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Risk Factors Associated with Tuberculosis and the Impact of the Introduction of Genexpert on the Diagnosis of Tuberculosis in Presumptive cases of a Hospital in Nigeria

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Abstract

Objective: *To investigate the risk factors and impact of the introduction of XPERT MTB/RIF test on the diagnosis of pulmonary tuberculosis (TB) in presumptive cases in a General Hospital in Nigeria.*

Design and setting*: A retrospective study that examines the record of the hospital, from January, 2015 to December, 2017. A logistic regression analysis was utilized to identify the associated factors.*

Results*: There were total of 753 TB cases out of a total of 3639 people investigated. The rate of TB was 0.207. The multivariable regression analysis revealed that TB was significantly associated with all age groups: 15 -24 years [odds ratio (OR) = 5.316, 95% CI: 3.299 – 8.566], 25-34 years (OR = 4.584 95% CI: 2.899 – 7.248), 35 -44 years (OR = 4.388, 95% CI: 2.765 - 6.964), 45-54 years (OR = 3.044 95% CI: 1.875 - 4.940), 55 -64 years (OR = 2.165, 95% CI: 1.273 - 3.681) and >64 years (OR = 2.135, 95% CI: 1.201 - 3.793).*

HIV positivity (OR = 0.519, 95% CI: 0.411 – 0.655) and unknown HIV status (OR = 0.277, 95% CI: 0.197 – 0.390) and females, (OR = 0.437, 95% CI: 0.368-0.517), were less likely to have TB.

Conclusion*: Age group 25-54 is an independent predictor of positive tuberculosis results in presumptive cases.*

Keywords: *Xpert MTB/RIF, tuberculosis, risk factors, Nigeria.*

Introduction

Nigeria has a high burden of tuberculosis (TB). The country presently ranked 7th globally in new reported TB cases. Only India records higher number of death due to TB than Nigeria (WHO, 2018). The estimated incidence of TB as at 2017 in Nigeria was 407,000, with 115,000 dying due to TB, despite the availability of a very effective treatment for TB (WHO, 2018).

The national survey of TB of 2012 showed that males and those aged 45-54 have the highest TB ratios in Nigeria (NTBLCP, 2012). Almost half of them, (49%), reported taking treatment in general hospitals (NTBLCP, 2012). Most patients often take inappropriate action, which could be responsible for the continued transmission of TB (NTBLCP, 2012). Many of those who sought any form of care (37%), consulted the general hospitals (NTBLCP, 2012).

The report left a huge gap in the knowledge of TB in people <15 years in Nigeria. This, with poor case ascertainment, hamper the accurate quantification of the disease burden associated with childhood TB (Newton, Brent, Anderson, Whittaker, & Kampmann, 2008). Meanwhile, TB is increasingly contributing, and forming an important cause of global child morbidity and mortality. Despite this, childhood TB is still largely being underdiagnosed and underreported; as a result of the challenging diagnostic confirmation inherent in the paucibacillary nature of TB, and the difficulty in obtaining expectorated sputum from children (Marais, et al., 2006).

WHO recommended automated nucleic acid amplification test (NAAT); Xpert MTB/RIF (Xpert; Cepheid, Sunnyvale, California), for the diagnosis of HIV-associated and drug-resistant TB in adults (Boehme, Nabeta, Hillemann, & al., 2010; WHO, 2011). And by 2014, WHO further recommended its use as the initial diagnostic test in all children suspected of having TB (WHO, 2014).

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Presumptive TB refers to those with symptoms or signs suggestive of TB. This study, becomes significance because most presumptive TB patients in Nigeria, that sought treatment, have preference for General Hospitals. Hence, the reason why a General Hospital was the locale for this study.

Materials and methods

Study design and location

This is a retrospective study of presumptive TB patients of a General Hospital, in Lagos. The state is populated by 6.4% of Nigerians (LASG, 2018), yet it is burdened with about 9.4% of Nigeria TB cases (Adejumo, et al., 2017). This study is with the consent of the management of the hospital. Patients' consent was not sought at the time of data retrieval; hence, their identities were concealed. All patients investigated for TB between 2015 and 2017 were included. Xpert MTB/RIF was introduced as a first-line test at the hospital in March, 2016. Prior to this time, diagnosis of TB was done using Ziehl-Neelsen's method.

