent	Rare	Frequent	Very frequent
Overall	20.9% (10.0-43.7); n=19	20.9% (15.7-27.8); n=19	62.6% (49.9-78.6); n=57	42.1% (29.5-60.1); n=16	36.8% (20.2-49.5); n=14	31.6% (20.2-53.9); n=12	16.7% (6.3-44.4.); n=1	50.0% (28.4-88.0.); n=3	83.3% (49.6-99.9); n=5	12.3% (8.3-24.5); n=8	5.4% (0.7-42.3); n=3	83.9% (71.7-98.2); n=47
Village												
Kambi-Muru	57.1% (36.3-90.0); n=8	14.3% (4.0-51.5); n=2	28.6% (12.5-65.4); n=4	71.4% (44.7-90.3); n=5	14.3% (2.3-87.7); n=1	14.3% (2.3-87.7); n=1	0	0	0	14.3% (2.3-87.7); n=1	42.9% (18.2-100.0); n=3	42.9% (18.2-79.8); n=3
Lindi	0	16.7% (4.7-59.1); n=2	83.3% (64.7-99.2); n=10	0	0	0	0	0	0	16.7% (4.7-59.1); n=2	0	83.3% (64.7-99.2); n=10
Silanga	6.3% (0.9-41.7); n=1	31.3% (15.1-64.6); n=5	62.5% (42.8-91.4); n=10	16.7% (2.8-99.7); n=1	66.7% (37.9-98.3); n=4	16.7% (2.8-99.7); n=2	0	0	0	18.2% (5.2-63.7); n=2	0	81.8% (61.9-96.4); n=9
Soweto-East	28.6% (8.9-92.2); n=1	28.6% (8.9-92.2); n=2	42.9% (18.2-99.3); n=3	33.3% (10.8-70.3); n=2	33.3% (10.8-70.3); n=2	33.3% (10.8-70.3); n=2	0	0	0	0	0	100% (95.0-100); n=1
Soweto-West	12.0% (4.2-34.7); n=3	16.0% (6.5-39.3); n=2	72.0% (56.4-91.9); n=18	37.5% (15.3-91.7); n=3	37.5% (15.3-91.7); n=3	25.0% (7.5-83.0); n=2	0	0	0	5.9% (0.9-39.4); n=1	0	94.1% (83.6-99.7); n=16
Kianda	28.6% (8.9-92.2); n=2	14.3% (2.3-87.7); n=1	71.4% (44.7-90.4); n=5	50.0% (18.8-80.7); n=3	25.0% (4.6-91.3); n=1	50.0% (18.9-80.8); n=2	0	0	0	0	0	100% (95.0-100); n=3
Laini-Saba	30.0% (11.6-77.3); n=3	30.0% (11.6-77.3); n=3	70.0% (46.7-96.3); n=7	42.9% (18.2-90.6); n=2	42.9% (18.2-90.6); n=1	57.1% (30.1-98.3); n=4	25.0% (4.6-91.3); n=1	50.0% (18.8-80.7); n=2	100 (95.0-100); n=4	0	40.0% (13.7-80.5); n=2	100% (95.0-100); n=5
Gender												
Male	16.7% (8.5-32.8); n=7	23.8% (13.9-40.9); n=10	66.7% (53.8-82.6); n=28	35.0% (19.3-63.5); n=7	40.0% (23.4-68.4); n=8	40.0% (23.4-68.4); n=8	0	75.0% (42.6-98.5); n=3	75.0% (42.6-98.5); n=3	16.7% (6.8-40.8); n=4	0	91.7% (81.3-99.6); n=22
Female	24.5% (15.0-40.0); n=12	18.4% (10.2-33.1); n=9	59.2% (46.9-74.7); n=29	50.0% (31.5-79.4); n=9	33.3% (17.3-64.1); n=6	22.2% (9.4-52.7); n=4	50.0% (12.5-90.6); n=1	0	100% (95.0-100); n=2	9.4 (3.2-27.5); n=3	12.5% (5.0-31.3); n=4	78.1% (65.0-93.8); n=25

n= total number of individuals, CI = confidence interval

TABLE 4: Prevalence of the Co-Infections with Helminths and Protozoans

Co-infections %(95%CI); n	Helminths %(95%CI); n			Protozoans %(95%CI); n			Co-infection with any helminths or protozoan %(95%CI); n
	One species	Two species	Three species	One species	Two species	Three species	
Overall	10.8%(6.9-17.0); n=44	2.0% (0.6-6.6); n=8	0.2%(0-1.7); n=1	20.7%(14.0-30.5); n=84	1.2%(0.5-3.3); n=5	0.5% (0.1-3.5); n=2	2.7% (1.7-4.3); n=11
Village							
Kambi-Muru	15.5%(8.5-28.3); n=9	0	0	24.1%(15.3-38.1); n=14	0	0	5.2%(1.7-15.6); n=3
Lindi	13.8%(7.2-26.2); n=8	3.4%(0.9-13.5); n=2	0	20.7% (12.5-34.2); n=12	0	0	1.7%(0.2-12.0); n=1
Silanga	12.1%(6.0-24.2); n=7	0	0	24.1%(15.3-38.1); n=14	3.4%(0.9-13.5); n=2	0	3.4%(0.9-13.5); n=2
Soweto East	20.7%(12.5-34.2); n=12	8.6%(3.7-19.9); n=5	1.7%(0.2-12.0); n=1	12.1%(6.0-24.2); n=7	0	0	3.4%(0.9-13.5); n=2
Soweto West	6.9%(2.8-17.8); n=4	1.7%(0.2-12.0); n=1	0	41.4%(30.5-56.2); n=24	1.7%(0.2-12.0); n=1	0	3.4%(0.9-13.5); n=2
Kianda	1.7%(0.2-12.0); n=1	0	0	12.1%(6.0-24.2); n=7	0	0	1.7% (0.2-12.0); n=1
Laini Saba	5.2%(1.7-15.6); n=3	0	0	10.3%(4.8-22.1); n=6	3.4%(0.9-13.5); n=2	3.4%(0.9-13.5); n=2	0
Gender							
Male	8.2%(5.1-13.1); n=16	2.6%(1.1-6.1); n=5	0.5%(0.1-3.6); n=1	19.5%(14.7-25.9); n=38	1.0%(0.3-4.1); n=2	1.0%(0.3-4.1); n=2	3.6% (1.7-7.4); n=7
Female	12.9%(9.1-18.4); n=27	1.4%(0.5-4.4); n=3	0	22.0%(17.1-28.4); n=46	1.4%(0.5-4.4); n=3	0	1.9% (0.7-5.1); n=4

n= total number of individuals, CI = confidence interval

TABLE 5: Multivariable Analysis of Risk Factors Associated With Any Intestinal Helminth and Protozoan Infections

Factors	Risk factors for any helminth infections aOR (95%CI), p-value	Risk factors for any protozoan infections aOR (95%CI), p-value
Village		
Kambi-Muru	Reference	
Lindi	1.13 (0.32-4.02), p=0.842	1.12 (0.40-3.12), p=0.835
Silanga	0.29 (0.06-1.36), p=0.116	1.23 (0.38-4.03), p=0.729
Soweto East	6.45 (0.95-43.52), p=0.056	2.55 (0.49-13.19), p=0.264
Soweto West	0.26 (0.05-1.28), p=0.097	3.64 (1.16-11.46), p=0.027**
Kianda	0.12 (0.01-1.23), p=0.074	1.12 (0.34-3.66), p=0.849
Laini Saba	1.30 (0.14-11.68), p=0.814	3.50 (0.65-18.80), p=0.144
Child gender		
Male vs Female	0.64 (0.31-1.30), p=0.215	0.90 (0.53-1.54), p=0.698
Child age		
2 vs 5 years	1.16 (0.31-4.40), p=0.828	0.58 (0.22-1.55), p=0.278
3 vs 5 years	0.74 (0.21-2.63), p=0.642	0.87 (0.35-2.17), p=0.765
4 vs 5 years	2.04 (0.59-7.02), p=0.257	0.83 (0.33-2.05), p=0.683
Parent's age		
≤20 vs >40 years	4.67 (0.41-53.70), p=0.216	0.35 (0.06-2.15), p=0.256
21-30 vs >40 years	3.49 (0.21-2.63), p=0.642	0.47 (0.13-1.72), p=0.253
31-40 vs >40 years	1.65 (0.24-11.48), p=0.612	0.43 (0.11-1.64), p=0.219
Parent's marital status		
Single vs Married	1.39 (0.54-3.60), p=0.499	0.57 (0.24-1.33), p=0.192
Separated vs Married	0.40 (0.07-2.25), p=0.299	0.90 (0.28-2.90), p=0.860
Parent's level of education		
Primary vs None	0.79 (0.31-2.05), p=0.632	1.04 (0.43-2.53), p=0.923
Secondary vs None	0.27 (0.08-0.89), p=0.032**	0.78 (0.30-2.06), p=0.618
Post-secondary vs None	0.94 (0.10-9.09), p=0.960	0.34 (0.06-2.06), p=0.242
Parent's earnings (Ksh)		
(5,000 – 10,000) vs < 5,000	3.34 (1.40-7.96), p=0.007**	1.74 (0.88-3.46), p=0.112
> 10,000 vs < 10,000	4.40 (0.76-25.37), p=0.097	1.27 (0.35-4.59), p=0.720
Floor type		
Dirt vs Cement	2.22 (1.01-4.88), p=0.046**	1.67 (0.85-3.29), p=0.135
Tile vs Cement	0.89 (0.07-10.81), p=0.924	1.04 (0.13-8.02), p=0.971
Source of drinking water		
Borehole vs Communal tap	Omitted	1.71 (0.07-39.18), p=0.736
Water vendor vs Communal tap	0.42 (0.11-1.66), p=0.218	0.27 (0.09-0.81), p=0.019**
Latrine cleanliness		
Dirty vs Clean	1.52 (0.63-3.69), p=0.352	2.33 (1.19-4.55), p=0.014**
Waste water drainage channel		
Yes vs No	1.16 (0.43-3.10), p=0.771	1.48 (0.71-3.10), p=0.292
Flooding during rainy season		
Yes vs No	0.81 (0.32-2.03), p=0.650	0.87 (0.46-1.68), p=0.687
Child wash hands after visiting toilet		
Yes vs No	0.69 (0.20-2.42), p=0.564	0.42 (0.14-1.26), p=0.121
Child bite nails		
Yes vs No	1.51 (0.69-3.29), p=0.305	0.63 (0.32-1.23), p=0.178
Child wear shoes/sandals		
Yes vs No	8.20 (0.91-73.84), p=0.061	1.25 (0.42-3.69), p=0.684
Child nails are trimmed		
Yes vs No	0.74 (0.26-2.17), p=0.589	2.36 (0.72-7.73), p=0.158

