PREVALENCE AND RISK FACTORS OF MULTI DRUG RESISTANT TUBERCULOSIS AMONG REFUGEES IN THE RESETTLEMENT CAMPS OF ADJUMANI, MOYO AND YUMBE DISTRICTS WEST NILE REGION.

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LAURENT NSHIZIRUNGU[a,1,2], IZALE WEWEDRU[a,3], DOREEN AMULEN[a,4], PAUL LUWUNA[a,5], DENISH OLET[a,6], MICHAEL OMING[a,7]

[a] Faculty of Medicine, Mbarara University of Science & Technology,
Mbarara, Uganda.
Tel.: +256-4854-21373, Fax: +25648520782

[1]Corresponding author.
[2]E-mail: nshizirungu33laurent@gmail.com
[3]E-mail: wewedruiza@hotmail.com
[4]E-mail: amulendoreen2@gmail.com
[5]E-mail: luwunapaul@gmail.com
[6]E-mail: olet.denis@yahoo.com
[7]E-mail: mike.omex9@gmail.com

Abstract Background: Multidrug-resistant tuberculosis (MDR-TB) is a name given to tuberculosis agents when the bacteria are resistant to at least isoniazid and rifampicin, two of the most effective TB drugs. The study aimed to determine the prevalence and risk factors of MDR-TB among the refugees in the resettlement camps of Adjumani, Yumbe, and Moyo districts, West Nile region.
Method: This was a cross-sectional study where questionnaires were used to capture risk factors associated with MDR-TB and sputum samples (n=223) collected were examined using the gene expert machine. P values and corresponding 95% CI were calculated. All statistical tests were two-tailed and P-values less than 0.05 were considered significant. **Results:** From the study,143(64.1%) were males while 80 (35.9%) were females, with the age range of 3- 64 years and mean age of 32 years, out of 223 sputum samples analyzed on GeneXpert machine; 178 (79.8%) tested negative for *Mycobacterium tuberculosis* (MTB) while 45 (20.2%) tested positive for *Mycobacterium tuberculosis*. Of the 45 samples that tested positive for MTB; 39 (17.5%) were rifampicin sensitive and 6 (2.7%) were rifampicin-resistant. Of the 39 case MTB cases detected in the refugee resettlement camps of Bidibidi, Itula, and Mungula, 17 (43.6%), 14 (35.9%), and 8 (20.5%) were from each mentioned camp respectively; whereas of the 6 MDR-TB cases detected; Mungula camp had the majority cases 3 (50%), Bidibidi camp had 2 (33.3%) cases and Itula had 1 (16.7%) cases. The Risk factors associated with MDR-TB among refugees was overcrowding 5 (83.3%) and not enrolled on DOTs, 5 (66.7%). There was no significant association between MDR-TB and age (P=0.43; 95%CI=0.163-0.233)
Conclusions and recommendations: The general prevalence of *Mycobacterium tuberculosis* is 20.2% and MDR-TB is 2.7%.

1 Background:

Tuberculosis (TB) is a chronic infectious multi-systemic disease caused by bacteria of *Mycobacterium Tuberculosis* Complex (MTC) that is spread from person to person through the air and one of the leading causes of mortality worldwide. Mycobacteria belong to the family Mycobacteriaceae and order Actinomycetes. TB usually affects the lungs, but it can also affect other parts of the body, such as the brain, the kidney, or spines. According to CDC, TB is treatable and curable; however, persons with TB can die if they do not get proper treatment (longo *et al*.,2012). The MTC are genetically related and show high conservation of DNA (benon *et al.*,2008). Some species such as *M. tuberculosis, M. africanum* and *M. cannettii* are specific to humans and *M. microti* to rodents while *M. bovis* and its variants are zoonotic. The disease is globally distributed; however, the geographical distribution of MTC differs with some species and strains being specific to a particular human sub-population (Gagneux, 2005). Nonetheless, the prevalence is high in urban areas with high population densities (Gandhi.2006). Multidrug-resistant tuberculosis (MDR-TB) is a name given to TB when the bacteria are resistant to at least isoniazid and rifampicin, two of the most effective TB drugs. However, in May 2016 WHO issued guidance that people with TB resistant to rifampicin (RR-TB), with or without resistance to other drugs, should be treated with an MDR-TB treatment regimen. This includes patients with MDR-TB as well as patients with TB resistant to rifampicin. This group of patients (effectively an expanded MDR-TB group), is sometimes referred to as MDR-TB/RR-TB. MDR-TB is an important threat to global TB control. There are two ways that people get MDR-TB. According to Kanabus *et al.,* (2020) people get acquired drug-resistant TB when their TB treatment is inadequate. This can be for a number of reasons, including the fact that patients fail to keep to proper TB treatment regimens (WHO, 2019).

According to Kanabus *et al*.,(2020) It can also be that the wrong TB drugs are prescribed, or substandard TB drugs are used for treatment. Secondly, transmitted or secondary MDR-TB, results from the direct transmission of drug-resistant TB from one person to another. The emergence of drug resistance is promoted by ineffective TB control programs and interruption of drug supplies, often due to political and other social disruption (longo *et al*., 2012). Each year, approximately 480,000 people become ill with MDR-TB, and 170,000 dies (WHO *et al.*,2016). The same article further reports that drug-susceptible TB can be cured in >95% of patients within 6 months of standardized treatment, treatment for MDR-TB takes up to 2 years and succeeds in just 55%–67% of cases (WHO, 2016).

According to the medical service administration of Vietnam et al., (2015), an estimated 480,000 people worldwide developed MDR-TB, and an additional 100,000 people with rifampicin-resistant TB were also newly eligible for MDR-TB treatment. India, China, and the Russian Federation accounted for 45% of the 580 cases. It has been estimated that 9.5% of these cases were XDR-TB. Extensively drug-resistant TB (XDR-TB) has been reported by 105 countries in 2014 (CDC, 2013). Some countries have been reported to have an extremely very high prevalence (Calve et al., 2010). In Swaziland, 7.7% and 33.8% of TB smear-positive NCs and PTCs, respectively, had MDR-TB. This represents an 8.5-fold and 3.7-fold increase compared with MDR-TB prevalence among other African countries. In neighbouring countries like South Africa, the estimated MDR-TB prevalence was 1.8%, and in Mozambique 3.5% (Calver, 2010).

