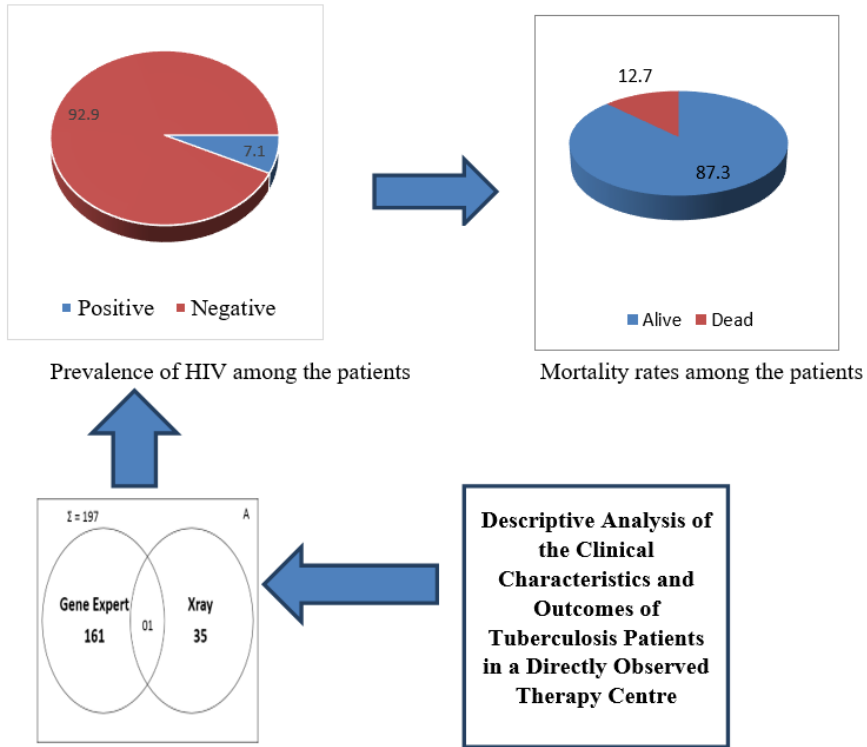


RESEARCH ARTICLE

Assessment of mortality rate in tuberculosis / human immunodeficiency virus (HIV) co-infected patient

A. E. Ojo*, O. A. Ojo, S. O. Adebajo, A. T. Ajibola, A.R. Oloyede, H. A. Popoola, A. S. Babalola and D. A. Ojo



Highlights

- Co-infection of HIV/TB was 7.1% while mortality rate was 28.6% in the age group of 43 and above.
- Co-infection with TB and HIV is associated with high mortality.
- Age was a significant determinant of TB infectivity among the investigated patients.

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Assessment of mortality rate in tuberculosis / human immunodeficiency virus (HIV) co-infected patient

A. E. Ojo^{1,*}, O. A. Ojo², S. O. Adebajo¹, A. T. Ajibola¹, A.R. Oloyede¹, H. A. Popoola¹, A. S. Babalola¹ and D. A. Ojo¹

¹Department of Microbiology, Federal University of Agriculture, Abeokuta, Nigeria

²Department of Pharmacognosy, Faculty of Pharmacy, Madonna University, Elele, River-state, Port-harcourt, Nigeria.

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Abstract: Prior to the discovery of Human Immunodeficiency Virus (HIV), the pattern of tuberculosis (TB) prevalence witnessed a gradual drawdown and the mode of presentation was usually pulmonary. This study assesses the mortality rates of TB and HIV co-infected patients in a directly observed therapy (DOT) centre in Nigeria. The retrospective study retrieved 18 months of data from 197 patients on the TB register of a centralized DOT centre in the Ogun State, Nigeria. Data collected included age, sex, and HIV status, with TB results obtained from Genexpert. The data obtained from 197 TB patients were analyzed using descriptive statistics and chi-square. Out of the 197 TB patients, 67.0% were males and 33.0% were females. A majority of the patients (41.6%) were within the age category of 43 years and above. This was followed by 35 – 42 years (25.4%) and 27 – 34 years (19.8%), while the lowest proportion of patients (0.5%) falls within the age brackets of 3 - 10 years. Furthermore, 92.9% of the patients were HIV negative. Using Chi-squared test, no significant difference was seen in TB occurrence to sex ($p>0.05$) while age contribute significantly to mortality. Co-infection of HIV/TB was 7.1% while mortality rate in this group was 28.6% as observed in the age group 43 and above. Overall, the mortality rate in the TB patients was 2.0%. Results showed that the age was a significant contributor ($p<0.05$) to HIV TB co-infection among the patients. Age regressed positively with TB infection in the study population. The study concludes that the co-infection of TB and HIV was significantly associated with high mortality.