aOR- Adjusted odds ratio
** Indicates a significant p-value (<0.05)

habit of biting fingernails, and having untrimmed fingernails were not associated with IPs infections (Table 5). The likelihood of being infected by helminths was high in children whose parents/guardians had no formal education (aOR = 0.27, 95% CI: 0.08-0.89, *p = .032*), compared to those whose parents/guardians had attained secondary level education (aOR= 0.78, 95% CI: 0.30-2.06, *p=.618*). Similarly, children from families who earned less than Kenya shillings (Ksh) 5000 were more infected with helminth parasites (aOR= 3.34, 95% CI: 1.40-7.96, *p=.007*) and less infected with protozoans (aOR=1.74, 95% CI: 0.88-3.46, *p=.112*) compared with children from families that earned more than Ksh 5000. Likewise, children from houses with dirt floors were at significant risk for any helminth infection (aOR = 2.22, 95% CI:1.01-4.88, *p = .046*) and at non-significant risk for any protozoan infection (aOR = 1.67, 95% CI:0.85-3.29, *p = .135*), compared to children from houses with cemented floors. In addition, children from households that used water from the communal taps were at less risk for any helminth infection (aOR = 0.42, 95% CI: 0.11-1.66, *p=.218*) and at high risk for any protozoan infection (aOR = 0.27, 95% CI: 0.09-0.81, *p=.019*), compared to children from households that buy water from water vendors. Similarly, children whose parents/guardians reported using dirty toilets were at a high significant risk of protozoan infection (aOR = 2.33, 95% CI: 1.19-4.55, *p=.014*) and at non-significant risk for any helminth infections (aOR = 1.52, 95% CI: 0.63-3.69, *p =.352*). Regarding residence, children in Soweto West village (aOR = 3.64, 95% CI: 1.16-11.46, *p =.027*) were at a significantly high risk for protozoan infections, than other villages. Kambi-Muru village was used as the reference category (Table 5).

DISCUSSION

This study's findings indicate that protozoa infections were more prevalent than STH infections, which is consistent with a study conducted in Uganda among pre-school children.[27] Possible reasons could be due to contaminated water and poor sanitary conditions. In this study, children from households that used dirty toilets or used water from the community taps were at significantly high risk of having protozoa infections. Reports from similar studies in urban slum settings have shown that water contaminated with human faeces would be the infection source of the protozoa such as *Entamoeba* species and *G. lamblia*.[28,29] In contrast, higher rates of infestation with STHs[18] and protozoans[14] were previously reported in studies conducted Kenya. Differences in the prevalence of various parasites in this study could be related to sample size, study population, as well as the techniques used for diagnosis.[30] The predominant helminth parasite was *A. lumbricoides* followed by *T. trichiura* and hookworm respectively, similar to findings from studies conducted in other localities in SSA[31,32] where *A. lumbricoides* and *T. trichiura* were the most common helminth parasites. According to the WHO classification of infection intensities, *A. lumbricoides*, *T. trichiura*, and hookworm had light infections. No moderate or heavy infections were recorded in this study. The overall prevalence of STH parasites found in this study was lower than WHO population treatment level[33] and could be attributed to morbidity control through deworming of school going -

children in the study area. The most common protozoan parasite was *G. lamblia* followed by *E. histolytica/dispar*, and commensal *Entamoeba coli* respectively. This finding is consistent with results from similar studies conducted from other SSA countries[27,34-36], that indicate that *G. lamblia* and *E. histolytica/dispar* infections are more prevalent in under-five children. Most children had very frequent-intensity protozoa infections. Protozoans' *G. lamblia* and *E. histolytica/dispar* had very frequent and rare intensity infections respectively.

The prevalence and intensity of protozoan infections among children in this study is of concern and deserves consideration in the development of control and prevention policies by Kenya's Ministry of Health. Although modified ZN staining was applied to identify *Cryptosporidium* parasites, no *cryptosporidium* infection was identified in this study. Possible explanations could be due to the selection/ choice of the study population and intermittent excretion of cryptosporidium oocysts. The present study investigated asymptomatic children sampled in the community and used a single stool examination. However, this is in contrast to reports on cryptosporidiosis in children aged below 5 years.[27,37] Regarding co-infections, some of the children harboured multiple species of helminth and protozoa parasites concurrently. This could be due to shared risk factors such as poor sanitation, improper hygiene, and behaviour of participating children. Co-infection as a marker of poor sanitation and poverty is of clinical significance as individuals with multiple parasite species may suffer from multiple morbidities and increased susceptibility to other infections.[38] Single infection rate was higher for protozoans compared to helminths. This can be attributed to the common route of transmission, i.e., faecal-oral pathway, especially when people do not practice proper personal and environmental hygiene. In addition, no significant difference was observed in intestinal helminth and protozoa infection between male and female children in this study. Possible reason could be that both girls and boys have similar behavioural habits and engage in similar outdoor activities around their households that could expose them to the same sources of infections. However, higher prevalence rates for helminth infections were observed in Soweto East village than other villages. In this study, children whose parents/guardians have no formal education were significantly at risk for helminth infections compared to those with secondary education. Similar findings have been reported in studies among children showing a significant association of infection rate with the education status of the caregiver.[3,39] Furthermore, this study showed evidence of a significant association of low family income and dirt floors with helminth infections. Previous studies have demonstrated that poor hygienic and sanitary conditions and other factors related to low socioeconomic status facilitate the transmission of IPs.[40]

Limitations

Due to limited resources, this study relied on a single stool examination for detection of IPs instead of the recommended standard three samples collected in different days.[41] The overall prevalence of protozoa infection was probably underestimated since formol-ether concentration and iodine mounting methods are -

unable to detect trophozoites. In addition, light microscopy was used to detect and identify the amoebic cysts and therefore differentiations of *E. histolytica* from the morphologically identical species *E. dispar* was not done.

CONCLUSION

This study showed that both helminth and protozoan parasites are prevalent among pre-school aged children in the Kibera informal settlements. Hence, intervention measures including education on personal hygiene and health, provision of safe drinking water, improvement of socioeconomic status, and sanitation should be taken into account to reduce the prevalence of these infections in the study area. Also, further studies using larger sample size and molecular tools should be conducted to determine the prevalence and intensities of IPIs in the area.

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One Week Prevalence and Incidence of Diarrhea: Baseline Status of Cluster Randomised Controlled Trial of Nano Maji Filter System in Geita, Tanzania

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ABSTRACT

Background: We have developed Nano Maji (NMM) filter system for water treatment which is currently being evaluated in a definitive cluster randomised controlled trial.

Objectives: This paper descriptively presents the baseline status of one-week incidence and prevelence of diarrhoea water, sanitation and hygiene and their determinants.

Methods: Recruited households in the three villages of Geita district were allocated to either intervention (NNM filter system) or control (usual practice). The primary outcome of the trial is to reduce episodes of diarrhoea at 6months post-randomisation. Secondary outcomes are to improve water, sanitation and hygiene (WASH) status. Although households were sampled, individuals living in the selected households are used as unit of analysis for estimation of prevalence and incidence of diarrhea.

Results: A total of 1,281 individuals (1,070 above 5 years and 211 under the age of 5 year children) lived in 186 households (7 individuals per household). The reported one-week prevalence and incidence of diarrhea was 10.8% and 8.4% respectively. Children under the age of five years had high incidence (22.7%) of diarrhea than individuals aged 5 years and above (5.6%). Among under five children, boys had high incidence and prevalence of diarrhea than girls. Individuals with diarrhea were likely to live in poor household, not using safe water and toilet. Over 70% of households had unacceptable latrines 135 (72.7%) and poor water situation 138 (74.3%) in terms of practice of storing, treating and drawing water from storage container. Majority of respondents had limited knowledge on handwashing and rarely used soap when washing hands.

Conclusion: Substantial proportion of individuals living in project areas are affected by diarrhea. Children below the age of five years are more affected than individuals aged five years and above. The baseline findings are representative of local status of WASH, and reflects the prevailing poor water, sanitation and hygiene status in rural areas of Tanzania. Trial approval number NIMR/HQ/R.8a/Vol.IX/3045

BACKGROUND

Although simple and cost effective interventions to prevent and treat diarrhoea are available, childhood diarrheal disease is still among the leading causes of mortality and morbidity.[1,2] In 2016, mortality due to diarrhoea was 22·4 deaths (16·8–32·0) per 100,000 globally. Higher rates were recorded among children younger than 5 years (70·6 deaths per 100,000) and among individuals older than 70 years (171·7 deaths per 100,000. In the same year, diarrhoea contributed 8.9% of all deaths in children younger than 5 years. The estimated episodes of diarrhoea among children younger than 5 years were 1,105,406,865 which translated into 1.75 episodes (1·52–2·02) per child.[3] The highest burden of diarrheal related mortality is carried by developing countries with nearly four fifths of all under-five mortality occurring in Sub-Saharan Africa and south Asia.[4,5]

Substantial progress has been made globally in reducing the burden of diarrhoeal diseases, driven by decreases in several primary risk factors. However, this reduction is not equally distributed across locations. Evidence shows that diarrhoeal diseases disproportionately affect communities with poor access to health care, safe water, and sanitation, and low-income or marginalised populations.[6] In Tanzania, diarrheal diseases are major contributors to under-five mortality. According to the 2016 Tanzania Demographic and Health Survey report, 12% of under-five children had a diarrheal episode in the 2 weeks prior to the survey.[7] The 2016 Tanzania Demographic and Health Survey reported that while there was no notable difference in diarrhoea prevalence among children by source of household drinking water and toilet facility, the prevalence varied with mother's le vel of education and household wealth.[8]

Several other studies conducted in Tanzania and elsewhere have also reported similar and varying prevalence and incidences of diarrhoea among under-five children.[9-12]

The areas where artisanal mining activities are taking place are characterised with high population and poor provisions of water, hygiene and sanitation services. As a result, these areas have a high burden of water borne diseases. Previous study conducted in Geita region, reported two weeks' diarrhoea prevalence of 28.3% among under-five children and 15.5% among their mothers/caretakers.[12] It should be noted that there is paucity of data regarding the magnitude of diarrheal disease burden among individuals aged five years and above living in mining areas of Geita. This study was conducted with the aim to determine prevalence and incidence of diarrhoea among individuals living in randomly selected households in Busolwa and Mgusu wards in Geita region, Tanzania. The results of this study will be used to increase knowledge on the burden of diarrhoea in the selected villages which are in proximity to mining areas, and monitor and evaluate the effect of Nano Maji Filter System (NNM) intervention on health outcomes.

