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Original article

PREVALENCE AND RISK FACTORS OF ACTIVE TUBERCULOSIS AMONG HIV- POSITIVE CLIENTS RECEIVING ANTIRETRO VIRAL THERAPY AT VILLA MARIA HOSPITAL, KALUNGU DISTRICT: A CROSS SECTIONAL DESCRIPTIVE STUDY.

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ABSTRACT

Background

With the introduction of antiretroviral therapy (ART), TB remains a leading Co-infection among people living with HIV while on ART, responsible for 30% of deaths among PLHIV in Uganda. This study was designed to determine the prevalence and risk factors leading to the development of active tuberculosis among HIV-positive clients receiving ART from Villa Maria Hospital in Kalungu district.

Methodology

A cross-sectional descriptive study that employed qualitative data collection methods was conducted among 160 HIV-positive clients. Participants with TB symptoms were diagnosed with TB using smear microscopy (Zn), gene-expert, and urine TB lam and chest x-ray. Data was collected, and analyzed by Microsoft Excel 2013, and results were presented in tables & figures.

Results

Among the participants, 44.4% and 55.6% were male & female respectively with a median age of 45 years. 25 (15.6%) of the patients had developed active TB infection, which was independently associated majorly with advanced HIV disease & non-users of TPT. The use of IPT & good adherence to ART reduced the risk of developing TB by over 80%. 33.8% didn't know how TB spreads, and coughing, and living with a TB patient were the most identified ways in which TB spreads, Lack of food & long distances to the health centers were the major hindrances to completing TB treatment. Pill burden & frequent movement to health centers were the major challenges faced during TB treatment.

Conclusions

HIV clients with cough, advanced HIV disease, and non-users of TPT had an increased risk of developing TB infection. However, the use of TPT and good adherence to ART reduced the risk of TB among HIV-infected patients. Therefore, the researchers recommended intensified early screening of TB among HIV patients with cough, and involvement of VHTs/CHWs and community-based organizations (CBOs) to increase the awareness and control measures of TB in the communities.

Keywords: Mycobacterium Tuberculosis, TB Lam, People living with HIV, TB preventive Therapy (TPT)

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Introduction

Tuberculosis (TB) infection is the leading co-infection among HIV/Aids patients in the world. Approximately 43.8 million people live with HIV globally, 24.4 million in east and southern Africa, and 1.4 million in Uganda *(UNAIDS 2022*).

More than 4100 people die from tuberculosis (TB) every day and approximately 30,000 people fall ill with TB disease despite TB being preventable and treatable *(UNAIDS, 2022*). TB is the leading cause of death among people living with HIV (PLHIV) where in 2020; it was ranked 13th leading cause of death after COVID-19 and above HIV/AIDS. A total of 1.5 million people died from TB including 214,000 people living with HIV Worldwide *(WHO: Global TB Report 2020).*

Throughout sub-Saharan Africa, the dramatic spread of the HIV epidemic has been accompanied by up to a fourfold increase in the number of TB cases registered by national TB programs *(UNAIDS, 2022).* Globally a quarter of a million die of TB and 30% of deaths among PLHIV in Uganda are due to TB.

Uganda is among the 30 highly burdened countries for TBHIV co-infection with the risk of developing TB being 20 times greater in people living with HIV (PLHIV) according to the World Health Organisation Global TB Report *(WHO), 2020*. TB is a leading opportunistic infection (OI) in PLHIV in Uganda.

The TB incidence rate is 196 per 100,000 per year 16 per 100,000 HIV-negative people die per year and 90,000 incidents are TB cases *(Bolton L, et al; 2022*). The advent of antiretroviral therapy (ART) and TB preventive therapy (TPT) has generally reduced the development of TB illness among PLHIV, as reflected by an overall reduction of HIV/AIDS-related morbidity and mortality thus improving the survival among PLHA. HIV infection is the most important risk factor for developing active tuberculosis, which increases the susceptibility to primary infection or reinfection and also the risk of tuberculosis (TB) reactivation for patients with latent TB (WHO, 2020) however mal-nutrition, diabetes, or tobacco also increases the risk of developing TB in PLHIV WHO, 2020).

With the above innervations, the occurrence of TB has been reduced by 67–80% in most studies. Even with these advantages of antiretroviral therapy (ART) and TB preventive therapy (TPT), still, a significant proportion of patients on ART still develop active TB with a varying prevalence rate of 2.5–30.1% in most studies *(WHO Global TB Report, 2020).*

In our setting, the literature on the magnitude of this problem is still scarce, especially in the Kalungu district part of central Uganda. So, this study aims to determine the prevalence and risk factors leading to the development of active tuberculosis among HIV-positive clients receiving antiretroviral therapy from Villa Maria Hospital in Kalungu district.

The general objective of the study:

To determine the prevalence and risk factors of active tuberculosis among HIV-positive clients receiving antiretroviral therapy at Villa Maria Hospital in Kalungu district.

Specific objective

To determine the prevalence of active tuberculosis among HIV-positive clients receiving anti-retroviral therapy at Villa Maria Hospital in Kalungu district.

To investigate the risk factors leading to active tuberculosis infections among HIV-positive clients receiving ART from Villa Maria Hospital in Kalungu district.

To access patients' Knowledge and awareness on how TB spreads and factors that hinder clients from completing TB treatment.

Materials and Methods

Study Design

A cross-sectional descriptive study design was used to enroll clients who were HIV positive and receiving antiretroviral therapy (ARV) from Villa Maria Hospital. Consent was obtained from all participants. The clients who qualified for the study were tested for Tuberculosis using microscopy/ZN, gene expert, TB LAM, or X-ray, and a structured questionnaire was used to collect data and to determine the risk factors that led to active tuberculosis. Data was summarized on data sheets and analyzed using an Excel program.

Study area

The study was carried out at Villa Maria Hospital (HIV clinic) covering patients in Kalungu district and some parts of neighboring districts of Gomba, Bukomansimbi, Ssembabule, and Masaka.

