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Pulmonary Tuberculosis in the Bo District of Southern Sierra Leone.



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Assessing Influence of HIV Status on Management outcomes of Drug Sensitive Pulmonary Tuberculosis in the Bo District of Southern Sierra Leone.

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Abstract

Purpose: Tuberculosis in Human immunodeficiency virus is a predictor of unfavourable outcome during the management of TB cases due to the synergy both bear in the patient. This study is to test the hypothesis that patient is more likely to be unfavourable in the co infected than the TB stand-alone patients with standard treatment in patients. The associated factors might not be exhaustive that leads to outcomes factored in the study.

Methodology: The retrospective cohort study data of 1,947 patients admitted from 1st January 2020 to 1st January 2022 at TB treatment centres in Bo district of Sierra Leone was analysed using datatab software after data completeness was checked and cleaned. Both bi-variable and multi-variable logistics regression and other statistical methods were employed to assess the relationship between HIV+TB synergic as well as TB alone outcomes. Data was analysed based on 95% CI and $p < 0.05$.

Findings: When an ANOVA was used to test for significance from zero, $F=3.41$, $p = 0.002$, $R^2 = 0.01$. Regression coefficients for exits = $1.17 - 0.02$., gender = -0.02 , literacy = -0.1 , family bread winner with TB = -0.02 and foods insecurity = $+0.07$. A point-biserial correlation was also computed to determine the relationship between HIV status and TB interms of outcome which showed a positive correlation between HIV status and exit code information, although no statistically significance ($r_{pb} = 0.04$, $n = 1987$, $p = .065$).

Unique contribution to theory, practice and policy: Successful treatment outcome was high among HIV/TB co-infected as well as TB mono-infected should both be treated with standard treatments. Strengthening patient management in a collaborative approach and use of novel

drugs as well as research will increase the survival rate of patients treated. With standard treatment and patient centered care the outcome of TB patient management will not be hinged on their HIV status. The adoption of this theory into policy in TB programmes will improve the success rate in TB management.

Keywords: *Tuberculosis, Cohort study, Determinants, Outcome*

1. INTRODUCTION

Mycobacterium spp. bacilli, which are transferred by infectious people through the inhalation of a droplet nucleus by another person, are the cause of tuberculosis (TB). It is a communicable disease that can damage practically all of the body's organs, making it a major contributor to ill health and one of the world's top causes of mortality. Prior to the coronavirus-2019 (COVID-19) pandemic, TB was the top infectious cause of mortality, surpassing HIV/AIDS, according to the 2022 World Health Organization Global TB Report.**Error! Reference source not found.**

HIV co-infection, alcoholism and other risky lifestyle, diabetes mellitus, silicosis, chronic renal impairment, overcrowding, incarceration, social injustice, profound immune response, corticosteroids, malnutrition, drug abuse, as well as other immune suppressive conditions and biological treatments such as anti-TNF therapy-immune-modulating drugs, drop in the quality of best mechanism for continuum of care.

About a quarter of the planet's population is estimated to be infected with TB, as according data provided by WHO in 2022,**Error! Reference source not found.** even though most people won't go on to develop TB disease because some people will clear the infection. About 90% of those who acquire TB yearly are adults, with men suffering from the disease at a rate higher than women. Even though disease more usually affects the lungs (pulmonary TB), it does also affect other organs.

Without treatment, the TB disease has a significant rate of death (about 50%). About 85% of patients can be treated with the currently recommended therapies (a 4-6 month regimen of anti-TB drugs for rifampicin and isoniazid susceptible bacilli).

To ensure that everyone who has the illness or infection could get access to these therapies, universal health coverage (UHC) is necessary. Through multisectoral action to address TB predisposing factors such poverty, undernourishment, HIV infection, smoking, and diabetes, the number of persons becoming sick and dying from TB can also be reduced. More than ten cases

and fewer than one death per 100,000 people per year have already been attained in some countries because to TB disease. To rapidly reduce the number of new cases each year (i.e., TB incidence) downward to the levels already attained in these low-burden nations, research breakthroughs such as a new vaccine) are needed. A report from the World Health Organization (WHO).**Error! Reference source not found.**

To now, the main causes of the high prevalence of tuberculosis worldwide are poverty and HIV. Although culture occasionally plays a part, poverty is what forces individuals to congregate in one shelter, consume an unbalanced diet that triggers the TB infection, and be unable to access medical facilities. (Lancet 2005; Dye C.; Lancet 2006)**Error! Reference source not found.**

The COVID-19 pandemic made the already difficult task of diagnosing and treating TB much more difficult. There are many sick people, but the infamous lockdowns and people's fear of being isolated and diagnosed with COVID-19, which occurred in some settings under cruel conditions, only made the management and control of TB much worse.

Conflict in many developing countries also had a negative impact on vaccination rates, rendering patients in high-prevalence countries more susceptible to the infection. As it makes patient treatment difficult, the fight to lower HIV incidence is telling for both TB control and management. This is partially a result of a lack of resources to identify and treat cases, as well as social injustice towards individuals who have TB.

The majority of those who have received TB preventative treatment up to this point have been those living with HIV, according to the worldwide TB report, 2022.**Error! Reference source not found.** From less than 30 000 in 2005 to 3.0 million in 2019, the annual number increased globally. In 2020 and 2021, it declined (to 2.7 million and 2.8 million respectively). 2005 till the end.