Intervention with Nano Maji Filter System (NNM)
NNM is a water treatment system designed to remove heavy metals and microbial contamination in water. In this survey, we undertook a randomised controlled field trial to evaluate the effectiveness of NNM system to remove heavy metals and microbial contaminants in domestic water. The primary outcome of the trial was to reduce episodes of diarrhoea at 6months post-randomisation. Secondary outcomes were to improve water, sanitation and hygiene (WASH) status. The trial was implemented in 3 villages of Geita where 64 households were selected to receive the intervention (NNM system and WASH education) and 128 households were put in control arm (continue with usual practice). At baseline, information on episodes of diarrhoea in the past one week prior to ther survey was collected for all participating household members. Weekly visitations were made to participating households for a period of 3 months. Individuals in these households were the unit of analysis for estimation of prevalence and incidences of diarrhoea.

METHODS
Study Site
Most mines are located in remote areas and they lack adequate sanitation, thus making individuals living in these areas vulnerable to waterborne diseases.[13] For this reason, villages located in mine areas in Busolwa and Mgusu wards were selected. The selected wards are situated in Geita which is one of Tanzania's 31 administrative regions. It comprises of 5 districts and 6 councils, one of which (Geita) is a town council. The districts are divided into divisions that are further sub-divided into wards, villages, and sub- villages (hamlets). In total, the region is made up of 21 divisions, 122 wards, 474 villages, 65 streets, and 2219 sub-villages or hamlets.

The region covers an area of 20,054 square kilometres (7,743 square meters),bordered by Lake Victoria to the east, and home to Tanzania's largest gold mining industries. The Geita Gold Mine is the largest mining operation located within Geita Region, 4 km west of the town of Geita. Other major industries in the region are agriculture and fishing. Geita Region has moderate temperatures of between 220 degrees Centigrade and 300 degrees Centigrade with average rainfall ranging from 900 mm to 1200 mm per annum. Rainfall is fairly evenly distributed with short rains from September to December followed by a dry spell from January to February before long and heavy rains set in from March till the end of May. From June to September the region is subjected to dry season. During the hot season, humidity is 35%, and rises up to 60% during the rainy season. Water supply in Geita Region is satisfactory with Lake Victoria serving as the main water source in the area. Other water sources include rivers, streams, shallow wells, bore holes, rain water harvesting and springs. The demand for water in this region is driven by human and livestock population. In 2018, demand for water in Geita Region was reported at 53,149 cubic meters (m³) against availability of 27,637.5 m³, which is 53% of the region's total demand. Water supply in urban areas (i.e. Geita Town, Chato Town and Bukombe Town) was at 41%.[14]

Study Design
A cross sectional study was conducted to generate baseline data which was used to monitor and evaluate the performance and effect of NNM water filter system in removing heavy metals and microbial contaminations from domestic water.

Study Population
Study population include all individuals residing in selected households for a randomised field trial to evaluate the effectiveness of NNM water filter system in removing heavy metals and microbial contaminants from domestic water.

Sample Size
Sample size was calculated using StatCalc - Epi Info™ 7 which is an online sample size calculator. The assumptions used in sample size calculation were; 80% study power, 95% Confidence Intervals (CI), and risk ratio of 1.84 for exposed group (control arm), the calculated Kelsey sample size was 194 households. (Control group 129 and experiment group 65). Information on the occurrence of diarrhoea was collected from all individuals residing in each of the selected 194 households involved in the trial.

Sampling procedures
While wards and villages were purposeful selected, households were systematically selected from the list of all households with at least one child under the age of 5 years obtained from the 3 Village Executive Officers (VEOs). For each village, the total number of required households was divided by the total number of households in the sampling frame to get a number which was used to select the first and the next household. A total of 3 villages were selected from 2 wards (two villages from Mgusu ward and one village from Busolwa ward). From each village, 68 households were selected.

Inclusion Criteria
Villages were selected based on availability of water sources which are used by at east 80% of the population,

availability of health facility and proximity to the mining areas. Selection of household was based on availability of at least one child under the age of five years living in the household.

Exclusion Criteria
The village was excluded if it lacks health facility and a common water source which is used by at least 80% of village population, and not located close to the mining areas. Households without a child under the age of five years were also excluded from the sampling list.

Ethical Considerations
The study was reviewed by the National Health Research Review Committee (NatHREC) and granted certificate of approval with number NIMR/HQ/R.8a/Vol.IX/3045. Permission to conduct the study was obtained from local government authorities in Geita at all levels (region, district, ward and village).

The study used written informed consent form (ICF) for adults (18+ years). The form contained a general description of the study (e.g., procedures, lengths, goals and objectives) as well as a statement on risks and benefits associated with the study and an explanation of key rules such as confidentiality and voluntary participation. Contact information for the research team were also provided in case participant wished to reach out for further clarifications.

Verbal permission was sought for from household members aged 10 to 17 years to allow respondents share their information on diarrhoea episodes. Respondents and household members were assured that their decision not to participate in the project or to be interviewed or not to answer certain questions or to stop the participation at any stage of the study was ok and would not jeopardize their rights to access medical care or other social services.

Data Collection and Analysis
The study adopted data collection tools which were used to estimate one-week incidence and prevalence of diarrhoea among children under the age of five years in Mkuranga distriict.[10] The adopted data collection tools were translated into Swahili. Translation was done by native qualified translators and were back translated by a different person who had not seen the English questionnaire to see if the tools had the same meaning. Any inconsistencies in the translation were addressed. The approved translated tools were scripted into a table format. The tools were administered by Research Assistants who underwent a 3-day training prior to the data collection exercise.

Of the 486 eligible households in the intervention arm (Busolwa), 65 households were sampled and consented to participate in the project. In control arm, 995 households were eligible but the study sampled only 121 households, the response rate was 100%. Interviews with heads of households, observations and census of household members were the methods of data collection employed by this study. In the event that the head of the household was not present, any other member of household aged 15 years and above was interviewed. The tool used in the previous study[10] collected information on respondents' hygiene practice and knowledge, water

treatment practice and household sanitation, captured information on occurrence of episodes of diarrhoea among children below the age of five years and adults residing in visited households. Encouraged by other researchers,[14,15] this study used the World Health Organization's definition of diarrhoea to assess episodes of diarrhoea.[16]

Knowledge on hygiene was assessed by 9 items which had yes and no responses. Respondents were asked when is the critical time to hands. The final score was obtained by summing the items and then dichotomised into less and comprehensive hygiene knowledge.

Sanitation score was constructed by summation of five main observations around the household. These included presence or absence of animal or human faeces, trash and pit for dumping trashes around the homestead and utensil drying rack. Presence was coded 1 and absence 2. The sanitation score was constructed by adding all the five items and then dichotomised responses into poor sanitation and good sanitation.

Water situation was assessed by rating households' main water source, the practice of storage and treatment of drinking water and the practice of drawing water from the storage container. First, the water sources were rated as safe (coded 1 and included borehole) or not safe (coded 2 included shallow well, river, pond, lake, canal and stream). Frequency of each water treatment method was rated as always (coded 1), sometimes (coded 2) rarely (coded 3) and never (coded 4). After summation of frequencies of all the water treatment methods, the score was dichotomised into adequate water treatment practice (coded 1) and inadequate water treatment practice (coded 2). Water storage practice was coded 1 if the household use gallon, 2 if uses pot and 3 if the household uses bucket with no cock. However, in the analysis code 2 and 3 were combined and ended up with good water storage practice (code 1) and poor water storage practice (code 2). The practice of drawing water from the storage container was assessed by asking respondents to select the appropriate option which included a cup used only for drawing water (coded as 1), a cup used for drawing water and sometimes for drinking (coded as 2) and a cup used for both drawing and drinking (coded as 3). In the analysis, option 2 and 3 were merged and therefore this item remained with two options 1 being good water drawing practice and 2, poor water drawing practice. To get a composite index for water situation, the four items were summed up (water source safety, and water treatment, storage and drawing practices) with high score indicating poor water situation. The study used mean score as the cutoff point for dichotomising the resulted scores into good water situation coded as 1 and poor water situation coded as 0.

Occurrence of diarrhoea was assessed by asking respondent if any member of the household had diarrhoea in the previous 7 days. If the answer is yes, the respondent was asked on which days member of the household had diarrhoea and how frequently a person passed out loose or watery stool within 24 hours. In addition, respondents were asked how long the diarrhoea lasted (number of days with diarrhoea).

The approach used by Mashoto et al[10] to assess wealth index was adopted. Household assets such as house, toilet, land, radio, motorcycle, bicycle, car, phone, cow,

pig, goat, sheep, donkey, chicken and duck were recorded as 1 "available and functioning" and 0 not available or available not functioning. Use of sources of energy for cooking i.e. electricity, kerosene oil, fire woods, gas and solar were recorded as 1 "yes" or 0 "no". Assets and sources of energy for cooking were analysed using principal components analysis (PCA). The first component resulting from the analysis was used to categorise households into 4 approximate quintiles of wealth ranging from the 1st poorest to the least poor 4th quintile.

Data was analysed using IBM SPSS Statistics for Windows version 19.0 (IBM Corp, Armonk, NY, USA). Continuous variables were summarized into mean and standard deviation while categorical ones were summarised into proportions. Chi- square test and multi nominal logistic regression were applied to determine factors influencing knowledge of causes of diarrhoea. We calculated the prevalence of diarrhoea as the percentage of individuals suffering from diarrhoea assessed during a 7-day period.

