Prevalence and Characteristics of Multidrug Resistant Tuberculosis Notified in Abu Anga Hospital, Khartoum State, Sudan

ABSTRACT

Background: In 2020, there were 5.8 million cases of tuberculosis worldwide, making it a substantial public health concern. Drug-resistant strains of Mycobacterium tuberculosis, which are characterized by increased morbidity and mortality, have become a significant threat to the global control of tuberculosis. ***Objective:*** To determine the prevalence of multidrug-resistant tuberculosis reported at Abu Anga Hospital in Khartoum State between 2020 and 2022 is the goal of this investigation. ***Materials and Methods:*** A total of 204 samples were used in this retrospective analysis to identify MTB/RIF. From January 2020 to December 2022, use the Gene Xpert MTB/RIF assay to quickly identify M. tuberculosis complex (MTBC) strains and identify rifampicin-associated mutations of the rpoB gene directly from sputum samples. ***Results:*** All 204 samples tested positive for *Mycobacterium tuberculosis* (MTB), with confirmed drug resistance in all cases. Among drug-resistant TB cases, the prevalence of multidrug-resistant TB (MDR-TB) was 49 (24.0%) in 2020, increased to 97 (47.5%) in 2021, and then declined to 58 (28.5%) in 2022. New MDR-TB diagnoses predominated (134, 65.7%) compared to other categories. Rifampicin resistance (RR) was the most frequent pattern (162, 79.4%), followed by MDR-TB (41, 20.1%) and isoniazid monoresistance (1, 0.5%). Males represented most cases (134, 65.7%), and pulmonary TB was the primary presentation (193, 94.6%). ***Conclusions:*** Since tuberculosis (TB) is the second leading infectious disease-related cause of death worldwide, especially among individuals with co-infections of HIV and TB, its detection and treatment remain top priorities for all countries. According to the study's findings, MDR was more prevalent. Pulmonary tuberculosis was the most common form of TB in 2021, and rifampicin was the most common drug-resistant type. These findings highlight the ongoing challenges of TB and antibiotic resistance in Khartoum. It is also advised to establish additional treatment centers in rural areas of Sudan, along with programs that promote treatment adherence, such as patient counseling, to improve future outcomes.

Keywords: MDR-TB, Prevalence, Rifampicin, Tuberculosis, Sudan

1. INTRODUCTION

Until the middle of the 20th century, tuberculosis (TB) was widely believed to be incurable. As shown by Crofton in 19591, the advent of anti-TB medications altered the course of TB patients' lives (Sir John Crofton passed away on November 3, 2009, at the age of 97) **[1].** According to estimates from the World Health Organization (WHO), more than 10 million individuals worldwide contracted tuberculosis (TB) between 2017 and 2018 **[2],** In addition to their socioeconomic impact, tuberculosis (TB) and multidrug-resistant TB (MDR-TB) continue to pose a danger to global public health **[3].** During the COVID-19 pandemic, the most noticeable effect was a significant worldwide drop in the number of newly diagnosed TB cases, which fell from 7.1 million in 2019 to 5.8 million in 2020, according to WHO data in the 2021 Global Tuberculosis Report. TB mortality has gone up due to limited access to TB diagnosis and treatment. TB will claim 1.3 million lives worldwide in 2020 **[5].** The two main medications used to treat tuberculosis are rifampicin (RIF) and isoniazid (INH). Ethambutol (EMB), streptomycin (STM), and pyrazinamide (PZA) are the other first-line medications **[3].** The 85% and 70% treatment success targets are explained by the risk of tuberculous infection and its trend, which is crucial in controlling the TB pandemic. Even when HIV is present, the detection of smear-positive TB cases can help reduce the TB burden **[9].** MDR-TB, or multidrug-resistant tuberculosis, is characterized by resistance to at least isoniazid and rifampicin **[4].** Patients with relapses and failures had higher levels of rifampicin resistance (RR-MTB). In 2018, there were almost half a million new cases of rifampicin-resistant (RR) TB, 78% of which had MDR TB **[6].** According to WHO (2021), up to 71% of the world's population, or 2.1 million people, received a diagnosis of bacteriological tuberculosis in 2020, which is drug-resistant to rifampin **[5].** High HIV prevalence and a delay in early diagnosis and effective treatment initiation are linked to the high burden of TB and MDR-TB in low-income countries **[6].** Sudan accounted for 14.6% of the total TB burden and was ranked second in the East Mediterranean area for TB incidence (WHO, 2007) **[3].** Drug resistance may potentially be a consequence of the initial infection. Therefore, to address this, substantial measures are usually required. Compared to susceptible treatments, the second-line drugs of MDR-TB are characterized by higher treatment costs, longer therapy durations, lower efficacy, and more adverse treatment effects **[2].** TB produced by M tuberculosis isolates that are resistant to rifampicin, isoniazid, and fluoroquinolones, and at least one of the second-line injectable medications (capreomycin, kanamycin, and amikacin) is known as

