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Prevalence of MDR-TB Based on Demographic Factors Among Patients Attending Nauth and St Patrick's Hospital Mile 4 Abakaliki in Southeast Nigeria

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Abstract: This study was designed to determine the prevalence of multi-drug resistant tuberculosis (MDR-TB) among pulmonary tuberculosis patients attending NnamdiAzikiwe University Teaching Hospital (NAUTH) Nnewi and St Patrick's Hospital Mile 4 Abakaliki demographically. Patients with persistent cough for over two weeks were screened by Ziehl-Neelsen ZN technique for the presence of acid fast bacilli (AFB) in their sputum and a total of 103 patients with AFB positive sputum samples were recruited. The positive sputum samples were subjected to Xpert MTB/RIF assay (GeneXpert®, Cepheid USA) and culture on Lowestein Jensen medium for 42 days at 37°C. Drug susceptibility testing was done on the isolates using the nitrate reduction assay (NRA). Eighty-three 83 (80.6%) of the isolates were obtained from culture after suspected colonies were subjected to morphological, biochemical, and immunological tests and out of the 83 (80.6%) samples analysed by Xpert MTB/RIF assay 45 (67.2%) were rifampicin resistant. Age group 26-35 years showed the highest proportion of positive culture results (33.7%) followed by age group 18-25 (28.8%) years. Demographically, age group 26-35 years had a high prevalence rate of MDR-TB (50.0%) and female gender also showed high prevalence rate of MDR-RB (48.5%). Strikingly, educational status was significantly associated with MDR-TB (P=.020). St Patrick's hospital had a high prevalence rate of MDR-TB (46.94%) when compared with NAUTH (38.9%) and these indicates that there is high prevalence of MDR-TB among patients with pulmonary TB in these sites. The demographic results of this study calls for urgent and serious intervention as MDR-TB prevalence is increasing even in the face of intense national TB control program.

Keywords: Prevalence, MDR-TB, Demographic Factors, Patient

1. Introduction

Tuberculosis, one of the oldest recorded human afflictions, is still one of the biggest killers among the infectious diseases, despite the worldwide use of a live attenuated vaccine and several antibiotics. *Mycobacterium tuberculosis* is the causative agent of tuberculosis in humans. Other tuberculosis complex organisms are *Mycobacterium bovis* (causes tuberculosis in cattle and humans, as well as other carnivores) and *M. africanum* (the causative agent of human tuberculosis in tropical

Africa) [1]. It is the leading cause of death from a curable infectious disease and approximately 9 million new cases of TB are identified per year, with almost 2 million deaths related to TB, making *Mycobacterium tuberculosis* the single greatest cause of mortality due to a bacterial pathogen [2]. Multi-drug resistant tuberculosis (MDR-TB) is a type of TB that is resistant to Rifampicin and Isoniazid, two of the first line anti-TB drugs [3]. Of great concern is the fact that MDR-TB which is caused by *Mycobacterium tuberculosis* strains that do not respond to standard therapies not only poses problems for the treatment of individuals but also for the control of TB in populations as it represents lapses in public health [4]. Studies both locally and globally have been done to assess the burden of MDR-TB within the population. In Nigeria, Lawson *et al.,* [5] in an effort to ascertain the prevalence and risk factors associated with MDR-TB reported 13% prevalence rate of MDR-TB among studied population. According to the American Lung Association (ALA), 9.2% of cases of TB were resistant to Isoniazid, and 1.3% resistant to both Isoniazid and Rifampicin in the United States, although these cases had no history of previous treatment with TB drugs [6]. World Health Organisation (WHO) estimates that 26% of patients with TB infection in Nigeria are HIV positive [7].

Global surveillance programme showed variation in the magnitude and trends of drug resistance in different countries. Migration of population has also been reported to strengthen the transmission dynamics of TB as well as antimicrobial drug resistant organism [8]. However, the implementation of Directly Observed Therapy (DOTs) strategy in Nigeria since 1993 has achieved a case detection rate of 30% and treatment success rate of 79% which is still below the global target of 70% detection and 85% cure rate respectively [9]. This implies that majority of active cases are still not detected within the communities and this will continue to transmit TB infection [8]. It has been observed that MDR-TB has reached alarming levels worldwide with the emergence of strains that are virtually untreatable with the existing drugs and it has been indicated that MDR-TB is likely to be more prevalent in Africa than previous reports indicated [7, 10]. Therefore this study assessed the demographic prevalence of MDR-TB among pulmonary tuberculosis patients attending Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi and St Patrick's Hospital Mile 4 Abakaliki and the findings calls for urgent and serious intervention as MDR-TB prevalence is increasing even in the face of intense national TB control program.

