Association of Previous Smoking Habit and Oerceived Social Discrimination with the Risk of Multi-Drug Resistant Tuberculosis in Central Nepal

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ABSTRACT

Background: Multidrug-resistant tuberculosis (MDR TB) caused by Mycobacterium tuberculosis resistant to both Isoniazid and Rifampicin with or without resistant to other drug, is among the most alarming pandemic problem. The objectives of this study was to assess the risk factors of MDR TB in Central Nepal.

Methods: A matched case control study was conducted among 186 cases of MDR TB and 372 non-MDR TB controls from central region of Nepal. Pretested questionnaires containing socio-economic, cultural & behavioral; environmental, biological and health service factors were used. Variables significant in bivariate analysis were entered in multiple regression models for further analysis.

Results: After adjusting for confounders, previous smoking habit (aOR= 4.5,(95%CI(1.24-16.2)) (p=0.04), and perceived social discrimination (aOR=5.83,95%CI (1.77-19.71)) (P=0.021) independently predicted greater MDR TB risk.

Conclusions: Encouraging MDR TB cases for smoking cessation through awareness activities should be a priority. Stigma reduction programs should include the empowerment of patients and communities while promoting TB-related research for further exploration into the risk factors of TB and associated stigma.

Keywords: Tuberculosis; drug resistance; smoking; stigma; Nepal

INTRODUCTION

Multi drug resistant tuberculosis (MDR TB) remains one of the most serious challenges to global health. Drug resistant tuberculosis generally arises through the selection of mutated strains by inadequate chemotherapy by which diseases becomes resistant to at least two major anti-tubercular drugs: isoniazid and rifampicin.[1] Globally, 500,000 MDR TB cases have been reported.[2] The overwhelming burden of MDR TB is in resource-poor countries[3] like Nepal. The National Tuberculosis program (NTP) reported 262 MDR TB cases with 2.6 percent prevalence of MDR TB among the newly diagnosed and 17.6% in previously treated TB cases in Nepal.

Earlier study reported MDR TB cases were more likely to be associated with foreign born, younger

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than 65 years, male, and HIV positive individual.[4] In the context of impending emergence of MDR tuberculosis in Nepal, it is indispensable to have a clear picture of risk factors associated with MDR TB. This study aims to identify the risk factors of MDR TB in Central Nepal.

METHODS

The Central development region comprises of 19 districts, had over 10 million population[5] in 2011. The National TB control program had estimated 2.2 % prevalence of MDR TB in this region. There were 3 Directly Observed Treatment short course (DOTs) plus centers in this region.[6]

The diagnosed and under treatment MDR cases recorded from three DOTS plus centers after June 2008 (National Tuberculosis Center, Lalgadh hospital and National Medical College, Birgunj) formed the study frame of this study. National Tuberculosis Center is the tertiary referral center of tuberculosis, located in Kathmandu Valley. Lalgadh Hospital is a leprosy hospital situated at Lalgadh in Mahotarri district (Terai region of Nepal). National Medical College is a private medical college situated in Birjung.

This is a matched case-control study. Data were collected in from June 2010 to April 2011.The sample size was calculated assuming 15% exposed to MDR TB in the control group at 80% power and case to control ratio of 2:1, similar to a conducted in Spain.[7] Tuberculosis case with resistance to at least two major anti-tuberculosis drugs; isoniazid and rifampicin were defined as multidrug-resistant tuberculosis (MDR TB) case pertinent to the finding by drug sensitivity test and culture according to national tuberculosis Protocol.[6] The control constituted any sputum positive category-I tuberculosis patient (new smear positive pulmonary tuberculosis cases as per national tuberculosis protocol) undergoing DOTS treatment minium 5 months with negative finding on sputum microscopy at least a month apart, the last one being in the last month of treatment. Since these cases were certainly free from MDR TB, they serve as definite control group.[6]

Cases and controls were matched by sex, age,

geographical region. The frequency distribution of the matched variable was similar in both cases and controls. At least two control people were matched to a case. Age was matched in following age groups: <10 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years and >70 years. The controls were selected from the same geographic area (for example, same or adjacent VDCs or municipality) and the same type of community (urban or rural) as the case. They were selected from the same center diagnosed during the same time period as of MDR TB cases and representing the nearby geography of the cases.

