RESEARCH ARTICLE

Tuberculosis among Household Contacts of Multidrug-Resistant Tuberculosis Cases at a Tertiary Hospital in Lucknow, India

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ABSTRACT- Background- Multidrug-resistant tuberculosis (MDR-TB) is caused by the strain of *Mycobacterium tuberculosis*, it is transmitted through air droplets from an infected person and close contacts of MDR-TB patients have a high potential to developing TB. This study aims to determine the profile of TB/multidrug-resistant TB (MDR-TB) among household contacts of MDR-TB patients.
Methods- The cases were recruited from King George's Medical University, Lucknow, India. In this cross-sectional study, close contacts of MDR-TB patients were screened for tuberculosis, clinical, radiological and bacteriological experiments were performed to find out the evidence of TB/MDR-TB.
Results- The cases were enrolled between December 2015 to December 2016, total of 100 index MDR-TB patients were recruited, which initiated on MDR-TB treatment. A total of 428 contacts, who could be studied, 11 (2.57%) were diagnosed with MDR-TB and 4 (0.93%) had TB. The most frequent symptoms observed in patients were cough, chest pain and fever.
Conclusion- Tracing symptomatic contacts of MDR-TB cases could be a high yield strategy for early detection and treatment of MDR-TB cases to contribute to reduced morbidity, mortality and to cut the chain of transmission of infection in the community. The approach should be bringing about for wider implementation and dissemination.
Key-words- Household, MDR-TB, Symptomatic, TB, Transmission

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) is caused by strain of *Mycobacterium tuberculosis* that is resistant to at both isoniazid (INH, H) and rifampicin (RMP, R) that are two most powerful 1st line anti TB drugs, it is transmitted through air droplets from infected person and Close contacts of MDR-TB patients have a high potential to developing TB. Because of the emergence of resistant nature of *Mycobacterium tuberculosis* strains, tuberculosis adopted more alarming nature in the form of MDR-TB, is a global occurrence that poses a serious threat to ongoing national TB control programmes. India accounts for about a quarter of the global TB burden. Worldwide India is the country with the highest burden of both TB and MDR-TB [1]. There are an estimated 79,000 multi-drug resistant TB patients among the notified cases of pulmonary TB each year.

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According to WHO, In 2016 an estimated 28 lakh cases occurred and 4.5 lakh people died due to TB.
According to the 2017 World Health Organization global report, approximately 490000 people were infected by MDR-TB. In addition, there were an estimated 110,000 people who had rifampicin resistant TB (RR-TB). So the number of people estimated to have had MDR-TB or RR-TB in 2016 was 600,000 with approximately 240,000 deaths. Almost half (47%) of these cases were in India, China and the Russian Federation, in which India has highest TB incidence in Asia [1].
The prevalence of MDR-TB in India is reported to be around 3% in new cases and 12-17% in retreatment cases [2]. Close contacts of MDR-TB cases are expected to be at increased risk of developing TB due to intense and/or prolonged exposure to index cases in the weeks to months before diagnosis and treatment beginning [3]. However, contradictory statistics have emerged from different existing studies concerning the risk of TB in close contacts of drug-susceptible and MDR-TB patients. A number of studies have reported a comparable risk of transmission in the two groups [4–6], whereas others have not [7].
Global TB Report 2017 released by the WHO, India, along with China and Russia, accounted for almost of half

of the 490,000 multi-drug-resistant TB (MDR-TB) cases registered in 2016, but limited data are available from India to date on the occurrence of TB/MDR-TB among household contacts of MDR-TB patients. Contact tracing in general is supposed to provide two functions:
(1) identifies contacts with TB disease so that treatment can be initiated early when disease is more restricted- this in addition serves to decrease transmission and (2) identifies high-risk infected contacts who might assistance from either anticipatory treatment or close surveillance [8].
The objective of our study was to estimate the incidence of TB in household contacts of MDR-TB patents registered at the DR-TB center KGMU. Many risk factors that are associated to development of MDR-TB have been reported among contacts but have not been concurrently assessed. The present study was carried out to determine the proportion of household contacts, which develop active TB due to direct transmission from an index case in that household through the clinical, radiological, and bacteriological profile in household contacts of MDR-TB patients at a tertiary TB care center in Lucknow, India.

