

Prevalence of Multidrug Resistance Tuberculosis

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Abstract

Introduction

Tuberculosis is common in Pakistan. Due to various factors including socioeconomic factors, compliance is poor to anti-tuberculosis drugs, leading to resistance. We aim to determine the prevalence of Multidrug resistance (MDR) tuberculosis in Pakistani population.

Methods

A prospective observational study was conducted from April 1, 2019, to December 31, 2019, in the Pulmonology department of a tertiary care hospital in Pakistan. Culture and sensitivity were assessed using a sputum sample or, in cases of an absent sputum sample, from Broncho alveolar lavage.

Results

Approximately 71.3% percent patients who had tuberculosis were found to be resistant to Isoniazid and around 48.6% did not respond to Rifampin. Multi-drug resistant was found in 29.4% participants.

Conclusion

Multi-drug resistance tuberculosis is very prevalent in Pakistan, which may increase burden on health care system and may lead to various complications of tuberculosis.

Keywords

Multi-drug resistance, Tuberculosis, Pakistan

Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* that mainly affects the lungs causing respiratory disease along with systemic symptoms such as fever, anorexia and weight loss. Multidrug resistance tuberculosis (MDR-TB) is when the causative bacteria become resistant to the drugs used to cure tuberculosis. The commonly used drugs to treat non-resistant tuberculosis are isoniazid, rifampin, pyrazinamide and ethambutol. MDR-TB means strains of TB that do not respond to at least isoniazid and rifampin, the 2 most powerful anti-TB drugs [1].

Pakistan has the sixth largest population in the world and has the fifth greatest burden of TB [2]. The country is also estimated to have the fourth highest prevalence of multidrug-resistant TB (MDR-TB) globally. Drugs resistant TB has emerged due to multiple causes which include: late diagnosis, improper treatment, patients lost to follow-up, non-adherence to medications, and lack of a social support programme for high-risk populations [3]. Furthermore, socioeconomic problems, including hunger, homelessness, and unemployment, are common among MDR-TB patients [4]. Additionally, in a global systematic review and meta-analysis, unemployment and lack of health insurance coverage were risk factors of MDR-TB [5].

Developing of TB drug resistance is a major concern and is on the rise. However, there is not enough data on the incidence of MDR-TB in Pakistan. The aim of this study is to determine the prevalence of Multidrug resistance tuberculosis. Identifying patients with MDR-TB will help us identify the risk factors that are contributing to increase incidence of MDR-TB.

Materials and Methods

A prospective observational study was conducted from April 1, 2019, to December 31, 2019, in the Pulmonology department of tertiary care, Pakistan. The inclusion criteria were; patients older than 18 years registered for tuberculosis management, had been taking first-line anti-TB regimen

for a minimum of two months and were still positive for *Mycobacterium tuberculosis* (MTB), either on sputum smears or culture. Informed consent was taken from patients and the study was approved by the institutional review board. Drug adherence was confirmed from the patient's TB drug and dosage card.

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was taken from Liaquat university of health and medical sciences (LUMHS/2019/02).

Culture and sensitivity were assessed using a sputum sample or, in cases of an absent sputum sample, from Broncho alveolar lavage. Isolation of *Mycobacterium* from the specimens was achieved by Lowenstein-Jensen medium and *Mycobacterium* Growth Indicator Tube medium (Becton Dickinson, Franklin Lakes, NJ, USA). After that, MTB was isolated using the BACTEC NAP test [(p-nitro- α -acetyl amino- β -hydroxy-propiophenone) (Becton Dickinson)]. The MTB strains which were resistant to both isoniazid and rifampin were labeled as MDR strains.

The patients completed a brief questionnaire requesting patient demographics such as age, gender, and history of TB contact. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software Version 22.0 (Chicago, SPSS Inc.). Data was presented as frequencies and percentages.

