RESEARCH ARTICLE

Prevalence and risk factors of multi drug resistant tuberculosis in children

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Abstract

Objective: To assess the prevalence of drug-resistant tuberculosis and to identify possible risk factors in children.

Method: The descriptive, interview-based study was conducted at the Pulmonology outdoor clinic of Jinnah Hospital, Lahore, Pakistan, from January to August 2019, and comprised children aged up to 14 years who were either contacts of a multi-drug resistant tuberculosis patients or non-contacts. Data related to their demography as well as clinical and social characteristics was collected using a questionnaire. Data was analysed using SPSS version 22.

Results: Of the 202 subjects, 115(56.9%) were girls and 87(43.1%) were boys. There were 70(34.7%) subjects aged >13 years, followed by 45(22.3%) aged 9-12 years, 44(21.8%) aged ≤4 years and 43(21.3%) aged 5-8 years. Overall, there were 26(12.9%) cases positive for multi-drug resistant tuberculosis; 16(61.5%) girls and 10(38.5%) boys. In terms of age, 17(65.4) cases were positive in those aged >13 years. Age, previous history of tuberculosis, co-infection with any immune-compromising disease and close contact with patients of multi-drug resistant tuberculosis were significant risk factors identified.

Conclusion: The prevalence of multi-drug resistant tuberculosis was high in contacts of multi-drug resistant pulmonary tuberculosis patients, more prevalent in children aged 13-14 years.

Keywords: Mycobacterium tuberculosis, MDR in children, multi-drug resistance, MDR TB contacts.

(JPMA 73: 1978; 2023) **DOI: https://doi.org/10.47391/JPMA.7872**

Submission completion date: 19-09-2022- **Acceptance date:** 15-03-2023

Introduction

Globally, there are approximately 67 million children suffering from mycobacterium tuberculosis (MTB) infection. It is estimated that 5 million children are infected with isonicotinic acid hydrazide, or isoniazid, (INH) mono-resistant MTB strains and 2 million with multidrug-resistant (MDR) strains. In 2014 alone, an estimated 850,000 children developed pulmonary tuberculosis (PTB) with 25,000 MDR cases.[1] The statistics surged drastically, and in 2017, about a million new cases of paediatric TB were reported.[2] Adding to the current poor trajectory, there have also been reports of extensive drug resistance (XDR) in paediatric PTB, with almost 100,000 children found infected with XDR strains.[1]

In TB patients, drug resistance results from spontaneous genetic mutations in the MTB genome.[2] The risk of genetic mutation increases with increasing bacterial load, explaining why resistance is more commonly seen in adult cavitary PTB, which has large bacilli load. In children, the more common reasons of drug resistance are transmission of a resistant bacillus, and previous treatment with anti-TB therapy (ATT). Other factors that predispose to drug-resistant TB include inappropriate drug regimens, monotherapy and drug non-adherence.[3]

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Pakistan is among the top 20 TB-endemic countries, which share 84% of global TB burden and 87% of MDR TB burden, according to the World Health Organisation (WHO).[2] Though there have been various studies highlighting the incidence of MDR TB in Pakistan,[4] no study could be found focussing on the incidence of paediatric MDR TB in Pakistan. The current study was planned to fill the gap by assessing the prevalence of MDR TB and finding the risk factors among Pakistani children.

Patients and Methods

The descriptive, interview-based study was conducted at the Pulmonology outdoor clinic of Jinnah Hospital, Lahore, Pakistan, from January to August 2019. After approval from the institutional ethics review board, the sample size was calculated using the single population proportion formula as follows: n = z2 p (1-p)/d2; (1) where: n = the minimum required sample size; z = standard normal distribution value at 95% confidence interval (CI) 1.96; p = prevalence of paediatric MDR TB 29%[5] and d = margin of error 4%. The values were put into the formula: n= 1.962 x 0.292 / 0.042 leading to 3.8416 x 0.0841 / 0.0016 = 201.924 = 202. The sample was raised by enrolling the subjects till the target sample size was reached. Those included were children of either gender aged 0-14 belonging to Okara, Lahore, Sahiwal and Pakpattan districts of the Punjab province who were either contacts or non-contacts with confirmed MDR TB cases. Those excluded were clinically diagnosed individuals and those with extra-pulmonary TB.

Data was collected from parents/guardians/attendants using a predesigned and pretested questionnaire based on known and possible factors.

Demographic data was noted along with 8 different risk (R) factors; R1 = children with Bacille Calmette-Guérin (BCG) vaccine done, R2 = malnourished or low body mass index (BMI),[6] R3 = close contact with any MDR TB patient, R4 = previously treated for drug-sensitive TB (DSTB), R5 = coinfection with any immune compromising disease, R6 = children with positive Mantoux test, R7 = children living in congested areas with multiple families living in the same house, and R8 = children with latent TB infection.[3,7]

Data was entered into Microsoft Excel and its accuracy was checked by cross-verifying with hard copies of available data on treatment site. Data was analysed using SPSS version 22. P<0.05 was considered significant.