extensively drug-resistant TB (XDR TB) **[7].** Programs for disease management and control must prioritize early treatment initiation, ongoing surveillance, frequent monitoring, and rapid diagnosis of drug-resistant TB. To mitigate the issue of early TB diagnosis in low-income nations **[6].** According to the WHO, one of the main reasons disease resistance exists is that Directly Observed Treatment (DOT) has not been implemented. Furthermore, suboptimal therapy procedures have a direct impact on resistance to anti-TB medications, which is a reflection of the low caliber of TB programs in many nations **[8].** Consequently, this study aimed to detect the Prevalence of Multidrug-Resistant Tuberculosis Notified in Abu Anga Hospital, Khartoum State, Sudan, to help with future management strategies and to provide guidance on the potential ways to control the spread of MDR-TB in Sudan.

2. METHODOLOGY

This retrospective study aimed to identify the prevalence of Multidrug-Resistant Tuberculosis (MDR-TB) among TB patients in Khartoum State from January 2020 to December 2022. The hospital-based investigation took place at Abu Anga Hospital, the specialized facility in Sudan that receives referrals for suspected tuberculosis cases, provides medical services to the population of Khartoum, and functions as Sudan's primary MDR-TB reference hospital, where all documentation and reporting procedures are centralized. All MDR-TB patients recorded at the hospital during the study period were consecutively targeted for inclusion. Cases were included only if they were reported at Abu Anga Hospital and laboratory-confirmed as MDR-TB by GeneXpert testing between 2020 and 2022, while cases reported at the hospital without GeneXpert confirmation of MDR-TB were excluded.

Sampling and sample size

The study focused on all hospitalized patients, regardless of gender or age, who were registered between 2020 and 2022. During this time, 204 MDR-TB patients were recorded; as there was a cap on the total number of patients, all patients were recruited without any sampling.

Molecular screening

Hain MTBDRplus for RIF/INH resistance and MTBDRsl VER 1.0 for fluoroquinolones and injectable second-line anti-TB medications were used by the Sudan National Tuberculosis Control Program (NTP) to screen for XDR-TB in 2012. GeneXpert was introduced in 2014, and MTBDRsl version 2 was introduced in 2017. In less than two hours, GeneXpert offers both fast TB detection and RIF resistance. The national MDR-TB diagnosis algorithm formerly separated TB presumptive cases into two groups based on molecular screening. GeneXpert must screen patients in the first category, which is the high-risk group. This group consists of MDR contacts, HIV-positive patients, retreatment TB cases, and healthcare workers.

Data analysis

To process the data, appropriate statistical treatments and equations were used through the statistical software. After completing the study data collection, it was sorted, coded, and then analyzed, and the researcher entered the data of this sample into a computer using Statistical Packaged for Social Science (SPSS) (version 23), the researcher used of several tests and statistical methods "descriptive statistics (Frequency and Percentage) to describe the sample data', chi-square test, And run to summarize continuous and categorical variables of the socio demographic and clinical factors; the predictors were identified and considered significant at a *P-value* less than 0.05.

