RESEARCH ARTICLES

Epidemiology of tuberculosis in the context of HIV and AIDS in Sinazongwe district of Zambia: A retrospective analysis

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TB cure and completion rates have remained poor for Sinazongwe district in the past five years. Mortality, treatment failure and defaulter rates among TB patients have also been increasing in the same period. The reasons for the observed poor treatment outcomes are not well understood but could be attributed to high HIV co-infection among TB patients in the district.

This study was aimed at determining the prevalence of HIV/AIDS among TB patients and asses the association between the common TB treatment outcomes. A retrospective study of 484 TB patients' clinical files drawn from a total of 2,137 files was conducted at Sinazongwe Zonal Health Centre. HIV was more prevalent among female TB patients at 61.5% compared to their male counterparts, 54%. TB/HIV co-infection were higher for patients with extra pulmonary TB compared to patients with pulmonary TB (p= 0.002).

HIV prevalence among TB patients in Sinazongwe district was high and there was no evidence of declining trend observed across the reference period. HIV did not only fuel the number of new TB infections but was also, in part, responsible for reducing TB cure rate and increasing mortality rate among TB patients registered in the routine TB program.

Introduction

Tuberculosis is a chronic, progressive infectious bacterial disease that affects all species of mammals, including humans. Human tuberculosis (TB) is chiefly associated with infection by members of the *Mycobacterium tuberculosis* complex (MTC) which includes *Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium africanum, Mycobacterium caprae, Mycobacterium microti, Mycobacterium pinnipedii and Mycobacterium canetti* [1,2]. *Mycobacterium tuberculosis* is the common causative agent of human tuberculosis (TB). This bacterium mainly affects the lungs but

may progress to other parts of the body such as the meninges, kidneys, bones and lymph [3].

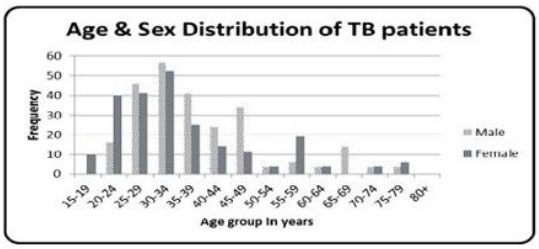

Figure 1: Distribution of TB patients by age and sex (n=484) in Sinazongwe district (2007-2012).

Human Immunodeficiency Virus (HIV) alone is a known cause of human mortality and when combined with TB, it becomes a lethal co-infection for human beings [4]. HIV affects the immune system and increases susceptibility to TB infection by causing depletion of CD4 T cells, which are important in the control of TB [4, 5]. HIV has effects on other cells, including macrophages, and influences cytokine production, which may also prevent a host from containing an initial or latent *Mycobacterium tuberculosis* infection [3]. Further, HIV increases the chance of relapse in TB cured persons [6].

Globally, TB–HIV co-infection accounts for 13% of TB deaths and about 8% of these are attributed to HIV [8]. Zambia, with a population of about 13 million people, is one of the countries experiencing high TB notification rates coupled with a high HIV disease burden in selected places [4, 9, 10]. The analysis of medical metadata has shown undesirable TB treatment outcomes strongly associated with high HIV co-infection rates [11]. The rapid increase of tuberculosis case notification in Zambia from 1985 onwards is mainly attributed to the HIV epidemic, but other factors like population growth, urban overcrowding and improved access to health care have also contributed [9, 12].

Arising from recent studies conducted in selected parts of the Country, medical metadata analysis indicates that incidence of TB/HIV co-infections has increased and that HIV is the major reason for high TB notifications in Zambia [12, 13, 14]. In Sinazongwe district, new HIV infection rates have increased by twenty two percent (22%) between 2007 and 2012 [15, 16]. The number of patients on ART has also grown by 18% between 2007 and 2012 [17]. TB cure and completion rates have remained poor for Sinazongwe characterized by high mortality, treatment failure and defaulter rates in the same period [13, 16, 17, 18]. The reason for the observed poor treatment outcomes is not well understood but could be attributed to high HIV co-infection among TB patients at this facility.

