

Multiple-drug resistant (MDR) tuberculosis among HIV sero-positive and sero-negative populations in Ilorin, North-Central Nigeria

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Submitted: December 2018

Accepted: June 2019

Published: August 2019

Citation:

Abdulazeez et al Multiple-drug resistant (MDR) tuberculosis among HIV sero-positive and sero-negative populations in Ilorin, North-Central Nigeria. South Sudan Medical Journal 2019; 12(3):93-96

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Introduction: Multiple-drug resistant tuberculosis (MDR-Tb) has become a global issue especially in many African countries. Regular studies are needed to ascertain its early detection and elimination in the endemic regions in order to reduce the morbidity and mortality rates

Objective: To assess the frequency of MDR-Tb among HIV sero-positive and sero-negative populations in Ilorin, North-Central Nigeria.

Method: Sputum samples were collected from 1,601 subjects provisionally diagnosed with pulmonary tuberculosis (TB) at Sobi Specialist Hospital, Ilorin-Nigeria. Inclusion criteria were based on a cough for at least three weeks with no response to antibiotics treatment or when the chest Xray indicated TB infection. From each patient three specimens were obtained for Ziehl Neelsen staining and 4ml of blood were collected for HIV antibody testing.

Results: The frequency of Acid Fast Bacilli (AFB) positive cases was 10.86% while 0.72% MDR-Tb and 3.2% concurrent infection with *Mycobacterium tuberculosis* and HIV were documented. Statistically, no significant association between age and MDR-Tb ($X^2=0.6731$, $P>0.05$) was found.

Conclusion: The study revealed 10.86% of AFB positive cases, 0.74% MDR-Tb cases and 3.2% concurrent infection between *Mycobacterium tuberculosis* and HIV. We therefore recommend aggressive and effective control measures to prevent further transmission of MDR-Tb between patients and health care workers while increased access to ART for HIV infected MDR-TB patients is also suggested.

Key words: multiple-drug resistant tuberculosis, co-infection, HIV, Nigeria

INTRODUCTION

Pulmonary tuberculosis (TB) is an infectious disease causing high morbidity and mortality throughout the world.^[1-5] In 2015, reports showed an estimated 10.4 million cases of tuberculosis globally, including 1.2 million (11%) people living with Human Immunodeficiency Virus (HIV). Recent reports showed that 57% of TB among people living with HIV was not promptly diagnosed or treated, resulting in 390,000 tuberculosis-related deaths in 2015.^[6, 7]

HIV infection increases the risk of TB infection^[8, 9] by 26 to 36 times.^[10, 11] TB causes about a third of HIV-related deaths.^[4, 6] *Mycobacterium tuberculosis* is defined as multidrug-resistant when it becomes resistant to first-line drugs as isoniazid and rifampin. This accounts for 5% of all TB cases globally.^[12, 13] The World Health Organization (WHO) endorsed the Gene Xpert MTB/RIF for use in countries where TB is endemic and declared it a major milestone for global TB diagnosis in December 2010.^[14]

In view of paucity of information about MDR-Tb in our locality, this study was carried out to determine the frequency among HIV sero-positive and sero-negative populations

METHOD

Selection of subjects and specimen collection

The study was carried out between June 2017 and May 2018 in the chest clinic

of the Specialist Hospital Ilorin, north -central Nigeria on sputum collected from 1,610 patients provisionally diagnosed with pulmonary TB. Ethical approval was obtained from Ethical and Animal Care Committee of the School of Basic Medical Sciences, Kwara State University. Informed consent of the subjects and the parents of children was obtained.

A cross-sectional simple random method was employed. Inclusion criteria were based on a cough for at least three weeks with no response to antibiotics or when the chest Xray indicated TB infection.

Three specimens were obtained per subject. The first specimen was produced on the first contact, the second produced early morning following the first day at home while the third was produced at the clinic. Four milliliters of blood were collected from each subject for HIV antibody testing.

Laboratory analysis of specimens.

Each sputum specimen was treated with a mixture of sodium hypochlorite and sodium hydroxide for decontamination before analysis. Smears were made from the sediment of the specimens and stained by Ziehl Neelsen techniques and examined for Acid-Fast Bacilli.

Assessment for multiple drug resistance was based on the use of the Gene Xpert machine which is an automatic sputum processor by real time amplification. The process was repeated for all the specimens and only the concordant results were considered in this study.

