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A Four-Year Hospital-Based Retrospective Study of the Predictors of Tuberculosis in People Living with HIV and Receiving Care at Bamenda Regional Hospital, Cameroon

Cho Sabastine Anye, MSc;[1,2] **Claude Ngwayu Nkfusai,** MSc;[1,2]✉ **Brenda Mbouamba Yankam,** MSc;[1] **Frankline Sevidzem Wirsiy,** MSc;[3] **Joyce Mahlako Tsoka-Gwegweni,** MSc, MPH, PhD;[4] **Samuel Nambile Cumber,** MPH, MSc, PhD[4,5,6]

[1]Department of Microbiology and Parasitology, Faculty of Science, University of Buea, Buea, Cameroon; [2]Cameroon Baptist Convention Health Services, Yaounde, Cameroon; [3]Department of Public Health and Hygiene, Faculty of Health Sciences, University of Buea, Buea, Cameroon; [4]Office of the Dean, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa; [5]Section for Epidemiology and Social Medicine, Department of Public Health, Institute of Medicine, The Sahlgrenska Academy at University of Gothenburg, Box 414, SE – 405 Gothenburg, Sweden; [6]School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria Private Bag X323, Gezina, Pretoria, 0001, Pretoria, South Africa

✉Corresponding author email: ngwayuclaude1@gmail.com

ABSTRACT

Background: Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) co-infections place immense burdens on healthcare systems with particularly diagnostic and therapeutic challenges. TB is high among opportunistic diseases and the most leading cause of death among patients with HIV/AIDS. HIV infection is the most-known risk factor for *Mycobacterium tuberculosis* infection and progression to active disease, which increases the risk of latent TB reactivation by 20-fold. We present a four-year descriptive analysis of TB in people living with HIV in the Bamenda Regional Hospital (BRH) from 2012-2016.

Methods: This was a hospital-based descriptive chart review. We conducted manual reviews of medical records of HIV/TB co-infected patients from June 2017-July 2017 at BRH's AIDS Treatment Centre, North West region of Cameroon. Socio-demographic and clinical characteristics of cases were captured using a pre-tested data collection sheet and analyzed with Statistical Package for Social Sciences (SPSS) software, version 25.

Results: Out of the 1078 HIV patients, 36.5% (393) of them were diagnosed with TB; 75% (808) of the People living with HIV (PLWHIV) were active; among the remaining 25%, 10.2% were bedridden, 13.0% were jobless, and 1.8% were retired. The greater proportion of the participants were females 65.5% (705).

Conclusion and Global Health Implications: The baseline anemia, smoking tobacco, drinking alcohol, detectable (≥50copies/mL), CD4 count ≤ 200cells/µl and gender of the PLWHIV were associated with the incidence of TB. We recommend early diagnosis and treatment of anemia, modification of patient's lifestyle, and strengthening of immunization programs to reduce the risk of TB occurrence among HIV-infected people.

Key words: • Chart review • Tuberculosis • People living with HIV • Bamenda regional hospital • Cameroon

1. Introduction

1.1. Background

Tuberculosis is among the leading opportunistic diseases and the leading cause of death among HIV/AIDS patients.[1,2] Tuberculosis (TB) and HIV co-infections place an immense burden on health care systems and pose particularly diagnostic and therapeutic challenges.[3] In addition, HIV infection is the most powerful known risk factor for *Mycobacterium tuberculosis* infection and progression to active disease, which increases the risk of latent TB reactivation by 20-fold.[4] Thus, M. tuberculosis and HIV act in synergy, accelerating the decline of immunological functions and leading to subsequent death if untreated.[4]

Tuberculosis occurs in every part of the world. In 2016, the largest number of new TB cases occurred in Asia, with 45% of new cases, followed by Africa, with 25% of new cases.[5] In 2016, 87% of new TB cases occurred in the 30 high TB burden countries. Seven countries accounted for 64% of the new TB cases: India, Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa. Global progress in addressing health of people with HIV infection depends on advances in TB prevention and care in these countries. Sub-Saharan Africa remains the region most heavily affected by HIV.[5]

In Cameroon, HIV prevalence for the population ages 15-49, 15-65 years are 0.2%, 3.4% and 3.7%, respectively.[6] Tuberculosis and HIV co-infection is associated with significantly increased likelihood of mortality with HIV co-infected TB patients having significantly lower cure rates and lower treatment success rates compared to non-HIV infected TB patients.[7] The incidence of TB in Cameroon was 194 cases per 100,000 populations in 2017.[8] In 2017, the incident rate of TB was 60 cases per 100,000 among People Living With HIV/AIDS (PLWHIV).[8] This indicates a considerable co-infection rate from both diseases. However, there is insufficient evidence on the situational analysis of TB in people living with HIV in the Bamenda Regional Hospital (BRH), North West region of Cameroon. There are no readily available data describing TB infection and associated factors among PLWHIV in the North West Region of Cameroon. An understanding of TB and HIV co-infection and associated factors may help to improve the management of TB infection.

