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Multi Drug Resistant Tuberculosis of (15-60 Years) of Far-Western Region of Nepal

Bhuwan Thakurathi[1*], Raksha Giri[2], Deepak Kumar Yadav[3], Vijay Khanal[3], Suman Chandra Gurung[4], Mohan Thakurathi[5] and Om Prakash Joshi[6]

[1]*Health for Life, RTI International, Dhangadhi, Kailali, Nepal*

[2]*Suaahara, Dhangadhi, Kailali, Nepal*

[3]*B.P Koirala Institute of Health Science, Dharan, Nepal*

[4]*Birat Nepal Medical Trust, Kathmandu, Nepal*

[5]*Seti Zonal Hospital, Dhangadhi, Kailali, Nepal*

[6]*Save the Children International, Dhangadhi, Kailali, Nepal*

[*]**Corresponding author:** Bhuwan Thakurathi, Health for Life, RTI International, Dhangadhi, Kailali, Nepal, Tel: +979849024751; E-mail: bhuwanthk@gmail.com

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Abstract

Background: Multidrug-Resistant Tuberculosis (MDR-TB) is tuberculosis that does not respond to Isoniazid and Rifampicin and remains one of the major public health concerns in the South-East Asia Region of World Health Organization.

Methodology: A descriptive analytical design with an unmatched case-control study was conducted in Kailali district of Far-Western Nepal among purposively selected 50 cases and 50 controls.

Results: Service, business, migrant labor and house wife were found three times more at risk of having MDR-TB than those who were involved in agriculture (OR 3.38; 95% CI 1.12-10.22). People who live in hill/mountain were also found three times more at risk than those who lives in Terai (OR 3.75; 95% CI 1.19-11.86). Similarly, people who had pulmonary tuberculosis were found eleven times more likely to have MDR-TB than those who had extra-pulmonary tuberculosis (OR 11.39; 95% CI 1.10 to-117.3).

Conclusion: The study revealed that there was significant association between occupation, place of residence, type of tuberculosis and MDR-TB.

Keywords: Multidrug-resistant tuberculosis; HIV; Pulmonary tuberculosis; Risk factors

Introduction

Multidrug-Resistant Tuberculosis (MDR-TB) is tuberculosis that does not respond to Isoniazid and Rifampicin that are the anti-tuberculosis drugs. The mortality in MDR-TB has been seen high both in HIV-infected and uninfected individuals [1]. There are about 440,000 cases of MDR-TB identified each year, causing at least 150,000 deaths from a disease that should be curable. Levels are much higher in those previously treated for tuberculosis [2]. The latest estimate of MDR-TB is 2.9 percent among new cases and 11.7 percent among retreatment cases [3].

The treatment cost of MDR- TB is very expensive comparing to first line TB treatment [1] and the cure rate of MDR-TB patient is almost 50 percent in Nepal [3] and MDR-TB takes two years or more to treat with drugs that are less effective, more toxic and more expensive [4].

Therefore, tuberculosis is the main public health problem in Nepal and MDR-TB being the new challenge. The main objective of our study is to assess the factors associated with MDR-TB in far-western region of the country and the specific objectives of the study are as follows:

- To find out the association between socio-demographic and economic factors with MDR-TB.
- To assess the association between type of tuberculosis and MDR-TB.
- To find out the association between disease history and MDR-TB.

Materials and Methods

The paradigm of the study was quantitative and the study was both descriptive and analytical. The study analyzed the association of MDR-TB with different factors.

Unmatched Case control study was conducted to identify the factors associated with MDR-TB. Kailali district of far western development region was purposively selected to carry out the study. Cases were selected from National partnership for Integrated Development (NAPID), Nepal. Controls were selected from the Seti Zonal Hospital, Nava Jeewan Hospital, and Jugada Sub Health Post. The study period started from September 2013 to February; 2014.