Multidrug-resistant tuberculosis is an emerging problem in many parts of the world, and its levels among new TB patients are increasing in sub-Saharan Africa (Benson *et al.*,2014). According to Kidenya *et al., (* 2014), the prevalence of MDR-TB among new cases ranges from 0.4% in Tanzania to 4.4% in Uganda, and among recurrent cases ranges from 3.9% in Tanzania to 17.7% in Uganda. About 500 new smear-positive MDR-TB cases are estimated to occur per year in Uganda. (WHO, 2010).

The study was done in the resettlement refugee camps in Adjumani, Yumbe, and Moyo districts, West Nile Region. It was among all refugee patients suspected to have TB who consented to the study and their sputum samples were tested using the gene Cepheid gene Xpert machine. The study was done in a period of nine months.

2 METHODOLOGY

Study Area

This study was conducted at different refugee resettlement camps in Adjumani, (Mungula), Moyo district (Itula), and Yumbe district (Bidibidi) which are located in the West Nile Region of Uganda.

West Nile consists of the following districts: Adjumani, Arua, Koboko, Maracha, Moyo, Nebbi, Yumbe, and Zombo. Uganda is now home to more than 500,000 refugees from South Sudan, living in 48 refugee resettlements in 4 districts of Northern Uganda. Since July 2016, Uganda has been receiving not less than 2500 refugees daily. Adjumani (147,000 refugee persons) and Arua (39,747 refugee persons) districts both have 17 refugee resettlements each; Koboko (1,439 refugee persons) has 8 while Yumbe has 6 resettlement camps. Uganda's Yumbe district has the second largest population size of refugees in East and Central Africa (270,000+ persons) with a capacity of more than 200,000 persons after the Dadbaab refugee camp in Kenya (320,000 persons). Bidibidi is the largest refugee camp in the world (Hattem, 2017). On average Yumbe receives 1000 new arrivals on a daily basis. Uganda has one of the most favorable refugee protection environments in the world: providing for freedom of movement, right to work, and also providing land for refugee settlements in line with the refugee Act of 2006. Mungula refugee camp is in Adjumani district and it accommodates over 30,000 refugees, just across the border from South Sudan.

Mogo-Palorinya settlement camp in Moyo district, West Nile has been reopened to accommodate about 80,000 refugees who are fleeing fragile South Sudan., it was a home for South Sudan since the 1990s.

Study Design

This was a cross-sectional study where questionnaires were issued to participants to capture their socio-economic, demographic data, and risk factors associated with MDR-TB. The sputum samples collected from the study participants were examined using the gene expert machine.

Study Variables

The study variables included the risk factors associated with MDR-TB among refugees in resettlement camps, social-economic, demographic variables, and the Gene expert test results.

Study Population

The study targeted refugees living in the resettlement camps of Adjumani, Moyo, and Yumbe districts, West Nile region presenting with signs and symptoms of tuberculosis who consented to participate.

Study selection criteria Inclusion Criteria

The study included only refugee patients presenting with signs and symptoms of tuberculosis who consented by signing the consent forms.

Exclusion Criteria

Refugee patients who had signs and symptoms of tuberculosis and did not consent.

Sample Size determination

The sample size was determined using the Standard formula by (Kish and Leslie, 1970).

n =z2 p q

d2

n = sample size required.

Z-is the z-score (1.96) on a normal standard variation corresponding to the 95% level of confidence.

p-is the estimated prevalence of MDR TB (17.7 %) in Uganda (WHO, 2010).

q = 1-p

d = desired precision at 5% (0.05)

q = 1-p = 1-0.177 = 0.823

0.05^2

n = 223 participants

Therefore, a total of 223 patients were considered in this study

Sampling Technique

Clients in the health facility were triaged to enable segregation of coughers from non-coughers. The coughers were then directed to sit in a place designated for them. They were briefed about the study and thereafter assessed using the questionnaire. Those who were eligible for the test were then taken through the consent form. Whoever accepted to sign the consent form was asked to provide a sputum sample which was examined using the gene expert machine.

Data Collection Tools

Data were collected using a questionnaire that was written both in English and Arabic with the help of a research assistant who translated in the local languages spoken by the refugee natives, presumptive TB register, laboratory TB register checklist, and gene expert machine.

Data collection

Data on demographic and socioeconomic characteristics and other risk factors associated with MDR-TB among refugees in the resettlement camps were collected using a printed questionnaire written both in English and Arabic after consent of the patients. A research assistant/language translator who was well versed with English, Arabic, and other languages are commonly spoken by refugees in the camps was used to ease communication for quality results. The presumptive TB register, laboratory TB register, and checklist were used to collect data from the printed gene expert result slips and the computer.

Quality assurance

The sputum samples were analyzed following the standard operating procedures (SOPs) for running GeneXpert machine and sample preparation. In order to quality control the study findings, only sputum samples collected well and in the recommended sputum containers were accepted. To keep good track of the results, proper labeling of the samples were noted, therefore all samples were labeled with a unique patient identifier, time and date of collection using a permanent pen marker. Only trained staffs were used at all the stages of the study. Data generated were double checked before being entered.

Data analysis and presentation

Data collected were coded, filtered, and checked for inconsistencies before being analyzed. They were securely kept in records, flash discs, and databases for future use. Data were entered into the computer using Epi data and analyzed with SPSS version 22 (Statistical Package for Social Sciences version 22). Results were presented in form of tables and charts preceded by descriptive statements.

Ethical Considerations

Approval was got from the Mbarara University of Science and Technology Faculty Research Committee (FRC) and the district health officers in the study districts of Adjumani, Moyo, and Yumbe. Consent was also got from all eligible clients who accepted to sign the consent form. Unique identification numbers were used for identification to avoid mixing client's identities. For clients who were diagnosed with MDR- TB their names were sent to the district TB and leprosy officers/focal persons for appropriate management. Confidentiality was highly maintained.

