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# A Study on Pulmonary Tuberculosis and Risk Factors in New and Re-Treated Presumptive Patients at Wad Madani Tuberculosis Center, Sudan (2018-2019): A Cross-Sectional Study

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## Abstract

**Introduction:** The increase in cases of drug-resistant pulmonary tuberculosis, especially in endemic areas, is mainly associated with re-treatment, although resistant tubercle bacilli can be easily transmitted between all susceptible persons. **Objective:** The study aimed to describe pulmonary tuberculosis, risk factors and MDR in new and re-treated suspected patients attending Wad Madani Tuberculosis Center that provides service in central Sudan. **Methods:** Cross-sectional laboratory based study among 300 presumptive pulmonary tuberculosis patients during 2018 and 2019 was conducted. Cases were divided into new and re-treated. *Mycobacterium tuberculosis* DNA and rpoB gene of multi-drug resistance (MDR) were detected in sputum samples by GeneXpert assay as manufacturer instructions. **Results:** Out of 300 suspected participants, 34% (103/300) were diagnosed as pulmonary tuberculosis using GeneXpert method. The frequency of males, the age group from 21 to 40 and rural housing were the most with percentage reach 68% (70/103), 51% (53/103) and 58.3% (60/103) respectively. All observed symptoms were significantly associated with pulmonary tuberculosis. New cases represented 59.2% (61/103) while re-treated was 40.8% (39/103). The overall frequency of MDR patients was 9.7% (10/103) of which 50% (5/103) had relapse situation. **Conclusion:** It appeared that the cases of MDR pulmonary

tuberculosis are on the increase compared to previous findings, recommended measures must be taken to control the spread of tuberculosis and the causes of re-treatment and relapse must be studied.

## Keywords

MDR, Pulmonary Tuberculosis, Relapse, Sudan

## 1. Introduction

During the time period from 2006 to 2015, Sudan recorded an increasing in cases of tuberculosis in both new and resistant cases, which indicates the absence or ineffectiveness of control measures for limiting the spread [1]. In many developing countries tuberculosis remains a major cause of morbidity and mortality and moreover, cases and deaths due to tuberculosis in developing countries are estimated at about 95% and 98% respectively [2]. Of the total cases of tuberculosis infection in the Eastern Mediterranean Region, Sudan includes 11% to 15%, with incidence to infection, which reaches the highest level in 2010 (119 per 100.000 population), then incidence rate was recorded to be 77 per 100.000 population in 2018 [1] [3].

Risk factors of acquiring TB could be categorized into factors that related to susceptible person and contact situation, this includes: age, sex, HIV confection, diabetes, immunosuppressive drugs medications, renal failure, alcohol intake. While risk factors related to drug resistance occurring include failure, relapse, and loss of follow-up [4]. Since the HIV is the most important pathogen that weakens the immune system, its spread in community increases the incidence of infectious diseases such as tuberculosis. In Eastern Sudan, which represents the border between Sudan and Ethiopia, TB/HIV co-infection constituted 18.3% as documented by Tajeldin *et al.* [5]. Records showed a significant difference in the susceptible to tuberculosis among health-care workers in the low- and middle-income and high-income countries; in most developing countries medical personnel work at non-preventable conditions beside environmental pollution in hospitals, shortage of disinfection and other infection control measures [6]. According to WHO Sudan classified as country with medium prevalence for diabetes [7] which is another risk factor for acquiring tuberculosis, in adult a percentage 7.7% had been reported as prevalence rate in Sudan [8].

In Sudan before 2017 MDR cases were ignored due to the inactivation of gene Xpert diagnosis system and thus resistance data are limited record, after 2017 drug resistance cases appear with frequency not recorded and in 2018 reported as 3.8% for new cases and 18% for re-treated cases of tuberculosis. Continuous monitoring of tuberculosis prevents spread of TB cases and helps control program [1]. In 2017 in Sudan, it was estimated about 600 patients among pulmonary TB patients; 3.5% of new TB cases and 18% of pre-treated cases are MDR/RR-TB cases [9]. From study data many reasons of drug resistance were ob-

served; these were due to description of incorrect practices and poor enrollment to anti-TB medications infection [10] [11] [12]. Drug resistance can occur also due to the consequences of primary infection. There for, for treated this cases need intensive interventions. MDR-TB is characterized by the cost of expensive treatment, long period of indication, decrease efficacy compared to susceptible medications, and enormous side-effects of treatment [13].

Indeed, few scattered data were directed to know the outcome of treatment of MDR-TB specially in Sudan where resources is limited. [14] [15] [16] furthermore, this situation makes Sudan at level lower than the goal required to be achieved by WHO [17].

