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Rifampicin (RMP) is associated with the lowest occurrence of resistance against tubercle bacilli (Mukinda et al 2012). It is estimated that nearly 60,000 MDR- TB cases occur annually in the sub- Saharan region and these comprise of 14% of the global burden of TB (WHO 2010).

The prevalence of rifampicin resistance according to this study's findings was 10%.

The predisposing factors to rifampicin resistance were cigarette smoking (P-Value = 0.001), history of prolonged stay with a TB infected patient, (P-Value = 0.001) and history of previous treated episode of TB among the study respondents (P-Value = 0.001).

The government of Uganda needs to carry out more intensified mass sensitization of people about the dangers of cigarette smoking particularly to HIV infected individuals.

In the same line of sensitization, people need to be continuously reminded by ministry of health about the signs and symptoms of TB so that community members can identify suspects and refer them for specialised diagnosis and management such that delayed detection of the disease is minimised which will also reduce on rifampicin resistance. It will also minimise exposure of people living with the infected individuals.

A Research Report Submitted to the Faculty of Hass of University O Kisubi in Partial Fulfillment of the Requirements for the Award of a Diploma in Medical Laboratory Technology .

Definition of Key Terms

MDR TB: This refers to a strain of TB that is resistant to isoniazid and rifampicin.

Sputum positive: A person known to have tubercle bacilli in their sputum when examined.

Immune compromised: This refers to a patient with a lower immune status than normal which makes him/her susceptible to infection.

I. CHAPTER ONE: INTRODUCTION

1.1 Background to the study

Tuberculosis (TB) remains one of the world's leading causes of adult morbidity and mortality resulting in an estimated 8.8 million incident cases and 1.4 million deaths. Up to 92% of the TB cases occur in low and middle-income countries with sub-Saharan Africa region hosting nine of the highest TB incidence countries globally (WHO 2011). Uganda is ranked 16th among the 22 high burden countries (NTLP 2010). Treatment of tuberculosis lasts at least 8-months using a combination of first line drugs: Isoniazid, Rifampicin, Pyrazinamide, Ethambutol and Streptomycin. Rifampicin and Isoniazid both form an integral part of the initiation and continuation phase of anti-tubercular treatment regimens in all defined categories of patients (WHO 2010).

Rifampicin (RMP) is associated with the lowest occurrence of resistance against tubercle bacilli (Mukinda et al 2012). It is estimated that nearly 60,000 MDR- TB cases occur annually in the sub-Saharan region and these comprise of 14% of the global burden of TB (WHO 2010).

Rifampicin-monoresistant TB (RMR-TB) has been noted as a problem in the United States, particularly in HIV infected individuals (Sandman et al 2000). A study in the Western Cape of South Africa by Mukinda et al (2010) reported a 12 % prevalence of RMR-TB and found alcohol, HIV co-infection and other factors as predisposing factors to resistance. Studies done in some sub-Sahara African countries indicate low rates of MDR-TB defined as resistance to at least INH and RIF among new patients of TB. The prevalence of MDR-TB was 1.4% in Burundi, 1.2% in Tanzania, 2.6% in Gambia and 3.4% in Mozambique (WHO 2010). In Rwanda, the prevalence of MDR-TB was 3.9 % (Umubweyi et al 2011).

A study by Jones-Lopez et al (2011) in Mulago Hospital on TB patients reported a 23% prevalence of MDR-TB and a 1% prevalence of Rifampicin Mono resistance. Lukoye et al (2011), in a Kampala survey among new cases of TB reported a prevalence of MDR Tuberculosis of 1.1% and rifampicin mono resistance of 0.8%.

They however found no association between MDR and HIV co-infection. A survey done by Lukoye et al (2011) in Uganda among old and new cases of TB reported a prevalence of rifampicin resistance of 0.4% among 1209 new TB cases and a rifampicin resistance of 23% among previously treated cases. All Rifampicin resistant cases were also Multi-drug resistant. Rifampicin plays a prominent role in TB treatment as one of the first line TB drugs and it is important that this drug does not develop resistance because of the limited treatment alternatives available. Furthermore, detection of rifampicin resistance is important in directing clinicians in the making of informed decisions (Karenye 2013). A number of factors influence development of TB resistance which can be due to the patient adherence, the treatment regimen itself or pre-treatment factors. In 2001, the MoH through National Tuberculosis and Leprosy Program formally adopted the community-based TB Care (CBTBC) strategy to address the TB challenges in the country. Much as chronic cases can be detected using sputum smears and resistance made by microbiological cultures, there is a need to increase the case detection rates of new and old resistance cases if TB is to be put under control. Scaling up the use of the Genexpert which is a faster, accurate and robust method needs to be done expeditiously so that the burden of MDR-TB does not reverse gains made in both TB and the HIV fight.

1.2 Problem statement

Drug resistance among tuberculosis patients is a major and emerging threat to its control and treatment both globally and in Uganda and this threatens to reverse the gains made so far in the fight against tuberculosis. TB had a death rate of 5.3% and in 2007 it claimed 9.3 million lives a good number who were drug resistant (WHO 2008). No national study has been done on TB drug resistance so far. However, a study done in some parts of Uganda reported a Rifampicin resistance prevalence of 0.8% while a study among 214 admitted patients at Mulago National referral hospital in 2000 reported a rifampicin prevalence of 1.4% (Lopez et al 2011). While these rates appear low, concern has to be raised with regard to the reducing cure rates of TB by rifampicin and isoniazid as reported in South Africa which is no different from Uganda thus highlighting the need for closer scrutiny of these rates (Wright et al 2009).

No drug resistance study has been done among Lubaga hospital TB patients. There needs to be a more comprehensive study about TB drug resistance and particularly about rifampicin since this drug is a surrogate marker of MDR- TB.

Relapses seem to be on the rise in Lubaga hospital and cure rates are not exactly known. The need for more elucidation about the resistance of TB primary drugs needs to be done to aid the better management of all categories of TB patients in Lubaga hospital.

1.3 General objective

To determine the prevalence of rifampicin resistant tuberculosis and its associated factors among patients in Lubaga hospital.

1.4 Specific objectives

1. To determine the prevalence of rifampicin resistant TB among patients in Lubaga hospital.
2. To assess the major factors associated with Rifampicin resistance among TB patients in Lubaga hospital.

1.5 Research questions

1. What is the prevalence of rifampicin resistant TB among patients in Lubaga hospital?
2. What are the major factors associated with rifampicin resistance among TB patients in Lubaga hospital?