Data Management
The data was entered automatically using the data collection software during the fieldwork. There were limited number of paper versions of the survey available to the interviewers in case of any problem with electronic devices; paper-based data were entered into the electronic devices at the end of the day when there was a connection. All data were checked on a daily basis via random verification checks by the field monitoring team. The data was checked for duplicated entries, outliers, spurious codes. Additional cross-checking was done to triangulate and eliminate entries with mutually exclusive answers on a range of questions. The team used call-backs to verify spurious or suspicious answers with the respondents. Where not possible, entries containing such answers were removed.

Two data sets were maintained – one with the respondent personal and contact information and the other one with the actual responses to the survey questions including diarrhoea information for all household members. Only the senior research team had access to the dataset with the respondent identifiable data.

RESULTS
Out of 194 households, interviews were possible in 186 households (response rate 95.9%). A total of 1,281 individuals (1,070 above 5 years and 211 under the age of 5 year children) lived in 186 households (on average household had 7 individuals). Almost 60% of the respondents were married male peasants who attained primary school education level. The majority of households (62.1%) use traditional pit latrine (Figure 1). Over 70% of the households have poor water situation in terms of water storage, treatment and practice of drawing water from the storage container. In 76.8% of the visited households, drinking water is not treated. Significantly high proportion of households in the intervention arm do not treat drinking water (Table 2).

Slightly over one third of the interviewed individuals reported to always use running water to wash their hands at critical moments. However, consistence use of soap when washing hand was affirmed by 16% of the -

respondents (Table 2). In few of the visited households, visible human and animal stools were spotted on the surroundings, and about a third of households had pit for dumping trash. The total sanitation score being lower in the control arm than in the intervention arm (Table 3).

The reported one-week prevalence and incidence of diarrhoea among 1,281 individuals living in the surveyed 186 households was 10.8% and 8.4% respectively. Individuals living in households allocated for intervention and control were equally affected with diarrhoea (Table 4). Compared to adults (5.6%), children under the age of five years had high incidence (22.7%) of diarrhoea. Within group variation existed with boys under the age five years being more affected than girls (Table 5). Table 6 depict results of multivariate analysis which indicate that individuals with diarrhoea were more likely to live in the households which occasionally use soap for hand washing (OR 6.3; 95% CI, 1.9 to 21.4) and less likely to use toilets (OR 0.1; 95% CI,0.03 to 0.4).

FIGURE 1: Types and Status of Households' Latrines
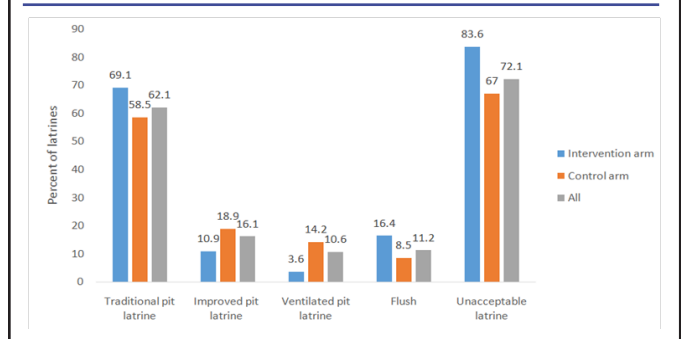
DISCUSSION
Provision of access to safe water, sanitation and hygiene are the most impactful interventions for reduction of diarrhoea. Poor water situation coupled with inadequate household sanitation and limited hygiene practice exposes both adults and under-five children to diarrhoea. One in four households are at risk of consuming contaminated drinking water, increasing their susceptibility to episodes of diarrhoea, particularly in under-five children who had high diarrheal incidence and prevalence than adults. The incidence and prevalence of diarrhoea among children under the age of five years reported in this study are higher than what have been reported in Mkuranga district[10] but lower than the incidence revealed by systematic review of diarrheal incidence in low and middle income countries[16] and diarrhoea prevalence reported in rural area of Nigeria.[17] However, the Nigeria study assessed two-weeks diarrhoea prevalence while the current and the previous studies conducted in Tanzania assessed one-week prevalence.

Previous studies have demonstrated that low socioeconomic status, lack of education, poor water storage practices, use of unsafe water, poor sanitation and overcrowding in terms of high number of children under the age five years living in a household are risk factors for diarrhoea.[10,18-21] In the present study, individuals

TABLE 6: Factors Associated with Diarrhoea (Those with Diarrhoea)

R2 = 0.229	OR	95% CI	P value
Sex			
Females	0.6	0.2 – 1.9	0.402
Males	1		
Wealth Index:			
Less poor quintile	0.8	0.6 – 4.4	0.842
Least poor quintile	1.3	0.3 – 0.5	0.691
Poorer quintile	0.5	0.1 – 2.3	0.374
Poorest quintile	1		
Intervention group			
Yes	1.6	0.6 – 4.3	0.307
No	1		
Household water situation			
Good	1.1	0.3 – 5.0	0.858
Poor	1		
Defecation place			
Toilet	0.1	0.03 – 0.4	0.002
Open	1		
Wash hands at critical moments			
Yes	1.1	0.4 – 3.2	0.811
No	1		
Use running water to wash hands			
Yes	0.31	0.1 – 1.1	0.070
No	1		
Soap use to wash hands			
Occasionally	6.3	1.9 – 21.4	0.003
Always	1		

belonging to the poorest wealth quintile were more likely to have diarrhoea but the significant association disappeared in the multivariate analysis. Our study adds to the body of knowledge that use of toilets and soap when washing hand is critical for prevention of diarrhoea.

Results of our study revealed that children under the age of five years have high incidence and prevalence of diarrhoea than individuals aged 5 years and above. However, in the first stage of multivariate analysis, the significant association between prevalence of diarrhoea and age disappeared. Thus, in order to prevent or reduce episodes of diarrhoea among children and adults, it is important to implement water, sanitation and hygiene interventions at individual, household and community levels.

The observed differences in the water treatment practice and sanitation status between households in intervention and control arm disappeared in the multivariate analysis, and thus it is unlikely such slight difference will have any impact on outcome of the trial.

Study Limitations
It should be noted that the prevalence of diarrhoea is seasonal and subject to the respondent's reporting of the episode of diarrhoea. We collected data during dry season and hence the reported prevalence and relied on

information provided by respondent on behalf of him/herself and other members of the household. Thus it is possible that the study under estimated the incidence and prevalence of diarrhoea due to both seasonal variations and recall bias or respondent not having correct information on diarrhoea episodes for all of his/her household members because they did not disclose the information to the respondent.

CONCLUSION
Substantial proportion of individuals living in the study area are affected by diarrhoea. Children below the age of five years are more affected than individuals aged five years and above. However, it is likely that the study under estimated the incidence and prevalence of diarrhoea among individuals aged 5 years and above due to the biases described in the study limitations section. Nevertheless, the study provides baseline data for monitoring and evaluating the health outcome of NMM water filter system.

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TABLE 1: Response Rate and Respondents' Profile

	Intervention arm (n= 65)	Control arm (n = 121)	All (N = 186)
Response rate	100%	94.5%	96.9%
Mean Age (SD)	40.9 (10.7)	44.2 (11.5)	43.0 (11.3)
Sex			
Males	58 (89.2)	98 (81.0)	156 (83.9)
Females	7 (10.8)	23 (19.0)	30 (16.1)
Position in houses			
Head of house	25 (38.5)	88 (72.7)**	113 (60.8)
Spouse/Partner	30 (46.1)	24 (19.8)	54 (29.0)
Child/Relative	10 (15.4)	9 (7.4)	19 (10.2)
Marital status			
Married	39 (60.0)	71 (58.7)	110 (59.1)
Cohabiting	21 (32.3)	29 (24.0)	50 (26.9)
Other	5 (7.7)	21 (17.4)	26 (14.0)
Went to school			
Yes	63 (96.9)	100 (82.6)	163 (87.6)
No	2 (3.1)	21 (17.4)**	23 (12.4)
Education level			
Primary school	56 (88.9)	82 (82.0)	138 (84.7)
Secondary school	7 (11.1)	18 (18.0)	25 (15.3)
Occupation			
Peasant/livestock keepers	45 (69.2)	65 (53.7)	110 (59.1)
Small business	11 (16.9)	28 (23.1)	39 (21.0)
Employed	0 (0.0)	5 (4.1)	5 (2.7)
Small scale mining	9 (13.8)	23 (19.0)	32 (17.2)
Wealth Index			
1st least poor	17 (26.2)	37 (30.6)	54 (29.0)
2nd poor	23 (35.4)*	24 (19.8)	47 (25.3)
3rd poor	16 (24.6)	25 (20.7)	41 (22.0)
4th poorest	9 (13.8)	35 (28.9)*	44 (23.7)

*P<0.05; **P<0.001

TABLE 2: Respondents' Wash Hand Practice, and Households' Water and Hygiene Status

	Intervention arm (N= 65)	Control arm (N = 121)	All (N = 186)
Household do not treat drinking water	80 (86.0)*	82 (69.5)	162 (76.8)
Household poor water storage	29 (31.2)	42 (35.6)	71 (33.6)
Household poor water situation	71 (76.3)	93 (78.8)	164 (77.7)
Respondents wash hands at critical moments	30 (32.3)	48 (40.7)	78 (37.0)
Respondent always use running water to wash hands	40 (43.0)	39 (33.1)	79 (37.4)
Respondent always use soap to wash hands	15 (16.1)	19 (16.1)	34 (16.1)
Always respondent use toilet	80 (86.0)	108 (91.5)	188 (89.1)
Knowledge on soap kill germs	60 (92.3)	108 (89.3)	168 (90.3)

*P<0.05

TABLE 3: Household Hygiene and Sanitation

	Intervention (n = 65)	Control arm (n = 121)	All (N = 186)
Human stool near house	3 (4.6)	5(4.1)	8 (4.3)
Animal stool near house	16 (24.6)	16 (31.2)	32 (17.2)
Trash near house	32 (49.2)*	42 (34.7)	74 (39.8)
Pit for dumping trash	17 (26.2)	34 (28.1)	51 (27.4)
Utensil rack	11 (16.9)	38 (31.4)*	49 (26.3)
Household Sanitation Score			
Good	37 (56.9)	85 (70.2)	122 (65.6)
Poor	28 (43.1)*	36 (29.8)	64 (34.4)

*P<0.05

TABLE 4: One-Week Incidence and Prevalence of Diarrhoea among Individuals Living in Households Assigned to Intervention and Control Arm

