

Epidemiological profile of multidrug-resistant tuberculosis patients in Gorakhpur Division, Uttar Pradesh, India

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ABSTRACT

Introduction: Multidrug-resistant tuberculosis (MDR-TB) poses a major threat to control of TB worldwide. Adequate information on socioepidemiological factors and their interaction is required for its control. The aim was to study the social and epidemiological profile of MDR-TB patient in Gorakhpur division. **Methodology:** A cross-sectional study of 157 MDR-TB patients from Gorakhpur division admitted at DR-TB Center of a tertiary care center were interviewed during initiation of MDR-TB treatment using structured questionnaire and collected data were described using descriptive statistics. **Results:** More than 2/3rd of patients were male and the mean age was 32.15 ± 13.19 years. Overcrowding was present in 82.8% of households and ventilation of living room was inadequate in 72.7% of households. About 21.7% had history of contact with TB cases. Two-third of the patients practice unhygienic sputum disposal practices at home and at public places it was more than 90%. More than 60% of patients have the history of irregular treatment in intensive phase and 80% in continuation phase. Nearly 68.8% of patients were resistance to isoniazid (H) and rifampicin (R) and 18.5% were resistance to H, R, and S (streptomycin) followed by H, R and E (Ethambutol). Nearly 3.8% of patients were HIV positive and 7% had history of diabetes. 64.3% were under severe thinness category according to the WHO classification. **Conclusion:** Study point out need of nutritional counseling and support throughout the treatment. Use of incentives, enhancing contact tracing and increasing awareness regarding sputum disposal practices are recommended for effective control.

Keywords: Drug-resistant tuberculosis, epidemiology, multidrug-resistant tuberculosis, tuberculosis

Introduction

Drug-resistant tuberculosis (DR-TB) poses a major threat to control of TB worldwide. In 2015, there were an estimated 480,000 new cases of multidrug-resistant TB (MDR-TB) and an additional 100,000 cases with rifampicin-resistant TB (RR-TB) who were also newly eligible for MDR-TB treatment. As in 2015, 3.9% of new and 21% of previously treated TB cases were estimated to have had rifampicin- or MDR/RR-TB and caused 250,000 deaths. Most cases and deaths occurred in Asia. In India,

there were an estimated 79,000 new cases of MDR-TB/RR-TB cases are notified and drug resistance shows that 3.5% of new and 16% of previously treated TB cases were estimated to have MDR/RR-TB in 2015.^[1] Factors such as inadequate chemotherapy, poor adherence to treatment, treatment failure, prior treatment, pulmonary cavity TB, diabetes, and HIV infection are mainly accounted for the progress of drug resistance in TB.^[2,3] Of these, the supreme predictor for the presence of MDR-TB is a previous history of treatment of TB.^[2] Psychiatric illness, drug addiction, alcohol consumption, symptom relief, homelessness, adverse drug reactions, and inability to afford treatment do predict nonadherence to treatment. The new Post-2015 Global TB Strategy recognizes action on social

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determinants of TB as a main element of the valiant policies and supportive systems vital for TB control. In line with this approach, there is a general agreement that research is necessary to assess and measure how social determinants affect TB risk.^[4] Adequate information on socioepidemiological factors and their interaction is required for control and effective treatment of TB as well as MDR-TB. However, there is scarcity of information in the study area as well as in our country and the magnitude and direction of interaction of these socioepidemiological factors may vary in different setting. With this background, our aim was to study the social and epidemiological profile of MDR-TB patient in the Gorakhpur division.

