Multi Drug Resistance: A Continuous Challenge by a Century Old Mycobacterium Tuberculosis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: Tuberculosis is a mycobacterial infection caused by mycobacterium tuberculous bacillus. Anti-tuberculous drugs are drugs used to treat tuberculosis which include first line anti-tuberculosis drugs used to treat tuberculosis initially when the infection is non-resistant these include Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol. Second line anti-tuberculosis drugs which are used to treat resistant tuberculosis or when first line drugs are contraindicated these include Ethionamide, Capreomycin, ciprofloxacin etc. Multidrug-resistant tuberculosis is tuberculosis not responding to 2 first line anti-tuberculosis drugs.
Methods: This study was aimed at determining the frequency of MDR pattern in multidrug-resistant tuberculosis cases. The design was cross sectional and the study was conducted at Tuberculosis and chest diseases Center Mirpur Khas in 2017 over two years.
Results: Total 458 MDR patients were evaluated 252(55%) females and 206(45%) were males. Isoniazid and Rifampicin were resistant in 97 (21.17%) cases while Isoniazid, Ethambutol and

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Rifampicin were found to be resistant in 40(8.73%) cases. The resistance for Isoniazid, Pyrazinamide and Rifampicin was observed in 50(10.92%) cases whereas 60(13.10%) patients were resistant to Isoniazid, Rifampicin and Streptomycin. Isoniazid, Ethambutol, Rifampicin and Streptomycin were resistant in 75(16.38%) cases. Isoniazid, Pyrazinamide, Rifampicin and Streptomycin resistance was seen in 40(8.73%) patients and 96(20.96%) of the cases shoed resistance to Isoniazid, Ethambutol, Pyrazinamide and Rifampicin.

Conclusion: Multidrug-resistant tuberculosis is highly prevalent in the region.

1. INTRODUCTION

Tuberculosis a mycobacterial infectious disease which has progressed over a century all over the globe, it still persists as a health challenge in the form of drug resistance. The primary target of the mycobacterium tubercle bacillus is the lung tissue secondarily affecting the all body tissues like bones, GIT, brain etc. Although the complete cure is available but remittance and resistance continue to add the morbidity. Immuno-compromised patients are on greater risk along with people of low socio economic status and poor hygienic conditions. The disease has an annual mortality of 1.3 million deaths globally [1].

The treatment consists of an intensive phase and a continuation phase of two months with four drug combination (Isoniazid, Rifampicin, Ethambutol and Pyrazinamide) and a six month continuation phase with 2 drugs (Isoniazid and Rifampicin). Multi drug resistance phenomenon is an emerging challenge because the mycobacterium frequently develops resistance against the first line drugs. Drugs used in the management of Multi drug tuberculosis are termed as 2nd line drugs which include quinolones, aminoglycosides and macrolides etc.

There are 110000 annual deaths approximately due to Multidrug-resistant tuberculosis and there is 50% annual increase in new MDR cases which is an evidence of poor infection control [2]. The prevalence of multi drug tuberculosis in India is 23.3% [3]. Likewise the Multidrug-resistant tuberculosis cases are highly prevalent in Afghanistan China, Indonesia, Iran and Nigeria. According to the global report on tuberculosis 2015, there were 14000 MDR tuberculosis cases in Pakistan with 4.2% as cases new cases whereas 16% were relapse cases [4]. There are estimated 110,000 deaths due to multi drug resistant tuberculosis annually and there are about half million new cases of MDR/year [5]. Chronic illness puts adverse effect on the economic as well as mental status of the individuals and families leading to poverty and depression [6].

In this study we have tried to estimate the exact figures regarding the MDR tuberculosis, like its frequency and resistance patters n this part of the land. Although studies were published from different provinces of Pakistan on this subject but very few are found from Sindh province.