1.2 Objective

This study assessed TB infection and its associated factors among PLWHIV in the Bamenda Regional Hospital, in the North West Region of Cameroon. We hypothesized that there will be a relationship between socio-demographic and clinical characteristics and TB/HIV co-infection.

2. Methods

2.1. Study Design

This was a descriptive chart review carried out within a period of two months in accredited HIV care and treatment center of the Bamenda Regional Hospital in the city of Bamenda, Cameroon. The study was conducted in the BRH's AIDS Treatment Centre, which receives over 2,000 patients per year for routine HIV care including follow-up by doctors and other health personnel. In the hospital, all HIV positive people are enrolled in the day care hospital for comprehensive HIV care. There is a multidisciplinary professional team which includes physicians, nurses, public health professionals, laboratory technologists, pharmacists, etc. Antiretroviral therapy (ART) is provided to HIV-infected patients according to their CD4 count and the World Health Organization (WHO) clinical guide.

2.3. Study Population

All HIV infected individuals that were registered between January 2012 and December 2016 at BRH and who met the inclusion criteria were sampled in the study. The study included all PLWHIV aged 15 years and above enrolled at the day care hospital and presumptive TB cases (those who had TB symptom) and initiated ART before or in the absence of TB diagnosis workup. We also excluded HIV positive adults who started anti-TB treatment at the beginning of the follow-up and those with incomplete baseline information such as CD4 count and hemoglobin (Hb) level. Patients were considered to have prevalent TB only if they were documented to be on TB treatment at baseline (as is the convention for TB diagnosed before ART initiation), and were excluded from subsequent incidence analysis. Finally, any individual with incomplete chart and diagnosed clinically without sputum examination, culture and chest X-ray was excluded.

2.5. Sampling Technique

All available information on patient records was checked and an appropriate data extraction tool was prepared to collect the patient's data. All patient files were used to fill the epi info data template, where just specific variables which summed up to 54 different variables were collected from the patients' medical record files (booklets).

2.6. Data Analysis

For the determination of the associated risk factors from the extracted data, the cox proportional hazard regression model was used which allows analyzing the effect of several risk factors on survival to the endpoint called hazard, which in this case is being diagnosed of TB (hazard). Data were extracted from a total of 1077 patient's files (HIV patients 15 years and above, and HIV presumptive TB cases who had initiated ART treatment in the absence of TB diagnosis workup) using Epi-Info version 7.5.2 (Centers for Disease Control and Prevention, Atlanta, GA, USA, 2011). The data were then cleaned and descriptive analyses completed using SPSS version 25 (IBM Corporation, Armonk, NY, USA).

3. Results

3.1. Clinical and Socio-Demographic Characteristics of the Participants

Out of the 1077 HIV patients 36.5% (393) of them were diagnosed with TB; 75% (808) of the PLHIV were active, while 25% (where 10.2% were bedridden, 13.0% were jobless and 1.8% were retired. Out of those who completed the viral load test Out of 1078 who completed the viral load test, 29.8% had viral load <40copies/mL which is generally recorded as being undetectable. Of these, 11.1% (119) had detectable viral load that is >40copies/mL, 35% (366) had CD4 count <200cells/µl and 65% had CD4 count greater than 200cells/µl. In all, 33.6 % (329) of PLHIV were at WHO clinical stage I; 41.9 % (451) were at WHO clinical stage II; 18.6 % (200) of them were at WHO clinical Stage III, and 5.7% (61) were at WHO stage IV. Out of the 1,077 patients, 25.9 % (279) had HB counts greater than or equal to 13g/dL. 55.7% (600) had an Hb count between 10-12g/dL, while 6.5% (70) had Hb count between 6-9, 7.4% (80) less than or equal to 5g/dL Hb count, excluding the missing values (Table 1).

3.2. Tobacco Smoking, Alcohol Intake among PLWHIV With or Without TB

Out of 283 PLHIV who smoke, 74.2% (210) of them had TB and out of the 795 non-smokers, about 193 had TB (figure 1). Out of 613 PLHIV who drink alcohol, 248 had TB. Out of the 464 non-users of alcohol, about 159 had TB (Figure 2). Out of the 650 patients with a family size of 3-13, approximately 61.3% (247) developed TB.

