ORIGINAL ARTICLE

Risk Factors for Multi-Drug Resistant Tuberculosis in Patients at Tertiary Care Hospital, Peshawar

Fazli Wahab, Saadia Ashraf, Naveed Khan, Rukhsana Anwar and Mukhtiar Zaman Afridi

ABSTRACT

Objective: To determine the frequency of common risk factors for multi-drug resistant tuberculosis in patients presented at a tertiary care hospital, Peshawar.

Study Design: Cross-sectional, observational study.

Place and Duration of Study: Pulmonology Department, Khyber Teaching Hospital, Peshawar, from December 2006 to October 2007.

Methodology: Patients with positive AFB culture and sensitivity results and found resistant to both rifampicin and isoniazid with or with resistance to other first line anti-tuberculosis drugs, were recruited from both Pulmonology Ward and Outpatient Department (OPD). Informed verbal consent was taken and a questionnaire administered to all participants of the study. Information regarding demographics, education status, occupation, monthly household income, AFB C/S, details of past history of tuberculosis and family history of TB or Multi-Drug Resistant (MDR-TB) was recorded. Data was analyzed on SPSS version 11.

Results: A total of 30 patients of MDR-TB were interviewed. Male (n=17) and female (n=13) ratio was 1.3:1. Mean age was 34.2±15.3 years. Ninety-two percent female and 52.9% male were uneducated. In 56.7%, monthly income was less than 5000 rupees and in 40% between 5000-10,000 rupees. All patients had previous history of Antituberculous Treatment (ATT), in which 20% had undertaken ATT course once, 53.3% twice and 26.7% thrice in the past. In the study group, 13 (43.3%) patients had not completed their first ATT course and 11 of them were receiving ATT from a general practitioner (GP) at that time. Seven (23.3%) patients had family history of TB but no one had documented MDR-TB in the family. Resistance to RH was present in all patients; moreover, 56.7% had resistance to RHEZ+S.

Conclusion: The most common factors in the study group were previous history of tuberculosis, repeated courses of ATT, prescribed by different clinicians and unsupervised treatment by a GP during the initial course of ATT.

Key words: *MDR-TB. Multi-drug resistant tuberculosis. Factors.*

INTRODUCTION

Approximately one-third of the world population is infected with *Tubercle bacilli*. Around 8 million new cases of active disease develop each year and 3 million people die.[1] In Pakistan, its incidence is estimated to be 171/100,000 population.[2] Besides high incidence of *Tubercle bacilli* in Pakistan, prevalence of multi-drug resistant strains is also a cause of great concern.[3] Multi-Drug Resistant Tuberculosis (MDR-TB) is defined as simultaneous resistance of *Mycobacterium tuberculosis* to both isoniazid and rifampicin with or without resistance to other anti-tuberculosis drugs.[4,5]

Drug resistance is entirely a man-made problem and results from inadequate chemotherapy. Exposure to single drug due to irregular drug supply, poor drug quality, inappropriate prescription and/or poor adherence to treatment suppress the growth of *bacilli* susceptible to that drug but permits the multiplication of drug resistant organisms.[5]

In the community chronic cases, resulting from poor treatment, are the reservoir of drug resistant strains. Strategies need to be evolved to target these common risk factors to prevent emergence and spread of multi-drug resistant tuberculosis. The only way to prevent tuberculosis entirely is to effectively treat the active cases, so as to stop the transmission of this infection in the community.[6] This study was aimed to determine the frequency of established risk factors for MDR-TB, which are common in the local setup.

METHODOLOGY

This cross-sectional, observational study was carried out in the Pulmonology Department of Khyber Teaching Hospital, Peshawar, from December 2006 to October 2007. Informed verbal consent was obtained from all participants of the study. Only those patients were included in the study whose AFB culture and sensitivity report revealed isoniazid and rifampicin resistance with

Department of Pulmonology, Khyber Teaching Hospital, Peshawar.

Correspondence: *Dr. Fazli Wahab, C/o, Dr. Naveed Khan, House No. A-15, Police Colony, Nasir Bagh Road, Peshawar. E-mail: drwahab24@hotmail.com*

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or without resistance to any other first line anti-tuberculosis drugs. All those cases in which culture and sensitivity report was awaited or not available at time of interview were excluded. All the cases had culture reports from a single laboratory, with standard culture and sensitivity practice.

Demographics, education status, occupation, monthly household income, starting date of second line anti-tuberculosis drugs and culture/sensitivity report to all first line anti-tuberculosis drugs was recorded.

History of tuberculosis in the past, previous courses and duration of ATT used were recorded. In patients having past history of tuberculosis, further information under which supervision (DOTS, general physician, chest physician, surgeon, other) ATT was used. Data on 8 months ATT course completion during first course and reasons for interruption (could not afford, side-effects, felt better after few months, no improvement with treatment or others) were recorded. History of tuberculosis in the family including MDR-TB was asked.

Mean ± Standard Deviation (SD) for age and frequency of different known risk factors were calculated. Distribution of risk factors according to gender, age, educational status, occupation and monthly income basis was also calculated. As no comparative analysis was done, p-value was not calculated. Data entry and analysis was done using SPSS version 11.

