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Appraising Treatment Outcomes of Cohort of Smear-positive Patients with Tuberculosis (TB) alone and TB-HIV Co-infected on Directly Observed Treatment Short Course (DOTS) at a Teaching Hospital in Enugu State, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author ECA designed the study, performed the statistical analysis. Authors ECA, ODO CNO and OAI wrote the protocol and first draft of the manuscript. Authors ECA and ODO managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Tuberculosis and Human Immunodeficiency Virus are overlapping monsters presenting an enormous economic burden, suffering, pain and grief globally. They have high mortality rates and most international efforts to control infectious diseases focus on these diseases yet they still pose a great threat.
Methods: This study was conducted at the Chest Clinic of University of Nigeria Teaching Hospital (UNTH) Enugu. It involved a retrospective appraisal of treatment outcomes of cohort of smear-

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positive patients with Tuberculosis (TB) alone and TB-HIV co-infected on Directly Observed Treatment Short-course (DOTS) who were initiated on TB treatment and completed treatment in the period 2008 to 2011. A proforma was used in collecting data. Chi-square test and Binary Logistic regression to establish associations and identify predictors of treatment outcomes

Results: Most patients 322(73.7%) were declared cured at end of treatment [TB alone 281(75.7%) and TB/HIV coinfection 41(65.1%)]. Treatment outcome were associated with disease status (p =0.022) and distance to the clinic (p =0.017). Those that had TB alone were about 0.6 times (AOR 0.56; 95% CI 0.33-1.63) likely not to be cured than those with TB/HIV. Those that travel 0-20 km to the clinic were about 0.5 times (AOR 0.50; 95% CI 0.28-0.91) likely not to be cured than those that travel more than 80 km.

Conclusion: Even with the moderately high cure rate among these patients, effort are needed by stakeholders and all populace in curbing this ravaging menace. Equally the identified predictors of treatment outcome were TB/HIV co-infection and distance from residence to the clinic which should be addressed.

Keywords: Tuberculosis; HIV; co-infection; treatment outcome.

1. INTRODUCTION

Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) are among the three most recognised and targeted communicable diseases afflicting developing countries. It constitutes an enormous burden regarding suffering, pain and grief globally [1]. TB was declared a global emergency in 1993 when an estimated 7–8 million cases and 1.3–1.6 million deaths occurred in a year [2]. Human Immunodeficiency Virus (HIV) has contributed to a global resurgence of tuberculosis. In 2014, about 9.6 million people were estimated to be suffering from TB out of which 12% of newly diagnosed TB cases among them were HIV-positive [3]. TB is the most significant single cause of death in the setting of AIDS, accounting for about 26% of AIDS-related deaths out of which 99% occur in developing countries [4]. In 2010, an estimated 39% of new TB cases in sub-Saharan Africa were HIV-co-infected [5]. Sub-Saharan Africa constitutes just 12% of the global population, nevertheless accounts for 82% of the global burden of HIV-associated TB with 71% resulting in deaths [3,5]. Concisely HIV pandemic accounts for 31% of all new TB cases in adults [6,7].

HIV is driving the TB epidemic in many countries, especially in sub-Saharan Africa and Asia. Most of the estimated number of cases in 2010 occurred in Asia (59%) and Africa (26%) [8]. HIV and TB co-infection is a fast-growing problem in Africa and Asia [9]. In sub-Saharan Africa, the prevalence of HIV is about 5%-35% of the adult population, and one-third to one-half of HIV-infected individuals is co-infected with Mycobacterium tuberculosis [10]. The proportion of TB cases co-infected with HIV is highest in countries in the African Region with African Region accounting for 82% of TB cases among people living with HIV. Women account for an estimated 3.2 million incident cases (range, 3.0 million–3.5 million), equivalent to 36% of all cases [11]. Nigeria is among the 22 high TB burden countries that contributed 80% of global TB burden in the world. TB was declared an emergency in 2003 in the country. Nigeria used to be fifth(5^{th}) in the world prevalence having 600 and 610 per 100,000 by year 2000 and 2008 respectively with an annual incidence rate of 270 and 300 per 100,000 in 2000 and 2008 respectively [12] but recently tenth(10^{th}), with an estimated incidence and prevalence of is 133/100,000 and 199/100,000 populations respectively [11]. There are 12.1% and 22.6% case detection rates in 2000 and 2007 under DOTS with mortality of 86 and 93 per 100 000 in 2000 and 2007 respectively [13]. The TB burden is further compounded by the high HIV prevalence of 4.4% in the country [14]. According to the Nigeria Federal Ministry of Health in 2010, the recorded HIV prevalence among TB patients increased from 2.2% in 1991 to about 27% in 2008 [15].