Methodology

From November 1, 2015, to October 31, 2016, 157 MDR-TB patients who are ≥ 18 years of age and diagnosed as confirmed case of MDR TB from a Revised National TB Control Programme (RNTCP) accredited CDST or CBNAAT lab from Gorakhpur division admitted at drug-resistance TB Management Centre (DR-TB Centre) of BRD Medical College, Gorakhpur were enrolled in a Cross sectional study. DR-TB Centre at BRDMC is established under RNTCP and it covers four district of Eastern UP (Gorakhpur, Maharajganj, Deoria, and Kushinagar). All suspected cases of MDR-TB from these districts are referred to this center and from here patient's samples are collected for drug sensitivity test and sent to nearest RNTCP certified laboratories (IMS, Banaras Health University, and Varanasi). Patient diagnosed as DR-TB are registered under directly observed *treatment*, short-course (DOTS) plus treatment regimen. All registered patients were initiated treatment and kept under observation for 7 days at DR-TB ward and after that patients referred to their nearest DOTS Provider. The sample size was calculated with the help of Epi-info software version 7.2.0.1 (developed by Centers for Disease Control and Prevention). using population survey option. Prevalence of MDR-TB in previously treated TB patients was taken as 16%. With 95% confidence interval and 6% acceptable margin of error, the calculated sample size was 143. The minimum sample size to represent the study population was 143. By considering the previous record of inpatient admission we decided the sampling technique, sample size (margin of error adjustment) and data collection period. Consecutive sampling (All the patients fulfilling inclusion criteria during the study period of 6 months were enrolled). Severely ill patient unable to participate in the interview and patients who have not given consent to participate in the study were excluded. Structured schedule is used to assess the social and epidemiological determinants. Questionnaire has five section which includes demographic profile, previous treatment history, clinical profile, assessment of housing conditions and health seeking behavior and hygiene practices of MDR-TB patients. The study was approved by the Institutional Ethics Committee, and we obtained written informed consent from all the participants.

Results

A total of 174 patients were admitted at DR-TB ward over the period of 6 months duration, out of them 17 were excluded from the study as they did not met the eligibility criteria of age (≥ 18 years). Distribution of patients is shown in Figure 1. The mean age of patients was 32.15 ± 13.19 and median age was 29 (22–40). The minimum and maximum age was 18 and 78, respectively. Demographic characteristics are described in Table 1. The difference in frequency of employment status in past and present were cross tabulated and difference compared using Chi-square test and found statistically highly significant ($P < 0.001$). Among 157 patients, 43% were employed in the past and at present this proportion is 12.7% as shown in Figure 2. Loss of income was present in 42.67%, among them 85.07% were male and 14.9% were female. The difference in proportion of existence of loss of income between gender was compared and found statistically significant ($P < 0.001$). Characteristics of previous treatment history of MDR-TB patients are presented in Table 2. In our study, all 157 (100%) patients found to be previously treated cases. Time interval between TB and MDR-TB was compared with gender and found statistically insignificant ($P = 0.46$) with Chi-square test. Nearly 49.1% of males and 38.8% of females had 6–12 months duration between TB and MDR-TB. 28.7% males and 36.7% females was under 6 months interval category. Education status among patients who took insufficient duration treatment were compared using Chi-square and found insignificant with $P = 0.77$. 76.3% in illiterate and 73.9% in literate were claimed history of insufficient duration of treatment during the anti-tubercular treatment.

Clinical characteristics of MDR-TB patients are presented in Table 3. 97.5% were pulmonary MDR-TB patients and rest were accompanying with other system. 64.3% in female MDR-TB patients were under < 16 body mass index (BMI) which is the cut off value to classify severe thinness according to the WHO Classification. BMI and Gender of MDR-TB patients were compared using Chi-square test and was found insignificant with

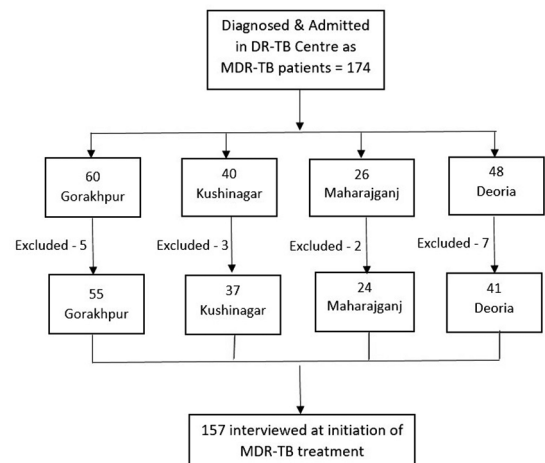


Figure 1: District-wise distribution of multidrug-resistant tuberculosis patients

Table 1: Demographic characteristics of multidrug-resistant tuberculosis patients enrolled in this study (n=157)

