Prevalence of chest symptomatics of tuberculosis among diabetes patients in Udupi taluk

Swapnil Nimkar

United Nations Development Programme, Mysuru, Karnataka, India

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ABSTRACT

Context: Diabetes is becoming prevalent dramatically in the Asian countries. In India, 15% of tuberculosis (TB) cases are attributed to diabetes mellitus (DM).

Objectives: 1. To determine the prevalence of chest symptomatics among diabetes patients in Udupi taluk. 2. To assess the factors associated with diabetes mellitus which might predispose to tuberculosis.

Methods and material: A cross-sectional study was done from March 2013 to Aug 2013. Convenience sampling was adopted. Interviews of 132 diabetes patients were conducted in Udupi taluk. Data was analyzed using descriptive and univariate analysis.

Results: The study revealed the prevalence of chest symptomatics of TB among diabetes patients as 10.6%. In the study, 78.6% of subjects had history of cough associated with sputum. Approximately, two third of the chest symptomatics (66.7%) reported that they were smoking for more than 25 years. The significant association of chest symptoms of TB was found with the factors such as; history of TB ($p = 0.017$), history of intermittent cough ($p < 0.0001$), per capita income of the respondents ($p = 0.023$) and total monthly family income of respondents ($p = 0.028$).

Conclusions: Occurrence of chest symptoms elucidated poor socioeconomic conditions among respondents. History of intermittent cough and history of TB in the past, contributed as a major factor for predisposition to TB. It is recommended to design; feasible and cost effective, integrated public health care approach for bidirectional screening model within primary health care system in India.

1. Introduction

In the context of economic development, causal pathway of health issues progressed from infectious to non-infectious diseases, leading to increased burden on public health system. Sir William Osler (1892) described TB (Tuberculosis); as most universal scourge of human race.¹ Susruta, the first Indian physician (600 A.D) addressed the link of diabetes and tuberculosis.² In recent decades, tuberculosis incidence decreases in high income countries but remains high in the countries comprising of; high prevalence of malnutrition and HIV (Human Immunodeficiency Virus) as well as crowded slums situations. Currently, more than 80% of adults with diabetes live in low-income or middle-income countries, and diabetes generally presents at a younger age in these countries.³

Around 46% of diabetics are reckoned to be undiagnosed worldwide, and 84% of those undiagnosed, live in (LMICs) low and middle-income countries, where tuberculosis prevalence is high.⁴

The shift in the paradigm between the positive effect of reducing food insecurity in the world and the negative effects of increased

obesity and diabetes prevalence, is considered as crucial element in TB epidemiology.⁵

Diabetes with TB represents intricate intersection between communicable and non-communicable diseases. The revised epidemiological targets in new global tuberculosis strategy are based on unprecedented decrease of tuberculosis incidence, from the present 2% per year to 10% per year globally, by 2025. At the same time, the tuberculosis case fatality rate is expected to be halved from 15% to 6-5%, by 2025⁶

At cellular level, T helper 1 cytokines play a crucial role in controlling mycobacterium infection. This cytokine response is observed less among diabetes patients.⁷ In this weak knee-jerk reaction, person does not get any symptom and cannot spread any infection to other people. Bacteria break out through the scar and cause reactivation of tuberculosis.⁸ The massive destruction of lung tissues precedes to present more cavities and exaggerated chest symptoms. In this scenario, Ketone bodies in the blood of diabetes patients provides favorable environment for reactivation of TB. It is also known, that diabetic autonomic neuropathy can lead to variation in basal airway tone which

E-mail address: nilmanipal@gmail.com.