There are promising interventions in Nigeria like the adoption of new Stop TB Strategy, DOTS and increased access of People Living With HIV/AIDS) PLWHA to Antiretroviral Therapy (ARV) from 21% to 26% between 2007 and 2009. Extra-pulmonary and smear-negative TB cases, which are more difficult to diagnose account for an increased proportion of total cases. The concomitant treatment of HIV and active TB poses significant challenges, particularly relating to the duration and frequency of dosing of anti-TB drugs and the optimal timing of Highly Active Antiretroviral Therapy (HAART) initiation relative to TB treatment. This has

significant consequences vis-à-vis overlapping drug toxicities and drug-drug interactions between anti-TB drugs and antiretroviral drugs as well as the Immune Reconstitution Inflammatory Syndrome (IRIS). There are also higher chances of adverse drug reactions.

Although a lot of studies has been done on HIV, TB as well as TB/HIV co-infection occurrence rates, there is still need to investigate the treatment outcome among TB/HIV co-infected patients in Nigeria This study aims to compare treatment outcome among patients with TB alone and those with TB co-infected with HIV placed on DOTS presenting at the chest clinic in UNTH Enugu. The information provided in this study will be a useful guide in planning or modifying TB control programs among HIV infected persons especially in this era of the HIV pandemic.

2. MATERIALS AND METHODS

2.1 Study Area

The study area was at the Chest clinic of University of Nigeria Teaching Hospital (UNTH) Old site in Enugu. UNTH is the oldest and biggest tertiary hospital in South Eastern Nigeria. It serves as a major referral centre for all states in the region and even beyond. The clinic runs a week thrice; Mondays, Wednesdays and Fridays with an average of two new patients per clinic, twenty-four a month and about three hundred in a year. The clinic is for management of TB cases. Doctors in the clinic also consult at HIV clinic. This arrangement allows for comprehensive management of the patients especially those with TB/HIV co-infection.

2.2 Study Design

This was a cohort study. It involved a retrospective review of the treatment outcomes among a cohort of patients with TB alone and those with TB co-infected with HIV who were initiated on TB treatment and completed treatment in the period 2008 to 2011.

2.3 Study Population

This comprised patients attending Chest clinic in UNTH Enugu who have TB alone and those having TB co-infected with HIV commenced on, completed DOTS and then discharged from treatment scheme**.** All sputum smear positive Acid Fast Bacilli (AFB) patients that enrolled during the study period were included while patients that were smear negative AFB even if on treatment, with other illnesses, with TB or TB co-infected with HIV/AIDS but still on treatment were not studied. They were followed for eight (8) months each.

2.4 Study Instrument and Procedure

Medical records, treatment or case files and discharge summary records of selected patients for the study were reviewed using a Proforma with relevant information and data collected.

2.5 Data Analysis

Data were analyzed using IBM Statistical Package for Social Sciences (SPSS) version 20. Frequency tables were used to present data. Chi-square test was used to investigate an association of socio-demographic variables, distance to facility and disease status with treatment outcomes. Binary Logistic regression was used to identify predictors of treatment outcome. Level of significance was at $p \leq 0.05$.

2.6 Ethical Consideration

Ethical clearance was sought from the Ethics committee of University of Nigeria Teaching Hospital (UNTH), Enugu. Permission was also obtained from Head of the chest clinic. Confidentiality was maintained by making data collected as anonymous as possible.

2.7 Definition of Treatment Outcomes (WHO)

Cured Patient that started treatment as sputum smear positive and at seventh month follow up tested negative goes on to complete treatment and discharged.

Failure Patient that started treatment as sputum smear positive and at fifth month follow up still tested positive.

Relapse Patient that started treatment as sputum smear positive and at seventh month follow up tested negative, complete treatment and discharged from the scheme but returns later to the clinic with sputum positive result.

Return After Default (RAD) Patient that started treatment as sputum smear positive, has been on treatment for four weeks (one month) and defaulted on follow up for eight weeks then comes back for treatment.

Others (unknown) Defaulted without returning (lost) or outcome unknown.

3. RESULTS

Table 1 shows the socio-demographic characteristics of patients. The mean age of those with TB alone was 28.4 years. Majority were aged 21-30 years 172(46.4%), males 232(62.5), students 91(24.5%) and travelled 0-20 km 294(79.2%). The mean age of those with TB/HIV coinfection was 32.3 years. Majority were aged 21-30 years 27(40.9%), males 232(62.5), traders 18(27.3%) and travelled 0-20 km 40(60.6%).