For selecting the sample size, all the participants from the Drug Resistant Hostel were selected as cases, therefore, considering it as a census, those who are resistant to both drugs isoniazid and rifampicin in the Drug Resistant Hostel are considered as cases.

Likewise, controls (those having only Tuberculosis) were selected purposively from three sites and interviewed on first come first basis (35 from Seti Zonal Hospital, 10 from Nava Jeewan Hospital and 5 from Jugada Health Post).

Therefore, there were altogether 50 cases selected from Partnership for Integrated Development (NAPID)-Nepal and 50 control, the overall sample size of the study with comparison ratio 1:1 was 100.

Face to face interview was conducted to gather information from both case and control and all questions were asked in local language. Questions asked in interview were their age, sex, educational background, marital status, family size, family type, occupation, educational status place of residence, history of tuberculosis, alcohol uses, illicit drug uses, smoking, ventilation status, disease history and history of hospitalization were tested in bivariate and multivariate analysis to find out the association. Similarly, questions regarding reasons for non-compliance of anti-tuberculosis drugs were also asked. HIV status was taken from the detail history of subjects and confirmed with laboratory reports. No other clinical factors were included in questionnaire.

Informed verbal consent was taken from individual subject prior to interview.

Validity and reliability

Previous studies which shows the factors that are associated with MDR-TB and consultation with experts' on Tuberculosis, questionnaire was developed. Questionnaires were pretested before actually applied in the field. Necessary change in the questionnaire was made on the basis of pretesting. For testing internal validity (questionnaire), Cronbach's alpha was calculated which value was more than 0.7. The collected raw data were checked and edited at the time of data collection. Coding list was prepared manually and data were entered in excel software. The data was analyzed in SPSS version 16.0. Descriptive statistics of data was carried out to calculate frequency, percentage and mean. The Chi-square was applied for comparison between two variable of binary outcome. Odds ratio (OR) and 95 percent confidence interval (CI) was estimated by bivariate analysis and forward regression model was used to find out the associated factors of multivariate analysis of MDR-TB.

Results

The total number of the respondents were 100 (62 were male and 38 female) making sex ratio of almost 7:3. About 8 out of 10 (76%) of the respondents were above 30 years which showed more young people infected of Tuberculosis. Majority of respondents in case and in control were married (80%). Brahmins/Chettris were found predominately in both case and control (82%). Half of the respondents of cases were from nuclear family whereas only 36 percent controls were from nuclear family. Likewise, 56 percent in cases and 64 percent in control were found to have family member more than five.

Similarly, 22% respondents from case and 50% respondents from control involved in agriculture and remaining involved in other occupations such as service, business, migrant labor and housewife (Table 1). Majority of respondents from case and control were literate i.e., 80 percent in case and 78 percent in control. Majority of the respondents in controls had the family income more than 10000 compared to cases. Majority of respondents were from terai in both cases and controls.

Characteristic	Case N	Percent (%)	Control N	Percent (%)
Age categories				
<30 yr	35	70	38	76
>30 yr	15	30	12	24
Sex				
Male	35	70	31	62
Female	15	30	19	38
Marital Status				
Married	36	72	40	80
Unmarried	14	28	10	20
Ethnicity				
Brahmin/Chettri	32	64	41	82
Others	18	36	9	18
Family Type				
Nuclear	25	50	18	36
Joint	25	50	32	64
Family Size				
<5	22	44	18	36
>5	28	56	32	64
Occupation				
Agriculture	11	22	25	50
Other	39	78	25	50
Educational Status				
Illiterate	10	20	11	22
Literate	40	80	39	78
Family Income				
>10000	28	56	41	82
<10000	22	44	9	18
Residence				
Terai	32	64	42	84
Hill/Mountain	18	36	8	16

Table 1: Socio-demographic status of the respondents.

Majority of respondent were found to have pulmonary tuberculosis in both case and control i.e., 98 percent in case and 82 percent in control.