Villa Maria Hospital is located approximately 17 kilometers (11 mi), by road along Masaka Ssembabule road, north of Masaka Regional Referral Hospital, in the city of Masaka. Villa Maria Hospital is also located approximately 140 kilometers (87 mi), by road, southeast of Mubende Regional Referral Hospital, in the town of Mubende. The geographical coordinates of Villa Maria Hospital are 0°13'50.0"S, 31°44'35.0" E (Latitude: -0.230556; Longitude: 31.743056).

The hospital serves as the district hospital of Kalungu with an official catchment area of more than 183,232 people and other four neighboring districts of Bukomansimbi, Gomba, Ssembabule, and part of Masaka City. The hospital has approximately 4,350 HIV patients enrolled in HIV care, approximately 300,000 OPD attendances, and 6,000 admissions annually.

Study Population

The targeted population was HIV-positive clients receiving antiretroviral therapy at Villa Maria Hospital during the time of the study. The study included clients of all ages, and sex and independent of their duration spent on ART.

Sample size determination

The sample size was determined based on the formula used by

n = 4PQ/d2

Where P= estimated prevalence = 10%

n = Sample size

z = Standard deviation at a confidence level of 95%

Q= (1-p) proportion of the population without characteristics (=0.5)

1= Error term

d = degree of accuracy 0.05

Therefore, substitution in the formula n = $\frac{4x0.1x0.5}{0.05\ 2}$

n = 144 study subjects

To meet the target sample size, n was increased by 10% getting an approximate sample size of 160 respondents.

Sampling strategy

Inclusion criteria

Only HIV-positive clients receiving antiretroviral therapy at Villa Maria Hospital during the period of the study were eligible and enrolled in the study.

Exclusion criteria

HIV-negative clients and HIV-positive clients who were on tuberculosis treatment at the time of the study were excluded.

HIV-positive clients receiving antiretroviral therapy from other facilities other than Villa Maria Hospital were also excluded from the study.

Determination of prevalence of active tuberculosis among HIV-positive clients receiving anti-retroviral therapy at Villa Maria hospital in Kalungu district.

General steps to follow

TB Symptom screening tools were used to screen for all clients attending the HIV clinic for TB.

All patients with positive symptom screens provided sputum samples for laboratory diagnosis of TB using ZN staining (smear microscopy) or gene expert.

For patients with CD4 cells less than 200 cells/mm3, urine samples were collected and tested using TB LAM (Alere lateral flow assay).

Patient's results were recorded in the laboratory TB register, patient's result form, TB presumptive and Unit TB register.

Patients' Tuberculosis (TB) results were collected from the laboratory TB register and verified using the unit TB register.

Laboratory diagnosis method for active TB infection

Microscopy diagnosis of TB using Ziehl Neelsen (ZN) staining

Principle of the test: In the Ziehl Neelsen staining (ZN) is performed on sputum and other body fluids to detect mycobacterium species. In the Ziehl Neelsen staining (ZN) procedure, Acid Fast Bacilli (AFBs) mycobacterium retains the primary stain (strong carbol-fuchsin) even after exposure to decolorizing acid-alcohol and stains pink hence the "acid-fast". A counter stain of 0.5% methylene blue is then used to differentiate between the AFB and non-AFBs or debris.

Smear preparation and staining procedure

- New grease-free and clean slides were used and correctly labeled using a diamond or lead pencil.
- Fish out suspicious portions i.e. purulent, muco-purulent, or muco-salivary from the sputum container and place them on a glass slide using applicator sticks.
- Spread the material evenly at the center of the slide with an approximate area of 2cm X 1cm and allow it to air dry.
- Fixed the smear by passing it over a gentle flame 3 times and allowing it to cool before staining.
- Placed slides on the staining rack without touching each other including positive and negative control slides.
- Covered the smear with freshly filtered strong carbol-fuchsin.
- Heated gently with fresh a flame until steam rose from the slides for a maximum of 15 minutes i.e., heat 3 times at an interval of 5 minutes.
- Wash gently with clean water and drain off excess water.
- Covered the slides with 20% Sulphuric acid for 3 minutes

- Washed thoroughly with clean water, if the slide is not decolorized properly, repeat the decolorizing process if necessary.
- Drained off excess water and covered the smear with 0.5% methylene blue for 1 minute.
- Drained off the stain, washed the smear with clean water, and wiped the back of the slides with tissue paper.
- Allowed the slides to air dry in the slide rack.
- Examined the smear microscopically using X 100 objective and AFBs appear as fine red rods against a blue background

Laboratory diagnosis of TB by a lateral flow urine lipoarabinomannan assay (Urine TB LAM)

Principle

TB LAM antigen is an immune chromatographic test for the quantitative detection of lipoarabinomannan (LAM) antigen of Mycobacteria in human urine. It employs highly purified antibodies specific to the major polysaccharide antigen of the genus Mycobacterium which are used for capture and the detection tracer. The capture antibodies are adsorbed onto the nitrocellulose membrane of the strip and the detection antibody is labeled by conjugation to colloidal gold particles.

When the urine sample is added to the sample pad, the colloidal gold conjugated antibodies attached to the LAM antigen are released by the specimen from the conjugated pad. This immunological complex is then captured by anti-LAM antibodies immobilized on the nitrocellulose membrane and made visible due to the presence of a colloidal gold label. A positive result (a visible purple/pink line) indicates that the LAM antigens of mycobacteria are present in the sample or above the detection limit of the test whereas a negative result (no visible purple/pink line) indicates it is not present or below detection limit. To ensure the validity a procedural control bar is incorporated in the assay device.

Test procedure

- Collected afresh midstream urine at room temperature in a clean urine container.
- Removed the protective foil cover from each test.
- Pipetted 60 ul of urine and applied it to the sample pad
- Waited for 25 minutes and read the results under standard indoor light conditions.

Results interpretation:

The results are interpreted and recorded as summarized below:

TB LAM Antigen positive result: Two bars (purple/pink line) appear in both the control and patient window of the test strip.

TB LAM Antigen negative result: One bar (purple/pink line) appears in the control window of the test strip.

Invalid results: No bar (purple/pink line) appears in the control window of the test strip.

