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Confirmation of Symptomatic Tuberculosis Using Gene Xpert (MTB/RIF) among Patients within Zuru Emirate Council, Kebbi State, Nigeria

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Abstract

Tuberculosis (TB) is a bacterial infectious disease which is caused by Mycobacterium tuberculosis (MTB) and is spread from person to person via airborne droplets. It is among the 12 Global disease of epidemic importance that needs a periodic surveillance for better prevention and control. It primarily affects the lungs. Gene Xpert MTB/RIF (GXMR) is an automated, real-time polymerase chain reaction (PCR) test for detecting TB as well as rifampicin resistance (RIFR). It remains the only fully automated cartridge based test which can detect both TB and RIFR in less than two hours. This survey aimed at assessing GXMR among Symptomatic TB Patients within Zuru Emirate Council, Kebbi State. It was prospective cross-sectional survey conducted among 185 GXMR attendees at Martha Bamaiyi General Hospital Zuru. GXMR test was conducted for all the participants. IBM SPSS Statistics version 20 Statistical Software was used for statistical analysis. The prevalence of TB and RIFR were 32 (17.3%) and 0 (0%) respectively. Among sex, male had higher prevalence of 19 (59.4%) than female 13 (40.6%). For prevalence among age group, 15 (46.9%) was the highest in 25-34 years. Overall prevalence of HIV was 40 (21.62%) while the prevalence of HIV among TB positive patients was 4 (12.5%). Among the local government areas, Danko/Wasagu had the highest prevalence of 17 (53.1%) followed by Zuru 7 (21.9%) while Fakai and Sakaba were having the least prevalence of 4 (12.5%) respectively. The rural settlement had the highest prevalence of 18 (56.3%) while urban and semi-urban had 7 (21.85%) respectively. The study indicates the need to aggressively deploy personnel and chemotherapeutic facilities to cover the population in the area.

Keywords: Tuberculosis, Gene Xpert, Symptomatic, Patients and Resistance.

INTRODUCTION

Tuberculosis (TB) is an infectious bacterial disease caused by *Mycobacterium tuberculosis*-MTB(WHO, 2006). It is spread from person to person via airborne droplets through coughs or sneezes (Wang *et al.*, 2016). Inhalation of these bacteria is the most common mode of infection (WHO, 2006). TB primarily affects the lungs (causing pulmonary TB), but it can also affect other organs, e.g. central nervous system, lymphatic system, and circulatory system among others, resulting in extra pulmonary TB (Wang *et al.*, 2016).

About one-third of the human population is infected with the causative agent MTB(Joanne *et al.*, 2008). After establishing residence in immune system cells in the lung, it often remains in a dormant state until the host's immune system is compromised. The disease kills about 3 million people annually and is the direct cause of death for many AIDS patients. Predictably, MTB is becoming ever more drug resistant. Genome studies is of great importance in the fight to control the renewed spread of TB (Joanne *et al.*, 2008).

According to World Health Organization there were 8.6 million new TB cases in 2012 and even 1.3 million TB deaths. In the under-developed countries 95% of infections occur due to pitiable diagnostic and treatment facilities(Sajed *et al.*, 2014). It is estimated that approximately 70 million people will die from TB within next 20 years and it is because of inadequate measures for the TB control (Sajed *et al.*, 2014).

The newer tests for diagnosing TB are needed because of the difficulties associated with the test that are currently used both to diagnose as well as to detect drug resistance. Traditionally TB has been diagnosed through the use of chest X- ray, smear microscopy and through the culture. One of the most significant disadvantage of culture being the time that it takes and for sputum the matter of accuracy (Bhadke *et al.*, 2016).

The newer tests for diagnosing TB are needed because of the difficulties associated with the test that are currently used both to diagnose as well as to detect drug resistance (Bhadke *et al.*, 2016).

Multidrug resistance TB (MDR-TB) is an increasing concern globally and directly threatens disease-control efforts in many countries. Globally, 3.6 % of new TB cases and 20.2 % of previously treated cases are estimated to have MDR TB (Bhadke *et al.*, 2016).