According to WHO classification, tuberculosis patients' status could be identified as new and re-treated cases; re-treated patients include relapse and failure treatment. Relapsing involves those who infected again after completing the period of 6-month treatment, and failure treatment characterized by positive ZN smear after first two months of starting anti-tuberculosis treatment [1]. This study identified MDR among new and re-treated pulmonary tuberculosis cases attending Wad Madani Tuberculosis Center using GeneXpert assay.

## 2. Methods

### 2.1. Settings of the Study

The study followed cross-sectional design during 2018 and 2019. Conducted area was Wad Madani Tuberculosis Center where the majority of admitted patients were from Gezira State. According to 2017 Gezira State population was estimated to be 5,096,920.

### 2.2. Case Definition and Sample Size

This study enrolled patients whom suspected to have pulmonary tuberculosis and referred to the Wad Madani Tuberculosis Center during the study periode. Admitted patients had tuberculosis suspected chest X-ray report and they complain of chronic pulmonary signs and symptoms according to inclusion criteria. Cases were categorized into new and re-treated. The later more classified into relapse, failure of treatment and loss of follow-up. Three hundred cases were recruited.

### 2.3. Sputum Collection and De-Contamination

Early morning sputum was targeted and collected in a suitable plastic container. Patients were constricted to collect more 2 ml of sample after deep coughing. Saliva and food remnants contaminated sputum was rejected. Macroscopical examination is done for the presence of blood. Safety considerations followed were; sodium hydroxide decontamination and personal protective equipments [18].

### 2.4. GeneXpert Assay Test and Interpretation of Results

Immediately after sputum collection, MTB DNA and rpoB gene were examined

in the Medical Laboratory of Wad Madani Tuberculosis Center using (Cepheid, GeneXpert IV) Specimens were prepared to be proceed by GeneXpert machine according to the manufacture instruction [19]. Results were interpreted for the presence of MTB DNA by 5 fluorescent labeled probes; A, B, C, D and E. Detection of 2 or more probes considered positive while no or one probe detection indicated negative result. Degrees of positivity for each sample were determined as high, medium, low and very low. MDR MTB was recorded by the presence of rpoB gene which indicated rifampicin resistant strain; one probes or more negative indicated MDR and all probes positive resulted in no MDR.

## 3. Results

From total of 300 studied patients with pulmonary tuberculosis symptoms, 34% (103/300) were diagnosed as sputum positive by GeneXpert assay. High, medium, low and very low DNA positivity were reported with 16.5% (17/103), 51.5% (53/103), 23.3% (24/103) and 8.7% (9/103) frequency respectively. Males were predominated and represented 68% (70/103). Age group from 21 to 40 was the most frequent 51.5% (53/103) and rural residence occurred with 58.3% (60/103). Symptoms; fever, night sweat, bloody cough, weight loss and appetite loss were significantly associated with pulmonary tuberculosis. Prolong cough was recorded in all cases. No association was found between pulmonary tuberculosis and studied risk factors; contact history (Chi-Square 0.309) and HIV (Chi-Square 0.282) (**Table 1**). While diabetes and renal failure were not documented. New cases of pulmonary tuberculosis among studied subject equal 59.2% (61/103), relapse status was 22.3% (23/103) and failure treatment 16.5% (17/103). MDR tuberculosis was revealed in 9.7% (10/103) of all cases of which relapse involved 50% (5/10) (**Table 2**).

## 4. Discussion

The dilemma of tuberculosis drug resistance cases is increased with the spread of disease transmission and, accordingly, the resistant causative agent. Regrettably, these drug-resistant cases are associated with an increase in the number of deaths [20]. In the near time during 2018, rifampicin as the most functional first line anti-tubercular expressed resistance of 500.000 cases world-wide [9]. Many factors make drug-resistant tuberculosis an exceptional problem to deal with. In terms of medication, the alternative use of second treatment line includes additional antibiotics with more side effects, high cost and a longer duration [21] [13]. Molecular tests for drug-resistant tuberculosis are characterized by rapid and accurate diagnosis, which made them the most widely used [22]. As documented by WHO in 2015, Sudan occurred in the 30 high TB burden countries. The data related to the drug-resistance is of great importance, especially since Sudan is not among the countries in which resistant tuberculosis is spread [23].

This study found 9.7% of pulmonary TB cases as multi-drug resistance and this percentage is slightly more than the last recorded in Sudan in 2018, which

amounted to 7.7% [1]. Near finding was obtained by Aricha and his group in Kenya in 2019 [24] and Ethiopia [25]. However low and or/very low frequency occurred in North Africa and developed countries. It is noted that the increase in MDR-TB is directly proportional to the cases recorded in the country, therefore, the spread must be controlled first in order to reduce the number of drug resistant cases.

