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Tuberculosis prevalence and rifampicin resistance among presumptive patients in Nasarawa State: A three−year retrospective study

Ibrahim Hassan Ikrama[1,2], Amadou Talfi Zakou[1], Ngolo Jebes Lamini[1], Celestine Osanga[1], Attari Nasara Dogara[1], Lambo Yamusa Wakili[1], Daniel Abah Augustine[1], Muhammad Maryam Hassan[1], Regina Aluku[1], Caleb Luka Kyari[1], Agbawu M. Agbawu[1], Godwin Attah Obande[2], Aleruchi Chuku[2]✉

[1]*Laboratory Services, Dalhatu Araf Specialist Hospital Lafia, Nasarawa state 950001, Nigeria*

[2]*Department of Microbiology, Faculty of Science, Federal University of Lafia, Lafia, Nasarawa State 950101, Nigeria*

ABSTRACT

Objective: To investigate the prevalence and rifampicin resistance of tuberculosis among presumptive patients in Nasarawa state, Nigeria.

Methods: Patient data collected from January 2019 to December 2021 were retrospectively computed from the register at the tuberculosis laboratory of Dalhatu Araf Specialist Hospital, Lafia. A total of 91 884 patient records were analyzed to determine tuberculosis prevalence, rifampicin resistance, and patients' characteristics using *Chi*-squared test.

Results: An overall prevalence of 8.0% was recorded among presumptive patients over the three-year period with a decreasing trend in prevalence from 10.0% (2019) to 6.5% (2021), though the number of samples progressively increased each year and more than doubled in 2021. Most of the patients tested for tuberculosis were females (52.6%) and were mostly older than 15 years (84.1%). Conversely, a higher resistance to rifampicin was observed among tuberculosis positive male patients (55.6%) than in females (44.4%). Similarly, tuberculosis positive patients older than 15 years (84.6%) showed greater resistance to rifampicin than those younger than 15 years (15.4%). Statistically, no relationship was established among age, sex, year of sampling and tuberculosis prevalence or rifampicin resistance rate.

Conclusions: Despite the downward trends in tuberculosis prevalence and rifampicin resistance rate observed in this study, measures at maintaining the gains achieved in the fight against tuberculosis must remain paramount as the race towards reducing tuberculosis incidence and mortality by 2025 continues.

KEYWORDS: Tuberculosis; Rifampicin; Resistance; Nasarawa; *Mycobacterium*

1. Introduction

Tuberculosis is a highly infectious airborne disease caused by the bacterium *Mycobacterium tuberculosis*, which affects the lungs (Pulmonary tuberculosis) as well as other extra-pulmonary organs such as the liver, kidney, skin, spleen and brain, resulting to non-pulmonary or extrapulmonary tuberculosis[1]. Transmission occurs when a healthy person inhales droplet nuclei of *Mycobacterium tuberculosis* released into the air from another person with active pulmonary or laryngeal tuberculosis. This can be through coughing (the most efficient means of generating infectious droplet nuclei

Significance

This study has revealed a downward trend in both the prevalence and rifampicin resistance of tuberculosis, and also underscores the urgent need to continue implementing measures aimed at sustaining the progress made in the fight against tuberculosis in the study area. While the efforts to reduce the incidence and mortality rates have been fruitful, it is essential to sustain these interventions to ensure that the gains achieved are not lost.

✉To whom correspondence may be addressed. E-mail: aleruchichuku14@gmail.com.

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aerosols), sneezing, shouting, singing or other forceful processes that release respiratory secretions[2]. The droplet nuclei move through the buccal or nasal passages, through the upper respiratory tract and bronchi to reach the alveoli of the lungs or becomes deposited in other body organs or tissues. Constitutional symptoms such as anorexia, fever, fatigue, cough, malaise and weight loss may be observed in infected individuals[3].

