Original Research Article

Contributing Factors Associated with Multi-Drugs Resistance Tuberculosis among MDR-TB Clients of Kathmandu, Nepal

Sanju Bhattarai[1], Shanti Awale[2]

[1]Lecturer, Lalitpur Nursing Campus, Sanepa, Lalitpur, Nepal.
[2]Associate Professor, Lalitpur Nursing Campus, Sanepa, Lalitpur, Nepal.

Corresponding Author: Sanju Bhattarai

ABSTRACT

Introduction: The emergence of Multi-Drug Resistant Tuberculosis (MDR-TB) has become a significant public health problem and an obstacle to effective TB control measure.
Objective: The objective of this study was to assess the contributing factors of MDR-TB.
Materials and Methods: This study entitled "Contributing Factors Associated with Multi-Drugs Resistance Tuberculosis among MDR-TB Clients of Kathmandu, Nepal" was a descriptive cross sectional study. The study population consisted of 103 MDR-TB clients of National Tuberculosis Center, Bhaktapur, and German Nepal Tuberculosis Project (GENETUP) Kathmandu. Non probability purposive sampling method was used and data was collected using semi-structured questionnaire through face to face interview. Descriptive statistics was used for data analysis with the help of SPSS version 20.
Results: Of the total 103 respondents, 79.6% of the respondents were literate, 97.1% were employed at the time of diagnosis, 69.9% lived in rural areas, and 65.05% lived in crowded room at the time of MDR-TB diagnosis. Likewise 89.3% had past TB history, among them 75% had unfavorable treatment outcome of past TB and 35.9% respondents had interrupted TB treatment in past. Nearly seventy percent respondents had close contact with TB patients in past. Regarding personal habits 35.9% had ever smoked, 62.1% are passive smoker and 46.6% ever drank alcohol. Regarding co-morbidity 10.7% had suffered from COPD and 1.9% had HIV and diabetics each.
Conclusion: Overcrowding, close contact with TB patient, passive smoking, past TB treatment, self administered modality in past TB treatment and unfavorable outcome of past TB treatment have been observed as the contributing factors for MDR-TB.

Key words: MDR-TB, Contributing factors, Nepal.

INTRODUCTION

Tuberculosis (TB) is an infectious bacterial disease caused by Mycobacterium tuberculosis, which most commonly affects the lungs. One in three people in the world is infected with Mycobacterium tuberculosis. People become ill with TB only when the bacteria become active. Bacteria become active as a result of anything that can reduce the person's immunity, such as HIV, advancing age, or some medical conditions. [1]

Resistance to anti-tuberculosis (anti-TB) drugs is an important challenge in global TB control. Mutations in Mycobacterium tuberculosis is the result of misuse of anti-TB drugs. [2]

Multi Drug Resistant Tuberculosis (MDR TB) is defined as TB caused by strains of Mycobacterium tuberculosis that are resistant to at least Isoniazid and Rifampicin; the most potent anti TB drugs. MDR-TB takes longer to treat with second-line drugs, which are more expensive and

have more side-effects (WHO, 2014c). Cure rate of MDR-TB is 50%- 70% which is lower than the drug-susceptible TB. Failure to control MDR-TB may lead to another era with TB being regarded as a fatal disease. [3]

Globally in 2012, an estimated 450000 people developed MDR-TB and there were an estimated 170000 deaths from MDR-TB. Data from drug resistance surveys and continuous surveillance among notified TB cases suggest that the highest levels of MDR-TB are found in Eastern Europe and central Asia. Almost 50% of MDR-TB cases worldwide are estimated to occur in China and India. [4]

TB is one of the most widespread infectious diseases in Nepal, and poses a serious threat to the health and development of the people of this country. About 60% of adults and 45% of the general population have been infected with the disease. Nearly 2% of people are infected every year. As TB spreads through the air, it is not surprising that the highest rates of infection have been found in the most densely populated areas, such as Kathmandu valley and other urban areas in Nepal. [5]

Multi-Drug Resistance in the world as well as in our country is in increasing trend, it may create a big issue in future if control measures are not addressed in present.