Results

In our study, we included 101 participants approximately. The mean \pm standard deviation (SD) age of participants was 28 ± 13 years. There were 58 women (57.4%) and 43 men (42.6%) in the study. There were 63 (62.3%) patients who had a positive history of household TB contact. Around 71.3% percent patients with tuberculosis were resistant to Isoniazid and 48.6% were resistant to Rifampin. Multi-drug resistant was found in 29.4% participants. (Table 1)

Drug	Sensitivity n (%)	Resistance n (%)
Streptomycin	56 (55.4%)	45 (44.6%)
Isoniazid	29 (28.7%)	72 (71.3%)
Rifampin	52 (51.4%)	42 (48.6%)

Isoniazid + rifampin (MDR)	70 (70.4%)	31 (30.6%)
Pyrazinamide	50 (49.5%)	51 (50.5%)

Among second line of treatment, participants had maximum resistant to Ofloxacin (59.7%), followed by Ethionamide (9.9%).

Drug	Sensitivity n (%)	Resistance n (%)
Kanamycin	92 (91.1%)	9 (8.9%)
Capreomycin	98 (97.1%)	3 (2.9%)
Ethionamide	91 (90.1%)	10 (9.9%)
Ofloxacin	61 (60.3%)	40 (59.7%)

Discussion:

Tuberculosis infection is a global burden and is a major cause of mortality in Pakistan [6], such that Pakistan holds 8th rank according to a report by WHO on the total number of tuberculosis cases reported [7]. In the following study, we have studied patients on anti-tuberculosis therapy and have concluded the presence of drug resistance. According to our study, the majority of the patients on Isoniazid or Rifampin have developed resistance to the particular drug therapy. We

have also confirmed the presence of multidrug resistance (MDR) in patients who were on Isoniazid as well as rifampin regime. In our study the patients who were given second-line drug therapy, out of which majority of them have developed resistance to Ofloxacin followed by Ethionamide.

Similar to our study, a study conducted at Civil Hospital, Jamshoro has also concluded high drug resistance in patients on Isoniazid and Rifampin. The study also concluded a high frequency of multidrug resistance (MDR) [8]. A survey on Isoniazid drug has also predicted point mutations contributing to the Isoniazid resistance [9]. A similar study has also concluded that the most common second-line drug resistance was to Ofloxacin which is consistent with our results [8].

The major risk factor for the development of tuberculosis infection includes increasing age, male gender, smoking history, heavy alcohol consumption [10]. Low socioeconomic status and underlying medical conditions have also contributed to the development of the infection [10]. HIV co-infection has also contributed to the active tuberculosis infection due to impaired immunity [11]. Patients with immune-mediated inflammatory disorders (IMID) have also raised the likelihood of acquiring the infection [11]. Studies have also linked immunosuppression and malnutrition to the development of tuberculosis infection [12]. Higher risk was observed in patients suffering from diabetes [13]. Children on the other hand are also susceptible to getting infected [14].

Studies have confirmed the presence of resistance to second-line drugs. The drug Ofloxacin is a broad-spectrum fluoroquinolone antibiotic that is used as a second-line drug treatment for tuberculosis infection. Studies have shown poor treatment results with Ofloxacin resistance despite the addition of other fluoroquinolones [15]. The widespread abuse of the use of fluoroquinolone antibiotics has significantly contributed to the rise of Ofloxacin resistance. Strategies are required to stop the misuse of antibiotics for other infections thus improving the efficacy of Ofloxacin for the treatment of tuberculosis [16].

Tuberculosis is the major cause of mortality and morbidity in Pakistan thus, making it evident to provide proper treatment strategies to control the spread. The lack of diagnostic facilities, improper and inadequate drug therapies have contributed to drug resistance. The rising global burden calls for the establishment of Directly Observed Treatment Strategy (DOTS) to eliminate

inadequate and partial treatment strategies [7]. It is important to spread awareness regarding proper treatment protocols. The surveillance strategies should be launched to collect data regarding the risk factors present in the population. Efforts should be made to counsel the patients regarding smoking, alcohol cessation, and to adopt a healthier lifestyle [11]. Maintenance of hygiene should be made the top priority. The early and accurate screening procedures can be employed which will help limit the epidemic.

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