

Prevalence of Pre-XDR-TB, XDR-TB among MDR-TB patients

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MAUM AM conceived idea, SN AM drafted the study, AM MAUM MS collected data, MS SN did satisfied analysis & interpretation of data, MAUM AM critical reviewed manuscript, All approved final version to be published

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The Authors declares that there is no conflict of interest.

Abstract

Background: Tuberculosis (TB) still remain a challenge to health authorities through out the world. It is most dangerous in the form of drug resistant TB (DR-TB). Programmatic management is need of the day to stop the transmission and conversion of susceptible TB into DR-TB. Present study was conducted to evaluate the prevalence of pre-extensively drug resistant tuberculosis (Pre-XDR), extensively drug resistant tuberculosis (XDR) among the MDR TB patients.

Material and Method: We reviewed the record of all patients registered in PMDT site at Nishtar Medical hospital, Multan, Pakistan between June 2012 and March 2016. Data was obtained about clinical details and resistance pattern.

Results: A total of 531 patients were enrolled during this period. 295 (55.5%) were male and 236 (44.5%) were female. Most of the patients 377/531 (71%) belong to younger age group i.e from 15-44. The prevalence rate of Pre-XDR and XDR –TB among MDR TB patients were 171/531 (32.2%) and 18/531 (3.4%) respectively. Out of 18 XDR-TB patients 10 were resistant to Am (Amikicin), Km (Kanamycin), Cm (Capreomycin) and FQ (Fluoroquinolone). 05 were resistant to Km+FQ. 02 were resistant to Am+Km+FQ and 01 patient was resistant to Cm+FQ. Out of 171 PRE-XDR TB patients all were found to be resistant to FQ and no one was resistant to 2nd line Injectibles (Am,Km,Cm) .

Conclusion: There is high prevalence of Pre-XDR tuberculosis in patients registered at PMDT site, at Nishtar Medical hospital, Multan, Pakistan Pakistan. Similarly XDR-TB patients were also reported and registered during this time period. There is a desperate need to closely follow new TB patients and to emphasize on treatment compliance in order to prevent drug resistant tuberculosis. There is also a need to ban over the counter sale of Anti Tuberculous Drugs especially second line drugs.

Keywords: Pre-XDR; XDR; Fluoroquinolone; PMDT

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Introduction

Pakistan currently ranks fifth amongst countries with highest burden of Tuberculosis alongside the fourth highest burden of drug resistant TB globally. In an estimated population of 180 million with annual incidence of TB being 231/100,000, Pakistan produces about 420,000 new cases annually.¹ The estimated percentage of new TB cases with MDR-TB

was reported to be 3.5%.² Extensively Drug-resistant Tuberculosis (XDR-TB) is defined as TB caused by a Multi-Drug-Resistant (MDR) strain (i.e., resistant to at least Rifampicin and Isoniazid) that is also resistant to any Fluoroquinolone (FQ) and one of the second-line injectable drugs, such as Capreomycin, Kanamycin, or Amikacin (AK).² Pre-XDR TB is defined as MDR-TB strain that is resistant to either Fluoroquinolone or second line injectable drug but not to both.³

According to the WHO, levels of MDR-TB will reach an alarming state in South Asia if prompt steps are not taken.⁴ The incidence of TB increases rapidly in settings where TB control is poor, patients are immuno compromised and also among those with HIV/AIDS or malnutrition.⁵ Globally an estimated 20 % of patients with TB default or fail to respond to therapy and develop MDR-TB.⁶⁻⁸ Several factors are responsible or contribute to the development of MDR-TB. These include programmatic and patient factors such as poor adherence of patients to first line anti-TB drugs, inappropriate treatment regimen, dosage and duration for treatment and non-compliance to national guidelines and TB treatment protocol by clinicians among others. The inappropriate use of second line anti-TB drugs in MDR-TB patients will lead to amplification of resistance and the development of XDR-TB.⁹

The aim of the study was to determine the prevalence of Pre-XDR and XDR tuberculosis among the patients registered during June 2012 to march 2016 by using drug susceptibility testing.

Objectives

To determine the prevalence of Pre XDR and XDR tuberculosis among the patients registered at the PMDT site at Nishtar Medical hospital, Multan, Pakistan

Methodology

This was a retrospective audit conducted at the PMDT site at Nishtar Medical hospital, Multan, Pakistan from June 2012 to march 2016. All the patient charts with the diagnosis of drug resistance tuberculosis were retrieved. Complete previous history of anti-tuberculosis drugs was explored from the patients and all the samples underwent gene expert and then drug sensitivity testing (DST) for 1st and 2ndline drugs.

Results

A total of 531 patients were enrolled during this period. 295 (55.5%) were male and 236 (44.5%) were female. Most of the patients 377/531 (71%) belong to younger age group i.e. from 15-44 (Table 1). The prevalence rate of Pre-XDR and XDR-TB (Figure 1) among DR TB patients were 171/531 (32.2%) and 18/531 (3.4%) respectively (Table 2). Out of 18 XDR-TB patients 10 were resistant to Am (Amikacin), Km (Kanamycin), Cm (Capreomycin) and FQ (Fluoroquinolone) (Table 3). 05 were resistant to Km+FQ. 02 were resistant to Am+Km+FQ and 01 patient was resistant to Cm+FQ. Out of 171 PRE-XDR TB patients all were found to be resistant to FQ and no one was resistant to 2nd line Injectables (Am, Km, Cm). Base line characteristics of the patients are given in Figure 2,3.