Assessment of the risk factors leading to active tuberculosis infections among HIV-positive clients receiving ART at Villa Maria Hospital in Kalungu district.

HIV-positive Patients were interviewed using researcher or researcher-administered questionnaires to determine the risk factors leading to TB infection among HIV-positive clients. Formal consent or assent (patients below 14 years) was sought before taking part in the study.

Assessment of the Knowledge and awareness of how TB spreads and factors that hinder clients from completing TB treatment at Villa Maria Hospital in Kalungu district.

HIV-positive Patients were interviewed using researcher or researcher-administered questionnaires to determine their knowledge and awareness of how TB spreads and factors that hinder clients from completing treatment using a structured researcher-administered questionnaire. Formal consent or assent (patients below 14 years) was sought before taking part in the study.

Data management and analysis

Data collected was collected using data sheets, stored on a master data sheet, and transferred to Microsoft Excel. Data was kept with utmost security by the use of codes, passwords, and encryption. Data was exported to Microsoft Excel and analyzed using statistical functions. The statistics were computed and presented in the form of tables of results, bar graphs, pie charts, measures of central tendency (especially the mean, mode, and median), and measures of dispersion. The existence of any significant differences between patients' categories or correlations was investigated.

Quality control and quality assurance aspects

The standard operating procedures for laboratory diagnosis of TB were observed as recommended by Uganda's national TB reference laboratories. Also, a blind check of TB slides was carried out by another laboratory technician. All patients were assigned unique numbers to avoid bias, and positive and negative control slides were used to check the quality of the stains during staining procedures.

Ethical consideration

Ethical approval was sought from the University of Kisubi Research Ethics and Review Committee and an

introduction letter was obtained from the University of Kisubi Faculty of Health Sciences introducing the researchers to Villa Maria hospital administration (study site). Permission and authorization from the Villa Maria hospital administration were obtained to carry out the study. Information to be obtained from the participants was treated with utmost confidentiality. Informed consent was obtained from clients before recruiting them into the study and study numbers (not names) were used for data collection as a way of keeping the clients' results identity anonymous.

RESULTS

Socio-demographic characteristics of the participants.

According to the table 1, one hundred sixty (160) HIV-positive clients receiving ART were enrolled in the study. Eighty-nine (55.6%) of the patients were female and seventy-one (44.4%) were male. The median (IQR) age of the patients was 45 years. More than half (54.4%) of the patients were married and living in rural areas. 60.6 % (97) of the patients were Catholics, 15.6% (25) were protestants, 14.4% (23) were Muslims and 9.4 % (15) were affiliated with other religions.

One hundred and one patients were peasant farmers (63.1%), 10.6 % (17) of the patients were school-going students, 8.8 % (14) were boda-boda and taxi drivers, 7.5% (12) were formally employed (teachers and health professionals), 6.9 % (11) of the patients were small business persons and the least 3.1 % (5) were security personnel. Most of the patients 65 % (104) had primary education, 18.8 % (30) of the patients had secondary education level, 8.1 % (15) had educational level of tertiary and above and 6.9 % (11) had never attended school.

Table 1: shows socio-demographic characteristics of the participants.

Variable		Frequency	Percentage (%)	Laboratory confirmed TB case	
				Positive TB cases	% TB cases
Age	< 18	12	7.5	0	0
	18 -24	27	16.9	01	3.7
	25-39	39	24.4	07	17.9
	>40	82	51.2	17	20.7
Total		160	100	25	
Gender	Male	71	44.4	16	10.0
	Female	89	55.6	09	5.6
Religion	Muslims	23	14.4	02	8.7
	Catholics	97	60.6	20	20.6
	Protestants	25	15.6	03	12.0
	Others	15	9.4	00	6.7
Marital status	Married/ cohabiting	87	54.4	17	19.5
	Single	20	12.5	03	15
	Separated	38	23.8	02	5.3
	Widow	15	9.3	03	20
Total		160	100	25	
Level of Education	Primary	104	65	20	19.2
	Secondary	30	18.8	03	10.0
	Tertiary / university	15	8.1	0	0
	Never attended school	11	6.9	02	18.2
Total		160	100	25	
Occupation	Peasant farmers	101	63.1	21	20.8
	Formal employed	12	7.5	0	0
	Drivers (taxi+ boda-boda)	14	8.8	2	14.3
	Business personnel	11	6.9	2	11.2
	Security personnel	05	3.1	0	0
	None	17	10.6	0	0
Total		160	100	25	

Table 2: shows the clinical characteristics and TB symptoms among HIV-positive clients

Variable		Frequency	Laboratory confirmed TB case	
			Positive TB cases	% of TB cases
WHO clinical stage	Clients in stages III & IV	15 (9.4%)	7	46.7
	Clients in stages I & II	145 (90.6%)	18	12.4
TB symptoms	Cough of no duration	160(100%)	25	15.6
	Persistent fevers for 2 or more weeks	42(26.2%)	19	45.2
	Noticeable weight loss	79(49.4%)	23	29.1
	Excessive night sweets for 3 weeks or more	32(20.0%)	19	59.4
	Contacts of pulmonary TB patients	15(9.3%)	05	33.3
Advanced HIV disease status	Clients with CD4 < 200	10(6.2%)	07	70
	Clients with CD4 >200	150 (93.8%)	18	22
Viral suppression status	Virally suppressed	05 (3.1%)	3	60
	virally non-suppressed	155 (86.9%)	22	14.2
History of TB exposure	Contacts to TB patients	05 (3.1%)	03	60.0
	Non-contacts to Tb patients	155(96.9%)	22	14.2

Client's clinical characteristics and TB symptoms among HIV-positive patients

Majority, 90.6 % (145) of the patients had WHO clinical stage I and II and 9.4 % (15) of the patients had WHO clinical–Stages III & IV. All 160(100%) clients in the study had a cough, 49.4 % (79) had noticeable weight loss, 26.2 % (42) had a persistent fever for 2 or more weeks, 20 % (32) had excessive night sweats for 3 or more weeks and 9.3% (15) were contacts of pulmonary TB patients. 6.2 % (10) had advanced HIV disease, 3.1 % (05) were virally non-suppressed and 3.1% were contacts of TB clients. This data is presented in Table 2.

