

## Multidrug-Resistant Tuberculosis (MDR-TB) Control Activities in Kano State, North West Nigeria: Progress so Far

Article by Musa K. Bawa<sup>1</sup>, Mustapha Mukhtar<sup>2</sup>, Ado Umar<sup>3</sup>

<sup>1</sup>African Field Epidemiology Network (AFENET), Abuja, Nigeria

<sup>2</sup>Bayero University Kano, Nigeria

<sup>3</sup>Aminu Kano Teaching Hospital, Bayero University Kano, Nigeria

E-mail: musabawa56@yahoo.com<sup>1</sup>, mmukhtar.eco@buk.edu.ng<sup>2</sup>, adoumar2014@gmail.com<sup>3</sup>

### Abstract

**Background.** The emergence of MDR TB poses a great treat to global health. Progress in response to the global MDR/RR-TB crisis is dismal. There is need to intensify efforts.

**Methods** We mapped the gene experts in Kano state. We reviewed the MDR-TB patients line list using the National tuberculosis and leprosy control program (TBLCP) line listing template. The data was analyzed using Epi Info version 3.5.4 and Microsoft Excel 2007.

**Results** The number of Cepheid gene Xpert machines increased from 1 in 2013 to 18 in 15 (34.1%) of the 44 LGAs in 2018. A total of 288 MDR TB cases were managed in 2017 and 2018 in Kano state, of which 262 (90.1%) were cases identified within the 2 years, 26 (9.0%) were referred in from other states. Of the 288 cases managed, 225 (78.1%) were enrolled, 6 (2.1%), died, 8 (2.7%) refused enrollment and 18 (6.3%) loss to follow up. Of the 68151 reported and tested cases, 60479 (88.7%) were MTB negative, 7672 (11.3%) were MTB positive. Of the 7672 MTB positive cases, 7313 (95.3%) were drug sensitive (DS MTB), 280 (3.7%) were MDR TB and 79 (1.0%) were indeterminate.

**Conclusions** We conclude that there is progress in the MDR TB control program of Kano state with number of gene Xpert machines increased over time. We found improvement in MDR TB enrollment rate by 24.4% from 2017 to 2018. However, there is need to intensify tracking of MDR TB cases for enrollment.

**Keywords:** Multidrug-resistant tuberculosis (MDR-TB), control, progress, Kano state, north west Nigeria.

### Introduction

Global declines in tuberculosis incidence provide evidence that political commitment together with aggressive plans to curb the disease can make a difference [1]. These efforts not only stopped the upward spiral of tuberculosis incidence but reversed the trend. The World Health Organization (WHO) has now set targets to end tuberculosis by 2035 and is directing efforts at accelerating the rate of decline, with the expectation of reducing the incidence rate by 90% and mortality by 95% compared to levels in 2015 [2]. The greatest disaster that can happen to a patient with tuberculosis is that his organisms become resistant to two or more of the standard drugs [3]. Drug resistance poses serious threat to the global health because it requires treatment for a long period of time, frequent hospitalization and subsequent higher cost of treatment and results in a considerable number of mortalities. Treatment of drug resistant tuberculosis is difficult because second line drugs must be used which are less potent than the first line and are not as well tolerated [4-5].

The National Tuberculosis and Leprosy Control Programme (NTBLCP) was established in 1989 by the Government of Nigeria to coordinate TB and leprosy control efforts in Nigeria. The emergence of MDR TB is a great concern in Nigeria [6]. MDR TB was described in Nigeria as early as 1976 by Fawcett in Zaria. Since then, there have been other reports of TDR in various parts of the country using mycobacterial culture and drug susceptibility test [7-8]. A lot of progress has been made in TB and MDR TB, however, there has been set back in the achievement by the increasing occurrence of MDR TB cases. Several factors threaten the potential to realize these targets, and key among these is drug resistant tuberculosis [9]. Unfortunately, much like the global situation, drug resistant tuberculosis in Africa is largely missed with 93 000 cases estimated in 2016, while only 27 828 (30%)

were diagnosed. Even when the diagnosis is made, only 59% achieve a successful treatment outcome [10].