Table 2 shows distribution of patients by treatment outcome. Generally, majority of the patients 323(73.7%) were declared cured at end of treatment. Those with TB alone 281(75.7%) were cured while those with TB/HIV coinfection 41(65.1%) were cured. Failure cases were 8(2.2%) for TB alone and 0(0.0%) for TB/HIV.

Table 1. Sociodemographic characteristics of patients

Sociodemographic variables	TB alone Frequency (%) (n = 371)	TB/HIV Frequency (%) (n = 66)
Age in categories (Yrs)		
<20	36(9.7)	4(6.1)
21-30	172(46.4)	16(24.2)
31-40	93(25.1)	27(40.9)
41-50	61(16.4)	10(15.2)
51-60	42(11.3)	8(12.1)
>60	29(7.8)	1(1.5)
Mean(SD)	**28.4(5.7)**	**32.3(8.6)**
Sex		
Male	232(62.5)	31(47.0)
Female	139(37.5)	35(53.0)
Occupation		
Civil servant/public servant	64(17.3)	16(24.2)
Student	91(24.5)	7(10.6)
Artisan	57(15.4)	9(13.6)
Applicant/apprentice	60(16.2)	9(13.6)
Farmer	32(8.6)	7(10.6)
Others mainly traders	67(18.1)	18(27.3)
Distance to clinic		
0-20	294(79.2)	40(60.6)
21-40	45(12.1)	13(19.7)
41-60	7(1.9)	4(6.1)
61-80	4(1.1)	1(1.5)
>80	21(5.7)	8(12.1)

Table 2. Distribution of patients by treatment outcome

Treatment outcome	Disease status (n = 437)		Total (%)
	TB alone	TB/HIV	
	Frequency (%)	Frequency (%)	
In 5 categories			
Cured	281(75.7)	41(62.1)	322(73.7)
Failure	8(2.2)	0.0(0.0)	8(1.8)
Return After Default (RAD)	6(1.6)	10(15.2)	16(3.7)
Relapse	5(1.3)	0.0(0.0)	5(1.1)
Others (uknown)*	71(19.1)	15(22.7)	86(19.7)
In 2 categories			
Cured	281(75.7)	41(62.1)	322(73.7)
Not cured	90(24.3)	25(37.9)	115(26.3)
Total	**371(100.0)**	**66(100.0)**	**437(100.0)**

Table 3. Relationship between factors and treatment outcome

	Treatment outcome (n = 437)		Bivariate analysis	Multivariate analysis
	Cured (%)	Not cured (%)	χ^2 (p value)	AOR(95%CI)
Age in categories				
< 20	32(80.0)	8(20.0)		
21-30	131(76.2)	41(23.8)		
31-40	67(72.0)	26(28.0)		
41-50	42(68.9)	19(31.1)	3.04(0.766)	NA
51-60	31(73.8)	11(26.2)		
>60	20(69.0)	9(31.0)		
Sex of patient				
Male	193(73.4)	70(26.6)		
Female	130(74.7)	44(25.3)	0.10(0.824)	NA
Occupation of patient				
Civil/public servant	56(70.0)	24(30.0)		
Student	75(76.5)	23(23.5)		
Artisan	51(77.3)	15(22.7)	3.31(0.652)	NA
Applicant/apprentice	54(78.3)	15(21.7)		
Farmer	26(66.7)	13(33.3)		
Others Esp Traders	61(71.8)	24(28.0)		
Disease status				
TB alone	282(76.0)	89(24.0)		0.56(0.33-1.21)
TB/HIV coinfection	41(62.1)	25(37.7)	5.62(0.022)	1
Distance to clinic				
0-20	259(77.5)	75(22.5)		0.50(0.28-0.91)
21-40	36(62.1)	22(37.9)		0.40(0.12-1.35)
41-60	6(54.5)	5(45.5)	11.96(0.017)	0.20(0.03-1.34)
61-80	2(40.0)	3(60.0)		0.71(0.30-1.63)
>80	20(69)	9(31.0)		1

NA: Not applicable,
Bivariate analysis using Chi square test
Multivariate analysis using Binary Logistic Regression
AOR-Adjusted Odds Ratio

Table 3 shows the relationship between factors and treatment outcome. There was a statistically significant association between disease status (p =0.022) and distance to clinic (p =0.017) with treatment outcome. The respondents that had TB alone were about 0.6 times (AOR 0.56; 95% CI 0.33-1.63) likely not to be cured than those with TB/HIV. Those that travel 0-20 km to the clinic were about 0.5 times (AOR 0.50; 95% CI 0.28-0.91) likely not to be cured than those that travel more than 80 km.