Characteristic	Frequency (%)	95% CI
Age (years)		
18-29	80 (51)	43.2-58.6
30-40	45 (28.7)	22.1-36.1
>40	32 (20.3)	14.8-27.3
Area of residence		
Urban	52 (12.7)	8.4-18.8
Rural	137 (87.3)	81.1-91.6
Sex		
Male	108 (68.8)	61.1-75.5
Female	49 (31.2)	24.4-38.8
Education		
Illiterate	38 (24.2)	18.1-31.4
Primary (standard 1-7)	72 (45.9)	38.2-53.6
Secondary (standard 8-10)	24 (15.3)	10.5-21.7
Higher secondary (standard 11-12)	17 (10.8)	6.8-16.6
Graduate and above	6 (3.8)	1.7-8.0
Religion		
Hindu	133 (84.7)	78.2-89.5
Muslim	22 (14)	9.4-20.3
Others	2 (1.3)	0.3-4.5
Type of family		
Nuclear family	26 (16.6)	11.5-23.1
Joint family	69 (43.9)	36.4-51.7
Three generation	62 (39.5)	32.1-47.3
Marital status		
Married	87 (55.4)	47.6-62.9
Unmarried	48 (30.6)	23.9-38.1
Widow/widower	13 (8.3)	4.9-13.6
Separated/divorced	9 (5.7)	3.0-10.5
Loss in income		
Yes	67 (42.7)	35.2-50.5
Dependent	90 (57.3)	49.5-64.7
Occupation		
Housewife	30 (19.1)	13.7-25.9
Daily laborer	37 (23.6)	17.6-30.7
Farmer	8 (5.1)	2.6-9.7
Employee	8 (5.1)	2.6-9.7
Student	12 (7.6)	4.4-12.8
Merchant	8 (5.1)	2.6-9.7
Unemployed/dependent	46 (29.3)	22.7-36.8
Skilled worker	7 (4.5)	2.1-8.9
Others	1 (0.6)	0.1-3.5
Present employment status		
Employed	20 (12.7)	8.4-18.8
Occasionally going for work	16 (10.2)	6.3-15.9
Unemployed/dependent	121 (77.1)	69.8-82.9
Past employment status		
Employed	68 (43.3)	35.8-51.1
Occasionally going for work	2 (1.3)	0.3-4.5
Unemployed/dependent	87 (55.4)	47.6-62.9
Loss in income		
Yes	67 (42.7)	35.2-50.5
Dependent	90 (57.3)	49.5-64.7

Contd...

Table 1: Contd...

Characteristic	Frequency (%)	95% CI
Food habits		
Vegetarian	113 (72)	64.4-78.4
Nonvegetarian	44 (28)	21.5-35.5

CI: Confidence interval of proportion

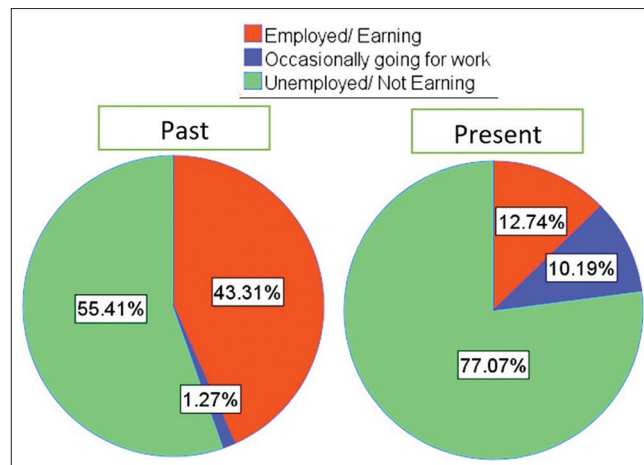


Figure 2: Distribution of employment status in the past and at present

$P = 0.59$. 100% of patients of MDR-TB claimed that they do not smoke at present. Among them, 43.31% had smoking habits at past. The mean BMI in Nonsmokers was 15.89 ± 3.02 and 15.48 in Past Smokers. The mean BMI between past smoker and those who never smoked was compared with independent t -test and was found statistically insignificant. 100% of patients of MDR-TB claimed that they do not consume alcohol at present. Among them, 41.4% had alcohol habits at past. The mean BMI in Nonalcoholic was 15.37 ± 2.67 and 15.77 in past alcoholic. The mean BMI between past alcoholic and those who never consumed alcohol was compared with independent t -test and was found statistically insignificant ($P = 0.41$). Overcrowding was present in 82.8% of households and ventilation of living room was inadequate in 72.7% of households. Other characteristics are given in Table 4. Overcrowding in Nuclear and Joint/Three generation family was compared using fisher exact test and found statistically significant with $P = 0.004$ [Figure 3]. Health seeking behaviors and hygiene practices of MDR-TB patients which includes sputum disposal, cough hygiene practices, usage of facemask, etc., as shown in Table 5.