2. MATERIALS AND METHODS

This study was a cross sectional design study conducted at Centre for Tuberculosis and chest diseases situated in Mirpur Khas district of Sindh province. Inclusion criteria were patients of different age groups from 10 years to no upper age limit, known MDR cases without any gender discrimination whereas the exclusion criteria were non-tuberculous respiratory infections, non-MDR tuberculosis patients. The data acquisition forms were developed for collecting information required which were filled under ethical guidelines with informed consent from either patients or their relatives. Selection of patients involved the non-probability type of sampling which was purposive sampling. No statistical test was applied as it was not required. Resistance patterns were confirmed by the associated lab though gene expert. Tables, pie charts and bar charts were used to represent frequency and percentage of the obtain data.

3. RESULTS

Total 458 MDR patients were evaluated 252(55%) females and 206(45%) were males [Fig. 2]. Isoniazid and Rifampicin were resistant in 97 (21.17%) cases while Isoniazid, Ethambutol and Rifampicin were found to be resistant in 40(8.73%) cases. The resistance for Isoniazid, Pyrazinamide and Rifampicin was observed in 50(10.92%) cases whereas 60(13.10%) patients were resistant to Isoniazid, Rifampicin and Streptomycin. Isoniazid, Ethambutol, Rifampicin and Streptomycin were resistant in 75(16.38%)

Table 1. Multi drug resistance pattern

| Multi drug resistance pattern	N (%)
Isoniazid+ Rifampicin	97(21.17%)
Isoniazid+ Rifampicin+ Ethambutol	40(8.73%)
Isoniazid+ Rifampicin + Pyrazinamide	50(10.92%)
Isoniazid+ Rifampicin + Streptomycin	60(13.10%)
Isoniazid+ Rifampicin + Ethambutol+ Streptomycin	75(16.38%)
Isoniazid+ Rifampicin + Pyrazinamide +Streptomycin	40(8.73%)
Isoniazid+ Rifampicin + Ethambutol+ Pyrazinamide	96(20.96%)
Total number of MDR-cases	**458(100%)**
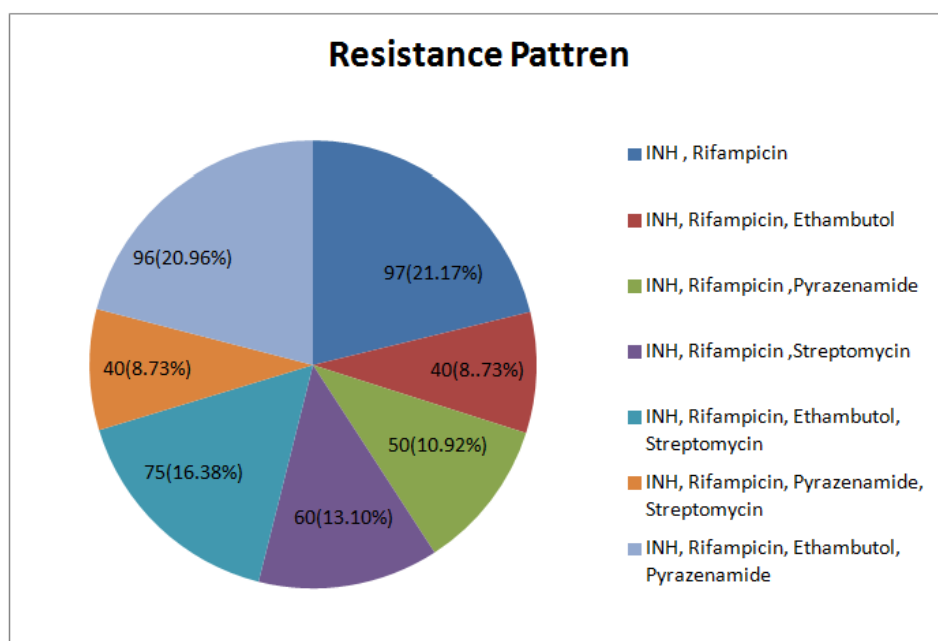
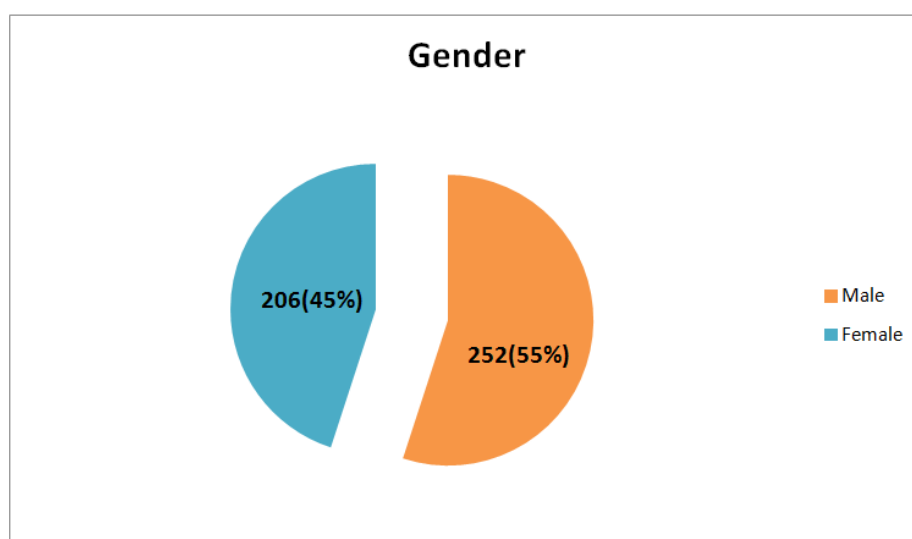**Fig. 1. Pie chart representation of MDR pattern**