The enormous incidence and mortality rate of tuberculosis globally, regionally and locally is alarming and requires timely assessment of the available treatment therapies as well as their efficacy. In 2021, with a total mortality of approximately 1.6 million, the global incidence of tuberculosis was 10.6 million cases, of which adult males accounted for 6 million cases, while women and children accounted for 3.4 million and 1.2 million cases respectively. These values represent a 4.5% increase in incidence compared to 2020 and increase in mortality from 1.5 million previously reported in 2020. Similarly, the yearly number of new cases per 100 000 population also increased by 3.6% in 2021. Previously, new cases had continuously declined by 2.0% annually over the past two decades[4]. The high mortality rate of tuberculosis may qualify its ranking as the second leading causal agent of death arising from a single infectious agent, next to COVID-19[5].

The burden of antibiotic resistance in tuberculosis treatment poses a serious challenge to efforts being channelled towards global reduction of prevalence rates. In 2020, 7.5% of people diagnosed with pulmonary tuberculosis showed multidrug and extensively drug resistance. In 2021, 3.6% of people diagnosed with new tuberculosis cases had multidrug-resistant tuberculosis (MDR-tuberculosis) or rifampicin-resistant tuberculosis (RR-tuberculosis). Among those previously treated for tuberculosis, 18% developed MDR/RR-tuberculosis. Incidence cases of MDR-tuberculosis or RR-tuberculosis (MDR/RR-tuberculosis) increased by 3.0 % from 437 000 in 2020 to 450 000 in 2021[4].

Available data on the WHO country profile as of March 2023 showed that Nigeria holds about 4.4% (467 000) of the global burden and 8.0 % (125 000) of the global death cases, with treatment coverage of 44.0%, fatality ratio of 28.0% and 2.5% new cases of drug resistance in 2021[6]. Nigeria is top among West African countries to be on WHO's global list of high burden countries for tuberculosis, HIV-associated tuberculosis and MDR/RR, and one of the few in Africa to be captured on these lists, alongside Central African Republic, Democratic Republic of Congo, South Africa, Mozambique, Malawi, Liberia, Zambia and others. Along with 10 other high tuberculosis burden countries, treatment coverage in Nigeria was below 50.0% in 2021. Additionally, Nigeria has been listed among the top 5 countries with disparity (6.3%) between estimated tuberculosis incidence and the number reported for newly diagnosed tuberculosis cases, due to both underreporting and underdiagnosis of tuberculosis cases[4].

Several results may occur throughout the course of tuberculosis treatment. These outcomes can be influenced by factors such as coexisting diseases like HIV. The success or failure of tuberculosis treatment has also been significantly associated with HIV treatment and retreatment, defaulting treatment by patients, poor implementation of Directly Observed Therapy (DOT) and inefficient patient counselling[7]. Failed treatment can result in increased morbidity and mortality, and can substantially influence community spread of the disease[8], thereby worsening the health and socioeconomic wellbeing of people. The WHO and its partners aim to reduce tuberculosis deaths and incidence rate by 75.0% and 50.0% respectively by 2025. The fulfilment of these goals revolves around the combination of early diagnosis of all tuberculosis infections, treatment of all tuberculosis forms, vaccination with bold policies and supportive systems, coupled with intense research and innovation[4].

Nigeria targets eradication of tuberculosis by 2030[9], a feat that can only be achieved through concerted efforts at continuous testing, diagnosis and treatment of infected persons. Previous studies conducted in Nasarawa state revealed a prevalence rate of 32.0% in children, and between 11.3% to 18.8% among the general population[10–12]. A study by Pennap and coworkers reported a HIV prevalence of 44.20% among tuberculosis patients in a Nasarawa state referral centre[13], while a prevalence of 34.5% was reported by Gyar and coworkers in Lafia[14]. Resistance to rifampicin has also been reported among tuberculosis patients in Nasarawa state[12]. Over a period of 4 years (2015 – 2019), 12 733 cases of tuberculosis were recorded in Nasarawa state[15], making it imperative to keep track of tuberculosis infections in Nasarawa state. This study aims to provide data-driven information that can guide the drive towards eradication of tuberculosis, and better management of the disease among the populace. This present study compares tuberculosis incidence and resistance among presumptive tuberculosis patients in Nasarawa state from 2019 to 2021.

