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Prevalence of Multidrug-Resistant Tuberculosis (MDR-TB) and Laboratory Efficiency in Detection in Kano State, North West Nigeria, 2018

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Abstract

Background: *Multidrug-resistant tuberculosis (MDR-TB) is an increasing global problem. Good laboratory diagnosis is key to prompt treatment. This study aimed at assessing the laboratory performance in the multidrug-resistant tuberculosis (MDR-TB) control activities in Kano state, north west Nigeria, 2018.*

Methods: *We reviewed data and used a check list for assessment and analysis of secondary data of Kano state DR TB component of the state tuberculosis and leprosy control programme (STBLCP). The data was analyzed using Epi Info version 3.5.4 and Microsoft Excel 2007.*

Results: *Kano state in 2018 had a total of 37496 presumptive Mycobacterium tuberculosis (MTB) cases reported and 37496 (100%) tested. Of the 37496 presumptive MTB cases tested, 36641 (97.7%) were presumptive pulmonary MTB cases and 855 (2.3%) were presumptive extra pulmonary MTB cases. Of the 37496 tested, 33781 (90.1%) were MTB negative, 3715 (9.9%) MTB positive. Of the 3715 MTB positive cases, 3531 (95.0%) were MTB positive but drug sensitive (DS MTB), 140 (3.8 %) were MDR TB cases and 44 (1.2%) were indeterminate. Of the 140 MDR TB cases, 3 (2.1%) were <15 years of age, 137 (97.9%) were* ***≥15 years*** *age, 101 (72.1%) were males and 39 (27.8%) were females.*

Conclusions: *The laboratory performance of Kano state MDR-TB control programme activities is good with good detection rate and 100% testing rate. There is high number of MDR TB cases. Majority of MDR TB cases are males and aged* ***≥15 years of age.*** *There is need for the state TBLCP and partners to intensify community awareness on MDR TB*

Keywords: *Assessment, laboratory performance, Multidrug-resistant tuberculosis, Kano state, north west Nigeria.*

Introduction

Tuberculosis (TB) kills almost 30,000 people each week. The disease is caused by *Mycobacterium tuberculosis (Mtb),* which is transmitted through the air from person to person. Currently, more than two billion people, nearly one-third of the world's population, are estimated to be infected with *Mtb* (latent TB) and are at risk of developing the disease. TB is curable, but inappropriate treatment can lead to multidrug-resistant TB (MDR-TB), which is resistant to the two most effective anti-TB drugs, and extensively drug-resistant TB (XDR-TB), which is resistant to many anti-TB drugs [1, 2].

Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDRTB) increasingly occur in resource-constrained settings. In the context of a national response to MDR- and XDR-TB, health workers in TB clinics (in district hospitals and some accredited health centers) will need to diagnose MDR-TB, initiate second-line anti-TB drugs, and monitor MDR-TB treatment [3]. This year alone, more than 480,000 people will develop MDR-TB (including XDR-TB).1 Fewer than 20 percent of individuals with MDR-TB access treatment; of that small fraction, fewer than half are cured, due to health systems that are unable to appropriately diagnose and treat the disease [4].

Multidrug-resistant tuberculosis (MDR-TB) is an increasing global problem, with most cases arising from a mixture of physician error and patient non-compliance during treatment of susceptible

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TB. The extent and burden of MDR-TB varies significantly from country to country and region to region. As with TB itself, the overwhelming burden of MDR-TB is in high-burden resource-poor countries. The diagnosis depends on confirming the drug susceptibility pattern of isolated organisms, which is often only possible in resource-rich settings. There should be a strong suspicion of drug resistance, including MDR-TB, in persons with a history of prior treatment or in treatment failure cases. Culture is the gold standard method and drug sensitivity testing (DST) can be done but it is costly and therefore unavailable in most sites. There is also the risk of contamination and prolonged turnaround time due to the slow growth rate of the TB bacilli [5]. Available newer and faster methods like MODS (Microscopic Observation Drug Susceptibility Assay), MGIT (Mycobacterium tuberculosis Growth Indicator Tube) and colorimetric assay all require specialized skills and bio-safety laboratories that are often unavailable in the regions where these methods are mostly needed. The gene Xpert machine (Xpert MTB/RIF Assay method) has the potential to revolutionize the diagnosis of TB based on its speed, sensitivity and specificity [6, 7]. Treatment in developed countries is expensive and involves an individualized regimen based on drug susceptibility data and use of reserve drugs. In resource-poor settings a WHO retreatment regimen may be used, but increasingly the move is to a directly observed treatment based 'DOTS-plus' regimen in a supported national TB programme. However, even where such treatment is given, the outcome for patients is significantly worse than that for fully susceptible TB and has a much higher cost [8].

