Original Research Article

DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20172828

Risk factors of multi-drug resistant tuberculosis in urban Allahabad, India

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Received: 26 April 2017 Accepted: 24 May 2017

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ABSTRACT

Background: India has the highest burden of tuberculosis globally while second highest in estimated MDR-TB cases after China. The prevalence of MDR-TB is estimated to be 3% among new cases and 14-17% amongst the retreatment cases. The Objective of the study was to identify the risk factors of MDR-TB in patients registered at tuberculosis units of urban Allahabad.

Methods: A cross-sectional study was carried out on TB patients registered at the urban tuberculosis units of Allahabad district in the year 2015. A total of 54 MDR-TB and 1016 non-MDR TB patients were included in the study. A pre-tested structured questionnaire was used to collect the data on the various factors. The chi-square test was used to study the association of various risk factors for MDR-TB patients.

Results: MDR-TB was more common in 26-45 year age group (59.26%), males (62.96%), previously treated TB case (83.34%), positive history of contact with MDR-TB patient (5.55%), patients previously on non-DOTS treatment (37.78%), patients with associated co-morbidities (37.03%) and in substance abuse (74.07%) while Non-MDR is more common in >45 years (46.75%) age group, females (56.69%), new cases (87.20%), patients on DOTS therapy (85.16%), without any co-morbidities (83.46%) and in patients having positive history of substance abuse (60.04%).

Conclusions: The younger age, male gender previous TB treatment, patients previously on Non-DOTS treatment, incomplete previous TB treatment, positive contact history of MDR-TB cases, presence of associated co-morbidities and substance abuse was significantly associated with MDR-TB patients than Non-MDR-TB patients (p<0.05).

Keywords: Risk factors, MDR-TB, Allahabad

INTRODUCTION

Tuberculosis (TB) is as old as the mankind.¹⁻³ TB ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV).⁴ India and China alone accounted for 24% and 11% of global cases, respectively.⁵

Globally, emergence of drug resistance is a dangerous alarm. The increase in the incidence of MDR-TB and the emergence of XDR-TB presents tremendous challenges to the global efforts to battle tuberculosis. MDR-TB,

defined as resistance to both Isoniazid and Rifampicin, is difficult to cure and requires prolonged treatment with expensive and often toxic multidrug regimens.⁶

Globally, an estimated 3.5% of new cases and 20.5% of previously treated cases have MDR-TB. India has the second highest total number of estimated MDR-TB cases after China (1,00,000 cases).

Patients infected with MDR strains are less likely to be cured from TB particularly if they are co-infected with HIV or suffer from other immune- suppressive diseases. MDR-TB is associated with a two to four fold increase

period of treatment, psychological problems, economic wastage, poor treatment adherence and consequently treatment failure. $^{9-11}$ It is also associated with higher case fatality rates (50 – 80%) as a result of drug toxicity. 9,10

It is known that epidemiologic information on risk factors of MDR-TB is important for prevention and control of the spread of the disease in countries where drug resistance is a major threat. The disease is not only a medical problem or a public health problem but is also a critical social problem of great magnitude. There is scarcity of information in the study area and at large to our country.

With this background, the present study was conducted to study the risk factors that are associated with the development of MDR-TB.

Objective

To identify the risk factors of MDR-TB in patients registered at tuberculosis units of urban Allahabad.

METHODS

This cross-sectional study was conducted among all TB cases registered at urban tuberculosis units (TUs) of Allahabad during the year 2015.

There are 29 tuberculosis units (TUs) in the district, out of which six tuberculosis units are situated in urban areas (Swaroop Rani Nehru Hospital, Beli Hospital, Government TB Hospital Teliarganj, Motilal Nehru Hospital (Colvin Hospital), Keedganj & Sulemsarai).

At the beginning, the permission was taken from the District Tuberculosis Officer, Allahabad to obtain the information from the records of the registered patients at various urban TUs.

The listing of all the registered TB cases with the residential address and contact numbers at the six urban tuberculosis units was done. The number of cases registered during the year 2015 was 1092 out of which the total confirmed MDR-TB patients residing in urban Allahabad were 57.

An interview of all the participants were made in the local language after obtaining the informed consent and assuring full confidentiality, a pre-designed and pretested questionnaire was filled. The socio-demographic variables that were included in the study were age, gender, religion, marital status and type of family. For the purpose of identification of risk factors of MDR-TB, patients were asked about history of previous TB treatment, mode of previous TB treatment, status of previous TB treatment, family history of TB and history of contact with MDR-TB case and history of migration. Further, information was taken about the history of substance abuse, history of immunosuppressive therapy/anti-cancer therapy and presence of comorbidities including diabetes and HIV status.

