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Sociodemographic and clinical profile of multi drug resistant tuberculosis patients: a study at drug resistant tuberculosis centers of Kolkata

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Abstract:
Background*:Emergence of drug resistant tuberculosis, particularly multi drug resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB) has become an obstacle to effective TB control in India.*
Objectives*: To study the sociodemographic and clinical profile of MDR/XDR-TB patients in Kolkata.*
Methodology*: A retrospective study was performed on MDR patients admitted in Jadavpur and Boral TB hospitals, the two designated drug resistant tuberculosis centers (DR-TB center) of Kolkata, in 2013.*
Results*: Out of 172 admitted cases, majority (30.23%) were between 21-30 years. Males were predominant (61.62%). Females were significantly younger compared to males (p=0.002). Most patients (59.9%) were underweight (BMI<18.5kg/m^2). Among the patients, HIV seropositivity and XDR-TB was found in 2.9% each. According to MDR-TB suspect criteria majority were relapse cases (35.46%). The commonest associated comorbidity was COPD (17.44%). Most patients had bilateral (81.39%) and moderately extensive (38.95%) lesions in chest x-ray. Drug sensitivity testing (DST) showed lowest resistance (1.16%) to pyrazinamide.*
Conclusion: *Relapse of previous antituberculosis treatment was found to be major contributor of MDR-TB suspect cases in Kolkata. Prevalence of resistance to 2nd line drugs is still low. Early diagnosis of drug resistance from all re-treatment cases, quality DOTS services and more controlled and rational use of second-line anti-TB drugs can prevent emerging of MDR/XDR-TB as a major public health problem.*
Keywords *- drug resistant tuberculosis center (DR-TB center), drug sensitivity testing (DST), extensively drug resistant tuberculosis (XDR-TB), multi drug resistant tuberculosis (MDR-TB)*

I. Introduction

Emergence of drug resistant tuberculosis (TB), particularly multi drug resistant tuberculosis (MDR−TB) and more recentlyextensively drugresistant tuberculosis (XDR−TB) has been an area of growing concern and is posing a threat to global efforts of TB control.In 2013, there were an estimated 480 000 new cases of MDR-TB worldwide, and approximately 210 000 deaths from MDR-TB. Highest levels of MDR-TB were reported from Eastern European and central Asian countries.[1]

India is one of the high tuberculosis burden countries in the worldaccounting for nearly 24% of the global incidence. According to the latest World Health Organization (WHO) global tuberculosis report released in 2014, India has surpassed China in harboring MDR-TB cases and there were 62,000 cases of MDR−TB from India in 2013. An estimated 2.2% (95% CI: 1.9-2.6) of new cases and 15% (95% CI: 11-19) of retreatment cases in India have MDR-TB.[1]

Mismanagement of MDR−TB with erratic use of second−line drugs may lead to development of XDR−TB. In the global scenario, about 9% of all MDR cases are XDR-TB.[1] Although, the exact extent of XDR-TB in India is not known, Ramachandranetal had reported 3.2% of XDR strains among the MDR isolates in a field study from Gujarat.[2]

The HIV-TB co-infection has been aptly described as the "cursed duet". [3] WHO estimated5.7% HIV prevalence in incident TB cases in India in 2013 while 13% prevalence was reported worldwide. [1] Patients with HIV-TB co-infection frequently have advanced HIV disease and are at an increased risk of death and new opportunistic infections. [4]

Programmatic management of drug-resistant TB (PMDT) is being implemented in West Bengal in a phased manner since 2011.In this study we present data regarding the sociodemographic and baseline clinical characteristics of MDR/XDR−TB patients of Kolkata who started DOTS Plus in the year 2013 .

II. Materials And Methods

This was a retrospective record based study of MDR-TB patients of Kolkata who were admitted in drug resistant tuberculosis center (DR-TB center) between Ist January to 31st December 2013 for initiation of DOTS Plus. The research proposal was submitted to the Ethical Committee of R.G. Kar Medical College and Hospital, Kolkata for approval and the study was started after getting permission from the concerned authority.