Progress in response to the global MDR/RR-TB crisis is dismal. M/XDR-TB constitutes both a public health and international health security crisis which requires urgent, innovative and sustained interventions involving multiple state and non-state sectors. Unfortunately, the essential political will – which should translate into adequate financial and human resources to address the MDR/RR-TB crisis – is lacking in many countries, often those hardest hit by the epidemic. Complacency about TB as an “ancient” disease and reluctance by policy-makers to embrace innovations (notably rapid diagnostics and new drugs) threaten the strides made in TB control over the last ten years and poses a major barrier to containing and reversing the MDR/RR-TB crisis [11]. As with all TB, 99% of MDR-TB occurs in high-burden resource-poor countries. However, increasing globalization and population mobility will mean an increase in MDR-TB cases in developed countries. It is clear that without both political will and money, the number of cases of MDR-TB in both developed and developing countries will continue to rise. It is also clear that, in the long term, the costs of inaction are likely to be greater than those of action. We conducted a descriptive correctional study to assess progress of MDR TB control in Kano state, north west Nigeria.

## **Methods**

### **Study area**

The study was conducted in Kano state, the capital city of Kano State, north west Nigeria.[12]. Kano state tuberculosis and leprosy control programme (STBLCP) which coordinates tuberculosis control activities in the state is located at the state infectious disease hospital (IDH) domiciled under the state ministry of health. 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. The state is made up of 44 local government areas (LGAs), the highest in Nigeria. The Nigerian north west zonal TB reference laboratory is also located at Kano state.

### **Study design**

This is a descriptive cross-sectional study. The study included the profiling of the personnel of the state tuberculosis and leprosy control programme (STBLCP) and the availability of gene Xpert machines in the state.

### **Study scope**

The study scope was Kano state TBLCP activities for 2017 to 2018.

### **Study population**

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

### **Inclusion criteria**

All MDR-TB patients identified by the Kano STBLCP in 2017 and 2018.

### **Exclusion criteria**

Those that did not test positive for RIF resistance or MDR TB positive on gene Xpert.

### **Sample size determination**

A data of a total of 68007 suspected Mycobacterium tuberculosis (MTB) cases was analyzed.

### **Study instruments**

We used the National Tuberculosis and Leprosy Control program (NTBLCP) line listing report for suspected Mycobacterium tuberculosis (MTB) cases and rifampicin (RIF) resistant TB cases forms, quarterly reporting form for presumptive and confirmed TB form, RIF resistant cases managed by the state in the previous year, RIF resistant cases managed by state in the quarter under review, line listing

of each RIF resistant cases enrolled on 2<sup>nd</sup> line DR TB treatment in the community, line listing of each RIF resistant cases referred to the treatment center enrollment on 2<sup>nd</sup> line DR TB treatment forms. We used a structured checklist to profile the personnel of the state tuberculosis and leprosy control programme (STBLCP) and the availability of gene Xpert machines in the state.

### Data management

We reviewed the data of Kano state MDR TB which 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 an assessment and secondary analysis. A few of the data were missing. However, that was not significant to impact on the data. Also, the study mainly focused on the progress in the process of tracing patients from MDR-TB detection to enrollment in treatment. Treatment success rates were not assessed. Thus, these data may not reflect the overall effects of MDR-TB control program.

### Results

The number of personnel supporting the state TBLCP is made up of 51 personnel. Of the 51 personnel, 7 (13.7%) are state officers including the MDR TB focal person (FP) and 44 (86.3%) are LGA TBLCP officers also referred to as LGA TBLCP supervisors. Assessment of the MDR TB diagnosis center showed that the number of Cepheid Xpert MTB/RIF (*gene Xpert*) machines used for MDR TB diagnosis has increased from 1 (2.3%) the of 44 LGAs in 2013 to 18 in 15 (34.1%) of the 44 LGAs in the state in 2018 (Fig 1).

A total of 288 MDR TB cases were managed in the years 2017 and 2018 in Kano state, of which 262 (90.1%) were cases identified within the 2 years, 26 (9.0%) were referred in from other states within the year. In the year 2017 and 2018, no MDR TB was transferred to another state. Of the 121 cases managed, 187 (64.9%) were males.

Sex distribution of the MDR TB cases showed male preponderance from Q1 to Q4. The highest male dominance was at Q3 where males accounted for 52 (67.5%) of the 77 MDR TB cases in the quarter. The least male dominance was in Q1 where males accounted for 33 (55.0%) of the 60 MDR TB cases (Fig 2).

