

**RISK FACTORS OF HIV/DR-TB CO-INFECTION AMONG PATIENTS MANAGED AT  
NIGERIAN TREATMENT CENTERS: ANALYSIS OF NIGERIAN TUBERCULOSIS  
REFERENCE LABORATORY DATA, ZARIA, 2017**

**ADO U. ADAMU**  
Nigerian Field Epidemiology and Laboratory Training Program  
[adoumar2014@gmail.com](mailto:adoumar2014@gmail.com)

**SUFIYAN, M. B**  
Ahmadu Bello University Zaria  
[sufyanmb@gmail.com](mailto:sufyanmb@gmail.com)

**S. AHMED**  
National Tuberculosis and Leprosy Training Center, Zaria  
[sahmednl@yahoo.com](mailto:sahmednl@yahoo.com)

**&**  
**UMAR FARUK ABUBAKAR**  
Aminu Kano University Teaching Hospital, Kano  
[famzarab@gmail.com](mailto:famzarab@gmail.com)

**Abstract:**

*HIV and Mycobacterium tuberculosis (MTB) co-infection constitutes serious public health challenge in many parts of the world including, Africa. To date, HIV/MDR-TB prevalence is estimated by the National Tuberculosis and Leprosy Control Program (NTBLCP) based on existing HIV/TB surveillance data, which lack accuracy due to questionable quality of the routine surveillance information, completeness of TB notification and instances of TB under-diagnosis. Data from Laboratory register of MDR-TB patients sent for TB culture and DST at the National TB reference Laboratory of the NTBLTC, Zaria were reviewed from January 1 to December 31, 2017. HIV/MDR- TB was defined as co-infection as any person with positive laboratory HIV and MDR- TB test. Data were analyzed using descriptive statistics and logistics regression model ( $\alpha = 0.05$ ). Prevalence of HIV/MDR-TB co-infection was 92(17.0%). Almost half of all the HIV/MDR-TB co- infection falls within the age group 20 – 59 years among all sexes. The likelihood of having HIV/MDR-TB co-infection was 1.8 (OR 1.8: CI = 1.1 – 2.8;  $p = 0.024$ ) times higher among females than male's patients. HIV/MDR-TB co-infection rate was high in National Tuberculosis Reference Laboratory data, Zaria and it was found to be more prevalent among the most economically important age group, hence exerting a negative impact on Nigeria's economy. The study recommended that the NTBLCP implement measures that will improve adherence to prevention and control practices across the country.*

**Key words:** Tuberculosis; TB/HIV Co-infection; treatment outcome; Mortality; Risk factors.

**Introduction**

Tuberculosis (TB) and human immune deficiency virus (HIV) co-infection is a serious public health challenge because of associated mortality globally.(1) TB is the most common opportunistic disease and cause of death for those infected with HIV. Similarly, HIV infection is one of the most important risk factors associated with an increased risk of latent TB infection progressing to active TB disease. (2) In the individual host the two pathogens, *M. tuberculosis* and HIV, potentiate one another, accelerating the deterioration of immunological functions and resulting in premature death if untreated(3). Some 14 million individuals worldwide are estimated to be dually infected. TB is the largest single cause of death in the setting of AIDS, accounting for about 26% of AIDS-related deaths , 99% of which occur in developing

countries(4). Globally, people living with HIV (PLWHA) are about 30 times more likely to develop TB than HIV-negative individuals 99% of which occur in developing countries(ref)....

Prevalence of HIV infection among TB patients varies from country to country, the highest rates have been reported in areas where HIV prevalence is high in the general population. For example a high co-infection rate of 44% - 52% has been reported in Kenya , while a lower co-infection rate of 8.8% was obtained in Southern California, USA(5).

TB burden in Nigeria (318 per 100,000) is one of the highest in the world (6) and according to the National Agency for the Control of AIDS (NACA) the prevalence of HIV in Nigeria is 3.4% as at 2012 (7). However, the proportion of patients with TB/HIV co-infection in Nigeria is projected to be 19.1%.(8) Several studies from Nigeria and other high TB burden countries have shown that TB/HIV co-infected patients have poorer treatment outcome (9).

However, Accurate data on TB/HIV co-morbidity in different parts of Nigeria were not available due to limited access to HIV Counseling and Testing (HCT) by individuals with TB infection.(10) This study determines the prevalence and associated risk factors of HIV/DR-TB co-infection among TB patients sent for laboratory diagnosis in the reference center of the National Tuberculosis and Leprosy Training Center (NTBLTC), Zaria.

