Original article

Prevalence of rifampicin resistance among tuberculous patients in Khartoum State, Sudan

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A R T I C L E   I N F O

A B S T R A C T

Background: Tuberculosis (TB) is an infectious disease usually caused by *Mycobacterium tuberculosis* (MTB) bacteria. Rifampicin resistant tuberculosis (RR-TB) defined as resistance to rifampicin detected using genotypic or other first method with or without resistance to other first line anti-TB drugs, RR-TB is emerging as a major problem due to poor management of drug sensitive as well as drug resistance TB. **Objectives:** The study aimed to determine the prevalence of the drug resistant (rifampicin among TB patients) in Khartoum state. **Material and methods:** This study was cross-sectional study performed on 75 Sudanese individuals; sputum samples were collected from 75 patients with tuberculosis; whose are sub divided according to their severity into mild patients and high patients. The drug resistance (rifampicin) among T.B patients detected by GeneXpert. The statistical analysis was conducted using SPSS 26 computer program. **Results:** This study was conducted among 75 Sudanese patients with tuberculosis as case group. Mean and SD of age was (30.6 ± 6.4 years). Age was grouped to four age group; the most common age group was between 21-30 years. It was found that two patients had resistant strains of *M. tuberculosis*. **Conclusion:** The study concluded that Gene-Xpert MTB/RIF is a useful tool for detection of TB and RIF resistance on primary respiratory specimens.

Introduction

Tuberculosis (T.B) is an airborne infectious disease caused by *Mycobacterium tuberculosis* and is a major cause of morbidity and mortality, particularly in developing counties. T.B is a communicable disease, whose main reservoir is man, but infrequently with another *mycobacterium* belonging to the *Mycobacterium tuberculosis* complex. Pulmonary tuberculosis (T.B) is a common infection [1]. Rifampicin resistant tuberculosis (RR-TB) defined as resistance to rifampicin detected using genotypic or other first method with or without resistance to other first line anti-TB drugs. RR-TB is emerging as a major problem due to poor management of drug sensitive as well as drug resistance TB. RR-TB is treatable, but is very expensive and requires long duration of treatment and contains potentially toxic drugs [2]. The detection of rifampicin resistance serves as a

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surrogate marker for detection of multi-drug resistant tuberculosis resistant to at least isoniazid and rifampicin [3]. Rifampicin resistance mechanism involves missense mutations in the rifampicin resistance- determining region (RRDR) of *rPOB* gene and 95% of strains that are resistant to rifampicin harbor a mutation within the 81-pb region of the *rPOB* gene [4]. Reports indicate that in Africa the prevalence of resistance to one or more anti-TB drug and of MDR-TB range from 3% to 37.3% [5]. Molecular assays such as Gene-Xpert are changing the landscape of the diagnosis and management of drug resistant TB and may prove to be a cost-effective solution to this problem [6]. Gene-xpert uses real-time polymerase chain reaction (PCR) to detect the specific sequence for *Mycobacterium tuberculosis* as well as that of rifampicin [7].

The study was done to evaluate the role of Gene Xpert for diagnosis of rifampicin resistant *M. tuberculosis* in order to see the percentage of cases of rifampicin resistance.

The study aimed to determine the prevalence of the drug resistant (rifampicin among TB patients) in Khartoum state.

Material and methods

Study design

Cross-sectional study.

Study area

Khartoum state, Sudan.

Study population

The target group in this study was Sudanese patients who had tuberculosis.

Study variables

Age:15-50 years old

Sample size

75 patients as case study number fulfilled the required number to represent tuberculosis patients

$$N = \frac{Z^2 PQ}{d^2}$$

Where:

N = sample size

P = prevalence rate

Z = 1.96 at C=0.05 [C=desired confidence level]

D = desired width of confidence [precision]

Q = 100-p

Specimens collection

Sputum samples were collected in sterile wide mouth containers for analysis. The samples were preserved in fridge at 4° C.

Ethical considerations

Ethical clearance has been obtained from the ethical committee of Gharb El-Niel Collage. Written informed consents have been pre-requested from participants in the study. Patients were looked after by medically qualified doctors with special training in tuberculosis.

Methodologies

Principle of GeneXpert

Gene-Xpert systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequence using real-time reverse transcriptase PCR (RT-PCR) and real -time PCR assay. Each Gene-Xpert module processes one sample. The sample and applicable reagents are inserted into a GeneXpert cartridge, and a test is created on the Gene-Xpert system to run the test. The cartridge is then loaded into an available instrument module and then is started [8,9].