2. Materials and Methods

2.1. Study Area

This study was conducted at NnamdiAzikiwe University Teaching Hospital (NAUTH), Nnewi and St Patrick's Hospital, Mile 4 Abakaliki. Nnewi is the second largest city in Anambra State and is home to nearly 388,805 residents. Abakaliki is the capital of Ebonyi state and has a population of 149,683 persons [12]. NAUTH is a tertiary health institution and serves as a site for treatment and management of both TB and HIV patients. It is also a referral centre for both cases. St Patrick's Hospital, Mile 4 Abakaliki is a faith-based health facility and offers both antiretroviral therapy and TB care to patients.

2.2. Sample Size

Minimum sample size was calculated using the formula stated by [13] and a total of 103 sputum smear positive AFB samples were colleted for the study.

2.3. Ethical Approval

Ethical approval for this study was obtained from NAUTH research and ethics committee. Consent was obtained from each participant and participants' confidentiality was maintained throughout the study. Participants received no financial motivation for their involvement in the study. Participants were free to withdraw from the study at any point and their withdrawal would not affect their treatment. This study was conducted between January 2015 and September 2016.

2.4. Sample Collection and Analysis

Consenting, eligible participants were screened for presence of AFB in their sputum. Two sputum samples (spot and early morning) were collected in sterile screw-cap universal containers from each participant on 2 consecutive days and stained by Ziehl-Neelsen's method.

Progressively, early morning mucoid or mucopurulent sputum specimen was collected from each participant with smear positive AFB test result into a sterile screw-cap universal bottle. The specimen was then stored in the refrigerator until transported to the TB reference laboratory of Dr Lawrence Henshaw Memorial Hospital (DLHMH) in Calabar, Cross River State. Transport was done within 72hrs of collection.

After appropriate sample preparation, two Lowestein Jensen (LJ) medium slants were cultured for each sample. Tubes were loosely capped and incubated as such at 37°C for one week in a slanted position to ensure even distribution and absorption of inoculum. After 1 week, tubes were incubated upright for up to 6 weeks and the caps tightened. An in-house strain H37RV and an uninoculated tube were used as positive and negative control respectively.

After Colonies was confirmed by Ziehl-Neelsen (ZN) staining for acid-fastness, niacin test was carried out on each inoculated and control tubes. The formation of a yellow colour was interpreted as positive reaction; absence of colour was regarded as negative reaction for production of Niacin. Catalase test, p-Nitrobenzoic Acid (PNB) and TB Ag MPT64 Rapid Test was carried out in this study and *M. tuberculosis* identification was based on its slow growth rate, no pigmentation, no growth on Lowestein Jensen (LJ) medium containing p-nitrobenzoic acid, niacin production, catalase negative at 68°C and positive Ag MPT 64 test.

Drug susceptibility testing (DST) was carried out on all confirmed *M. tuberculosis* colonies and nitrate reduction

assay (NRA) method was used [11].

GeneXpert MTB/RIF assay for detection of Rifampicin Resistance was carried out on the sputum samples of the participants. Sputum sediments were mixed with sample buffer in a ratio of 1:3 in a screw cap tube and screwed tightly. The tube was vortexed for 20 seconds. Sample was incubated at room temperature for 10mins. After 10mins the sample was vortexed again for 20 seconds and incubated at room temperature for 5mins. After incubation, 2ml of sample was inoculated into the genexpert cartridge. Cartridge was scanned into the GeneXpert machine and allowed to run for 2hrs. After 2hrs the test result was read off the screen of the GeneXpert machine monitor.

2.5. Data Analysis

Data was statistically analyzed using statistical package for social sciences SSPS for windows version 20.0 software. A standard questionnaire was completed for each recruited patient to collect demographic parameters. Frequencies were calculated as percentages. Comparison of categorical variables and significance testing was done with $\chi 2$ test. P-value of less than 0.05 ($P<0.05$) was considered statistical significant.

3. Results

Demographically, table 1 showed the culture positivity result of the study. Age range 26-35 years had the highest culture positivity prevalence (33.7%). It shows also that male (59.0%) was more infected with TB than female (41.0%). Table 2 showed that educational status was statistically associated with MDR-TB and the study had a prevalence rate of 44.8%. In Figure 1, mile 4 Abakaliki had MDR-TB prevalence of 46.94% compared to 38.89% from NAUTH.