Majority of case were found to have history of tuberculosis treatment and only 2 (4%) of control had history of tuberculosis treatment.

There were only 2 respondents in control having history of tuberculosis and none of them had history of non-compliance whereas 48 out of 50 respondents had history of tuberculosis due to which it was not possible to calculate association.

Reason for non-compliance of anti-tuberculosis drugs among the respondents

The reason for non-compliance or irregularity of anti-tuberculosis drugs was explored (Table 2). Majority of the respondents had forgotten to take the drugs i.e., 35 percent followed by feeling better (23%), home far from health center (12%) and remaining had shortage of money, no time for medication, misprescription by health worker, migration during medication or stigma.

Reason for Non-Compliance	Number	Percentage (%)
Forget to take drugs	6	35
Feeling better	4	23
Home far from Health Centre	2	12
Shortage of Money	1	6
No time for Medication	1	6
Misprescription by Health Worker	1	6
Migration at the time of Medication	1	6
Stigma	1	6

Table 2: Reason for non-compliance of anti-tuberculosis drugs among the respondents.

In bivariate analysis, ethnicity, occupation, family income, and residence showed significant association with MDR-TB. Among the ethnic group, Dalit, Janajati and Tharu were found at 3 times higher risk than Brahmin/Chettri for MDR-TB (95% CI 1.017 to 6.457). The respondents who were engaged in occupation such as service, migrant labor, and business were found 4 times more risk to MDR-TB than agriculture (95% CI 1.487 to 8.454).

In this study, respondents having family income less than 10000 were found to had about 4 times more risk of MDR-TB than respondents having family income more than 10000 (95% CI 1.437 to 8.913).The respondents who lives in hill/mountain area were found at 3 times higher risk to MDR-TB than who lives in terai (95% CI 1.141 to 7.646). Age, marital status, family type, family size and educational status were not found significantly associated with MDR-TB. The study found significant association between type of tuberculosis and MDR-TB. Having MDR-TB among people suffering from pulmonary tuberculosis was found 11 times higher than their counterparts (95% CI 1.308 to 88.473).

Similarly, history of tuberculosis treatment was found strongly associated with MDR-TB. Those who had history of tuberculosis treatment had been found 576 times higher risk for MDR-TB (95% CI 77.924 to 4257.713). The big range in confidence interval could be due to relatively smaller sample size.

Knowledge of MDR-TB was found significantly associated with MDR-TB (Table 3). This association could be due to the better knowledge and understanding after contacting MDR-TB.

Characteristics	OR	95% CI	P-value
Age categories			
<30 years	1		
>30 years	0.737	(0.303 -1.789)	0.499
Sex			
Male	1		
Female	0.699	(0.304-1.607)	0.398
Marital Status			
Married	1		
Unmarried	1.556	(0.615-3.935)	0.349
Ethnicity			
Brahmin/Chettri	1		
Others	2.562	(1.017-6.457)	0.043
Family Type			
Nuclear	1		
Joint	0.562	(0.253 -1.252)	0.157
Family Size			
<5	1		
>5	0.599	(0.265-1.354)	0.216
Occupation			
Agriculture	1		
Other	3.545	(1.487 -8.454)	0.004
Educational Status			
Illiterate	1		
Literate	1.128	(0.431- 2.956)	0.806
Family Income			
>10000	1		
<10000	3.579	(1.437-8.913)	0.006
Residence			
Terai	1		
Hill/Mountain	2.953	(1.141-7.646)	0.023
TB type			
Extra-Pulmonary	1		
Pulmonary	10.756	(1.308- 88.473)	0.027
History of tuberculosis treatment			
No	1		
Yes	576	(77.92 -4257.71)	0
MDR-TB Knowledge			

No	1		
Yes	32.667	(4.167- 256.076)	0.001
Illicit Drug User			
No			
Yes	1	(0.061 -16.44)	1
Alcohol Use			
No			
Yes	1.181	(0.530- 2.63)	0.683
Smoking			
No			
Yes	0.773	(0.34 -1.74)	0.534
Disease History			
No	1		
Yes	1.194	(0.37 - 3.84)	0.766
History of hospitalization			
No	1		
Yes	0.432	(0.148 - 1.261)	0.118
Ventilation Present			
Not adequate	1		
Present	0.699	(0.304 - 1.607)	0.398
OR = Odds Ratio, CI = Confidence Interval, Significant = P-value <0.05			

Table 3: Bivariate analysis of the factors associated with MDR-TB.