Multidrug-resistant tuberculosis (MDR-TB) is tuberculosis due to organisms which show high-level resistance to both isoniazid and rifampicin, with or without resistance to other anti-TB drugs. The molecular basis of resistance to isoniazid and rifampicin (and some other drugs) is now largely understood. Resistance to isoniazid is due to mutations at one of two main sites, in either the *katG* or *inhA* genes [8, 9]. Resistance to rifampicin is nearly always due to point mutations in the *rpo* gene in the beta subunit of DNA-dependent RNA polymerase [10]. These mutations are not directly connected, and so separate mutations are required for organisms to change from a drug-susceptible isolate to MDR-TB. The accurate diagnosis of MDR-TB requires a positive culture of *Mycobacterium tuberculosis* and drug susceptibility testing. However, genetic probes which detect drug resistance to rifampicin with >95% accuracy are very suggestive of MDR-TB; <10% of rifampicin resistance is monoresistant, and so rifampicin resistance is a marker for MDR-TB in >90% of cases [11]. Because of its increasing prevalence MDR-TB is now subdivided into 'basic' MDR-TB, with resistance only to rifampicin and isoniazid, and 'MDR-TB-plus', with a similar resistance pattern but with resistance to one or more additional first- and/or second-line drugs. In MDR TB management, laboratory diagnosis is very important in identifying cases, initiating treatment and treatment monitoring of the MDR TB disease. Gene expert machine is the commonly used machine in Nigeria in MDR TB diagnosis [6]. We conducted an assessment study to assess the laboratory performance in the multidrug-resistant tuberculosis (MDR-TB) control activities in Kano state, north west Nigeria, 2018.

Methods

Study area

The study was conducted in Kano, the capital city of Kano State, north west Nigeria.[12]. Kano is very cosmopolitan and is reported to be the second most populous state in Nigeria after Lagos state with a total population of 12.6 million. Kano state is made up of 44 local government areas (LGAs), this is the highest in a single state in Nigeria. Each of the LGAs is made up of one tuberculosis leprosy supervisor (TBLS). The Cepheid Xpert MTB/RIF (*gene* Xpert) is the machine used for MDR TB diagnosis. The Nigerian north west zonal TB reference laboratory is also located at Kano state.

Study design

This is a cross-sectional descriptive study that included the use of a check list for assessment and analysis of secondary data of Kano state DR TB component of the state tuberculosis and leprosy control programme (STBLCP).

Study population

The study population was all MDR TB patients identified in Kano state, north west Nigeria. Nigeria 2017.

Inclusion criteria

All presumptive Mycobacterium tuberculosis (MTB) cases identified by the Kano STBLCP in the year 2018. A presumptive TB is a patient who presents with symptoms or signs suggestive of TB (previously TB suspect).

Exclusion criteria

Those that did not test positive for RIF resistance or MDR TB positive on g*ene* Xpert.

Sample size determination

A laboratory data of 121 MDR TB cases was analysed.

Study instruments

We used the National Tuberculosis and Leprosy Control program (NTBLCP) line listing report for rifampicin (RIF) resistant TB cases forms, quarterly reporting form on Xpert MTB/RIF Assay.

Data management

We reviewed the MDR TB laboratory data of Kano state. This is a component of the state tuberculosis and leprosy control programme (STBLCP) data. The data was analyzed using Epi Info version 3.5.4 (US Centers for Disease Control and Prevention) and Microsoft Excel 2007.

Ethical considerations

Ethical clearance was obtained from the ethical review board, ministry of health, Kano state. Respect to participants' rights was observed including the right to refuse participation with explanation through participant's information form and provision of individual consent forms for the consent of the participants.

Limitations

This was a secondary analysis. A few of the data were missing. However, that was not significant to impact on the data. This study mainly focused on the assessment of the laboratory performance. The process of tracing patients from MDR-TB detection to enrollment in treatment, detection rates and treatment success rates were not assessed. Thus, these data may not reflect the overall effects of MDR-TB control.

Results

Kano state had 18 Cepheid Xpert MTB/RIF (*gene Xpert*) machines used for MDR TB diagnosis 15 different MDR TB diagnosis sites of the state. As at 2018 The Nigerian north west zonal TB reference laboratory also located in Kano state had in addition to gene Xpert machine, the line probe assay and MDR TB culture facilities.