Of the 288 cases managed in the years 2017 and 2018, 225 were enrolled giving an enrolment rate of 78.1%, 6 died before enrolment giving a death rate of 2.1%, 8 refused enrollment giving a refusal rate of 2.7% and 18 could not be tracked giving a loss to follow up of 6.3% (Table 1).

The MDR TB enrollment rate was higher in 2018 (88.1%) than in 2017 (66.6%) and that reflected across the quarters, Q1 to Q4. Trend of enrollment rate showed highest enrollment in 2017 (89.5%) and 2018 (100%) were both in Q3. The least enrollment rate in 2017 (17.9%) and 2018 (78.6%) were in Q4 (Fig 2).

Analysis of the laboratory result of tuberculosis in Kano state in 2017 to 2018 showed that a total of 68151 suspected Mycobacterium tuberculosis (MTB) cases were reported and 68151 (100%) tested. Of the 68151 reported cases, 60479 (88.7%) had no MTB detected (MTB negative), 7672 (11.3%) had MTB detected (MTB positive). Of the 7672 MTB positive cases, 7313 (95.3%) had MTB detected (MTB positive) but not RIF (rifampicin) resistant (RR) i.e. drug sensitive (DS MTB), 280 (3.7%) had MTB detected (MTB positive) with RR (MDR TB cases) and 79 (1.0%) MTB detected (MTB positive) but with RR indeterminate.

## Discussion

Our study found a good progress in the MDR TB control program of Kano state with number of Cepheid Xpert MTB/RIF (*gene Xpert*) machines used for MDR TB diagnosis has increased from only 1 LGA in 2013 to 18 in 15 of the 44 LGAs in the state in 2018. Also, all the suspected Mycobacterium tuberculosis (MTB) cases reported in the year 2017 to 2018 amounting 68151 were all tested giving the testing rate of 100%. More so, the enrollment rate of the MDR TB cases was seen to have improved from 2017 to 2018 with increase of 24.4%. In Nigeria and elsewhere, the gene Xpert machine is very critical in the MDR TB control programme.

The importance of the gene expert machine in the prompt diagnosis thereby enabling prompt treatment of MDR TB cannot be over emphasized. It is also important in the treatment monitoring of the MDR TB disease. 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 [13]. 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 [14].

The gene Xpert machine (XpertMTB/RIF Assay method) has the potential to revolutionize the diagnosis of TB based on its speed, sensitivity and specificity [15]. It is a cartridge-based automated diagnostic test that can, in less than 2 h, simultaneously detects Mycobacterium tuberculosis organisms as well as rifampicin resistance by using three specific primers and five unique molecular probes which ensure a high degree of specificity.

The use of sealed and disposable cartridges apparently overcomes the problem of cross contamination. There is minimal bio-hazard so that bio-safety cabinets are not compulsorily needed. The Xpert MDR/Rif assay method which is a nucleic acid amplification test (NAAT) based on the principle of polymerase chain reaction (PCR) has opened a new era of widespread molecular diagnosis of TB. Its hands-on operation is easy and requires minimal technical expertise [16].

It was developed by the laboratory of Professor David All of the University of Medicine and Dentistry of New Jersey together with Cepheid incorporation and FIND (Foundation of Innovative New Diagnostics) with additional financial support from the United States National Institute of Health (NIH), Bill and Melinda Gates Foundation [17]. The gene Xpert system was launched in 2004 while the first clinical validation studies were carried out in 2009 in some countries including South Africa and India, after which the machine was endorsed by WHO in 2010 for use in TB endemic countries [18].

With technical assistances of WHO, KNCVT Tuberculosis Foundation (TBCARE 1 Consortium) and international partners including Family Health international (FHI) 360 and Institute of Human Virology, Nigeria (IHVN), the National TB and Leprosy control Programme (NTBLCP) has been able to install the machine in a number of facilities across Nigeria [16].