1.6 Significance of the study

The study generated new information with regard to rifampicin-TB resistance and its associated factors among patients at Lubaga hospital. This information generated can be used to improve TB such that resistance to TB treatment is minimised for better health.

The findings can also be used as a source of reference for people who wish to conduct further research in related areas of study.

The study has been used by the researcher as a partial requirement to be fulfilled for the award of a Diploma in Medical Laboratory Technology.

Since the introduction of the community based care programme of TB management by Ministry of Health, there have been major milestones achieved such as the treatment targets reaching 80% from 70%. However the emergence of resistance threatens to make TB incurable once again and treatment 100 fold more expensive. The need to address resistance is urgent and needs an extensive study to identify MDR-TB as early as possible to minimise resistance.

1.7 Scope of the study

This study was limited to TB patients at Lubaga hospital who consented to take part in the study between Apriland June 2015.

II. CHAPTER TWO: LITERATURE REVIEW

2.1 Prevalence of Rifampicin resistant TB

In a study about prevalence of rifampicin mono resistant mycobacterium tuberculosis among suspected cases accessing services at Yirgalem Hospital in Israel, a total of 236 participants were included under this study. Among these, 57.6% were males and 42.4% were female. Concerning to treatment history, 177 (75.0%) were new cases and the rest, 59 (25.0%) were old cases. The overall prevalence of pulmonary tuberculosis was 16.5% and out of these, the prevalence of rifampicin mono-resistant Tuberculosis was 3.4% (Mesfinand Teshome 2015).

According to a report by Fasih et al (2012), 7738 strains of Mycobacterium tuberculosis were isolated from pulmonary specimens submitted in an Iranian study from 2009 to 2011. These included 54% (n 4183) rifampicin susceptible and 46% (n: 3555) rifampicin resistant strains. Analysis of rifampicin susceptible strains showed resistance to at least one of the first line drugs in 27% (n: 1133) of the isolates.

In a study conducted about the global isoniazid resistance patterns in rifampicin-resistant and rifampicin-susceptible tuberculosis, out of the 673 strains tested, 95 (14.11%) showed mono-resistance, 365 (54.23%) strains were found to be resistant to more than one drug. A total of 118 (17.53%) strains were found to be resistant to all the four drugs tested. MDR was seen with 320 (47.54%) isolates. This study observed maximum resistance with rifampicin (74.4%) followed by streptomycin (70.0%), isoniazid (53.2%), and ethambutol (21.7%) (Menon, et al 2012)

The emergence and spread of multi-drug resistant tuberculosis (MDR-TB) is threatening to destabilize global tuberculosis control. The prevalence of MDR-TB is increasing throughout

the world even among newly diagnosed cases of sputum-positive pulmonary tuberculosis.A total of 218 cases of sputum-positive pulmonary tuberculosis were enrolled between 2008 and 2009 and of these, 41 (18.8%) cases had negative mycobacterial cultures and DST was carried out in 177 cases. The mean age of the patients was 27.8 ± 10.2 years; 59 patients (27%) were female. All patients tested negative for HIV infection. Out of 177 cases, two cases of MDR-TB were detected.

Thus, the prevalence of MDR-TB among newly diagnosed pulmonary tuberculosis patients was 1.1 per cent. (SurendraK et al 2010)

Studies done in the United States indicate that TB drug resistance had decreased down to 3% (CDC, 2004) while in neighboring East African countries such as Rwanda, a prevalence rate of rifampicin resistance of 3.9 % was reported and it was 2.7 % in Northern Tanzania (Kibiki et al 2007). A study done in Mbarara Uganda by Bazira et al (2011) reported a 5.6% prevalence of TB rifampicin resistance. A 1996-1997 National TB drug resistance survey reported 0.8% prevalence (Bretzel et al, 1998), while another study in the peri-urban areas of Kampala reported a prevalence of rifampicin resistance of 4.4 % (Nieman et al 2008). The differences in this figure might be due to the sampling strategies that were used in each of the studies above where one sampled the whole country while the other looked at one division of Kampala which is highly burdened with TB.

Identification of rifampicin-resistant tuberculosis is an important event, both for the individual patient and from a public health perspective, triggering a cascade of interventions, including additional drug susceptibility testing, appropriate patient referral for extended and potentially toxic treatment, and contact tracing. The definitive diagnostic test should therefore have very high specificity. A recent Cochrane review (6) estimated the sensitivity and specificity of Xpert for rifampicin resistance as 94% (95% CI, 87 to 97) and 98% (95% CI, 97 to 99), respectively.

With these parameters and a prevalence of rifampicin resistance of 5%, the positive predictive value of a rifampicin-resistant result on Xpert would be 71%. The measured positive predictive value in this study of the Xpert version 4 assay is 99.5% (95% CI, 98.47 to 100) (Muhammad et al 2011).

2.2 Major factors associated with Rifampicin resistant development TB

Mesfin et al (2015) conducted a study in which fifty eight (24.6%) of the total subjects were suspected for MDR tuberculosis. Twenty two (9.3%) of the subjects were smear positive andthe highest positive finding of rifampicin susceptible Mycobacterium tuberculosis bacilli were observed within the age group of 16-30 years.

Non-adherence to treatment is a problem in Tuberculosis (TB) management as with other long term illnesses which can be categorized into patient, drug and provider related factors (MoH 2011). TB treatment presents particular challenges for adherence because the treatment is long and involves taking a number of medications.

Side-effects are common and the patient usually feels better long before treatment has been completed coupled with a high pill burden in HIV patients (Macllean 2003). Non-adherence has been cited as one of the reasons for failure of achievement of the global treatment success rates by Uganda (WHO 2007). As a consequence retreatment failure has been singled out as the leading indicator of resistance failure. TB second line regimen entails in most cases use of one of the drugs previously taken in regimen one as recommended by the WHO thus when retaken, this compounds resistance of the TB to the drug such as rifampicin yet it tends to be more toxic (WHO 2008).

Transmission has been known to generate resistant genotypes even in those with good adherence. This is because in the process of transmission, strains develop new resistance capabilities hence creating resistance in the next host. Health care workers and those caring for the TB patient are at an increased risk of acquiring resistant strains. However transmission of an already existing strain has been observed among those who are exposed (Menon et al 2012).

There is a clear link between TB and HIV, with 13% of the global TB cases occurring among HIV infected individuals. Incidence of HIV-positive TB cases is even higher in Africa, where 79% of the newly diagnosed cases are found (WHO 2012).

According to Bazira et al (2011), TB resistance has been linked to HIV which has caused an increase in Mycobacterium tuberculosis complex (MTC) infection and rapid progression of the infection. It is also known to increase MTC transmission rates at the community level, further threatening the health and survival of HIV sero-negative individuals as well.