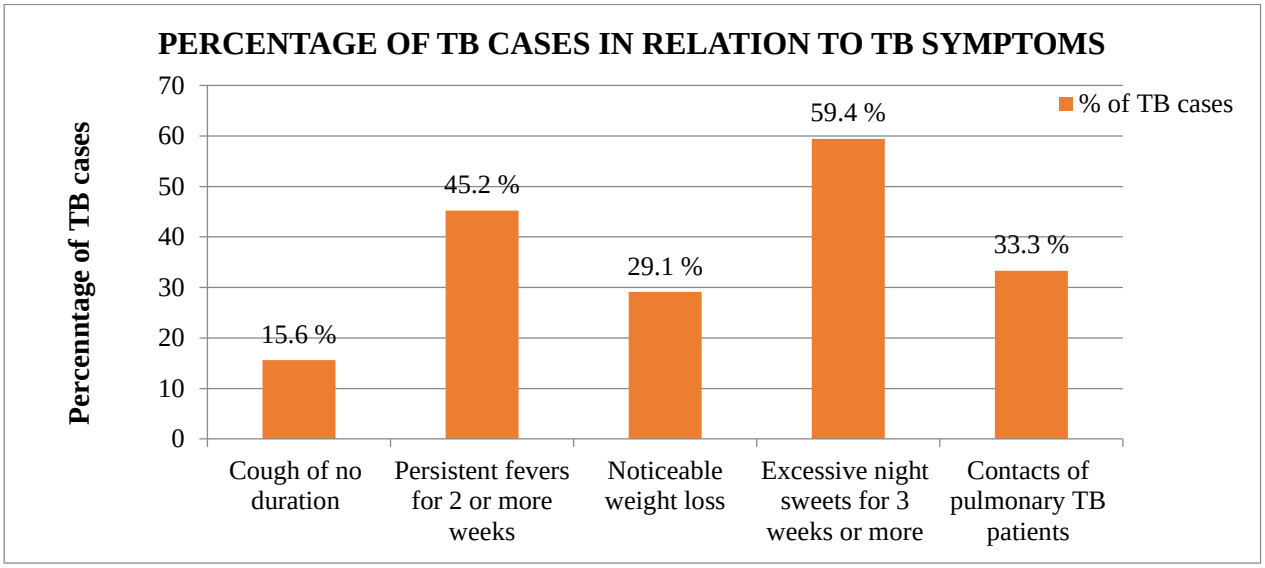

Figure 1a; bar chart showing the percentage of TB cases per symptom

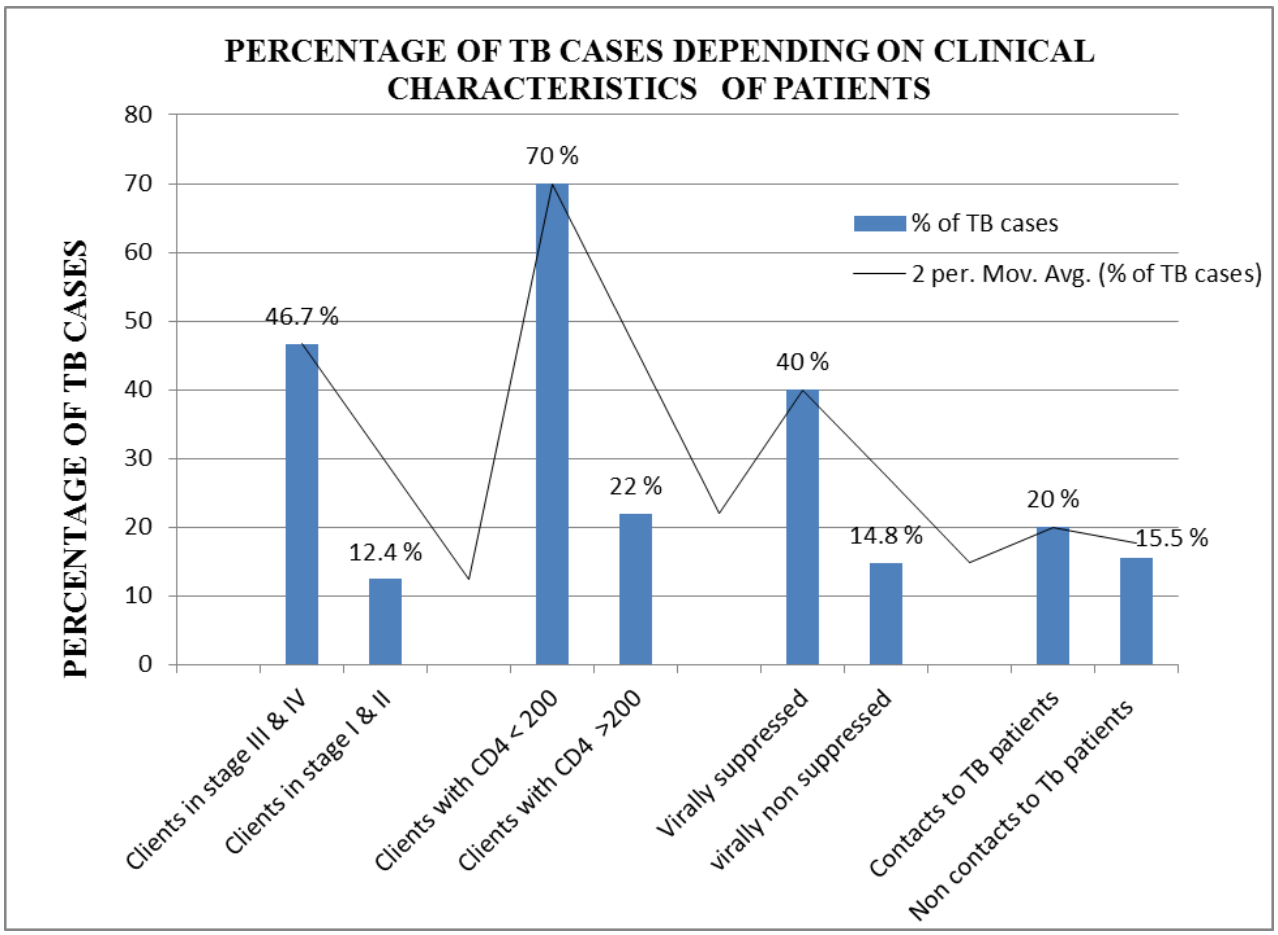

Figure1b: bar chart showing the percentage of TB cases per clinical characteristics of patients