4. Discussion

In this retrospective study of records of 1077 HIV patients under care in the Bamenda Regional Hospital, smoking tobacco (26.2%), detectable viral load (27.3% that is >40copies/mL), drinking alcohol (59.6%), CD4 counts <200 (34.0%) and specific Hb counts were found to be risk factors associated with the development of TB. Previous studies have reported that TB incidence among HIV patients varies from one country to another, depending on the country's health policy regarding HAART use and the local TB prevalence rate. In Ethiopia, where the policy on the use of HAART was established in 2000[9] and in Kenya where TB rates were high according to the study by Abdullahi *et al.,*[10] the co-infection incidence reached 3.7 per 100 person years. However, prevalent TB at the time of ART initiation (defined as being on TB treatment) was slightly lower (about 9.5% on average) in each year (since at the BRH each year is being considered as a new cohort in which the patients were followed up) compared to prior studies in countries such as Ethiopia and South Africa which have documented TB prevalence rates at ART initiation ranging from 11±31.5%.[11] This may indicate that, although screening occurs routinely at the BRH based on the doctor's recommendations, it may not detect all patients with TB prior to their ART initiation. In this study, the overall incidence of TB was 9.12 per 100 person years (PY). The incidence was similar to rates reported in other studies done in Ethiopia and many other Sub-Saharan African countries with reported incidences ranging from 5.4 to 11 per 100 PY.[12]

Table 1: Clinical and socio-demographic characteristics of the patients living with HIV

Clinical and socio-demographic characteristic	Response	No (%)
Alcohol	No	464 (43.1)
	Yes	613 (56.9)
	Total	**1,077 (100.0)**
Smoking	No	795 (73.8)
	Yes	282 (26.2)
	Total	**1,077 (100.0)**
Occupational Status	Bedridden	110 (10.2)
	Employed-active	808 (75.0)
	Jobless	140 (13.0)
	Retired	19 (1.8)
	Total	**1,077 (100.0)**
TB	No	684 (63.5)
	Yes	393 (36.5)
	Total	**1,077 (100.0)**
Viral load copies/mL	**<=40**	**321 (29.8)**
	41-933394	116 (10.8)
	933395-1866748	2 (0.2)
	1866749+	1 (0.1)
	Total	**440 (40.9)**
	Missing	**637 (59.1)**
	Total	**1,077 (100.0)**
CD4 Count cells/µl	<=200	366 (34.0)
	201-497	456 (42.3)
	498-793	185 (17.2)
	794+	38 (3.5)
	Total	**1,045 (97.0)**
	Missing	32 (3.0)
	Total	**1,077 (100.0)**
HB count g/dL	<=8	78 (7.2)
	8-10.9	151 (14.0)
	10-13+	661 (61.4)
	14+	139 (12.9)
	Total	1,029 (95.5)
	System	48 (4.5)
	Total	**1,077 (100.0)**
WHO Clinical Staging	S1	329 (33.6)
	S2	451 (41.9)
	S3	200 (18.6)
	S4	61 (5.7)
	Total	**1,077 (100.0)**