Gene Xpert (MTB/RIF) is an automated, real-time polymerase chain reaction (PCR) test incorporating integrated sample processing, for detection of TB as well as resistance to Rifampicin. In 2010 the WHO endorsed Xpert as a replacement test for smear microscopy in patients suspected of HIV-associated TB or MDR-TB(Nicol *et al.*, 2013). The Gene Xpert system provides rapid results within 2 hours of specimen reception in the laboratory and WHO has advocated it as an initial diagnostic tool test in individuals suspected of MDR-TB or HIV-associated TB (Wang *et al.*, 2016).

In addition, conventional culture and drug susceptibility testing(DST) will be required to detect resistance to anti- TB agents other than Rifampicin. Because Xpert MTB/RIF detects resistance only to Rifampicin (WHO, 2014b).

The Xpert MTB/RIF assay remains the only fully automated cartridge based real-time DNA based test which can detect both TB and resistance to rifampicin in less than two hours, and the only mature technology representing a new generation of automated molecular diagnostic platforms (WHO, 2013). WHO has advocated it as an initial diagnostic tool test in individuals suspected of MDR-TB or HIV-associated TB (Wang *et al.*, 2016).

This research was aimed to Asses Gene Xpert (MTB/RIF) among Symptomatic TB Patients within Zuru Emirate Council attending Martha Bamaiyi General Hospital Zuru Kebbi State, North West geopolitical zone of Nigeria.

MATERIALS AND METHODS

StudyArea

This study was carried out among population of Zuru Emirate Council in Martha Bamaiyi General Hospital Tuberculosis Laboratory Zuru, Kebbi State, Nigeria between the periods of April-June 2018.

Study Design

This was a prospective cross-sectional study that was done in Martha Bamaiyi General Hospital Tuberculosis Laboratory Zuru, Kebbi State Nigeria.

Study population

This prospective cross-sectional study involves 185 GXMR attendeesat the Martha Bamaiyi General Hospital Tuberculosis Laboratory Zuru, Kebbi State Nigeria been the only center of GXMR within the Emirate Council between the period April-June 2018.GXMR test was conducted for all the participants.

The sample size was determined using the following equation as described by (Naing *et al.*, 2006).

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where;

n= sample size

z= statistics for a level of 95% confidence interval =1.96

p= prevalence rate at 26.3% (0.263) Nassarawa State (Kingsley *et al.*, 2016)

d= precision (allowable error) = 5% = 0.05

Therefore;

$$n = \frac{1.96^2 \times 0.263(1-0.263)}{(0.05)^2}$$

$$n = \frac{3.8416 \times 0.263 \times 0.737}{0.0025}$$

n=297.85

n=298 samples

The calculated sample size was 298. To minimize error and make it balance 185 samples was used for the study. The age range was from 0-65 years and above. They are farmers, businessmen and civil servants.

Inclusion Criteria

All unconfirmed symptomatic TB patients within Zuru Emirate Council that underwent Gene Xpert test at Martha Bamaiyi General Hospital, Zuru Kebbi State within the research period.

Exclusion Criteria

All asymptomatic TB patients within and outside Zuru Emirate Council that did not participated in Gene Xpert test at Martha Bamaiyi General Hospital, Zuru Kebbi State within the research period.

Sample Collection

All the participants were given appropriate serial numbers for easy identification. Moreover, each patient was given two (2) clean, sterilized and appropriately labeled specimen bottles for the collection of early morning and on the spot sputum samples. The samples were then collected in such a way that they corresponded with the patients' serial number on the form. Patients were advised neither to add saliva nor particles to the sputum. Relevant socio-demographic data were also collected from patients; age, gender, settlement and local government area.