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elicits vagal inhibitory response, causing reduced bronchial reactivity as well as bronchodilation; progressively, induce Lower Respiratory Tract Infection (LRTI).⁹ Apart from this, genetic studies have also shown the connection of genes with diabetes-tuberculosis co-morbidity. HK2 gene encodes for hexokinase 2 enzyme, which has a crucial role in aerobic glycolysis. The process of glycolysis provides energy to macrophages. So, abnormality of HK2 gene leads to impairment of macrophages activity. Eventually, it increases susceptibility to respiratory infections. Similarly, reduced expression of gene CD28, leads to lower the immune responses to T cell receptors on surface of CD cells and tends to decline the level of IL-2 by activating T lymphocytes.¹⁰

Diabetes can create its adverse outcomes during management of TB as; hyperglycemia results in reduced bioavailability of Rifampicin.¹¹ DM (Diabetes Mellitus) might be responsible to increase the time of sputum conversion and it may develop the drug resistance as well.¹² People with DM are more likely to fail anti-TB treatment and eventually; tend to die during treatment, compared to those without diabetes.

One third of the world population is currently infected with tuberculosis. India contributes one fifth of the global burden of tuberculosis. Prevalence of tuberculosis in India was 249 per 100000 in 2010.¹³ About 70% of DM patients live in developing countries especially in South East Asian and Western pacific countries.¹⁴ In 2011, India had 6.13 crore people living with diabetes with 983,000 deaths attributable to it (IDF 2011). Karnataka attributes approximately 11% of total diabetes patients in India.¹⁵

According to Millennium Development Goal (MDG) and Diabetes report, IDF, in India, 15% tuberculosis is attributed to diabetes.¹⁶ Mexico emerged as a global leader in implementing collaborative efforts for diabetes-TB co-morbidity.¹⁷ People with diabetes are around 2.5 times more prone to develop TB (IDF Diabetic atlas, fifth edition). In India, there is a great need of addressing chest symptomatics of tuberculosis among diabetics; to render them towards enhanced passive case detection. This would contribute to early case detection, which is the principal strategy of tuberculosis control. The current study will turn out to be contemporary evidence for public health scientists.

Objectives of the study were to determine the prevalence of chest symptomatics of tuberculosis among diabetes patients in Udupi taluk and to assess the factors associated with diabetes which might predispose to tuberculosis.

2. Material and methods

Study design: Descriptive cross-sectional study was conducted from March 2013 to August 2013.

Setting: 'Random blood sugar (RBS) above normal level' was considered as the criteria for diagnosis of diabetes mellitus among normal individuals. The study involved the individuals who were already diagnosed for diabetes mellitus in government primary health care system in Udupi taluk.

Data collection method: Convenience sampling was adopted. Data was collected from sampled diabetic patients by doing survey in various identified sites in Udupi taluk.

List of all PHCs (Primary Health Centers) and CHCs (Community Health Centers) was obtained from District health and family welfare office, Udupi. Medical officers and health workers of respective PHCs were contacted and appointments were fixed with them. List of diagnosed diabetes patients was obtained from health workers of selected health care facility. Available addresses of diabetes patients were searched with the help of health workers to conduct survey. Before conducting interviews, health workers as well as respondents were oriented about the questions and method of conducting interview. A translated Kannada version of semi-structured questionnaire was prepared to conduct face to face interviews. Pilot study was done to validate the questionnaire. Modifications were done in questionnaire after pilot study. Apart from this, questionnaire was validated by research experts in Manipal University.

Table 1

Distribution of respondents according to age, sex and religion, DM status, duration of DM, DM treatment status (N = 132).

Variables		N (%)
Age (years)	18–29	1 (0.8)
	30–39	8 (6.1)
	40–49	22 (16.7)
	50–59	34 (25.8)
	60–69	42 (31.8)
	70 & above	25 (18.9)
Sex	Male	68 (51.5)
	Female	64 (48.5)
Religion	Hindu	115(87.1)
	Muslim	15(11.4)
	Christian	2(1.5)
DM status	IDDM	10(7.6)
	NIDDM	122(92.4)
Duration of diabetes	< 1 year	18 (13.6)
	1–5 years	71 (53.8)
	> 5 years	43 (32.6)
DM treatment status	Regular	125 (94.7)
	Irregular	7 (5.3)

N = Number

DM = Diabetes Mellitus

IDDM = Insulin Dependent Diabetes Mellitus

NIDDM = Noninsulin Dependent Diabetes Mellitus

Inclusion criteria: 1. Clinically diagnosed cases of diabetes mellitus 2. Subjects of age at least 18 years or above 3. Respondents who gave written informed consent clearly.