3. RESULTS

Table 1. Distribution of demographic data for MDR.TB patients

Age	Frequency	Percent %
0-15	7	3.4%
16-30	120	59.3%
31-45	59	28.4%
more than 45	18	8.9%
Gender		
Male	134	65.70%
Female	70	34.30%
Nationality		
North Sudan	196	96.1%
South Sudan	6	2.9%
Other	2	1%
Patient occupation		
Employed	14	6.9%
Self employed	107	52.5%
Without job	83	40.6%

Table 2. Frequency of MDR.TB categories

MDR. TB categories	Frequency	Percent %
New case	134	65.7%
Failure in treatment	33	16.2%
Lots of follow-up	21	10.3%
Relapse	16	7.8%
Total	**204**	**100%**

Table 3: Frequency of Type drug resistance

Type of drug resistance	Frequency	Percent %
INH	1	0.5%
RR	162	79.4%
MDR	41	20.1%
XDR	0	0%
Total	**204**	**100%**

Table 4. Frequency of Treatment outcome

Treatment outcome	Frequency	Percent %
Cure	57	27.9%
Treatment Complete	58	28.4%
Treatment failure	13	6.4%
Died	18	8.8%
Lots of follow-up	20	9.8%
Not evaluate	34	16.7%
Transfer out	4	2%
Total	**204**	**100%**

Table 5. Factors Significantly Associated with MDR-TB Categories

Variable	Category	New Case n (%)	Treatment Failure n (%)	Loss to Follow-up n (%)	Relapse n (%)	Total n (%)	p-value

Year of Diagnosis	2020	26 (19.4%)	10 (30.3%)	2 (9.5%)	11(68.8%)	49(24.0%)	**<0.001**
	2021	60 (44.8%)	19 (57.6%)	15 (71.4%)	3 (18.8%)	97(47.5%)	
	2022	48 (35.8%)	4 (12.1%)	4 (19.0%)	2 (12.5%)	58(28.5%)	
Age Group	0–15 years	5 (3.7%)	0 (0.0%)	0 (0.0%)	2 (12.5%)	7 (3.4%)	**<0.001**
	16–30 years	64 (47.8%)	29 (87.9%)	17 (81.0%)	11(68.8%)	121(59.3%)	
	31–45 years	48 (35.8%)	4 (12.1%)	4 (19.0%)	2 (12.5%)	58 (28.4%)	
	≥45 years	17 (12.7%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	18 (8.9%)	
Gender	Male	64 (47.8%)	33 (100%)	21 (100%)	16 (100%)	134(65.7%)	**<0.001**
	Female	70 (52.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	70 (34.3%)	
Patient Occupation	Employed	14 (10.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	14 (6.9%)	**<0.001**
	Self-employed	101(75.4%)	6 (18.2%)	0 (0.0%)	0 (0.0%)	107(52.5%)	
	Unemployed	19 (14.2%)	27 (81.8%)	21 (100%)	16 (100%)	83 (40.6%)	
Type of Drug Resistance	INH Monoresistance	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	**<0.001**
	Rifampicin-Resistant (RR)	117(87.3%)	23 (69.7%)	19 (90.5%)	3 (18.8%)	162(79.4%)	
	MDR	16 (11.9%)	10 (30.3%)	2 (9.5%)	13(81.3%)	41 (20.1%)	

Table 6. Association Between Treatment Outcomes and MDR-TB Categories

Treatment Outcome	New Case n (%)	Treatment Failure n (%)	Loss to Follow-up n (%)	Relapse n (%)	Total n (%)
Cure	55 (41.0%)	1 (3.0%)	0 (0.0%)	1 (6.3%)	57 (27.9%)
Treatment Completed	36 (26.9%)	21 (63.6%)	1 (4.8%)	0 (0.0%)	58 (28.4%)
Treatment Failure	13 (9.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (6.4%)
Died	2 (1.5%)	0 (0.0%)	7 (33.3%)	9 (56.3%)	18 (8.8%)
Loss to Follow-up	8 (6.0%)	7 (21.2%)	3 (14.3%)	2 (12.5%)	20 (9.8%)
Not Evaluated	20 (14.9%)	4 (12.1%)	7 (33.3%)	3 (18.8%)	34 (16.7%)
Transferred Out	0 (0.0%)	0 (0.0%)	3 (14.3%)	1 (6.3%)	4 (2.0%)
Total	**134 (100%)**	**33 (100%)**	**21 (100%)**	**16 (100%)**	**204 (100%)**