Additionally, it was noted in the report that seven nations—India, Nigeria, South Africa, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe—reported starting more than 200 000 HIV-positive patients on TB preventive treatment in 2021, making up a total of 82% of the 2.8 million cases reported globally. The prevalence of TB preventive treatment among HIV-positive individuals varies greatly among nations; in 13 high TB/HIV burden countries that supplied data for 2021, the median coverage among those just beginning antiretroviral therapy was 58% (32–65%). In the 20 countries that provided data, the median percentage of HIV-positive individuals who began TB preventative therapy in 2020 and finished it was 87% (IQR, 64–96%).

The tests for TB infection, according to the global TB report, can enable focus TB prophylactic

therapy on those who will benefit the most from it. In order to provide TB prophylactic therapy to individuals at risk, 115 nations reported adopting either interferon gamma release assays (IGRA) or tuberculin skin testing (TST) in the public or private sectors in 2021. 29 of the 36 countries that claimed they did not carry out TB infection tests belong to the WHO African Region.

In developed nations, immigrants from developing countries such as Sub-Saharan Africa, the Indian subcontinent, South East Asia, the Baltic states, and Russia are the most likely to get TB, while in the developed world, drug and alcohol addicts, the homeless, hostel residents, individuals with impaired immune systems, and others are more probable to contract the disease. Even though TB is one of the oldest diseases in history, it still poses a threat to survival, perhaps because normal management techniques are not strictly followed to provide the desired outcome. That may prevent TB from presenting to patients, whether they are immunocompromised or not, as a death sentence (Coker R, McKee M, et al. 2006). **Error! Reference source not found.**

In many developing nations, the diagnosis of PTB is performed either through the use of a direct smear examination of sputum for GeneXpert PCR, a reliable approach for confirming rifampicin susceptibility. There are situations where other crucial testing, such culture testing, is lacking (London: NICE, 2006). **Error! Reference source not found.**

The standard first-line treatment for drug-sensitive pulmonary tuberculosis (PTB) for six months comprises of:

1. Isoniazid (INH, H): It is a pro-drug. It is not effective as it is given, but once inside the bacteria, it is converted to an active form by a catalase. The drug inhibits synthesis of long-chain mycolic acids used in the formation of the cell wall. It has been shown to bind to an enzyme encoded by the *inhA* gene which catalyses the reduction of fatty acid 2-trans-enoyl thioesters involved in fatty acid synthesis, but it may also bind to other targets. It is thought to act as a structural analogue of the essential cofactor nicotinamide adenine dinucleotide (NAD⁺).
2. Rifampicin (R): A major step forward in the treatment of tuberculosis was the introduction of rifampicin in the 1960s. A broad-spectrum antimicrobial lipophilic ansamycin that can readily diffuse through the cell wall and inhibits synthesis of mRNA by binding to the β -subunit of bacterial RNA polymerase (*rpoB*). It is active against slowly growing organisms that are not readily killed by isoniazid. Resistance to rifampicin arises mainly from mutations in the gene (*rpoB*) that codes for the beta subunit of RNA polymerase (which is the protein

complex that transcribes genes). There are several sites in the gene that can mutate to produce a viable but rifampicin-resistant enzyme. The most common, but not all, mutations in the *rpoB* gene are exploited in the Xpert MTB/RIF diagnostic assay. Mutations associated without phenotypic resistance to rifampicin can also be identified by Xpert MTB/RIF (false positives). Resistance arises in two different ways. Most often the bacteria acquire a mutation in the catalase gene *katG* (which activates the isoniazid), or even lose the gene altogether. Thus INH enters the cell, but is never converted to an active form. Less commonly, mutations arise in the *inhA* gene, reducing the affinity of the protein for the active form of isoniazid. There have also been some mutations found in other genes, especially in *fabG2*. Whole genome sequencing continues to identify more mutations, especially in intergenic regions, that are associated with resistance to this drug.

3. Pyrazinamide (Z): Pyrazinamide is a synthetic analogue of nicotinamide (vitamin B3), and is only active under acidic conditions. Like isoniazid, it is a pro-drug that is converted to its active form, pyrazinoic acid (POA), by the bacterial enzyme pyrazinamidase, *pncA*. Some POA diffuses out of the *Mtb* bacillus, and under acidic conditions, becomes protonated. It then re-enters the cell where it accumulates, leading to acidification and disruption of the cytoplasmic membrane potential. This has an effect on many major cellular processes within the bacillus, including transmembrane transport; its actions are general and not linked with a specific molecular target. The main problem is that phenotypic resistance to pyrazinamide is difficult to detect in the laboratory. *M. bovis* is intrinsically resistant to pyrazinamide. Many mutations associated with resistance have been suggested. The importance of the drug was its effect on shortening the standard first-line drug regimen. In strains of *Mtb* resistant to pyrazinamide, the use of the drug was associated with poorer outcomes whereas its use in pyrazinamide-sensitive strains improved. outcomes.
4. Ethambutol (E): Ethambutol [(S,S')-2,2'(ethylenediimino)di-1-butanol] is a synthetic drug that disrupts biosynthesis of the cell wall. Mutations in genes encoding for arabinosyl transferases (*embC/A/B*) have been associated with resistance to the drug in clinical isolates of *Mtb*.

Combination drug therapy is widely accepted as a way to ensure that the treatment of TB disease is as short as currently possible. WHO recommends that the drugs be combined in tablet form as fixed-dose combinations. The Orange guide recommends only maintaining a limited set of formulations in order to simplify supply and prescription safety.