In addition to high testing rate, our study found good MDT TB detection rate with 11.3% of the total 68151 suspected Mycobacterium tuberculosis (MTB) cases found with MTB detected (MTB positive) 3.7% had MTB detected (MTB positive) with RR 1.0% MTB detected (MTB positive) but with RR indeterminate. This shows it will be difficult for the MTB and MDR TB cases to be missed. However, for public health importance of MTB and MDR TB diseases, the percentage positivity is alarming as the diseases are accompanied with high level morbidity and mortality must especially the MDR TB. Patients with drug-resistant TB face agonizing, prolonged suffering and often permanent disability while on second-line treatment, together with devastating economic hardship, stigma and discrimination. On top of the clinical toll taken by M/XDR-TB treatment, patients often face catastrophic economic repercussions, pushing them into extreme poverty. Once treatment options are exhausted, patients and health services are confronted by numerous ethical, legal and human rights challenges, given ongoing airborne transmission of the disease with explosive outbreaks described in congregate settings [19].

Our study found male preponderance among the MDR TB cases. This reflected all through from Q1 to Q4 2017. male preponderance among the MDR TB cases may be associated with occupation

and culture as males are busier and move around more than females Male MDR TB preponderance was also reported from other previous studies in Nigeria [20]. Cultural practices and occupation that predisposes men may be responsible.

Our study found a death rate of 2.1%, enrollment refusal rate of 2.7% and 6.3% loss to follow up. While the death rates in 2017 and 2018 was equal, there was a reduced enrollment refusal rate and loss to follow up in 2018 compared to 2018. This shows improvement in tracking of cases and adherence of cases to enrollment. and tracking However, the findings underscores the dare need to sustain intensified MDR TB cases tracking, enrollment and monitoring. Kano state had a fair number of personnel supporting the state TBLCP at state and LGA levels. We found a number of MDR TB cases were referred in from other states within the period of the study but none was transferred to another state. This also demonstrate the ability of the state MDR TB control program to manage their cases and as well support other states.

Our study is limited such that the findings may not reflect the overall effects of MDR-TB control study. We mainly focused on the process of tracing patients from MDR-TB detection to enrollment in treatment. Treatment success rates were not assessed.

## Conclusions

We conclude that there is a good progress in the MDR TB control program of Kano state with number of Cepheid Xpert MTB/RIF (*gene Xpert*) machines used for MDR TB diagnosis has increased over time from 1 in only 1 LGA to 18 in 15 LGAs in 2018. All the suspected MTB cases reported in the year 2017 to 2018 tested (100%) testing rate. There is good detection rate and improvement in MDR TB enrollment rate by 24.4% from 2017 to 2018.

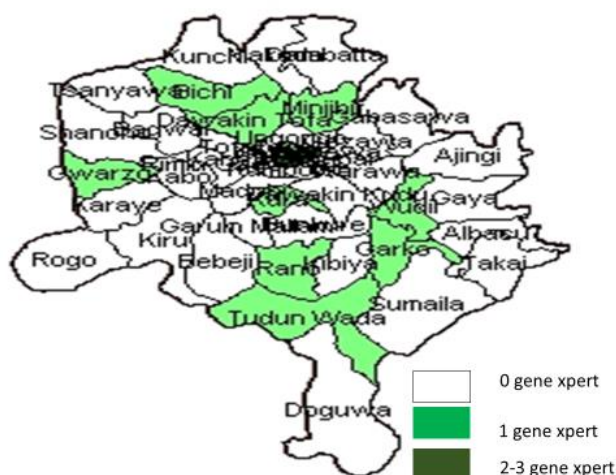
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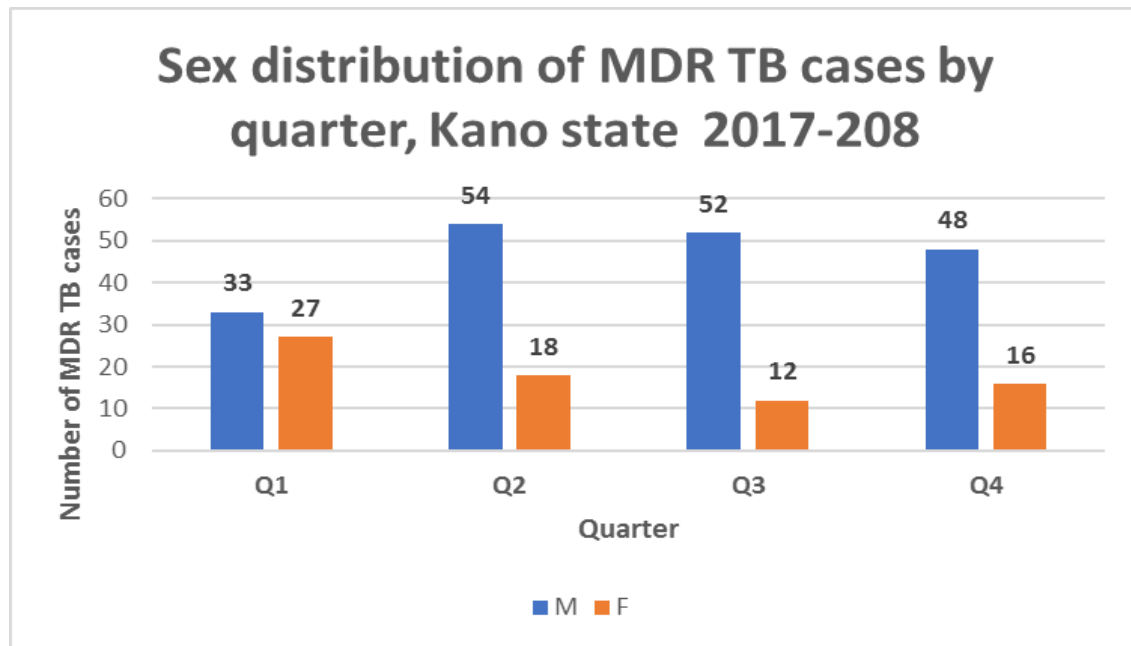
## Competing interest