The study questionnaire was adapted from earlier studies.[4, 8, 9] The questionnaire was pre-tested in the field to ensure that all questions are clear and understandable. First part of questionnaire was related to knowledge of tuberculosis and second part on the influential factors of the diseases. Social discrimination in this study refers to perceived stigma or felt stigma. It is the perception, expectation or fear of discrimination and the awareness of negative attitudes or practices in society.[10] However, two types of stigma were represented by the questions in this study. Perceived stigma was represented by questions addressing Shyness to talk of medication and Perceived social discrimination while experienced stigma were represented by questions addressing any experiences of social exclusion and the family support.

Trained enumerators administered the structured questionnaire amongst the MDR TB cases and Non-MDR TB cases. The cases were drawn from the DOTS plus center recently diagnosed or under treatment of MDR tuberculosis. The source of control constitutes hospital TB cases not diagnosed as MDR tuberculosis cases. All the eligible controls had an equal chance of being enrolled. Information about the risk factors was assembled in precisely the same manner for cases and control. The cases were confirmed as MDR TB by means of Culture and Drug Susceptibility Testing from German Nepal TB Project (WHO accredited diagnostic center). After that they were referred to nearby DOTS Plus Center for the registration and treatment. Once the patient get registered in the center,

they received the treatment from either the DOTS center or from any of the nearby 14 DOTS Plus sub-centers as per their convenience.[6] Regarding HIV status, the respondents received voluntary counseling prior doing HIV test as per the protocol of National Center for AIDS and STD Control.

Data were double entered in Epi-Info (Version 6 CDC, Atlanta, GA) and SPSS 13 version and transferred to STATA (Version 9, Stata Corporation, College Station TX) for analysis. Bivariate analyses were performed to examine the effect of each variable on the risk of MDR TB. Multivariate logistic regression models were then constructed, including variables that showed an effect ($p<0.05$) in the prediction of MDR TB in the bivariate analyses. To address possible confounders in the present study all variables analyzed in bivariate analysis which showed significant associations with outcome were included in Statistical multiple regression. Stepwise forward selection procedure with entry probability 0.05 and removal probability 0.10 was implemented. Adjusted odds ratios were calculated for identified risk factors for MDR TB after controlling the other variables.

Ethical permission for study protocol and consent form for the study was obtained from the Nepal Health Research Council, World Health Organization Ethical Review Committee (WHO-ERC), Health Research ethical board of Kathmandu University and Ethical Committee of Faculty of Tropical Medicine, Mahidol University, Thailand. The written consent was taken from all the participants; however, for those who were illiterate, oral consent was taken. For minors (10-18 years), their written consent and the written permission of their parents were taken. For oral consent, the information regarding the research was provided verbally and in comprehensible form to the participant and a literate witness was requested to sign on behalf of the participant after the participant has given oral consent. In addition to the signature of literate witness the thumb print of the participant was recorded in informed consent form.

RESULTS

During the study period, 186 MDR TB cases and 372 controls were recruited from the Central Development Region of Nepal. The ratio of the case to control was 1:2. A total of 131 (70.4%) males and 55 (29.6%) females participated in this study. Greater than one third (37.6%) of respondents were 20-29 years of age and nearly two third (68.8%) were from hill region of Nepal. *(Table 1)*

Table 1. Socio-demographic characteristics of cases and Controls.