Discussion

This study was conducted for the first time in the region to analyze various epidemiological factor and aspects related to DOTS plus regimen among MDR-TB patients put on Category IV during the first year of implementation of DOTS plus project in the district Gorakhpur.

More than 2/3rd of patients were male and the mean age was 32 years. Mean age of male was higher as compared to female, however difference was found to be statistically insignificant ($P = 0.10$).

Table 2: Distribution of previous treatment history characteristics of multidrug-resistant tuberculosis patients (n=157)

Characteristic	Frequency (%)	95% CI
Interval between TB and MDR-TB diagnosis		
<6 months	49 (31.2)	24.4-38.8
6-12 months	72 (45.9)	38.2-53.6
>1 year	36 (22.9)	17.0-30.1
Number of previous treatment		
1	139 (88.5)	82.6-92.6
2 and above	18 (11.5)	7.3-17.3
Took private diagnostic/treatment center		
Yes	125 (79.6)	72.6-85.1
No	32 (20.4)	14.8-27.3
History of irregular treatment during intensive phase		
Yes	95 (60.5)	52.7-67.8
No	62 (39.5)	32.1-47.3
History of irregular treatment during continuation phase		
Yes	123 (78.3)	71.2-84.0
No	34 (21.7)	15.9-28.7
Previous treatment with insufficient duration		
Yes	117 (74.5)	67.1-80.6
No	40 (25.5)	19.3-32.8
Reason to stop/miss medications in anti-TB drugs		
Forgetfulness	16 (10.2)	6.3-15.9
Symptoms not relived and took private treatment	35 (22.3)	16.4-29.4
Fear of side effects	6 (3.8)	1.7-8.0
Felt medication was not effective and decided not to take dose	13 (8.3)	4.9-13.6
Occupation related problems	22 (14.0)	9.4-20.3
Symptomatically cured	46 (29.3)	22.7-36.8
Took medication regularly	19 (12.1)	7.8-18.1

CI: Confidence interval of proportion; TB: Tuberculosis; MDR: Multidrug-resistant

A study from Mumbai, India, in which nearly 69% of patients belonged to the younger (15–35 years) age group with a median age of 26 years (interquartile range: 20–37 years).^[5] A study from Ahmedabad, India, in which 83.7% of patients were in reproductive age group of 16–45 years with mean age of 33.64 ± 11.03. 68.5% were males and majority of the patients belong to Hindu religion.^[6] Udwardia 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.^[7]

More than 3/4th of patients were from rural area and 1/3rd are illiterate. Majority (83.4%) of patients belongs to Joint/Three generation people and more than half (55.4%) are married. Before the diagnosis of TB 68% of patients were earning, but at present, only 20% of patients claimed that they go for their work. This difference is found to be highly statistically significant ($P \leq 0.001$). All working patients (42%) had loss of income because of illness, loss of income was significant ($P \leq 0.001$) in male. All

Table 3: Clinical characteristics of multidrug-resistant tuberculosis patients (n=157)

Characteristic	Frequency (%)	95% CI
Presence of BCG scar		
Yes	44 (28)	21.5-35.5
No	113 (72)	64.4-78.4
History of contact with TB cases		
Yes	34 (21.7)	15.93-28.74
No	123 (78.3)	71.2-84.0
Household contacts of TB		
Yes	17 (10.8)	6.8-16.6
No	140 (89.2)	83.3-93.1
Type of tuberculosis		
Pulmonary	153 (97.5)	93.6-99.0
Pulmonary + pleural	2 (1.3)	0.3-4.5
Pulmonary + other system	2 (1.3)	0.3-4.5
Resistance pattern		
H and R resistant	108 (68.8)	61.1-75.5
H, R and E resistant	17 (10.8)	6.8-16.6
H, R and S resistant	29 (18.5)	13.1-25.2
H, R, S and E resistant	3 (1.9)	0.6-5.4
HIV status		
Positive	6 (3.8)	1.7-8.0
Negative	151 (96.2)	91.9-98.2
Diabetes history		
Yes	11 (7)	3.9-12.1
No	146 (93)	87.8-96.0
BMI category		
Severe thinness (<16)	101 (64.3)	56.5-71.4
16 and above	56 (35.7)	28.6-43.4
Smoking		
Past	68 (43.3)	35.8-51.1
Never	89 (56.7)	48.0-64.1
Tobacco (chewing)*		
Past	23 (14.6)	9.9-21.0
Never	134 (85.4)	78.9-90.0
Alcohol past		
Habitual	20 (12.7)	8.4-18.8
Social	45 (28.7)	22.1-36.1
No	92 (58.6)	50.7-66.0