In Nepal, 2.3% of new tuberculosis patients, and 15% of previously treated tuberculosis patients are estimated to be MDR-TB by the year 2011.Although the proportion of MDR-TB is low, due to the overall high TB burden in Nepal the absolute number of MDR cases is quite large. [6]

The prospective case control study conducted in four europium Union countries: France, Germany, Italy, and Spain between 1997 and 2000 concluded that intravenous drug , living in a nursing home, pervious tuberculosis, prison, known tuberculosis contact, immunosuppression other than human deficiency virus, and health care worker were statically significant risk factors of MDR-TB. [7]

An observational study/ case-control study with a total number of 55 multi-drug resistant tuberculosis cases attending in the National Tuberculosis Centre, Bhaktpur Nepal revealed history of prior tuberculosis, smoking habit as the major factor for MDR-TB [8] similarly previous TB treatment was the strongest determinant of MDR-TB in Europe [9]

The incidence of MDR tuberculosis is progressively increasing in the world as well as in Nepal. The rapid progress in the incidence need to be halted by timely identifying the risk factor and promptly intervening the preventive and control measures. Failure to control MDR-TB may lead to another era with TB being regarded as a fatal disease.

Understanding factors associated with MDR-TB is critical in designing evidence guided intervention strategies that are best suited for the country's situation. Although these factors have been studied extensively in many parts of the world, a knowledge gap still exists in Nepal. This study intends to explore contributing factors that are associated with MDR-TB in Nepal. This information is crucial in formulating policies that will help in allocating resources, targeting surveillance activities, promoting early case finding, managing cases, and preventing MDR-TB.

MATERIALS AND METHODS

Descriptive cross-sectional research design was used to find the contributing factors of MDR-TB among the registered MDR-TB clients of two Drug Resistant Tuberculosis center of Nepal namely National TB center, Bhaktapur and GENETUP Kathmandu. National Tuberculosis Centre (NTC) is the focal point of the National Tuberculosis Programme in Nepal and German-Nepal TB Project (GENETUP) is a project working in the health sector under the premises of National Anti Tuberculosis Association (NATA).

These DR-TB centers had been selected purposively. The 103 sample was

drawn by using non-probability purposive sampling technique. Semi- structured questionnaire was used and face to face interview technique was used to collect the data.

Validity of the instrument was maintained by developing the research questionnaire on the basis of the objectives of the study, reviewing the related literature and guidance of subject expert. The Nepali translated tool was pretested in 11 MDR-TB clients of DR-TB center of Lumbini Zonal Hospital Butwal for clarity and feasibility and necessary modification was done..

Study was conducted after written permission from concerned authorities i.e. Lalitpur Nursing Campus, Institutional Review board of TU IOM, National Tuberculosis Center, Bhaktapur and NATA/GENETUP was obtained.

Study was conducted after getting ethical approval from Institutional Review Board TU, IOM. Permission was taken from National Tuberculosis Center, Bhaktapur and GENETUP, Kalimati. Written consent was taken from respondents after explaining the purpose and relevancy of the study. The confidentiality of respondent was maintained throughout the study.

Privacy was maintained during the course of interview by using the separate area. Respiratory masks were used as per need during the interview. The interviews were conducted in open areas with free circulation of airs to reduce the risk of transmission.

Verification of data was done in the field for completeness and consistency in the filled questionnaire. Data was edited coded and entered by using SPSS version 20 software. Data was analyzed by using descriptive statistics such as frequency, percentage, mean and standard deviation.

RESULTS

Table 1 shows that more than half (57.3%) of the respondents fall between age group 15-29 yrs and very few i.e. 15.5 % of the respondents fall in 45 and above yrs. Regarding sex of the respondents majority

(69.9%) were female. Regarding Religion majority of the respondents (62.1%) belongs to Hindu. It also unveils that more than half (53.4%) of the respondents were married followed by single (44.7%). Likewise majority (82%) of respondents were literate. Among literate nearly half (47.6%) had completed Higher studies followed by Primary Education (20.7%), Secondary Education (18.3%) and informal Education (13.4%).

Table 1. Respondents' Demographic Variables   n=103

Items	Frequency	Percent
Age at the Time of Diagnosis in years		
15-29	59	57.3
30-44	28	27.2
45 and above	16	15.5
Mean ± SD 30.72 ± 13.42 (yrs)		
Sex		
Female	72	69.9
Male	31	30.1
Religion		
Hindu	64	62.1
Buddhist	29	28.2
Christian	10	9.7
Marital Status		
Married	55	53.3
Single	46	44.7
Separated	1	1.0
Widowed	1	1.0
Educational Level		
Literate	82	79.6
Illiterate	21	20.4
If Literate (n=82)		
Informal Education	11	13.4
Primary Education	17	20.7
Secondary Education	15	18.3
Higher Studies	39	47.6

Table 2. Respondents' Residence Related Variables at the Time of MDR-TB Diagnosis   n=103

Items	Frequency	Percent (%)
Place of Residence at the Time of MDR-TB Diagnosis		
Rural	72	69.90
Urban	31	30.10
Type of Residence at the Time of MDR TB Diagnosis		
Own House	50	48.54
Rented House	39	37.86
Camp/Group	14	13.59
Crowded in Room		
Yes	67	65.05
No	36	34.95

Table 2 illustrates that majority of the respondents i.e. 69.9% had lived in rural area at the time of MDR-TB Diagnosis. Regarding type of residence nearly half (48.54%) of the respondent lived in their own house and very few i.e. only 13.6% respondents lived in a camp/ Group.