Exclusion criteria: 1. Seriously ill patients 2. Already diagnosed tuberculosis patients having history of diabetes mellitus.

Ethical clearance: The ethical clearance for the study was obtained from Institutional Ethics Committee, Manipal University. Permission was obtained from District Health and Family Welfare Office, Udupi to get technical support for the study. The patients were given brief information regarding study before conducting interviews. Written informed consent was obtained from all respondents.

Analysis: Data analysis was done with the help of statistical software SPSS (Statistical Package for the Social Sciences) version 15.00.

Case Definition: In the study, a person having cough since at least two weeks or more than two weeks; at the time of interview, is considered as a 'chest symptomatic'.

3. Results

Table 1 shows the distribution of diabetes patients according to age, sex and religion. Most of the respondents belonged to 60–69 years age group (31.8%). The age group of 50–59 years constitutes 25.8% respondents. Majority of the participants in the study, were Hindus (87.1%). Only 1.5% respondents were found to be Christians. Table 1 shows the distribution of the respondents according to DM status, duration of diabetes and treatment status. Around 92.4% patients indicated the pattern of having NIDDM (Non-insulin Dependent Diabetes Mellitus). Out of the total respondents, more than half of the respondents (53.8%) were having history of diabetes for one to five years. The table shows the trend about treatment status which; denotes that most of the patients were taking treatment for diabetes, regularly (94.7%). As shown in the Table 2, out of 25 respondents having cough, 44% respondents had cough associated with sputum. Apart from this, 20% of those respondents had history of chest pain along with cough. In this study, prevalence of chest symptomatics among diabetes patients was found to be 10.6% in Udupi taluk. According to Table 3, more than 20% respondents who had total monthly family income; in the range of rupees 5000 to rupees 10000, were chest symptomatics. More than 17% respondents, who had per capita income in the range of rupees 500 to rupees 1500, were chest symptomatics. Out of the total subjects, 2% of

Table 2
Distribution of respondents according to history of chest symptoms (N = 25).

Chest symptoms present	Yes N (%)	No N (%)
Cough associated with sputum	11(44)	14(56)
Cough associated with chest pain	5(20)	20(80)
Cough associated with fever	1(4)	24(96)
Cough associated with hemoptysis	1(4)	24(96)

N = Number.

Table 3
Distribution of respondents according to chest symptoms with respect to total monthly income (Rs) and per capita income (Rs), History of intermittent cough, history of TB, family history of DM, family history of TB, duration of diabetes (years), current smokers, duration of smoking (years), alcohol consumption, duration of alcohol consumption respectively. (N = 132).

Variables		Chest symptoms		p value
		Yes N (%)	No N (%)	
Total monthly family income (Rs)	< 5000	4 (5.1)	75 (94.9)	0.028 ^a
	5000–10000	8 (20.5)	31 (79.5)	
	> 10000	2 (14.3)	12 (85.7)	
Per capita income (Rs)	< 500	1 (2)	49 (98)	0.023 ^a
	500–1500	11 (17.7)	51 (82.3)	
	> 1500	2 (10)	18 (90)	
History of intermittent cough	yes	13(41.9)	18 (51.1)	< 0.0001 ^a
	no	1 (1)	100 (99)	
History of TB	yes	4 (36.4)	7(63.6)	0.017 ^a
	no	10(8.3)	111 (91.7)	
Family history of DM	yes	2(4.3)	45 (95.7)	0.137
	no	12(14.1)	73(85.9)	
Family history of TB	yes	2(28.6)	5(71.4)	0.161
	no	12(9.6)	113 (90.4)	
Duration of diabetes (years)	0–2	3(6.7)	42(93.3)	0.530
	2.1–5	6(13.6)	38(86.4)	
	> 5	5(11.6)	38(88.4)	
Current smokers	yes	3(16.7)	15(83.3)	0.407
	no	11(9.6)	103(90.4)	
Duration of smoking (years) (N = 23)	0–10	0(0)	3(100)	0.616
	11–25	1(33.3)	2(66.7)	
	> 25	2(11.8)	15(88.2)	
Alcohol consumption	yes	6(20.7)	23(79.3)	0.080
	no	8(7.8)	95(92.2)	
Duration of alcohol consumption (years) (N = 35)	≤ 10	1(12.5)	7(87.5)	1.000
	11–25	2(22.2)	7(77.8)	
	> 25	3(16.7)	15(83.3)	

N = Number.