Table3: showing the prevalence of TB among HIV clients

	Variable	Frequency	Confirmed TB cases	Prevalence of TB %
Age (Median age is 45years)	< 18 18 -24 25-39 >40	12(7.5%) 27(16.9%) 39(24.4%) 82(51.2%)	0 01 07 17	0 3.7 17.9 20.7
Gender	Male Female Overall prevalence is 15.6%	71(44.4%) 89(55.6%)	16 09	10.0 05.6
Religion	Muslims Catholics Protestants Others	23(14.4%) 97(60.6) 25(15.6%) 15(9.4%)	02 20 03 00	8.7 20.6 12.0 6.7
Marital status	Married/ cohabiting Single Separated Widow	87(54.4%) 20(12.5%) 38(23.8%) 15(9.3%)	02 20 03 00	8.7 20.6 12.0 6.7

Education level	Primary Secondary Tertiary / university Never attended school	101(65%) 30(18.8%) 15(9.3%) 11(6.9%)	20 03 0 02	19.2 10.0 0 18.2
Occupational	Peasant farmers Formal employed Drivers (tax + boda-boda) Business personnel Security personnel School going	101(63.1%) 12(7.5%) 14(8.8%) 11(6.9%) 05(3.1%) 17(10.6%)	21 0 2 2 0 0	20.8 0 14.3 11.2 0 0
Laboratory testing methods	Smear microscopy /ZN Gene expert Urine TB Lam Chest X-ray	125(78.1%) 34(21.3%) 10(6.3%) 13(8.1%)	6 7 7 9	4.8 20.6 42.9 69.2

Prevalence of active TB infection among HIV-positive clients

Of the total of 160 HIV positive clients who participated in the study, 15.6% of the patients had developed active TB infection. 4.8 % (6) of the TB patients had positive acid-fast bacilli (AFB), 20.6% (7) had positive gene expert, 42.9% (7) had a positive urine TB lam and 69.2% (9) had a positive X-ray for TB. 20.7 % (17) of the TB clients were 40 years and above and the rest (8) were between 18-39 years.

Males had the highest prevalence of 10% whereas Catholics had the highest prevalence of 20.6 % (20). Most of the TB cases were among Single clients (20.6%), clients with a primary level of education and those who never attended school at a prevalence of 19.2% (20) and 18.2% (2) respectively. Also, the peasant farmers had a higher prevalence of 20.8% (21) and the majority of the TB patients had a pulmonary TB infection as shown in Table 3.

Factors associated with the development of active TB

In this study, 160 clients were examined and interviewed patients to determine the factors leading to the development of active TB among HIV-positive clients receiving ART.

The various factors were as follows;

Clients with CD4 cell count less than 200 cells / μL, malnutrition, WHO clinical stage III & IV, non-use TB preventative therapy (TPT/ isoniazid), having viral load greater than 1000 copies/ml, patients with 40 years and above, low levels of income, history of being in contact with TB clients, low levels of formal education, poor ventilation and defaulting on TB treatment significantly increased the risk of developing active TB infection. While, good adherence to TB treatment, being formally employed, high level of education, good nutrition, non-exposure to TB clients, good adherence to ART with virally suppressed viral load of less than 1000 copies and use of TB preventive therapy (TPT/isoniazid), significantly reduced the risk of active TB infection.

However, WHO clinical stage III and IV, the use of isoniazid preventive therapy, and having poor adherence to ART medications are significantly associated with active TB infection.

Patients in WHO clinical stages III and IV were more than 4 times more likely to develop TB infection

Compared to clients with WHO clinical stage I and II. However, the use of isoniazid preventive therapy reduced the risk of TB infection by 84.8% compared to clients who did not use isoniazid preventive therapy. Similarly, HIV-positive clients with good adherence to ART medications were less likely to develop TB infection by 85.2% compared to those with poor adherence to ART the above information is summarized in Table 4.

Table 4: showing the risk factors leading to active TB among HIV-positive clients

RISK FACTORS		**Number / % (n=160)**	**Confirmed TB cases**		**OR(95 %CI)**	***P* -value**
			Negative (n=135)	**Positive (n=25)**		
Gender	Male Female	71 (44.4%) 89(55.6%)	55(77.5%) 80(89.9%)	16(22.5%) 09(10.1%)	2.5(1.1 – 6.2 0.3(0.1 – 0.9	0.035