Sample Processing

Xpert MTB/RIF cartridges [source; Federal Ministry of Health (National Tuberculosis and Leprosy Control Program), cartridge lot number; 23818 and 23822, expiry date; 25-11-2019 and 01-12-2019 respectively] were labeled with the corresponding specimen ID. One milliliter expectorated sputum was transferred to a conical, screw-capped tube using a sterile transfer pipette. Two milliliter Xpert MTB/RIF Sample Reagent (2:1) was added to the expectorated sputum using a sterile transfer pipette. The lid was replaced, and the tube was shaken vigorously for 10-20 times. The tube was allowed to stand upright for 5 minutes at room temperature and again the tube was shaken vigorously for 10-20 times (Bhadke *et al.*, 2016). The tube was allowed to stand upright for another 10 minutes at room temperature. Then sputum were allowed to liquefy with no visible clumps of sputum. The Xpert MTB/RIF cartridge lid was opened. Using the sterile transfer pipette, the liquefied specimen was aspirated into the transfer pipette until the meniscus is above the minimum mark and the sample was transferred into the open port of the Xpert MTB/RIF cartridge. The cartridge lid was closed and the test was started as per Gene Xpert System manufacturer instruction (Bhadke *et al.*, 2016). Results were obtained within 2 hours (Shukla *et al.*, 2017). Positive results display; MTB detected RIF not detected, MTB detected RIF detected, MTB detected RIF indeterminate while, negative result display MTB not detected RIF not detected.

Data Analysis

The data obtained were analyzedusing IBM SPSS STATISTICS VERSION 20to calculate percentages (%), tables and graph and Microsoft Excel 2010 was used for pie chart.

Ethical Approval

Ethical approval was obtained from the Hospital Ethical Committee; Kebbi State Ministry of Health with reference number SMOH/42/S/5/4679, also individual consent from eachpatient was assured of anonymity and confidentiality.

RESULTS

Table 1 shows the total number of TB and RIFR patients examined for Assessment of Symptomatic Tuberculosis using Gene Xpert (MTB/RIF) among Patients within Zuru Emirate Council, Kebbi State, Nigeria. Out of 185 patients screened, 32 (17.3%) emerged positive and 153 (82.7%) emerged negative. Therefore the prevalence of TB within the study area was 17.3%. Figure 1 represents the prevalence of TB sex distribution which was found to be highest among males with 59.4% and that of female with 40.6% infection.

Table 1. The Overall Prevalence of Tuberculosis and RIF Resistance in the Samples Examined

Sputum Samples	Tuberculosis (%)	Rifampicin Resistance (%)
Positive samples	32 (17.3)	0
Negative samples	153 (82.7)	0
Total	**185 (100)**	**0**

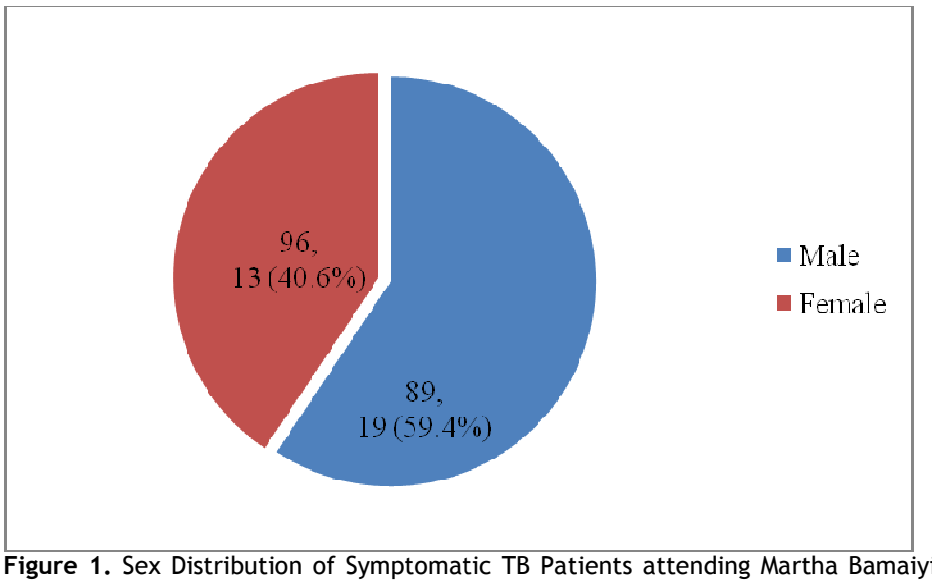

Figure 1. Sex Distribution of Symptomatic TB Patients attending Martha Bamaiyi General Hospital ZuruKebbiState