Likewise majority (65.05%) of the respondent's room was crowded.

Table 3. Respondents' Close Contact with TB Patient before MDR-TB diagnosis   n=103

Items	Frequency	Percent
Close Contact with TB patient		
Yes	69	66.99
No	34	33.10
Relationship with Close Contact (n=69)		
Family Members	32	46.38
Neighbor	18	26.09
Relatives	11	15.94
Co-workers	8	11.59

Table 3 shows that majority (66.99%) of the respondents had close contact with TB patient and among them majority (46.38%) were family members and very few (11.59%) were co-workers.

Table 4. Respondents' Personal Habits History   n=103

Items	Frequency	Percent
Ever Smoked by the Client		
No	66	64.1
Yes	37	35.9
Passive smoking		
Yes	64	62.1
No	39	37.9
Ever drank Alcohol		
Yes	48	46.6
No	55	53.4

Table 4 demonstrates that majority (64.1%) of the respondents were non smoker. Regarding passive smoker, majority (62.1%) of the respondents was passive smoker. Likewise more than half (53.4%) of the respondents had not ever drank alcohol.

Table 5. Respondents' Past History of TB   n=103

Items	Frequency	Percent
Ever been treated for TB in the past		
Yes (Old Case)	92	89.3
No (New Case)	11	10.7
Type of TB the client was suffered from in the past (n=92)		
Pulmonary (smear positive)	73	79.3
Extra pulmonary	10	10.9
Pulmonary (smear negative)	9	9.8

Table 5 shows that majority (89.3%) of the respondents had been treated for TB in past among them majority (79.3%) had pulmonary (smear positive) and minority (9.8%) had pulmonary (smear negative) type of tuberculosis.

Table 6. Respondents' Co-morbid Conditions   n=103

Items	Frequency	Percentage
Clients having diabetes		
No	101	98.1
Yes	2	1.9
Clients suffering from COPD		
No	92	89.3
Yes	11	10.7
HIV test Result of the client		
HIV Negative	101	98.1
HIV Positive	2	1.9

Table 6 shows that majority (98.1%) of respondents had no diabetes; minority (10.7%) of the respondent had suffered from COPD. Regarding HIV, majority (98.1%) had HIV negative result.

DISCUSSION

Regarding epidemiological charac-teristics of the MDR-TB clients, the mean and standard deviation of the age at the time of diagnosis was 30.72 ± 13.42 (yrs) which is quite similar to the research done in Nepal i.e. 29 yrs and Cameroon i.e. 33yrs. [10-11] In this study majority of the MDR-TB clients consisted of female (69.9%) which is contradictory to the finding of several studies. [12-14]

Majority (79.6%) of the MDR-TB respondents are literate which is supported by Bhatt et al., [14] among them 47.6% had higher education which is consistent with study conducted in china. [15]

Regarding place of residence, 69.9% lived in rural areas whereas 30.1% lived in urban areas. It is also found that nearly half (48.5%) respondents lived in their own house. These results were matched with research done by Ibrahim et al [16] who reported that higher incidence of MDR-TB was found in patients living in rural areas (81.5%) compared to those living in urban areas (18.5%).

Majority of the respondents (65.05%) lived in overcrowded room, most of the people staying together (75.75%) being family members. This finding is consistent with the study by Kliiman & Altraja [17] who reported that poor living conditions, homelessness, prisons and overcrowding are the risk factors for MDR-TB. Similarly a cross-sectional study done in 81 MDR-TB patients in India shows more than half of the respondents' house was overcrowded (58%). [14]

Regarding close contact with TB patient, majority 69 (69.99%) of the respondents gave history of close contact with TB patient among them nearly half (46.38%) of the close contacts (46.38%) were family members showing the fact that TB usually spread within close contacts, this is similar to study done in Bangladesh [18] that shows 38% of MDR-TB patients had a history of contact with TB patient. Likewise an unmatched case control study conducted on 2010 in Bangladesh revealed history of TB contact were four times more likely to influence multi-drug-resistant tuberculosis. [19] Similarly more than half (54%) people had contact with a known case of TB (either in their family or friends who had been diagnosed with TB) as revealed by study conducted in Bhim Hospital, Bhairahawa. [13] Likewise a cross-sectional study in 81 MDR-TB patients in India shows 48.2% MDR-TB patients had a history of contact with TB case before they suffered and among them 85 % of such contact were family members. [14]

As per study conducted by Massi et al. [20] which revealed that excess smoking have more chance of having MDR-TB, but in this study, it is found that only 35.9% of the respondents had ever smoked.