Study Limitations

- Since there was inflation in the economy, it affected the budget which led to financial constraints and hence delays in timely completion of the research.
- Language barrier affected the smooth flow of data collection.
- Policies involved in accessing the camps also caused some delay in the commencement of data collection.
- There was one gene x-pert machine per district serving a large workload.

Dissemination of research findings

A written research report was compiled 2 copies submitted to the Mbarara University of Science and Technology library, a copy was distributed to each of the respective District Health Officers in the study districts, Microbiology laboratory, and the research supervisor. Findings of the study will also be presented in conferences and thereafter summarized into a manuscript for potential publication in a peer-reviewed journal.

3 RESULTS

This study was conducted to determine the prevalence and risk factors associated with multidrug-resistant tuberculosis among refugees in the resettlement camps of Bidibidi (Yumbe district), Mungula (Adjumani district), and Itula (Moyo district) in the West Nile region. It was conducted from April 2017 to March 2018. Laboratory investigations were done on 223 sputum samples using the GeneXpert Method technique. Data were analyzed using the SPSS statistical package version

22 to determine the relationship between demographic variables and the outcome of the variables. The results of the analysis were presented in form of tables and figures.

Demographic characteristics

Of the 223 respondents, 143 (64.1%) were males and 80 (35.9%) were females, the age range of the respondents was from 3- 86 years with a mean age of 32 years and the median age of 22 years.

Sample distribution by Gender

Out of the 223 samples collected for the study, the majority 143 (64.1%) were from males, while females had 80 (35.9%). Statistically, there was no significant difference in the distribution of samples by sex (X2 = 0.465, P-value 0.359) (Figure 4.1).

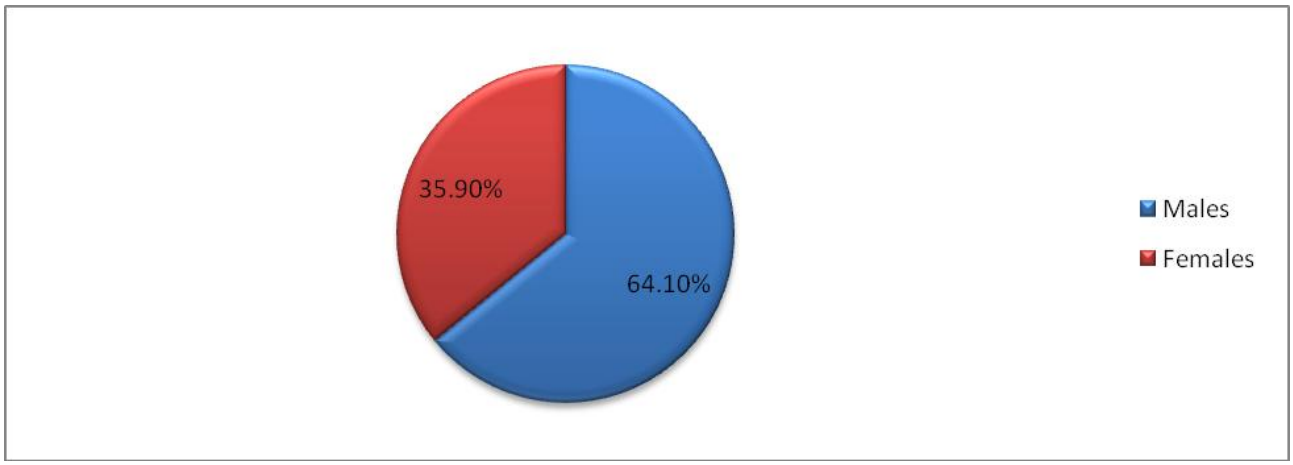

Figure 1. Sample distribution by Gender

X^2 = 0.465, P-value 0.359

Figure 4.1: Distribution of study samples by gender

4 Distribution of study samples by age

Out of the 223 sputum samples collected for the study, , majority 77 (35.5%) were from the age group of 21-30 years, followed by 50 (22.4%) from 31-40 years, 27 (12.1%) from 41-50 years,

22 (9.9%) from 11-20 years, 18 (8.1%) were from 51-60 years, 16 (7.2%) were from 61 plus years and least 13 (5.8%) were from the age group of 1-10 years old (Figure 4.2).

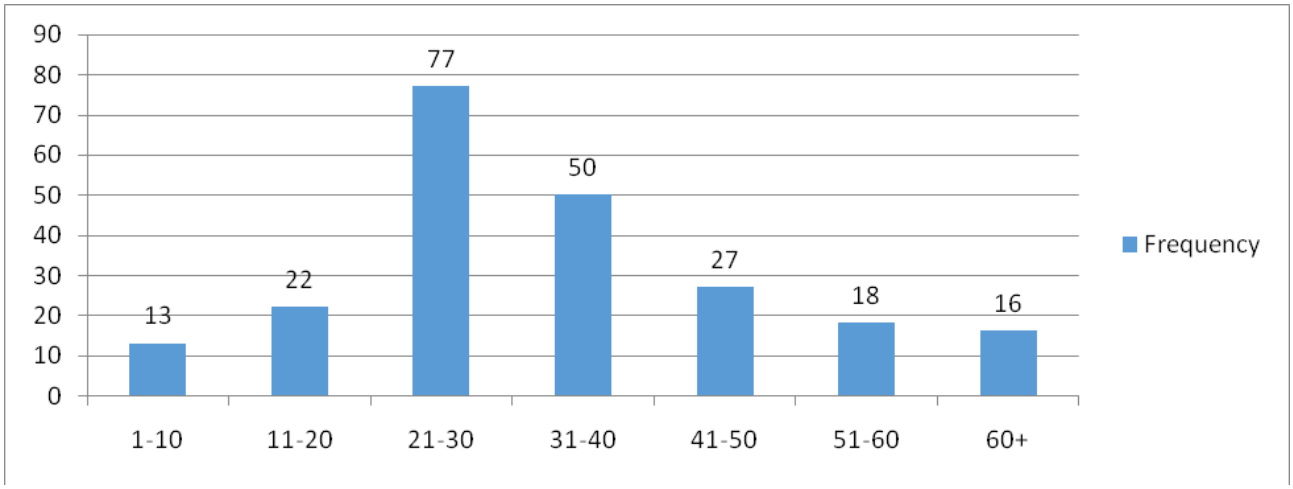

Figure 2. Sample distribution by age

5 Age group

Sample distribution by resettlement camps

Majority of the sputum samples 135 (60.5%) collected for examination were from Bidibidi camp (Yumbe district), followed by 51 (22.9%) from Mungula (Adjuman district) and the least 37 (16.6%) were from Itula camp (Moyo district) (Figure 4.3).