RESULTS

Gender ratio was 1.3 (17 males): 1 (13 females). Mean age was 34.2±15.3 years. Mean age of males was 32 ±15.3 and that of females was 36±13.7 years. Sixty percent patients were aged between 20-40 years; 13.3% were younger than 20 years and 26.7% were older than 40 years of age (Table I). Seventy percent patients were uneducated (Table I). All females were housewives and 64.7% males were labourers. The monthly household income was less than 5,000 and between 5,000-10,000 rupees in 56.7% and 40% respectively (Table I). Previous history of tuberculosis was present in all the patients. Twenty percent patients used ATT course once, 53.3% twice and 26.7% thrice in the past (80% used twice or more time). Thirteen patients (43.3%) did not complete their first 8 months ATT course and 11 (84.6%) of them were receiving treatment under GP supervision at that time. The reasons for interruption were affordability and side-effects in 46.2% each (Table II). Family history of tuberculosis was present in 23.3% but history of MDR-TB in the family was not documented. According to AFB culture and sensitivity report, RH resistance was present in all patients, moreover, in 23.3% patients *Mycobacterium tuberculosis* was resistant to RHEZ+S+Thiacetazone and in 56.67% to RHEZ+S.

Table I: Gender distribution of risk factors of MDR-TB.

Risk factors	Male n: 17 (56.7%)	Female n: 13 (43.3%)	Total n: 30 (%)
Age			
Below 20 years	3 (17.6)	1 (7.7)	4 (13.3)
20 to 40 years	10 (59)	8 (61.5)	18 (60)
Above 40 years	4 (23.4)	4 (30.8)	8 (26.7)
Education			
Uneducated	9 (53)	12 (92)	21 (70)
Under Matric	7 (41)	1 (8)	8 (26.7)
Above Matric			1 (3.3)
Income (monthly)			
<Rs. 5000	10 (59)	7 (54)	17 (56.7)
Rs. 5000 to 10,000	6 (35)	6 (46)	12 (40)
> Rs. 10,000	1 (6)	0	1 (3.3)
Occupation			
Labourer	11 (64.7)	0	11
Student	1 (5.8)	0	1
Govt employee	2 (11.8)	0	2
Others	3 (17.7)	0	3
Housewife	NA	13 (100)	13

Table II: Details of patients who had used ATT in the past.

Under whose supervision ATT used	Male n (%)	Female n (%)	Total n (%)
DOTS*	8 (47.1)	4 (30.8)	12 (40)
G.P**	7 (41.2)	7 (53.8)	14 (46.7)
Physician	1 (5.9)	1 (7.7)	2 (6.7)
Chest Physician	0	1 (7.7)	1 (3.3)
Surgeon	1 (5.9)	0	1 (3.3)
Total	17 (56.7)	13 (43.3)	30
ATT course (8 months) not completed			
DOTS	1 (12.5)	1 (20)	2 (15.4)
G.P	7 (87.5)	4 (80)	11 (84.6)
Total	8 (26.7)	5 (16.7)	13 (43.3)
Reasons for interruption of ATT course			
Could not afford	3 (37.5)	3 (60)	6 (46.2)
Side effects (nausea/vomiting)	4 (50)	2 (40)	6 (46.2)
Not improving	1 (12.5)	0	1 (7.6)

**Directly Observed Treatment Short Course, **General Practitioner*

DISCUSSION

MDR-TB is an increasing global problem arising from a combination of physicians' error and patients' non-compliance during treatment of susceptible tuberculosis.[7] Wild strains of *Mycobacterium tuberculosis* that have not been exposed to anti-tuberculosis drugs are almost never resistant.[8]

As a matter of fact, previous history of tuberculosis is the most common risk for developing MDR-TB. In this study, all 30 participants were having history of tuberculosis in the past and 80% had ATT twice or more in the past. This is the documented most common risk factor in national and international literature.[7,9-16]

In this study, the gender difference was not significant to the level to be as a risk for developing MDR-TB, as the sample size was small. The ratio of male and female was 1.3: 1 and the mean age was 34.2±15.29. Faustini

et al. determined the risk factors for MDR-TB in six countries of Europe and found that MDR-TB patients were more likely to be male and younger than 65 years of age besides other more common risk factors.[14]

In this study, majority of MDR-TB patients were of low socioeconomic status and uneducated. The poor compliance in tuberculosis treatment is often due to the cost of drugs when taking treatment outside DOTS, and lack of education and/or understanding on the part of patient as well as on treating physician. The study by Khan *et al.* found that MDR-TB is more common in those patients with secondary tuberculosis and poor compliance.[10] Almani *et al.* also pointed out that MDR-TB was common in non-compliance of patients, which is due to lower education and lower socioeconomic status.[17] Bastian reported that MDR-TB is caused by improper treatment, inadequate drug intake or poor patient supervision.[18] Thirteen (43.3%) patients in the present study had not completed ATT course in the past and a majority of them was taking treatment under GP supervision. World Health Organization (WHO) has recommended multi-faceted programme, known by the acronym DOTS, that promotes effective treatment of the drug susceptible TB as the prime method of limiting drug resistance.[18-20]

In Pakistan, tuberculosis is mostly diagnosed on clinical suspicion and on therapeutic response to anti-tuberculosis drugs, rather than on the basis of sputum microscopy and culture isolation. This results in in-appropriate use of anti-tuberculosis drugs. Furthermore, compliance with treatment remains poor.[21]

The results of this study are limited by small sample size, observational study design and lack of control for comparison. The results remain important since the increasing level of drug resistance among mycobacterial isolates in our population is most alarming. Adequate control strategies have already been devised but the implementation of these strategies needs sincere commitment.

CONCLUSION

The most common factors found in those with MDR-TB were previous history of tuberculosis, repeated courses of ATT by different clinicians and unsupervised treatment by GPs during the initial course of ATT.

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