In this study, it is found that most of the respondents were exposed to passive smoking (62.1%), and, this finding is supported by study of Somdatta et al., [21] where passive smoking is revealed as one of risk factor for childhood tuberculosis. Alcohol intake is considered as a major risk factor for MDR-TB, which is supported by

the study of Massi et al., [20] which revealed that excess alcohol users have 4.01 times more chance of having MDR-TB then non alcohol users. Similarly study done by Kliiman & Altraja [17] also revealed alcohol intake as risk factor for MDR-TB. In this study it is found that nearly half (46.6%) of the respondents were alcohol users.

Most of the respondents (89.3%) in this study had history of past TB Treatment. Meta analysis of 29 papers has shown previous TB treatment as the strong determinant for MDR-TB i.e 10.23 times than new cases. [9]

According to the National Tuberculosis Program's Nepal National Survey 2011, MDR among new cases of TB is 2.2% and MDR among previously treated cases of TB is 17.2% thereby giving a ratio of approximately 8:1 for prevalence of MDR in these two groups. [5] And this pattern holds true in our study with same (8:1) ratio of previously treated case (89.3%) to new case (10.7%). This might be due to lack of patients' adherence to chemotherapy or inappropriate regimens of treatment.

In this study, among the patients who were previously treated for TB, majority (79.3%) were suffered from Pulmonary (Smear Positive) TB type. This finding resembles with the case control study conducted in Addis Ababa where among the 134 MDR-TB cases majority (91.8%) had suffered from pulmonary smear positive tuberculosis in past. [22]

In this study, only 1.94% respondents were co-infected with diabetes and HIV each and 10.7% are suffered from COPD. This study resembles with the study done by Pant et al. [13] which shows, only 2 out of 31 MDR-TB cases were infected with HIV. This finding resembles with the study conducted in Nepal [10] where HIV, diabetics and COPD are negatively associated with MDR-TB.

CONCLUSION

Overcrowding, rural as a place of residence, close contact with TB patient,

passive smoking, alcohol consumption past TB treatment history was observed as most prevalent contributing of MDR-TB.

A better understanding of contributing factors for MDR-TB would help to determine groups of patients who would be more likely to have MDR-TB there by helping in early diagnosis and decreasing the chance of further transmission.

REFERENCES

1. WHO. *Global Tuberculosis Report*. World Health Organization, Geneva; 2014 Retrieved September 16, 2014, from http://www.who.int/topics/tuberculosis/en/
2. Daniel TM. The history of tuberculosis. *Respiratory Medicine* 2006 *100*(11), 1862-1870. Available from doi:10.1016/j.rmed.2006.08.006
3. National Tuberculosis Centre. 2014. *Annual report 2069/70B.S.* National Tuberculosis Center, Thimi, Bhaktapur, 2014. Available from http://nepalntp.gov.np/theme/images/uploads/1395815121000000000Annual_TB_report_2069-70.pdf
4. World Health Organization (2012). *Tuberculosis in the South-East Asia Region*. WHO, Geneva, 2012 Available from http://reliefweb.int/sites/reliefweb.int/files/resources/Tuberculosis_WHO-TB-Report-2012.pdf
5. National Tuberculosis Center. *National tuberculosis control programme Nepal-Annual report 2010-2011*. National Tuberculosis Centre, Thimi, Bhaktapur, 2011 Available from : http://nepalntp.gov.np/theme/images/uploads/1359021203l_Report_NTP_2011.pdf
6. World Health Organization. *Global tuberculosis report 2013*. WHO, Geneva, 2013 Available from: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf
7. Casal M, Vaquero M, Rinder H, Tortoli E, Grosset J, Rusch-Gerdes S, . . . Jarlier V. A Case-Control Study for Multidrug-Resistant Tuberculosis: Risk Factors in Four European Countries. *Microbial Drug Resistance.* [Online] 2005; *11*(1): 62-67. Available from doi:10.1089/mdr.2005.11.62
8. Marahatta SB, Kaewkungwal J, Ramasoota P, & Singhasivanon P. Risk factors of Multidrug Resistant Tuberculosis in central Nepal: A pilot study. *Kathmandu University Medical Journal*. [Online] 2010; *9*(32): 392-397. Available from http://www.kumj.com.np/issue/32/392-397.pdf
9. Faustini A, Hall AJ, & Perucci CA. Risk factors for multidrug resistant tuberculosis in Europe: a systematic review. *Thorax*. [Online] 2006; *61*: 158-163. Available from doi:10.1136/thx.2005.045963
10. Health Research and Social Development Forum. Risk factors of MDR TB: a case control study in selective DOTS Plus Clinics in Nepal. Health Research and Social Development Forum. 2012 Retrieved from http://www.herd.org.np/resources/research-survey/risk-factors-mdr-tb-case-control-study-selective-dots-plus-clinics-nepal
11. Kuaban C, Noeskae J, & Rieder H. High effectiveness of a 12-month regimen for MDR-TB patients in Cameroon. *Int J tuberc Lung Dis*. [Online] 2005; *19*(5). Available from doi: 10.5588/ijtld.14.0535
12. Marahatta SB, Kaewkungwal J, Ramasoota P, & Singhasivanon P. Risk factors of Multidrug Resistant Tuberculosis in central Nepal: A pilot