Based on the clarification by all the authors in this work, I wish to declare that none of the authors have any competing interest in the manuscript.

## Tables and figures



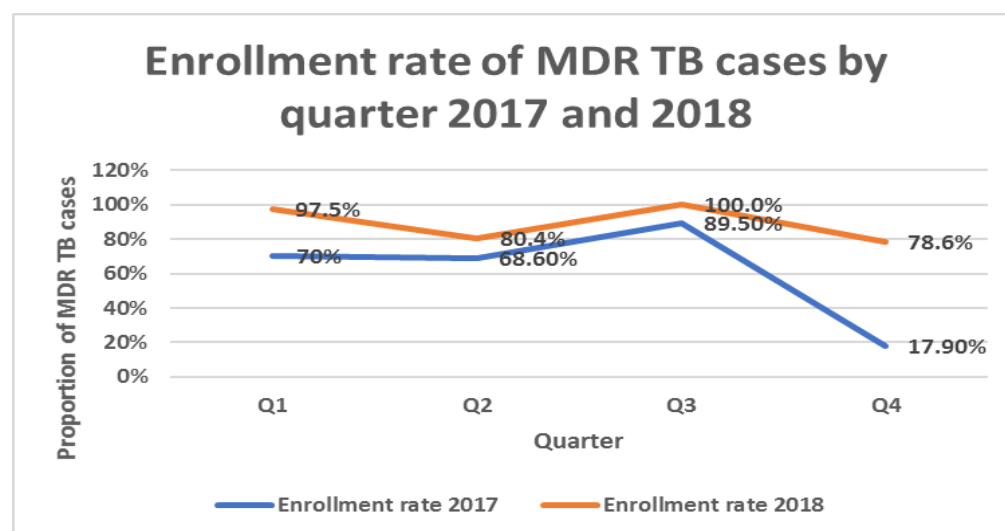
**Figure 1.** Showing map of Kano state with the LGAs with cepheid Xpert MTB/RIF (*gene Xpert*) highlighted



**Figure 2.** Showing sex distribution of MDR TB cases Q1 – Q4 in Kano state, north west Nigeria 2017 and 2018

**Table 1.** Showing total number of MDR TB cases managed in the year, number of number of enrollments, number of deaths before enrollment, number that refused enrollment and number of those that could not be traced for enrollment /loss for follow up in Kano state, north west Nigeria 2017-2018

Quarter	Total number of cases managed in the year	Number of enrollments	Number of deaths before enrollment	Number that refused enrollment	Number of those that cannot be traced for enrollment /loss for follow up
2017	121	77 (66.6%)	3 (2.5%)	5 (4.1%)	14 (11.6%)
2018	168	148 (88.1%)	3 (1.8%)	3 (1.8%)	4 (2.4%)
Total	288	225 (78.1%)	6 (2.1%)	8 (2.8%)	18 (6.3%)



**Figure 3.** Showing trend of MDR TB enrollment rate Q1 – Q4 in Kano state, north west Nigeria 2017 and 2018

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