This study was carried out at the National TB reference Laboratory of the NTBLTC, Zaria, Kaduna State Nigeria. Management of drug resistant TB commenced in Nigeria in 2007 and is coordinated by the National Tuberculosis and leprosy control program (NTBLCP) and State TB and Leprosy Control Programme (STBLCP). The total DOTS and microscopic coverage as at December 2014 stood at 5,728 DOTS and 1,765 microscopy sites respectively(11).

By 2011 there were (5,728) DOTS centers and (1,765) microscopy sites and centers, in addition the GeneXpert (MTB/Rif ) has been adopted as point of entry in the diagnosis of drug resistant Tuberculosis in Nigeria which propelled the increase in the detection of RIF resistance TB cases(11).

### **Methodology**

A retrospective review of Laboratory register of all MDR-TB patients sent for TB culture and DST at the National TB reference Laboratory of the NTBLTC, Zaria hospital between January, 1st and December 31st, 2017 was conducted.

### **Patient Population**

Patients with microbiologically confirmed pulmonary MDR-TB and positive cultures for *Mycobacterium tuberculosis* from respiratory samples who were admitted to the various treatment centers for treatment between January 2016 and December 2016 were included in the study.

### **Data Collection**

Patients were identified using the Laboratory register, which included all patients with MDR-TB hospitalized at the sites. Entries were cross-referenced to identify *M. tuberculosis* strains with rifampicin and isoniazid resistance. Patient records were reviewed for socio-demographics, HIV status, treatment outcome data, and information was recorded in an anonymized database, which was further analyzed.

### **Drug Susceptibility Testing**

Drug susceptibility testing was performed in a specialized section of the laboratory at the NTBLTC, one of the national reference laboratories for TB evaluation, in Nigeria. All patients included in the study had a positive *M. tuberculosis* culture available for drug susceptibility testing. Susceptibility testing was performed for the following drugs: isoniazid, rifampicin, rifabutin, ethambutol, pyrazinamide, streptomycin, amikacin, capreomycin, fluoroquinolones, prothionamide, cycloserine, paraaminosalicylic acid, and linezolid.

### **Treatment and Outcome**

Patients were considered to have received an appropriate MDR-TB treatment regimen once they had received at least four drugs in combination therapy that were thought to be effective according to the results of drug susceptibility testing, including a second-line injectable drug for the intensive phase of treatment (9). TB treatment was directly observed during the entire course of therapy. To ascertain the microbiological response to treatment, sputum cultures were collected on a monthly basis during hospitalization and every 1–2 months afterward until the end of therapy. Outcome was ascertained using the revised WHO definitions (9). Patients were considered to have a successful outcome if they were cured or if they had completed the treatment or had an unsuccessful outcome in the case of default, treatment failure, or death.

### **Statistical Analysis**

Data processing and analysis were performed using Microsoft Excel 2017 and Epi-info version 7.2 software. Descriptive statistics were used to summarize the data and the results were presented as frequency and proportions. Bivariate analyses were conducted to determine the associations between dependent and independent variables. Those variables that had significant association at  $\leq 0.2$  on bivariate level were further analyzed using unconditional multivariate logistic regression to identify independent predictors of HIV/MDR-TB co-infection. The level of significance was set at  $\alpha=0.05$  and 95% CI level.

### **HIV testing**

HIV test was conducted for some confirmed TB cases. Determine (determine HIV-1/2 Alere Determine™, Japan 2012) and Uni-Gold™ (Trinity Biotech PLC, Wicklow, Ireland 2013) were used in parallel algorithm. However, STAT-PAK® was used as tie breaker when there was discordant result.

### **Ethical issues**

Data for this study were retrieved from the MDR-TB Laboratory register of the National Reference Laboratory NTBLTC Zaria. Permission for the data use was obtained from the management of NTBLTC, Zaria. The ethical committee of management of NTBLTC, Zaria ensured that the research is in compliance with ethical principles and was granted approval. The general principles of ethics such as beneficence, non-maleficence, respect for autonomy and justice was considered. The research is non-invasive and did not carry any potential risks or harm to the participants. Confidentiality of the data and information obtained was maintained and was used only for the purpose of the study.