Table 2 shows the prevalence of TB in relation to Settlements. Those in the Rural settlement had the highest percentage of occurrence (positive results) 18 (56.3%). Followed by the Semi-Urban and urban which are having the same number of patients positive 7 (21.85%). None of the settlements examined were positive to RIFR. Table 2 presents the prevalence of TB and RIF resistance based on the LGAs within the study area, where Danko/Wasagu was found to have high prevalence with 53.1% positive followed by Zuru with 21.9% out of 55 patients, the least was found among Fakai and Sakaba with 12.5% out of 19 and 7 patients respectively while RIF resistance was not detected.

Table 2. Prevalence of Tuberculosis by Socio-Demographic data of Symptomatic TB Patients attending Martha Bamaiyi General Hospital Zuru, Kebbi State

Variables	Frequency	Number of Positive (%)
Settlements		
Rural	96	18(56.3)
Semi-urban	35	7(21.85)
Urban	54	7(21.85)
Local Government Areas		
Danko-Wasagu	104	17(53.1)
Fakai	19	4(12.5)
Sakaba	7	4(12.5)
Zuru	55	7(21.9)

Figure 2 shows the prevalence of TB among age groups, the group which falls between 25-34 was recorded the highest 15 (46.9%) during the study followed by the age group of 35-44 6 (18.8%) and the least was among age group 55-64 2 (6.3%). The prevalence rate of HIV in Zuru Emirate Council in this study was 21.62%, 40 of the 185 patients tested positive to HIV as shown on Table 3. From Table 4, out of the 32 samples that tested positive for tuberculosis, 4 (12.5%) were HIV positive. While, 28 (87.5%) were HIV negative. Also those resistant to RIF were 0 (0%).

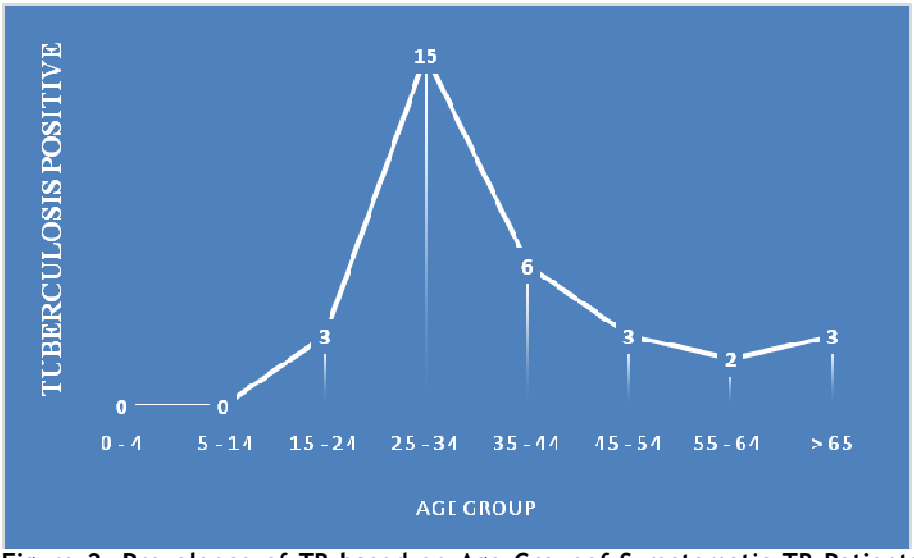

Figure 2. Prevalence of TB based on Age Groupof Symptomatic TB Patients attending Martha Bamaiyi General Hospital ZuruKebbi State