Therefore, a retrospective study was undertaken with the overall objectives of determining (i) period prevalence of

HIV/AIDS among TB patients and (ii) factors associated with treatment outcomes of patients in the routine TB program from 2007 to 2012 at Sinazongwe Zonal Health Centre. Due to limited information generated in the routine TB program, the extent to which HIV/AIDS influences TB treatment outcome has remind unknown since the initiation of TB and ART services in the study district. Thus, this article intends to provide baseline data on understanding the major issues that need to be addressed in TB control in the context of HIV/AIDS and inform policies that will ensure implementation of effective interventions for impact.

Methods

A retrospective study was used to review TB clinical files and charts for TB patients registered in the routine TB care program at Sinazongwe Zonal Health Centre for the period between 2007 and 2012.

Sinazongwe has an estimated population of 118,000 people [19]. The district is part of the Zambezi valley in the southern part of Zambia covering approximately 4200 square kilometres. Being a retrospective study, the study did not have any direct interaction with the patients but rather reviewed all adult patients (15 years and above) data, diagnosed with TB by symptoms, positive sputum smear, culture or chest x-ray, who were entered into the TB register and received treatment at Sinazongwe Zonal Health Centre at least a month prior to initiation of the study. Medical files that did not meet these criteria were thus excluded from the study. A

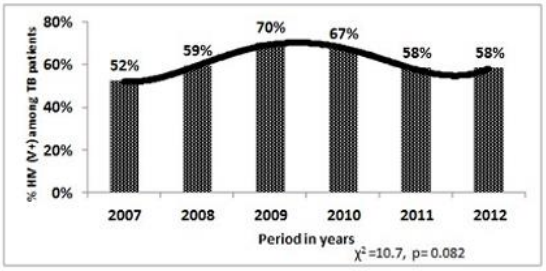

Figure 2: Prevalence of HIV among TB patients at SZHC from 2007-2012 (n=484)

TB patient file for this study was defined as any suspected TB patient with a sputum smear on microscopy examination (SSM) indicating presence of acid fast bacillus (AFB) or chest x-rays (CXR) results appearing abnormal (showing some whitish spots in the lungs) or the results of a bacterial culture and acid fast bacteria (AFB) culture indicating growth of *Mycobacterium* [20, 21].

Patients' clinical files were stratified into six strata with each stratum representing the year in which the patient's files were opened. Hospital TB registers were used to generate sampling frames for each of the years under review. The study aimed at soliciting medical metadata from patients aged 15 years and above who were diagnosed with TB by sputum smear microscopy examination or

chest x-ray and or culture. Using this inclusion criterion, 2, 137 clinical files were eligible for inclusion out of the total of 3,821 registered files. Random samples were drawn from each stratum using the simple random formula described by Dahiru [22].

Table 1: Patients history of TB treatment (N= 484) at SZHC between 2007 and 2012

		Patient's TB treatment history		
		equency	percent	95% CI
Treatment history	New	341	70.5	(66.4 – 74.5)
	Relapse	18	3.7	(2.0 – 5.4)
	Transfer-in	109	22.5	(18.8 – 26.2)
	Treatment after failure	12	2.5	(1.1 – 3.9)
	Treatment after default	4	0.8	(0.02 – 1.6)
	Total	484	100.0	

It was planned that the prevalence estimate would be determined at 5% precision at a confidence level of 95% assuming that patient clinical files were drawn from a normally distributed population. Consequently, using simple random sampling for each stratum (period stratum) with the design effect of stratified random sampling estimated at 2, TB prevalence of 3.2% [42] the sample size required for the study was calculated as 484 [22].

A review of records was accomplished by trained data collectors who were oriented in the data collection procedures prior to the activity. Variables of interest included age, sex, diagnosis, type of TB, treatment history, HIV/AIDS status and treatment outcomes. Validity and reliability issues were addressed through pre-testing of the research instruments.

Data was cleaned and entered into the Statistical Package for Social Sciences (SPSS) version 16.0, where all the statistical analyses were performed including descriptive statistics. Prevalence of HIV among TB patients was calculated. The Chi-square (χ^2) test was used to test for associations between categorical variables. A stepwise logistic regression model was used to determine predictors of TB treatment outcomes among the patients. All variables with p-values less than 0.250 in the univariate analysis were included in the model. The variables under consideration were sex of patients, weight, age, and level of education, type of TB, type of patient, HIV status and marital status. The Logit link function reported the coefficient, p-value, odds ratio (OR) and 95% lower and upper confidence interval values for the OR. Criteria used in determining whether the constructed model adequately fitted the data were, a non-significant Hosmer and Lemeshow Test ($p > 0.05$) and a significant Omnibus Test of Model Coefficients ($p < 0.05$). All statistics were considered significant at $p \leq 0.05$.