	Intervention (n =524)	Control (n = 757)	All (N = 1281)
Diarrhoea events	48	60	108
Incidence (%)	9.2	7.9	8.4
Prevalence (%)	62 (11.8)	76 (10.0)	138(10.8)

TABLE 5: One-Week Incidence and Prevalence of Diarrhoea among Individuals Living in the Surveyed Households by Age Group (N = 1281)

	Incidence		Prevalence	
	<5 years	≥ 5 years	<5 years	≥ 5 years
All	22.7**	5.6	29 (13.7)	109 (9.5)
Sex				
Males	43.6**	0.7	18 (17.8)*	51 (9.7)
Females	20.0	9.0**	11 (10.0)	58 (10.7)
Group				
Intervention	20.4	3.7	15 (16.1)	47 (10.9)
Control	24.6	6.9	14 (11.9)	62 (9.7)
Wealth index				
Less poor quintile	15.4	1.8	9 (13.8)	24 (7.4)
Least poor quintile	22.8	9.8*	9 (13.8)	36 (12.2)
Poorer quintile	6.4	2.7	4 (8.5)	22 (8.6)
Poorest quintile	52.4**	9.3*	7 (16.7)*	27 (14.0)*

*P <0.05; **P< 0.001

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ORIGINAL ARTICLE

Proportions of Pathogenic Bacteria Isolated from Door Locks and Working Benches in Clinical Laboratory: A Laboratory Based Study

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ABSTRACT

Background: Numerous studies have revealed the association of the door handle and contamination of pathogenic bacteria. Door handles of clinical and research laboratories have higher chances of contamination with pathogenic bacteria during closing and opening with contaminated gloves on, or sometimes after visiting the toilets without the use of disinfectant materials. There is limited epidemiological data regarding bacteria cross contamination of door locks of the Clinical laboratory at Kilimanjaro Christian Medical Centre. This study aimed at providing the proportions of bacteria contaminating medical laboratory doors
Methods: A cross section laboratory-based study was conducted and it involved collection of swab samples from doors and working benches in the clinical laboratory
Results: Prevalence of *Staphylococcus aureus, Escherichia coli*, Coagulase Negative *Staphylococcus, Bacillus spp., Pseudomonas aeroginosa* and coliforms were (26%, 22%, 18%, 8%, 4% and 4% respectively.
Conclusion: This study has reported high proportion of pathogenic bacteria. The results entails that, internal and external environments are responsible for laboratory door contamination.

BACKGROUND

A door lock is a mechanical or electronic fastening device that is released by a physical object (such as; a key, keycard, fingerprint, RFID card, security token, coin, etc.), by supplying secret information (such as a number or letter permutation or password), or by a combination thereof or only being able to be opened from one side such as a door chain.[1] Numerous studies have revealed the association of the door handle and contamination of pathogenic bacteria.[2,3] Door handles of clinical and research laboratories have higher chances of contamination with pathogenic bacteria during closing and opening with contaminated gloves on, or sometimes after visiting the toilets without the use of disinfectant materials.[4] Laboratory workers may acquire infection or be contaminated with these pathogenic bacteria after holding the contaminated door locks.[1,5] A study conducted in Morocco in 2017 reported that 176(88%) of collected swabs from different hospital surfaces had positive bacterial growth. Gram-negative and positive isolates were 51.5% (101/196) and 48.5% (95/196) respectively. The main isolates being *Enterobacter* (31.6%), *Staphylococcus aureus* (24%), *Pseudomonas aeroginosa* (9.2%) and *Acinetobacter* spp (3.3%).[6]

Another study conducted in Nasarawa State University, Keffi, Nigeria, reported that out of a total of 200 handles sampled, 34 (17%) *E.coli* isolates were identified.[7] Other studies have also shown that 50% of healthcare associated infections are due to contaminated medical devices.[8,9] According to a World Health Organization (WHO) report, the incidence of Health Care Associated Infections (HCAI) is still high in many parts of the world including Tanzania.[10] Overall prevalence of HCAIs in developed countries varies between 5.1% and 11.6%, while the overall prevalence of HCAIs in Tanzania is approximately 14.8% which is high compared to prevalence in developed countries. A study conducted in Altnagelvin hospital showed that among pathogenic bacteria contaminating door frames, *Pseudomonas aeruginosa* was the predominant bacteria species.[11]

Contaminations from door locks or door handles associated infections are infections that an individual can get when they come in contact with the door that is contaminated with such pathogenic bacteria and such infection was not present at the time before contact, and the source of the bacterial contaminants is from the environment.[12,13,14]

In some cases, the microorganism originates from staff's own skin, normal flora becoming opportunistic after touching or doing other procedure that compromise the protective skin barrier.

One of the studies that was conducted in Ghana reported that door handles had the highest isolation[23] and the highest number of differential isolates were from working surfaces.[7] Of the total bacterial isolates, 46.14% were pathogenic, with *S. aureus* being the highest (14.42%), while 53.86% were non-pathogenic, made up of 45.2% of *Bacillus spp.*[15] Other studies conducted in Volta regional hospital in Ghana with an estimate of 218 swab sample taken from door handles and working benches showed that a total of 187 (88.8%) bacterial isolates were obtained from the swabs (*P<.0017*) made up of 55.5% non-pathogenic isolates, 33.3% pathogenic isolates and 14.2% no bacteria growth. There was significant difference between pathogenic isolates and no bacterial growth (*P=.0244*). The largest pathogenic isolates were S. aureus (57.6%) and *E. coli* (39.4%) whilst *Bacillus spp.* was the only identified non-pathogenic isolate.[16] Another study conducted in Ghana in 2017 had a total of 120 swab samples taken from door handles, stair railings and other points of contact at Tamale Teaching Hospital, Tamale Central Hospital and Tamale West Hospital; a total of 47 (39%) positive *S. aureus* samples were isolated from door handles of the 3 hospitals. These findings are in line with what was reported other studies conducted in Ghana and Nepal.[17,18] Although staff members might not get infected due to contaminated door handles and working benches, patients with open wounds like burns and scratches may be at high risk to infection.

Bacterial cross-contamination is mostly reported to be high in door handles which are never cleaned with cleaning agents or never cleaned at all.[19] A study conducted in Japan, described the survival of bacteria under dry conditions, mycobacterium species were detected more than two months after inoculation, since most gram positive and gram negative bacterial can survive for weeks up to months under dry condition.[20] This fact potentiates regularcleaning and disinfection of working benches and would involve implementing protocol based guidelines for cleaning and decontaminaion.[21] These procedures must be performed more often during working hours so as to minimise chances of contamination among workers.[22,23] Failure to perform appropriate disinfection and decontamination can lead to spread of pathogenic bacteria and multidrug resistance organisms.[24]

There is limited epidemiological data regarding bacteria cross contamination of door locks of the Clinical laboratory at Kilimanjaro Christian Medical Centre. This study aimed at providing the proportions of bacteria contaminating medical laboratory doors. The study results will ultimately promote infection prevention and control programs of healthcare associated infections.

METHODOLOGY
Study Design, Period and Study Area
A cross section laboratory-based study was conducted and it involved collection of swab samples from doors and working benches in the clinical laboratory. In and out door handles and working benches with higher chance of contamination were considered. Door handles which are not in use or closed doors and working bench with minimal exposure to contamination for a period of more than one month prior to the time of the study were excluded.

The study was conducted from July to August 2020. A total of 34 swab samples were collected; 14 swab samples collected from the inside and outside door locks respectively, and 6 swab samples from the working benches. The study was conducted at Kilimanjaro Christian Medical Centre (KCMC), department of Clinical laboratory located in Moshi, Kilimanjaro, North East Tanzania. KCMC hospital is one of the 4 Zonal consultant hospitals of Tanzania. The hospital is 70Km away from Arusha, situated on the slopes of mount Kilimanjaro (M8JG+2X7 on google map).

Sample Population and Sampling Method
Samples were collected from clinical laboratory door handles (inside and outside) and working benches. All door handles and sample reception benches and sample processing benches were sampled in the study. Sample size was calculated by using TaroYamane formula $[n=N/(1+Ne^2)]$[31] and a minimum sample size of 25 was estimated. The study collected 34 samples.

Sample Collection
Sterile cotton swabs were moistured using sterile normal saline and used for sample collection on both external and internal surface of door handles and working benches. All swabs were put into stuart media for transportation to the microbiology laboratory. Samples were given unique identification numbers and were all immediately transported to Microbiology departments for microbiological analysis.

Culture for Swabbed Doors and Benches in Laboratory Sections
34 swab samples were collected; 14 samples were from the inside and out door locks respectively, making a total of 28 swab samples plus 6 swab samples that were collected from working bench surfaces, making a total of 34 swab samples.

Bacteria Culture
Bacteria culture was used to isolate specific bacteria. Quantitative culture method using calibrated loop technique was used by streaking on the following media;

Sheep blood agar (BA): This was used for growth of both gram positive and gram-negative bacteria. Gram positive bacteria show characteristics of haemolysis of blood and are classified as alpha, beta and gamma haemolysis.

MacConkey Agar (MCA): Was used for growth of gram-negative bacteria in order to classify lactose from non-lactose fermenters. All the inoculated plates were incubated in the incubator at 35 to 37°C for 18 to 24 hours. The growth rate on culture plates was quantified as +1, +2, and +3 for the growth on primary, secondary and tertiary streaking on the culture plate respectively.

Biochemical tests were performed in order to properly identify the bacteria to spp levels.

Tests such as; Triple Sugar Iron (TSI), Simon's citrate test, Urease test, Sulphur-Indole-Motility agar (SIM), Catalase

test, Coagulase test and Oxidase test were performed according to Clinical Laboratory Standard Institute guidelines-M100 (32).

Bacitracin and Optochin
Bacitracin and optochin were used to identify group A and beta haemolytic Streptococci species respectively by assessing the sensitivity or resistance of the two discs. Optochin disc is sensitive to Streptococcus pneumonia, while bacitracin is sensitive to *Streptococcus pyogenes*. Other Streptococcus species such as *S. agalactiae* were identified by using CAMP test and bile esculin was used to identify Enterococcus faecalis *(E. faecalis)*

Novobiocin
This disc was used to differentiate coagulase negative Staphylococcus species. *Staphylococcus epidermidis* is sensitive to novobiocin while *Staphylococcus saprophyticus* is resistant to novobiocin disc.