Keywords: Tuberculosis (TB); Human Immunodeficiency Virus (HIV); Retrospective study; Age; Sex; Directly Observed Therapy Centre.

INTRODUCTION

The issue of tuberculosis (TB) in developing countries cannot be swept under the carpet (Ziemlé *et al.*, 2014). Four decades ago, TB has been a re-emerging global public health concern because of its intensity on the standard of living in diverse countries (Popejoy *et al.*, 2017). Tuberculosis plays the leading role in causing nearly 40% of deaths among human immunodeficiency virus (HIV)-infected individuals (Gupta *et al.*, 2015). Africa has the most prevailing incidence of HIV infection. TB co-infection with HIV is a major element in the TB epidemic alongside mortality. Southeast Asia has a close figure to Africa in terms of TB incidence but with a low HIV infection prevalence (MacNeil *et al.*, 2019).

Globally, Nigeria remains one of the 30 countries highly burdened with TB, TB/HIV, and multidrug-resistant TB (MDR-TB) (WHO, 2016). TB was reported to have infected approximately ten million people in 2017. In 2018, the incidence of TB accounted for 0.22% of the population, and close to 407,000 developed TB, with nearly 100,000 notified, resulting in 24% treatment coverage (Federal Ministry of Health, 2019). The overpopulated environment, penury, and compromised immune system of the host enhance the transfer of this disease among residents. These conditions started over the past millennium and have been affecting the trends of TB incidence for decades in the United States, the rest of the world, and specific subpopulations (Popejoy *et al.*, 2017). Hence, this study assesses the mortality rate of TB HIV co-infected patients.

METHODOLOGY

Study design and settings

This retrospective study retrieved data that were routinely collected from patients who attended Sacred Heart Hospital (SHH), Abeokuta (DOTs centre), from 1st July 2019 to 31st December 2020 (18 months). Records of 197 TB patients enrolled in TB treatment at the facility were utilized. Abeokuta is the largest city and capital of Ogun State in southwest Nigeria. It is situated on the east bank of the Ogun River, near a group of rocky outcrops in a wooded savanna: 77 kilometers (48 m) north of Lagos by railway, or 130 kilometers (81 mi) by water. Latitude: 7° 09' 23.40" N, Longitude: 3° 20' 32.40" E.

SHH is located in the heart of the Abeokuta South Local Government Area of Abeokuta, the Capital of Ogun State, in the southwestern region of Nigeria. It is the backbone of Ogun State healthcare delivery and has a workforce of approximately 500. The hospital was selected because it is a reference center for the diagnosis and treatment of TB. It has a 70-bedded DR (drug resistant)-TB ward to ensure that 100% of diagnosed DR-TB patients in Ogun State and their care. SHH has been described as one of the largest tuberculosis treatment centers in Africa and one of the WHO-assigned hospitals for the diagnosis and treatment of TB and MDR-TB in the country. A total of 197 participants

*Corresponding Author's Email: ojae@funaab.edu.ng



were ultimately recruited for the study. The relationship between HIV infection, sex and age in children and adults with TB was established using descriptive statistics and chi-square and probit regression models.

Diagnosis of TB patients

Since 2016, the country has adopted Genexpert as the most preferable diagnostic means for all types of tuberculosis, restricting smear diagnosis to only geographic areas where Genexpert was not decentralized (Gidado *et al.*, 2019).