2. Materials and methods

2.1. Study Location

Study was conducted at the Dalhatu Araf Specialist Hospital Lafia (DASH) in Nasarawa State, Nigeria. The hospital is a secondary level health facility located in the heart of the town with laboratory facilities for tuberculosis and HIV testing. The hospital receives referred patients with suspected tuberculosis cases from all other Local Government areas within the state for tuberculosis testing and treatment.

2.2. Ethical approval

The study was approved by the ethical research and review committee of the DASH, Nasarawa State (Ethical approval number: DASH/L/ADM/0490). Since there was no direct contact with the patient or their samples, informed consent of the patients was not required. Patient personal information were also excluded during data collection, to ensure strict confidentiality.

2.3. Study design and population

This was a three-year retrospective, descriptive cross-sectional study conducted among tuberculosis patients from 10 Local Government Areas in Nasarawa state, who were referred to DASH for tuberculosis diagnosis from January 2019 to December 2021. Diagnosis of tuberculosis was performed in this facility using the Xpert MTB/rifampicin assay using the GeneXpert system. A patient was considered to be a suspected tuberculosis cases when a patient shows symptoms such as prolonged cough, night sweating, fever, weight loss and haemoptysis[16] Laboratory records of all patients who presented for tuberculosis testing within the period, and were captured in the register of suspected tuberculosis patients were included in this study. A total of 91 884 patients data met the inclusion criteria and were included in the study. Patients with incomplete data in their records were excluded from the study.

2.4. Source and method of data collection

Data collection involved the use of a structured data extraction tool. Initial data collection and extraction was done by two trained Laboratory Technicians. tuberculosis laboratory registers were the primary sources of data used in this study. Data were collected retrospectively and included patient's age and sex, tuberculosis test results, drug resistance status. Data collectors were trained, and the data collection instrument was independently assessed to ensure accuracy of the data collection process. Also, the data collectors were strictly supervised to further guarantee quality in the data.

2.5. Statistical analysis

All data collected in this study were pooled together and cleaned up using Microsoft Excel (Microsoft Corp., Redmond, WA,USA). Descriptive analysis was performed using Statistical Package for the Social Sciences (SPSS, version 21; SPSS Inc., Chicago, IL, USA). Frequencies and percentages were computed. Associations and observed differences in tuberculosis cases, and rifampicin as well as between gender and age categories were compared using either Pearson *Chi*-Square Test or Fisher's Exact Test. P value < 0.05 was considered statistically significant.

3. Results

Table 1 shows the demographic characteristics of of presumptive patients tested for tuberculosis in Nasarawa state from 2019 to 2021. The number of patient samples tested with Xpert for each year were 21 013 (22.9%), 23 483 (25.6%) and 47 388 (51.6%) respectively, making a total of 91 884 samples in 3 years. More females were tested in each of the 3 consecutive years than men, although the difference was not statistically significant (P = 0.474). Overall, 52.6% (48 295) of the patients were females while 47.4% (43 589) were males. Similarly, most of the samples analysed between 2019 to 2021 were from patients older than 15 years (77 252; 84.1%). There was no statistically significant difference between the number of patients tested in the two age groups (P = 0.159). The total number of samples tested progressively increased from 2019 and almost more than doubled in 2021, with no significant difference observed (P = 0.229).

Table 1. Demographic characteristics of of presumptive patients tested for tuberculosis in Nasarawa state in relation to sex and age over the three-year period.

Variables	2019	2020	2021	Total	P	χ^2
Sex						
Male	9 696 (46.1)	11 441 (48.7)	22 452 (47.4)	43 589 (47.4)	0.474	2.951
Female	11 317 (53.9)	12 042 (51.3)	24 936 (52.6)	48 295 (52.6)		
Age						
<15	2 648 (12.6)	2 012 (8.6)	9 972 (21.0)	14 632 (15.9)	0.159	-
>15	18 365 (87.4)	21 471 (91.4)	37 416 (79.0)	77 252 (84.1)		-
Total	21 013 (22.9)	23 483 (25.6)	47 388 (51.6)	91 884 (100.0)	0.229	2.951

Data are presented as n (%).