Among HIV infected patients on ART especially efaverinz, malabsorption of RMP and INH occurs and may be a contributing factor to consider, although the pharmacokinetics of RMP may be variable even without HIV (Gurumurthy et al 2004).Furthermore, it is possible that, in immune-compromised patients with TB, bacterial mutations confer drug resistance to anti-TB (Gagneux et al 2006).

According to Pablo-Mendez (1998), previous treatment has been widely recognised as inducing multidrug resistance of *M. tuberculosis* and the prevalence of MDR-TB has been estimated to be up to 10 times higher after unsuccessful treatment.

In a study carried out by Van et al *(*2010) in Cape Town, South Africa, tobacco smoking causes bronchitis, chronic obstructive pulmonary disease (COPD) and chronic pulmonary disability which are risk factors for MDR-TB. This implies that people who smoke cigarettes have nearly twice the risk of TB drug resistance than non-smokers.

Disease states including alcoholism and diabetes mellitus can increase the risk of developing tuberculosis. Certain medications, such as corticosteroids and infliximab (an ant i- α TNF monoclonal antibody) are becoming increasingly important risk factors for drug resistance, especially in the developed world (Rajani*et al*, 2013).

Delayed recognition of drug resistant TB due to poor detecting techniques, inappropriate chemo-therapy regimens, inadequate or irregular drug supply, and poor compliance by both patients and clinicians have each been reported as a reason for unsuccessful TB treatment (Pablo-Méndez A 1998).

III. CHAPTER THREE: METHODOLOGY

3.1 Study site

The study was carried out in Lubaga hospital. The hospital is located on Rubaga hill just adjacent to Lubaga cathedral, about 5km from the city Centre. Lubaga hospital is one of the oldest hospitals in Uganda having been founded in 1899, over 100 years ago. It is the second oldest hospital in the country and has offered health care to millions of people during its long history of existence. Over the years the hospital has built a reputation as a provider of affordable health care services and therefore has continued to attract and treat people of mainly mid-level and low level status. The hospital serves a low-income community of an official catchment area of 130,000 people in urban Kampala–Lubaga Division (KCCA data).

Lubaga Hospital is a 275 bed, private-not-for-profit hospital of the Archdiocese of Kampala. It provides medical services in pediatrics, maternity /gynaecology, internal medicine, surgery, Public Health, and HIV Care and Treatment.

In October 2012 the Board decided that the name of the hospital should be changed: from previously Rubaga Hospital to Lubaga Hospital.

The Board also clarified that the full name of the hospital is now “Uganda Martyrs Hospital Lubaga.”

3.2 Study design

Thiswas a cross sectional descriptive study that enrolled clients who were on TB treatment.

3.3 Study population

The study population comprised of all TB patients accessing services from Lubaga hospital during the time of the study.

3.4 Sample size determination

The sample size was determined following the formula Kish and Leslie (1965)

$N = \frac{Z^2 PQ}{d^2}$

Where: n = Sample size

Z =Standard normal deviation usually set at 95 % (1.96)

p =Prevalence. Using 50% as the prevalence since the prevalence of Rifampicin resistant TB is not known (0.5)

Q = (1-p) = (1-0.5) = 0.5

d =Standard error allowed in the study set at, 5% = (0.05)

Therefore $N = \frac{1.96^2 0.5 \; X \; 0.5}{0.05^2} = 384$

384 TB clients were enrolled into the study.

3.5 Selection criteria

3.5.1 Sampling method

Study participants were selected using simple random sampling method. For this research, 384 papers had the words "yes" written on them and another 384 papers had the words "no" written on them. The papers were carefully rolled in approximately similar ways before being shuffled in a cup. The TB clients were then asked to each pick a paper from the cup and only those picking the paper with the words "yes" were selected into the study. In the selection process, papers were shuffled after every pick.

3.5.2 Inclusion criteria

Only TB patients at Lubaga hospital TB clinic who were attending the TB clinic during the period of the study were eligible for enrolment into the study and were recruited if they consented to taking part in the study. For children, they were only enrolled upon consent of their parents or care takers.

3.5.3 Exclusion criteria

Non TB patients plus the ones who refused to consent during the time of study were excluded from the study.

3.6 Data collection tool

The instrument to be used for data collection was a structured questionnaire.

3.6 Data collection procedure and management

The structured questionnaire was self-administered for literate participants and interviewer-administered for illiterate clients. The questionnaire was reviewed to see if it was completely filled and all those questionnaires found to be partially filled in were handed back to their respective respondents for completion before re-submission to the researcher. One sputum specimen was also collected from the study participants and was analyzed by geneXpert machine (See appendix IV).

3.7 Data management and analysis

Data collected was stored in a data master sheet and transferred to Microsoft excel. Data was kept with utmost security by use of codes, passwords and encryption.

Data was exported to SPSS for Windows version 17 and analyzed with the help of a statistician.

Descriptive statistics were computed and presented in form of diagrams, measures of central tendency (especially the mean, mode, median) and measures of dispersion. Existence of any significant differences between patients' categories was investigated.

3.8 Quality control

Furthermore temperature logs, maintenance logs of the machine and routine maintenance were

used. Laboratory controls were run and monitored during the study period.

3.9 Ethical consideration

The researcher sought permission from Lubaga hospital research committee to do the study.

Information to be obtained from the respondents was treated with utmost confidentiality. Study numbers but not names were used on questionnaires for data collection as a way of keeping the respondents' identity anonymous.

Informed consent was also sought from each of the respondents before enrolling them into the study.

3.10 Dissemination of results

Results of the study were compiled into a research report, copies of which were disseminated to Lubaga hospital and the faculty of HASS of University of kisubi such that the information can spread to all concerned people.