Diagnosis of HIV patients

Following the national guidelines, HIV testing was conducted on all the patients captured in the register using Determine (DT) HIV-1/2 (Alere Medical Company Limited, Chiba, Japan), Unigold and Stat Pak rapid diagnostic test kits (HIV-1; Chembio Diagnostic Systems, Medford, NY) by adhering strictly to the manufacturers' instructions. The Determine kit was used as the first line strip for HIV testing, and positive results were rerun using the Unigold kit. This study was approved by the Sacred Heart Hospital Ethical Committee (Reference number SHH/EC/EA/03/06/21). Patient data were taken anonymously, thus assigned serial numbers to maintain their confidentiality. As this was routinely collected program data, patients' consent was waived.

Data analysis

Cleaned coded qualitative and quantitative retrieved data were input into Microsoft Excel® version 2013 and analyzed using descriptive statistics and chi-square test the relationship between TB and HIV. Information was presented as frequencies and percentages in tables and charts. A p value ≤ 0.05 was considered statistically significant

RESULTS

Demographic characteristics of the patients

The results showed that most TB patients (132 of 197 = 67%) were males, while the remaining 33% were females. Furthermore, the majority of the patients (82, 41.6%) were within the age brackets of 43 years and above. This was followed by 35 – 42 years (25.4%) and 27 – 34 years 39 (19.8%), while the lowest proportion of patients 1 (0.5%) fell within the age brackets of 3 -10 years (Table 1).

The results showed no significant difference in the HIV infection prevalence between females (10.8%) and males (5.3%), ($p>0.05$). With respect to age, no observable pattern was recorded in terms of HIV prevalence. Zero prevalence of HIV was recorded in children aged 3 – 10 years and adults within age brackets 19 – 26 years, while

the highest prevalence (14.3%) was recorded among children within the age range of 11-18 years (Table 2). The results showed that females recorded a slightly higher mortality rate (16.9%) than males (10.6%); however, the differences observed did not reach a statistically significant level ($p>0.05$). Mortality rate was 28.6% among HIV/ TB co-infected patients (Table 3).

Table 1: Socio-demographic characteristics of the studied patients

Variables	Frequency (n = 197)	Percentage
Gender		
Male	132	67.0
Female	65	33.0
Age Group (years)		
3 - 10	1	0.5
11 - 18	7	3.6
19 - 26	18	9.1
27 - 34	39	19.8
35 - 42	50	25.4
> 43	82	41.6

Table 2: Prevalence of HIV with respect to gender and age among the patients.

Variables	No. Examined	Prevalence	P values
Gender			0.160
Male	132	7(5.3)	
Female	65	7(10.8)	
Age group			0.534
3 - 10	1	0(0.0)	
11 - 18	7	1(14.3)	
19 - 26	18	0(0.0)	
27 - 34	39	1(2.6)	
35 - 42	50	5(10.0)	
>43	82	7(8.5)	

Mortality rates among HIV/ TB co-infected patients

The results showed that HIV and TB co-infection was significantly ($p<0.05$) associated with higher mortality among the patients. The results showed that 92.9% of the patients were HIV-negative. Furthermore, Co-infection of HIV and TB was 14 cases. Co-infection of HIV/TB was 7.1% while mortality rate in this group was 28.6% as observed in the age group 43 and above. Overall, the mortality rate in the TB patients was 2.0% (Table 3). Co-infected patients were 14 and were evenly distributed between the sexes. It occurs singly in age groups 11-18 and 27-34. Five of them were found within the age bracket 35-

Table 3: Mortality rate in HIV/TB co-infection

Infection Status	No. Examined	Mortality (%) in HIV/TB		P value
		Alive	Dead	
Coinfection	14(7.1)	10(5.1)	4(28.6)	0.043*
Non-Coinfection	183(92.9)	183	00	
Total	197	193	04	

42 while majority 7 occur in age group 42 and above. The mortality cases were also found in this age group (Table 4).

Table 4: Mortality rate in HIV/TB patients in relation to their age and gender.