Table 1: Baseline characteristics of the patients

Total Patients	Age group	Male	Female	Pre XDR	XDR
531	15-44	295	236	171	18
		55.5 %	44.5 %	32.2 %	3.4 %

Table 2: Resistance pattern in Pre XDR-patients

Pre XDR	FQ	Am	Km	Cm
171	171	0	0	0

Table 3: Resistance pattern in XDR patients

XDR	Am	Km+FQ	Am+Km+FQ	Cm+FQ
18	10	5	2	1

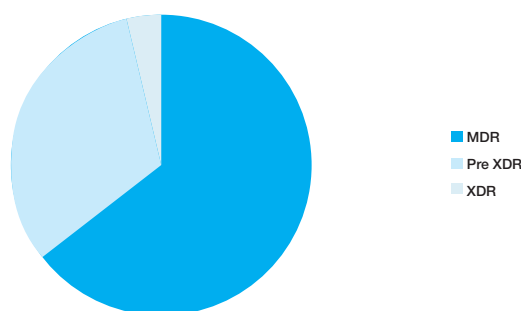


Figure 1: Prevalence of Pre-XDR and XDR Patients

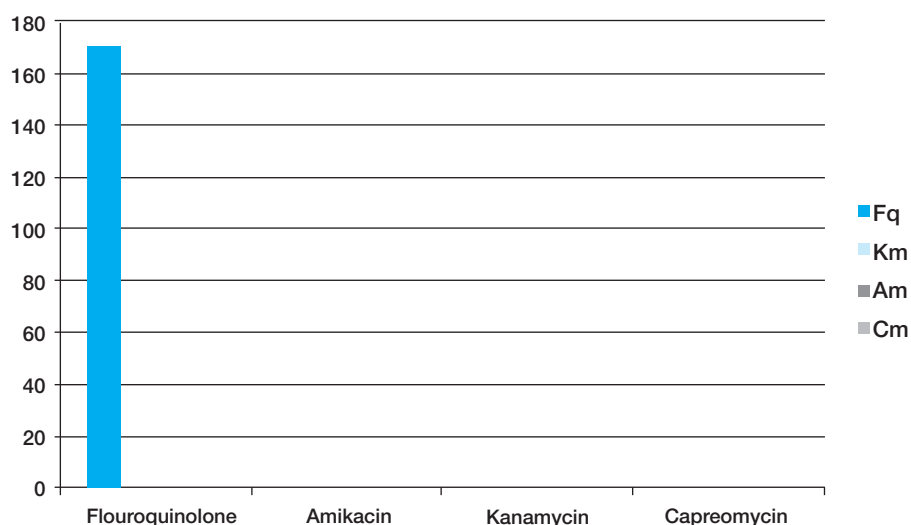


Figure 2: Resistance pattern in Pre-XDR patients

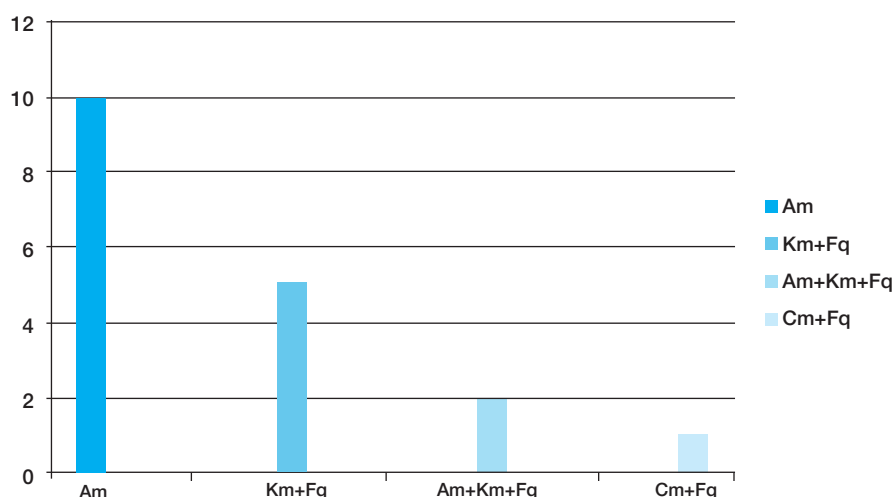


Figure 3: Resistance pattern in XDR patients

Discussion

We have conducted this study in order to determine the baseline pattern of drug resistance tuberculosis in MDR-TB patients. As per WHO guidelines DST were sent for Fluoroquinolone (FQ), Amikacin (Am), Kanamycin (Km) and Capreomycin (Cm). In our study prevalence of Pre-XDR TB and XDR-TB were found 32.2% and 3.4% respectively. Among Pre-XDR patients all were found resistant to Fluoroquinolone. In one study conducted by Nisar Rao et al at Ojha Institute of chest diseases Karachi, prevalence of Pre XDR and XDR TB were found 39.5% and 2% respectively.¹⁰ Both these studies show that there is a rising trend in Pre XDR and XDR TB patients in Pakistan.

Majority of Pre XDR-TB patients were resistant to FQ. Pre-XDR rates reported from other countries include 16.7% in Nigeria, 12.1% in Poland, 31% in China and USA, 28% in Taiwan.¹¹⁻¹⁵ Main problem in our country is that most of our MDR TB patients are already exposed to Fluoroquinolones like Levofloxacin, Moxifloxacin, Ofloxacin and Sparfloxacin, as these all are freely available in open market. The exposure of these patients to Levofloxacin can amplify resistance to all the other quinolones as well as there is cross resistance among Fluoroquinolones. So, Clinicians need to be sensitized about the rational use of Fluoroquinolones in patients suspected of having TB or have failed the conventional 1st line anti tuberculosis treatment. There is also strong need to ban the sale of over the counter medicine specially

Fluoroquinolones or if at all used, should be used judiciously in order to prevent the misuse of these medicines and in future to decrease this high incidence of drug resistance. Further studies are also needed from various parts of the country in order to make a clear picture of FQ resistance so that this matter can be raised on a national level.

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