ORIGINAL ARTICLE

Risk Factors Associated with Occurrence of Multidrug Resistance Tuberculosis

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ABSTRACT

Aim: Multidrug-resistant tuberculosis (MDR-TB) is a significant threat to community health. This study aimed to ascertain risk factors that contribute to the high incidence of MDR-TB.

Methods: A cross-sectional study was designed, in which 55 MDR-TB and 55 non-MDR-TB patients were included. Patients were identified based on their sputum examination and culture sensitivity report. Detailed data regarding possible risk factors were taken from the patients and analyzed in SPSS v. 24. Regression analysis was done to explore the association between potential risk factors and MDR-TB.

Results: Results of this study indicate the statistically significant association of patients age <40 years ($p = 0.005$), prior TB treatment ($p = 0.005$), contact with TB patients ($p= 0.002$), illiterate for health education ($p = 0.01$) and diabetes ($p<0.01$) with MDR-TB cases. However, gender, family history for TB, monthly income, smoking history, and alcohol consumption were not significantly associated with MDR-TB. An independent association of MDR TB with age less than 40 years ($p = 0.01$), patients had prior TB treatment ($p< 0.001$), and diabetes ($p< 0.001$) was observed.

Conclusion: In light of these results, practices to control MDR-TB should stress on the adequate treatment of TB; patients should be informed of the consequences if they do not adhere to the guidelines of therapy.

Keywords: Multidrug resistance, Antituberculosis drugs, Risk factors, MDR-TB

INTRODUCTION

Tuberculosis (TB) is an airborne infectious disease produced by *Mycobacterium tuberculosis.* It is a significant community health concern across the world; TB is the second leading fatal infection for humans after HIV-AIDS. In 2017, TB was amongst the top 10 contagious diseases, with approximately 1.6 million mortalities across the world[1-3]. Despite all the efforts to control tuberculosis, the incidence of multidrug resistance TB (MDR-TB) is growing, and it continues to represent a threat to public health. In a recent report of WHO in 2018, 1.86 million MDR-TB cases were identified[2].

The emergence of drug resistance TB magnifies the current grim of TB epidemic, creating a severe threat for TB control authorities and also imposes immense burdens on developing countries because of its complex, costly, less efficient and toxic treatment. MDR-TB is caused by *Mycobacterium tuberculosis* strains that become resistant to isoniazid and rifampin, the two best effective anti-tuberculous drugs. It is of great concern to recognize the emergence and dissemination of MDR-TB as it contributes in a high rate of morbidity and mortality. Apart from this, MDR-TB also contributes to considerable economic loss, expensive therapy, which is approximately 100 times greater than treating a non-MDR individual, cause a substantial economic burden on developing countries like Pakistan[4].

Unfortunately, Pakistan enlisted in the top 10 nations with the maximum number of TB patients, and the rate of MDR-TB cases range from 2.3% to 17.9%[5,6]. It is indispensable to understand the determinants of MDR-TB so that more feasible approaches can be adopted for the prevention of MDR-TB cases. Studies suggested that spontaneous mutation, which causes drug resistance in many microorganisms, rarely occurs in MTB. The most common factors identified in different countries for MDR-TB are retreatment, contact with TB patients, comorbidity, age, and alcohol use[4,7,8].

As the frequency of MDR-TB cases is growing in Pakistan, there is a need to identify the determinants of MDR. This study intended to evaluate the risk factors related with the occurrence of multidrug-resistant tuberculosis.

METHODS

An observational study conducted on 55 cases of MDR-TB patients and 55 susceptible TB patients, also known as non-MDR cases were included. The initial screening of MTB was done by the conventional microscopic Ziehl-Nielsen (ZN) technique[9]. Preliminary drug sensitivity test using GeneXpert MTB was done for all those cases who had sputum smear-positive after two weeks of TB therapy. Samples positive for this test were further processed for culture and phenotypic antimicrobial sensitivity testing[10].