## **RESULTS**

Of the 574 patients' records analyzed, 33(5.7%) had their HIV status unknown and so were excluded in the descriptive analysis, more than half of patients 315(58.0%) were in the age group 20 – 39 years, followed by 175 (32.0%) in age group 40-59 years, the least being the age groups 0-19 years and  $\geq 60$  years with 26(4.8%) and 25(4.6%) patients respectively as shown in table 1. Mean age is  $36.5 \pm 0.52$  years.

Males constitute the majority with 370 (68.4%) study participants as shown in Table. 2. The proportion of overall HIV/MDR – TB co-infected patients was found to be 92 (17.0%). Males were more infected than females in the age groups 0-19 years with 2 (7.7%) males and 1(3.8%) female respectively. In 40- 59 years age group, males were 24 (13.7%) and females were 8 (4.5%) respectively, but for age group 20-39 years males have 27 (8.6%) while females have 30 (9.5%) participants respectively. More than half of all the HIV/MDR-TB co- infection occurs within the age groups 20 – 59 years among all sexes as shown in Table 2.

Data from treatment centers of twenty-five states among 5 geopolitical zones with the exception of southwest zone were analyzed. These are Abia, Adamawa, Akwa-Ibom, Bauchi, Bayelsa, Benue, Borno, Delta, Edo, Enugu, FCT, Gombe, Imo, Kaduna, Kano, Katsina, Kebbi, Kogi, Nassarawa, Plateau, Rivers, Sokoto, Taraba, Yobe and Zamfara. Taraba state had the highest prevalence of 50.0% among all the states,

followed by Benue with 33.0%, FCT, 28.5%, Akwa Ibom 25.0%, Edo 18.5%, Gombe, Kaduna and Kano had 16.7% each, Abia 15.0%, Adamawa 12.5%, Delta 10.7%, Kogi 8.1%, Imo 5.0%, Bauchi 4.5%, Enugu 0.6% while Borno, Bayesa, Katsina, Kebbi, Yobe and Zamfara, had not recorded any case as shown in Table 3.

The odds of having HIV/MDR-TB co-infection among females is 1.8 times higher than males patients (OR= 1.8, CI 1.1 – 2.8; p = 0.024). There is no statistically significant difference between all age groups and HIV/MDR-TB co-infection.

Table 1: Prevalence of HIV/MDR-TB co-infection by patient’s age group at NTBLTC Zaria, 2017. N=541

Age group	Positive (%)	Negative (%)	Total
0 – 19	3(11.5)	23(88.5)	26
20 – 39	57(18.1)	258(81.9)	315
40 – 59	32(18.3)	143(81.7)	175
≥60	0	25(100)	25
Total	92(17.0)	449(83.0)	541

Table 2 Prevalence of HIV/MDR-TB co-infection by patient’s sex at NTBLTC Zaria, 2017. N=541

Age groups	Positive(%)		Negative(%)		Total
	M	F	M	F	
0-19	2(7.7)	1(3.8)	9(34.6)	14(53.8)	26
20-39	27(8.6)	30(9.5)	184(58.4)	74(23.4)	315
40-59	24(13.7)	8(4.5)	104(59.4)	39(22.2)	175
≥60	0	0	20(80)	5(20)	25
Total	53(9.7)	39(7.3)	317(58.6)	132(24.3)	541
Grand total	92(17.0)		449(83.0)		541

Table 3: Prevalence of HIV/MDR-TB by patient’s State at NTBLTC Zaria, 2017. N=541

S/N	State	Negative	Positive	Unknown	Total	Prevalence (%)
1	Abia	17	3	-	20	15.0
2	Adamawa	7	1	-	8	12.5
3	Akwa Ibom	20	7	-	27	25.0
4	Bauchi	18	1	3	22	4.5
5	Bayelsa	1	0	0	1	0.0
6	Benue	16	8	0	24	33.0
7	Borno	21	0	1	22	0.0
8	Delta	49	6	1	56	10.7
9	Edo	13	3	0	16	18.5
10	Enugu	1	3	1	5	0.6
11	FCT	13	6	2	21	28.5
12	Gombe	5	1	1	6	16.7
13	Imo	38	2	0	40	5.0
14	Kaduna	55	12	5	72	16.7
15	Kano	5	1	0	6	16.7
16	Katsina	9	0	1	10	0.0
19	Kebbi	6	0	0	6	0.0
20	Kogi	31	3	3	37	8.1
21	Nasarawa	9	0	2	11	0.0
22	Niger	34	3	1	38	7.8
23	Plataeu	1	0	0	1	0.0
24	Rivers	36	9	3	48	18.5
25	Sokoto	13	1	6	20	5.0
26	Taraba	20	20	0	40	50.0
27	Yobe	4	0	1	5	0.0
28	Zamfara	7	0	4	11	0.0