*No current smokers. CI: Confidence interval of proportion; BMI: Body mass index; TB: Tuberculosis; H: Isoniazid; R: Rifampicin; E: Ethambutol; S: Streptomycin; BCG: Bacille Calmette-Guerin

patients experienced substantial socioeconomic impact of TB disease, most importantly due to inability to work and job loss. These results are consistent with other reported findings.^[8-12] The occupational profile of patients revealed that a majority of them were unemployed (29.3%) and daily laborers (23.6%) followed by housewife (19.1%), student (7.6%), merchant (5.1%), farmer (5.1%), employee (5.1%), and skilled worker (4.5%). In the study of Mukherjee *et al.*, the majority of them were household workers (27.90%) and laborers (20.34%).^[11]

In 2/3rd of patients the interval between diagnosis of TB and MDR-TB was found to be duration of more than 6 months. More than 60% of patients have the history of irregular treatment in intensive phase and 80% in continuous phase and when they were enquired about the reason behind the issue

Table 4: Housing condition of multidrug-resistant tuberculosis patients (n=157)

Characteristic	Frequency (%)	95% CI
Over crowding		
Present	130 (82.8)	76.13-87.9
Absent	27 (17.2)	12.1-23.8
Type of house		
Independent	112 (71.3)	63.8-77.8
Attached	45 (28.7)	22.16-36.18
Construction of house		
Pucca	78 (49.7)	41.9-57.4
Semi-pucca	46 (29.3)	22.7-36.8
Kutchha	33 (21)	15.3-28
Floor of the house		
Mud	79 (50.3)	42.5-58
Cement/tiles	78 (49.7)	41.9-57.4
Sharing bedroom		
Yes	25 (16.4)	11-22.4
No	132 (83.6)	77.5-88.9
Housing ventilation of living room		
Adequate	40 (27.3)	19.3-32.8
Not adequate	117 (72.7)	67.1-80.6
Cross ventilation		
Present	35 (25.5)	16.4-29.4
Absent	122 (74.5)	63.8-77.8
Kitchen condition		
Separate	47 (29.9)	23.3-37.5
Combined	110 (70.1)	62.4-76.6

CI: Confidence interval of proportion

of Nonadherence of anti-TB treatment the listed reason were dispersed. 30% of patients discontinued their medication because they were symptomatically felt cured. On the other side, 18% of patients were not satisfied by the treatment as their symptoms continued and took private doctor consultation and treatment. Other reason includes forgetfulness (19.7%), occupation related problems (14%), and felt medication was not effective and decided not to take dose (7.6%). Occupational-related problems were found common in male. In Bhatt *et al.*, the common reason for default was financial problem follow by no improvement in symptoms.^[9]

Nearly 97.5% of patients are pulmonary MDR-TB patients and rest are accompanying with other system. 2/3 of patients are resistance to isoniazid (H) and rifampicin (R) only and rest 18.5% were accompanying with resistance to streptomycin and 10.1% with ethambutol. Mukherjee *et al.* demonstrated a low proportion of resistance to pyrazinamide (1.16%) ethambutol (1.74%), and streptomycin (1.74%). Among the second-line drugs only 2.90% resistance was found to both ofloxacin and kanamycin.^[11] In a study from Mumbai, the proportion of resistance to three or more drugs including HR (20%) was greater than that of resistance to HR only (4%).^[13]

In our study, nearly 65% of patients were under severe thinness category according to WHO classification. Past exposure of alcohol and smoking was found in 41% and 43%, respectively.

Table 5: Health seeking behavior and hygiene practices of multidrug-resistant tuberculosis patients

Characteristic	Frequency (%)	95% CI
Sputum disposal practices-at home		
Hygienic	105 (66.9)	59.1-73.7
Unhygienic	52 (33.1)	26.2-40.8
Sputum disposal practices-at public place		
Hygienic	13 (8.3)	4.9-13.6
Unhygienic	144 (91.7)	86.3-95.1
Knowledge about cough hygiene		
Correct	20 (12.7)	8.4-18.8
Incorrect	137 (87.3)	81.1-91.6
Seek advice from doctor other than medication		
Yes	101 (64.3)	56.5-71.4
No	22 (14.0)	9.4-20.3
Sometime	34 (21.7)	15.9-28.7
Facemask use		
Yes	123 (78.3)	71.2-84.0
No	34 (21.7)	15.9-28.7
Handwashing after coughing/sneezing		
Yes	23 (14.6)	9.9-21.0
No	105 (66.9)	59.1-73.7
Sometime	29 (18.5)	13.1-25.2
People per sleeping room		
1-2	53 (33.8)	26.8-41.4
3-4	76 (48.4)	40.7-56.1
>4	28 (17.8)	12.6-24.5