4. DISCUSSION

Tuberculosis poses significant challenges to developing economies as it primarily affects people during their most productive years just like in this study and other previous reports in developing countries [16-19]. The disease is closely associated with poor living conditions, poverty and low socioeconomic status. From this study, there was no obvious occupational predominance, though students, artisans and applicants (young dependents) with poor means of livelihood, live in congested apartments like hostels and camps were the majority. Similarly, a study at Ile-Ife low socioeconomic status, overcrowding, and poor living conditions were identified as major risk factors in the development of pulmonary TB [19].

The distribution of the patients by disease status shows that over eighty percent of the patients had TB alone. There is an equally higher proportion of males having TB alone but a higher proportion of females with TB/HIV co-infection. This is similar to the national values for 2007 TB which documented that up to 65% of males have sputum smear-positive results [20]. This value is expected, as males in sub-Saharan Africa are more exposed to predisposing factors for the infection than females. Like being more active

and socializing. However, social inequalities including gender and power relations, have an important impact on HIV transmission [21]. Recent reviews also suggest that women in many parts of the developing world have no control on how, when, and where sex takes place thereby increasing the likelihood of HIV infection among them [21]. The implication is that if not checked the ravaging effect of HIV will continue even to yet unborn population since it can be transmitted to unborn during pregnancy and to the babies during delivery and breast feeding.

This study shows that majority of the patients 73.9% were declared cured at end of treatment for the two cohorts of patients with TB alone and those with TB/HIV. The findings are similar to study carried out among pregnant women in south western Nigeria with cure rate of 78.7% [22]. Other studies in Nigeria [16,18,23] and a study in Europe [24] reported a cure rate of about 75%. Even with this encouraging result, finding from the study is below the recommended target of 85% by the WHO, so there is need to improve on this [25].

There was no significant association of treatment outcome with age, sex and occupation. This is corroborated by study on treatment outcomes done in General hospitals in Ogbomosho, Southwest, Nigeria where there was no difference among any age category and sex.[23] However, this result contrasts findings in similar studies where there were higher cure rate in females [18,26] Likewise another study showed traders, health workers and food vendors as having higher prevalence but no association with treatment outcome [27].

Distance from residence to the clinic was identified as a predictor of treatment outcome. Patients that cover > 20km are likely not to be cured when compared to those that cover < 20km Previous studies have equally found the distance patient covers before getting to clinic to be important [28]. This most likely is due to better compliance to treatment as stipulated in DOTS strategy (direct observation by health worker) by WHO in 2005. The proximity to clinic will make attendance to clinic as well as adherence better with consequent positive outcome.

Patients that have TB co-infected with HIV are almost twice more likely not to be cured as compared to the patients who are infected with TB alone. This is buttressed by some studies which have shown that compared with HIV negative TB patients, HIV infected TB patients have substantially higher case fatality rates and default rate [29-31]. Concisely, this may be as a result of effect of each disease on the other ranging from manifestation of the disease in co-morbid condition to drug- drug interaction. The dual infection of a person by TB and HIV seen-as double monster-with its consequences has been seen contributing to poor treatment outcome. Moreover, the emergence of more interaction of TB with human immunodeficiency virus (HIV) infection might be one of the ways HIV has contributed to a global resurgence of tuberculosis [32].

Low socioeconomic class and poor living condition are ascribed factors in TB, consequently, government at all levels should strive to improve the living condition of the masses as this will on its own reduce both the prevalence and incidence of the disease. Similarly prevalence, treatment outcome of TB cases as well as the set targets for control of TB cannot be improved on or achieved without first reducing the ravaging consequences of HIV. However, this can partly be achieved by increasing the awareness about the diseases, behavioral change communication especially among youths, increasing number of health facilities with resources for voluntary counseling and testing, access to anti-retroviral drugs, and empowering the youths through the creation of job opportunities, improving the wellbeing and care for the dependent ages.

5. CONCLUSION

The factors identified as predictors of treatment outcome were TB/HIV co-infection and distance from residence to the clinic. Even though there is a moderately high cure rate among smear-positive pulmonary TB patients, it falls short of expectation, if Nigeria is to achieve set target for TB cure rate hence the need for stakeholders in TB control to intensify efforts in identifying and developing solutions.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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