Ethics Statement

The reviewed data/documents were anonymized /de- identified and permission to perform the study in the district was obtained from the Provincial and District Medical

Officer (DMO) as well as Sinazongwe Rural Health Centre. Being a retrospective study, waiver of consent was sought and granted. Further the study was approved by the Institutional Review Board (ERES converge IRB) ethical review committee (ref. number: 2014-Mar-001).

Results

A total of 484 TB patient files from 2,137 eligible files were reviewed during this study. The analysis of basic demographic and clinical characteristics of patients indicated that majority (52.5%, 95%, CI: 48.0 – 56.9) of TB cases registered at Sinazongwe Zonal Health Centre between 2007 and 2012 were male and compared to females (47.5% (95% CI: 43.7 – 52.0). Further, the mean age of males (38.9 years, 95%, CI: 36.3 – 41.4) was slightly higher than females (35.4 years; (95%, CI: 32.8 - 38.0) (Figure 1). Figure 1 further shows that, there were relatively more young females between the age groups of 15-24 years with TB compared to males of the same age group. The trend changed slightly after 25 years when there proportionally were more males with TB compared to females (Figure 1).

With regards to education, the level of education for about 45% of the patients was not indicated in the files and amongst those who indicated that they had been to school, 46.6% (95%, CI; 40.6– 52.6) reached primary level of education, 39.2% (95%, CI; 33.3 – 45.0) reached secondary school, and only 14.2% (95%, CI; 10.3 – 18.8) had attained tertiary education. With respect to marital status, it was observed that most of the TB patients at this facility in the period under review were married 48.6% (95%, CI 42.3 – 50.1) followed by the singles 19.6% (95%, CI 17.8 -20.3). It was further observed that 70.5% (95%, CI 66.4 – 74.5) of the TB patients at Sinazongwe Zonal Health Centre registered between 2007 and 2012 were new TB patients and 23% (95% CI, 21.1 – 24.7) transferred-in from other facilities. Relapses and treatment failure accounted for 3.7% and 2.5%, respectively (Table 1).

Table 2: HIV testing results among TB patients at Sinazongwe Zonal Health Centre 2007-2012

HIV testing results					
Sex of patient			CT results		Total
			Positive	Negative	
Male	Date of registration	2007	4	13	17
		2008	10	11	21
		2009	13	8	21
		2010	23	7	30
		2011	8	2	10
		2012	8	14	22
	Total male		**66**	**55**	**121**
Female	Date of registration	2007	10	16	26
		2008	6	10	16
		2009	23	2	25
		2010	14	4	18
		2011	19	10	29
		2012	11	10	21
	Total female		**83**	**52**	**135**
Grand total (male and female)			**149**	**107**	**256**

An estimated 79.8% (95% CI: 76.2 – 83.3) of TB patients at this facility were diagnosed using sputum smear microscopy examinations, followed by X-ray (12.4%, 95% CI: 9.5 – 15.3); and culture (7.8%, 95%

CI: 5.4 – 10.2). Further, it was observed that among the smear diagnosed patients, majority were males (57.2%, 95%, CI; 52.3 – 62. 189), whereas among those diagnosed using X-ray and culture majority were females (75%, 95% CI: 64.0 – 86.0) and (52.6%, 95% CI: 36.8 – 68.5), respectively. Further, the study observed that about 84% (95% CI: 80.3 – 87.3) of the TB cases at this facility were diagnosed with pulmonary TB, whereas extra-pulmonary TB accounted for only 16% (95% CI: 12.6 – 19. 2) of the cases. Notably among the pulmonary cases, majority were males 55.3% (95%, CI: 50.4 – 60.1), while the majority of patients with extra-pulmonary TB were females 62.4% (95% CI: 51.5 – 73.2). The study established an association between type of TB and sex. Females were more likely to get extra-pulmonary TB, than their male counterparts (OR 2.1, 95% CI: 1.6 – 2.7, p=0.03) and that HIV positive individuals had a higher risk of presenting with extra-pulmonary TB than the pulmonary form, when compared to HIV negative patients (OR 2.0, 95% CI: 1.6 – 2.5, p=0.00).