MATERIALS AND METHODS

Setting and Study design- A cross-sectional study was conducted at the Department of Respiratory Medicine King George's Medical University DOTS-PLUS center, which covered the 24 Districts of Uttar Pradesh, India. The study population includes all the household contacts MDR-TB patient registered under category IV drug regimen of DOTS-PLUS program at DR-TB centre were recruited from December 2015 to December 2016. A total of 100 MDR-TB cases were recruited for this study after given informed consent. The study was ethically approved by the institutional ethics committee. All index cases were retreatment patients, who had unsuccessful treatment with 1st line drug regimen. The majority was residing in urban slum areas and was of poorer socio-economic position. After an initial phase of hospitalization of about one month, all index cases received supervised ambulatory treatment with second line drugs.

Screening contact practice at the hospital- At the DOTS-PLUS center, it was a regular work practice to enquire all index cases if any their family member had pulmonary symptoms (fever, weight lose, cough and loss of appetite) suggestive of TB. If any symptomatic family members were recognized, the index case was encouraged to take the family member for further examination at the hospital.
The DOTS-PLUS center team did through clinical examination of the symptomatic family member together with detailed history, physical examination, and laboratory work up as per the guideline of Revised National Tuberculosis Control Programme. Close contacts with no active TB disease were monitored carefully for at least two years. It was more important to careful and close follow-up was encouraged for infants and children less than 5 years of age because they were more prone to suffer from the disease. Household contacts with no suggestive signs and symptoms of active TB were aware regarding the signs and symptoms of TB, about their contact with an MDR-TB index case and about the significance of seeking treatment immediately if they develop signs and symptoms of TB disease. Follow up monitoring was done every 1–2 months. Contacts from Lucknow and nearby places, a team composed of community health workers and medical officer conducted home visits after every 1–2 months to trace. Those contacts, which came from outside Lucknow were motivated to visit the DOTS-PLUS center KGMU after every 1–2 months to undergo the study investigations.

Data collection- After obtaining informed consent, a standardized case-report form was filled out for all contacts of each index patient. Sex, age, weight clinical examination assessment, radiological assessment, closeness to the index case, bacille Calmette-Guerin (BCG) scar (presence/absence to assess infection rates among vaccinated and unvaccinated groups) and any history of TB (pulmonary/extra-pulmonary) were also recorded.
Socioeconomic status based on education, occupation and family income were classified by using a modified Kuppuswamy scale [9]. Nutritional status was assessed using the body mass index [10]. Sputum examination for acid-fast bacilli (AFB) on two early morning samples on 2 consecutive days was carried out in all contacts and in case of any positive result for sputum microscopy, these cases were referred to Intermediate Reference Laboratory (IRL) for Xpert MTB/Rif resistance testing. On confirmation from IRL for Rifampicin resistance on Xpert MTB, these patients were registered at DOTS-PLUS to start cat 4 treatments. Those cases with no Rif resistant to Xpert MTB although positive for sputum microscopy were referred to respective DOTS centres for registration and treatment initiation. Tuberculin skin testing (TST) using 5 tuberculin units (TU) purified protein derivative (PPD) was performed in all contacts and was recorded after 48-72 h at the study center. A reading of $\geqslant$10 mm was taken as positive. All contacts were also offered the human immunodeficiency virus and diabetes testing.
Some of the contacts that were not available at the time of home visit for interview, their history were obtained from the index cases or from other relatives of the family. In the case of casualty of any contact members because of TB, a history was obtained from the index patients or from other relatives of the family.
The 'Index case' was defined as the first identified case of MDR-TB in the house. All index cases were confirmed by sputum culture as having MDR-TB. A household contact case was defined as any person who shared the same enclosed living space for least 3 months prior to the identification of the index case and included spouses, children, parents, siblings and other family members (uncles, grandfathers, cousins).

RESULTS

Between December 2015 to December 2016, 100 index patients were reviewed that were started anti-tuberculosis treatment. Their demographic profile is shown in Table 1. Over 67 (67%) were male and 33% female. 54% of index cases belong to urban and 46% belong to rural areas. Out of 100 index cases Seven (7%) had previous and Nine (9%) had presented history of tuberculosis and majority of index cases were retreatment patients that received treatment either of first-line anti TB drugs of WHO treatment category regimen previously. In the study population, 410 (80.7%) were HIV negative, ninety-eight (19.3%) of confirmed MDR-TB index cases were also HIV positive.