**Table 1.** Baseline data of pulmonary tuberculosis subject. No 103

| | | Frequency | Percent | Chi-Square |
|---|---|---|---|---|
| **Gender** | Mae | 70 | 68.0 | 0.611 |
| | Female | 33 | 32.0 | |
| **Age category/year** | Less than 20 | 14 | 13.6 | 0.179 |
| | 21 - 40 | 53 | 51.5 | |
| | 41 - 60 | 23 | 22.3 | |
| | More than 60 | 13 | 12.6 | |
| **Occupation** | House wife | 15 | 14.6 | 0.082 |
| | Worker | 39 | 37.9 | |
| | Student | 8 | 7.8 | |
| | Farmer | 24 | 23.3 | |
| | Employer | 9 | 8.7 | |
| | Unemployed | 8 | 7.8 | |
| **Residence** | Rural | 60 | 58.3 | 0.888 |
| | Urban | 43 | 41.7 | |
| **Fever** | Yes | 38 | 36.9 | 0.000 |
| | No | 65 | 63.1 | |
| **Night sweat** | Yes | 28 | 27.2 | 0.000 |
| | No | 75 | 72.8 | |
| **Bloody cough** | Yes | 58 | 56.3 | 0.000 |
| | No | 45 | 43.7 | |
| **Weight loss** | Yes | 73 | 70.9 | 0.004 |
| | No | 30 | 29.1 | |
| **Appetite loss** | Yes | 93 | 90.3 | 0.000 |
| | No | 10 | 9.7 | |
| **Contact history** | Yes | 5 | 4.9 | 0.309 |
| | No | 98 | 95.1 | |
| **HIV** | Yes | 4 | 3.9 | 0.282 |
| | No | 99 | 96.1 | |

**Table 2.** Distribution of pulmonary tuberculosis cases according to the admission status and MDR detection. No 103

| Patient's status | Frequency | Percent | MDR positive | MDR negative |
|---|---|---|---|---|
| **New** | 61 | 59.3 | 3 | 58 |
| **Relapse** | 23 | 22.3 | 5 | 18 |
| **Failure treatment** | 17 | 16.5 | 2 | 15 |
| **Loss of follow-up** | 2 | 1.9 | 0 | 2 |
| **Total** | 103 | 100 | 10 | 93 |

Because of importance, we could not detect highly resistant cases such as extensive drug resistance tuberculosis XDR-TB due to lack of advance laboratory technology for testing [26] especially in Sudan. There for there is a need to detect the actual occurrence of XDR in tuberculosis endemic regions.

Although the proportion of female in the community is equal or more than male, we observed low rate of TB among studied women. Similarly, high rate of male infection reported in Sudan [27] and India [28]. From our result which revealed 69.8% of TB positive cases as workers and farmers, male more likely to be expose to MTB during day work [29]. Other behaviors common in male rather than female are smoking and tobacco [30]. In line, some studied elicited hormonal and immunological variation between female and male to be susceptibility determinant to infectious diseases [31] [32]. In contrast to above mentioned the incidence of pulmonary TB in female was greater than male in three related countries; Iran [33], Afghanistan [34] and Pakistan [35], social-cultural and economic factors supposed to be predictors for this situation, hence, studies are needed for more explanation.

The rural population formed a larger proportion of pulmonary tuberculosis in this current study although we showed no significant relationship, there is no doubt that the quality of living and health is lower than that of urban residents. The most affected age group among studied patients was from 21 to 40 years which had been noted in many other findings; in Sudan 27 and Kenya [36]. These results encourage further studies to re-evaluate host status in terms of susceptibility to infection and immunity status, prevalence of the causative agent [37] and vaccination.

With pulmonary tuberculosis, many studies deal with the social, clinical factors and admission status of patients some of these studies did not show a relationship between the tuberculosis and social factors [38] [39], and the results of our studies are in agreement.

In the present study cases of treatment failure was repeated by 16.5%, and this was determined by positive ZN smear after the first two months of treatment. The possible reasons of failure could be; the inadequate TB treatment centers and their far distance from the rural areas which included most cases [40]; in addition to the prolong medication period and the general weakness of the patients due to the loss of appetite and weight [41] [42].

Relapse after completing tuberculosis treatment is of a global concern [43] and our study recorded alarming rate of 22%; confirming that tuberculosis is still an endemic in Sudan. It is worth noting that, relapse is associated with drug-resistance tuberculosis, and it is not surprising that 50% of relapse cases in this study were MDR [44] [45], for comparison the MDR rate of new TB cases in Sudan was estimated in 2019 to be 3.5% [46].

In fact, this study did not identify the level of rifampicin resistance through rpoB gene sequencing for the detection of existent mutations, which can improve the drug selection and physician decisions [47].

In conclusion, the rates of drug-resistant tuberculosis are increasing even more in cases of relapse, which requires dealing with this problem in its initial stages, for example, increasing treatment centers and early diagnosis in peripheral places, and accuracy in following up on patients.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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