Procedure of GeneXpert (GeneXpert diagnostics, Langdorp, Brabant, Belgium)

- ❖ Sputum sample was collected in vacutainer.
- ❖ NaOH solvent was added to sputum sample in percent of 2:1 and was shacked well.
- ❖ The sample was incubated for 15 minutes, after that we took not less than 2 ml from the sample in cartridge, then cartridge was entered in GeneXpert machine.
- ❖ Put the sample and reagents into different chambers in the cartridge for sample preparation.
- ❖ Do probe checks to ensure that the sample preparation was successful.
- ❖ Run the RT-PCR and PCR cycles and real-time detection [8,9].

Data collection

Primary data were collected from the respondents in the form of a questionnaire and also from the analytical result of the patients who had

made tests. Secondary data were collected from medical textbooks, medical journals and internet web sites.

Quality controls

The standards and measurements of quality control of all materials and reagents that were used in this study were done according to standardized quality control measures.

Data analysis

Data was analyzed by using SPSS 26 computer program.

Results

This study was conducted among 75 Sudanese patients with tuberculosis as case group to determine prevalence of drug resistant (rifampicin) among *Mycobacterium tuberculosis* patients. Mean and SD of age was (30.6 ± 6.4 years). Age was grouped to four age group; the most common age group was between 21-30 years. Two patients had resistant strain of *M. tuberculosis*.

Table 1. Shows the frequency of Sudanese patients with tuberculosis in different age (year) groups, expressed as number and percentage (%)

Age groups	N (%)
Under 20	2(2.6 %)
21-30	41(54.7%)
31-40	26(34.7%)
Above 41	6(8%)
Total	75(100%)

Table 2. Shows the frequency of Sudanese patients with tuberculosis according to gender

Gender	Frequency	%
Female	8	10.7%
Male	67	89.3%
Total	75	100.0%

Table 3. Shows the frequency of Sudanese patients with tuberculosis according to severity of diseases

Severity of diseases	Frequency	%
High	34	45.3 %
Mild	41	54.7 %
Total	75	100 %

Table 4. Shows the frequency of Sudanese patients with tuberculosis according to sensitivity to rifampicin

Sensitivity to Rifampicin	Frequency	%
Sensitive	73	97.3 %
Resistant	2	2.7 %

Table 5. Shows the frequency of Sudanese patients with tuberculosis according to gender and severity of disease

Severity	Gender	
	Male	Female
Mild	36	5
High	31	3

Table 6. Shows the frequency of Sudanese patients with tuberculosis according to gender and sensitivity to rifampicin

Sensitivity	Gender	
	Male	Female
Sensitive	65	8
Resistant	2	0

Discussion

This study was cross-sectional, conducted in Khartoum State during the period between January to June 2023. 75 sputum samples were obtained from tuberculous patients during the period between January to June-2023. The average age ranged from 15-50 years, mean age was 30.6 ± 6.4 years. Tuberculosis was higher in males 89.3% (6,7) than females 10.7%. Most of the cases encountered were in the age group from 21-30 years 54.7%. The frequency of Sudanese patients with tuberculosis according to sensitivity to drug was in agreement with previous study which included 446 samples tested by Gene Xpert automated system , revealed that 22.9% of the sputum specimens were positive for *Mycobacterium tuberculosis* ,with 14.7% rifampicin resistant [10,11]. Tuberculosis generally affects the lungs, but can also affect other parts of the body. Most infections do not have symptoms, in which case is known as latent tuberculosis. About 10% of latent infections progress to active disease which if left untreated kills about half of those infected. The classic symptoms of active TB are chronic cough with blood containing sputum, fever, night sweats, and weight loss. Treatment requires the use of multiple antibiotics over a long period of time. Antibiotic resistance is a growing problem with increasing rates of multiple drug resistant tuberculosis (MDR-TB) [12,13].

MDR-TB treatment in transplant recipients is associated with many complications. MTB/RIF detected RR early and guided early empiric therapy [14,15].

The global dissemination of drug resistance across *Mycobacterium tuberculosis* strains, causative of TB, resulted in an estimated 450, 000 cases of drug-resistant (DR) TB in 2021. Dysregulated immune responses have been observed in patients with multidrug resistant (MDR) TB, but the effects of drug resistance acquisition and impact on host immunity remain obscure [16,17].

Conclusion

The study concluded that Gene-Xpert MTB/RIF is a useful tool for detection of TB and RIF resistance on primary respiratory specimens. Two patients had resistant strain of *M. tuberculosis*.

The study recommends use of Gene-Xpert test in all towns for diagnosis and follow up of tuberculosis in the state.

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