However, many of the 4-drug combinations lead to lower doses of several drugs.

Pyrazinamide is usually below the effective dose as defined by its minimum inhibitory concentration (MIC) in the available FDCs.

The dose of isoniazid in adults should remain at 300 mg, the dose at which the killing of Mtb is maximal, but is often less than 300 mg in FDCs.

If the patient weighs less than 54 kg, rifampicin is also below its expected MIC with the FDCs currently available.

Low serum levels of pyrazinamide have been especially associated with treatment failure and relapse (Perumal et al. 2019).**Error! Reference source not found.**

The combination of the four-HRZE is administered for two months, followed by HRE (in areas of high TB drug resistance) or HR, given over a four-month continuation phase. However, the effect of HIV on PTB treatment outcomes has not been well established in Africa. It is not clear whether there is poor management including that of response to immune reconstitution inflammatory response (IRIS) or other precipitating factors not observed.

The most frightening prospect is the appearance and spread of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains, rendering antibiotic treatment very difficult or impossible. In Mtb, multidrug resistance can arise especially by sequentially acquiring different mutations hence only Rif/INH sensitive PTB will be included in the study.

Other mechanisms for antibiotic resistance have come to light: Protein heterogeneity by mistranslation (Javid et al. 2014),**Error! Reference source not found.** an efflux pump, where a protein is acquired or mutated to pump antibiotics out of the pathogen such that lethal concentrations are never reached; when this happens, several different classes of antibiotic can be pumped out by one protein, causing multiple drug resistance. Deletions in cell wall synthesis operons (e.g. RD105), enhanced expression of enzymes adding lysine to surface phospholipids. Their importance is becoming more apparent as genotypic resistance is compared to phenotypic resistance.

The aim of the study is to assess the impact of HIV infection on PTB treatment outcomes by using data from January 2020 to January 2022 collected from TB treatment centers in the Bo district of Southern Sierra Leone.

Smear-positive PTB is the most infectious form of TB. Previous studies on the effect of HIV and antiretroviral therapy on TB treatment outcomes among these highly infectious patients

demonstrated conflicting results, reducing understanding of important issues.

1.1 Trigger and Rationale

It is generally perceived that pulmonary TB (PTB) in a HIV negatives has better treatment outcomes than those of their HIV positives peers even with standard management, a perception that will be looked into carefully by this study. TB being one of the common opportunistic infections /co-morbidities in people living with HIV (PLWH) especially in Sub-Saharan Africa needs better understanding of the dynamics between the two conditions in relation to treatment outcomes in Sierra Leone.

Sierra Leone has about 170 TB/HIV treatment centers across the country to serve its about 8-million populations that are all at risk of TB the country and a growing number of HIV infection incidence rate.

1.2 Methodological tool adopted

The study is a retrospective cohort study using multicenter secondary data collected from 1st January 2021 to 1st January 2023 of TB in HIV positive patients i.e. patients' personal files and the registers generated by staff at TB centers in the country be used to extract data. This method can throw better light on the relationship between HIV and TB.

2. RESEARCH QUESTION, AIMS, OBJECTIVES AND HYPOTHESIS

2.1 Research Questions

- a) How can unnecessary morbidity and mortality from TB be prevented among people living with HIV?
- b) What is the impact of co-infection with TB and HIV?

2.2 Study Aims

To compare treatment outcome between drug susceptible PTB in HIV and drug susceptible PTB and the factors associated with it.

2.3 Study Objectives

To assess the impact of HIV infection on standard PTB treatment outcomes by the use of existing data from 1st January 2021 to 1st January 2023 from TB treatment centers in the Bo district of Southern Sierra Leone.

2.4 Hypothesis testing

Tested hypothesis that with standard tuberculosis management, success rate $\geq 90\%$ achieved irrespective of HIV status.

- a) How can unnecessary morbidity and mortality from TB be prevented among people living with HIV?
- b) What is the impact of co-infection with TB and HIV?

3. LITERATURE REVIEW I

According to Karo B, et al. (2016)**Error! Reference source not found.** HIV-TB co-infection is commonly associated with higher mortality than HIV-negative TB patients however, added that it is encouraged to investigate the positive outcome of optimal duration of TB treatment in HIV coinfecting individuals for whom the planned study will be relevant. The study would have given a breakdown of categories that influenced higher mortality in HIV-positives. It is also a bit not clear the deaths due to an advanced HIV stage such as CD4 counts < 200 , cryptococcal, PCP, misdiagnosis of the type of TB, etc? The mentioned factors are predictors of poor treatment outcomes indicating that TB/HIV co-infection has remained a major public health problem in the world. Hence, the need for sustained strengthening and expansion of the national TB/HIV programmes. Abiodun Hassan, Ogbuji, et al (2016)**Error! Reference source not found.** stated that unsuccessful TB treatment outcomes are predicted to be higher among rural than urban resident patients more of which are present in the re-treatment category than new, and patients with other chronic diseases. Therefore, due emphasis should be given to these high-risk groups, and specific strategies to address these groups should be designed.

In their review, Hannock T et al. (2013)**Error! Reference source not found.** concluded that amid limitations in their study around 5% of eligible patients were not available and their exclusion might have introduced bias, therefore did not find significant differences in terms of age, gender and HIV status between TB treatment outcomes. Despite the limitations, their findings were useful to inform policy makers and programmes that aim to improve management of new smear-positive TB/HIV patients in Malawi and other comparable settings.