Characteristics	Cases (n=186)	Control (n=372)
Sex		
Male	131(70.4%)	262 (70.4%)
Female	55(29.6%)	110 (29.6%)
Age in years		
10-19	11(5.9%)	22 (5.9%)
20-29	70(37.6%)	140 (37.6%)
30-39	34(18.3%)	68(18.3%)
40-49	26(14.0%)	52(14.0%)
50-59	24(12.9%)	48(12.9%)
60-69	18(9.7%)	36(9.7%)
≥70	3 (1.6%)	6 (1.6%)
Location		
Mountain	5(2.7%)	10(2.7%)
Hill	128(68.8%)	256(68.8%)
Terai	53(28.5%)	106(28.5%)

Table 2. Bivariate analysis of Clinical characteristics in relation to MDR TB.

Characteristics	Cases	Control	Odds	p-value
	(n=186)	(n=372)	Ratio (OR)	
HIV positive	3(1.6%)	0(0%)		**0.037***
Prior history of TB	179(96.4%)	0(0%)		**<0.001***
Cirrhosis/liver infection	16(8.6%)	0(0%)		**<0.001**
TB surgery	2(1.1%)	0(0%)		0.11*
Mental diseases	2(1.1%)	0(0%)		0.11*
Drug allergy	2(1.1%)	1(0.3%)	1.01	0.26
Seizure	4 (2.2%)	1 (0.3%)	8.15	**0.045**
Heart related diseases	5(2.7%)	2 (0.5%)	5.1	**0.044**
Diabetes	14(7.5%)	7 (1.9%)	4.24	**0.002**
Chronic renal failure	3(1.6%)	2 (0.5%)	3.03	0.34
Gastritis	24(12.9%)	24(6.53%)	2.15	0.015
Injecting drug users	33(17.7%)	15(4.0%)	5.13	**<0.001**
History of alcohol consumption	69(62.9%)	3 (8.1%)	6.72	**0.001**
TB in family at present	25 (13.4%)	42(11.3%)	1.22	0.49
TB in family in past	50(26.9%)	61(16.4%)	1.87	**0.005**
Body weight in kg	47.42±8.24	51.5±9.41		0.21**

*Fisher exact test, **Independent sample t-test

Table 3. Bivariate analysis of socio-demographic characteristics in relation to MDR TB.

Characteristics	MDR TB (n=186)	Control (n=372)	Odds Ratio (OR)	p-value
Family Type				
Nuclear	124(66.7%)	216(58.1%)	1	
Joint	54 (29.0%)	143(38.4%)	0.65	0.032
Expanded	8(4.3%)	13(3.5%)	1.07	0.88
Marital status				
Unmarried	42 (22.6%)	118(31.7%)	1	
Married	136(73.1%)	249(66.9%)	1.53	0.004
Divorced	8(4.3%)	1(0.3%)	4.49	0.012
Religion				
Hindu	138(74.2%)	285(76.6%)	1	
Buddhism	38 (20.4)	63 (16.9%)	1.24	0.34
Muslim	3 (1.6%)	17 (4.6%)	0.36	0.11
Christian	7(3.8%)	7(1.9%)	2.06	0.18
Occupation				
Service	18 (9.7%)	106(28.5%)	1	
Unemployed	15 (8.1%)	24 (6.4%)	3.68	0.002
Labor	52 (32.8%)	100(26.9%))	3.06	0.001
Farmer	61 (32.8)	3 4(9.14%)	10.56	0.001
Student	18 (31.0)	40 (69.0%)	1.45	0.001
Housewife	4 (2.1%)	23(6.2%)	1.02	0.97
Others (foreign employment, business drivers)	17(9.1%)	8(2.2%)	12.5	0.001
Major source of family income				
Service	31 (16.7%)	152(40.9%)	1	
Agriculture	69(37.1%)	44(11.8%)	7.68	0.001
Business	44 (23.7%)	92 (24.7%)	2.34	0.02
Foreign Employment	8(4.3%)	13(3.5%)	3.01	0.034
Others (labour, maid, drivers)	9(4.8%)	7(1.9%)	6.3	0.001
Gross monthly income of family				
>Rs 15000	33(17.8%)	67(18.0%)	1	
Rs 1000-Rs 15000	30 (16.1%)	83 (22.3%)	0.73	0.3
Rs. 5000-Rs 9999	39 (21.0%)	132(35.5%)	0.59	0.68
<Rs 5000	54(29.0%)	62(16.7%)	1.76	0.04
Not mentioned	30(16.1%)	28(7.5%)	2.17	0.02
Education				
Literate	25 (13.4%)	58(15.6%)	1	
Illiterate	77(41.4%)	46(12.4%)	3.88	0.001
Primary School	31 (16.7%)	76 (20.4%)	0.94	0.86
Secondary School	31 (16.7%)	89(23.9%)	0.8	0.5
Higher Secondary School	15(8.0%)	84(22.6%)	0.41	0.017
University level	7 (3.8%)	58(15.6%)	0.85	0.75