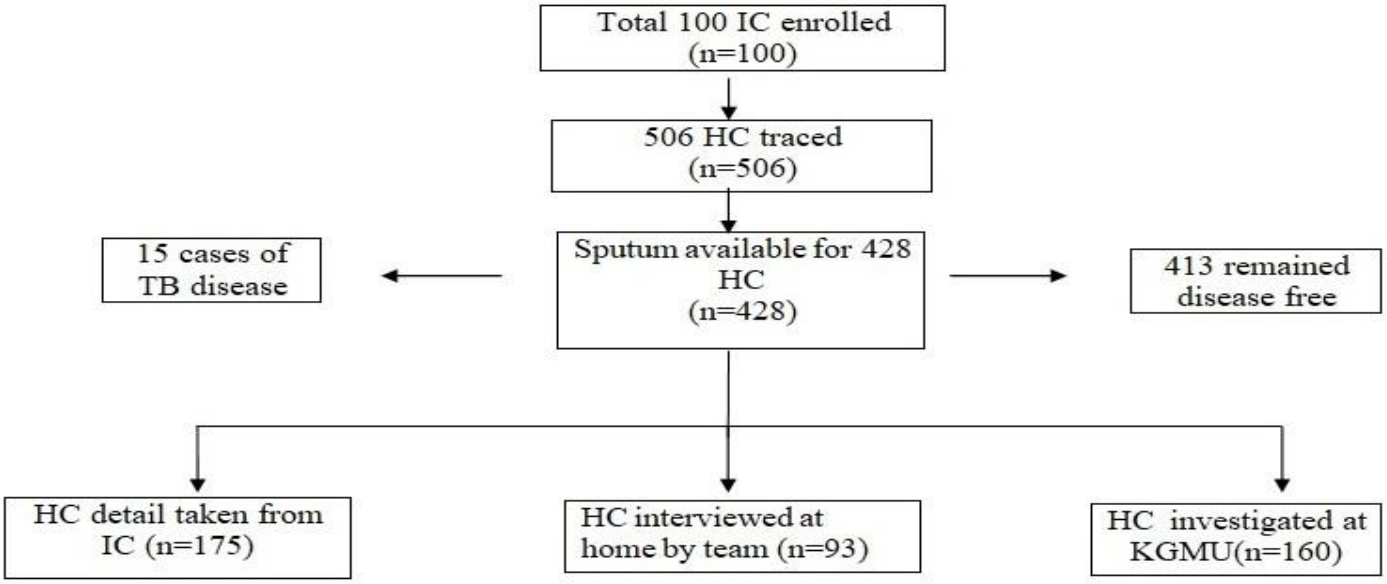

Fig. 1: Flow diagram representing contact tracing and outcomes of household contacts

(TB= Tuberculosis**, IC=** Index cases**, HC=** Household contact**, KGMU=** King George's Medical University, **n=** Number of patients)

Table 1: Socio-Demographic characteristics of Index case (IC)

Variables	Frequency (n=100)	(%)
Sex		
Male	67	67
Female	33	33
Age		
≤ 40	58	58
>40	42	42
Residence		
Urban	54	54
Rural	46	46
Personal habit		
Alcoholic	17	17
Non alcoholic	83	83
Smoker	27	27
Ex-smoker	4	4
Non-smoker	69	69
HIV status		
Positive	22	22
Negative	88	88
Contact history		
Present	7	7
Past	9	9
Absent	84	84
Smear Grading		
3+ or 2+	54	54
1+ or scanty	46	46
Culture Result		
Positive	98	98
Negative	2	2

The household contacts of the index cases were identified using the medical records of the index cases that were present in DR-TB center and through interviews of index cases and their family members; symptomatic contacts or family members recognized on the screening form and attached with the respective index case file.

There were 506 household contacts of 100 index patients were screened for tuberculosis. Their demographic profile is shown in Table 2. Majority of contacts (67.6%) were male and most of them (70.4%) belong to the urban area.