The Ethiopia study conducted by Tola A. et al. (2019)**Error! Reference source not found.** established that even though outcome of co-infected patients can be unpredictable, with effective case management, 86.8% of the TB-HIV co-infected patients are successful as TB treatment outcomes. On the contrary, a study in Vietnam by Thanh H et al, (2016)**Error! Reference source not found.** showed adverse outcomes in TB-HIV patients at about 26 %. It is not clear whether the outcome is due to differences in case management, inherent factors or HIV stage of the patient. Osei E et

al. (2019)**Error! Reference source not found.** showed that in Ghana treatment success was not only below the WHO end TB strategy set target of > 90% but those co-infected with HIV strongly predicted unsuccessful treatment outcomes more than the others. However, the study fell short of HIV co-infected WHO stage stratification like several other studies discussed above.

In a systematic review, Abay S et al, (2015)**Error! Reference source not found.**, the conclusive evidence on the reduction of all-cause mortality as a result of early initiation of ART was counteracted with the confirmation of the high rate of TB-IRIS and the death associated with it. The coexistence of pulmonary of PTB with HIV infection leads to high morbidity and mortality in the study population assessed by Wu Y et al.(2021)**Error! Reference source not found.** although antiretroviral therapy (ART) has decreased TB incidence in HIV-infected patients.

Despite overall treatment success of 75%, the high mortality in HIV co-infected in Vijay S et al, (2011)'s**Error! Reference source not found.** study group, further investigations may be needed to ascertain the main reasons for the high mortality. Successful TB treatment outcome among TB/HIV co-infected patients was lower than the target set by Global Plan to Stop TB 2011-2015. In conclusion, Yenework Sinshaw et al., (2017)**Error! Reference source not found.** strongly recommended that strengthening collaborative TB/HIV management activities that would trace the identified factors shall lead to increased successful treatment outcome of TB. Tuberculosis/HIV co-infection constitutes several problems including diagnostic and therapeutic challenges in the healthcare settings (Nglazi MD, Bekker LG et al 2015)**Error! Reference source not found.**, (Wondimeneh Y, Muluye D,Belyhun. 2012)**Error! Reference source not found.** It is supported by a study conducted in USA that revealed treatment of TB in co-infected patients differ from those patients who are infected with TB only (Sterling TR, Pham PA, Chaisson RE. 2010).**Error! Reference source not found.** Some of these challenges: clinical problems about duration of treatment, frequency of drug administration, pill burden, management of drug interactions, and complications of therapy like drug toxicity and immune reconstitution inflammatory syndrome (IRIS). Since such patients are being treated for two infectious diseases, the goals of treatment for both must be balanced through therapy integration, use of concurrent Antiretroviral Therapy (ART), prevention of HIV-related co-morbidities, controlling drug toxicity, and monitoring of IRIS (Sileshi B, Deyessa N, et al. 2013),**Error! Reference source not found.** (Bruchfeld J, Correia-Neves M et al 2015).**Error! Reference source not found.** This would bring optimal outcomes in terms of treatment response and prevention of drug resistance.

4. LITERATURE REVIEW II

According to David .O.H et al, 2019,**Error! Reference source not found.** Sierra Leone has a

high tuberculosis (TB) burden with a prevalence of 441 cases per 100 000 population. As a result of the Global Fund, some facilities in the country have access to improved diagnostics, including GeneXpert MTB/RIF testing, of particular use in diagnosing those at risk of drug resistance, in the form of rifampicin-resistant (RR) TB.

Despite decades of the implementation of the directly observed therapy short-course (DOTS), Sierra Leone is ranked among the 30 highest TB-burdened countries according to WHO report 2021. Several factors account for unfavorable treatment outcomes, among which are patient characteristics.

Previous studies have only focused on treatment outcomes without any consideration for the factors that lead to the outcomes in the management of DSPTB. The purpose of this study was to investigate not only patient characteristics but HIV infection in TB that is associated with treatment outcomes among TB patients undergoing the DOTS program in Sierra Leone.

A retrospective cohort design was used to analyze secondary data from the completed records of 2000 DST-PTB patients. Descriptive statistics, bivariate and multivariate logistic regressions were used to analyze the data. On the other hand, being HIV-positive decreases the odds of treatment completion. Also, the educational level, geographic location, and year of treatment were significantly associated with treatment completion.

According to World Health Organization, 2018a, World Health Organization, 2018b, Sierra Leone is among the 30 high TB burden countries that collectively accounted for 87% of all new TB cases globally in 2017, yet studies are lacking on the TB epidemic in this country. In the WHO, 2018a, 2018b articles ninety-eight percent of all TB patients were tested for HIV infection, yielding a TB/HIV co-infection prevalence of 12%. “Although there is a well-outlined national policy to provide treatment for all TB patients in Sierra Leone cost-free, only 70% of incident cases received anti-TB treatment in 2017, with a treatment success rate of 89%” (World Health Organization, 2018a, World Health Organization, 2018b). “Currently, the Global Fund provides 70% of TB control program costs in Sierra Leone, with other local and international agencies providing additional technical and logistical support towards control efforts” (The Global Fund, 2019).