IV. CHAPTER FOUR: RESULTS

4.1 Socio-Demographic Characteristics

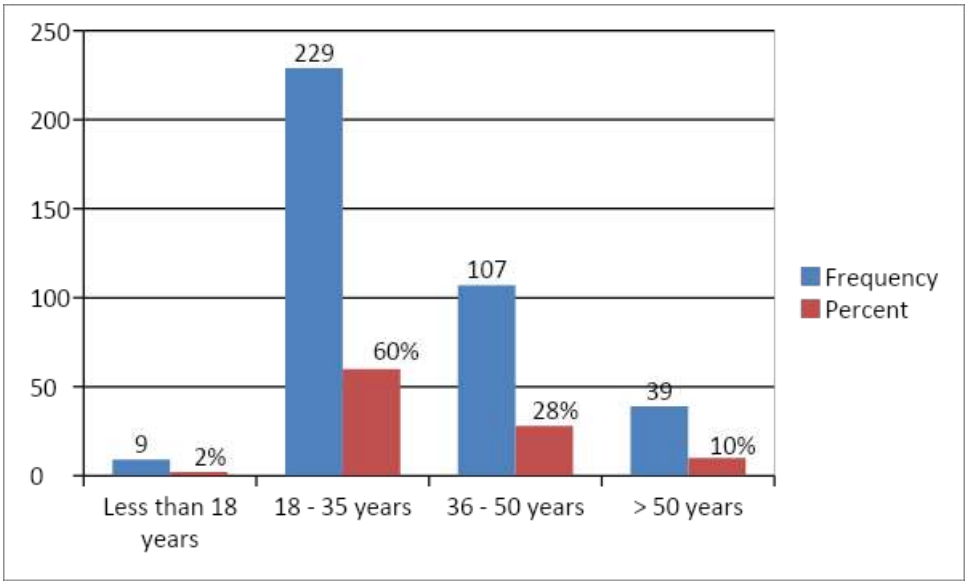

Figure 1: Distribution of the study respondents by their ages

Figure 1 above shows that 229 (60%) of the respondents were aged 18 to 35years, 107 (28%) were 36 to 50years, 39 (10%) were above 50years and 9 (2%) were less than 18 years.

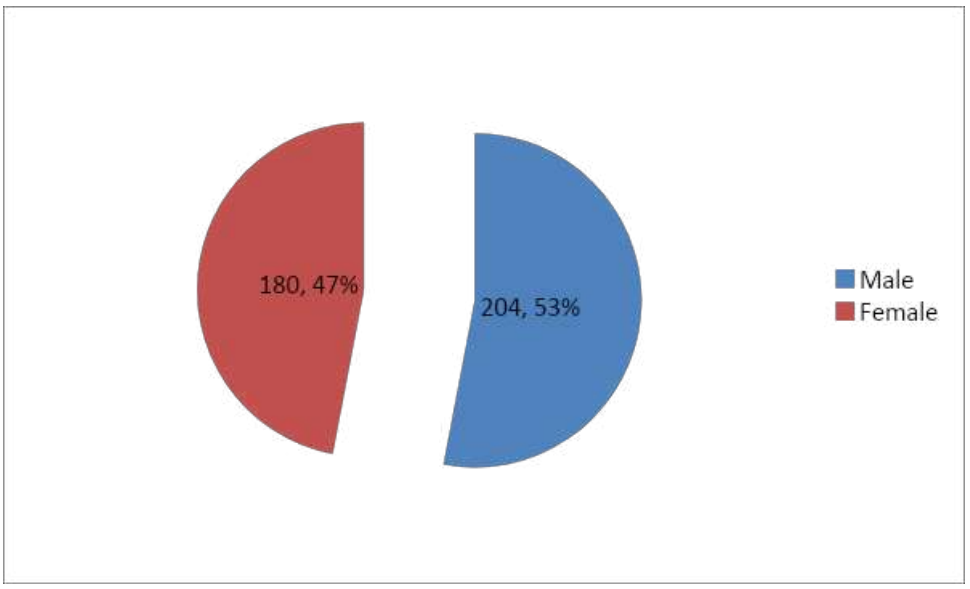

Figure 2: Distribution of respondents by their gender

Figure 2 above shows that 204 (53%) of the respondents were male and 180 (47%) were females.

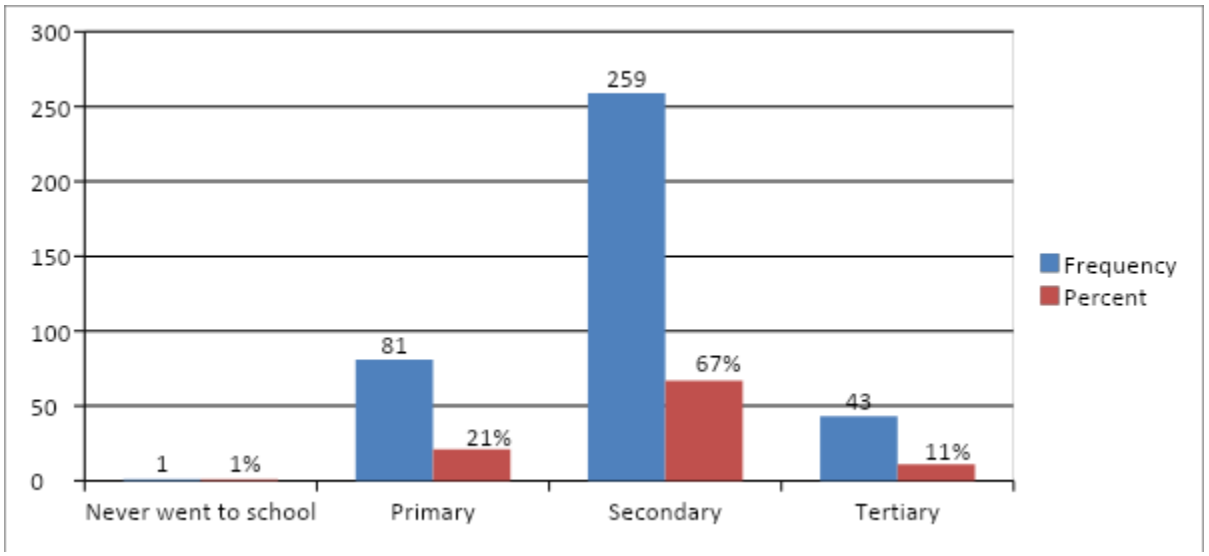

Figure 3: Distribution of respondents by their education status

Figure 3 above shows that 259 (67%) of the respondents had gone up to secondary school for their education, 81 (21%) had stopped in primary school, 43 (11%) had attained tertiary level of education and 1 (1%) was illiterate.