Table 3. The Overall Prevalence of HIV Status among Symptomatic TB Patients attending Martha Bamaiyi General Hospital Zuru, Kebbi State from Samples Examined

Samples examined	Frequency	Percentage (%)
Positive samples	40	21.62
Negative samples	145	78.38
Total	**185**	**100.00**

Table 4. Prevalence of Tuberculosis among HIV Positive Patients at Martha Bamaiyi General Hospital Zuru, Kebbi State

HIV STATUS	Tuberculosis Positive (%) N = 32
HIV Positive	4 (12.5)
HIV Negative	28 (87.5)
Total	**32 (100)**

DISCUSSION

The overall prevalence of TB and RIF resistance were 32 (17.3%) and 0 (0%) respectively. In comparison with a study, similar study of Tuberculosis and Rifampicin Resistance among Patients Seeking Medical Care in Nasarawa State, Nigeria higher prevalence of TB to be 26.3% (Kingsley *et al.,* 2016). A closely related prevalence of 25.5% was reported in a study of Prevalence of Pulmonary Tuberculosis (PTB) in Minna and Suleja, Niger State, Nigeria (Oyeleke *et al.,* 2015). But the prevalence in this study was higher than the prevalence of 6.9% recorded in Ibadan, Nigeria (Kehinde and Okesola, 2010). The reasons for the higher prevalence of patients infected with TB found from this study could be as a result that the study was carried out in the Hospital that serves as a referral sites for other smaller hospitals who do not have DOTS services.

Accurate, rapid detection of *M. tuberculosis* and TB drug resistance is critical for improving patient care and decreasing TB transmission. Therefore Xpert MTB/RIF assay was used in detecting rifampicin resistance. Rifampicin resistance of 0.00% found in this study was contrary to the 7.0% reported in samples collected from Jos and Lagos, Nigeria (Dinic *et al.,* 2012). Another study in Calabar, Nigeria, reported a rifampicin resistance of 6%, although no patient was found with resistance to only rifampicin (Otu *et al.,* 2013). Furthermore, 6 (21%) patients had rifampicin resistance in Amritsar, India (Shukla *et al.,* 2017). Globally, 3.5% of new TB cases and 20.5% of previously treated cases are estimated to have MDR-TB, while the estimated percentage of new tuberculosis with MDR-TB in Nigeria is 2.9 (WHO, 2014a).

The prevalence in relation to gender showed that out of the 96 female that participated, 13 (40.6%) were positive for tuberculosis and out of 89 male that were screened, 19 (59.4%) were positive. Males were shown to have the highest prevalence of tuberculosis than the females. This could be as a result of behavioral attitude of males of this age group (25-34 years old) and in addition to this; higher prevalence could also be as a result of indiscriminate use of drug and its abuse. The findings of this research that men are more prone to TB than women agree with report of higher TB rate among men than women (WHO, 2014a). There is lack of information explaining the role of gender in *M. tuberculosis* transmission and why TB seems to occur more in men than women(WHO, 2014a). A higher TB rate in males was reported in Kenya (Nyamogoba *et al.,* 2012). This study is in line with an earlier reported works in Uyo, Port Harcourt and Ibadan of Akwa-Ibom, Rivers and Oyo states respectively (Alfred and Silas, 2005; Obioma *et al.,* 2011; Kehinde and Okesola, 2010). But this finding is not in agreement with a research done in Abia State of Nigeria (Nwachukwu *et al.,* 2009).

Those in the Rural settlement had the highest prevalence of TB 18 (56.3), urban and semi-urban are having 7 (21.85) respectively. The reasons for the high prevalence of Patients infected with TB in Rural settlement found from this study could be as a result that the study was carried out in the Hospital that serves as a referral sites for other smaller Hospitals who do not have Directly Observed Treatment short course (DOTS) services. It is quite far from the rural regions and also quite expensive. The prevalence of RIF resistance was 0% amongst all settlements.