The patients who refused to give consent or died during the course of the study were excluded. Nineteen TB cases did not give the consent for interview. Three MDR-TB patients had died during the course of the treatment. Thus, the final sample size came out to be 1070.

The collected data were entered in the Microsoft excel data sheet and analysed using statistical software, SPSS version 18.0. Chi-square test was used to test for the statistical significance in the difference between different variables. P-value less than 0.05 were considered as significant.

RESULTS

A total of 54 MDR-TB patients and 1016 non MDR-TB patients were included in the study. Out of a total of 54 MDR-TB patients, majority 241 (23.72%) of the patients were registered at Moti Lal Nehru Hospital (Colvin) followed by Swaroop Rani Nehru Hospital, 13 (24.07%). Beli hospital had 11 (20.37%) patients. The TU at Sulem Sarai, Keedganj and Government TB hospital, Teliarganj had 6 (11.11%), 4 (7.40%) and 2 (3.70%) patients respectively whereas among 1016 non MDR-TB patients, majority 241 (23.72%) of the patients were registered at Beli hospital followed by Swaroop Rani Nehru Hospital, 206 (20.28%). Moti Lal Nehru Hospital (Colvin) had 194 (19.09%) patients followed by Government TB hospital, Teliarganj 184 (18.11%). The TU at Sulem Sarai and Keedganj had 109 (10.73%) and 82 (8.07%) patients respectively (Table 1).

Table 1: Distribution of TB patients registered at the urban tuberculosis units of Allahabad.

Tuberculosis units		MDR-TB (54)	(%)	Non-MDR TB (1016)	(%)
1.	SRN Hospital	13	24.07	206	20.28
2.	Beli Hospital	11	20.37	241	23.72
3.	Government TB Hospital, Teliarganj	02	3.70	184	18.11
4.	M.L.N Hospital (Colvin)	18	33.33	194	19.09
5.	TU, Keedganj	04	7.40	82	8.07
6.	TU, Sulem Sarai	06	11.11	109	10.73

Table 2: Demographic characteristics of registered TB patients.

Variables	MDR N =54	Percentage (%)	Non-MDR N =1016	Percentage (%)
Age				
<26 year	13	24.07	124	12.20
26-45 year	32	59.26	417	41.04
>45 year	09	16.67	475	46.75
Gender				
Male	34	62.96	440	43.31
Female	20	37.03	576	56.69
Religion				
Hinduism	36	66.66	732	72.05
Islam	17	31.48	244	24.02
Christianity	01	0.01	10	0.98
Others	00	00	30	2.95
Marital Status				
Unmarried	11	20.37	250	24.61
Married	40	74.07	683	67.22
Widow/ widower	03	5.55	73	7.19
separated	00	00	10	0.98
Family type				
Nuclear	38	70.37	780	76.77
Joint	16	29.63	236	23.23

MDR-TB was found to be more common in 26-45 year age group 32 (59.26%). On the other hand, in non MDR-TB group majority 475 (46.75%) were more than 45 years of age. The difference in the proportion between the two groups was found to be statistically significant (p<0.05) (Table 3).

Majority, 34 (62.96%) of the MDR-TB patients were males followed by females 20 (37.03%). On the other hand, in non MDR group, 576 (56.69%) females were affected and 440 (43.31%) males were affected. The difference in the proportion between the two groups was found to be statistically significant (p<0.05) (Table 3).

In MDR-TB category, most of the patients 45 (83.34%) had received previous treatment for TB while only 9 (16.66%) were new cases. Of the total of 1016 Non-MDR patients, 888 (87.20%) were new cases while only 128 (12.59%) patients were previously treated. It was found that the previous TB treatment history was significantly associated with MDR-TB compared to Non-MDR TB patients (Table 3).

Of the total 45 MDR-TB patients who had previous TB treatment history, 28 (62.22%) patients were receiving treatment from DOTS centre while 17 patients were receiving treatment from Non-DOTS sources. In Non-MDR TB group, most of the patients 109 (85.16%) took treatment from DOTS centre while only 19 (14.84%) patients took Non-DOTS treatment. On applying statistical test, the mode of treatment came out to be statistically significant. Among MDR-TB cases, 5.88% patients had a positive history of contact with MDR-TB

cases. None of the patient under non MDR-TB category gave any history of contact with MDR-TB case. The history of contact with MDR-TB case was statistically significant in both the groups (Table 3).