The study was designed to investigate the association of some risk factors and explore the impact of Xpert MTB/RIF. The risk factors studied are those recorded in the register of the laboratory. I included patients investigated using bacteriological test during a year (January – December, 2015); before Xpert MTB/RIF was introduced. During a transitional year: when bacteriological test was used (January 2016 - March 2016), and Xpert MTB/RIF method (April 2016 - December 2016). And during another year when patients were investigated using the Xpert MTB/RIF alone (January 2015 – December, 2017).

Data sources and inclusion criteria

All patients with TB symptoms were sent to the chest clinic for investigation and recording in the presumptive TB register. Patients referred from other TB treatment centres were excluded, so as to avoid double entry. The preference for laboratory register is because the data of those excluded, as per above, are kept there. All patients, of all ages, with known and unknown HIV status were included, except those with omitted ages and those unable to produce sputum or with extra pulmonary TB.

Statistical analysis

Data was analysed using SPSS 20.0 (Statistical Package for the Social Sciences, Chicago, Illinois) and presented as number of cases, mean ± standard deviation. The t-test, ANOVA and chi-square (χ^2) tests were used where applicable. Logistic regression analysis was employed to analyze the relationship between positive TB results and risk factors. A two-sided p value < 0.05 was considered significant for all analyses.

Results

Descriptive statistics

The mean age of TB negatives was 36.95 ± 17.30 years, which was significantly higher than TB positives (35.68 ± 14.05 years; $t = 2.07$, $p = 0.039$). Also, 513 of the 753 TB positives were males (68.1%), while 240 (31.9%) were females. The male to female ratio was 2.14:1.

Of the 714 TB positives investigated for HIV, 98 (13.7%) were positive, while 616 (86.3%) were negative. Another 39 (5.2%) have unknown HIV status. The average age of HIV positives was 37.45 ± 11.89 years, whereas that of HIV negatives was 36.51 ± 17.45 years ($t = 1.62$, $p = 0.105$).

The frequency of pulmonary TB and HIV

All patients were first seen at the out-patient department (OPD). During the study period, 218,705 patients were seen: 98,191 (44.9%) are males and 120,514 (55.1%) are females. The patients investigated during this period were 3639 with 753 positives for TB, a yield of 0.207 (753/3639). This rate is 0.362 (201/555) for 2015, 0.198 (238/1204) for 2016 and 0.167 (314/1880) for 2017. Overall, 1906 (52.4%) are males and 1733 (47.6%) are females. The overall ratio of male to female was 1.1:1.

The age groups with the highest frequency of TB positivity are: 25-34 (227), 35-44 (195) and 15-24 (132). TB positive cases increase annually for each age group, except for 45-54 and >64 age groups, with frequencies relatively same for 2015 and 2016. But astronomically increased for 2017 (Table 1).

Also, annually, TB positive cases were most in age groups: 25-34 (6.238%), 35-44 (5.359%) and 15-24 (3.627%). And also highest among 25-34 age group with a prevalence of 10.811% (2015), 5.897% (2016) and 5.106% (2017). The TB prevalence among <15 age group is 0.605% (Table 1).

Males are at a higher risk of having TB (Figure 1). The overall ratio of a male positive TB compared to their female counterparts is 2.14:1. Females (448) however, stand a higher risk of positive HIV than males (227) with a ratio 1.97:1. For HIV positives who also tested positive to TB, male (48) to female (50) ratio is almost 1:1. This is the trend for each of the year studied (Figure 1).

Logistic regression

In the univariate analysis of the relationship between positive TB and potential risk factors, multiple logistic regression model was employed. The following variables were used: Age (<15, 15-24, 25-34, 35-44, 45-54, 55-64 and >64); sex (male, female) and HIV status (negative, positive).

All the age groups: 15 -24 years [odds ratio (OR) = 5.316, 95% CI: 3.299 – 8.566], 25-34 years (OR = 4.584 95% CI: 2.899 – 7.248), 35 -44 years (OR = 4.388, 95% CI: 2.765 - 6.964), 45-54 years (OR = 3.044 95% CI: 1.875 - 4.940), 55 -64 years (OR = 2.165, 95% CI: 1.273 - 3.681) and >64 years (OR = 2.135, 95% CI: 1.201 - 3.793) were significantly associated with positive TB.