Table 4. Bivariate analysis of Knowledge and behavior in relation to MDR TB.

Characteristics	Cases (n=186)	Control (n=372)	Odds Ratio (OR)	p-value
Is TB communicable				
No	14(7.5%)	26(7.0%)	1	
Yes	172(92.5%)	346(93.0%)	0.92	0.47
Causes of TB				
Microbes	170(91.4%)	294(79.0%)	2.81	0.002
Close Contact	150(80.6%)	289(77.7%)	1.19	0.445
Malnutrition	125(67.2%)	90(24.2%)	6.42	<0.001
Lack of ventilation	111(59.7%)	200(53.8%)	1.27	0.21
Sexual intercourse	54(29%)	69(18.5)	1.79	0.007
Sins	41(22%)	8(2.2%)	12.86	<0.001
Hard work	124 (66.7%)	85 (22.8%)	6.75	<0.001
Poverty	104(55.9%)	58 (15.6%)	6.87	<0.001
Witch	14(7.5%)	7(1.9%)	4.24	0.002
Knowledge of symptoms				
Cough	182(97.8%)	34793.3%)	3.28	0.025
Chest Pain	174(93.5%)	314 (17.6)	2.67	0.002
Mild Fever	173(93.0%)	327(87.9%)	1.83	0.077
Blood in Sputum	162(87.1%)	329(86.0%)	1.09	0.79
Weight loss	170(91.4%)	325(87.4%)	1.53	0.2
Is TB curable				
No	5(2.7%)	10(1.8%)	1	0.31
Yes	181(97.3%)	548(98.2%)	0.49	
Heard of HIV				
No	33(17.7%)	104(38.0%)	1	
Yes	153(82.3%)	268 (72.0%)	1.79	0.009
Heard of HIV and TB co-infection**				
No	39(25.5%)	114 (42.5%)	1	
Yes	114(74.5%)	154 (57.5%)	2.6	0.001
Knowledge of MDR TB				
No	90 (48.4%)	341 (91.7%)	1	<0.001
Yes	96(51.6%)	31(8.3%)	11.73	
Knowledge on DOTS plus				
No	104(55.9%)	361(97.0%)	1	
Yes	82(44.1%)	11(3.0%)	25.87	<0.001
Present Habit of smoking				
No	179(96.2%)	368(98.7%)	1	
Yes	7 (3.8%)	4(1.3%)	3.58	0.044
Past habit of Smoking				
No	99 (53.2%)	315 (84.7%)	1	
Yes	87 (46.8%)	57 (15.3%)	4.85	<0.001
Smokes per day**				
<5	25(29.1%)	26(45.6%)	1	
5-10	15 (17.4%)	11 (19.3%)	1.41	0.47
11-15	11(12.8%)	7(12.3%)	1.63	0.37
16-20	15(17.4%)	9(15.8%)	1.73	0.27
21-25	10(11.6%)	2(3.5%)	5.2	0.045
>25	10(11.6%)	2(3.5%)	5.2	0.045

Table 5. Bivariate analysis of social stigma in relation to MDR TB.