Fundamentally, tuberculosis remains a disease of poverty, housing insecurity, stigmatization, and other social inequities (Lönnroth K, et al. 2009).**Error! Reference source not found.** Kamara and colleagues (Kamara RF, et al.2022)**Error! Reference source not found.** were unable to specifically explore these factors in their analysis, due to the retrospective design of their study. However, as

the largest single-country study to date from west Africa, their findings provide crucial insight into the current MDR-TB epidemic in this region and underscore the importance of integrative clinical care. Notably, their findings support current calls advocating for the urgent tackling of entrenched socio-cultural and economic inequities, as countries in this region intensify public health efforts towards meeting the End Tuberculosis goals by 2030

The characteristics of the TB epidemic in Sierra Leone are poorly understood and have not previously been investigated in detail. In this study, we describe the demographic characteristics, clinical presentation, treatment outcomes, and predictors of TB-related mortality at the largest TB clinic in an urban setting with high HIV prevalence in Sierra Leone (Lakoh et al., 2019b)^{Error! Reference source not found.}, using secondary data extracted from medical records of patients who started TB treatment at the facility during 2017.

According to world data atlas 2021, of the total country population of 8,141,343, Sierra Leone has 298 TB cases per 100,000 people. The nation has 76,000 persons living with HIV. The world data atlas went on to further state that in 2020, TB death rate of 31 cases per 100,000 people and AIDS estimated deaths of 3,000 persons.

Suboptimal TB treatment outcomes were observed in Sierra Leone in 2017. More local and international action is warranted to help achieve the 2035 global TB elimination targets (Lakoh, S. et al. 2020)^{Error! Reference source not found.}.

5. METHODOLOGY

The number of patients that die during treatment is higher in HIV/PTB than those that have PTB alone. There is perceived unnecessary death due to management gap in the treatment of patients. The described below methods used to do the study

5.1 Study Design with study variables

This study was retrospective cohort study that assessed DSTB cases with outcomes that are either HIV positive or negative.

It was retrospective cohort study of multicenter routine data collected from 1st January 2020 to 1st January 2022 on pulmonary TB cases irrespective of their HIV status i.e. patients' personal files and the registers generated by staff at TB treatment centers in the Bo district of the Southern province of Sierra Leone.

The study variables include Gender, Age, Cured, Treatment completed, Successful outcome (cure and completed), Died, Failed, Lost to follow-up, Transferred out, distance from health facility,

CD4 count, HIV status, HIV staging, Literacy, Available Meals per day, Patient being bread winner, period of death since enrolment, treatment facility, whether admitted or treated at OPD, length of stay, secondary drug resistance detected, etc.

5.2 Study area

The study area was the catchment areas of all the TB treatment centres including the referral facilities run/collaborated with by the ministry of health in Bo district of Southern Sierra Leone.

5.3 Study population

Patients commenced on treatment between 1st January 2020 and 1st January 2022 with outcomes (death, cured, completed treatment, failure, etc.) and came from the catchment district were selected as participants.

Bo district where the study population lives is located in the southern province of Sierra Leone with a area of 5463km² with a population of 756,975 and a density of 138.6/km² of (2021 census). The rate of natural increase stands at 4.7% (2015 → 2021 census). Females make up 51.6% (389,629) while the males make up of 48.4%(366,346).

The bulk of the population of Bo district like other parts of Sierra Leone are poor. The common occupation in the district are petty trading, gold and diamond mining, coffee, cacao subsistence rice farming, and oil palm agriculture.

Bo District is home to 385 Primary Schools and 40 Secondary Schools but the number of schools increase in the last 10 years, the reason why the literacy rate stands at about 45%.

The data was collected on 1,947 patients with complete data and outcomes that were as well resident in the data collection district at the time of admission. Initially the data collection was planned for 2000 patients but all the data collected did not sum up to the target.

5.4 Sampling

Because the estimate showed that the data will not be enough for random sampling, decision was made that all data be collected as long as it is enough. So instead of 2000 patient data, 1947 outcomes were available at that fell within the prescribed study period in the catchment area in Bo district.

Stratification of the samples will be done based on gender, age and HIV status, staging, etc.

5.5 Data Management and Analysis

The data captured demographic, socio-economic, clinical status, management and outcome.

Review of patients' files was carried out to enabled analyses of the desired variables. Patient's consultation cards/files available at designated treatment centers were used as reliable source of information. When computer data entry was accomplished, its processing and analyses commenced via datatab software to get derieved results that can be analysed for the link to treatment outcomes of HIV and TB infected only patients.

The data collectors were trained and piloted in the field as a test case before the actual data collection was done. Supportive supervision to the team in the field was carried out by a statistician to ensure quality data collection.

Collected data was computed using through hypothesis testing, chi-square, regression, hazard survival and other analyses programmes to compare outcomes of TB cases relative to HIV status and more so the WHO stage. The data was also used to capture demographics such as socio-economic, gender, clinical status, management and outcomes.

Collected data generated demographics, clinical characteristics, and laboratory findings extracted from medical records were used to assess relationship, predictors of death, including age adjusted hazard ratio with 95% confidence interval.

5.6 Ethical Considerations

Data collection was void of variables that can identify individual patients. Data usage was restricted for the purpose of this study and not otherwise. Any future use of the data will trigger a new consent or assent of authorization from the same ethical committee that validated its use. Although data cannot identify individuals, password used to open it. Stored data including the transcripts shall remain password-protected.