Analysis of the laboratory result of tuberculosis in Kano state in 2018 showed that a total of 37496 presumptive Mycobacterium tuberculosis (MTB) cases were reported and 37496 (100%) tested. Of the 37496 presumptive MTB cases reported, 36641 (97.7%) were presumptive pulmonary MTB cases and 855 (2.3%) were presumptive extra pulmonary MTB cases (Fig 1).

Of the 37496 reported cases, 33781 (90.1%) had no MTB detected (MTB negative), 3715 (9.9%) had MTB detected (MTB positive). Of the 3715 MTB positive cases, 3531 (95.0%) had MTB detected (MTB positive) but not RIF (rifampicin) resistant (RR) i.e. drug sensitive (DS MTB), 140 (3.8%) had MTB detected (MTB positive) with RR (MDR TB cases) and 44 (1.2%) MTB detected (MTB positive) but with RR indeterminate (Fig 2).

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Of the 3531 MTB positive cases, 3119 (88.3%) were pulmonary MTB cases and 412 (11.7%) extra pulmonary MTB cases. Of the 140 MDR TB cases, 140 (100%) were pulmonary MTB cases. None of the MDR TB cases was extra pulmonary MTB cases (Fig 3).

Of the total 37496 presumptive Mycobacterium tuberculosis (MTB) cases that were reported and tested, 6165 (16.4%) were <5 years of age, 31331 (83.6%) were ≥15 years age, 19275 (51.4%) were males and 18225 (48.6%) were females. Of the 140 MDR TB cases, 3 (2.1%) were <15 years of age, 137 (97.9%) were ≥15 years age, 101 (72.1%) were males and 39 (27.8%) were females (Table 1).

Discussion

Our study found the laboratory performance laboratory performance of the multidrug-resistant tuberculosis (MDR-TB) control programme activities in Kano state, north west Nigeria in 2018.good with all the 37496 presumptive Mycobacterium tuberculosis (MTB) cases were reported in the year tested. This implies 100% testing rate. For every reported presumptive Mycobacterium tuberculosis (MTB) case to be found tested, gives a clear indication of the capacity of the laboratory in the state to test every suspected MTB case as well as the MDR TB. This surely enables detection of cases for prompt enrollment and treatment. The gene Xpert machine (Xpert MTB/RIF Assay method) is highly recommended for MTB and MDR TB diagnosis. Most MDR TB diagnosis sites in Nigeria uses the gene Xpert machine (XpertMTB/RIF Assay method). Our study found by 2018, Kano state had 18 Cepheid Xpert MTB/RIF (*gene Xpert*) machines used for MDR TB diagnosis 15 different MDR TB diagnosis sites of the state. This is good for the state to enable ease detection of MDR TB cases. However, the population dynamics of Kano state where the is the most populated in Nigeria with a total population of 12.6 million [12, 13], more of the gene Xpert machines might be required. In addition to the 18 gene Xperts that Kano state has, the state also has a line probe and MDR TB culture facility located at Aminu Kano Teaching Hospital (AKTH), Kano state. This is the location of the Nigerian north west zonal TB reference laboratory. This Nigerian north west zonal TB reference laboratory serves the entire northwest Nigeria and such, presumptive MTB and MDR TB patients or laboratory samples are referred to the laboratory for analysis. The location of this reference laboratory in Kano state serve a lot of advantage to the MDR TB control programme of the state as the line probe and MDR TB culture facilities helps further screen patients for MDR TB and extensively drug resistant tuberculosis (XDR TB) after analysis by gene Xpert, where the need may arise.

We found of the 37496 presumptive MTB cases reported, 36641 (97.7%) were presumptive pulmonary MTB cases. This implies more than 95% of the presumptive MTB cases reported were presumptive pulmonary MTB cases. Whereas only about 2% were presumptive extra pulmonary MTB cases. Also, our study found of the 3531 MTB positive cases, 88.3% were pulmonary MTB cases while 11.7% were extra pulmonary MTB cases. However, all 140 MDR TB cases found in the study were pulmonary MTB cases. None of the MDR TB cases was extra pulmonary MTB case. Pulmonary MTB usually account for most of MTB Cases however extra pulmonary MTB is said to be on the raise as extra pulmonary MTB accounted for more than 11% of the MTB cases. After primary infection, TB may reactivate at anytime and anywhere in the body. Recent studies have suggested that the sites of extra-pulmonary tuberculosis (EPTB) may vary according to geographic location and population [14]. Clinical manifestations of TB are variable and depend on a number of factors that are related to the microbe, the host and the environment [15]. Our understanding of the role of host-related factors responsible for the occurrence of TB at extra-pulmonary sites is limited. Some studies have reported that the proportion of TB that is EPTB is on the rise due to the HIV epidemic [16] and possibly also improvement in diagnostic facilities [17]. Some studies have examined the role of host-related factors on the risk of development of EPTB.