The final regression model (forward logistic regression model) showed that respondents involves in occupation other than agriculture such as service, business, migrant labor and house wife were found at three times higher risk for the MDR-TB. Respondents who lived in hill/mountain were found 3 fold risk for MDR-TB than that lived in terai region (Table 4). Similarly, respondents who had pulmonary tuberculosis were found 11 times higher risk for MDR-TB than those who had extra-pulmonary tuberculosis. Family type, history of hospitalization and family income were not found significantly associated with MDR-TB despite the significant association in bivariate analysis.

Characteristics	AOR	95% CI	P-value
Ethnicity			
Brahmin/Chettri	1		
Other (Janajati, Dalit, Tharu)	1.58	(0.54 - 4.56)	0.39
Family type			
Nuclear	1		
Joint	0.52	(0.91 - 1.43)	0.2
Occupation			
Agriculture	1		
Others	3.38	(1.12 - 10.22)	0.031
Residence			
Terai	1		
Hill/mountain	3.75	(1.19 - 11.86)	0.024
TB type			
Extra-Pulmonary	1		
Pulmonary	11.39	(1.10 - 117.3)	0.041
History of Hospitalization			
No	1		
Yes	2.99	(0.76 - 11.70)	0.11
Family income			
>10000	1		
<10000	0.44	(0.15 - 1.26)	0.12
Educational status			
Literate	1		
Illiterate	0.67	(0.18 - 2.53)	0.56
AOR = Adjusted Odds Ratio, CI = Confidence Interval, Significant= P – Value < 0.05			

Table 4: Multivariate analysis of the factors associated with MDR-TB.

Discussion

In Nepal Multi Drug Resistant Tuberculosis management program has been launched subsequently in 2005, which is considered a global model for ambulatory treatment. Levels of drug resistance are high, with nearly 14.7 percent of new patients resistant to at least one drug.

This study attempted to explore associated factors that influences occurrence of MDR-TB. Age is one of the important determinants of MDR-TB. Previous studies had also shown influence of age on MDRTB [5-16]. The study on Spain showed that people who were 45 years and above are at higher risk for MDR-TB than people below the age of 45 year [17]. But the study on Iran showed that people who were below 45 years of age are at higher risk for MDR-TB than people above the age of 45 years [11]. However, this study showed no any association between age and MDR-TB.

Majority of the respondents in both cases and controls were male i.e., 70 percent in cases and 62 percent in controls. The study carried out by pant et al. also found majority of cases were male. Having less access of women to diagnostic facilities than man, could be the reason. However, this study had not shown any association between sex and MDR-TB. The study conducted in Iran and Central Asia showed sex of the respondents associated with MDR-TB [11,14]. The study conducted in Iran showed male sex had higher chance for MDR-TB but study on Central Asia showed female sex had higher chance for MDR-TB. Similarly, study in Rio de Janeiro, Brazil, had found male had higher occurrence of MDR-TB [15].

Majority of the respondents were Brahmin/Chettri i.e., 64 percent in cases and 82 percent in controls. This might be because Brahmin/Chettri was dominant in number and Dalit, Janajati and Tharu had no access to DOTS compared with Brahmin/Chettri. In contrast, the study conducted by Marahatta et al. showed upper caste (Brahmin/Chettri) had less occurrence of MDR-TB than other caste i.e., 29.1 percent in case and 21.8 percent control [18]. In bivariate analysis association was found between ethnicity and MDR-TB (OR 2.56 95% CI 1.017 to 6.45 p 0.048) where it was not found in multivariate analysis (p>0.05). The finding was similar to the study carried out in central Nepal by Marrahatta et al. [5].