Quality Control
Quality control was performed to all biochemical identification test and all media by using ATCC control strains. For performance control, *E. coli* ATCC 25922 (Ref. R4601971. Thermo scientific Lenexa KS 66215 USA), *Pseudomonas aeruginosa* ATCC 27065 (Ref. R4607892. Thermo scientific Lenexa KS 66215 USA) and *S. aureus* ATCC 25923 (Ref. R4609022. Thermo scientific Lenexa KS 66215 USA) strains were used as reference strains. These control Bacteria were inoculated on MCA for lactose and non-lactose fermenters respectively and *S. aureus* onto blood agar. Also, these strains were used in different identification tests such as; catalase test, coagulase test and oxidase test. For sterility control, the media were incubated at 37°C, incubator for 18 to 24 hours to see if the media were contaminated or not.

Data Management and Data Analysis
Every sample was given its identification number, data was recorded in a logbook before being transferred to excel sheet for coding and cleaning. Coded and cleaned data was then transferred to STATA version 14 for analysis. Tables and figure were used to summarise the results in form of percentage proportions.

Ethical Considerations
The study was approved by Kilimanjaro Christian Medical University College (KCMUCo) ethical committee with certificate number PG 12/2020., Permission to conduct the study was requested from Kilimanjaro Christian Medical Centre administration via the Head of the Clinical Laboratory department.

RESULTS
General Results from the Cultured Samples
From the 34 samples recruited, total isolates were 50; of which 45 were from door lock and 5 from the surface of working benches with some samples having mixed bacteria isolated. The inner door lock surfaces had a total of 18 isolates and 32 isolates were from outer door lock surfaces and working benches (Table 1).

Proportion of Bacteria Isolated from the Door Locks and Working Benches (N=50)
The overall door lock swabs were 28 which resulted into

45 isolates. In door locks were highly contaminated by pathogenic *E. coli* (8.0%) and *S. aureus* (12.0%) and out door lock were also highly contaminated with same the pathogenic *E. coli* (8.8%) and *S. aureus* (14.0%), however, Coagulase negative Staphs isolates were high (18.0%) (Table 2).
Figure 1

Overall Proportions of the Bacteria Isolated
Prevalence of *S. aureus*, *E. coli*, Coagulase Negative *Staphylococcus*, *Bacillus spp.*, *P. aeroginosa* and coliforms were (26%, 22%, 18%, 8%, 4% and 4% respectively. Other bacteria isolates and moulds account for 18%, each of which contributing to less than 2% (Figure 2).

FIGURE 1: Schematic Presentation of Sampling

FIGURE 2: Overall Bacterial Isolates (N=50)
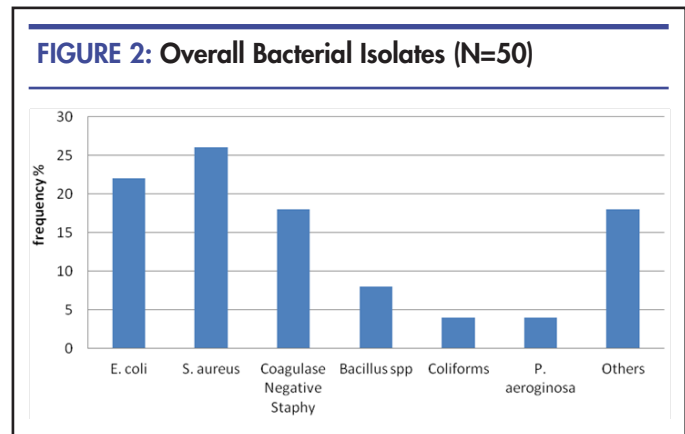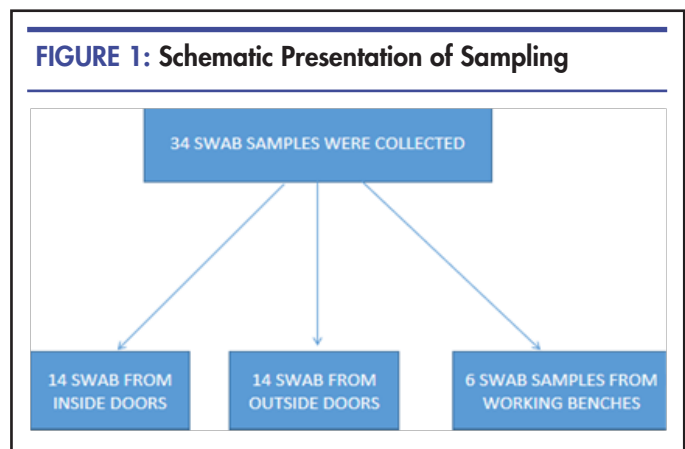
DISCUSSION
The high rate of hospital associated infections are associated with contaminations that occurs as a results of poor hygienic practices and failure to adhere to proper hospital infections control programs.[1] The high rate of contamination is facilitated by practices such as; inappropriate operation of doors while wearing contaminated gloves, use of toilets without washing hand and non-use of disinfectant material.[3]

This study reported high proportion of bacteria colonising the studied sites (73%). This is high when compared to a study conducted in U.S.A involving elevator buttons of

TABLE 1: Culture Results for Swabbed Doors and Working Benches in the Laboratory (N=50)

Section/Area	Sample	Out lock (sample A)	In lock (sample B)	Total isolates
Sterility	Control 1	-	-	Pass
Performance	Control 2	-	-	Pass
Swab	Control 3	-	-	Pass
Microbiology	S1	S. aureus	No Bacteria growth	1
Chemistry 1	S2	No Bacteria growth	S. aureus, E. coli, CNS	3
Hematology	S3	E. coli	No Bacteria growth	1
Serology	S4	S. aureus, CNS	No Bacteria growth	2
Doctors waiting area door	S5	E. coli, S. aureus, Bacillus spp	Coliforms, S. aureus, Bacillus spp	6
Reception door	S6	CNS	S. aureus	2
Molecula Biology 1	S7	No Bacteria growth	No Bacteria growth	0
Secretary door	S8	S. aureus, E. coli, CNS	-	3
Exit door	S9	E. coli, S. aureus, Citrobacter spp	E.col, CNS	5
Changing room	S10	CNS, Corynebacterium	S. aureus, Citrobacter spp	4
Molecular Biology 2	S11	S. aureus, CNS, Bacillus spp	Enterococci	4
Chemistry 2	S12	No Bacteria Growth	E.coli	1
Board room	S13	E. coli, P. aeroginosa	Coliforms	3
Parasitology	S14	Citrobacter spp	No Bacteria growth	1
Sluice room	S15	E. coli, CNS	P. aeroginosa, E. coli, Bacillus spp, Mould	6
Store 1	S16	S. aureus,	-	1
Store 2	S17	CNS, Corynebacterium	-	2
Store 3	S18	No Bacteria growth	-	0
Working Benches				
Blood transfusion	S19	E. coli, S. aureus corynebacterium	-	3
Reception bench	S20	S. aureus, GPC undetermined	-	2
Total isolates		**32**	**18**	**50**

Key: CNS is Coagulase Negative Staphylococcus; GPC is Gram positive cocci; NLF is Non   Lactose fermenters
     1-6 Number of isolates

4 different hospitals which reported the proportion of bacteria colonisation to be 61%.[34] The high proportion of bacteria colonisation reported in this study can be explained by the fact that, samples in this study were collected from the laboratory area, which is the most contaminated area in the hospital since it is where infectious materials are handled. The study reported high number of Bacteria isolate from the door locks and working benches. The leading bacteria isolates reported are; *S. aureus* followed by *E. coli* and Coagulase Negative Staphylococcus accounting for about 26%, 22% and 18% respectively. These findings are in line with previous studies conducted elsewhere. [5, 25] However, this study reported slightly higher proportion of *E. coli* isolated from doors compared to a study which was conducted in Nigeria.[33] The differences in the two study's findings can be accounted for by the fact that, the Nigerian study was conducted in a University premises doors. Such doors are obviously less likely to be as contaminated as Clinical laboratory doors. Hospital environment is highly contaminated and substantially infectious and thus,

chances of isolating high number of pathogenic bacteria in such an environment is high.[25,26] Furthermore, in a study conducted in USA[5], the predominant bacteria isolated reported was *S. aureus* and this is in line with this study's results, however, the proportions of the S. aureus in the current study is low compared to the USA study. This might have been attributed by the larger samples size utilised in the USA study.

With the rapid increase of the point prevalence of nosocomial infections among hospital inpatients in developing countries, there is still a big challenge on how best hospital associated infections can be controlled.[27] Despite the differences in the compared studies' set ups and geographical locations, the colonisation of bacterial in hospital settings is still high and poses a substantially high risk of continued exposure of healthcare workers, patients and patients relatives.[27,28]

This study also reported significant proportion of Coagulase Negative Staphylococci, which is in line with studies conducted in Florida USA, detailing with the fact

TABLE 2: Percentage proportion of the Bacteria Isolated (N=50)

	In lock n(%)	Out lock n(%)		Total N(%)
Total Bacteria growth	9(26.5)	16(47.0)		25(73.5)
Total Negative growth	5(14.7)	4(11.8)		9(26.5)
			Total	**34(100)**
Bacteria isolated				
E. coli	4 (8.0)	6(12.0)		10(20.0)
S. aureus	4(8.0)	7(14.0)		11(22.0)
Citrobacter spp	1(2.0)	2 (4.0)		3(6.0)
Corynebacterium	0(0)	2 (4.0)		2 (4.0)
Enterococci	1(2.0)	0(0)		1(2.0)
P. aureginosa	1(2.0)	1(2.0)		2 (4.0)
CNS	2 (4.0)	7(14.0)		9(18.0)
Coliform	2(4.0)	0(0)		2 (4.0)
Bacillus spp	2(4.0)	2(4.0)		4(8.0)
mould	1(2.0)	0(0)		1(2.0)
	Working benches surface	Bench surface		
E. coli	-	1(2)		1(2)
S. aureus	-	2(4)		2(4)
Corynebacterium	-	1(2)		1(2)
GPC undetermined	-	1(2)		1(2)
Total	**18(36)**	**32(64)**		**50(100.0)**

that; Coagolase negative Staphylococci are colonisers of the skin and are among laboratory contaminants, but are infectious if they penetrate bleached skin.[29,30] Hospital acquired infections as a result of surface contamination is being implicated in the propagation of drug-resistant bacteria.[13,14]

More interesting in this study, it was found that, more bacteria (CNS, *S. aureus and E. coli*) have been isolated from doors entering Doctor's waiting area before they come into contact with the reception area. This implies that, laboratory premises get contaminated from within source materials as well as from outside, that is to, Laboratory immediate clients who are the Doctors and Nurses during sample receiving process and results issuing.