Patients' unique IDs used and not names in addition to other variables such as age, sex, geo-origin, type of outcome, etc.

Approval from the ethics and scientific research committee was received from the health and sanitation ministry as well as the TB and Leprosy department at district also consented before collection. In fact, some of the data collectors were from the latter.

6. RESULTS

	<14yrs	≥15 yrs	literate	illiterate	HIV+ 64	HIV-	3 meals/day	<3meals/day	Bread winner	Not bread winner
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Females	16	686	297	405	53	649	483	219	109	625
Males	15	1230	679	566	53	1192	890	355	620	593
Total	31	1916	976	971	106	1841	1373	574	729	1218

Table 1. Age, Literacy, HIV Status and Food Security

6.1 Gender

There were 702(36.05%) females and 1245(63.94%) males initiated on anti-TB regimen in the period under review. Studies general has seen more males with the disease than women.

6.2 Age

Of the 1,947-patient data collected, 31(1.59%) were <15 years while 1916 (98.40%) were ≥15 yrs. The age distribution was mainly skewed towards ≥15 years old in the cohort which is again common in a stable population. However, 68.05% (1325) of the cohort in the study were 15-45 years.

6.3 Literacy

The literacy rate was 50.12% (976). The is so because the bulk of the patients were 15-45 years otherwise the overall literacy rate in the country is not that high.

6.4 HIV status

There were 106 (5.44%) patients were living with HIV among the 1,947 initiated cases. Interestingly there same number of males and females in the cohort are living with HIV. Proportionally the females have are higher considering the denominators.

6.5 Food security

6.6.1 Meals/day

For those who get 3 meals per day stood at 70.51% (1373).

6.6.2 TB in bread winner

Those among patients that were breadwinners of their homes were 729(37.44%) of the study cohort which may mean that the family would struggle with food while the person is sick.

Table 2. Treatment Outcomes

	cured	completed	LTFP	Death	Transferred	Death <24hrs	Death ≥24h-48hrs	Death ≥48hrs
Females	674	5	17	2	4	1	0	1
Males	1185	15	40	4	1	0	2	2
Total	1859	20	57	6	5	1	2	3

6.6 treatment outcomes

Number of patients cured were 1859(95.48%), completed treatment 20(1.02%) totaling to 96.50%(1879) success rate. Other outcomes were LTFP as 2.92%(57), death rate was 0.30%(6) and transferred out was 0.25%(5).

Half of the deaths were below 48hrs which might have occurred anyways. None of the deaths were a patient living with HIV.

6.7 Hypothesis testing

Table 3. t-Test for Independent Outcomes with Respect to HIV status

t	df	p (2-tailed)		
Exit code: 1= cured , 2= completed treatment 3= LTFP 4= Died 5= Transferred out	Equal variances	-1.13	974	.26
	Unequal variances	-0.81	60.42	.421

A two-tailed t-test for independent samples (equal variances not assumed) showed that the difference between TB in HIV- and TB in HIV+ with respect to the dependent variable Exit code: 1= cured , 2= completed treatment 3= LTFP 4= Died 5= Transferred out was not statistically significant, $t(60.42) = -0.81$, $p = .421$, 95% confidence interval [-0.25, 0.11]. Thus, the null hypothesis is retained which means with standard treatment of DSPTB the outcome in the patients living with HIV is not different from those that are HIV negative.

6.8 Point biserial correlation values

Table 4. Point Biserial Correlation values of HIV Status and Exit Outcomes

rpb	0.03
df	1945
t	1.53
p (2-tailed)	.127

A point-biserial correlation was run to determine the relationship between HIV status: HIV negative, HIV positive and Exit code: 1= cured, 2= completed treatment 3= LTFP 4= Died and 5= Transferred out. The correlation between HIV negative, HIV positive and Exit code: 1= cured, 2= completed treatment 3= LTFP 4= Died 5= Transferred out, was statistically not significant (rpb = 0.03, n = 1947, p = .127). Therefore, there is no difference in treatment outcome between the two groups and therefore the null hypothesis retained.

7. DISCUSSION

The study showed that nearly two-thirds (63.94%) of the 1,947 participants in the study were males that is similar to studies done on the TB demography of Sierra Leone where 2013 Kangbai, J. in his Evolutionary Trends for Pulmonary Tuberculosis Treatment Using DOTS in Sierra Leone assessed data collected treated from 1992-2010 retrospectively with a total of 2,958. He discovered that 1,881 (63.59%) were men and 1,077 females mostly adults of age range 15-65 years at the various German Leprosy Relief Association diagnostic centers, chest clinic at Lakka in Freetown and the Department of Environmental Health Sciences, Njala University in Bo, Sierra Leone.

The study Sesay, M.L in 2018 in his patient characteristics and treatment outcomes among tuberculosis patients in Sierra Leone show that there was no significant association between treatment completion and age, gender, and TB-case category. On the other hand, being HIV-positive decreases the odds of treatment completion. Also, the educational level, geographic location, and year of treatment were significantly associated with treatment completion.

The study data collected in 2020 and 2021 showed less incidence rate of TB than the nation rate of 289 cases/100,000 population in both years. The year 2020 had an incidence rate of 126 cases/100,000 population while 2021 was 131 cases/100,000 population. This may show that TB

incidence is either reducing or that suspected TB cases are being missed in the consultation to be sent for further investigation. There is likelihood of distance or past bad experience in the health facility that keeps patients from attending clinic.