A study conducted by Merza et al. showed unemployment as risk factor for MDR-TB [11]. The study in China had also shown significant association between occupation and MDR-TB [10]. This study had also showed that occupation was significantly associated with MDR-TB (95% CI 1.12 to 10.22). Respondents involved in other occupation such as service, business, migrant labor, and housewife were found 3 times higher risk of MDR-TB than those who involved in agriculture. This might be due to people engaged in service, migrant labor, housewife and business had more contact to MDR-TB or TB than those involved in agriculture. In contrast to this study, a study in US showed occupation was not associated with MDR-TB [18].

In this study, bivariate analysis showed association between family income and MDR-TB (0R 0.44 95% CI 0.155 to 1.26) while multivariate analysis showed no any association between MDR-TB and family income similar to the study conducted in Bangladesh and Kenya [6,8].

The study revealed only 20 percent cases were illiterate whereas study conducted by Pant et al. showed 78 percent of the cases were illiterate [16]. Bivariate analysis of the study showed surprising result as literate people had 1.12 times higher risk of MDR-TB (95% CI 0.431 to 2.95) while in multivariate model of analysis association was not found between educational status and MDR-TB.

Majority of the respondent lived in terai region i.e., 64 percent cases and 84 percent controls but study conducted by Marahatta et al. in Central Nepal found majority of the respondents lived in hill/mountain region i.e., 83.7 percent in cases and 92.7 percent in controls [5]. This study showed place of residence significantly associated with MDR-TB as supported by previous studies [6,19]. Those who lived in hill/mountain were found 3.75 times at higher risk for MDR-TB than those who lived in terai. This might be due to most of the hill/mountain population had no access to DOTS facility in comparison to terai. In contrast to this study, study conducted by Suchindran et al. showed no clear association of place of residence and MDR-TB [17].

Majority of the respondents had the pulmonary tuberculosis i.e., 98 percent in cases and 82 percent in controls. In this study, type of TB was found significantly associated with MDR-TB. Those who had pulmonary tuberculosis were at 11 times higher risk of MDR-TB than those who had extra-pulmonary tuberculosis (95% CI 1.10 to 117.57 p<0.041). In support of this study, a study conducted by Casal et al. in European Union countries showed previous tuberculosis (OR 2.03) with pulmonary location significant risk factor for MDR-TB and similarly study in South Africa had also showed pulmonary tuberculosis as the risk factor for MDR-TB. Ninety six percent of cases were found to have previous history of tuberculosis treatment. A study conducted by Wahab et al. showed all the cases had previous history of TB [9]. The study conducted by Zai et al. showed 68 percent of the MDR-TB patient had previous history of TB and the study conducted by Baghaei et al. showed 95.8 percent cases had previous history of tuberculosis [10,12]. Other studies had also shown previous history of tuberculosis treatment significantly associated with MDR-TB. In bivariate analysis, history of tuberculosis treatment was found highly significantly associated (OR 576; 95% CI 77.92 to 4257 p<0.00). However, due to very less cell value, it could not be included in multivariate model analysis.

Among the cases who had the previous history of tuberculosis treatment, more than one third had not taken the anti-tuberculosis drugs regularly and cross sectional study in Peshawar, Pakistan also showed 43.3 percent had not taken the anti-tuberculosis drugs regularly [9]. A study conducted by Barroso et al. showed not taking drugs regularly as a risk factor for MDRTB [20]. However, this study did not showed any association between drug compliance among history of tuberculosis treatment and MDR-TB.