Fig. 2. Pie chart of gender distribution

cases. Isoniazid, Pyrazinamide, Rifampicin and Streptomycin resistance was seen in 40(8.73%) patients and 96(20.96%) of the cases shoed resistance to Isoniazid, Ethambutol, Pyrazinamide and Rifampicin [Table 1,Fig. 1].

4. DISCUSSION

The frequent exposure to anti-microbial agents and poor compliance tuberculosis drugs is among the most common risk for MDR tuberculosis [7]. Surveillance data on MDR-tuberculosis conducted by WHO in 2017 shows 4.1% cases of MDR-tuberculosis are new cases, whereas 19% of the MDR cases were those which were previously treated for tuberculosis [8]. Results of study by Goyal et al. from Indian part of the subcontinent showed the MDR tuberculosis prevent at a rate of 23.3% as a total including all old and new cases [3]. Shivekar et al reported mono resistance for Rifampicin as 2.5% and for Isoniazid as 11.4% while MDR was reported as 5.4% which was much lesser from the previous Indian study [9]. A previous study from Sindh province of Pakistan by Ashique Ali Arain et al reported the MDR tuberculosis as 184 (89.32%) and non-MDR cases as 19 (10.68%) with males as 101 (49%) and females as 105 (51%). INH was resistant in 4 (1.94%) patients while Rifampicin was mono resistant in 15(7.28%) patients [10]. Another Pakistani study conducted in KPK province by Qadeer et al (2017) on the close contacts of tuberculous patients (n=1467), they found 3.8% (56) as tuberculosis positive with a MDR-tuberculosis rate of 96%(54) which was very high only 4% (2) patents were found to be susceptible to 1st line drugs [11].

Javaid et al (2016) reported MDR-tuberculosis to be present in 17.4% of the close contacts (n=610) whereas 4.2% of the cases non-MDR tuberculosis [12]. The cure rate for MDR tuberculosis is reported as 78.7% in Pakistan which is very effective and may due attributed healthy regional climate [13]. Some researchers have also explored the gender impact on MDR tuberculosis which does not seem to make a big sense and we didn't observe such results as well [14]. Liu et al. however reported positive association with female gender and MDR-Tuberculosis but again inconsistency lies between the two studies [15]. MDR-Tuberculosis is on rise despite of the availability of a wide range of 2nd line drugs which shows continuous challenges from mycobacterium over a century of years making the eradication of this disease still

a dream but the hope and struggle are alive too to deal this challenge.

5. CONCLUSION

The prevalence of MDR-tuberculosis is on rise and need further newer therapeutic agents in future to deal this challenge of mycobacterium tuberculosis.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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