Table 2: Socio-Demographic characteristics of Household contact (HC)

Variables	Frequency (n=506)	(%)
Sex		
Male	342	67.6
Female	164	32.4
Age		
≤ 40	318	62.8
>40	188	37.2
Residence		
Urban	356	70.4
Rural	150	29.6
Personal habit		
Alcoholic	54	10.7
Non alcoholic	401	89.3
Smoker	94	18.5
Ex-smoker	37	7.31
Non-smoker	375	74.1
Smear Grading	(n=15)	
3+ or 2+	11	73.3
1+ or scanty	4	26.7
Culture Result	(n=428)	
Positive	15	3.50
Negative	413	96.5
Drug susceptibility testing		
Resistance	11	73.3
Susceptible	4	26.7
Number of contacts, who developed MDR-TB/ household		
One	11	73.3
Two	3	20
Three	1	6.7

Three hundred eighteen (62.8%) of the contacts had ages below to 40 years that were the most susceptible age group of the population. Asymptomatic household contact was identified in 15 of 428 (3.50%) index cases. The most common symptoms were a cough followed by fever loss of appetite and haemoptysis. History of loss of weight was also present in all 15 contacts. Sputum specimens were collected and examination was performed for 428 (83.99%) household contacts, whereas the remaining 78 (15.4%) were unable to provide sputum for examination. Chest X-ray was performed in 228 contacts. Sputum for AFB yielded negative result for 413 (96.4%) cases while it was positive in 15 (3.50%), sputum smear positive cases had smear grading 3+ or 2+ for 11and 1+ or scanty for 4.

All sputum positive and other suspected cases were referred to Intermediate Reference Laboratory (IRL) for Xpert testing and Drug susceptibility testing (DST). Xpert and DST results of 11 (73.3%) contacts confirmed MDR-TB, while 4 (26.7%) was declared drug-susceptible TB. Four contacts that were diagnosed with pulmonary TB was referred back to their respective district for registration at DOTS center for category first whereas the remaining 11 contacts that were diagnosed as MDR-TB patients were registered for drug-resistant TB treatment at DR-TB center KGMU, Lucknow, India.

DISCUSSION

In India, the main objective of National DOTS-Plus Programme is to reduce tuberculosis transmission by providing early diagnosis and treatment of MDR-TB patients, for that, it follows the entire protocol of MDR-TB to facilitate prevention, diagnosis, treatment, and to cover the entire nation with the scheduling and monitoring in a phased manner. Household contacts constitute a high-burden group for developing TB and MDR-TB and the significance of selective case detection in these groups can't be overemphasized. Recently infected contacts carried an eightfold risk of developing TB compared with persons infected more remotely [11]. While not all cases found through household contact tracing were the result of transmission from the index

case, early detection and treatment of the contagious cases will greatly reduce the transmission rate in the population [12,13]. Because of frequent exposure to index patient, household contacts of MDR-TB have more recurrent threat to developing active TB and MDR-TB. On the other hand, available information on subsequent risk of developing active TB/MDR-TB disease among MDR-TB contacts had not been reliable. There are very few studies reported from India on the burden of disease and infection among contacts of MDR-TB patients. Singla *et al.* [2] reported that TB prevalence among contacts was 5.3% of whom only 0.7% had MDR-TB.

In the present study, we measured the factors that were related to contacts such as residence, any history of TB treatment, HIV status, sex, age, and number of confirmed MDR-TB in the house. In this study, a total 428 contacts of index patient studied, of which, 11(2.57%) contacts developed MDR-TB while 4(0.93%) cases developed drug-susceptible TB subsequent to the index case. The Overall rate of disease in the present study was 3.50 % which is very low as compared to an earlier study conducted by Dhingra *et al.* [14], who reported a 53.5% prevalence of TB infection in household contacts. We could not determine that household contact gets infected by transmission from index case as we were not performed genetic study of mycobacterium. However, as we know it is a communicable disease, there is significant proof to support the transmission of MDR-TB strain from person-to-person in the community. It was shown by Bayona *et al.* [15] that over half figure of global MDR-TB cases were thought to result from primary transmission. In addition, the transmission may have taken place previously, when they were drug-susceptible, as most of the index cases were retreatment cases. This study had a number of functioning problems with the simple contact tracing and testing strategies used. Almost a third of close contacts with cough for more than two weeks could not provide sputum samples for smear microscopy. While a number of contacts were unable to produce sputum sample when needed, many others were simply not present at their home at the time of visiting the team of DR-TB center. There were a number of limitations to our study. First, the small sample size of drug-resistant contact cases due to the inability to trace all the contacts. Second, data on several determinants for the MDR-TB disease were absent from analysis because they were not in the routine registers patients. Third, we considered only household contacts that were living with index patient and not other casual or close contacts.