This is further explained from the observations of our findings: Outside doors were having more bacterial contaminations, this is in line with previous study reports.[17] This implies that, good hygienic practice is still a problem in hospital settings. With the observed high proportion of pathogenic bacteria isolates. This signifies that, There is need for continued infection and prevention control programs to be in place and operational which goes in line with the COVID 19 era and its recommended control programs.[13]

CONCLUSION
This study has reported high proportion of pathogenic bacteria. The results entails that, internal and external environments are responsible for laboratory door contamination. Good hygiene practice and infectious control programs should be adhered to and implemented.

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Predictors of Surgical Site Infections among Patients Undergoing Open Urological Surgery at a Tertiary Hospital, Tanzania: A Cross Sectional Study

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ABSTRACT

Background: Surgical Site Infection (SSI) is one of the major hospital acquired infections, highly associated with prolonged hospitalisation, morbidity and mortality. In open urological surgeries, little is known on magnitude and factors associated with development of SSI.

Methods and Materials: The intervention was a cross-sectional prospective observational study performed between August 2015 and March 2016 at Muhimbili National hospital (MNH), Dar es Salaam, Tanzania. Patients who underwent open urological surgery at MNH during the study period and met inclusion criteria were consecutively enrolled, and followed up for 30 days. Patients´ and operative characteristics were recorded using standard structured questionnaires. Wound/ pus swabs were collected from patients with clinical evidence of SSI for bacteriological processing. Data analysis was performed using SPSS version 20.

Results: Of 182 patients who underwent open urological surgery, 22% (40/182) developed SSI. Pre-operative urinary tract infection (aOR 9.73, 95%CI 3.93-24.09, *p<.001*) and contaminated wound class (aOR 24.997, 95%CI 2.58-242.42, p = .005) were independent predictors for development of SSI. Shaving within 30 hrs before surgical procedure was found to be protective for developing SSI (aOR 0.26, 95%CI 0.09-0.79, *p=.02*). *Escherichia coli* (20/40) was the most predominant pathogen in SSI followed by *Klebsiella pneumoniae* (7/40) and *S. aureus* (6/40). Gram-negative bacteria were highly resistant to ceftriaxone, gentamicin, amoxicillin-clavulanic acid and trimethoprim-sulfamethoxazole.

Conclusion: Surgical Site Infection was high in open urological interventions. Pre-operative urinary tract infection and contaminated wound class predicted SSI. Bacteria causing SSI were highly resistant to commonly used antibiotics.

BACKGROUND

Surgical Site Infection (SSI) is among the major hospital acquired infections in patients undergoing surgical procedures. It is highly associated with prolonged hospital stay, increase in health care costs and mortality.[1,2] Certain patient and operative (preoperative, operative and postoperative) characteristics have been documented to be contributing to the risk of SSI development.[3,4]

Despite improvement in infection prevention and control practices in surgical procedures, such as; improved operating rooms, trained medical personnel, sterilisation techniques and provision of surgical antimicrobial prophylaxis, SSI remains a common hospital acquired infection and this has significantly limited the realisation of the valuable effects of surgical interventions. The incidence of SSI is approximately four times higher in Low and middle-income countries than in high-income countries.[4]

Depending on geographical location, the rates of SSI in developing countries accounts between 10.9 and 26% among patients undergoing major surgeries.[5-7] In addition, appreciable morbidity and mortality is attributed to SSI.[1,8] In Tanzania, studies have reported surgical site infections rate of 24% and 19.4% in district and tertiary hospitals respectively.[6]

Determining the magnitude and identifying risk factors associated with the incidence of SSI in preoperative and operative stage is critical for prevention and control of SSI. There is limited data about predicting factors for SSI incidence among patients admitted in general surgical ward, and among pregnant mothers undergoing caesarean sections in Tanzania.[6,9] Also, there is hardly any data about factors associated with SSI incidences among patients undergoing open urological surgery. In this study, we performed a cross-sectional observation study to determine the rate and predictive factors for SSI, aimed at establishing

evidence- based preventive protocols against SSI at Muhimbili National Hospital and other settings with similar context.

METHODS
Study Design and Settings
This was a cross-sectional prospective observational hospital-based study conducted between August 2015 and March 2016 at the urology ward of Muhimbili National Hospital (MNH), located in Dar es Salaam, Tanzania. MNH is the main specialised tertiary and training hospital for Muhimbili University of heath and Allied Sciences. It has 1500-bed capacity and attends 1000 to 1200 outpatients weekly. It serves approximately 6 million people living in and around Dar es Salaam and Pwani regions. The urology unit has approximately 70 bed capacity and performs at least 5 urological procedures daily.

Sample Size Estimation
The sample size calculation formula for finite population was applied to calculate the minimum required sample size

$$n=\frac{Nz^2pq}{d^2(N-1) + z^2pq}$$

where N=size of population from observational pilot study for patients who underwent open urological surgeries at MNH; about 256 underwent open surgeries for a period of 8 months
n=sample size
d= margin of error at 95% Confidence Interval which was considered to be 3%
q=1-p
p = proportion of patients with surgical site infection in general surgery at MNH which is 15.6% (add ref).

After adjusting for the non-response rate at 10 % the minimum required sample size was 195 patients. However, a total of 212 patients were recruited during the study period.

Study Population
All patients who underwent open urological procedure at Muhimbili National Hospital during the study period and consented to participate in the study were included in the study and were followed up for a period of 30 days. Patients who were malnourished and those with chronic illnesses such as HIV were excluded from the study. Surgical wounds were examined 48 hours after surgery and thereafter on each day until the patient was discharged. At the 7th day, during suture removal, the wound was examined again and whenever required, until day 30. During examination, the attending surgeon determined whether the patient had signs and symptoms of SSI. Clinical and microbiological evidence of SSI was defined as previously described by the Centre for Disease Control and Prevention.[3] A total of 212 patients underwent open urological surgery during the study period, 182 patients were followed for a period of 30 days, 9 patients died before completion of follow up period and 21 patients were lost to follow up.

Data Collection
A Standard structured questionnaire adopted from a previous study conducted in the same settings was used to collect information.[22] Prior to using the questionnaire, it was pretested by using a pilot sample of 10 patients admitted in general surgery ward and had developed SSI. The questionnaire questions were asked in Tanzania's National Language (Swahili). Data collection was performed by registered nurses who were trained on the study protocol. Information recorded included sex, age, co-morbidities, history of cigarette smoking, number of days of hospitalisation before surgery, history of abdominal hair removal before surgery, class of surgical incision, pre-operative urinary tract infection, duration of surgery, and pre-catheterisation before operation.

Specimen Collection and Laboratory Procedures
Patients with clinical evidence of SSI had two pus swabs or pus collected under aseptic procedure from the base of the wound and immediately transported to the laboratory in Amie's transport media (Oxoid, UK) for processing. Gram´s stain was performed on the first swabs for assessing the quality of the specimens and stain morphology. When the first swab was of good quality, then the second pus swab or pus from wound was plated onto MacConkey agar (Oxoid, UK) and blood agar (Oxoid, UK) and incubated under aerobic condition at 37°C for 18 to 24 hours. Bacteria isolates were identified based on colonial morphology, Gram stain and a set of biochemical tests including Analytical Profile Index for Enterobacteriaceae (API 20 E).

Antibiotic susceptibility testing was performed using the Kirby Bauer's disc diffusion method, in line with the Clinical and Laboratory Standard Institute (CLSI) guidelines.

Data Analysis
Data was entered and analysed using IBM SPSS software version 20, Armonk, NY IBM Corp. Data was summarised as; frequency, percentage and proportion. Binary logistic regression analysis was performed to identify the association between independent and dependent variables. Odds Ratios were used to test the strength of association between predictor variables. Significance was defined as a p-value of less than.05.

Ethical Considerations
Permission to carry out the study was obtained from Muhimbili University of Health and Allied Sciences, Senate Research and Publications Committee. Written informed consent was obtained from all study participants prior to enrolment. For participants below 18 years of age, informed consent was obtained from parents/guardians. Patient identification numbers were used instead of names to ensure confidentially.

RESULTS
Prevalence of Surgical Site Infection (SSI)
The rate of SSI in relation to various factors among patients who underwent open urological surgeries at MNH is summarised in Table 1. Of 182 patients who were followed up for 30 days, 40, 22% (95% CI 16.6 – 28.5) developed SSI. SSI was more common in males (32/144; 22.2%) and those aged between 54 and 71 years (13/47; 27.7 %). Patients with diabetes had high rates of SSI (2/6; 33.3%) compared to patients with other co-morbidities. Interestingly, SSI was observed more among non-smokers

TABLE 1: The rate of SSI among Patients who Underwent Open Urological Surgeries between August 2015 and March 2016 at MNH

Variables	Total	Frequency	SSI(%)
Age in years			
<17	27	3	11.1
18-35	29	9	20.7
36-53	39	8	20.5
54-71	47	13	27.7
>71	40	7	28
Sex			
Male	144	32	22.2
Female	38	8	21.1
Comorbidities			
Diabetic mellitus	6	2	33.3
Hypertension	50	13	26.0
Diabetic mellitus+Hypertension	27	7	25.9
No comorbidities	99	18	18.2
Cigarette smoking			
Yes	18	3	16.7
No	164	37	22.6
Days admitted			
One day	69	14	20.3
2 days	47	7	14.9
3 days	16	1	6.2
>3 days	50	18	36
Shaving			
Within 30 minutes	38	12	31.6
>30 minutes	23	9	39.1
No need	121	19	15.7
Catheterisation			
inserted	71	24	33.8
Not inserted	111	16	14.4
Pre-operative urinary tract infection			
Yes	44	26	59.1
No	138	14	10.1
Duration of surgery (Minutes)			
< 90	55	7	12.7
>90	127	33	26.0
Type of wound			
Clean	38	2	5.3
Clean contaminated	127	29	22.8
Contaminated	17	9	52.9

(37/164; 22.6%) compared to cigarette smokers(3/18;16.7). The rate of SSI was higher in patients who were admitted for more than 3 days (18/50; 36%) compared to those admitted for lesser days. Patients who shaved more than 30 minutes before operation had high rate of SSI (9/23; 39.1%) compared to those who shaved within 30 minutes (12/38; 31.6%) and those who did not require shaving (19/21; 15.7%). Participants who had pre-operative urinary tract infections had increased prevalence of SSI compared to those without (26/44; 59.1% vs 14/138; 10.1%). SSI rate was more common (24/71; 33.8%) in catheterised patients compared to those who were not catheterised (16/111; 14.4%). Patients who's surgery duration was more than 90 minutes presented with higher rate of SSI compared to those who had less (33/127; 26% vs 7/55; 12.7%).