The prevalence of of tuberculosis among presumptive patients in Nasarawa state from 2019 to 2021 was 8.0% (Table 2). The highest prevalence of tuberculosis cases among presumptive patients was observed in 2019 (10.0%). Although the number of positive tuberculosis cases increased from 2019 (2 099) to 2021 (3 080), a steady decline in prevalence was observed from 2019 (10.0 %) to 2021 (6.5%). Most of the tuberculosis cases recorded among the study population from 2019 to 2021 were pulmonary tuberculosis (99.99%) and only one case (0.01%) of extrapulmonary tuberculosis was recorded within the 3 years studied. The only case

Table 2. Prevalence of tuberculosis among presumptive patients in Nasarawa state over the three-year period.

Variables	2019	2020	2021	Total	*P*	χ^2
Positive pulmonary tuberculosis cases	2098 (99.95)	2186 (100)	3080 (100)	7364 (99.99)		
Positive extrapulmonary tuberculosis cases	1 (0.05)	0 (0.0)	0 (0.0)	1 (0.01)		
Total diagnosed positive cases	2099 (10.0)	2186 (9.3)	3080 (6.5)	7365 (8.0)	0.499	1.391
Total negative samples	18914 (90.0)	21297 (90.7)	44308 (93.5)	84519 (92.0)		
Total tested samples	21013 (22.9)	23483 (25.6)	47388 (51.6)	91884 (100)		

Data are presented as *n* (%).

of extrapulmonary tuberculosis recorded was in 2019 (0.05%). No statistically significant difference was observed among positive tuberculosis cases for the three years studied (*P*=0.499).

Rifampicin resistance in positive cases among presumptive tuberculosis patients recorded from 2019 to 2021 was higher in male patients (55.6%) than in female patients (44.4%) (Table 3), although the differences were not statistically significant (*P*=1.000). A prevalence of 2.44% (180/7365) rifampicin resistance was observed among the positive tuberculosis cases within the study period in Nasarawa state. Higher resistance to rifampicin among tuberculosis positive females (50.8%) than tuberculosis positive males (49.2%) was observed only in 2019. In relation to age, the highest rate of resistance was recorded among tuberculosis positive patients older than 15 years (84.6%) than those less than 15 years (15.4%), although no significant association was observed between rifampicin and age group of patients (*P*=0.055). No case of rifampicin resistance was recorded among tuberculosis positive patients less than 15 years in 2020. A total of 180 rifampicin resistant tuberculosis was recorded in the three-year period, with highest in 2019 (35.0%) and lowest in 2020 (31.1%), although the observed differences were not statistically significant (*P*=0.381). Overall rifampicin resistant tuberculosis rate among total diagnosed tuberculosis positive patients was 2.4% (*n*=7365), with the highest rate in 2019 (3.0%; *n*=2099) and the lowest in 2021 (2.0%; *n*=2186). Difference in rifampicin resistance rate among tuberculosis positive patients was not statistically significant (*P*=0.074).

Table 3. Comparison of rifampicin resistant tuberculosis infection among presumptive patients in Nasarawa in relation to sex and age over the three-year period.

Variables	2019 *n*=2099	2020 *n*=2186	2021 *n* =3080	Total *n* =7365	*P*	χ^2
Sex						
Male	31 (49.2)	30 (53.6)	39 (63.9)	100 (55.6)	1.000	-
Female	32 (50.8)	26 (46.4)	22 (36.1)	80 (44.4)		
Age						
<15	4 (6.3)	0 (0.0)	5 (8.2)	9 (5.0)	0.055	-
>15	59 (93.7)	56 (100.0)	56 (91.8)	171 (95.0)		
Total	63 (35.0)	56 (31.1)	61 (33.9)	180 (100)	0.381	1.930
Rifampicin resistance %	3.0	2.6	2.0	2.4	0.074	5.213

Data are presented as *n* (%).