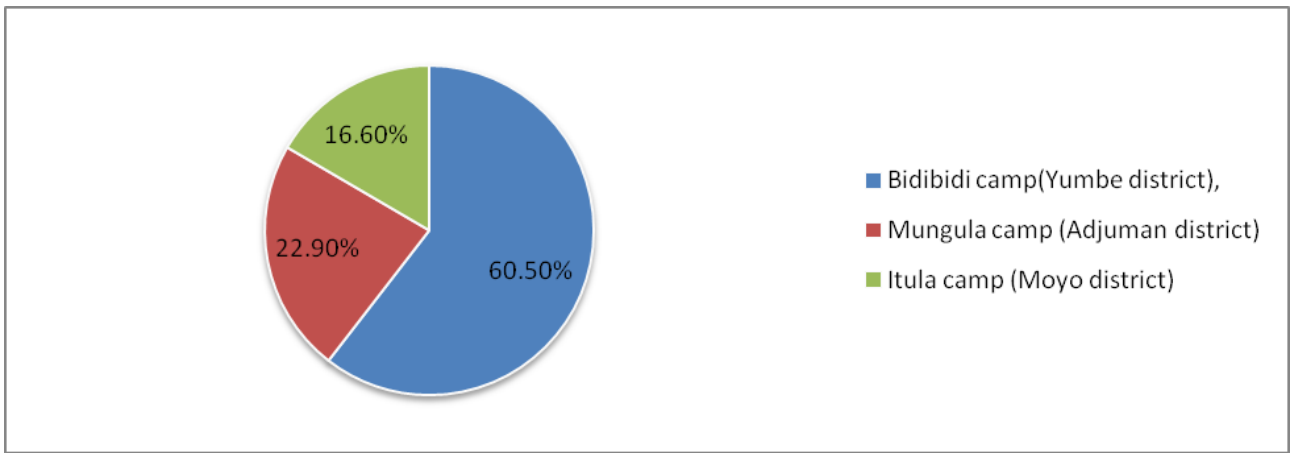

Figure 3. Sample Distribution by Resettlement Camp

6 Sputum GeneXpert test results

Out of 223 sputum samples analyzed on GeneXpert machine; 178 (79.8%) tested negative for *Mycobacterium tuberculosis* (MTB) while 45 (20.2%) tested positive for Mycobacterium tuberculosis. Of the 45 (20.2%)

Table 1. a: MTB among Respondents by Sex

Sex	MTB Status		Total, n (%)	X2	P-value
	Positive, n (%)	Negative, n (%)			
Female	11 (13.8)	69 (86.2)	80 (100)		
Male	28 (19.6)	115 (80.4)	143 (100)	0.238496	0.138
Total	**39 (17.5)**	**184 (82.5)**	**223 (100)**		

samples that tested positive for MTB; 39 (17.5%) were rifampicin sensitive and 6 (2.7%) were rifampicin resistant. Therefore, the overall prevalence of Mycobacterium tuberculosis (i.e. tuberculosis) among the refugees was 20.2% while that of MDR-TB was 2.7%.

7 Distribution of MTB and MDR-TB in the resettlement camps

Of the 39 (17.5%) MTB (rifanpicin sensitive) cases diagnosed in the refugee resettlement camps in West Nile region; 17 (43.6%) were from Bidibidi camp, 14 (35.9%) were from Itula camp and 8 (20.5%) were from Mungula camp. Of the 6 MDR-TB cases detected; Mungula camp had the majority of the cases 3(50%), followed by Bidibidi camp 2 (33.3%) cases, and Itula had only 1 (16.7%) case. The distribution of MTB and MDR-TB strongly varies according to camp. The difference in the distribution of MTB and MDR-TB by camp was statistically significant with a X^2= 16.09, P value: = < 0.001 (Figure 4. 4)