Majority of more than 83% of the total 37496 presumptive Mycobacterium tuberculosis (MTB) cases that were reported and tested were **≥15 years** of age while 16.4%. Also, more than 97% of the 140 MDR TB cases found in the study were ≥15 while only about 2% were <5 years of age. Higher age is associated with MTB infection but this seem to be more of the pulmonary MTB. But for extra pulmonary MTB, younger people are said to be more at risk [18]. We also found majority of the presumptive Mycobacterium tuberculosis (MTB) cases that were reported and tested were males. Also, was the case for the MDR TB cases with males accounting for more than 72%. Male MDR TB

preponderance was also reported from other previous studies in Nigeria [19, 20]. A similar study somewhere in Nepal found the overall male to female ratio of MTB cases was 1.6 (289/185). For extra pulmonary MTB patients, the male to female ratio was 1.07 (119/111), but 2.29 (170/74) for pulmonary MTB patients. The difference was statistically significant ($p < 0.001$) [18]. The male to female ratio is marginal among the extra pulmonary MTB unlike in the cases of pulmonary MTB.

Our study is limited such that the findings may not reflect the overall effects of MDR-TB control study. Our study mainly focused assessment of laboratory performance in the MDR TB control activities. Detection rates and treatment success rates were not assessed.

Conclusions

We conclude that the laboratory performance of the multidrug-resistant tuberculosis (MDR-TB) control programme activities in Kano state, north west Nigeria in 2018.is good with good detection rate and 100% testing rate. There is high number of MDR TB cases. Majority of the presumptive Mycobacterium tuberculosis (MTB) cases, MTB positive cases, MDR TB cases are males and aged **≥15 years of age.** There is need for the state tuberculosis and leprosy control programme (TBLCP) and partners to intensify community awareness on MDR TB

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Tables and figures

Table 1: Showing the number of presumptive MTB cases and MDR TB cases by sex and age, Kano state, north west Nigeria, 2018

	Total presumptive MTB cases tested			**MDR TB cases**		
Sex	**Total**	**<15 years**	**≥15 years**	**Total**	**<15 years**	**≥15 years**
Male	19271 (51.4%)	3120 (8.3%)	16151 (43.1%)	101 (72.1%)	2 (1.4%)	99 (70.7%)
Female	18225 (48.6%)	3045 (8.1%)	15180 (40.5%)	39 (27.9%)	1 (0.7%)	38 (27.1%)
Total	37496 (100%)	6165 (16.4%)	31331 (83.6%)	140 (100%)	3 (2.1%)	137 (97.9%)

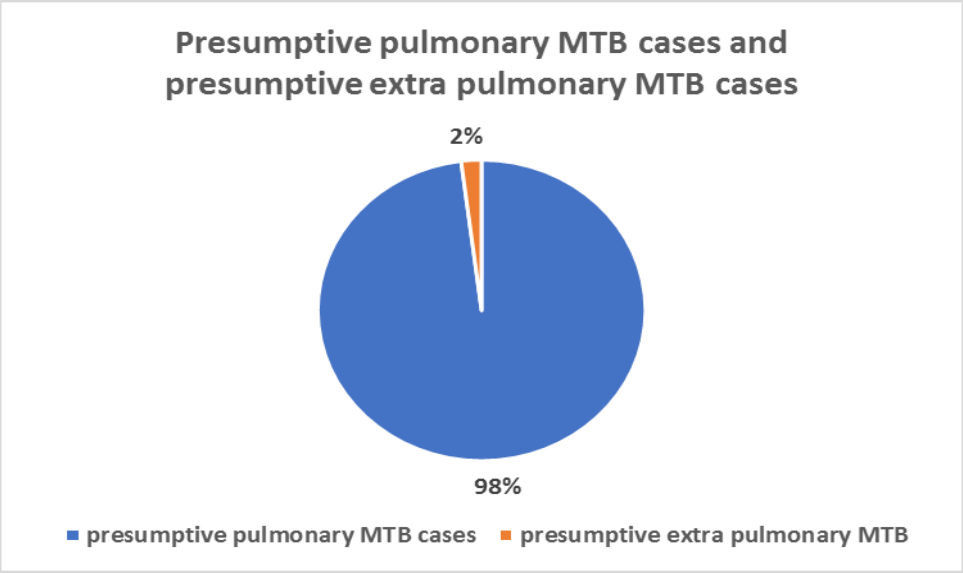

Figure 1. Showing the proportion of presumptive pulmonary MTB and presumptive extra pulmonary MTB cases, Kano state, north west Nigeria, 2018