4. Discussion

One of the major contributors to the eradication of infectious diseases, is the establishment of efficient, accurate, robust and rapid large-scale testing within a population[17,18]. Consequently, one of the WHO pillars in the quest of terminating tuberculosis globally, is early testing and diagnosis[4]. The present study shows a considerably large number of patient samples collected for tuberculosis testing over a three-year period spanning from 2019 to 2021. Each consecutive year witnessed an increase in the total number of patients tested, although no significant association between the observed increase and sampling years was statistically established. There was an 11.8% increase in the number of patients tested for tuberculosis in Nasarawa state between 2019 to 2020, and a 101.8% increase between 2020 to 2021, which may be associated with the increase in testing centres across the state. In 2003, Nasarawa state had only one tuberculosis testing centre, which had increased to 13 as of 2020[15]. The sharp rise in the number of tested samples observed in 2021 could be associated with the lifting of movement restrictions earlier imposed in 2020 within the country due to COVID-19. This may have afforded patients more access to healthcare facilities in their localities. Despite COVID-19 restrictions, more samples were tested in 2020 than in 2019. This is in contrast to the report of Deutsch-Feldman and colleagues who observed a 20.0% reduction in reported tuberculosis cases in the same year within the USA, due to COVID-19 restrictions [19].

Samples of females collected for tuberculosis testing within the 3-year period were higher than those of males, though the observed differences were not statistically significant. This finding is similar to earlier reports[20,21]. Although the actual reason for this observation may not be obvious, it may suggest that women in Nasarawa state are presenting more for tuberculosis testing than their male counterparts. A study conducted in the United Kingdom reported a higher consultation rate of 32.0% in women than in men, and the rate was higher in people who were associated with less socioeconomic affluence[22]. Furthermore, men may view visits to the hospital as a sign of weakness and therefore choose to act tough and show masculinity by not visiting the hospital even when they are sick[23,24]. The desire to be self-assisting and the feeling of embarrassment also prevent men from seeking medical assistance when they feel sick[25,26]. Our findings also revealed a higher

number of tuberculosis samples in the age range >15 years. This is in consonance with several earlier reports which reported similar observations among tuberculosis patients in Nasarawa state[12,27], some parts of Nigeria [17,28,29], Pakistan[20,21] and South Africa[30].

An important finding of this study is the reducing prevalence of tuberculosis among presumptive patients in Nasarawa state from 10.0% to 6.5% from 2019 to 2021. The overall prevalence of tuberculosis among presumptive patients within the 3-year period was 8.0%. This figure is much lower than earlier reports within the state. A prevalence of 18.8% was reported between January and April 2015[12]. Other studies reported a prevalence of 41.2% for March 2007 to October 2008[13], 26.3% for January to October 2015[31] and 11.3% for September 2017 to October 2018[11]. The pattern of progressive decrease in prevalence of tuberculosis among presumptive patients in Nasarawa state from 2019 to 2021 observed in this study is, hence, consistent with previous studies. This observation may be suggestive of improved services at the designated testing and treatment centres within the state. Also, the effect of the COVID-19 pandemic may not be ruled out of this observation. The WHO reported a sharp drop in tuberculosis notifications from high burden countries in 2020 during the COVID-19 pandemic[32]. Increased awareness of the disease and how to prevent its spread among the populace, occasioned by increased advocacy and enlightenment efforts may also be responsible for the decreasing prevalence observed in this study. Additionally, there is evidence that not all persons exposed to *Mycobacterium tuberculosis* eventually develop an active tuberculosis infection. Some end up as latent tuberculosis infections, which could later reactivate into active disease[33,34]. Such untreated cases can eventually transmit tuberculosis disease to healthy individuals and this can negatively impact tuberculosis treatment and control programmes within a population[35].