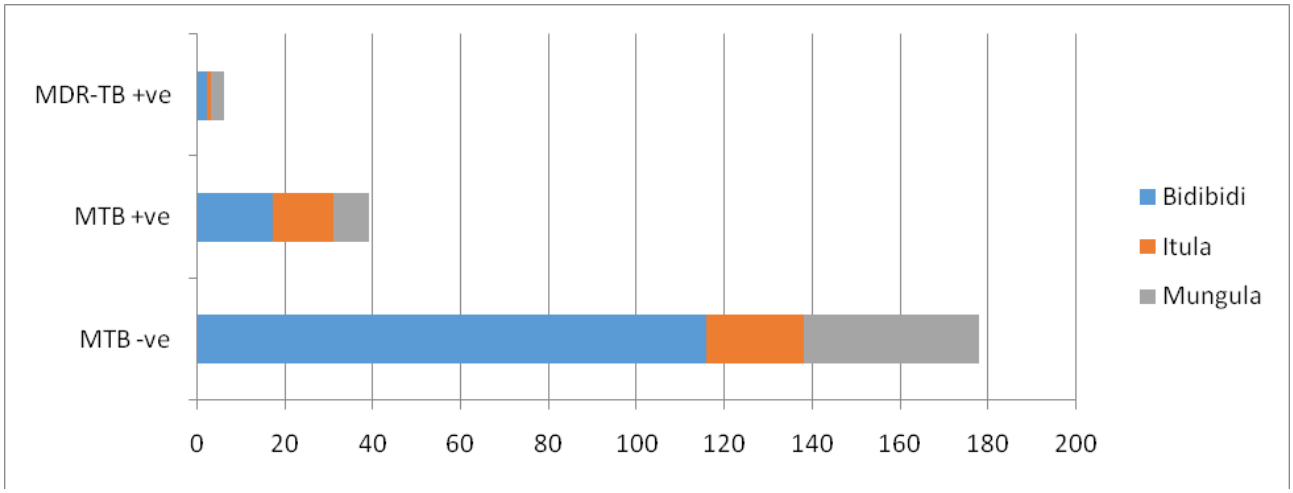

Figure 4. The difference in the distribution of MTB and MDR-TB by camp

X^2= 16.09 p value=0.001

8 MTB and MDR-TB distribution by gender

Of the 39 (17.5%) MTB (Rifampicin sensitive) cases detected; 28 (71.8%) were from males and 11 (28.2%) from females. The distribution of TB is not affected by sex (X^2=1.17, P=>0.1) (Table 4.1a); whereas out of the 6 MDR-TB cases detected; 3 (50%) each from both females and males: And statistically there was a significant difference in distribution of MDR-TB by sex score among the refugees with X^2 = 0.169893, p = 0.021 (Table 4.1 a and Table 4.1b).

X^2 = 0.238496, p = 0.138.

X^2 = 0.1698, p = 0.021

Table 2. b: MDR-TB among the Respondents by Sex

Sex	MDR-TB Status		Total, n (%)	X2	P-value
	Positive, n (%)	Negative, n (%)			
Female	3 (3.8)	77 (96.2)	80 (100)		
Male	3 (2.1)	140 (97.1)	143 (100)	0.1698	0.021
Total	**6 (2.7)**	**217 (97.3)**	**223 (100)**		

Table 3. Risk Factor Status

Risk Factors	MDR-TB status		Total, n (%)	X2	P-value
	Positive, n (%)	Negative, n (%)			
Recurrent TB	4 (66.7)	2 (33.3)	6 (100)		
HIV-TB co- infection	2 (33.3)	4 (66.7)	6 (100)		
Poor adherence	4 (66.7)	2 (33.3)	6 (100)	12.83	0.05≤p≤0.01
Overcrowding	5 (83.3)	1 (16.7)	6 (100)		
No DOTs	5 (83.3)	1 (16.7)	6 (100)		
Total	**20 (66.7)**	**10 (33.3)**	**30 (100)**		

9 MTB and MDR-TB distribution by age

Out of the 39 MTB (Rif-sensitive) cases detected; majority 14 (35.9%) were from age group 31- 40 years, followed by 12 (30.8%) from 21-30 years, 6 (15.4%) from 11-20 years, 3 (7.7%) from 51-60 years, 2 (5.1%) from 1- 10 years, and 1 (2.5%) each from 41-50 years and 61 (3%) plus years. From the 6 MDR-TB cases detected; 3 (50%) from 31-40 years, and 1 (16.7%) each from 21-30 years; 41-50 years and 1-10 years (Figure 4.5).4.5:age

10 Distribution of MDR-TB by risk factors

Of the 6 respondents diagnosed with MDR-TB, 5 (83.3%) were living in overcrowded homes and not enrolled on DOTs; 4 (66.7%) had recurrent MTB infections and poor adherence to their prescribed treatment, whereas 2 (33.3%) had TB-HIV co-infection. Statistically there is significance difference in the relationship between MDR-TB and the associated risk factors (X^2=12.83, P=0.05≤P≤0.01) (Table 4.2).

X^2 = 12.83, p = 0.05≤p≤0.01.

DISCUSSIONS

This study determined the prevalence of MDR-TB and the risk factors associated with the disease among the refugees in the resettlement camps of Mungula (Adjumani district), Itula (Moyo district), and Bidibidi (Yumbe district), West Nile region.

Out of 223 samples analyzed, the majority 143 (64.1%) came from the males. This was so probably because men have poor health-seeking behaviors and go for health care services when their health condition has worsened. Men are also prone to the risk factors associated with the acquisition of MDR-TB because of their lifestyles like drinking alcohol, smoking, and exposure to dusty work which are less common in women. According to other studies, alcohol consumption, non-adherence to the prescribed treatment, traveling to different places, and smoking are also significantly associated with MDR-TB (Marahatta *et al.*,2012). These findings agree with the study that was done to determine the epidemiology of TB among refugee arrivals in Minesota, the majority of them were men 74 (5%) (PrathibhaVarkey et al, 2001). However, statistically, there was no significant difference in the distribution of samples by sex (X2 = 0.465, P-value 0.359).

From the study, most samples 77 (35.5%) came from the age group of 21-30 years. This was so because this age group is socially and economically active, hence prone to MDR-TB risk factors like alcohol drinking, cigarette sharing, and smoking and buying sex whereby they may get HIV infection which is also a risk

factor for MTB infection since it lowers the immunity greatly. This, therefore, makes them vulnerable to the risk factors of contracting MDR-TB. This same age group being economically stable can easily seek health care services. The majority (75%) of TB cases in developing countries are in the economically productive age group of 15-50 years (Harries et al.,2004). The age group 1-10 years had the least samples 13 (5.8%) because they are always under parental guidance and care hence not much exposed to some of the risk factors of TB like alcohol drinking and smoking. Studies have also shown that TB is less common among children less than 10 years. According to the studies done, there are limited data on the prevalence of drug-resistance in African children with tuberculosis. In Cape Town, South Africa, between 2005 and 2007 the prevalence rates of MTB isoniazid resistance were 14.4% and 6.7% respectively in the general population. These prevalence rates had increased compared to one

The majority of the sputum samples 135 (60.5%) collected for examination came from Bidibidi camp because it has the largest population and most of the risk factors associated with TB could have been present. Bidibidi is also the largest in the West Nile region of Uganda and the second largest in East Africa after the Dadbaab refugee resettlement camp in Kenya. It, therefore, has the highest influx of refugees hence overcrowded, leaving many exposed to TB risk factors. This is in line with studies that show that the Bidibidi camp (Yumbe district) has the second largest population size of refugees in East and Central Africa (270,000+ persons) with a capacity of more than 200,000 persons after Dadbaab refugee camp in Kenya (320,000 persons). Bidibidi is also the second-largest refugee camp in the world (Hattem, 2017). With a large population of refugees in a camp, cases of TB are also bound to be rampant. The least sputum samples 37 (16.6) came from the Mungula camp because of the smaller population compared to others.