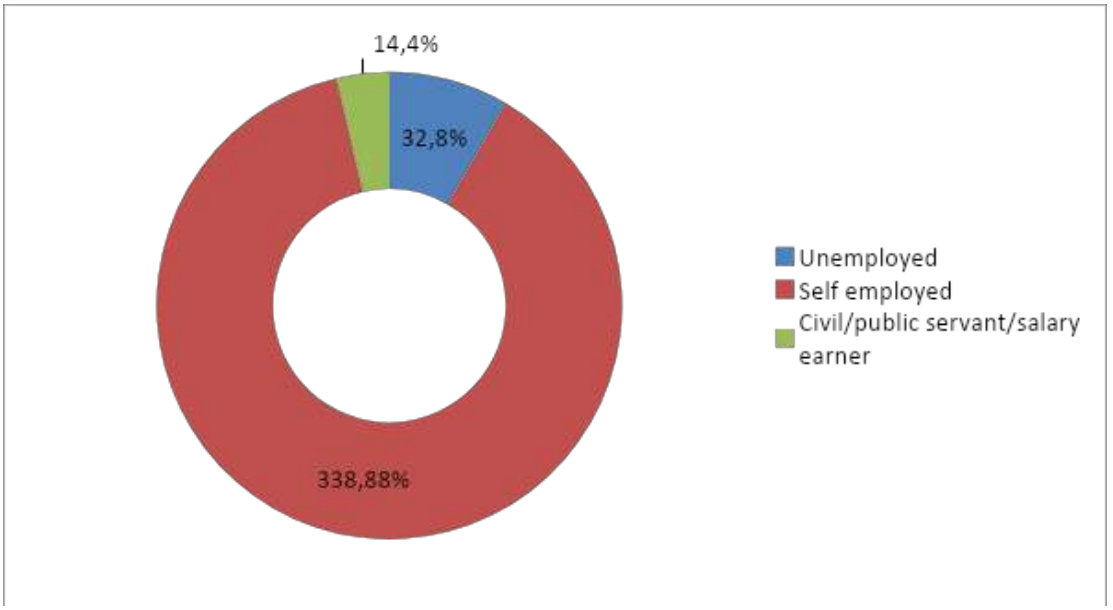

Figure 4: Distribution of respondents by their occupations

Figure 4 above shows that by occupation, 338 (88%) of the respondents were self-employed, 32 (8%) were unemployed and 14 (4%) were Civil/public servants/salary earners.

4.2 Prevalence of rifampicin resistant TB among patients in Lubaga hospital

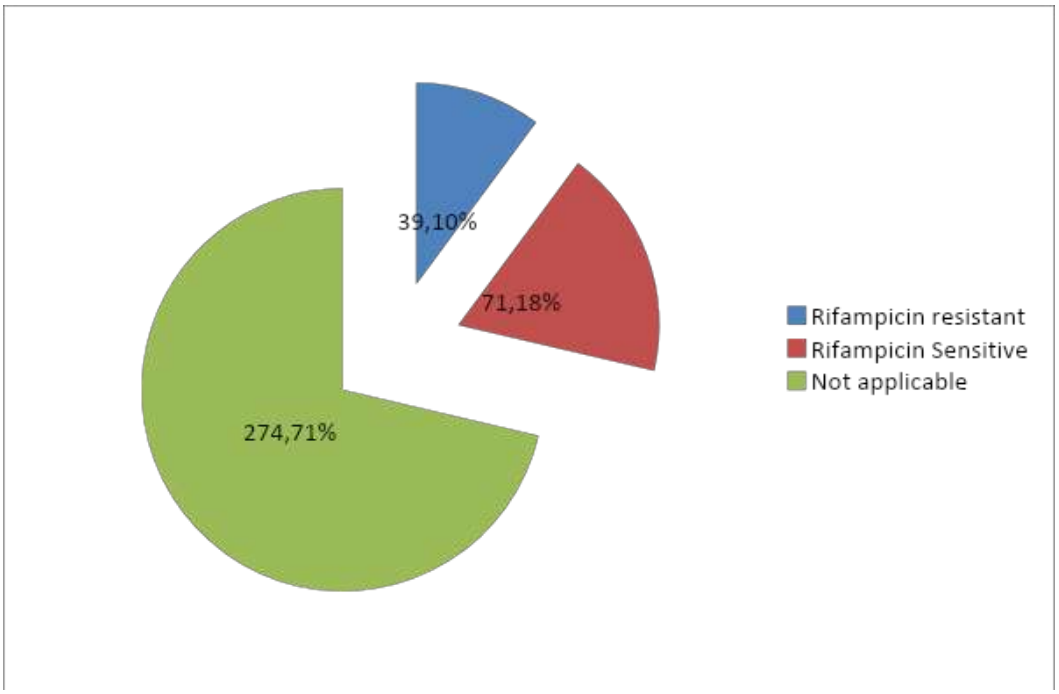

Figure 5: Showing rifampicin resistance among the study respondents

Figure 5 above shows that 39 (10%) of the respondents had rifampicin resistant strains of *Mycobacterium tuberculosis*, 71 (19%) had sensitive strains and 274 (71%) of the respondents had this non-applicable.

4.3 Factors associated with Rifampicin resistance among TB patients in Lubaga hospital

Table 1: History of previous TB treatment of the study respondents related with their rifampicin sensitivity status

		Have you been treated for TB before?		Total
		Yes	No	
Status of mycobacterium sensitivity to rifampicin	Sensitive	13	58	71
	Resistant	7	32	39
	Not Applicable	4	270	274
Total		24	360	384

P-Value = 0.001

Table 1 above show that of the 24 patients who had been treated for TB before, 13 had rifampicin sensitive tubercle bacilli, 7 had rifampicin resistant strains and for 4 respondents, this wasn't applicable. The table further shows that of the 360 respondents who had never been treated for TB before, 58 had rifampicin sensitive tubercle bacilli, 32 had rifampicin resistant strains and for 270, this was not applicable.

Table 2: Status of completion of treatment among previously TB positive patients related with their rifampicin sensitivity status

		If yes to question e) above, did you complete treatment		Total
		Yes	No	
Status of mycobacterium sensitivity to rifampicin	Sensitive	4	10	14
	Resistant	2	4	6
	Not Applicable	0	4	4
Total		6	18	24

P-Value = 0.438

Table 2 above shows that of the 6 respondents who had completed TB treatment before, 4 hand rifampicin sensitive tubercle bacilli and 2had rifampicin resistant tubercle bacilli strains. The table further shows that of the 18 respondents who hadn't completed the anti-TB treatment, 10 rifampicin sensitive tubercle bacilli, and 4 had rifampicin resistant tubercle bacilli strains and to 18 respondents, this wasn't applicable.

Table 3: History of prolonged contact with TB patient in respondent's history related with their rifampicin sensitivity

		Have you ever stayed with a TB patient or treated one		Total
		Yeas	No	
Status of mycobacterium sensitivity to rifampicin	Sensitive	2	69	71
	Resistant	3	36	39
	Not Applicable	1	273	274
Total		6	378	384

P-Value = 0.002

Table 3 above shows that of the 6 respondents who had ever had prolonged contact with a patient in their past, 2 had rifampicin sensitive tubercle bacilli,3 had rifampicin resistant tubercle bacilli and 1

had it not applicable. The table further shows that of the 378 respondents who had not had a prolonged stay with a TB patient in their past, 69 had rifampicin sensitive tubercle bacilli, 36 had rifampicin resistant tubercle bacilli and to 273 respondents, this was not applicable.