In MDR-TB group, the most common associated morbidity was Diabetes seen in 14 (25.92%) patients. HIV/AIDS was observed in 2 (3.70%) patients. The rest 4 (7.40%) were having other co-morbidities like multiple joint pain, Bronchial Asthma and Psoriasis. Similarly, in Non-MDR TB group also, Diabetes was the most commonly associated morbidity in 140 (13.77%) patients. Seven (0.68%) patients were having HIV/AIDS. The rest 21(2.06%) of the patients were having other comorbidities. There was a statistically significant difference in the associated co-morbidities in both the groups (Table 3).

In MDR group, the most common substance abuse was tobacco in 24 (44.44%). Nine (16.66%) patients had a history of alcoholism. Seven (12.96%) had a history of both smoking and alcoholism. Fourteen (25.92%) had no addiction. Similarly, in Non-MDR TB group also, 499 (49.11%) patients had a history of tobacco abuse. Ninety (8.85%) patients had a history of alcoholism. Twenty one (2.06%) patients had a history of both tobacco and alcoholism. There was no history of substance abuse in 406 (39.96%) patients. It was found that the substance abuse pattern was statistically significant in both the groups. It was found that the difference of immune-suppressant use in both the groups was statistically insignificant (Table 3).

Table 3: Possible risk factors of MDR-TB.

Variables	MDR n =54	Percentage (%)	Non-MDR n =1016	Percentage (%)	Test statistics	P value	
Age (year)	11 –34	(/0)	11 –1010	(/0)	statistics		
< 26	13	24.07	124	12.20	2	<0.05	
26-45	32	59.26	417	41.04	$\chi^2 = 19.956$		
>45	09	16.67	475	46.75	- df =2		
Gender		10.07	173	10.75			
Male	34	62.96	440	43.31	$\chi^2 = 8.028$,	<0.05	
Female	20	37.03	576	56.69	df=1		
Previous TB trea			370	30.07	ur r		
Previously treated	45	83.34	128	12.59	$\chi^2 = 189.28$	<0.05	
New case	09	16.66	888	87.20	- df =1		
Mode of previous							
induc of providu	MDR (n =4		Non MDR (n =128)				
DOTS	28	62.22	109	85.16	$\chi^2 = 10.627$	< 0.05	
Non DOTS	17	37.78	19	14.84	df = 1		
Status of previous							
Complete	15	33.33	60	46.88	$\chi^2 = 2.486$	>0.05	
Incomplete	30	66.66	68	53.12	df = 1		
Family History o							
Yes	11	20.37	316	31.11	$\chi^2 = 2.783$ df = 1	>0.05	
No	43	79.63	700	68.89			
History of contac							
Yes	03	5.88	00	00	$\chi^2 = 56.6$		
No	51	94.44	1016	100	df = 1	< 0.05	
History of migra	tion						
Yes	02	3.70	31	3.05	$\chi^2 = 0.07$	0.07	
No	52	96.29	985	96.95	df = 1	>0.05	
Co-morbidities							
Yes	20	37.03	168	16.54	$\chi^2 = 14.8$	-0.07	
No	34	62.96	848	83.46	df = 1	< 0.05	
Substance abuse							
Yes	40	74.07	610	60.04	$\chi^2 = 4.23$	<0.05	
No	14	25.92	406	39.96	df=1	< 0.05	
Immuno-suppres	ssant therapy						
Yes	03	5.56	21	2.06	$\chi^2 = 2.84$	>0.05	
No	51	94.44	995	97.93	df = 1		

DISCUSSION

In the present study, it was found that the occurrence of MDR-TB was more common in 26-45 year age group 32 (59.26%). On the other hand, in non-MDR group majority 475(46.75%) were more than 45 years of age. There was a significant difference in the age of patients affected with MDR-TB and Non-MDR-TB groups. The younger age of the patients could be a possible risk factor for MDR-TB compared to Non-MDR TB patients. Similar finding was obtained by Elmi et al where they found young age (25-44 year) to be associated with MDR-TB patients. ¹⁴

In the present study majority, 34 (62.96%) of the MDR-TB patients were males followed by 20 (37.03%) females. On the other hand, in non MDR group, 576 (56.69%) females were affected and 440 (43.31%) males were affected. The difference in the proportion between the two groups was found to be statistically significant (p<0.05). The male gender could be a risk factor for the development for MDR-TB. Mor et al found 57.9% males were affected with the development of MDR-TB which is nearer to present finding. ¹⁵