Characteristics	Cases (n=186)	Control (n=372)	Odds Ratio (OR)	p-value
Shyness to talk of medication				
No	5(2.7%)	10(1.8%)	1	<0.001
Yes	90(48.4%)	97(26.1%)	2.65	
Perceived social discrimination				
No	71(38.2%)	261(70.2%)	1	<0.001
Yes	115(61.8%)	111(29.8%)	3.81	
Social exclusion				
No	80(43.0%)	252(67.7%)	1	<0.001
Yes	106(57.0%)	120(32.3%)	2.78	
Family Support				
No	16 (8.6%)	78(21.0%)	1	0.002
Yes	170(91.4%)	294(79.0%)	2.81	

Table 6. Bivariate analysis of Health services in relation to MDR TB.

Characteristics	Cases (n=186)	Control (n=372)	Odds Ratio (OR)	p-value
Health institution first attended				
Private	13(7.0%)	189(50.8%)	1	
Government	173(93.0%)	183(49.2%)	13.74	<0.001
Distance from treatment center to home (minutes)				
	129.8±29.2	69.4±76		0.09
Travel cost (Rs)				
	202±130	123±81		0.015
Health care provider took detail information before diagnosis				
No	11(5.9%)	23(6.2%)	1	
Yes	175(94.1%	349(93.8%)	0.95	0.53
Health care provider provided detail information about disease and treatment				
No	7(3.8%)	35(9.4%)	1	
Yes	179(96.2%)	359(93.0%)	1.08	0.53
Presently seeking alternative care				
No	76(40.9%)	337(90.6%)	1	
Yes	110(59.1%)	35(9.4%)	13.93	<0.001
Patient's opinion of health condition				
Excellent	8(4.3%)	22(5.9%)	1	
Good	51(27.4%)	139(37.4%)	1.01	0.98
Satisfactory	117 (62.9%)	205(55.1%)	1.56	0.29
Poor	10(5.4%)	6(1.6%)	4.58	0.02

* Independent sample t test

Table 7. Multivariate logistic regression analysis for risk factors of MDR TB.

Variables	Adjusted Odds ratio	95% CI	P value
Gastritis	1.5	0.96-2.35	0.083
Diabetes	1.67	1.18-2.56	0.076
History of alcohol	2.47	1.05-5.82	0.069
TB in family in past	1.29	0.88-1.87	0.19
Heard of TB and HIV	1.19	0.83-1.71	0.34
Past habit of smoking	4.5	1.24-16.2	**0.04**
Present habit of smoking	2.47	1.21-2.79	0.071
Perceived social discrimination	5.83	1.77-19.71	**0.021**
Health institution first attended	1.65	1.21-2.24	0.08

Findings from bivariate analysis are shown in Table 1-6. Among all the variables which were significant (p<0.05) in bivariate analysis, variables which were significant by regression analysis were present habit of smoking OR = 2.47 (p=0.04) and social discrimination OR = 5.83 (p=0.021). (Table 7)

DISCUSSION

Our study revealed that those who had past habit of smoking were 4.5 times more likely to have MDR TB compared to control. An earlier study from Nepal revealed that 74% of the MDR TB patients had the history of smoking.[11] Another study in Pakistan found that, MDR TB was statistically different among smokers and non-smokers.[12] However, study done in Korea amongst the military worker found no significant differences in terms of smoking history (P=0.658).[13] In North India, of the risk factors studied for MDR TB, tobacco smoking had no relation to MDR TB infection.[14] Earlier literature described association of smoking with isoniazid resistance but more evidence is needed to explain this association.[15]

Immunological mechanisms that underpin the pathophysiological link between smoking and TB are unclear. A large body of scientific evidence in non-cigarette-smoke-associated animal and human models suggests that macrophages, CD4+ and CD8+ T-cells apoptosis of infected cells autophagy anti-mycobacterial peptides interferon (IFN)-γ, interleukin (IL)-12 and tumor necrosis factor (TNF)-α are important in host immunity against *Mycobacterium tuberculosis*. Other potential mechanisms whereby smoking may attenuate host defense mechanisms include oxidative stress at the site of infection and impairment or mechanical disruption of cilial function in the tracheobronchial tree.[16] The nicotine stops the production of TNF-alpha by the macrophages in the lungs, making the patient more susceptible to the development of progressive disease.[17]