The proportion of TB in children (less than 15 years of age) showed 1.59% of the study population, which is less than the WHO estimate of 11.66%. The age distribution mainly skewed towards ≥ 15 years old in the cohort, which is again common in a stable population. However, 68.05% (1325) of the cohort in the study were 15-45 years.

According to M. Majigo, G. Somi, A. Joachim, J. et al 2020, assessment was conducted of the occurrence of a first episode of pulmonary tuberculosis (PTB), involving individuals whose first visits at HIV care and treatment services occurred between January 2011 and December 2014. As a result, the study included a total of 527,249 individuals with a total of 11,539,844 clinical encounters at health facilities implementing TB and HIV collaborative activities. The overall TB incidence rate was around 16.7 (95% CI 16.4–16.9) cases per 1000 person-years with annual incidence rate decreasing from 17.0 to 14.9 per 1000 person-years, representing around 12% decrease over the 4 years. The TB incidence in the study was significantly associated with advanced HIV disease defined by WHO clinical stages. Our findings are consistent with previous findings and support the known benefit of early HIV diagnosis and treatment. There is a much higher risk of HIV and TB co-infected patients to develop active TB either from the latent infection or rapid progression of a new infection, especially in advanced HIV disease. TB incidence as a result of immune reconstitution after initiation of ART is likely to occur in advanced HIV disease. Although this study did not record immune reconstitution inflammatory syndrome, the majority of TB incidence among patients with advanced HIV disease occurred within 2 months after ART initiation, as previously observed.

According to Korzeniewska-Koseła, M., Wesołowski, S., 2021 states that the incidence rates of tuberculosis were growing along with the age group from 1.4 per 100,000 among children (0-14 years) to 23.9 per 100,000 among subjects in the age group 45-64 years, the incidence rate in the age group ≥ 65 years was 19.8 per 100,000. There were 81 cases in children up to 14 years of age (1.5% of the total) and 48 cases in adolescents between 15 and 19 years of age - rates 1.4 and 2.6 per 100,000 respectively. In 2019, there were 3897 cases of tuberculosis in men and 1424 in women. The TB incidence in men - 21.0 per 100,000 was 2.9 times higher than among women - 7.2. The biggest difference in the TB incidence between the two sex groups occurred in persons aged 50-54 years - 40.2 vs. 8.1 and in age group 55 to 59 years - 45.1 vs. 9.0. In 2019, there were 121 patients of foreign origin among all cases of tuberculosis in Poland (2.3%). In 2018, TB was

the cause of death for 519 people (mortality rate - 1.4 per 100,000).

The literacy rate was 50.12 % (976) higher than the national as the district is one of the regions with a relatively higher literacy rate. This is so because the bulk of the patients were 15-45 years otherwise the overall literacy rate in the country is not that high.

In 2002, Singh et al. suggested the need for extensive health education by community involvement to create awareness about TB in the slum communities of Delhi. Although literacy rates did not contribute to the correlation matrix in our study, the positive regression weights indicate that a level of awareness is more essential than literacy status for availing TB program services.

There were 106 (5.44%) HIV+ participants among the 1,947 initiated cases and none of them died during treatment. About 66.7% of the deaths were ≥ 40 years of age.

Some of the socio-economic determinants that were reviewed included having 3 meals/day. There were 70.51% (1373) of the study participants reported having 3 meals per/day. 37.44% (729) of the study participants were breadwinners of their respective families which means the family would struggle in getting food while the he/she is sick. In a similar social science study results Gregory J. Fox, Robyn S. Lee et al 2015, explained that untangling the nexus between concurrent socioeconomic factors and tuberculosis is challenging in settings where tuberculosis is prevalent given the close relationship between poverty, tuberculosis, and their determinants. Poor nutrition can be both cause and effect of the disease. Ecological studies of populations at risk for tuberculosis have reported associations between socioeconomic factors and disease; however, their findings are limited by problems of unmeasured confounding. Hence, the careful characterization of a large number of potential determinants of latent tuberculosis infection and disease was an additional strength of this study. These included demographic housing, social, environmental, and lifestyle factors, as well as the HIV status of people with disease. Although this inevitably means that the results of our comparative analyses should be considered hypothesis generating only, nevertheless, the estimates of effect of each potential social determinant could be adjusted for the potentially confounding effects of other possible determinants. Furthermore, as malnutrition is widespread among patients with tuberculosis, further studies into the relationship between nutrition, socioeconomic factors, and tuberculosis in other settings are also warranted.

In the Brazilian study by De Albuquerque. 2007 on the 'Factors associated with treatment failure, dropout, and death in a cohort of tuberculosis patients in Recife, Pernambuco State, Brazil. 2007,

treatment failure was associated with treatment delay, illiteracy, and alcohol consumption. Dropout was associated with age group, prior TB treatment, and illiteracy. Death was associated with age group, treatment delay, HIV co-infection, and head-of-household's low income. The main factors associated with combined unsuccessful treatment outcomes were age group, HIV co-infection, illiteracy, alcoholism, and prior TB treatment. The highest population-attributable risk percentages were related to HIV infection and alcohol consumption, both potentially modified by public health interventions. Treatment delay of more than 60 days was associated with treatment failure and death. Treatment delay allows progression of the disease to a more severe clinical phase in which cure becomes more difficult.