The highest prevalence of tuberculosis based on Local Government Area was in Danko/Wasagu Local Government Area with 17 (53.1%) compared to that of Zuru 7 (21.9%). This may be due to urban migration, environmental factor, traditional believes, inadherence to drug intake. This study is closely related to the findings that reported the prevalence of TB in Minna 58.2%) and Suleja 41.7% (Oyeleke *et al.,* 2015).

The highest rate of tuberculosis was found within the age range of 25-34 years compared with all other age groups, this is represented in Figure 2. The high prevalence of tuberculosis among this age group could be as a result of increase in reproductive activities among this age group as they always refer to them as "reproductive age". Higher prevalence of infection at this age group could also be attributed to increase in outdoor activities, overcrowding in most of the settlements and poor personal hygiene. This findings agrees with the research done in Nassarawa state (Kingsley *et al.,* 2016). While this study is not in agreement with the findings of Okonko *et.,al,* (2012) that reported TB infection was higher in age group 40years and above. One striking observation is thatamong 185 patients 21.62 % were HIV positive.

This finding is closely related to the findings in Yavatmal, Maharashtra where 23.5 % HIV positive and 76.5% HIV negative were recorded (Bhadke *et al.*, 2016).

The co-infection prevalence rate of HIV among the TB patients was determined to be 12.5% as presented in Table 4. Among the 40 (21.62%) participants that tested HIV positive, 4 (12.5%) were HIV positive and 28 (87.5%) are HIV negative among TB positive patients. The prevalence of HIV and TB co-infection (12.5%) is similar to the findings of some studies conducted in Kano (Iliyasu and Babashani, 2009), 10.5% and 14.9% among children and adults respectively found in Sagamu (Daniel *et al.*, 2004; Daniel *et al.*, 2007). Elsewhere, 11.6% TB and HIV co-infection in Jamaica was reported (Akpaka *et al.*, 2006). Also, 11.4% was found in Northwest Ethiopia (Tadesse and Tadesse, 2013). In Western Kenya, 55.5% was reported (Nyamogoba *et al.*, 2012) and 8.6% in India (Rajam and Muhammad, 2013). The variation among co-infection of HIV and TB patient could be associated with differences in behavioral factors, ignorance/educational status, and poverty level in different geographical locations (Abiodun *et al.*, 2015; Jemikalajah and Okogun, 2009). The variation could be due to life style such as practice of polygamy, patronage of traditional birth attendants, poor sanitary/hygiene practices and crowded environment (Abiodun *et al.*, 2015; Jemikalajah and Okogun, 2009). The high prevalence of TB-HIV co-infection that occurs in area could be due to high level of poverty and destitute (Olaniran *et al.*, 2011). Furthermore, the immune system of the patient also play essential role in TB-HIV co-infection (Olaniran *et al.*, 2011). Balanced diet is recommended for the infected patients. The value in this study is also lower than prevalence of 5.3% that was reported among MDR-TB in HIV positive patients in Addis Ababa, Ethiopia (Eyob *et al.*, 2004). In contrast, 17.7% TB-HIV was reported in India (Chakraborty *et al.*, 2010). The high prevalence rate in India compared to the findings of this study could be due to the fact that India is the leading TB high burden nation as reported by WHO (Okorie *et al.*, 2016). The occurrence of positive RIF resistance-TB in HIV patients is an indication of poor infection control and implementation in hospital setting (Okorie *et al.*, 2016).

CONCLUSION

Current study reported that TB is still prevalent in Zuru, Kebbi State, Nigeria with more males exposed and higher prevalence of HIV positive patients. RIF resistance was not detected. Therefore, further research in the study area which will cover the whole year is recommended.

RECOMMENDATIONS

Educating and enlightening campaigns should be embarked by religious and traditional leaders on the risk of TB transmission and Early diagnosis with treatment. Creation of DOTS services with qualified staff should be done in all the rural areas of the Emirate Council.Further studies that will include more antibiotics are highly recommended. Based on period of Research and data obtained, RIF resistance was not detected. Therefore, further research in the study area which will cover the whole year is recommended.

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