There was significant difference in the report of social discrimination experienced by MDR TB cases compared to controls. The social discrimination as a result of stigma against TB is existent since a long time. The negative perceptions from the community[18] and the self-harbored perceptions[19] towards diseases like TB and Leprosy[20] are common. The disease has been labeled as a "dirty disease", "a death penalty" or a punishment meted out to "guilty people" for ages.[21] The study done in eastern Africa revealed that stigma plays a significant role in non-adherence, both at individual level and on disease control activity especially

in developing nations.[22] Stigma causes people to reject the diagnosis, leading to the infection of more people and potential drug resistance.[23] In a study done in Kathmandu valley, TB stigma was found to increase TB diagnostic delay and treatment non-compliance.[20] The stigma has not been only problem with the perception in patients but also the community perception which has been largely attributed to fear of infection.[24,25] Health education of masses by community health programs to dispel the myths and stigma surrounding the disease and its treatment is necessary.[26] Stigma reduction programs should be conducted in affected communities. Awareness raising activities should be conducted to encourage MDR TB cases for smoking cessation.

This is the largest study till date reporting risk factors of MDR TB in Nepal. However, we have many limitations. Firstly, this study was conducted in central region of Nepal that limited generalizability of our findings to other geographic regions of Nepal. Past history of smoking and social discrimination is largely subjective and is prone to recall biases. Similarly, for controls, all patients under the primary treatment of non-MDR TB could have had the strain of MDR TB which could have been only confirmed by DST (Drug Susceptibility Test), however, this was beyond the scope of our study. Protocol guided (unconfirmed by DST) were considered as non-MDR controls.

CONCLUSIONS

In Conclusion, our study revealed that there was significant association of smoking habit and social stigma with MDR TB. Encouraging MDR TB cases for smoking cessation through awareness activities should be a priority. Stigma reduction programs should include the empowerment of patients and communities while promoting TB-related research for further exploration into the risk factors of TB and associated stigma.

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REFERENCES

1. Zager EM, McNerney R. Multidrug-resistant tuberculosis. BMC Infect Dis. 2008;8:10.

2. Caminero JA Multidrug-resistant tuberculosis: epidemiology, risk factors and case finding. Int J Tuberc Lung Dis. 2010 Apr;14(4):382-90.

3. Ormerod LP Multidrug-resistant tuberculosis (MDR TB): epidemiology, prevention and treatment. Br Med Bull. 2005;73-74:17-24.

4. Faustini A., Hall AJ and Perucci CA Risk factors for multidrug resistant tuberculosis in Europe: a systematic review. Thorax. 2006 Feb;61(2):158-63.

5. Central Bureau of Statistics Government of Nepal. National population and housing census 2011 (National Report). 2012;01 NHPC 2011.

6. National Tuberculosis Program. Annual Report of Tuberculosis Control Programme of Nepal. 2007.

7. Suarez-Garcia I., Rodriguez-Blanco A., Vidal-Perez JL, Garcia-Viejo MA, Jaras-Hernandez MJ, Lopez O, Noquerado-Asensio A. Risk factors for multidrug-resistant tuberculosis in a tuberculosis unit in Madrid, Spain. Eur J Clin Microbiol Infect Dis. 2009 Apr;28(4):325-30.

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 (KUMJ). 2010 Oct-Dec;8(32):392-7.

9. Espinal MA, Laserson K, Camacho M, Fusheng Z, Kim SJ, Tlali RE Smith I, Smith I, Suarez P, Antunes ML, George AG, Martin-Casabona N, Simelane P, Weyer K, Binkin N, Raviglione MC. Determinants of drug-resistant tuberculosis: analysis of 11 countries. The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. 2001 Oct;5(10):887-93.

10. Adhikari B, Kaehler N, Raut S, Marahatta SB, Gyanwali K, Chapman RS. Risk factrs of stigma related to leprosy

– A systematic review. Journal of Manmohan Memorial Health Sciences. 2013;1(2):3-11.