2.1 Setting

The area under Kolkata municipality has been divided into 10 urban health districts each of which is headed by the district tuberculosis officers (DTO). Under the urban health districts there are total 21 tuberculosis units (TU) which is under the supervision of medical officer tuberculosis control (MOTC).The chief tuberculosis officer (CTO) is in overall charge of the RNTCP programme in the city. The urban health districts refer sputum samples of suspected MDR-TB cases to the Intermediate Reference Laboratory (IRL) in Beleghata, for culture and drug sensitivity testing (DST). Three diagnostic technologies are used: Cartridge-Based Nucleic Acid Amplification Testing (CBNAAT), Line Probe Assay (LPA), Mycobacterial Growth Indicator Tube (MGIT) method. After confirmation of MDR-TB, patient is referred to the drug resistant tuberculosis center (DR-TB center) forinitiation of regimen for MDR-TB. The K.S Roy T.B. Hospital in Jadavpur was the designated DR-TB center of Kolkata but from 20th November 2013 Mother Teresa Memorial TB Hospital in Boral has been designated as the DR-TB center of this area. At the time of starting DOTS Plus detailed history was taken including screening for drug or alcohol abuse .Weight and height were measured .Routine investigations like complete blood count with platelets, blood sugar to screen for Diabetes Mellitus, liver function tests, blood urea and creatinine to assess the kidney function, screening for HIV at Integrated Counselling and Testing Center and chest X-ray were done at baseline. Cases with extra-pulmonary TB (EPTB) were subjected to tissue biopsy and culture DST.

2.2 Definitions

2.2.1 MDR-TB case: A TB patient whose sputum is culture positive for Mycobacterium tuberculosis and is resistant in-vitro to isoniazid and rifampicin with or without resistance to otheranti-tubercular drugs based on DST results from an RNTCP-certified Culture & DSTLaboratory. [5]

2.2.2 XDR-TB case: A MDR TB case whose recovered M. tuberculosis isolate is resistant to at least isoniazid, rifampicin, a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and a second-line injectable anti-TB drug (kanamycin, amikacin, or capreomycin) at a RNTCP-certified Culture & DST Laboratory. [5]

As rifampicin resistance is quite rare without isoniazid resistance RNTCP has taken the programmatic decision that patients who have any rifampicin resistance, should also taken to be resistant to isoniazid and managed as if they are an MDR TB case. In the present study we followed the same protocol. [5]

2.2.3 MDR suspect category: A MDR suspect in the present study was defined as a patient suspected of drug-resistant tuberculosis, based on RNTCP criteria for submission of specimens for drug-susceptibility testing [Annexure-1]. [5] During the study period, in West Bengal, suspects were being identified based on criteria C.

Annexure-1

Guidelines for MDR TB suspect case
Criteria A
All failures of new TB cases
Sputum smear positive previously treated cases who remain smear positive at 4 th month onwards
All Pulmonary TB cases, who are contacts of known MDR-TB cases
Criteria B– *in addition to Criteria A*
All smear positive previously treated pulmonary TB cases at diagnosis
Any smear positive follow-up result in new or previously treated cases
Criteria C– *in addition to Criteria B*
All smear negative previously treated pulmonary TB cases at diagnosis
HIV-TB co-infected cases at diagnosis

2.3 Data collection

Data on various parameters of the patients' viz. demographic, socioeconomic, clinical presentation, radiology, previous treatment history and results of drug sensitivity testing were recorded from the PMDT treatment register, PMDT treatment card and clinical information booklet. The data were entered in a pre-designed proforma.

2.4 Data analysis

For demographic and DST data, frequencies, percentages, means and ranges were calculated as appropriate. Means were compared by Independent samples T-test. A two-sided p value less than 0.05 was considered as statistically significant.The data was analyzed using the SPSS version 16.0 software.

III. Results

Table 1 shows the distribution of the study subjects according to their sociodemographic characteristics. Out of a total 172 MDR-TB patients, majority (30.23%) were in the age group 21-30 years (mean age = 32.52 years, standard deviation (SD) 13.05 years; range 14 – 85 years). The male to female ratio was 1.7:1. Mean age of females (28.59 ±12.50 years) was less than that of males (34.97±12.84).This difference was found to be statistically significant (t=-3.202, p=0.002). Majority of patients were Hindus (58.13%) and the rest were Muslims (41.86%). The occupational profile of patients revealed that a majority of them were household workers (27.90%) and labourers (20.34%) followed by skilled workers (18.60%), students (10.46%), business men (9.30%), unemployed (6.97%) and service men (6.39%).While 160 (93.02%) patients had history of having some kind of addiction; the most common form was chewing tobacco 62(36.04%) followed by smoking and alcohol (28.48% each).