Table 4: Smoking status of respondents related with their rifampicin sensitivity status

Count		Do you smoke cigarettes		Total
		Yes	No	
Status of mycobacterium sensitivity to rifampicin	Sensitive	8	63	71
	Resistant	3	36	39
	Not Applicable	4	270	274
Total		15	369	384

P-Value = 0.001

Table 4 above shows that of the 15 respondents who were cigarette smokers, 8 had rifampicin sensitive tubercle bacilli, 3 had rifampicin resistant strains of tubercle bacilli and 4 had this as not applicable. The table further shows that of the 369 respondents who were not cigarette smokers, 63 had rifampicin sensitive bacilli, 36 had rifampicin resistant strains of tubercle bacilli and for 270 respondents this was not applicable.

Table 5: Alcohol consumption of respondents related with their rifampicin sensitivity status

Count		Do you drink alcohol		Total
		Yes	No	
Status of mycobacterium sensitivity to rifampicin	Sensitive	14	57	71
	Resistant	6	33	39
	Not Applicable	4	270	274
Total		24	360	384

P-Value = 0.001

Table 5 above shows that of the 24 respondents, who were consumers of alcohol, 14 had rifampicin sensitive tubercle bacilli, 6 had rifampicin resistant strains of the tubercle bacilli and for 4 respondents this was not applicable. The table further shows that of the 360 respondents who were non-alcohol consumers, 57 had rifampicin sensitive tubercle bacilli, 33 had rifampicin resistant strains of tubercle bacilli and to the 270 respondents this was not applicable.

Table 6: Marijuana or Cocaine or Mairungi use among respondents related with their rifampicin sensitivity status

Count		Do you use Marijuana or Cocaine or Mairungi		Total
		Yes	No	
Status of mycobacterium sensitivity to rifampicin	Sensitive	4	67	71
	Resistant	1	38	39
	Not Applicable	4	270	274
Total		9	375	384

P-Value = 0.116

Table 6 above shows that of the respondents, who were users of Marijuana or Cocaine or Mairungi, 4 had rifampicin sensitive tubercle bacilli, 1 had rifampicin resistance and to the remaining 4, it was not applicable. The table also shows that of the 275 respondents, who were not usingMarijuana or Cocaine or Mairungi, 67 had rifampicin sensitive tubercle bacilli, 38 had rifampicin resistant tubercle bacilli and to 270, this was not applicable.

Table 7: HIV status of the respondents related with their rifampicin sensitivity status

Count		What is your HIV status?		Total
		Positive	Negative	
Status of mycobacterium sensitivity to rifampicin	Sensitive	50	21	71
	Resistant	33	6	39
	Not Applicable	204	70	274
Total		287	97	384

P-Value = 0.256

Table 7 above shows that of the 287 respondents who were HIV positive, 50 had rifampicin sensitive tubercle bacilli, 33 had rifampicin resistance and 204 had the question as not applicable. The table also shows that of the 97 respondents who were HIV negative, 21 had rifampicin sensitive tubercle bacilli, 6 had rifampicin resistant bacilli and to 70 respondents, it was not applicable.

V. CHAPTER FIVE: DISCUSSION OF RESULTS, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter presents a discussion where this study's findings are compared with the findings of other authors in similar studies done prior to this one. In this chapter, conclusions are drawn and based on the research findings, recommendations are drawn.

5.2 Socio-Demographic Characteristics of the study respondents

It was revealed that majority, 229 (60%) of the respondents in this study were aged 18 to 35 years, followed by 107 (28%) who were 36 to 50 years old, then by 39 (10%) who were above 50 years and lastly by 9 (2%) respondents who were less than 18 years old (Figure 1).

Slightly more than half, 204 (53%) of the respondents were male and 180 (47%) were females (Figure 2) whereas by educational status, slightly more than two thirds, 259 (67%) of the respondents had gone up to secondary school, about one fifth, 81 (21%) had stopped in primary school, about one tenth 43 (11%) had attained tertiary level of education and 1 (1%) were illiterate (Figure 3).

By occupation, 338 (88%) of the respondents were self-employed, 32 (8%) were unemployed and 14 (4%) were Civil/public servants/salary earners (Figure 4).

5.3 Prevalence of rifampicin resistant TB among patients in Lubaga hospital

Up to 10% of the respondents had rifampicin resistant strains of *Mycobacterium tuberculosis* and this reveals a prevalence of rifampicin resistance of 10%. This finding is a little higher than the prevalence of rifampicin mono-resistant Tuberculosis of 3.4% reported in a study by Mesfinand Teshome (2015). The prevalence finding of rifampicin resistance of 3.9% in Rwanda and 2.7% in Tanzania is also lower than this study's prevalence of 10% reported by Kibiki et al (2007).

Some studies done by Bazira et al (2011) and Nieman et al (2008) reported prevalences of 5.6% and 4.4% respectively in other Kampala studies which were also lower than this study's prevalence of rifampicin resistance of 10%.

This study's prevalence findings of 10% is however lower than the prevalence of rifampicin resistance of 46% reported in an Iranian study by Fasih et al (2012) and the prevalence of 74.4% reported by Menon, et al (2012)

5.4 Factors associated with Rifampicin resistance among TB patients in Lubaga hospital

It was discovered in this study that out of the 24 patients who had been treated for TB before, 13 had rifampicin sensitive tubercle bacilli and 7 had rifampicin resistant strains (Table 1; P-Value = 0.001). This shows that a strong association existed between the two variables and as such makes the finding to be similar to that of Pablo-

Mendez (1998), who reported that previous treatment was widely recognised as inducing multidrug resistance of *M. tuberculosis*.

Of the 6 respondents who had completed TB treatment before the current relapse, 4 had rifampicin sensitive tubercle bacilli and 2 had rifampicin resistant tubercle bacilli strains (Table 2., P-Value = 0.438). Based on the p-value, there was no significant statistical association between completion of treatment and sensitivity and makes this finding contrary to the observation made by (WHO 2007) that non-adherence is one of the reasons for failure of achievement of the global treatment success rates of TB by Uganda.