4. DISCUSSION

Global TB control is often seen as being seriously threatened by the advent of multidrug-resistant tuberculosis (MDR-TB) and, more recently, extensively drug-resistant TB (XDR-TB). Every year, more than 400,000 new cases of MDR-TB are reported, and XDR-TB cases have been found in every nation with the ability to detect them, even

though their rates are currently unknown. Strains, the kind of mutations they include, and their frequency in the mycobacterial genome differ depending on the geographic location **[11,12].** Therefore, success measures for these diagnostic procedures on a country-by-country basis may be contentious because the accuracy of current molecular diagnostic assays to identify MDRTB is reliant on global polymorphism frequencies. For instance, although being found in 100% of resistant strains in nations like Turkey, Canada, and France, the S315T (katG) polymorphism exhibits a large range in prevalence **[13–15].** In the current study, the age group of 16–31 had a greater frequency of MDR, and the total sample size was 204. TB 121 (59.3%) and 134 (65.70%) are more often found in men than in women. Our results are in line with the 2021 study conducted by Araya Gebreyesus Wasihum and associates **[6],** and S.A. Aricha and his colleagues in 2017 **[10]** demonstrated that the frequency of infection was higher in men than in women. Although more research is required to confirm this point, the reasons for these gender differences may be preferable to the work conditions and immunity status of men compared to women. When compared to other groups, the self-employed group had a higher incidence of 107 (52.5%), indicating low economic status and inadequate health education. Six individuals (2.9%) had HIV co-infection, according to the current study. However, HIV/AIDS is a contributing factor to poor treatment outcomes; according to a 2019 study by Monadil H. Ali et al. **[2],** patients with MDR-TB who were HIV/AIDS-positive had a threefold higher risk of dying than seronegative patients. This is most likely because second-line TB medications and antiretroviral therapy have serious interactions. Of the MDR TB categories, 134 (65.7%) were new cases, 33 (16.2%) did not respond to first-line medication treatment, 21 (10.3%) did not receive follow-up, and 16 (27.2%) exhibited multidrug resistance recurrence. According to our research, rifampicin had a high rate of drug resistance (162; 79.4%), followed by multidrug resistance (41; 20.1%; resistance to several drug types) and isoniazid 1; 0.51%). In contrast, there were no documented cases of substantial drug resistance in XDR. 51 instances showed negative outcomes (deaths, treatment failure, and loss of follow-up); 115 cases showed successful treatment (cure and treatment complete); 4 cases were in the remaining transferred group, and 34 cases were in the not-evaluated group. According to the varying rate of MDR-TB, 49 cases were reported in 2021, 97 cases in 2021, and 58 cases in 2022. The central

system for therapy may be impaired, and patient loss to follow-up may be the cause. Our study demonstrated low HIV prevalence (2.9%) and no significant association with MDR-TB categories or treatment results (p=0.358), despite the fact that HIV co-infection is an established global risk factor for TB outcomes **[2,6].** Although we only looked at adults in our analysis, paediatric MDR-TB outcomes in Nigeria **[16]** also show hazards of loss to follow-up. Multidrug-resistant tuberculosis (MDR-TB) affects society and poses a hazard to public health worldwide. Given the current high prevalence rates, we evaluated MDR-TB treatment results and factors that predict poor treatment outcomes in Sudan **[2].**

5. CONCLUSION

The study found that in 2021, the rate of MDR TB reached a record high (47.5%), high burden among males (65.7%) and new cases (65.7%), and predominance of rifampicin resistance (79.4%) highlight critical challenges in Khartoum. TB classifications, however, the rifampicin registry demonstrates the highest level of medication resistance and a noteworthy association with MDR. The most outcome-oriented treatment is recorded in TB categories with treatment outcomes and cure instances.

CONSENT

The patient's written consent has been collected.

ETHICAL APPROVAL

The study was approved by the Department of Medical Microbiology in Medical Laboratory Sciences at Shendi University, and the study was matched to the ethical review committee board. Sample collection was done after signing a written agreement with the participants. Permission for this study was obtained from the local authorities in the study area. This study's aims and benefits were explained with the assurance of confidentiality. All protocols in this study were done according to the Declaration of Helsinki (1964).

Disclaimer (Artificial intelligence)

As a result, the Author (s) declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during the writing or editing of manuscripts.

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