Low socioeconomic status, expressed either as illiteracy or low income for the head of household, increased the risk of all three negative outcomes. The increased risk of death among individuals for whom the head-of-household's income was unknown probably reflects sporadic earnings. Illiteracy can reflect both poor access to information (an obstacle for patients in this setting, which involves mainly written educational materials) and (given its strong association with low socioeconomic status) the inability to afford transportation to the health unit or losses in workdays. Because of social stigma, patients often prefer to be treated away from their place of residence. Such conditions contribute to irregular treatment, which may in turn lead to failure. Although low income and poor formal education measure similar attributes, in this setting illiteracy represents a lower cut-off point on the social scale and is likely to be related to greater deprivation, which explains its closer association with negative prognosis. According to a study in Pelotas, a city in the South of Brazil, among the socioeconomic variables, only skin color (non-white) was associated with treatment noncompliance. The authors suggested that poorer patients, probably non-whites, are more likely to get the disease and to experience more adverse conditions, making personal and family adaptation to treatment more difficult. The lack of association with other variables was probably due to the sample size. In another Brazilian study, at the ecological level, the correlation between TB death rates and poverty in São Paulo showed higher mortality in low-income areas. A study that reviewed mortality data for all U.S. residents that died in 1990 with TB as the underlying cause of death or with TB listed anywhere on the death certificate as a contributing cause of death suggested a contribution to TB mortality by substance abuse (including alcohol).

The outcome was generally very favorable with those discharged as cured been 95.48% of the total initiated on treatment within the period under review, 1.02% completed treatment and overall success rate standing at 96.50%. The unfavorable outcomes were 2.92% LTFP, 0.30%

death rate and transferred out was 0.25%. 50% of the deaths occurred in the first 48hrs of patient admission.

The treatment success rate of patients that were living with HIV was 94.33 % (100 of 106), LTFP was 4.71% (5) and 0.94% (1) transferred to inpatient facility because of worsening condition. It is also worth noting that none of the deaths were HIV+ participants/patients. Probably those who were very sick didn't make it to health facilities or even if they did were not initiated on anti-TB treatment but referred straight for inpatient care.

Similarly according to a study by Park, S., Moon, N. et al 2021, 3605 TB patients were enrolled in this program in Morocco's five prefectures (Rabat, Salé, Kénitra, Khemisset, Skhirat-Témara) from January 2018 to December 2019. Patients were managed based on demographic characteristics, socioeconomic status, areas (rural or urban), health literacy levels, and distance to primary health centers. After mobile health intervention was interposed with high-risk TB patients, along with patient education. The rate of successful treatment was 92.2%, which was higher than the national rate (88%). The "lost to follow-up" rate was 4.1%, which was significantly lower than the existing non-adherence rate of 7.9%. Therefore, integrated patient management for TB patients seem more effective than the existing conventional programs.

8. STUDY LIMITATIONS

It is not easily possible to if some of the lost to follow-up died or not as some of the patients' geo-origin are very hard to reach terrain by contact tracers. The lost to follow up might influence the outcome of the comparison between DS-PTB of HIV negatives and positives.

Errors or skipped entry of variables of patient's information into forms, registers, etc during patient management will affect the inclusion of certain patients of interest and hence affects outcome.

Lost to follow-up of patients responding well to treatment close to time of discharge may give negative outcome that was going to be success.

The number of patients who are HIV positive might not be enough for drawing judgement.

Another limitation is that the data collected is retrospective secondary data. Some study participants were left out due to issues with missing and/or inaccurate data.

9. CONCLUSION

A bit more than half (59.21%) of the participants were ages between 25 and 49 years. In this study the overall success rate was very high (96.50%) and so was the success rate of participants

that were living with HIV (94.33%) of which are by far higher than previous study done by Lakoh et al., 2019 at Connaught hospital in Western Sierra Leone in 2020. The reason is likely that the hospital is a tertiary referral hospital which means severely sick patients are referred there that will have effect on the outcome.

A two-tailed t-test for independent variables showed in the study that with standard treatment there is no statistically significant treatment outcome between TB participants with TB in HIV positive and TB in HIV negative, $t(60.42) = -0.81$, $p = .421$, 95% confidence interval [-0.25, 0.11]. That means the null hypothesis is retained and alternative hypothesis rejected.

The point-biserial correlation run to determine the relationship between HIV status in TB versus treatment outcome showed that it was statistically not significant ($r_{pb} = 0.03$, $n = 1947$, $p = .127$). Therefore, there is no difference in treatment outcome between TB in HIV positive and TB in HIV negative groups and therefore the null hypothesis retained as mentioned above.

10. RECOMMENDATION

Early and standard treatment of drug sensitive pulmonary tuberculosis is to be adopted in order to reduce mortality in cases irrespective of their HIV status. In this way the lungs will not be heavily compromised and at the same time easier to manage IRIS in patients that are living with HIV.

System strengthening to ensure continuity in patient counselling to treatment adherence, follow-up, community health education all to ensure good treatment outcomes.

Universal coverage of transport fare to and from treatment facility shall improve patient treatment outcomes. Family may unconsciously mount huge pressure on TB patients that are family breadwinners and as such will lead to lost to follow up or other adherence issues, so it is recommended that TB programs cater for food for families of TB patients as it is not everything that medicine can do without finance.

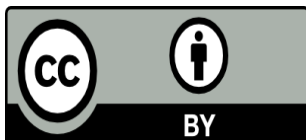
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