study.*Kathmandu University Medical Journal*. [Online] 2010; *9*(32), 392-397. Available from http://www.kumj.com.np/issue/32/392-397.pdf

13. Pant R, Pandey K, Joshi M, Sharma S, Pandey T, & Pandey S. Risk factor assessment of Multidrug-Resistant Tuberculosis. *Journal of Nepal Health Research Council*. [Online] 2010; Available from doi:10.3126/jnhrc.v7i2.3013

14. Bhatt G, Vyas S, & Trivedi K. An epidemiological study on MDR-TB cases registered under revised national tuberculosis control program of Ahmedabad City. *Indian Journal of Tuberculosis.* [Online] 2011; *59*: 18-27. Available from http://medind.nic.in/ibr/t12/i1/ibrt12i1p18.pdf

15. Yang X, Yuan Y, Pang Y, & Wang B. The burden of MDR/XDR tuberculosis in coastal plains population of China. *PLoS One*. [Online] 2015;*10*(2): Available from doi:10.1371/journal.pone.0117361

16. Ibrahim M, Hadejia S, Nguku P, Dankoli R, Waziri P, Akhimien O, . . . Ogiri S. Factors associated with interruption of treatment among pulmonary tuberculosis patients in Plateau State, Nigeria. *Pan Afr Med J.* [Online] 2014; *17*(78). Available from doi:10.11604/pamj.2014.17.78.3464. eCollection 2014

17. Kliiman K, & Altraja A. Predictors of extensively drug-resistant pulmonary tuberculosis. *Annals of Internal Medicine*. [Online] 2009;*150* (11), 766-775: Available from http://annals.org/aim/article/744523/predictors-extensively-drug-resistant-pulmonary-tuberculosis

18. Rifat M, Milton AH, Hall J, Oldmeadow C, Islam MA, Husain A, .

Siddiquea BN. Development of Multidrug Resistant Tuberculosis in Bangladesh: A case-control study on risk factors. *PLOS ONE*. [Online] 2014 *9*(8). Available from http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0105214

19. Flora MS, Amin MN, Karim MR, Afroz S, Islam S, Alam A, & Hossain M. Risk factors of multi-drug-resistant tuberculosis in Bangladeshi population: a case control study. *Bangladesh Medical Research Council Bulletin. [Online]* 2011; *39*(1), 34-41: Retrieved from http://www.banglajol.info/index.php/BMRCB/article/view/15808/11209

20. Massi MN, Wahyuni S, Halik H, Yusuf I, Leong FJ, Dick T, Phyu S. Drug rsisitance among tuberculosis patients attending diagnostic and treatment centers in Makassar, Indonesia. *Int J Tuberc Lung Dis* [Online] 2011; 15 (4), 489-495: Available from: https://www.ncbi.nlm.nih.gov/labs/articles/21396208

21. Somdatta P, Sharma S, & Behera, D. (2012). Passive smoking, indoor air pollution and childhood tuberculosis: A case control study. *Indian Journal of Tuberculosis*, *59*(3), 151-155. Retrieved from http://www.journals.elsevier.com/indian-journal-of-tuberculosis/most-cited-articles/

22. Hirpa S., Medhin, G., Birma, B., Melese, M., Mekonen, A., Suarez, P., & Ameni, G. (2013). Determinants of multidrug-resistant tuberculosis in patients who underwent first-line treatment in Addis Ababa: a case control study. *BMC Public Health*, *13*. doi:10.1186/1471-2458-13-782

****