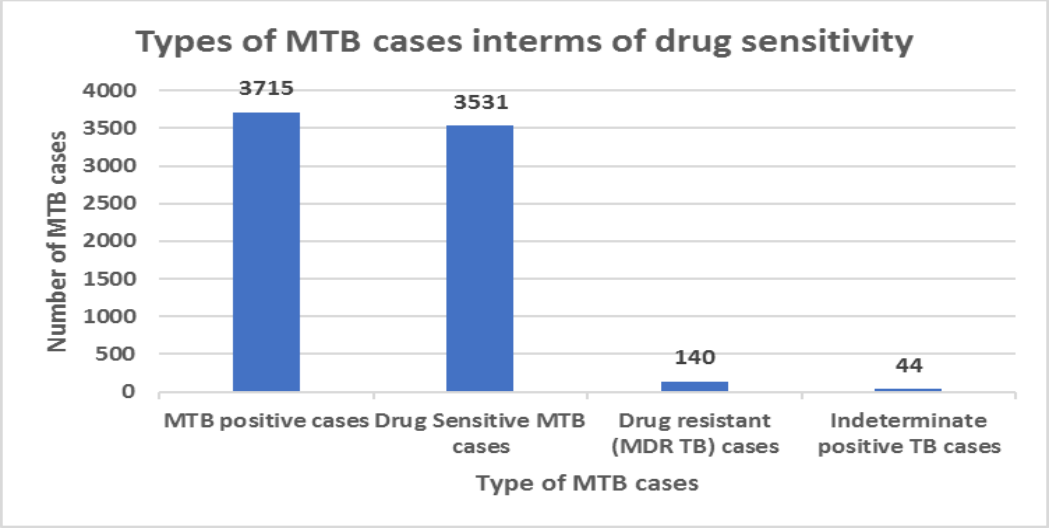

Figure 2. Showing the total MTB cases, drug sensitive cases, drug resistant (MDR) cases and the indeterminate MTB positive cases, Kano state, north west Nigeria, 2018

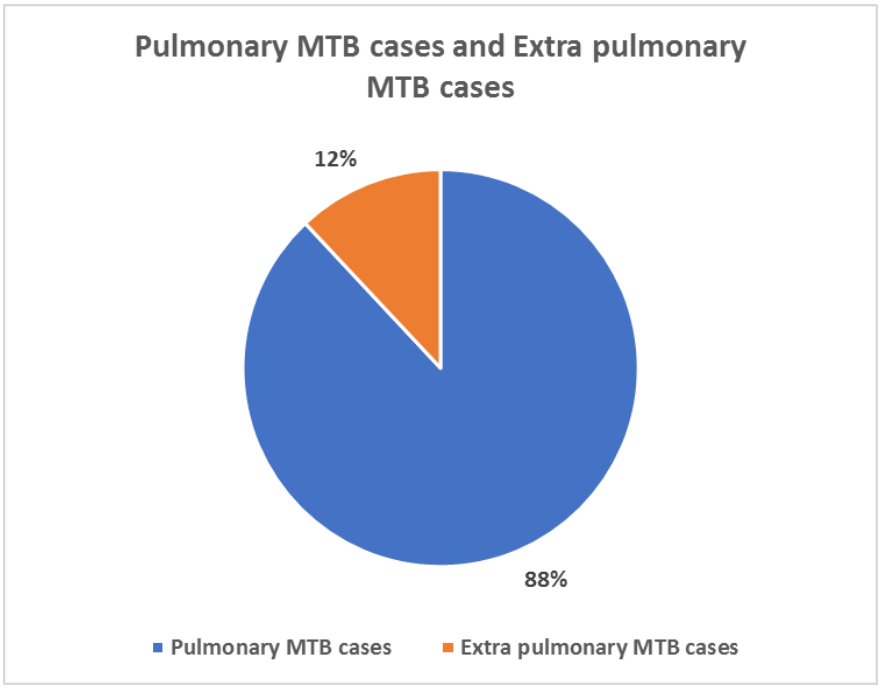

Figure 3. Showing the proportion of pulmonary MTB and extra pulmonary MTB cases, Kano state, north west Nigeria, 2018