This study revealed that of the 223 samples analysed, 178 (79.8%) tested negative for Mycobacterium tuberculosis while 45 (20.5%) tested positive. Therefore, the general prevalence of TB among refugees in the resettlement camps of Bidibidi, Mungula, and Itula was at 20.2%; rifampicin sensitive MTB was at 17.5% whereas MDR-TB was 2.7% compared to the study in Kenya done by(Ogaro *et al*.,2012), the level of MDR-TB was 0.5% in new TB cases and 8.5% in recurrent tuberculosis cases. The general TB prevalence of 20.2% among the refugees could possibly be due to the risk factors associated with MTB which include; recurrent TB infections, poor adherence to TB treatment, TB-HIV co-infection, and overcrowding leading to close contact with infected individuals. The MDR-TB prevalence is attributed to the high cases of recurrent MTB infections, poor adherence to treatment, overcrowding, and inadequate implementation of DOTs.

Among the 39 (17.5%) MTB (Rifampicin sensitive) cases diagnosed in the resettlement camps, 17 (43.6%) came from Bidibidi camp, 14 (35.9) from Itula camp, and 8 (20.5%) from Mungula camp. Most of the MTB cases were from Bidibidi camp because it is the largest population. The difference in the distribution of MTB and MDR-TB by the camp was statistically significant with a

10.1 Value: = < 0 001

The majority 28 (71.8%) of rifampicin-sensitive MTB cases were detected among males than females 11 (28.2%). Many males were diagnosed with MTB probably because most of them have poor health-seeking behaviors, poor adherence to treatment, and high-risk social practices like smoking; drinking alcohol, and drug abuse which could have predisposed them to MTB. Females were less prone to MTB (Rifampicin sensitive) possibly because of their good health-seeking behavior, and this agrees with studies that revealed globally that, men are significantly more at risk of contracting and dying from TB than women. However, the distribution of MTB (rifampicin sensitive) is not affected by sex (X2=1.17, P=>0.1,). But the distribution of MDR- TB cases 3 (50%) from females and 3 (50%) from males though the same, statistically there was a significant difference in the distribution of MDR-TB by sex score among the refugees with $\chi 2$ = 0.169893, p = 0.021. Gender can affect M. tuberculosis exposure because of different social roles, risk behaviours, and activities. Males may travel more frequently; have more social contacts; spend more time in settings that may be conducive for transmission, such as bars; and engage in professions associated with a higher risk for tuberculosis such as mining (WHO, 2018).

The highest number of cases caused by rifampicin sensitive MTB was from the age of 21-30 and 31-40 years. This could be attributed to their social behaviours and economic status which make them more prone to MTB. Thus exposing them to HIV infection which is a serious risk factor in lowering immunity

and TB infection. The least cases of MTB were from the age groups of 1-10 years and more than 41 years. These groups are economically or socially less active hence less prone to MTB. Most of the MDR-TB case 3 (50%) came from the age group of 31-40 years who are also the most affected by TB and exposed to the risk factors. Resistance to the major standard anti-tuberculosis drugs (rifampicin and isoniazid tablets) is the major challenge that is hindering the TB control and treatment programs in the refugee camps (Romero et al., 2006; Zignol et al., 2006). Therefore, the establishment of the prevalence of MDR-TB among refugees in resettlement camps of Moyo, Yumbe, and Adjumani districts is critical in patient management and control of the deadly disease.

The majority of the respondents who developed MDR-TB; 5 (83.5%) were living in overcrowded places and not yet enrolled on DOTs, 4 (66.7%) had recurrent MTB infections with poor adherence to their prescribed treatment and 2 (33.3%) had TB-HIV co-infection. Statistically

there is a significant relationship between MDR-TB and the associated risk factors (, $X2=12.83$, $P=0.05 \leq P \leq 0.01$). Other studies have not reported HIV infection as a risk factor and there are no reports of a statistical association between spoligotype and drug resistance pattern (Kidenya,2014).

As per these study findings, having TB infection, living in crowded places, and not being enrolled on DOTs and HIV infection could be risk factors to the development of MDT-TB as well as having recurrent TB infections. According to studies done in 2010, the reported incidence of TB among Tibetans living in India was 431cases out of 100 000 persons (KerryL.et al, 2010). The prevalence of HIV among MDR-TB patients was less than 1% (Mishra et al. 2011)

11 Conclusion

According to this study, the general prevalence of MTB (i.e TB) is 20.2% while MTB (Rifampicin sensitive) was 17.5% and that of MDR-TB is 2.7%. The most affected by MTB are males (12.6%). On the other hand, MDR-TB affected both males and females at the same frequency of (1.4%) but statistically more males were infected than females. The most affected age group was 31-40 years and the least affected was 1-10 years. Most of the cases were detected in the Mungula resettlement camp. The study also found out that overcrowding and not being on DOTs, recurrent Tb infections, and poor adherence to treatment are strong risk factors to the development of MDR-TB, unlike HIV infection. It is also worth noting that refugee resettlement camps of Moyo, Yumbe, and Adjumani districts in the West Nile region receive an influx of refugees from mostly South Sudan and the neighbouring countries hence resulting in extensive social mixing with people of different ethnicity for a long period of time which increases the risk of spread of MDR-TB as well as MTB. It is likely that the uncontrolled influx of refugees in the country creates high risks of the fast spread of the disease resulting in the observed results.