Mortality	No. Examined	Prevalence	P values
Gender			0.210
Male	7(5.3)	2(1.0)	
Female	7(10.8)	2(1.0)	
Age group			0.954
3-10	0(0.0)	0(0.0)	
11-18	1(14.3)	0(0.0)	
19-26	0(0.0)	0(0.0)	
27-34	1(2.6)	0(0.0)	
35-42	5(10.0)	0(0.0)	
>43	7(8.5)	4(2.0)	

DISCUSSION

From this study, sex had no implication on TB. Result showed that age was a significant contributor ($p < 0.05$) to HIV/TB co-infection among the patients. The consequence of HIV on the world tuberculosis pandemic cannot be swept under the carpet. Long before HIV was unveiled, the prevalence of tuberculosis experienced a gradual drawdown, and the model of presentation was usually pulmonary (Affusim *et al.*, 2012). In this study, the prevalence of TB slightly increased with increasing age. However, the probit regression model computed to estimate the determinants of TB among three variables (age, sex, HIV infection) revealed that age regressed positively with TB infection in this study. This implies that the prevalence of TB will always increase with age according to the model. Epidemiological studies on risk factors for TB have presented contradictory results with respect to the effect of age (Cui *et al.*, 2020). However, the findings in this study were similar to those of Affusim *et al.* (2012), who reported the highest prevalence of TB among older groups (Affusim *et al.*, 2012). Several studies have provided reasons for these age-related dynamics in the prevalence of TB, and these include risk factors such as diabetes (Stevenson *et al.*, 2007), indoor air pollution due to alterations in the immune system as a result of aging (Cui *et al.*, 2020). For timely TB diagnosis, the World Health Organization (WHO) in 2010 recognized Cepheid Xpert® MTB/RIF (Xpert) as a bedside test for the diagnosis of HIV-associated TB (WHO, 2011). Gene-Xpert is a nucleic acid amplification test that coevally detects *Mycobacterium tuberculosis* and resistance to rifampicin and has shown high sensitivity (79.7–100%) with an effective bedside diagnostic duration (<2 h) when compared to TB culture (Rie *et al.*, 2010; Helb *et al.*, 2010; Boehme *et al.*, 2010). The fact that X-ray showed a highly significant lower prevalence of 18.3% compared to 82% was shown by using a gene expert buttresses the low and/or poor performance of X-ray in the diagnosis of TB, as previously reported (Nakiyingi *et al.*, 2021; Wilson *et al.*, 2021; Theron *et al.*, 2012; Kanaya, *et al.*, 2001). Studies have reported that a normal chest X-ray could

reliably exclude TB in HIV-positive patients with negative sputum smears, owing to its high negative predictive value (Nakiyingi *et al.*, 2021).

Sex was not significantly associated with the prevalence of TB and HIV in this study population. The reason for this might be due to the fact that nowadays, both sexes are actively involved in outdoor jobs. Research confirms that men hardly seek medical care in most communities when compared to women (Horton *et al.*, 2016), and women are more opportune in tapping and remaining within HIV care facilities (Auld *et al.*, 2014; Druyts *et al.*, 2013). Thus, the probability of men remaining undetected and not treated for HIV co-infection is high. They also remain unavailable for TB screening that lies within HIV care settings.

This study provides data on TB cases in Abeokuta city and also provides information on the mortality of TB patients when co-infected with HIV. Studies have shown that both HIV and tuberculosis are major causes of morbidity and mortality in developing countries. Studies have shown that access to adequate health care and improvement in living standards has resulted in success in reducing the mortality associated with TB infections (Li, 2019; Nakiyingi *et al.*, 2021).

CONCLUSION

Co-infection of HIV/TB was 7.1% while mortality rate in this group was 28.6%.as observed in the age group 43 and above. Overall, the mortality rate in the TB patients was 2.0%. Result showed that age was a significant contributor ($p < 0.05$) to HIV TB co-infection among the patients. Age regressed positively with TB infection in the study population. Coinfection of TB and HIV was significantly associated with high mortality.

DECLARATION OF CONFLICT OF INTEREST

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The authors have no relevant financial or nonfinancial interests to disclose.

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