HIV positives (OR = 0.519, 95% CI: 0.411 – 0.655) and patients with unknown HIV status (OR = 0.277, 95% CI: 0.197 – 0.390) and females, (OR = 0.437, 95% CI: 0.368-0.517), were less likely to be TB positive (Table 2).

In a multivariate model, all the age groups: 15 -24 years (OR = 5.298, 95% CI: 3.267 - 8.591],

25-34 years (OR = 4.708 95% CI: 2.961 - 7.485), 35 -44 years (OR = 4.361, 95% CI: 2.732 - 6.963), 45-54 years (OR = 2.794, 95% CI: 1.710 - 4.563), 55 -64 years (OR = 2.100, 95% CI:

1.227 - 3.596) and >64 years (OR = 1.839, 95% CI: 1.028 - 3.291) remained significant (Table 2).

Discussion

The incidences of TB for 2015, 2016 and 2017 were 36.22%, 19.77% and 16.70%. An average rate of 20.7% for the periods. This is similar to the rates reported by similar studies in Nigeria. For example (Sani, Garba, Oyeleke, & Abalaka, 2015), reported 25.5% and (Egbe, Ike, & Aleruchi, 2016) reported 26.3%. This attested to the importance and great public health concern, this disease still poses in the area this study was conducted.

The drop in the incidence of TB, in 2016 and 2017 compared to 2015, was mainly because patients investigated in 2015 were those with a high suspicion of TB, whereas for 2016 and 2017, mere presence of any of the symptoms and signs of TB was enough for investigation.

Xpert MTB/RIF allowed processing of more samples; from other smaller centres to be processed at our laboratory, as well as making more HIV positives, with slightest suspicion of TB, to be investigated. This explains why of the 675 HIV positives investigated for TB, 15% were in 2015, 45% in 2016 and 40% in 2017. Positive TB and HIV patients are then visited at home or contacted on phone, so as to be initiated into appropriate treatments.

Xpert MTB/RIF also ensures that TB results become available within a few hours, unlike the previous average waiting time of 3 – 5 days when sputum smear microscopy method was the main diagnostic tool. This further explains the progressive increase in the number of cases investigated for 2016 (1:2.2) and 2017 (1:3.4) when compared to 2015. This is in line with the result from similar researches in other centers. For example, (Pereira, Barbosa, Dias, Almeida, & Silva, 2018), noticed a 1:2.0 increase pre - and post-Xpert MTB/RIF introduction in Brazil.

The highest prevalence was in the age group 25-34 years. This is contrary to the prevalence reported in the national survey of Nigeria where the highest estimate was in the 45-54 age group (NTBLCP, 2012). This difference may be because the survey was in 2012 and this study was between 2015 and 2017.

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There is an increase TB case finding by health workers, which made more presumptive cases to be referred to the laboratory. This is evident in the number of those investigated significantly increasing from 15% in 2015 to 45% in 2016 and 40% in 2017. Even, when there was no significant change in the number of patients seen at the OPD during the same period. Of the 218,705 patients: 70, 035 (32.0%) were seen in 2015, 70,304 (32.2%) in 2016 and 78,366 (35.8%) in 2017.

Also, the highest number of people investigated are in the age group 25-54 (62.2%), which had the lowest participation in the national survey (NTBLCP, 2012). This high participation rate, among this age group, was also observed in many similar studies, done after the national survey. For example (Egbe, Ike, & Aleruchi, 2016), observed 72.3% and (Nwachukwu, Onyeagba, Nwaugo, Ugbogu, & Ulasi, 2016) observed 75.1%. This further confirmed the increase efforts of health workers at case findings in Nigeria.

About seven out of ten positive TB are males (68.1%). The overall ratio of male to female positive TB is 2.14:1. This indicates a higher incidence of TB in males. It is consistent with the findings of the national survey (NTBLCP, 2012), and those of other similar studies (Dim & Dim, 2013; Igu, Enete, & Olaniyan, 2013; Egbe, Ike, & Aleruchi, 2016). Therefore, TB may be more prevalent in males in Nigeria. This may be because males socialize more at work and leisure than females and so are often more exposed to the risk factors of TB (Long, Johansson, Diwan, & Winkvist, 1999). Exposure of men to other risk factors of TB may also be responsible. For example: smoking, alcoholism, substance abuse and the nature of work (Nhamoyebonde & Leslie, 2014). Many new cases of TB have been attributed to these factors (WHO, 2018).