Results

Of the 202 subjects, 115(56.9%) were girls and 87(43.1%) were boys. There were 70(34.7%) subjects aged >13 years, followed by 45(22.3%) aged 9-12 years, 44(21.8%) aged ≤4 years and 43(21.3%) aged 5-8 years. Overall, there were 26(12.9%) cases positive for multi-drug resistant tuberculosis; 16(61.5%) girls and 10(38.5%) boys. In terms of age, 17(65.4) cases were positive in those aged >13 years (Table).

Table: Demographic characteristics and their relationship with multi-drug resistant tuberculosis (MDR TB).

	n (%)	MDR TB Positive [(%)]
Age Group		
≤ 4 years	44 (21.8)	3 (11.5)
5 - 8 years	43 (21.3)	1 (3.8)
9 - 12 years	45 (22.3)	5 (19.2)
≥13 years	70 (34.7)	17 (65.4)
Gender		
Male	87 (43.1)	10 (38.5)
Female	115 (56.9)	16 (61.5)
Total	202 (100)	26 (100)

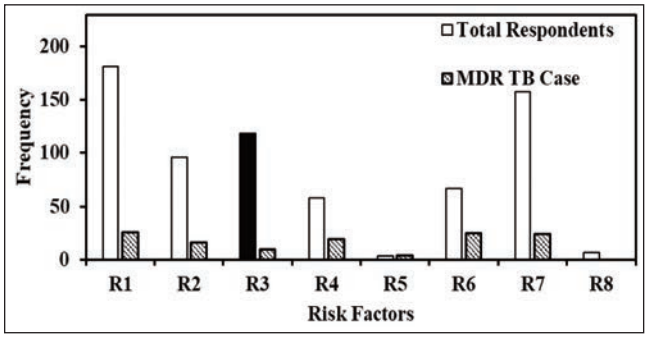

Figure: Relationship between risk factors and multi-drug resistant tuberculosis (MDR TB) prevalence in children.

Age, previous history of TB,[8] co-infection with any immune-compromising disease and close contact with patients of MDR TB were significant risk factors (Figure).

Discussion

Many studies have shown that MDR TB is linked with age, and younger ones are more susceptible.[9,10] According to the WHO, about 1.2 million children aged <15 years were infected with TB and 230,000 suffered death because of TB in a single year.[11,12] Besides, 25,000 to 32,000 children develop MDR TB every year.[13]

The current data regarding gender showed that 61.5% respondents were females, but the relationship of MDR TB with gender was not significant, which is in line with literature.[14,15] In contrast, many studies have shown that gender has significant impact on MDR TB prevalence.[8,9,16]

In the current study, 89.6% children had had BCG vaccine, and the relationship between vaccination status and MDR TB was non-significant (p=0.063). BCG has shown modest protection against TB and plays an important role in the prevention of TB, especially the patients having compromised immunity.[17] Another study showed that BCG vaccine provided varied degree of protection against PTB disease, especially in children.[18]

In the current study, patients having normal body weight had lower risk of MDR compared to overweight people. In contrast, one study showed a strong relationship between low BMI and PTB infection.[15,18]

Close contact with MDR TB patient had a significant (p=0.027) relationship with MDR TB occurrence in the current study. MDR TB is highly transmissible and people living in the same family have greater chances of developing active disease.[17] MDR TB cases actively increase the occurrence of the problem in the household and the people in close contact.[1,12] The current finding is supported by an earlier study.[1]

Further, patients with DSTB history were significantly more positive for MDR TB (p=0.0001). The finding is in line with previous studies.[18]

The current study showed that co-infection with any immune compromising disease had a strong relationship with MDR TB (p=0.0001), as has been reported earlier.[2,3]

Congested living conditions did not have a significant association with MDR TB (Figure) in the current study, which is in contrast with other studies.[10] Finally, the current study found no relationship between latent TB and MDR TB (Figure). An earlier study has mentioned that contact with MDR TB patients causes prevalence of latent TB infection.[14]

The current study has limitations as it did not address extra-pulmonary TB. Another limitation is the study's small sample size that was raised at a single centre.

Conclusion

Highest MDR rates were seen in contacts of MDR TB patients, children with other concomitant diseases and children with positive Mantoux test.

Acknowledgement: We are grateful to PMDT (Programmatic management of Drug resistant Tuberculosis) Site, Jinnah Hospital, Lahore, and Registrar of the Pulmonology Department, Jinnah Hospital, Lahore.

Disclaimer: The text is based on an academic thesis.

Conflict of Interest: None.

Source of Funding: None.

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