^a Statistically Significant.

the subjects; having monthly per capita income less than Rs 500, reported chest symptoms. It can be seen from the Table 3, that approximately 42% respondents having history of intermittent cough were found to be chest symptomatics. More than 36% respondents, who had previous history of TB, reported chest symptoms. It is also seen, that 4.3% of the respondents with family history of diabetes mellitus, were found as chest symptomatics of TB and 28.6% of the subjects having family history of TB were found to be chest symptomatics of TB. Both factors, family history of DM ($p = 0.137$) and family history of TB ($p = 0.161$) were not found to be much significant respectively.

Comparatively, during first five years from onset of diabetes mellitus, chest symptomatics were almost double than they were found during more than five years of period after diabetes onset. It was reported that; duration of diabetes ($p = 0.530$) was not significant with chest symptomatics, in this study. From Table 3, it is seen that 16.7% of the total smokers reported chest symptoms related to TB. Current smokers ($p = 0.407$) and duration of alcohol ($p = 0.616$) both were not found significant with chest symptomatics.

Distribution of chest symptomatics with respect to alcohol

consumption and duration of alcohol consumption is shown in the Table 3. About 20.7% of the alcoholics were found to be chest symptomatics. Respondents smoked for more than 10 years have made large contribution among chest symptomatics. Approximately 22.2% of the alcoholic respondents with drinking habit for 11–25 years, admitted having cough for two or more than two weeks. Alcohol consumption ($p = 0.080$) and duration of alcohol consumption ($p = 1.000$) didn't show any significant association with chest symptomatics.

4. Discussion

The study comprises of the age group of 18 years and above. In the study, the prevalence of chest symptomatics among diabetes patients in Udipi taluk was found to be 10.6%. The comparison will help to point out the strength and weakness inherent; in the current study. Looking back, a study done in US highlighted the importance of including the subjects more than 40 years, who have tendency to complicate with TB.¹⁸ In another study in Pakistan, 82% patients were in the middle age group (40–70 years).¹⁹ Moreover, Patel et al.²⁰ stated that 57% of the study subjects of his study, belonged to 40–60 years age group. Ibrahim KK et al.⁹ reported that more than half of the subjects in his study were belonging to 40–60 years age group (64%). Hamid Ullah et al.²¹ explained that all patients having TB were older than 40 years. In comparison with all these studies, in current study; more than half of the respondents were belonged to 50–70 years age group.

Male participation was more than half of the total respondents in the current study (51.5%). Around 64 females contributed in the current study. In contrast, female's contribution was only around 20% in the study done in Iraq.⁹

Study population consisted of 80% NIDDM, 9% IDDM (Insulin Dependent Diabetes Mellitus) and 11% diet-controlled subjects as stated by Jabbar et al.²² This quite corresponds with current study. In this study, among all respondents, 32.6% of respondents had history of diabetes since more than five years. In the converse of that, 51% study subjects had history of diabetes mellitus for more than 10 years duration till diagnosis of tuberculosis.²² According to Ibrahim KK et al.,⁹ in their study; 32% subjects were having TB from zero to five years from the onset of diabetes. Another study revealed that around 56% of the total subjects had cough.¹⁹ Hamid U et al.²¹ revealed that fever (93%) contributed to the major symptoms of TB in their study; Cough (45%) and cough associated with sputum (29%) were partly instrumental for TB. According to Jabbar et al.,²² fever (72%) and cough (66%) represented the chest symptoms. In comparison with that, in our study, 21.2% of the respondents were found to be having cough. Only one person reported that he was having fever at the time of interview (4%) and same proportion of patients (4%) reported to be having haemoptysis. P value was < 0.0001 for haemoptysis as well as for chest pain in the study by Ramdevrajani B et al.²³ which is not significant in our study. About 36.8% diabetic tuberculosis patients had no symptoms. Therefore diagnosis was made with the help of radiological examination.²⁴ Case series by Deshmukh et al. reported that 43.4% of TB patients had history of diabetes mellitus in their study.¹ Prevalence of TB among DM patients was found as 11.9%.²² Whereas, according to one of the study done in Pakistan, prevalence of TB among DM patients was estimated as 14%.¹⁹ Another study done in Imphal, India; estimated the prevalence of tuberculosis among DM patients with the help of radiological diagnosis as 27%.⁹ In a previous study, Holden and Hitz explicated that out of 106 patients, 48 patients had diabetes before appearing TB.² Among 380 diabetes patients, 121 patients (30.2%) had co-morbid infections. Among them, one fifth of those infections were due to pulmonary TB.²¹