For Nigeria (WHO, 2018), further reported females accounting for more than 50% of the estimated incident TB cases and with a better prevalence to notification ratio (about 4) compared to men (about 6). A suggestion that women are accessing available diagnostic and treatment services more effectively than men. All these made (Horton, MacPherson, Houben, White, & Corbett, 2016) to suggest a need for strategies to improve access to and use of health services among men.

Also, 66.4% of positive HIV are women. This is significantly higher than the 58% of the Nigeria estimates for women (NACA, 2018). This may be because the hospital harbors the two busiest seaports in Nigeria, with many sex workers to satiate sea farers sexually. And HIV prevalence has been found to be higher among port workers (ITF, 2013) and sex workers (NACA, 2015), when compared to the general population.

Unlike in many similar studies (Swaminathan, et al., 2000; WHO, 2018), I observed a significant lower risk of positive TB among HIV positives. This may be because, many HIV positives are now placed on Isoniazid Preventive Therapy (IPT) for six months, alongside the antiretroviral therapy (ARV).

The mean age of positive TB, in this study, was significantly lower than negative TB. This may be because many young people in Nigeria are becoming jobless. According to (Statista, 2018), youth unemployment rate in Nigeria increased from 8.05% in 2015 to 13.41% in 2017. Youth unemployment may be a cause of hunger and malnutrition and increase the occurrence of certain diseases. For example (George, 1984), cited in (Ugai, Nwagbara, & Uyang, 2011) attributed it to the increased occurrence of Kwashiorkor in Ghana. Furthermore, malnutrition is known to have a conjoined relationship with TB (Macallan, 1999).

The prevalence of TB in <15 years, in this study, is lower than the global prevalence in this age group (WHO, 2018). This is due to the challenging diagnostic confirmation faced with the use of gastric aspirate to obtain expectorated sputum in children as noted by (Marais, et al., 2006). This is worsened by the delay in processing the expectorated sputum samples, since the recommendation is that, the processing should start by the bed side and not later than half an hour after collection (CITC, 2018). Another factor is the almost impracticability of making very small children to fast overnight before aspirate collection.

Conclusion

The main findings of this study are along the trend in previous studies. But other important results were also obtained. In my analysis, HIV positives were not at a higher risk of developing TB, malnutrition was probably more adduced. The incidence of TB in <15 years was found lower than the global average due to challenges observed in diagnostic process in children.

Recommendations

I will recommend based on the result of this study:

[1]. Improvement of the diagnosis of childhood TB. Alternative diagnostic methods, such as sputum induction and other non-invasive methods such as stool samples on Xpert MTB/ULTRA, etc. should be more explored. Since evidence is becoming abundant to suggest that there are still many childhood TB that remain undiagnosed.

[2]. The age groups most affected by the disease is the working-class group. This in effect, means reduction of needed manpower to improve the economy of the country. More jobs need to be created for these young people, so as to reduce malnutrition which has been established to be a serious contributory factor to an individual developing TB.

[3]. National TB programs should intensify case findings among males, since many studies have found higher prevalence among them.

[4]. Case findings among HIV positives, especially females, should also be intensified in areas with high HIV prevalence because of HIV being a known risk factor for the development of TB disease.

[5]. There should be an increase integration of TB diagnosis and treatment in: women's clinics, mother and child centres. This should include increasing TB awareness among women.

[6]. Establishment of strong contact tracing. As well as better involvement of community members in case finding.

[7]. Finding cases should be extended beyond HIV positives. Other risk factors are becoming increasingly important to the development of TB.

Limitations

This study is limited by several factors. First, is that the study was conducted in a General Hospital and so the result may not be generalizable to Lagos. I only used the data in the register of the laboratory. Therefore, the impact of the other proven risk factors was excluded. It is thus pertinent that future studies should explore these.