Patients were classified as MDR or non-MDR based on their culture and drug sensitivity report. Patients were declared MDR-TB cases if mycobacterium strain resistant to minimum two potent primary line anti TB drugs (isoniazid and rifampicin). Patients from both gender and age above 18 years were included. Data from the selected cases were collected on a detailed questionnaire and information including age, gender, residence, monthly income in PKR, family history that presence of another tuberculosis case in the family, history of previous treatment, and diabetes were recorded. Several questions were asked by the patients to know about their health education. Patients were also being asked about smoking and alcohol consumption.

Statistical analysis was done using SPSS v. 24.0. Descriptive analysis was done for all variables to calculate frequencies and percentages. To find the association of risk factors with MDR-TB univariate binary logistic regression analysis was done. Those associated with

p<0.05 were considered in multivariate logistic regression analysis. A result was assumed statistically significant at a p-value of less than 0.05.

RESULTS

A total of 110 patients were included in this study, 55 MDR TB cases, and 55 non-MDR-TB cases. The sociodemographic analysis revealed that the majority of the patients were male (56%) with a mean age of 34.5±20.24 s.d. ranging from 18 to 62 years. Comparative analysis of MDR and non-MDR-TB cases indicate a higher proportion of male patients (62%), age less than 40 years (78%), monthly income <10,000 PKR (87%). Family history of TB cases, prior TB treatment, and smoking history were higher in MDR cases, 47%, 76%, and 55%, respectively. More MDR-TB cases reported having contact with any TB patients, illiterate for health education and found with diabetes. Results of univariate regression analysis indicate the statistically significant association of patients age <40 years (OR 3.21, 95% CI 1.40-7.37, p = 0.005), prior TB treatment (OR 4.3, 95% CI 1.87-9.87, p = 0.005), contact with TB patients (OR 3.35, 95% CI 1.52-7.36, p= 0.002), illiterate for health education (OR 2.62, 95% CI 1.17-5.87, p= 0.01) and diabetes (OR 4.8, 95% CI 2.05-11.20, p<0.01) with MDR-TB cases. However, gender, family history for TB, monthly income, smoking history, and alcohol consumption were not significantly associated with MDR-TB (Table-I).

Results of multivariate logistic regression analysis revealed an independent association of MDR TB with age less than 40 years (OR_{adj} 5.22, 95 % CI 1.50-18.14, p = 0.01), patients had prior TB treatment (OR_{adj} 16.14, 95 % CI 4.15-26.77, p< 0.001), and TB patients with diabetes (OR_{adj} 7.25, 95 % CI 2.23-14.55, p< 0.001). The results are presented in Table-II.

Table I: Association of risk factors with MDR TB cases by univariate regression analysis

Variable		MDR-TB (n = 55)	Non-MDR-TB (n = 55)	p-value	Odd ratio (95 % CI)
Gender	Female	21 (38%)	27 (49%)	0.24	1.56 (0.73-3.33)
	Male	34 (62%)	28 (51%)		
Age	<40 years	43 (78%)	29 (53%)	0.005	3.21 (1.40-7.37)
	> 40 years	12 (22%)	26 (47%)		
Monthly income	<10,000 PKR	48 (87%)	42 (76%)	0.13	2.2 (0.77-5.81)
	>10,000 PKR	7 (13%)	13 (24%)		
Family history of TB	Yes	26 (47%)	19 (35%)	0.17	1.7 (0.78-3.66)
	No	29 (53%)	36 (65%)		
Smoking history	Yes	42 (76%)	19 (35%)	0.13	0.52 (0.22-1.23)
	No	13 (24%)	36 (65%)		
Prior TB treatment	Yes	30 (55%)	12 (22%)	<0.001	4.3 (1.87-9.87)
	No	25 (45%)	43 (78%)		
Contact with TB patients	Yes	38 (69%)	22 (40%)	0.002	3.35 (1.52-7.36)
	No	17 (31%)	33 (60%)		
Health education	Illiterate	41 (75%)	29 (53%)	0.01	2.62 (1.17-5.87)
	Educated	14 (25%)	26 (47%)		
Residence	Rural	34 (62%)	27 (49%)	0.17	0.6 (0.27-1.27)
	Urban	21 (38%)	28 (51%)		
Diabetes	Yes	44 (80%)	25 (45%)	<0.001	4.8 (2.05-11.20)
	No	11 (20%)	30 (55%)		
Alcohol consumption	Yes	23 (42%)	15 (27%)	0.1	1.91(0.86-4.26)
	No	32 (58%)	40 (73%)		