Total monthly family income ($p = 0.028$) and per capita income ($p = 0.023$) were found statistically significant with chest symptomatics respectively. Around 75% of the total respondents were having monthly family income less than Rs 5000 in our study. Previous study done in Peshawar, reported less proportion of low socio-economic class

(54%).²¹ The study done by Ibrahim KK et al.⁹ showed that 24% of the total subjects in their study had previous history of TB at some point in their life, which can be considered in a higher extent. The factors, history of intermittent cough ($p < 0.0001$) and history of TB ($p = 0.017$) were found to be significant with chest symptoms respectively in our study. Apart from this, Webb EA et al.²⁵ reported that, contact with TB case was a significant risk factor for developing TB disease ($p < 0.002$) in their study. This factor was not found to be significant in our study. Previous study in Pakistan showed that, highest prevalence of TB (42.8%) was estimated among the patients having duration of diabetes more than 10 years.¹⁹ Contradicting with this, in a Turkish study, within first five year after diagnosis of diabetes mellitus, proportion of patients developing TB was maximum (38%).²⁴ According to Ibrahim KK et al.,⁹ in their study; 32% subjects were having TB from zero to five years from the onset of diabetes. Equating with this, in our study; it was seen that, 13.6% of the respondents who suffered from diabetes for two to five years, were considered as chest symptoms of TB.

Finally, it was concluded from the study that the poor socio-economic conditions turned out to be the major factor, responsible for occurrence of chest symptoms. Apart from that, the respondents having age more than 60 years were more likely to get chest symptoms of TB. It was seen from the study that, within first five years after diagnosis of DM, there was high propensity of getting chest symptoms of TB. It was optically discerned that; the respondents having history of TB and history of intermittent cough in the past, has a major role in predisposition to TB. It was also discovered that, tendency of smoking and alcohol for longer duration might lead to get chest symptoms among diabetics.

Study would have been more comprehensive if large number of subjects could have been included.

There is need of designing; feasible and cost effective integrated public health care approach, for bidirectional screening within primary health care system in India. It will direct diabetes patients for early diagnosis and treatment which will improve health outcomes. Systematic screening of chest symptoms in TB prevalent areas will help to reduce the burden of tuberculosis among diabetics. It will help the health system to tackle the dual epidemic wave of TB and diabetes.

Conflicts of interest

Authors declare no funding and no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cegh.2019.06.010>.