Tables

Table 1. Prevalence rates of pulmonary TB in the hospital laboratory, 2015-2017

	2015		2016		2017		
Factors	Investigated *N = 555*	Positive (%) N = 201	Investigated N = 1204	Positive (%) N = 238	Investigated N = 1880	Positive (%) N = 314	Total (Average Prevalence)
Age							
<15	7	2 (0.360)	101	8 (0.664)	217	12 (0.638)	22 (0.605)
15-24	76	37 (6.667)	147	44 (3.655)	251	51 (2.713)	132 (3.627)
25-34	142	60 (10.811)	312	71 (5.897)	455	96 (5.106)	227 (6.238)
35-44	150	53 (9.550)	269	61 (5.067)	388	81 (4.309)	195 (5.359)
45-54	91	30 (5.405)	182	28 (2.326)	274	41 (2.181)	99 (2.721)
55-64	60	11 (1.982)	118	19 (1.578)	168	17 (0.904)	47 (1.292)
>64	29	8 (1.441)	75	7 (0.581)	127	16 (0.851)	31 (0.852)

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Sex							
Male	338	137 (40.533)	605	161 (26.612)	963	215 (22.326)	513 (14.097)
Female	217	64 (29.493)	599	77 (12.855)	917	99 (10.769)	240 (6.595)
HIV Status							
Negative	332	169 (50.904)	861	200 (23.229)	1303	247 (18.956)	616 (16.928)
Positive	104	24 (23.077)	304	35 (11.513)	267	39 (14.607)	98 (2.693)
Unknown	119	8 (6.723)	39	3 (7.692)	310	28 (9.032)	39 (1.072)
Total number investigated							3639

Table 2. Multiple logistic regression for pulmonary TB in the hospital laboratory, 2015-2017

Factors	Total Investigated	Positive TB N (%)	Unadjusted OR (95% CI) Enter	p-value	HIV and Sex adjusted OR (95% CI)	p-value
Age Group (years)						
<15	325	22 (6.8)	1		1	
15-24	474	132 (27.9)	5.316 (3.299 – 8.566)	<0.001	5.298 (3.267 - 8.591)	<0.001
25-34	909	227 (25.0)	4.584 (2.899 – 7.248)	<0.001	4.708 (2.961 - 7.485)	<0.001
35-44	807	195 (24.2)	4.388 (2.765 - 6.964)	<0.001	4.361 (2.732 - 6.963)	<0.001
45-54	547	99 (18.1)	3.044 (1.875 - 4.940)	<0.001	2.794 (1.710 - 4.563)	<0.001
55-64	346	47 (13.6)	2.165 (1.273 - 3.681)	0.004	2.100 (1.227 - 3.596)	0.007
>64	*231*	31 (13.4)	2.135 (1.201 - 3.793	0.010	1.839 (1.028 - 3.291)	0.040
Sex						
Male	1906	513 (26.9)	1			
Female	1733	240 (13.9)	0.437 (0.368-0.517)	<0.001		
HIV Status						
Negative	2496	616 (24.7)	1			
Positive	675	98 (14.5)	0.519 (0.411 – 0.655)	<0.001		
Unknown	468	39 (8.3)	0.277 (0.197 – 0.390)	<0.001		

Figures

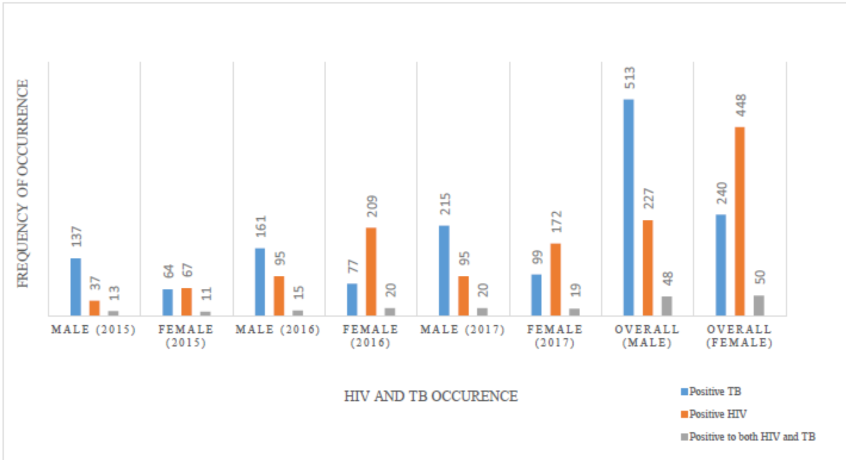

Figure 1. Sex distribution of frequency occurrence of positive TB and positive HIV in presumptive TB

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