Only 221 (45.7%; 95%, CI: 41.2 – 50.1) of TB patients knew their HIV status at TB registration and the majority of these were males 58.8% (130) (95% CI: 52.3 – 65.3). Those who did not know their HIV status at TB registration were further asked to concert for HIV testing and over 98% agreed to be screened and positivity rate was thus determined at 58.2% (95% CI: 52.2 – 64.2). Although most of the patients that tested positive for HIV were females at 61.5% (95% CI: 53.3 – 69.7), there was no statistically significant difference between sexes (p=0.164) (Table 2).

Overall, the study indicated that the mean prevalence of HIV among TB patients in the reference period was 62% (95% CI: 54.3 – 64.6), with the highest 70% (95% CI: 67.3 – 78.7) reported in 2009 and the lowest 52% (95% CI: 38.6 – 60.9) reported in 2007. The observed variations in HIV prevalence rates among TB patients was not statistically significant (p =0.082) (Figure 2).

Table 3: Maximum likelihood estimates of predictors of TB treatment outcome in Sinazongwe district of Zambia

Variable	Category	Odd Ratio (OR)	95% C.I. for OR		p-value
			Lower	Upper	
Age (years)	15 to 28	15.01	3.45	65.31	<0.000
	29 to 34	10.63	3.10	36.39	<0.000
	35 to 44	2.74	0.92	8.23	0.072
	➢ 44*	-	-	-	-
Type of TB	Pulmonary	24.83	5.74	107.41	<0.000
	Extra-pulmonary*	-	-	-	-
Treatment completed	completed	438.92	53.55	3597.85	<0.000
	Not completed*	-	-	-	-
	Constant	0.000			<0.000

C.I = confidence interval; *Reference category

A forward step-wise binary logistic regression model was used to determine predictors of TB treatment outcome in Sinazongwe district of Southern Province of

Zambia. The Omnibus test for model coefficients was significant ($p<0.001$) and the Hosmer and Lemeshow test was non-significant ($p=0.997$), indicating that the model fitted the data. However, the confidence intervals of the estimates were very wide due to uncertainty of the estimates. The variables that were found to be significant predictors of TB treatment outcome were the age of the patient, the type of TB and whether the patient completed the treatment or not (Table 3). Patients who were between 15 and 28 years old were more than fifteen times more likely to be cured than those who were more than 44 years old, while those who were between 29 and 34 years old were more than ten times more likely to be cured than those who were above 44 years old. Further, patients who had pulmonary TB were more than twenty-four times more likely to be cured than those who had extra-pulmonary TB. Furthermore, patients who had completed their medication were more than 438 times more likely to be cured than those who had not completed the treatment (Table 3).

Discussion

The study was aimed at determining the prevalence of HIV/AIDS among TB patients and determining factors associated with TB treatment outcomes of the patients registered in the routine TB care program at Sinazongwe Zonal Health Centre between 2007 and 2012. Generally, the demographic distribution of TB burden observed in Sinazongwe does not deviate from the global picture reported elsewhere [23, 24]. The study highlighted that the majority of the patients in this community had a humble education with only 39% having reached secondary level of education. This is in agreement with findings from elsewhere that there is a positive correlation between number of years spent in school and TB infections [42]. It has been hypothesised that increased schooling results into improved knowledge, decent work and work environment, improved health seeking behaviour and improved housing conditions to mention but a few [23, 25], thus reducing the risk of contracting TB.

The study documented that majority of patients were diagnosed using sputum smear microscopy, followed by x-ray and culture. Though this exemplifies the application of standard TB diagnosis and treatment guidelines as recommended for rural health facilities in Zambia [13], the use of microscopy comes with numerous challenges especially in the light of MDR-TB [20, 25, 26]. The current guidelines of World Health Organization and the International Union

against Tuberculosis and Lung Diseases specify that the essential step in the investigation of patients who are suspected of having pulmonary tuberculosis should have at least three microscopic examinations [27]. Sputum smear microscopy examination has a significant limitation in its performance in that sensitivity is compromised when the bacterial load is less than 10,000 organisms/ml sputum sample [28, 29].