Commercial Determine test strip (Global source, Shenyang LTH Tech, China) was employed for qualitative detection of HIV antibodies. Each test strip was removed from the foil, dipped in the serum for 30 seconds and allowed for 5 minutes on the work bench for the serum to flow through control and test columns. Appearance of two pinkish lines in the strip within 5 minutes was an indication of HIV positive while appearance of a single line at the control column was an indication of negative HIV serum.

Statistical analysis

Data were analyzed using SPSS version 23 software

(SPSS Inc. USA). The Chi Square test was used to assess the distribution of MDR-Tb and the frequency of co-infection between AFB and HIV infection.

RESULTS

Frequency of Multiple Drug Resistance and co-infection of AFB and HIV with respect to age is shown in Table 1. Out of 1,610 subjects examined, no case of MDR-Tb was reported among age groups of 15-29 years and 30-44 years while 1.10% and 8.0% MDR tuberculosis were documented in age groups of 45-59 years and 60 years and above respectively. Chi-Square test showed no significant association between age and MDR-Tb ($\chi^2=0.6731$, $P>0.05$). The highest rate (4.2%) of concurrent infection was reported within the age group 30-44 years while no case of co-infection was recorded among those aged 60-72 years. Statistically significant positive correlation was recorded between co-infection (of AFB and HIV) and age ($r = 4.9210$, $P<0.05$).

Figure 1 shows that a higher rate of TB was recorded among the male subjects ($n=98$, 6.1%) than among females ($n=75$, 4.7 %). Conversely, a higher rate of HIV infection was recorded for females ($n=36$, 2.2 %) than the males ($n=28$, 1.7 %). Our findings also revealed a higher rate (3.45%) of co-infection among females than in males with 3.10%. Out of 175 AFB positive cases recorded, 47 of them were also infected with HIV representing 26.90% of the AFB positive cases.

Figure 2 shows the frequency of MDR-Tb in relation to HIV status. Out of 62 subjects tested positive for AFB with unknown HIV Status, six (9.6%) were MDR. Also, out of 63 HIV sero-positive cases living with TB, 6 (9.5%) were MDR resistant while no case of MDR was recorded among 50 HIV sero-negative subjects with tuberculosis.

Occurrence of co-infection of AFB and HIV with respect to marital status is as shown in Table 2. The results showed no case of co-infection among the widows whereas 2.98% and 0.90% of the co-infections were documented among single and married subjects respectively. Chi-square test showed no significant difference in the rate of co-infection with respect to marital status ($\chi^2=0.9337$, $P>0.05$).

Table 1. Frequency of Multiple Drug Resistance and co-infection of AFB and HIV according to age

| Age – years | Number examined | AFB positive n (%) | MDR n (%) | HIV positive only n (%) | AFB + HIV Co-infection n (%) |
|-------------|-----------------|--------------------|-----------|-------------------------|------------------------------|
| 15-29 | 575 | 64 (11.13) | 0(0.0) | 28(4.9) | 20 (3.4) |
| 30-44 | 571 | 83(14.53) | 0(0.0) | 27(4.7) | 24(4.2) |
| 45-59 | 364 | 20(5.49) | 4(1.10) | 4(1.10) | 8(2.2) |
| 60-74 | 100 | 8 (8.00) | 8(8.00) | 4(4.0) | 0(0.00) |
| Total | 1610 | 175 (10.86) | 12(0.72) | 63(3.91) | 52(3.2) |