11. Pant R, Pandey KR, Joshi M, Sharma S, Pandey T, Pandey S. Risk Factor Assessment of Multidrug-Resi.stant Tuberculosis. Journal of Nepal Health Research Council. 2009;7(2):89-92.

12. Khan A, Usmani AQ, Sultana A, Hussian Z, Khan DA. Risk factor in development of MDR TB in hospitalised patients Pakistan Air Force Medical Journal. 2005;4:218-22.

13. Lee SW, Jeon K, Kim KH, Min KH. Multidrug-resistant pulmonary tuberculosis among young Korean soldiers in a communal setting. J Korean Med Sci. 2009 Aug;24(4):592-5.

14. Pande JN, Singh UB, Sinha S, Agarwal RC, Singh SPN. Evaluation of risk factors and prevalence of drug resistant tuberculosis in North India. Chest Journal. 2005;128(4).

15. Ruddy M, Balabanova Y, Graham C, Fedorin I, Malomanova N, Elisarova E, Kuznetznov S, Gusarova G, Zakharova S, Melentyev A, Krukova E, Golishevskaya V, Erokhin V, Dorozhkova I, Drobniewski F. Rates of drug resistance and risk factor analysis in civilian and prison patients with tuberculosis in Samara Region, Russia. Thorax. 2005 Feb;60(2):130-5.

16. van Zyl Smit RN, Pai M, Yew WW, Leung CC, Zumla A, Bateman ED, Dheda K. Global lung health: the colliding epidemics of tuberculosis, tobacco smoking, HIV and COPD. Eur Respir J. 2010 Jan;35(1):27-33

17. Davies PD, Yew WW, Ganguly D, Davidow AL, Reichman LB, Dheda K, Rook GA. Smoking and tuberculosis: the epidemiological association and immunopathogenesis. Trans R Soc Trop Med Hyg. 2006 Apr;100(4):291-8.

18. Adhikari B, Shrestha K, Kaehler N, Raut S, Chapman RS. Community attitudes towards leprosy affected persons in Pokhara municipality of western Nepal. J Nepal Health Res Counc. 2013 Sep;11(25):264-8.

19. Adhikari B, Kaehler N, Chapman RS, Raut S, Roche P. Factors affecting perceived stigma in leprosy affected persons in western Nepal. PLoS Negl Trop Dis. 2014 Jun;8(6):e2940. PubMed PMID: 24901307.

20. Baral SC, Aryal Y, Bhattrai R, King R, Newell JN. The importance of providing counselling and financial support to patients receiving treatment for multi-drug resistant TB: mixed method qualitative and pilot intervention studies. BMC Public Health. 2014;14:46.

21. Long NH, Johansson E, Diwan VK, Winkvist A. Fear and social isolation as consequences of tuberculosis in VietNam: a gender analysis. Health Policy. 2001 Oct;58(1):69-81.

22. Isaakidis P, Rangan S, Pradhan A, Ladomirska J, Reid T, Kielmann K. 'I cry every day': experiences of patients co-infected with HIV and multidrug-resistant tuberculosis. Trop Med Int Health. 2013 Sep;18(9):1128-33.

23. Cramm JM, Finkenflugel HJ, Møller V, Nieboer AP. TB treatment initiation and adherence in a South African community influenced more by perceptions than by knowledge of tuberculosis. BMC Public Health. 2010;10:72.

24. Baral SC, Karki DK, Newell JN. Causes of stigma and discrimination associated with tuberculosis in Nepal: a qualitative study. BMC public health. 2007;7:211. PubMed PMID: 17705841.

25. Dodor EA, Kelly S. 'We are afraid of them': attitudes and behaviours of community members towards tuberculosis in Ghana and implications for TB control efforts. Psychology, health & medicine. 2009 Mar;14(2):170-9.

26. Mathew AS, Takalkar AM. Living with tuberculosis: the myths and the stigma from the Indian perspective. Clin Infect Dis. 2007 Nov 1;45(9):1247.