It is also important to note that sputum smear microscopy has a poor track record in extra-pulmonary tuberculosis, paediatric tuberculosis and in patients co-infected with HIV and Tuberculosis [30, 31]. Studies have further showed that microscopic examination could cause treatment defaulters and loss to follow up due to repeated requirement for sputum samples for subsequent examinations [32, 33]. In view of the high prevalence of HIV among TB patients at this facility (62%), diagnosing TB by sputum smear microscopy would conceal valuable information. Therefore, it is important to consider the use of the rapid methods such as the automated Nucleic Acid Amplification Test, Xpert MTB/RIF) to revolutionaries TB diagnosis in Sinazongwe. The use of such technology provides improved sensitivity and specificity in people living with HIV with a detection rate of 80% (95% CI: 67% - 88%), which would represent an increased case detection of TB by 45% when compared to microscopy [34, 35, 36]. However, Expert MTB/RIF comes with its own challenges such as increased running costs, demand for trained manpower, infrastructure and investment requirements that are often beyond the scope of most diagnostic facilities that offer TB diagnosis to communities, particularly in resource limited rural communities [34, 37].

The study revealed that over, fifty-four percent of the TB patients did not know their HIV status at enrolment. This could have been largely due to non-availability of HIV testing kits, poor community sensitization and inactive TB/HIV working groups [12]. As part of diagnosis and treatment guideline of TB, all TB patients should be tested for HIV [13, 18]. Therefore, candidates who did not know their HIV status were requested to go for diagnostic counselling and testing for HIV during their follow up visits. Overall, HIV testing rates among TB patients was established at 98% (95% CI: 97.7 – 99.2). Screening over 90% of TB patients for HIV is a big success as observed by Wesen and USAID who reported, that most of the countries only manage to test between 87% and 90% [26, 38], respectively.

Overall, the study found that HIV prevalence was high among TB patients in the study

community with an average of 62% co-infection rate annually. Trend analysis indicated that the high HIV prevalence among TB patients reminded sustainably high during the 5 years period with no evidence of reducing. The persistently high HIV infection rates among TB patients could largely be attributed to the influx of people into the district due to increased social economic activities such as opening of two coal mines, opening of the thermal power plant, fishing and trade in livestock. As it is generally known that, the influx of people comes with numerous public health threats such mushrooming of shanty compounds, night clubs/bars, substance abuse, overcrowding, commercial sexual workers (prostitution) and all kinds of environmental pollution and social devices that predispose increased exposure to communicable diseases. These conditions are, in part, favorable risk factors for rapid spread of infectious diseases such as HIV and TB [4].

Furthermore, the study found that TB/HIV co-infection was high for both sexes. Particularly, it was observed that the mean age of female patients co-infected with HIV was lower (29 years) compared males (38 years). The results obtained in this study regarding age and sex distribution of TB/HIV co-infected individuals are in line with what has been reported elsewhere concerning Zambia's TB epidemiological patterns [4, 10, 12]. The findings also are consistent with findings from other HIV/AIDS studies conducted in Zambia showing the same age groups affected by TB to have high prevalence of HIV [4, 9, 14]. The observed pattern indicates no significant reduction in the disease progression from 2007 to 2012. The situation is worrisome and calls for scrutiny of public health approach such as the methods used by the district to deliver health education messages as well as models of health promotion.

The logistic regression model revealed that age was significant predictor in TB treatment outcome with younger persons having an increased chance of being cured or TB. The observed trend is as would be expected considering that the biology of young people support rapid system recovery [40]. Further, patients who had pulmonary TB were more likely to be cured than those who had extra-pulmonary TB. In extra-pulmonary TB infection, the pathogen sometime lodges in organs or tissues that are not easily accessed by drugs and thus contributing to treatment failure [41]. As would be expected, patients who had completed their medication were more than 438 times more likely to be cured than those who had not completed the

treatment, underpinning the importance completing the treatment.

This study has established that HIV prevalence among TB patients was high in Sinazongwe district. The high prevalence was observed in all individual years from 2007 to 2012 with no evidence of declining trend.

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