In this study, 6 respondents had had prolonged contact with a patient in their past and out of these, 2 had rifampicin sensitive tubercle bacilli, 3 had rifampicin resistant tubercle bacilli,P-Value = 0.001 (Table 3). It is possible that there was delayed recognition of TB in the patients they had lived with such that those patients had developed rifampicin resistant strains which they had passed on to this study's respondents who in turn developed rifampicin resistance which relates with the findings of Pablo-Méndez A (1998).

There was a total of 15 respondents who were cigarette smokers, and of these, 8 had rifampicin sensitive tubercle bacilli whereas 3 had rifampicin resistant strains of the tubercle bacilli (Table 4, P-Value = 0.001). This implies that cigarette smoking increased ones chances of getting resistance to rifampicin which is in line with the findings of Van et al(2010) who in a study carried out by in Cape Town, reported that tobacco smoking causes bronchitis , chronic obstructive pulmonary disease (COPD) and chronic pulmonary disability which are risk factors for MDR-TB. This implies that people who smoke cigarettes have nearly twice the risk of TB drug resistance than non-smokers.

According to this study, there were 24 respondents who were consumers of alcohol and out of these, 14 had rifampicin sensitive tubercle bacilli and 6 had rifampicin resistant strains of the tubercle bacilli (Table 5; P-Value = 0.116). Based on this study's p-value, alcohol consumption was not statistically associated with rifampicin resistance which makes it a contrary finding to the findings of Rajani*et al*, (2013) who reported in part that alcoholism an increasingly becoming an important risk factor for TB drug resistance.

Among the 9 Marijuana or Cocaine or Mairungi users in this study, 4 of them had rifampicin sensitive tubercle bacilli whereas 1 had rifampicin resistance (Table 6, P-Value = 0.116). This shows that there was no significant association between these drugs and rifampicin resistance.

Of the 287 respondents in this study who were HIV positive, 50 had rifampicin sensitive tubercle bacilli and 33 had rifampicin resistant strains (Table 7). Though by numbers there seems to be a variation between rifampicin sensitive tubercle bacilli and rifampicin resistant strains wasn't statistically significant (P-Value = 0.256). This is contrary to the findings of Bazira et al (2011), who reported TB treatment resistance as linked to HIV.

VI. CONCLUSIONS

The prevalence of rifampicin resistance according to this study's findings was 10%.

The predisposing factors to rifampicin resistance were cigarette smoking (P-Value = 0.001), history of prolonged stay with a TB infected patient, (P-Value = 0.001) and history of previous treated episode of TB among the study respondents (P-Value = 0.001).

VII. RECOMMENDATIONS

The government of Uganda needs to carry out more intensified mass sensitization of people about the dangers of cigarette smoking particularly to HIV infected individuals.

In the same line of sensitization, people need to be continuously reminded by ministry of health about the signs and symptoms of TB so that community members can identify suspects and refer them for specialised diagnosis and management such that delayed detection of the disease is minimised which will also reduce on rifampicin resistance. It will also minimise

exposure of people living with the infected individuals.

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List of Abbreviations and Acronyms

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
CT	Cycle Threshold
DNA	Deoxy Ribonucleic Acid
DST	Drug Susceptibility Testing
HAART	Highly Active Anti-retroviral Therapy
HIV	Human Immuno-deficiency Virus
INH	Isoniazid
LPA	Line Probe Assay
MDR	Multi- drug resistant
MoH	Ministry Of Health
MTB	Mycobacteria Tuberculosis
MTC	Mycobacteria Tuberculosis Complex
NTLP	National Tuberculosis and Leprosy Programme
PCR	Polymerase Chain Reaction
RIF	Rifampicin or its derivatives such as rifabutin
RIFR	Rifampicin Resistant
RMR	RifampicinMonoresistant Strain
RNA	Ribonucleic Acid
RT	Real Time
TB	Tuberculosis
WHO	World Health Organisation

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APPENDICES

Appendix I: Consent Form

My name is Nakiboneka Winnie, a final year student of university of Kisubi pursuing a diploma in medical laboratory technology currently doing a study entitled 'Prevalence of rifampicin resistant TB among patients in Lubaga hospital. You have been chosen as one of the participants in this study to provide us with answers which the questionnaire will ask you. Participation in this study is voluntary and you may leave it at any time if you so wish but will still be able to access services from the hospital.

You will be able to know about your resistance status of TB treatment and if found to be resistant, your doctor will be notified so that you can be treated accordingly.

I have read and understood the condition written herein or I have got an explanation about the study and have willingly accepted to take part in it

Signature/thumb print of participant.....Date.....

Appendix Ii: Questionnaire

Topic: Prevalence of Rifampicin Resistant Tuberculosis Among Patients in Lubaga Hospital

Participant's ID No.....

Instructions to study participants

Tick the answer of your choice or fill your answer in the spaces provided

Section A: Socio-Demographic Characteristics

a. What is your age in years? _____-

b. What is your gender?

1. Female 2. Male

c. What is your highest level of education attained?

1. Never gone to school
2. Stopped in primary school
3. Stopped in secondary school
4. Attained tertiary education

d. What is your occupation?

1. Unemployed 2. Self-employed 3. Civil/public servant/salary earner

Section B: Prevalence of rifampicin resistant TB among patients in Lubaga hospital

(e) Gene expert result

1) MTB positive 2) MTB negative

(f) If gene expert MTB positive, the result is.....

1) Very low 3) Medium
2) Low, 4) High

f) Status of mycobacterium sensitivity to rifampicin
   1) Sensitive 2) Resistant

Section C: Factors associated with Rifampicin resistance among TB patients in Lubaga hospital

g) Have you been treated for TB before?
   1) Yes 2) No
h) If yes to question e) above, did you complete treatment
   1) Yes 2) No
i) If no to question j) above, why?
   .....
j) Have you ever stayed with a TB patient or treated one
   1) Yes 2) No
k) Do you smoke cigarettes
   1) Yes always 3) No
   2) Yes sometimes
l) Do you drink alcohol?
   1) Yes always 3) No
   2) Yes sometimes
m) Do you use Marijuana or Cocaine or Mairungi?
   1) Yes 2) No
n) What is your HIV status?
   1) Positive 3) I don't know
   2) Negative
o) Do you have diabetes mellitus?
   1) Yes 3) I don't know
   2) No
p) Do you have a chronic cough?
   1) Yes 2) No

Appendix Iv: Specimen Collection and Processing Procedures

Sputum sample collection

The participants were provided with a sterile sputum collection container and then were instructed on how to collect a random sputum sample that very day of about 2 - 5mls.