CONCLUSIONS

The present study highlighted the requirement for early detection and treatment of TB in household contacts of MDR-TB, who represent a high-burden group, and also suggest that active tracing of symptomatic contacts; cases contribute to reduced morbidity, mortality, and transmission of infection in the society. This could be a very effective approach to saving more people as well as in cutting the chain of the transmission in the community. The conclusions from this study were believed to notify the national MDR-TB treatment carrying out plan as well as other similar countries in their attempt to roll out MDR-TB treatment services.

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REFERENCES

[1] WHO Global TB Report, 2017.

[2] Singla N, Singla R, Jain G, Habib L, Behera D. Tuberculosis among household contacts of multi drug-resistant tuberculosis patients in Delhi, India. Int. J. Tuberc. Lung Dis., 2011; 15(10): 1326–30.

[3] Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis, 2005; 34: 01–37.

[4] Teixeira L, Perkins MD, Johnson JL, et al. Infection and disease among household contacts of patients with multidrugresistant tuberculosis. Int. J. Tuberc. Lung Dis., 2001; 5: 321–28.

[5] Schaaf HS, Vermeulen HA, Gie RP, Beyers N, Donald PR. Evaluation of young children in household contact with adult multidrug-resistant pulmonary tuberculosis cases. Pediatr. Infect. Dis. J., 1999; 18: 494–500.

[6] Schaaf HS, Van Rie A, Gie RP, et al. Transmission of multidrugresistant tuberculosis. Pediatr. Infect. Dis. J., 2000; 19: 695–99.

[7] Siminel M, Bungerzianu G, Anastasaty C. The risk of infection and diseases in contacts with patients excreting *Mycobacterium tuberculosis* sensitive and resistant to isoniazid. Bull. Int. Union Tuberc., 1979; 54: 263.

[8] Mulder C, Klinkenberg E, Manissero D. Effectiveness of tuberculosis contact tracing among migrants and the foreign-born population. Euro Surveill. Rev. Artic., 2009; 14(11): 11.

[9] Kuppuswami B. Manual of socio-economic scale (urban). New Delhi, India: Manasayan, 1981.

[10] Kuczmarski RJ, Carroll MD, Flegal KM, Troiano RP. Varying body mass index cut-off points to describe overweight prevalence among US adults: NHANES III (1988 to 1994). Obes. Res. Nov., 1997; 5: 542–48.

[11] American Thoracic Society and Centers for Disease Control and Prevention. Targeted tuberculin and treatment of latent tuberculous infection. Am. J. Respir. Crit. Care Med., 2000; 161 (4 Pt 2): S221–S47.

[12] Long R, Schwartzman K. Pathogenesis and transmission of tuberculosis. In: Canadian tuberculosis standards. Vancouver: Canadian Thoracic Society Canadian Lung Association Public Health Agency of Canada, 2014.

[13] Devadatta S, Dawson JJ, Fox W, et al. Attack rate of tuberculosis in a 5-year period among close family contacts of tuberculosis patients under domiciliary treatment with isoniazid plus PAS or isoniazid alone. Bull. World Health Organ., 1970; 42: 337–51.

[14] Dhingra VK, Rajpal S, Aggarwal N, Taneja DK. Tuberculosis trend among household contacts of TB patients. Indian J. Community Med., 2004; 29: 44-48.

[15] Bayona J, Chavez-Pachas AM, Palacios E, Llaro K, Sapag R, et al. Contact investigations as a means of detection and timely treatment of persons with infectious multidrug-resistant tuberculosis. Int. J. Tuberc. Lung Dis., 2003; 7(Suppl 3): S501-S09.

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