Table 2 shows the distribution of the MDR-TB cases according to their baseline clinical characteristics. According to the MDR-TB suspect criteria 61 (35.46%) were relapse cases of previous antituberculosis treatment; 46(26.74%) were treatment failures; 39(22.67%) were defaulters; 25(14.53%) were smear positive follow up in new or previously treated cases and only 1 patient (0.58%)was MDR contact .

Chronic obstructive pulmonary disease (COPD) was the commonest comorbidity (17.44%) among the study group followed by Diabetes Mellitus (15.69%) and hypertension (2.32%). Five patients (2.90%) were HIV positive though HIV status was not checked in 15(8.72%) cases. The mean body mass index (BMI) was 18.5 ± 4.025 kg/m^2, range 12 – 31 kg/m^2).103 patients (59.88%) were undernourished with BMI less than18.5 kg/m^2.

Only pulmonary TB (PTB) was present in 167 (97.09%) patients, while both pulmonary TB and extra-pulmonary TB (EPTB) was noted in five (2.90%) patients (two – pleural effusion, one – pyopneumothorax, one – hydropneumothorax, one- cervical lymph node). Majority had moderately extensive Koch's lesion 74(43.02%) while extensive and mild lesion was noted on x-rays in 67(38.95%) and 31(18.02%) respectively. Bilateral lesion (81.39%) was more than unilateral lesion (18.60%). A total of 77(44.76%) cases had cavitary lesions. 12 patients (6.97%) had unilateral destruction of lung (11-left sided, 1-right sided). Cough was the most common symptom occurring in 92.44% patients followed by expectoration (81.97%).

Figure 1 shows the individual drug resistance pattern of the study group. While by definition, 100% of cases were resistant to isoniazid (INH) and rifampicin, lowest resistance was found to pyrazinamide (1.16%). Only one (0.58%) patient was resistant to four first-line drugs (rifampicin, INH, streptomycin, and ethambutol) and two (1.16%) were resistant to all five drugs (rifampicin, INH, streptomycin, ethambutol and pyrazinamide). Five (2.90%) patients met the criteria of XDR−TB and were resistant to rifampicin, INH, ofloxacin and kanamycin. [5] Overall, the study group was resistant to a mean of 2.06 drugs.

Figure 2 is a map of the area under Kolkata municipality with ten urban health districts (D) .The districts have been divided into four groups according to the number of MDR-TB cases detected from them viz- 0-10, 11-20, 21-30 and more than 30.Most of the urban health districts had 11-20 number of MDR-TB cases (area shaded green). Highest numbers of cases were from Hazi. Number of cases referred from different urban health districts were as follows- Hazi (37), Manasatala (28) ,Tangra (20), Maniktala (18), Alipore(17), Behala (15),Boral (12), Strand Bank Road(9), Baghbazar (8), Tollygunge (8).