Table 1. *Culture Positivity with respect to Socio-Demographic Factors.*

Variable	Number in the Study	Number Culture Positive	%
Age (years)			
18-25	30	23	28.8
26-35	35	28	33.7
36-45	19	18	21.7
46-55	11	10	12.0
56-65	5	3	3.6
>65	3	1	1.2
Gender			
Male	61	49	59.0
Female	42	49	41.0
Employment Status			
Civil servants	7	7	8.4
Self employed	71	57	68.7
Student	17	13	15.7
Unemployed	8	6	7.2
Educational Status			
None	14	11	13.3
Primary	32	26	31.3
Secondary	46	36	43.4
Tertiary	11	10	12.0
Location/Residence			
Rural	62	52	62.7
Semi-urban	9	5	6.0
Urban	32	26	31.3
Marital Status			
Married	61	53	63.9
Single	41	30	36.1
Widow/Widower	1	0	0.0

Table 2. *Prevalence of MDR-TB based on Demographic Factors.*

Variable	Resistant Isolates	MDR Isolates	Prevalence rate (%)	P-value
Age (years)				
18-25	21	9	42.9	
26-35	21	11	50.0	
36-45	15	6	40.0	.464
46-55	7	2	28.6	
56-65	2	2	100	
>65	1	0	0.0	
Gender				
Male	34	14	41.2	
Female	33	16	48.5	.548
Employment Status				
Civil servants	5	3	60.0	

Variable	Resistant Isolates	MDR Isolates	Prevalence rate (%)	P-value
Self employed	47	21	44.7	.776
Student	11	2	45.5	
Unemployed	4	1	25.0	
Edu. Status				
None	10	8	80.0	
Primary	20	8	40.0	.020
Secondary	30	9	30.0	
Tertiary	7	5	71.4	
Location/Residence				
Rural	41	20	48.8	
Semi-urban	4	2	50.0	.625
Urban	22	8	36.4	
Marital Status				
Married	43	20	48.8	
Single	24	10	41.7	.702

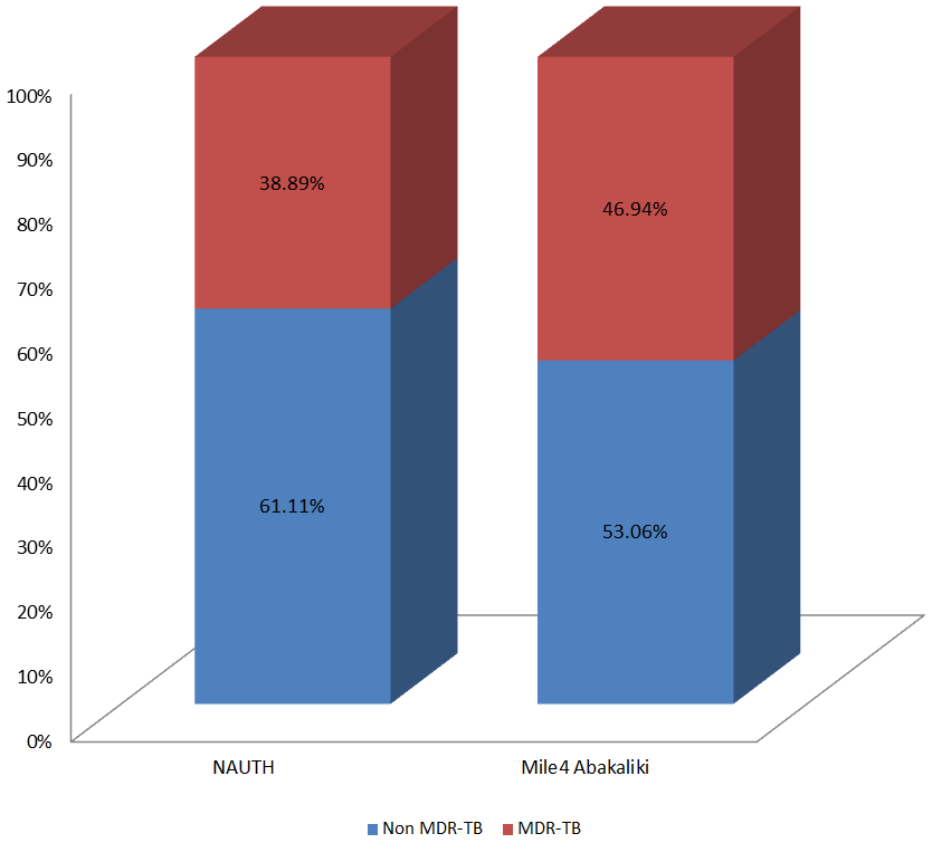

Figure 1. *Prevalence of MDR-TB in each Site.*

Abbreviations.
NonMDR-TB: Non multidrug resistance Tuberculosis.
MDR-TB: Multidrug resistance Tuberculosis.
NAUTH: NnamdiAzikiwe University Teaching Hospital.