Marital status	Married/ cohabiting Single Separated Widow	87(54.4%) 20(12.5%) 38(23.8%) 15(9.3%)	70(80.5%) 17(85%) 36(94.7%) 13(80%)	17(19.5%) 03(15%) 02(5.3%) 03(20%)	2.0(0.8 - 4.9) 1.0(0.3 - 3.5) 0.2(0.1 - 1.1) 1.3(0.3 - 4.9)	0.1 0.9 0.06 0.7
Occupation/income status	Peasant farmers Formal employed Drivers (tax + boda-boda) Business personnel Security personnel None	101(63.1%) 12(7.5%) 14(8.8%) 11(6.9%) 5(3.1%) 17(10.6%)	80(79.2%) 12(100%) 12(85.7%) 9(88.8%) 5(100%) 17(100 %)	21(20.8%) 0 2(14.3%) 2(11.2%) 0 0	3.6(1.2 - 11.1 0.2(0.01 - 3.4 0.9(0.2 - 4.2) 1.2(0.2 - 6.0) 0.5(0.02 - 8.7 0.1(0.008-2.3	0.02 0.3 0.9 0.8 0.6 0.2
Alcohol/substance use	Non-alcohol users Alcohol users	109 (66.3%) 51 (33.45%)	93 (58.1%) 42 (26.3%)	16(10.0%) 09 (06.0%)	0.8(0.3 - 2.0) 1.2(0.5 - 3.0)	0.6
Deity	Balanced Non-Balanced	145(90.6%) 15 (09.4%)	126 (87%) 09(60%)	19(13.0%) 06(40%)	0.2(0.07 – 0. 4.4(1.4 – 13.	0.0106
Smoking exposure	Smokers Non-Smokers	01 (0.6%) 159 (99.4%)	01 (0.6%) 134(83.8%)	0 25(15.7%)	1.8(0.07-44.4) 0.6(0.02-14.4)	0.7
Exposure to TB infection	Contacts to TB patients Non-contacts to Tb patients	05 (3.1%) 155(96.9%)	02(40%) 131(85.8%)	03(60.0%) 22(14.2%)	9.1(1.4 – 57. 0.1(0.01 – 0.69)	0.0192
Nutritional status	Poor (MUAC red + yellow) Good	05(3.1%) 155(96.9%)	02(40%) 133(85.8%)	03(60%) 22(14.2%)	9.1(1.4 - 57.4 0.1(0.02 - 0.7	0.02
Adherence to TB treatment status	Good Poor	02 (15.4%) 11 (84.6%)	02(100%) 09 (81.8%)	0 02(18.2%)	0.8(0.03 - 21.5) 1.3(0.05 - 37.2)	0.9
Adherence to ART	Poor (Virally non-suppressed) Good (virally suppressed)	05 (3.1%) 155 (86.9%)	2 (40%) 133 (85.8%)	3 (60%) 22 (14.2%)	9(1.4 – 56.9) 0.1(0.01 - 0.7	0.0196
TB Preventive Therapy (TPT) status	Non-use of TPT Completed TPT	15 (9.4%) 145 (90.6%)	9 (60%) 126(86.9%)	6(40%) 19(13.1%)	4.4(1.4 – 13. 0.2(0.07 – 0.	0.0106
WHO CLINICAL STAGE	Clients in stages III & IV Clients in stages I & II	15 (9.4%) 145 (90.6%)	8 (53.3%) 127(87.6%)	7(46.7%) 18(12.4%)	6.2(2.0 -19.1 0.2(0.05 - 0.50)	0.002
CD4 status	Clients with CD4 < 200 Clients with CD4 >200	10(6.2%) 150 (93.8%)	3 (30%) 132 (88%)	7(70.0%) 18(22%)	17(4.1 – 72.1 0.06(0.01-0.24)	0.0001
Ventilation status	Good Poor	98 (61.3%) 62 38.7%)	84 (85.7%) 51 (82.3%)	14(14.3%) 11(17.7%)	0.8(0.3 - 1.8) 1.3(0.5- 3.1)	0.6

Key; OR: Odds ratio, **95% CI:** 95% Confidence Interval, **P value:** Significance levels, **TPT:** TB preventive therapy.

Table 5: showing knowledge & awareness on how TB spreads and factors that hinders clients from completing TB treatment.

Variable	Categories	Frequency (n =160)	Laboratory-confirmed TB cases		Percentage of TB positive Cases %
			TB Negative	TB Positive	
TB spreads	Those who don`t know Those who know	054(33.8%) 106(66.2%)	49(90.7) 86(81.3)	05 20	9.3 18.7

Ways in which Tb spread	Coughing	37(23.1%)	32	05	13.5
	Being in contact with Tb patients	17(10.6%)	15	02	11.7
	Living with Tb patients	19(11.9%)	14	05	26.3
	Sneezing	22(13.8%)	17	05	22.7
	Breathing contaminated air	11(6.8%)	08	03	27.3
	Doesn't know	54(33.8%)	49	05	9.3
Previously suffered from TB	Yes	13(08.1%)	11	02	15.4
	No	147(91.9%)	124	23	15.6

Categories		Frequency (n = 13)	Percentage %
Factors that hinder clients from completing TB treatment	High transport costs	02	15
	Long distances & frequent movements to health centers	03	23
	Poor attitude of health workers	01	08
	Lack of food / increased appetite	07	54
Challenges faced by patients during TB treatment	Frequent movements to health centres	10	77
	Treatment fatigue	09	69
	Increased appetite/lack of food	07	54
	Pill overload/pill burden	13	100

Knowledge and awareness on how TB spreads and factors which hinders clients from completing TB treatment

On accessing knowledge and awareness on how TB spreads and factors which hinders clients from completing TB treatment and factors faced during TB treatment as shown in Table 5, only 33.8% (54/160) didn't know how TB spreads. 33.8% were not aware of way(s) in which TB spreads, the most known ways in which TB spreads were coughing, sneezing, living with Tb patients, being in contact with TB patients and breathing contaminated air at a percentage of 23.1%,13.8%,11.9%,10.6% & 6.8% respectively.

Only 8.1% (13) respondents had previously suffered from TB, lack of food, long distances to the health centres, high transport costs and poor attitude by health workers was the major hindrances to completing TB treatment.

Pill overload/burden, frequent movement to health centres, treatment fatigue and increased appetite /lack of food were the major challenges faced during Tb treatment at 100%, 77%, 69% and 54% respectively. This is shown in Figure2.