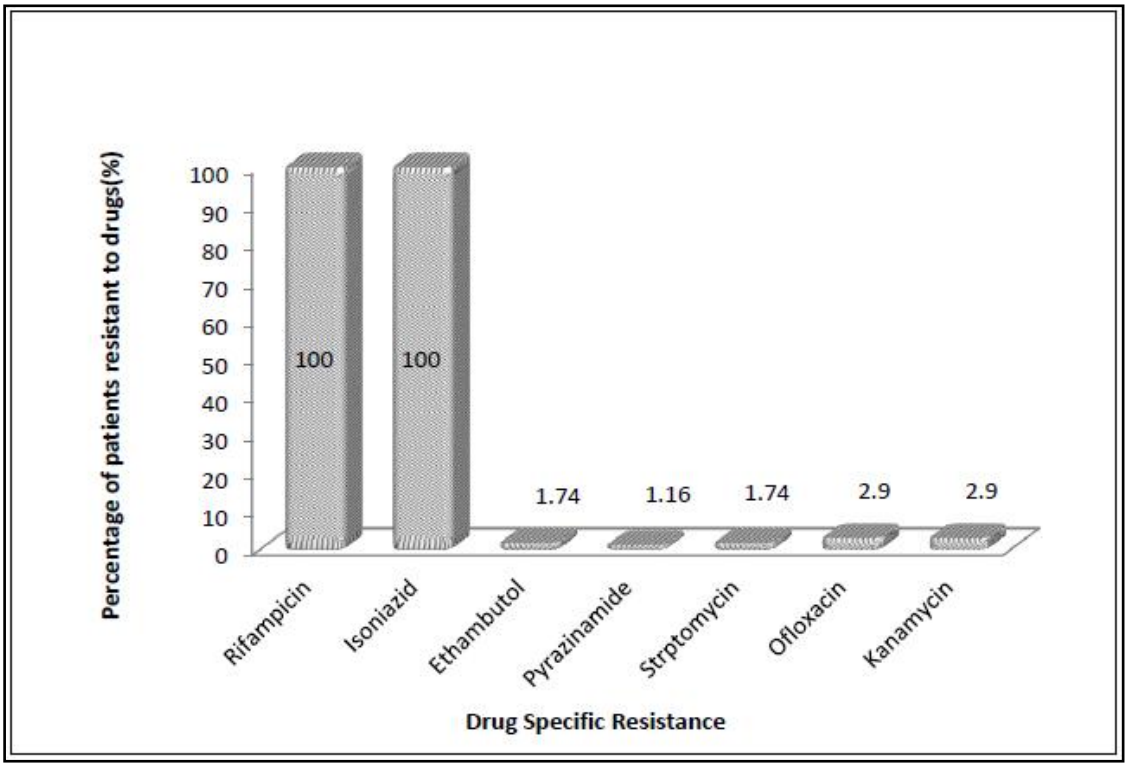

Figure 1: Individual drug- specific resistance patterns of MDR-TB cases.