The patient was then provided with a sterile collection container which was pre-labeled with their study number. Patient isolated him/herself in a well aerated space then coughed/expectorated with a productive cough into the container. Sample was then placed in a sample bag then brought to the laboratory where it was accessioned and clerked into the already established system following the standard operating procedures for acceptance or rejection of the sample. The samples were then analysed following the standard operating procedure by Gene Xpert analysis.

Sample storage

Samples were stored in a safety cabinet until analysis was done. For the samples which were not to be worked on that very day, they were kept in a fridge before being worked on.

Sample processing and analysis

The Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA) detects the presence of MTBC DNA and its susceptibility to rifampicin (RMP) in a single reaction. The assay is based on a heminested real-time PCR (RT-PCR) that targets the *rpoB* gene hot spot region. Any deviation from the wild type sequence

resulting in a delay in the appearance of the signal exceeding a predetermined CT value, between the earliest and latest cycle threshold (CT) values is reported as RIF resistant. The test is carried out within 2 hours in a disposable cartridge. The only manual step was the mixing of a bactericidal buffer with the sample prior to addition to the cartridge (Van Rie et al 2010).

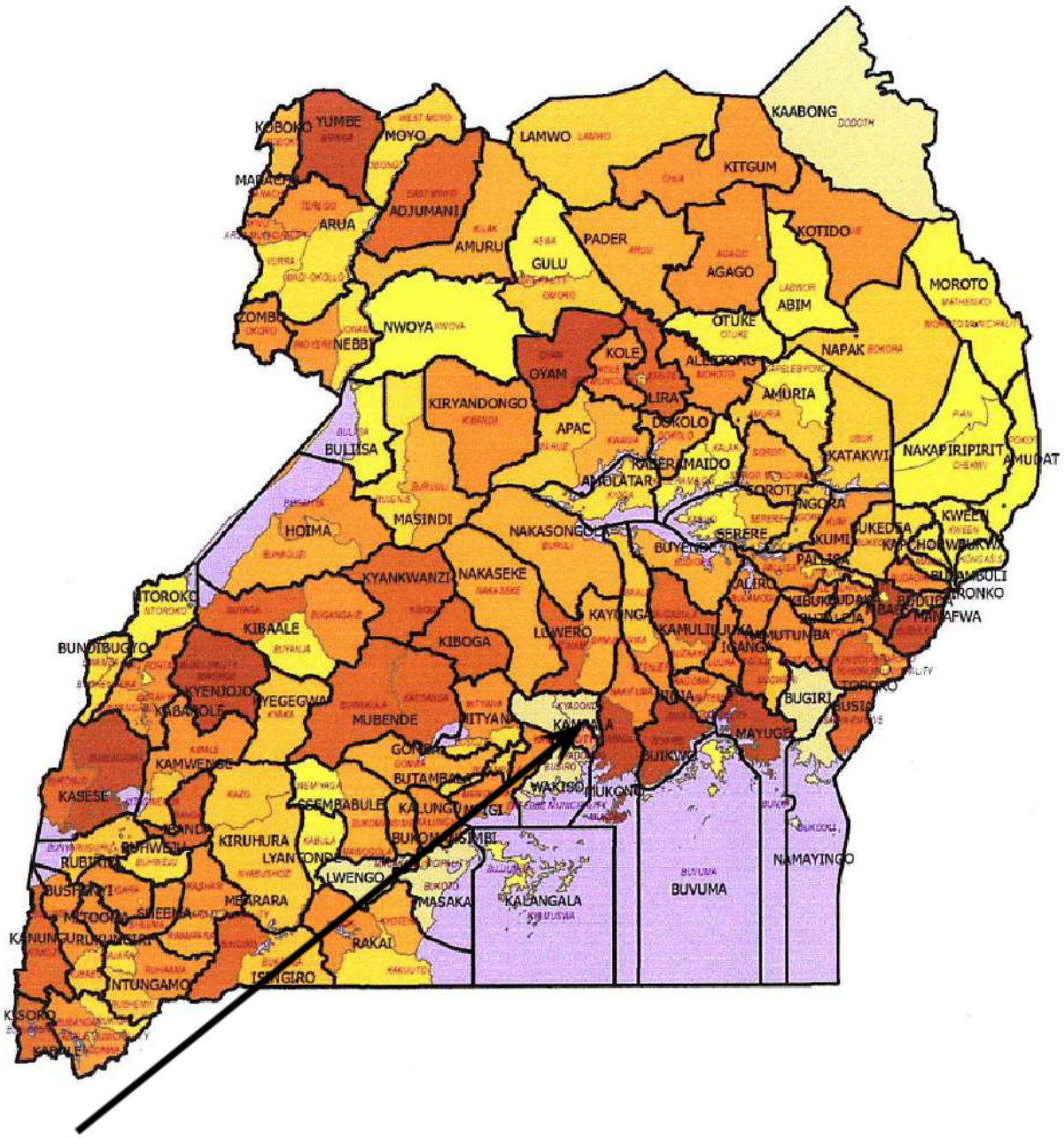
Waste collected from the study was disposed as per standard guidelines of the laboratory regarding sharps, infectious agents and other waste.

Procedure

- Each XpertMTB/RIF cartridge was labeled with a sample ID written on the side of the cartridge such that it did not obstruct the cartridge barcode.
- XpertMTB/RIF sample reagent was added to fresh sputum samples in a ratio of 2:1 i.e. 2 parts sample reagent to 1 part sample.
- The mixture was shaken vigorously 20 times then allowed to stand for 10 minutes. One back and forth movement was taken as a single shake. After 10 minutes, the mixture was shaken 20 times then allowed to stand for 5 minutes.
- Using the sterile pipette provided in the cartridge kit, the liquefied sample was aspirated until the liquefied sample meniscus, was above the minimum mark. No further processing was done if there was insufficient in volume i.e. <2 ml.
- Efforts were made to ensure that the liquefied sample being transferred to the cartridge had no bubbles as this could cause an error
- The cartridge lid was opened and the sample-reagent mixture transferred into the sample port of Xpert MTB/RIF cartridge.
- Once the sample had been loaded, the cartridge was closed making sure the lid snapped shut firmly into place.
- The patient I.D was scanned or patient's details entered manually then the cartridge barcode scanned.
- The cartridge was loaded into the assigned GeneXpert cartridge bay or module and the test run started. This was done within 30 minutes of loading the sample into the cartridge.
- The test took 2 hours to give results.

NB: The cartridge that had been standing and opened for more than 30 minutes was not used and also no cartridge was re-used in performance of the test.

Appendix VI: Map of Uganda Showing Kampala District



Kampala district