CI: Confidence interval of proportion

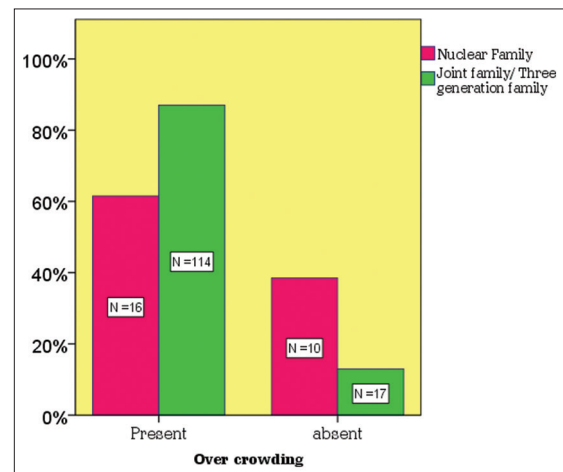


Figure 3: Distribution of overcrowding in different type of family

Diabetes and HIV positive patient were found only in 7% and 3.8%, respectively. We compared mean value of BMI with gender, smoking, and alcohol status, found statistically insignificant association. A study from Kolkata, India found the mean BMI of the patients in this study was 18.5 kg/m², 59.88% were undernourished.^[11] Undernutrition among MDR-TB cases was also reported from another study (mean BMI of 17.84 kg/m²) done in a tertiary care setting in New Delhi.^[14] 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, and testing for HIV is recommended for all TB patients.^[15,16] The literature regarding prevalence of HIV in MDR-TB is scanty from most parts of India. Datta *et al.* have reported 1.9% HIV seropositivity among MDR-TB cases.^[17] However in the present study, 3.8% of MDR-TB patients were HIV seropositive.

Most of the MDR-TB patients were living in poor environmental condition. Housing ventilation of living room was absent in 72.7% of patient's house and cross ventilation was present only in 25% of houses. In 70% of patient's house kitchen was combined with living room and nearly half of the households are not pucca and mud in the floor. A study from Wardha, Maharashtra describes distribution of chest symptomatic contact with relation to housing condition such as overcrowding, kitchen condition, and sharing of same bedroom with index case. Among symptomatic contacts 46.15% were residing in overcrowded houses and 15.39% chest symptomatic contact had separate kitchen, sharing of same bedroom with index case was up to the tune of 38.46%.^[18]

Knowledge and practices regarding hygiene was poor. 2/3rd of patients practice unhygienic sputum disposal practices at home and at public places it was more than 90%. Only 12% of patients have the correct knowledge regarding cough hygiene and 2/3rd do not wash their hands after coughing and sneezing. The probable reason for this could be lack of patient provider interaction. 78% have claimed that they use facemask when they go to public places. 65% have claimed that they seek advice from doctor other than medication. Dissatisfaction with treatment services and poor patient provider interaction were apparent determinants of default and barriers in utilization of services.^[19,20] Tsegaye, Abiy, Mesele, *et al.* found rural residence, seeking treatment from traditional healers and poor knowledge about TB were associated factors that predict patient delay. Chinenye concluded that practices of covering mouth and nose when coughing and sneezing, personal hygiene, immunization of family members were poor among the study participants.^[21]

Conclusion

Based on the findings of the present study, it is recommended to strengthen the patient's supervision during continuous phase of anti-TB treatment. The present study also point out need of nutritional counseling and support throughout the treatment. Motivation of private practitioner for increasing referrals needs to be strengthened. Use of incentives, enhancing contact tracing, and increasing awareness regarding sputum disposal practices are recommended for effective control of MDR-TB. Since the present study was confined only to MDR-TB cases and there was no comparison group, definite conclusion regarding the factors responsible for development of resistance and the relationship between various social, behavioral, and environmental aspects and drug resistance need to be explored and hence, further research is recommended.

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Conflicts of interest

There are no conflicts of interest.

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