Recommendations

- Adherence to the treatment regimen should be strengthened by the national tuberculosis control program to avoid the spread of MDR-TB disease.
- Conduct similar studies in other refugee resettlement camps countrywide.
- There is also a need to monitor the trend of acquired resistance to other anti-mycobacterial agents.
- Decongest overcrowding in refugee resettlement camps to reduce the spread of TB.
- Improve early TB case detection and treatment to reduce the development of MDR-TB and TB.
- Mitigate TB risk factors that predispose people to the acquisition of TB and MDR-TB infection.
- Conduct further studies to characterize Mycobacterium species that cause MDR-TB among refugees.

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References

[1] Joel Bazira, Benon B Asiimwe, Moses L Joloba, Freddie Bwanga, and Mecky I Matee. Mycobacterium tuberculosis spoligotypes and drug susceptibility pattern of isolates from tuberculosis patients in South-Western Uganda. *BMC Infectious Diseases*, 11(1):11–11, 2011.

[2] Harries, 2004.

[3] M J Zhang. Detection of mutations associated with isoniazid resistance in Mycobacterium tuberculosis isolates from China. *Journal of Clinical Microbiology*, 43(11):5477–5482, 2005.

[4] Cdc, 2008.

[5] R B Pierre, A Wierenga, M Barton, K Thame, J M Branday, and C D C Christie. Student self-assessment in a paediatric objective structured clinical examination, 2005.

[6] M A Espinal. Global trends in resistance to anti-tuberculosis drugs. *The New England Journal of Medicine*, 344:1294–1303, 2001.

[7] D Helb and J M Story. Rapid detection of Mycobacterium tuberculosis and rifampin resistance by use of on-demand, near-patient technology. *JClinMicrobiol*, 48:229–237, 2010.

[8] R. Frothingham and W. A Meeker-O'Connell. Genetic diversity in the Mycobacterium tuberculosis complex based on variable numbers of tandem DNA repeats. *Microbiology*, 144(5):1189–1196, 1998.

[9] S Gagneux. Variable host-pathogen compatibility in Mycobacterium tuberculosis. *Proceedings of the National Academy of Sciences, USA 103*, pages 2869–2873, 2005.

[10] Alastair J.J. Wood and Michael D. Iseman. Treatment of Multidrug-Resistant Tuberculosis. *New England Journal of Medicine*, 329(11):784–791, 1993.

[11] Benson R. Kidenya, Lauren E. Webster, Sehan Behan, Rodrick Kabangila, Robert N. Peck, Stephen E. Mshana, Oksana Ocheretina, and Daniel W. Fitzgerald. Epidemiology and genetic diversity of multidrug-resistant tuberculosis in East Africa. *Tuberculosis*, 94(1):1–7, 2014.

[12] Iseman, 1994.

[13] Tanaffos.

[14] *BMC Clinical Pathology*, 12:20–20.

[15] A. Umubyeyi, I. C. Shamputa, L. Rigouts, A. Dediste, M. Struelens, and F. Portaels. Evidence of 'amplifier effect' in pulmonary multidrug-resistant tuberculosis: report of three cases. *International Journal of Infectious Diseases*, 11(6):508–512, 2007.

[16] C Boehme. Rapid molecular detection of tuberculosis and rifampin resistance. *N. Engl. J. Med*, 363:1005–1015, 2010.

[17] W A Githui. Surveillance of drug-resistant tuberculosis and molecular evaluation of transmission of resistant strains in refugee and non-refugee populations in North-Eastern Kenya. *Int J Tuberc Lung Dis*, 4:947–955, 2000.

[18] A D Calver. Emergence of increased resistance and extensively drug-resistant tuberculosis despite treatment adherence. *South Africa. Emerg Infect Dis*, 16:264–335, 2010.

[19] Asiimwe B. Mycobacterium tuberculosis Uganda genotype is the predominant cause of TB in Kampala. *Uganda. Manual for TB diagnosis*, 12(14):386–391, 2015.

[20] Scotto, 2008.

[21] Longo, 2012.

[22] 2016.

[23] Who. *The stop TB strategy: building on and enhancing DOTS to meet the TB related millennium development goals*. Geneva, 2014.

[24] P A Otto. MDR-TB is in town; and might be tugging along XDR-TB. *Southern Sudan Medical Journal*, 2(3):1–2, 2008.

[25] P B Bifani. The evolution of drug resistance in Mycobacterium tuberculosis: From a mono-rifampin-resistant cluster into increasingly multidrug-resistant variants in an HIVseropositive population. *The Journal of Infectious Diseases*, 198:90–94, 2008.

[26] H Traore. Low-cost rapid detection of rifampicin resistant tuberculosis using bacteriophage in Kampala, Uganda. *Annals of Clinical Microbiology and Antimicrobials*, 6:1–6, 2007.

[27] P Baghaei, 2009.

[28] A. G. M. Van Der Zanden, E. M. Te Koppele-Vije, N. Vijaya Bhanu, D. Van Soolingen, and L. M. Schouls. Use of DNA Extracts from Ziehl-Neelsen-Stained Slides for Molecular Detection of Rifampin Resistance and Spoligotyping of Mycobacterium tuberculosis. *Journal of Clinical Microbiology*, 41(3):1101–1108, 2003.

[29] N Range. Anti-tuberculosis drug resistance pattern among pulmonary tuberculosis patients with or without HIV infection in Mwanza, Tanzania. *Tanzania Journal of Health Research*, 14(4), 2012.

[30] B Iseman, 1993.

[31] Benon B Asiimwe, Solomon Ghebremichael, Gunilla Kallenius, Tuija Koivula, and Moses L Joloba. Mycobacterium tuberculosisspoligotypes and drug susceptibility pattern of isolates from tuberculosis patients in peri-urban Kampala, Uganda. *BMC Infectious Diseases*, 8(1):101–101, 2008.

[32] K. Weyer and H. H. Kleeberg. Primary and acquired drug resistance in adult black patients with tuberculosis in South Africa: results of a continuous national drug resistance surveillance programme involvement. *Tubercle and Lung Disease*, 73(2):106–112, 1992.