Rifampicin is among the most potent first line anti-tuberculosis drug for the treatment of tuberculosis. Hence, observance of resistance to this drug in tuberculosis patients is a serious public health issue. Our findings in this study revealed that 2.4% of rifampicin-resistant positive tuberculosis cases recorded among presumptive patients in Nasarawa state from 2019 to 2021. The yearly rifampicin resistance rate was 3.0% in 2019, 2.6% in 2020 and 2.0% in 2021, showing that the resistance rate reduced from 2019 to 2021. This prevalence is much lower than those reported in previous years, though more patients were tested in this study. Reported rifampicin resistance in Nasarawa state range from 6.6%[31] to 12.1%[12]. A meta-analysis conducted in 2017 reported 32% and 53% prevalence of drug-resistant tuberculosis, and multi-drug resistant tuberculosis of 6% and 32% in Nigeria among new and previously treated tuberculosis cases[36]. Differences in sample size, study period and patient data could have influence the observed variations[37]. In contrast to the findings of this present study, Dayyab and co-workers reported a 100.0 % resistance to rifampicin in 132 MTB isolates obtained from an Infectious Disease Hospital in Kano, Nigeria[38]. With respect to sex and age, rifampicin resistance was observed more among male tuberculosis positive patients than in females, and in patients older than 15 years. Similar findings in respect of higher rifampicin resistance in males was also previously reported in Enugu[39], Nasarawa[27] and Maiduguri all in Nigeria and in countries such as South Africa and China[40–42]. The greater rifampicin resistance observed in patients older than 15 years also agrees with several reports from Nigeria and other countries[40,37,42]. Drug resistance have detrimental effect on patients as it can lead to extended hospitalization, increased treatment cost and sometimes death[43]. Although no statistically significant association was established between age, gender and rifampicin resistance, factors such as lifestyle, level of exposure, differences in socioeconomic realities and non-adherence to treatment regimens can influence susceptibility or resistance in tuberculosis management[38]. Infection with a resistant tuberculosis strain or existence of untreated tuberculosis infection could also result in resistance to rifampicin[44]. Drug abuse and the use of substandard anti-tuberculosis drugs are also possible factors that influence the development of resistance in tuberculosis. Available reports also suggest that prolonged exposure to anti-tuberculosis drugs during a treatment course can increase the chance of developing resistance in tuberculosis patients[45]. The foregoing supports the fact that to fully and rapidly achieve reduction in tuberculosis cases globally, timely and accurate diagnosis must be coupled with prompt and effective treatment programs that ensure adherence to treatment regimens. Creation of incentives for patients who religiously follow their treatment schedules could also encourage adherence to treatment course and prevent defaulting or interruption. Drug resistance has remained a public health issue with increasing propensity for becoming a major challenge to the management of infectious diseases globally. In addition to already existing anti-tuberculosis drugs, efforts at developing more effective and efficient drugs for tuberculosis must be encouraged and supported as is being done for other infective agents.

5. Conclusions

Tuberculosis remains a disease of public health concern due to the effect it exerts on the socioeconomic wellbeing of patients. This study considered tuberculosis data obtained over a period of three years (2019 to 2021) among presumptive patients in Nasarawa state. Although the prevalence of tuberculosis in this study has shown a decreasing trend since 2019 to 2021, continuous testing

of suspected patients alongside increased creation of awareness about the disease in Nasarawa state remains important. The rate of resistance to rifampicin observed in this study is much lower than reports from other parts of Nigeria and the world. However, incentives that encourage commitment to treatment regimens among tuberculosis positive patients can ensure the sustenance of this gain in the effort to eliminate tuberculosis in Nasarawa state and globally. No significant association was established between factors such as age, sex and year of sample collection with the prevalence of tuberculosis, or resistance to rifampicin within the study period among presumptive patients in Nasarawa state. As the WHO targets to substantially reduce tuberculosis deaths and incidence by 2050, the sustenance of control models that encompass rapid diagnosis, effective treatment and continuous mitigation of resistance to existing anti-tuberculosis drugs while developing new ones, remains a crucial requirement.

Conflict of interest statement

The authors claim there is no conflict of interest.

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This study receives no extramural funding.

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

Ikrama IH, Zakou AT, and Lamini NJ designed the experiment. Chuku A drafted the first manuscript. Osanga C, Dogara AN, Wakili LY, Augustine DA, Hassan MM, Aluku R, Kyari CL, and Agbawu AM performed the experiments and collated the data. Obande GA performed the data analysis. Chuku A, Obande GA, and Lamini NJ read the manuscript, made corrections to the manuscript, reviewed and edited the content of the entire manuscript. All authors approved the final copy of the manuscript before submission.

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