4. Discussion

Multidrug-resistant tuberculosis (MDR-TB) has continued to be a challenge for tuberculosis control globally [14]. It has been observed that the main new barrier that challenges the control of TB is high burden of multidrug-resistant TB (MDR-TB). MDR-TB is a man-made problem due to poor management and quality of antituberculosis drugs and can be minimized by making tight identification of its predictors [15]. Though the major contributing factor identified for the spread of MDR-TB is poor infection control [7]. The result of this study showed high culture positivity rate demographically and this agrees with the report of [16] that stated 65.7% culture positivity rate in South-West Nigeria. Otu *et al.,* [17] reported that 100 out of 120 sputum samples were positive for *M. tuberculosis* on culture in a study in Calabar. This rate is however higher than the 33% culture positivity rate reported by [8]. In India, Guade *et al.,* [18] reported a lower culture positivity rate of 44%.

The high rate of TB culture positivity in this study could

be attributed to the pooled effect of analyzing samples from two centers with high population of pulmonary TB patients including referrals. Importantly, standard procedures were followed to avoid distortion of the organism; therefore samples were maintained in cold chain from collection until analysis at the laboratory. Samples were promptly couriered within 72 hrs to the testing laboratory. As a result, more of the acid fast bacilli contained in the samples were still viable at the time of culture and this reflected in the increased number of organisms isolated. Furthermore, the high rate could be due to the high proportion of the participants yet to commence treatment.

In patients receiving treatment, organisms may have lost their ability to grow on culture media; patients being treated with a rifampicin containing regimen often become culture negative by about the third week of treatment although they may still be sputum smear positive [18]. Lukoye *et al.,* [23] reported a 90.5% TB culture positivity in a national survey done in Uganda. In this survey also, 90.7% of patients enrolled were treatment naïve.

Demographically, age group 26-35 years had the highest proportion of positive results followed by age group 18-25. This age distribution of the culture positive results agrees with [8]. They reported that 65% of the culture positive results in their study at Nnewi were from age group 21-40 years. Also [16] reported that 45.8% of the culture positive results were from age group 25-34 years. Tuberculosis has been known to affect the economic (productive) age group [19]. The males in this study had a higher TB positivity rate than the females. This agrees with [8], who reported a statistically significant higher proportion of males with TB positive culture results than females in a study at NAUTH Nnewi. Also [17] reported that out of 100 cultures positive results in a study at Calabar 53 were from males. Das *et al.,* [20] reported that 72% of the culture positive results were from the males in a study in Odisha, India. This could be because men engage in more active lifestyle habits and are more to be seen in congregate settings like prisons.

The prevalence rate of MDR-TB in this study is similar to that reported by [21] in Georgia and [22] in Tanzania. It is however lower than that reported by [16] in South West Nigeria and [8] stated a lower rate of MDR-TB in Nnewi. The result of this study showed that level of education had a significant association with MDR-TB and this agrees with [18]. They reported that illiteracy contributed significantly to development of MDR-TB in India. Worthy of note, Illiteracy is always associated with ignorance and this could affect drug compliance. For instance many persons in our environment even in this century still believe that TB is a supernaturally acquired disease. They believe that TB is either due to spiritual invocations or as a result of harmful fetish practices of an aggrieved enemy. These set of individuals are more interested in assessing spiritual, herbal or traditional remedy. Even when they commence treatment in the hospital they do not hesitate to abandon their regimen for alternative unorthodox solutions and this could lead to treatment failure and exacerbation of illness.

5. Conclusion

Conclusively, MDR-TB is a major public health problem and mainly affects economically productive age group of the population as Age group 26-35 years showed the highest proportion of positive culture results (33.7%) followed by age group 18-25 (28.8%) years. The alarming increase in the prevalence of MDR-TB calls for intensified national TB control program and regulated treatment plan due to the fact that educational status was significantly associated with MDR-TB.

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