Ninety eight percent controls and 60 percent cases were found to have no knowledge of MDR-TB and a study by Marahatta et al. also showed more than 90 percent controls had no knowledge of MDR-TB [5]. It might be due to counseling of health workers to the MDR-TB patient about MDR-TB (cause, consequences, and side effects of drugs). Marahatta et al. showed knowledge about MDR-TB, significantly associated with MDR-TB (OR 9.643 95% CI 3.33 to 27.84 p<0.001) [17]. This study also showed association between MDR-TB knowledge and MDR-TB in bivariate analysis (OR 32.66 95% CI 4.16 to 256.07 p<0.001) but could not be included in multivariate analysis since less cell value.

Majority of the respondents had not taken any type of illicit drug. The respondents who had taken illicit drug were found to have taken intravenous drug. A study conducted by Casal M showed illicit drug use as the significant factor for MDR-TB [12]. This study showed illicit drug use not significantly associated with MDR-TB. Among the respondents, 38 percent cases, and 42 percent controls used to drink alcohol whereas the study conducted in Central Nepal showed alcohol use more in cases than controls i.e., 52.7 percent in cases and 38.2 percent in controls [5]. Descriptive study among MDR-TB patient in Bhairawaha, Nepal showed more than half of the cases used to take alcohol [13]. This study showed no association between MDR-TB and Alcohol use supported by Marahatta et al. [5]. However the study conducted by Barroso et al. showed alcohol with cigarette smoking as associated factor for MDR-TB [20]. In this study, 40% cases and 34% controls were found to smoke cigarette and none of the smoker were current smoker whereas in previous study smoking was found more in cases than controls i.e., 49.1 percent in cases and 29.1 percent in controls [5]. Descriptive study among MDR-TB patients in Bhairawaha, Nepal showed 74 percent of the cases were smoker [16]. This study did not found any association of smoking with MDR-TB supported by previous study [12]. In contrast with this study, smoking was found significantly associated with MDR-TB [5]. In some study, smoking in combination with alcohol was found significantly associated with MDR-TB [20].

Twelve percent cases and 14 percent of controls were found to have history of any disease. Cases were found to suffer from typhoid, kidney stone, and gastritis whereas controls were found to suffer from jaundice, diabetes, and asthma. A study conducted by Arévalo et al. in Spain found hepatic cirrhosis strongly associated with MDR-TB (OR 104, 95% CI 12.8 to 847) [21]. But this study showed no association between history of disease and MDR-TB which was supported by the study conducted in Iran [12]. Twenty-four percent from cases and 12 percent from controls had history of hospitalization. Studies carried

out by Rick et al. in Namibia showed history of hospitalization significantly associated with MDR-TB whereas this study had not shown any association between history of hospitalization and MDR-TB [7]. Sixteen percent respondents from cases were found to have family history of TB and none of the respondents from controls was found to have family history of TB. Therefore, there might be transmission of MDR-TB from infected family member to the cases that had family history of MDR-TB. In cross sectional observational study in Pakistan, none of the cases were found to have a family history of MDR-TB [9]. But due to very less cell value, it was not included in further analysis.

Majority of respondents were found not having proper ventilation in their room i.e., 31(62%) from cases and 36(72%) from controls whereas a study by Marahatta et al. showed only 14.5 percent cases and 29.1 percent controls had no adequate ventilation in room[5]. This study showed ventilation status in living and sleeping room was not associated with MDR-TB and also supported by findings of study by Marahatta et al. [5].

Conclusion

The study shows that people involved in occupation such as service, business, migrant labor, and housewife, those who were residents of Hill/Mountain, who had pulmonary TB, were found at higher risk of MDR-TB.

However, no significant association was seen between cigarette smoking, alcohol use, illicit drug use, economic status and MDR-TB. The strength and truthfulness of these associations need to be examined with multi-center case-control study so that risk factors can be unveiled. Such studies can be designed based on the finding of this study. Based on our finding; the related stakeholders could make plan and policy for the management of tuberculosis and- multi drug resistant tuberculosis.

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