References

1. Sen T, Joshi SR, Udwadia ZF. Review article. Tuberculosis and diabetes mellitus: merging epidemics. *JAPI*. 2009 May 57:399–404.
2. Guptan A, Shah A. Tuberculosis and diabetes: an appraisal. *Ind J Tub*. 2000;47:3–8.
3. International Diabetes Federation. . IDF Diabetes Atlas 2013 [internet] 2013 [cited Jan 22, 2014]. Available from: <http://www.eatlas.idf.org>.
4. Beagley J, Guariguata L, Weil C, Motala A. Global estimates of undiagnosed diabetes in adults. *Diab Res Clin Pract*. 2014;103:150–160.
5. Lönnroth Knut, Roglic Gojka, Harries Anthony D. Improving tuberculosis prevention and care through addressing the global diabetes epidemic: from evidence to policy and practice. *Lancet Diabetes Endocrinol*. 2014;2:730–739.
6. WHO Executive Board (2014). 134th session. *Global strategy and targets for tuberculosis prevention, care and control after 2015*. EB134.R4. Geneva: World Health Organization; 2014.
7. Young F, Critchley J, Unwin N. Diabetes & tuberculosis: a dangerous liaison & no white tiger. *Indian J Med Res*. 2009 July;130:1–4.
8. Sayed Sulaiman SA, Mohd Zain FA, Abdul Majid S, et al. Tuberculosis among diabetic patient. *Webmed Cent Infect Dis*. 2011;2(12).
9. Ibrahim KK. The relation between tuberculosis and diabetes mellitus in patients. *J Kufa Univ Life Sci* 3:1–11.
10. Qu Hui Qi, Rentfro AR, Lu Y, et al. Host susceptibility to tuberculosis: insights from a longitudinal study of gene expression in diabetes. *Int J Tuberc Lung Dis*. 2012;16(3):370–372.
11. Van Crevel R, Alisjahbana B. More on tuberculosis. *Lancet*. 2008;371:647–648.
12. Revised National TB Control Programme Annual Status Report [internet]2013[cited 9/05/2019]. . Available from: <https://tbcindia.gov.in/showfile.php?lid=3163>.
13. Sullivan T, Ben Amor Y. The Co-management of tuberculosis and diabetes: challenges and opportunities in the developing world. *PLoS Med*. 2012;9:7.
14. Behera D. TB and Diabetes- the dual epidemic: is it a matter of concern? *Indian J Tuberc*. 2011;58(4):143–147.
15. Angadi J. North Karnataka Focus of Survey on Diabetes, Bangalore [internet] 2012 [updated 2012Nov; Cited 29/06/2013]. . Available from: <http://www.deccanherald.com/content/291784/north-karnataka-focus-survey-diabetes.html>.
16. Balakrishnan S, Vijayan S, Nair S, et al. High diabetes Prevalence among tuberculosis Cases in Kerala, India. *PLoS One*. 2012;7(10).
17. Project concern International. A Person-Centered Approach to Disease Prevention [internet] [cited 14/07/13]. . Available from: <http://www.pciglobal.org/mexico/>.
18. Restrepo BI, Fisher-Hoch SP, Crespo JG, et al. Type 2 diabetes and tuberculosis in a dynamic binational border population. *Epidemiol Infect*. 2007;135:483–491.
19. Amin S, Khattak MI, Shabbier G, Wazir MN. Frequency of the pulmonary tuberculosis in patients with diabetes mellitus. *Gomal J Med Sci*. 2011 July-Dec;9(2):163–165.
20. Patel JC. Complications in 8793 cases of diabetes mellitus 14 years study in Bombay Hospital, Bombay, India. *Ind J Med Sci*. 1989 July;43(7):177–183.
21. ullah Hamid, Iqbal Z, Ullah Zia, Mahboob A, Masood-ur-Rehman. Frequency of pulmonary tuberculosis in patients presenting with diabetes. *PJCM*. 2009;15(4):1–7.
22. Jabbar A, Hussain SF, Khan AA. Clinical characteristics of pulmonary tuberculosis in adult Pakistani patients with co-existing diabetes mellitus. *EMHJ*. 2006;12(5):522–527.
23. Ramdevrajani B, Ghani MH, Shah ZA, Ghorri RA. Frequency of pulmonary tuberculosis in diabetes mellitus. *Med Channel*. Sept 2007;13(3):100.
24. Yurteri G, Sarac S, Orhan D, Oflluglu H, Demiroz F. Features of pulmonary tuberculosis in patients with diabetes mellitus: a comparative study. *Turk Respir J*. 2004;5(1):5–8.
25. Webb EA, Hesseling AC, Schaff H, et al. High prevalence of mycobacterium tuberculosis infection and disease in children and adolescents with type 1 diabetes mellitus. *Int J Tuberc Lung Dis*. 2009;13(7):868–874.