[33] ' Ndung and P W. Resistance patterns of Mycobacterium tuberculosisisolates from pulmonary tuberculosis patients in Nairobi. *J Infect Dev Ctries*, 6:33–39, 2012.

[34] Deus Lukoye, Frank G. J. Cobelens, Nicholas Ezati, Samuel Kirimunda, Francis E. Adatu, Joseph K. Lule, Fred Nuwaha, and Moses L. Joloba. Rates of Anti-Tuberculosis Drug Resistance in Kampala-Uganda Are Low and Not Associated with HIV Infection. *PLoS ONE*, 6(1):e16130–e16130, 2011.

[35] Kanabus, 2020.

[36] M Sanders. Rifampin mono-resistant Mycobacterium tuberculosis in Bujumbura, Burundi: results of a drug resistance survey. *Int J Tuberc Lung Dis*, 10:178–183, 2006.

[37] Kidenya, 2014.

[38] B E Thomas, 2016.

[39] Daily Monitor, 2015.

[40] L Kerry. *Improved Detection of Tuberculosis and Multidrug-Resistant Tuberculosis among Tibetan Refugees*. India, 2010.

[41] Who, 2016.

[42] Anthony S. Fauci and. Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis: The National Institute of Allergy and Infectious Diseases Research Agenda and Recommendations for Priority Research. *The Journal of Infectious Diseases*, 197(11):1493–1498, 2008.

[43] Je V Oeltmann. Multidrug-resistant tuberculosis outbreak among US-bound Hmong refugees. *Thailand. Emerg Infect Dis*, 14:1715–1721, 2005.

[44] B T Asiimwe. Mycobacterium tuberculosis Uganda genotype is the predominant cause of TB in Kampala. *Uganda. International Journal of Tuberculosis and Lung Diseases*, 12(4):386–391, 2008.

[45] H S Schaaf. Childhood drug-resistant tuberculosis in the Western Cape Province of South Africa. *ActaPaediatrica*, 95:523–531, 2014.

[46] Gibson S Kibiki, Bert Mulder, Wil MV Dolmans, Jessica L de Beer, Martin Boeree, Noel Sam, Dick van Soolingen, Christophe Sola, and Adri GM van der Zanden. M. tuberculosis genotypic diversity and drug susceptibility pattern in HIV- infected and non-HIV-infected patients in northern Tanzania. *BMC Microbiology*, 7(1):51–51, 2007.

[47] W A Githui. Isolation of multidrug-resistant tuberculosis strains in patients from private and public health care facilities in Nairobi. *Kenya. International Journal of Tuberculosis and Lung Disease*, 8(7):837–841, 2004.

[48] Sb and Marahatta. Multidrug resistant tuberculosis burden and risk factors. *Kathmandu University Medical Journal*, 8(1), 2010.

[49] Vareldzis, 1994.

[50] Global Tuberculosis control. *World Health Organization*, 2019.

[51] W J Githui. Identification of MDR-TB Beijing/W and other Mycobacterium tuberculosis genotypes in Nairobi, Kenya. *Int J Tuberc Lung Dis*, 8:352–360, 2004.

[52] Leslie Kish. Determining sample size for research activities. *Educational And Psychological Measurement*, 30:607–610, 1970.

[53] H Albert. Rapid screening of MDR-TB using molecular Line Probe Assay is feasible in Uganda. *BMC Infect Dis*, 10:41–41, 2010.

[54] Kr Steingart, 2014.

[55] *Procedings of National Academy of Sciences, USA*, 91:2428–2429.

[56] A Somoskovi. The molecular basis of resistance to isoniazid, rifampin, and pyrazinamide in Mycobacterium tuberculosis. *Respiratory Research*, 2:164–168, 2001.

[57] L David. *Control of communicable diseases manual 18th edn*. American Public Health Association, Washington, D.C, 2004.

[58] C Dye, 2008.

[59] Mishra. Treatment of drug-resistant Tuberculosis. The Lancet Infectious Disease. *Manual of the National Tuberculosis and Leprosy Program*, 2010.

[60] Philip LoBue. Extensively drug-resistant tuberculosis. *Current Opinion in Infectious Diseases*, 22(2):167–173, 2009.

[61] Yanis Ben Amor, Bennett Nemser, Angad Singh, Alyssa Sankin, and Neil Schluger. Underreported Threat of Multidrug-Resistant Tuberculosis in Africa. *Emerging Infectious Diseases*, 14(9):1345–1352, 2008.

[62] G E Pfyffer. Drug-resistant tuberculosis: Resistance mechanisms and rapid susceptibility testing. *Schweiz Med Wochenschr*, 130:1909–1913, 2000.

[63] E Kassa-Kelembho, B.-S G Takeng, E C Nambea-Koisse, T B Yapou, F Talarmin, and A. Surveillance of drug-resistant childhood tuberculosis in Bangui. *Central African Republic. IntTuberc Lung Dis*, 8(5), 2004.

[64] S Keshavjee. *Stemming the tide of multidrug resistant tuberculosis: Major barriers to addressing the growing epidemic. Institute ofMedicine, national academies*. Washington DC, 2008.

[65] T Ogaro. Anti-tuberculosis drug resistance in. *Afr J Health*, 20:21–27, 2012.

[66] J Gafirita, 2012.

[67] Matteo Zignol, Mehran S. Hosseini, Abigail Wright, Catharina Lambregts–van Weezenbeek, Paul Nunn, Catherine J. Watt, Brian G. Williams, and Christopher Dye. Global Incidence of Multidrug-Resistant Tuberculosis. *The Journal of Infectious Diseases*, 194(4):479–485, 2006.

[68] Bifani. Rapid molecular detection of tuberculosis and rifampin resistance. *N Engl J Med*, 363:1005–1015, 2010.

[69] *Journal of Medicine*, 329(11):784–791.

[70] *Guidance for national tuberculosis programmes on the management of tuberculosis in children*. Geneva, 2006.