The present study found that in MDR-TB category, most of the patients 45 (83.34%) had received previous

treatment for TB while only 9 (16.66%) had newly developed MDR-TB. Of a total of 1016 Non-MDR patients, 888 (87.20%) were newly developed case while only 128 (12.59%) patients were previously treated. So the history of previous treatment of tuberculosis was significantly associated with MDR-TB patients as compared to Non-MDR TB patients. Mulu et al also observed the previous history of antituberculosis therapy in 79.1% of MDR-TB patients. ¹² Rifat et al observed 98% patients who had a history of previous TB treatment. ¹⁶ Abdulrahman et al found the history of anti-tuberculosis therapy to be the only risk factor associated with drug resistant Mycobacterium tuberculosis, with an odds ratio of 19.9 (p<0.00001) which is again nearer to our finding. ¹⁷

In this study, there were 45 MDR-TB patients who had previous TB treatment history, of which 28 (62.22%) patients were receiving treatment from DOTS centre while 17 patients were receiving treatment from Non-DOTS places. In Non-MDR TB group, most of the patients 109 (85.16%) took treatment from DOTS centre while only 19 (14.84%) patients took Non-DOTS treatment. The treatment from Non DOTS centre came out to be significantly associated with MDR-TB patients compared to Non-MDR TB patients. This could be attributed to the fact that the drugs supplied under DOTS are supervised and free of cost. The patients are also counselled for the completion of the entire therapy and told about the consequences of non-compliance with the treatment. However, Non-DOTS therapy may lack the free supply of drugs, proper counselling and supervision of the treatment. Gnevaa Bhatt et al found that 60.5% MDR-TB patients received treatment from RNTCP while 39.5% patients from private health facility which is similar to our finding.¹⁸

In the present study, it was found that 11 (20.37%) patients had a positive family history of tuberculosis in MDR-TB category, while 16 (29.62%) patients had no family history. The family history was unknown to 27 (50%) patients. In Non-MDR category, 444 (43.70%) the family history was unknown. The family history was positive in 316 (31.10%) patients and negative in 256 (25.19%) patients. The family history was not found to be statistically significant in cases of MDR-TB. Similar finding was observed by Casal et al who reported positive history of contact with tuberculosis in 22.5% MDR-TB patients. ¹⁹

In MDR-TB patients, most 51 (94.44%) had either no or unknown history of contact with MDR-TB patient. Only 3 (5.55%) patients of MDR-TB gave positive contact history. In non-MDR TB patients, 531 (52.26%) had a negative contact history with MDR-TB patient while it was unknown to 485 (47.74%) patients. The contact history was not positive in any of the patients. Mulu et al conducted a case-control study in Amhara National Regional state, Ethiopia and observed a history of contact

with MDR-TB patients in 28.8% while 14.4% controls had a history of contact with MDR-TB patients. 12

In this study, it was found that in MDR-TB group, the most common associated morbidity was diabetes in 14 (25.92%) patients. HIV/AIDS was observed in 2 (3.70%) patients. The rest 4 (7.40%) had other co-morbidities. Similarly, in Non-MDR TB group, Diabetes was the most commonly associated morbidity in 140 (13.77%) patients. Seven (0.68%) patients had HIV/AIDS. The rest 21(2.06%) of the patients had other co-morbidities. The presence of co-morbidities was significantly associated with MDR-TB patients when compared to Non-MDR TB patients. Similar to the present study which demonstrated co-morbidities in 37.03% patients, Datta et al observed 40.3% patients with MDR-TB having co-morbid illnesses like Diabetes, COPD, HIV/AIDS etc.²⁰

CONCLUSION

It can be concluded from the study that the MDR-TB was more frequently associated with younger age (26-45 years), males, low socio-economic status, previous TB treatment, patients on Non-DOTS treatment, incomplete previous TB treatment, positive contact history of MDR-TB cases, presence of associated co-morbidities and substance abuse. The case-control study is warranted to assess the strength of association with possibly associated risk factors.

ACKNOWLEDGEMENTS

I am thankful to the District Tuberculosis Officer, Allahabad for co-operating with me in the entire study.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

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Cite this article as: Raazi J, Prakash S, Parveen K, Shaikh S. Risk factors of multi-drug resistant tuberculosis in urban Allahabad, India. Int J Community Med Public Health 2017;4:2383-8.