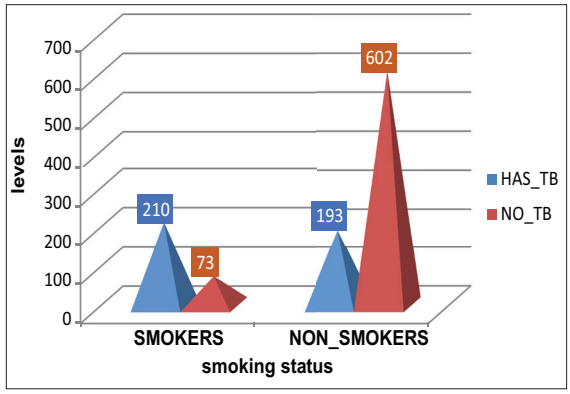

Figure 1: PLWHIV: Smoking Status and TB Diagnosis

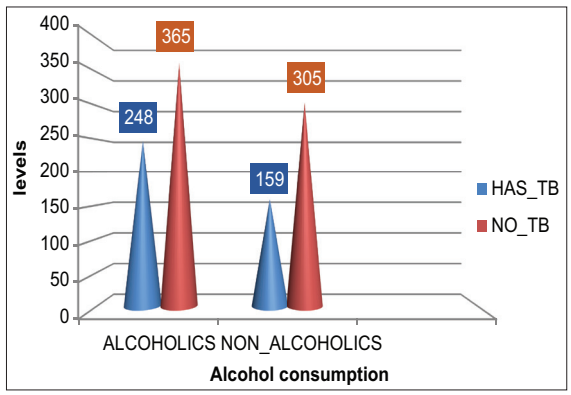

Figure 2: PLWHIV: Alcohol Use Status and TB Diagnosis

The incidence of TB was associated with history of cigarette smoking, as 74.2% (210 PLHIV) of the 283 patients who smoke came up with TB compared to the 24.3% (193 PLHIV) of the 795 patients who did not smoke but developed TB, thus indicating that cigarette smokers were 3 times (that is 74.2% vs 24.3%) at higher risk of developing TB than non-smokers. This might be cigarette smoking exposes smokers to low immunity and this increased the risk of developing TB among HIV infected patients who are already immuno-compromised. The finding was consistent with a study done in Taiwan.[13] In the same light, alcohol has been recognized as a strong risk factor for TB disease.[14] More than 50% of the HIV patients in our study consumed alcohol, where out of the 613 PLHIV who drink alcohol, 248 (40.45%) came up with TB, while out of the 464 non-alcohol drinkers, about 159 (34.5%) came up with tuberculosis. Out of the 650 patients with a

family size of 3-13, approximately 61.3% (247) of them developed TB. Thus, an individual who live in the family size of 3 - 13 was 1.74 times, that is, approximately two times, at higher risk of developing TB than an individual who lives in family with <2 individual. It is consistent with a prior study which showed that risk of TB was associated with the number of people living together in the household[15] but inconsistent with a study done in Addis Ababa[16] which depicted that risk of developing TB was not associated with the number of people living together in the household.

In this study, 330 out of the 384 TB cases had their CD4 counts >50 cells/µl and 54 patients had CD4 counts <50 cells/µl. Hence those with CD4counts <50cells/µl were at a higher risk (1.05 times) of developing TB compared to those with CD4 counts greater than 50cells/µl. These are consistent with other studies. For example, a study which was conducted in South Africa showed that having a low CD4 count increases the incidence of TB,[17] who took into account variations in CD4 count with time and therefore estimated the effect of the CD4 count at the nearest time before the TB occurrence. This was also similar to most studies that looked at effects of baseline CD4 count by Gupta *et al.* in 2014.[18] Baseline anemia has been established to be associated with increased risk of sputum positive TB.[19] Similarly, anemia has been reported to predict HIV progression to AIDS, and also besides independent of CD4 and viral load counts,[20] it is also potential risk factor for developing TB.

Recommendations for Further Studies: A unique patient record document type should be used to store patient's information (both at the main treatment center and the five satellite treatment centers) to enable a coherent data capture via the life-time follow up periods of the patients. Patient information from the different satellite centers should be distinguished and stored differently. In other words, patients' records should be differentiated not only by area of residence, but also by the satellite center where he/she was receiving treatment. Further studies can be initiated, such as knowledge, attitude, and practice (KAP) research, to better understand the key issues, such as the different prevalence/ incidence rates of a particular variable and why the differences exist.

5. Conclusion and Global Health Implications

The baseline anemia, smoking tobacco, drinking alcohol, detectable (≥50copies/mL), CD4 count ≤200cells/µl and gender of the PLWHIV were associated with the incidence of TB. Therefore, early diagnosis and treatment of anemia, modification of patient's daily hobbies/habits (such as excessive alcohol intake, smoking etc.) and strengthening immunization programs are recommended to reduce the risk of TB occurrence among HIV-infected people. The results clearly show that there is a relationship between socio-demographic, clinical characteristics, and TB/HIV co-infection, hence our study's null hypothesis was rejected.

Compliance with Ethical Standards

Competing interests: *The authors declare that they have no competing interest.* ***Funding:*** *There was no funding for this study.* ***Ethics approval:*** *Ethical approval was granted by the Institutional Review Board of the Faculty of Health Sciences of the University of Buea. Administrative approval was obtained from the Director of the Bamenda Regional Hospital. Data entry forms were coded to ensure anonymity of patient personal information.* ***Acknowledgements:*** *We are grateful to the Directorate of the Bamenda Regional Hospital for allowing us to have access to their data.*

Key Messages

- Baseline anemia, smoking tobacco, drinking alcohol, detectable (≥50copies/mL), CD4 count ≤200cells/µl and gender of PLWHIV were associated with the incidence of tuberculosis (TB).
- Timely diagnosis and treatment of HIV could potentially reduce the incidence of TB, while patients are receiving ART, as is Interpersonal therapy (IPT) and infection control in health-care facilities.
- Healthcare workers should strengthen health education for TB/HIV prevention and treatment and promote smoking and alcohol drinking cessation.

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