Table 4: Factors associated with HIV/MDR –TB co- infection at NTBLTC Zaria, 2017. N=541

Variable	HIV/MDR-TB	MDR-TB	COR (95%)	P-Value
Age group	n = 92(%)	n = 449(%)		
(years)				
0 – 19	3(13.6)	19(86.4)	1	-
20 – 39	49(16.3)	251(83.6)	0.81(0.23 – 2.33)	0.974
40 – 59	30(17.5)	141((82.5)	0.74(0.21 – 2.67)	0.875
>60	10(20.8)	38(79.2)	0.60(0.14 – 2.44)	0.698
<b>Sex</b>				
Females	39(22.8)	132(77.2)	1.8(1.1 – 2.8)	0.0204
Males	5.3(14.3)	317(85.7)	1	
<b>Treatment success</b>				
Unsuccessful	12(11.54)	92(88.46)	0.5(0.29 – 1.09)	0.3292
Successful	80(18.1)	357(81.69)	1	

This study found that 541(94.0%) patients had HIV counselling and Testing (HCT) across the country. This finding although not good enough, is higher than the national figure (86%).(8,(11).This may be due to improvement in the HCT in the treatment centers across the country, making it a standard practice for all presumptive TB patients to have HIV testing. The study also showed that there are 33(6.0%) unknown HIV status, this is a wide gap which needs to be closed in order to attain good prevention and control practices.

The proportion of HIV/MDR – TB co-infected patients was found to be low in the country but with varying proportions across the states. In sub-Saharan Africa, the risk of developing TB is high. This is partly due to high HIV prevalence. In 2014, an estimated 41% of African TB cases were HIV co-infected(12,(13). In this study, 17.0% had HIV/ MDR-TB co-infection which is lower than what was found in Lagos state (23%) (14), national (19%) figures (11) and a study from Eastern Nigeria(15) but higher than what was reported in a study from a south-western state in Nigeria (16). However southern Africa countries like Malawi and South Africa with high HIV prevalence reported TB/HIV co-infection rate between 56% – 62% (13,(17). The prevalence of TB/HIV co-infection was 43% in Africa (USAID, 2013) and between 50 – 80% in parts of sub-Saharan Africa in 2012(5). Our finding may be a reflection of the decline in the prevalence of HIV prevalence in the country as reported by NACA, earlier studies showed that TB/HIV prevalence in Nigeria was between 28% and 43%(18).

Majority of all the HIV/MDR-TB co- infection falls within the age group 20 – 59 years as shown in Table. This is similar to what is obtainable in the national HIV sero-prevalence survey.(7)This age group happens to be the most important and most active in terms of economy, sex, child bearing as well as all the occupational activities. This implies that sexual activities play very significant role in the transmission of both HIV and MDR-TB infections.

HIV/MDR – TB co-infection is found to be prevalent in most of the states analyzed as shown in Table. Taraba state had the highest prevalence of 50.0% among all the patients studied as shown in Table. This implies that HIV/ MDR – TB burden in the country is estimated as much higher than previously thought in some states particularly (based on data from the routine surveillance system), with considerable ongoing transmission. These results suggest that MDR-TB should be given focused improved surveillance and continue to be classified as a significant public health problem in Nigeria.

The odds of having HIV/MDR-TB co-infection among females is 1.8 times higher than male patients (OR= 1.8, CI 1.1 – 2.8; p = 0.024).This finding is in contrast to the reports of patients with TB and HIV/AIDS in New York (USA), Tanzania and Spain (19) in which the observed effect of gender on TB/HIV was not significant.

There is no statistically significant difference between age group and HIV/MDR-TB co-infection OR= 0.81, CI 0.23-2.33; p=0.974). This is contrary to what was reported in similar studies from Lagos and Ethiopia, where TB/HIV co- infection was associated with lower age groups(1). But similar to the findings of WHO(20) TB and HIV is known to affect people in the reproductive age groups. Also there is no statistically significant difference between treatment success and HIV/MDR-TB co- infection (OR= 0.5, CI 0.29-1.09; p=0.3292).

### **Conclusion**

HIV/MDR-TB co-infection rate was high in most of states reporting in the study area and was found to be more prevalent in the most economically important age group, hence, exerting a negative impact on the nation's economy. The NTBLCP need to put measures in place that will improve adherence to prevention and control practices across the country.

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