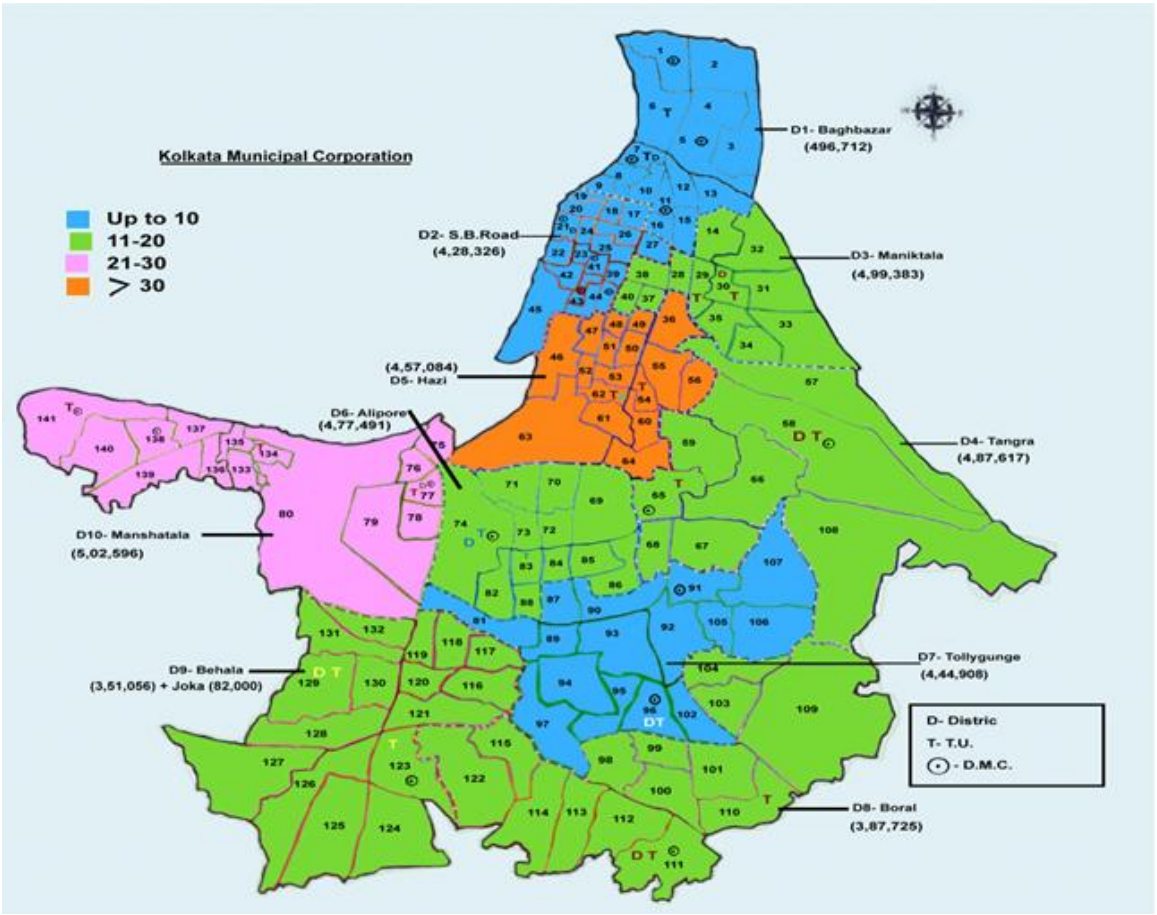

Figure 2: Distribution of MDR-TB cases in urban health districts of Kolkata

IV. Discussion

Drug resistance is not a new phenomenon in India. It has been reported even much before the era of RNTCP. [6] However, high level of resistance to second line drugs (SLD) including XDR-TB as shown in many recent studies across the country has generated concern. [2, 7- 9]

In the present study majority of the MDR-TB cases (30.23%) were in the younger age group (21-30 years); mean age was 32.52 years. In a retrospective study done in a TB unit in Mumbai, Dholakia and Shah noted that majority of the cases (67.6%) were in the age group 15-35 years with a mean age of 31years. [10]Udwadia and Moharil, Sharma et al. also reported prevalence of younger age group among MDR-TB patients with the mean age of their study groups being 29.7 years and 33.25 years respectively. [9, 11] Majority of our cases were male (61.62%).Male predominance among MDR-TB cases has been also reported by other authors.[8,12]

The occupational profile of our patients revealed that a majority of them were household workers followed by labourers and skilled workers. Gupta et al. observed a significantly higher prevalence of pulmonary TB in blue-collar and white-collar workersthan household workers, students and retired/unemployed people. However, they have not looked into drug resistance patterns in these patients. [13]

Our patients were a heavily pre-treated group of MDR-TB patients of which majority belonged to relapse cases (35.46%) of previous antituberculosis treatment. A recent meta-analysis also showed that relapse rate is high (almost 10%) in India and the risk factors for relapse included drug irregularity, initial drug resistance, smoking, and alcoholism. [14] However, in a prospective study conducted by Sethiet al. in North Indiaa major proportion of MDR-TB cases was due to treatment failure. [15]

The mean BMI of the patients in this study was 18.5 kg/m^2, 59.88% were undernourished. Undernutrition among MDR-TB cases was also reported from another study (mean BMI of 17.84 $kg/m^{2)}$ done in a tertiary care setting in New Delhi. [11]

The commonest comorbidity among our study group (17.44%) was chronic obstructive pulmonary disease (COPD). Dattaet al. also found COPD to be the commonest comorbid disease among MDR-TB cases in a tertiary care hospital of Kashmir. Diabetes was present as a comorbid illness among 7.6% in their study whereas in the present study higher proportion of cases (15.69 %) had diabetes. [8]

Globally, MDR-TB has been a particular concern among HIV-infected persons, whose rate of survival is substantially lower than that of those not infected, [3, 4, 16] and testing for HIV is recommended for all TB patients. The literature regarding prevalence of HIV in MDR-TB is scanty from most parts of India. Datta et al.reported 1.9% HIV seropositivity among MDR -TB cases. [8] However in the present study 2.90% MDR-TB patients were found to be HIV seropositive.