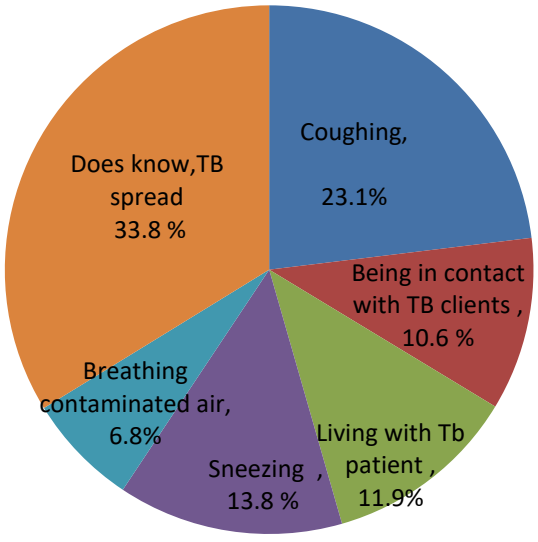

Figure 2a pie chart showing ways in which TB is spread

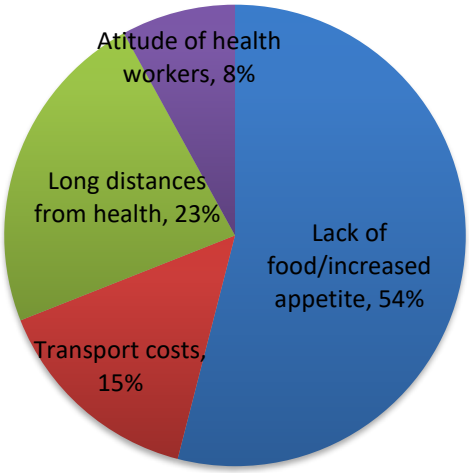

Fig 2b: pie chart showing factors which hinder TB clients from completing treatment

DISCUSSIONS, CONCLUSIONS, RECOMMENDATIONS

Prevalence and risk factors of active tuberculosis among HIV-positive clients receiving antiretroviral therapy at Villa Maria Hospital in Kalungu district.

The prevalence of developing TB infection while receiving ART was found to be 15.6%. The number of infected male patients outweighed female patients with a median age of 45 years. The overall prevalence of 15.6% is relatively in agreement with a similar previous study conducted by *Mulugeta. T et al; 2021* found the prevalence of TB among people living with HIV in southwest Ethiopia to be at 17.3%. It disagrees with findings of similar studies such as the study conducted by *Daniel W. Gunda et al; 2018* Northwest Tanzania which indicated the prevalence of active TB among HIV clients receiving ART to be at 11%, in another study conducted by *Kavitha. G et al; 2021* in four African countries indicated the prevalence of TB being 3% among people living with HIV and in the study conducted in Bududa among people receiving ART by *Kalyetsi. R et al; 2019* found the prevalence of TB among HIV-positive clients to be at 5.9%.

The majority, 78.1% (125) of the participants were diagnosed using smear microscopy (Zn) and this yielded the least positive cases at 4.8% (06), 21.3% (34) clients were diagnosed with gene expert with 20.6% (07) positive cases, followed with X-ray at 8.1% (13) with 69.2% (9) positive cases and TB lam at 6.1 % (10) with 42.9% (7) positive cases. The low positivity rate in smear microscopy was responsible for the low prevalence rate which was observed in most studies that were solely based on it such as the study conducted by *Kavitha. G et al; 2021* in four African countries indicated the prevalence of TB was 3% among people living with HIV and in the study conducted in Bududa among people receiving ART by *Kalyetsi. R et al; 2019* found that the prevalence of TB among HIV-positive clients was 5.9% since it's the cheapest and most commonly used method to diagnose TB.

Based on the client`s clinical characteristics and TB symptoms, developing TB was found to increase in clients with CD4 < 200cells/ul, followed by those in clinical stages III & IV, virally non-suppressed and history of exposure to TB patients with advanced HIV disease characteristics at positivity rate of 70%, 46.7%, 40%, and 20% respectively. All the 25 TB cases had a cough regardless of duration. Excessive night sweats for 3 weeks or more, persistent fevers for 2 or more weeks, contacts of pulmonary TB, and noticeable weight loss were the most common symptoms exhibited by the clients responsible for 59.4%, 45.2%, 33.3%, and 29.1% TB cases respectively. The above findings are in line with the reviewed literature for the study conducted by Kavitha.G.et al; 2021, *Mulugeta. T et al; 2021* and 2020 Uganda consolidated HIV treatment guidelines.

The development of TB among HIV-positive clients was proportional to age the most affected age group was 40 years and above with a prevalence of 10.6% followed by 25-39 years with a prevalence of 4.4 % then by those of 18 - 24 years with a prevalence of 0.6% and the median age was 45 years. The highest TB cases were recorded in the age group of 40 years and above which agrees with the study conducted by *Daniel W. Gunda et al; 2018* but in disagreement with the studies conducted by *Kavitha et al; 2021, Mulugeta T, et al; 2021 and Kalyetsi et al; 2019* in which the highest cases of TB were registered in the age group of 25-39 years.

In this study, male clients had the highest prevalence of TB at 10% than females at 5.6%. These findings agree with the previous studies conducted by *Daniel W. Gunda et al; 2018(*male 55.81%, female 44.19%) *and Kavitha et al; 2021*(male 53.8%, Female 44.19%), which indicated a higher prevalence of TB among males than females *and* disagreed with the study conducted by *Kalyetsi et al; 2019*(male 3.23%, female 8.06%) with higher prevalence recorded in females than in males. However, the rate of developing TB is independent of age and sex.

Risk factors leading to active TB among HIV-positive clients receiving ART

Although HIV infection is regarded as the highest predisposing factor of active TB, during this study,-several factors were investigated for their potential association with the occurrence of TB while receiving ART. In the study, male clients were found to have a high risk of developing TB at 10% (16) whereas female clients were at 5.6% (9) of developing TB. Several studies had similar findings including the study conducted by Muttuba. W et al 2019 in the five referral hospitals of Uganda to assess the prevalence and risk factors of TB with the risk of developing TB in males being at 23%.

Clients with low levels of education were at 37.4% risk of developing TB (primary education 19.2% and never attended school 18.2%) compared to those with higher levels of education with at 10% risk of developing TB. This agrees with the study conducted by Tegegne AS et al: 2022 with the risk of developing TB is higher in clients with low levels of education than those with a higher level of education.

Being with CD4<200cells/ul, malnutrition, being virally non-suppressed, patients in clinical stages III & IV, being a contact with TB patients, non-use of TPT, and poor ventilation were the most common factors to active TB among HIV-positive clients with risk of developing TB being at 70%, 60%, 60%, 60%,46.7%, 40%, & 17.7% respectively.