Predictors of Surgical Site Infection

Shaving patients more than 30 minutes before operation was significantly associated with development of surgical site infections, cOR 3.451 (95%CI 1.308–9.105, *P=.012*). Having urinary catheterisation in situ before operation was significantly associated with surgical site infections on univariate analysis cOR 3.032 (95%CI 1.472 – 6.246, *p value .003*). The odds of SSIs were 12 times more in patients who had had pre-operative urinary tract infections before surgery (cOR 12.794, 95%CI 5.655 – 28.94, *p value <.001*). On univariate analysis, contaminated surgical procedures were found to be significantly associated with development of surgical site infection cOR 20.3, (95%CI 3.651 – 112.3, *p=.001*) (Table 2). Age, history of cigarette smoking, comorbidities, duration of admission before surgery and duration of surgery were found not be associated with the development SSI among patients who underwent urological surgery.

On multivariate analysis, pre-operative urinary tract infection was found to be independently associated with the development of surgical site infections aOR 9.73 (95%CI 3.93-24.09, p <.001). Contaminated surgical procedures were also found to be an independent factor associated with surgical site infection aOR 24.997 (95%CI 2.58-242.42, *p .005*) (Table 2). Shaving more than 30 minutes and urinary catheterisation were found to be not independently associated with surgical site infections and shaving within 30 minutes before surgical procedure was found to be protective against developing SSI aOR 0.26 (95%CI 0.09-0.79, *P=.02*)

Bacteria Aetiology of SSI/ UTI and their Antimicrobial Susceptibility Pattern
A total of 40 bacteria were isolated from patients with SSI, majority of the isolates were Gram negative bacteria. *Escherichia coli* were the most predominant pathogens causing SSI in 50% (20/40) patients undergoing urological surgery. *Klebsiella pneumoniae* accounted for 17.5% (7/40), *S. aureus* 15% (6/40), *Pseudomonas aeruginosa* 10% (4/40) and *Proteus mirabilis* 7.5% (3/340).
Escherichia coli isolates from SSI were highly resistant to ceftriaxone (84.2%), gentamicin (86%), amoxicillin-clavulanic acid (84%) and trimethoprim-sulfamethoxazole (82.3%). Seventy eight percent (78%) of *Klebsiella pneumoniae* and 62% of *P. mirabilis* were resistant to ceftriaxone. *S. aureus* displayed high rate of resistance to amoxicillin –clavulanic (68.4%), while low rates of resistance were observed in ceftriaxone (42%), gentamicin (36%) and ciprofloxacin (27%).

DISCUSSION
The overall prevalence of SSI among patients undergoing open urological surgery at a tertiary hospital in Tanzania was 22%. Our finding was higher compared to a study from developed countries like Serbia 5.9%,[2] and a recent study in Egypt (9%) [10] among patients undergoing urological surgery. The contributing factors for the observed high rates of SSI in this study can be attributed to insufficient infection control and prevention measures. During this study's duration, wards were congested and patients who underwent surgery were mixed with other patients categories. In addition, most of the surgical procedure lasted more than 90 minutes, which also could have contributed to the increased rate of SSI. Conversely, the setting of this study was completely different from

TABLE 2: Predictors of SSI among Patients who Underwent Open Urological Surgery between August 2015 and March 2016 at MNH

Variable	Number of patients	Rate of SSI n (%)	cOR	95%CI	P value	aOR	95%CI	P value
Age (years)								
<17	27	3(11.1)	1					
18 – 35	29	9(31.0)	2.087	0.466 – 9.346	0.336			
36 – 53	39	8(20.5)	2.065	0.494 – 8.626	0.320			
54 – 71	47	13(27.7)	3.056	0.785 – 11.915	0.107			
>71	40	7(28.0)	2.667	0.659 – 10.786	0.169			
Cigarette smoking								
Yes	18	3(16.7)	0.686	0.188 – 2.500	0.568			
No	164	37(22.6)	1					
Comorbidities								
Diabetic mellitus	6	2(33.3)	2.25	0.38 – 13.24	0.37			
Hypertension	50	13(25.5)	1.54	0.68 – 3.46	0.25			
DM + Hypertension		27	7(26.9)	1.66	0.61 – 4.53	0.33		
No comorbidities	99	18(18.2)	1					
Days admit pre-operation								
1 day	69	14 (20.3)	1					
2 days	47	7(14.9)	0.687	0.254 – 1.859	0.460			
3 days	16	1(6.3)	0.262	0.032 – 2.155	0.213			
>3 days	50	18(36.0)	2.210	0.970 – 5.034	0.059			
Shaving								
Within 30 minutes	38	12(31.6)	2.478	1.068 – 5.747	0.035*	0.26	0.09-0.79	0.02*
>30 minutes	23	9(39.1)	3.451	1.308 – 9.105	0.012*	0.420	0.12 – 1.45	0.170
No need	121	19(15.7)	1					
Catheterisation								
Inserted	71	24(33.8)	3.032	1.472 – 6.246	0.003*	1.670	0.664-4.198	0.275
Not inserted	111	16(14.4)	1					
Pre-operative urinary tract infection								
Yes	44	26(59.1)	12.794	5.655 – 28.94	<0.001*	9.73	3.93-24.09	<0.001*
No	138	14(10.1)	1					
Wound class								
Clean	38	2(5.1)	1					
Clean contaminated	127	29(23.0)	5.327	1.209 – 23.46	0.027			
Contaminated	17	9(53.0)	20.250	3.651 – 112.3	0.001*	25	2.58-242.42	0.005*
Duration of surgery								
0 to 90 minutes	55	7(17.5)	1					
>90 minutes	127	48(33.8)	2.407	0.992 – 5.842	0.052			

SSI; Surgical site infection, cOR; Crude odds ratio, CI; Confidence interval, aOR; adjusted odds ratio

that in Serbia and Egypt, Tanzania being a developing country, with limited resources could count for the observed high prevalence rates. The rate of SSI reported in the present study was less than that reported by studies that considered general surgery,[6] but higher than reports from studies that considered obstetrics surgeries in Northern, Tanzania.[9] These findings from the same study settings suggest that patients' characteristics (risk factors) and surgical procedures determine the occurrences of SSIs. Patients from urology surgery might not share the same risk factors with their counterparts from general surgery and obstetrics.

Our study finding compares with reports from previous studies[11-13], which reported that having urinary tract infections before urological surgical procedures is a risk factor for development of SSI among patients undergoing open urological surgery. Besides, SSI still developed in this study's participants with urinary tract infections being treated with antibiotics before surgery. This study could not ascertain if the same bacteria isolated from urinary tract infection were causative of SSIs, further molecular studies need to be performed to establish the clonal relationship. However, previous studies elsewhere[11,14], documented that not all causative bacteria of SSI were of the same species as those from pre-operative urinary tract infections. Ideally, in a setting with culture facilities and elective surgery, urine culture needs to be performed before surgery.

Contaminated surgical incision was found to be a risk factor for development of SSI. This finding is consistent with reports of several previous studies performed in urology and general surgery wards.[2,4,10,15-17] Several studies have reported correlation between wound class and development of SSI, the risk increases with classification of incision, surgeries on clean and clean – contaminated incision carry low risk compared to surgeries performed on contaminated and dirty incisions, which can be accounted for by high loading dose of microbes.[7,18,19]

Interestingly, shaving less than 30 minutes before surgical procedure on univariate analysis was associated with development of SSI. However, after controlling other factors, on multivariate analysis, shaving less than 30 minutes before surgical procedure was found to be a protective factor against the development of SSI. This observation is similar to findings from studies carried out elsewhere in different geographical settings[7,20], which documented that increased time lapse between shaving and surgical procedure significantly increases risk for SSI.

The most common source of pathogens causing SSIs is endogenous from patients' own body flora. Bacteria are mainly transmitted to surgical sites during surgical manipulation. In this study, Gram negative bacteria such as *E. coli* and *Klebsiella pneumoniae* were the most common causes of SSI. Since all surgeries did not involve the opening of the gastro-intestinal tract, it was hardly unexpected to find predominance of these bacteria, which are flora of the gut. Due to close proximity of the rectum and site of incision, possibly the organisms may have ascended from the rectum. This study's results are consistent with results from reported by studies conducted among patients who underwent open urological procedures.[14,21]

Numerous studies in Tanzania have reported increased rate of antibiotic resistance among bacteria causing SSI.[6,22,23] In our study, Gram negative bacteria causing SSI were highly resistant to ceftriaxone, which is commonly used for surgical antimicrobial prophylaxis. This is Consistent with reports from other studies conducted elsewhere.[22,24,25], Bacteria resistance to third generation cephalosporin is on increasing trend in Tanzania, an observation that calls for further studies to assess the effectiveness of use of third generation cephalosporin as prophylaxis to prevent SSI.

This study was limited by the use of aerobic culture techniques and loss to follow up which could have cause under reporting of the reported prevalence.

CONCLUSION

The rate of SSI among patients undergoing urological surgery at MNH was high. History of pre-operative urinary tract infections and contaminated wounds were found to be predictors for SSI. Most of Gram-negative bacteria isolated from SSI were highly resistant to ceftriaxone and other commonly used antibiotics. We therefore, recommend culture and sensitivity testing to patients on urinary catheter prior to surgical procedures, and improvement of IPC measures in the wards. Furthermore, evidence-based treatment approach using laboratory culture and sensitivity results to treat SSI should be used and establishment of surveillance system for SSI, so as to give appropriate feedback to the surgeons for patient management.

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