Majority of patients in our study had pulmonary TB (97.09%), while 2.90% patients had both PTB and EPTB. Similar findings have been reported by others. [10] Radiologically our patients had more moderate (43.02%) to severely extensive disease (38.95%), usually bilateral (81.39%). This has also been reported by some other Indian observers. [9, 10] Worldwide, the prevalence of XDR-TB is on the rise. XDR-TB has been reported by 100 countries globally by the end of 2013. The proportion of MDR-TB cases with XDR-TB was highest in Georgia (20.0%). [1]Among our study group, 2.90% patients were found to have XDR-TB. This figure is almost consistent with some recently published reports from various other parts of India [2, 10, 17]. However some other Indian authors have reported a higher prevalence of XDR-TB among MDR-TB cases. [8, 9]

The present study demonstrated a low proportion of resistance to pyrazinamide (1.16%) ethambutol (1.74%) and streptomycin (1.74%). Among the second line drugs (SLD) only 2.90% resistance was found to both ofloxacin and kanamycin. Overall, the patients were resistant to a mean of 2.06 drugs. In another study reportedly the proportion of resistance to pyrazinamide, streptomycin and fluoroquinolone was greater with a mean resistance to 4.6 drugs. [9] We observed a 0.58% resistance rate to four first-line drugs - rifampicin, INH, streptomycin and ethambutol, which is less than that observed in the published reports of Dattaet al,Lahiri et al.[8, 18]Generalizability of the findings of this study however may be limited. The study was limited to MDR-TB patients who belonged to Kolkata, and therefore was not representative of the total MDR pool in the state.

V. Conclusion

The present study showed that younger age group particularly in the females were more affected with MDR-TB. Undernutrition was quite prevalent among the MDR-TB patients. Relapse of previous antituberculosis treatment was found to be the major contributor of MDR-TB suspect cases in Kolkata. DST profiles suggested low level of resistance to first line drugs (other than rifampicin, INH). Prevalence of XDR-TB was also found to be low. Overall the findings of this study emphasize the importance of studying the sociodemographic factors and drug resistance patterns of tuberculosis in different patient categories to timely modify and strengthen the national programs. Early diagnosis of drug resistance from all re-treatment cases, quality DOTS services and more control and rational use of second-line anti-TB drugs can prevent emerging of MDR/XDR-TB as a major public health problem.

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Table 1: Socio-demographic profile of MDR-TB patients (N=172)

Characteristics	Number	Percentage
Age		
11-20 years	36	20.93
21-30 years	52	30.23
31-40 years	44	25.58
41-50 years	25	14.53
51 and above	15	8.72
Sex		
Female	66	38.37
Male	106	61.62
Religion		
Hindu	100	58.13
Muslim	72	41.86
Primary occupation		
Unemployed	12	6.97
Household work	48	27.90
Labourer	35	20.34
Skilled work	32	18.60
Service	11	6.39
Student	18	10.46
Business	16	9.30
Addiction*		
smoking	49	28.48
tobacco chewing	62	36.04
alcohol	49	28.48

*There were multiple responses

Table 2: Baseline clinical characteristics of MDR-TB patients (N=172)

Clinical characteristics	Number	Percentage
Site of disease		
Only Pulmonary	167	97.09
Pulmonary +Extra-pulmonary	5	2.90
MDR suspect category		
Relapse of previously treated case	61	35.46
Treatment failure	46	26.74
Treatment after default	39	22.67
Any smear positive follow up	25	14.53
MDR contact	1	0.58
HIV status		
Negative	152	88.37
Not known	15	8.72
Positive	5	2.90
Comorbidities		
Diabetes	27	15.69
Hypertension	4	2.32
COPD	30	17.44
Status of drug resistance		
MDR	167	97.09
XDR	5	2.90
Nutritional status		
Normal (BMI $\geq$18.5kg/m^2)	69	40.11
Undernourished (BMI<18.5kg/m^2)	103	59.88
Presenting symptoms*		
Cough	159	92.44
Expectoration	141	81.97
Shortness of breath	57	33.13
Fever	56	32.55
Anorexia	45	26.16
Hemoptysis	44	25.58
Chest pain	43	25.00
Vomitting	31	18.02
Chest radiographic features		
Mild Koch's lesion	31	18.02
Moderate lesion	74	43.02
Extensive Koch's lesion	67	38.95

* There were multiple responses

Footnotes
Source of Support: Nil
Conflict of Interest: None declared.