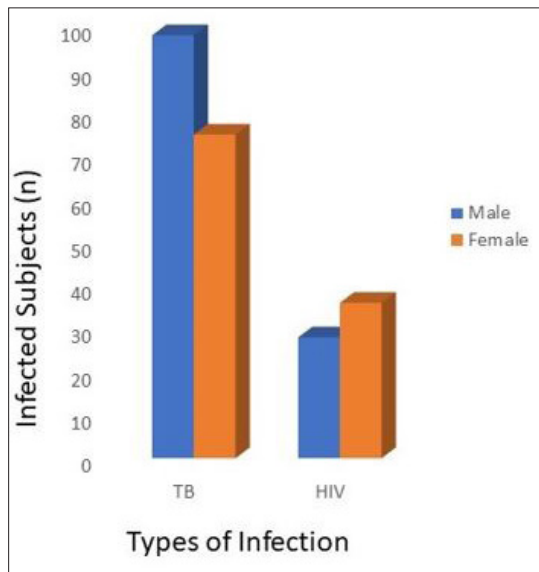


Figure 1. Distribution of AFB and HIV by gender

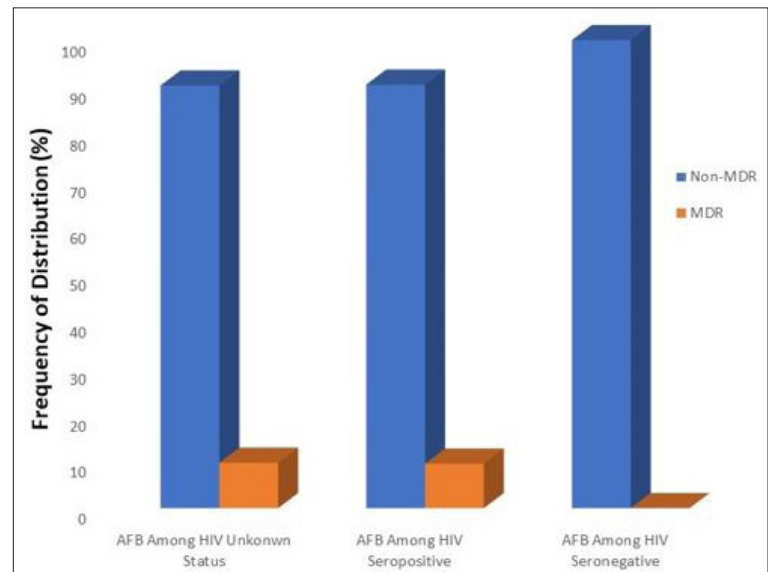


Figure 2. Prevalence of MDR tuberculosis in relation to HIV status

Table 2. Concurrent infection of AFB and HIV in relation to marital status.

| Marital Status | No examined | AFB positive n (%) | HIV positive n (%) | AFB + HIV Co-infection n (%) |
|----------------|-------------|--------------------|--------------------|------------------------------|
| Single | 436 | 43 (9.86) | 20 (4.58) | 13 (2.98) |
| Married | 1035 | 132 (14.00) | 43(4.15) | 10 (0.90) |
| Widow/Divorced | 139 | 0 (0.00) | 0 (0.00) | 0 (0.00) |
| Total | 1610 | 175 (10.86) | 63 (3.91) | 23 (1.43) |

DISCUSSION

This study reveals 0.74% prevalence rate of MDR-Tb while 3.2% of co-infection with *Mycobacterium tuberculosis* and HIV was documented. The frequency of AFB positive cases was 10.86%. This finding differs from the result of a previous study^[15] in which a 22% prevalence rate was found in the south-eastern part of the same country. Our sample size was larger and may explain this difference. Out of the 175 AFB positive cases recorded, only 12 cases were MDR positive representing 4.0 % of the AFB positive cases and 0.74% of the entire sampled population. Coincidentally, all the cases of MDR were documented among the HIV sero-positive population while none was reported among their sero-negative counterparts. The finding is similar to a previous WHO report.^[5]

The MDR result in the present study is however at variance with the 3.6% reported by Okorie et al.^[15] The difference could be attributed to the automated machine employed in this study while a manual technique was used by the previous authors. This requires further investigation.

Assessing the frequency of AFB positive cases with respect to age, the highest rate (14.53%) was recorded within the

age group 30-44 years, implying that this age group was more vulnerable to *Mycobacterium tuberculosis* infection. However, there was no record of MDR-Tb among this age group whereas 8.0% was recorded among subjects of 60 years and above. The reason for higher MDR among the older age group may be attributed to lower immunity with advancing age. Our finding differs from a previous study [8] where the highest rate was reported within the age of 50 years and above. Chi-Square test showed no significant association between age and MDR-Tb ($\chi^2=0.6731$, $P>0.05$) and between gender and MDR-Tb, ($\chi^2 = 0.912$, $P>0.05$).

Our study showed no case of co-infection with HIV and AFB among the widows while 2.98% and 0.90% co-infection was documented among the single and married subjects respectively. The reason for this could probably be due to a lower exposure by the widows to both infections as against single and married subjects. Also, non-uniformity of the specimens collected in the present study could probably be the cause of the variation.

Statistically, our findings showed a positive correlation between AFB and HIV prevalence in relation to age ($r = 4.9210$, $P < 0.05$). This observation implies that with

the rate of Mycobacterium tuberculosis infection, the frequency of HIV in the study area may be predicted in a model investigation.

CONCLUSION

This study revealed 10.86% of AFB positive cases, 0.74% MDR-Tb and 3.2% concurrent infection between Mycobacterium tuberculosis and HIV. We therefore recommend aggressive and effective control measures to prevent further transmission of MDR-Tb between patients and health care workers while increased access to ART for HIV infected MDR-TB patients is also suggested. Further studies that may lead to the discovery of new molecular markers are germane for prompt diagnosis and control of MDR-Tb.

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