Table II: Association of risk factors with MDR-TB cases by multiple logistic regression analysis

Variable		p-value	Crude odds ratio (95% CI)	Adjusted p-value	Adjusted odds ratio (95 % CI)
Age	<40 years	0.005	3.21 (1.40-7.37)	0.01	5.22 (1.50-18.14)
	> 40 years				
Prior TB treatment	Yes	<0.001	4.3 (1.87-9.87)	<0.001	16.14 (4.15-26.77)
	No				
Contact with TB patients	Yes	0.002	3.35 (1.52-7.36)	0.36	1.67 0.55-5.06)
	No				
Health education	Illiterate	0.01	2.62 (1.17-5.87)	0.79	0.86 (0.30-2.49)
	Educated				
Diabetes	Yes	<0.001	4.8 (2.05-11.20)	<0.001	7.25 (2.23-14.55)
	No				

DISCUSSION

This research work has established significant knowledge concerning the relationship between risk factors with MDR-TB. Identification of these factors can help planners and decision-makers for the implementation of policies to lessen the risks of MDR-TB. The patient's age, history of TB treatment, and diabetes were found influential independent risk factors associated with MDR TB.

The age of the patients showed a significant association with the occurrence of MDR-TB. Patients age <40 years presented five times higher odds of MDR compared to those aged >40years. Different studies in

various countries had documented this finding that younger age group is more prone to develop MDR-TB. A study in Ethiopia reported patients age <35 years have increased risk for MDR (ORa=7, p=0.001); another study from China reported a higher risk for MDR-TB in patients age <45 years[11,12]. The resistance at a young age may be due to failure to adhere to the therapy in this age group.

It is renowned that socioeconomic factors are responsible for tuberculosis, but it is not clear whether they play any significant role in MDR-TB[13]. In this study, the aim was to explore the relationship of monthly income with MDR-TB patients, and no significant difference was observed between MDR and non-MDR cases. The association of monthly income with multidrug resistance TB has not been consistently reported. Some of the studies reported the impact of low income with drug resistance TB, but few studies showed no significant difference in monthly income for MDR and non-MDR tuberculosis patients[14-16].

Results indicate that a family history of tuberculosis is not a risk factor for MDR-TB. The reason may be the people who already have a patient at home give more attention to treatment. They become aware of having a patient in their home already and are well prepared for future onsets. They give special attention to those factors which have been neglected by their relative patients, such as poor hygienic conditions, malnutrition, and their exposure to TB cases. All these aspects contribute directly to the onset of TB infection. The findings of this study suggest that smoking and alcohol consumption are not contributing to MDR-TB. However, diabetes is one of the main factors paying to the poor TB treatment outcomes declared by several studies[17,18]. Consistent with the previous reports in this study, diabetic patients showed higher odds of MDR TB.

In line with findings of earlier studies conducting in different countries, the current study also suggests, history of prior TB treatment is a potent risk factor associated with MDR TB[4,19,20]. Odd ratios indicate that patients have 16.14 times more likely to have MDR if they had past anti-tuberculous therapy. Acquired drug resistance may occur if there has been a history of inappropriate and inadequate use of first-line anti-TB drugs[21]. One of the most consistent independent factors contributing to high rates of MDR-TB is a prior TB therapy, suggesting that patients undergoing first-line TB drugs do not adhere to dosage and duration of treatment. To further explore the reason behind this behavior, a few questions from patients were asked to know about their knowledge for TB treatment. It was found that patient's knowledge towards their treatment and precaution was limited. On bivariate analysis in the current study, it was observed that poor health education also contributes to the higher cases of MDR; however, this factor does not show an independent association on multivariate analysis. Nevertheless, there is still a need to educate the patients towards the significance of proper dose, duration of treatment, and to aware them regarding the deadly outcome of poor compliance.

CONCLUSION

This study delineates several risk factors associated with the MDR-TB disease. Age <40 years, prior TB treatment and diabetes were found to be independent factors associated with MDR-TB. Based on this study, it is advised that health administrations and physicians should consider these factors for the effective management of multidrug-resistance TB.

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