Clients with CD4 <200 cells/ul were 3 times more at risk of developing TB than those with CD > 200 cells/ul whereas those in clinical stage III & IV were 4 times at risk of developing TB than those in clinical stage I & II. These findings agree with the study conducted by *Mulugeta T, et al; 2021, Daniel W. Gunda et al; 2018* and *Kavitha et al; 2021*. This implies clients with advanced HIV disease in clinical stages III & IV were at higher risk for TB infection and needed to use IPT as per guideline recommendations. In support of this, the study revealed that IPT reduced the risk of TB infection by 86.9% compared to those who did not use it. This is in line with WHO recommendations for IPT and 2020 HIV treatment guidelines.

Also, the risk of developing TB was high in peasant farmers and least in clients with formal employment. Peasant farmers were 20 times at risk compared to those with formal education due to high poverty levels and were less informed. This agrees with the study conducted by Muttuba. W et al 2019. In this study, the risk of developing TB was higher in contacts of TB patients and clients who use alcohol than those who smoke cigarettes. Contacts of TB patients were 60% at risk of developing TB and non-users of alcohol were 10% at risk of developing TB whereas non-smokers were 15 times at risk of developing compared to smokers. These findings agree with the study conducted by Muttuba. W et al; 2019 disagree with the risk in smokers. In the study conducted by Muttuba. W et al; 2019 the risk of developing TB in smokers was 19.9% in this study the risk was 0% this is due to the few numbers of smokers registered in the study.

Knowledge and awareness of how TB spreads and factors that hinder clients from completing TB treatment

On accessing the participant's knowledge and awareness of how TB spreads the study found out that 33.8% (54) participants didn't know how TB spread. 9.3% of the clients who didn't know how TB spreads developed TB whereas 18.9% of those who knew how TB spreads developed TB. The risk of developing TB was 2 times in the people who knew how TB spreads compared to those who didn't know how TB spreads. Coughing, being in contact with TB patients, living with TB patients, sneezing, and breathing contaminated air were the most known modes through which TB was spread by clients.

Breathing contaminated air registered the highest percentage of positive TB cases, followed by living with TB patients, sneezing, coughing, and being in contact with TB patients at 27.3%, 26.3%, 22.7%, 13.5%, and 11.7% respectively. Less information is given by previous studies on the relationship between knowledge and awareness of how TB spreads and its effect on the prevalence of TB among HIV clients. The study showed the spread of TB independent of one's knowledge of how TB spreads.

Out of 160 clients enrolled in the study, only 13 clients had previously suffered from TB infection high transport costs, long distances & frequent movements to health centers, poor attitude of health workers, lack of food, and increased appetite were the common factors that hindered them completing the TB treatment.

Pill overload/pill burden, frequent movements to health centers, treatment fatigue, and increased appetite in addition to lack of food were the major challenges faced by patients during TB treatment at a rate of 100%, 77%, 69%, and 54% respectively. Also, the findings affirm with WHO, 2020 which termed TB as a disease for the poor who need financial support during treatment.

Therefore, this study explains why there is increased prevalence of TB infection among HIV-positive clients receiving ART from Villa Maria Hospital and Kalungu district at large.

Conclusions

The prevalence of tuberculosis infection among HIV clients receiving ART from Villa Maria Hospital was 15.6%. The TB prevalence was higher in male clients compared to females, with a median age of 45 years.

Laboratory diagnosis of TB by Smear microscopy provided the least positive TB cases compared to other methods.

Clients with CD4 < 200cell/ ul, WHO clinical stage III & IV, virally non-suppressed, and contacts pulmonary confirmed Tb cases registered a higher prevalence of TB cases. Cough regardless of duration, excessive night sweats for 3 weeks or more, persistent fevers for 2 or more weeks, contacts of pulmonary TB, and noticeable

weight loss were the most common symptoms exhibited by the clients with TB infection.

Being male, low level of education, clients with CD4<200cells/ul, malnutrition, patients in clinical stages III & IV, being virally non-suppressed, non-use of TPT, being a contact with TB patients, and having poor ventilation were the most common risk factors leading to the development of active TB infection while receiving ART.

Only 33.8% didn't know how TB spreads but with a low prevalence of TB cases compared to 66.2% who knew how TB spreads. Coughing, being in contact with TB patients, living with TB patients, sneezing, and breathing contaminated air are the most known modes through which TB is spread by clients. High transport costs, long distances & frequent movements to health centers, poor attitude of health workers, and lack of food / increased appetite were the common factors that hindered them from completing the TB treatment with Pill overload/pill burden, frequent movements to health centers, treatment fatigue, and increased appetite/lack of food were the major challenges faced by patients during TB treatment

Recommendations

Thus, I recommend clinicians and other health service providers to intensify early screening of HIV-positive clients for tuberculosis and initiation of TB preventive therapy particularly for patients with advanced WHO clinical stage.

Multiple laboratory diagnostic methods should be employed in addition to smear microscopy to minimize delayed diagnosis and treatment.

The Ministry of Health should think of bolstering and reducing the treatment period of TB infection to reduce treatment fatigue.

Health workers should engage local government leaders, community-based organisations (CBOs) VHTs/CHWs, and community opinion leaders to increase awareness and control the spread of TB in the community.

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List of abbreviation and acronyms

AIDS: Acquired Immune Deficient Syndrome
ARVs: Antiretroviral Therapy
BCG: Bacille Calmette-Guerin
CBOs: Community Based Organizations
CD4: Cluster of Differentiation
CHWs: Community Health Workers
e.g.: Examples
et al: Many others
HIV: Human Immune Virus
i.e. That is to say
ICF: Intensified TB case finding form (guide)
IPs: Implementing Partners
IPT: Isoniazid Preventive Therapy
MOH: Ministry of Health
MTB/RIF: Mycobacterium Tuberculosis /Rifampicin
OI: Opportunistic infections
OPD: Out Patients Department
PLHIV: People living with HIV
SOPs: Standard Operating Procedure
TB: Tuberculosis
TPT: TB Preventive Therapy
UCMB: Uganda Catholic Medical Bureau
VHTs: Village Health Teams
WHO: World Health Organization
ZN: Ziehl- Neelsen

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Conflicts of interest

There were no conflicts of interest associated with this work

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