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EVALUATION OF 10-YEAR RISK OF A MAJOR CARDIOVASCULAR EVENT IN TUBERCULOSIS PATIENTS WITH AND WITHOUT DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

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Abstract

Objective: The present study aimed to estimate the 10-year risk of a major cardiovascular event in tuberculosis patients with and without diabetes mellitus in a tertiary care hospital.

Methodology: A cross-sectional study was conducted in patients aged 40 to 80 years, both gender, either pulmonary or extra-pulmonary tuberculosis with not less than 3 months were included for the study. Patients with any cardiovascular comorbidities were excluded from the study. WHO/ISH risk prediction charts was used to assess the prevalence of cardiovascular risk over 10 years. The association between various study categorical variables was calculated by using Chi-Square test.

Results: A total 136 patients were included in the study. Pulmonary tuberculosis was the most common type of tuberculosis (79%). 96% of the study patients belong to low-risk category according to WHO/ISH risk. Statistically significant difference is observed with respect to age ($p<0.001$), SBP ($p<0.001$), type of treatments ($p<0.05$).

Conclusion: The findings of the study revealed that there is a low risk of cardiovascular disease in tuberculosis patients.

Key words:

Cardiovascular risk, South Indian WHO/ISH risk, tuberculosis, diabetes mellitus

Introduction

Primary care prevention of Cardiovascular Disease (CVD) is essential as it is the leading cause of death and disability and continues to be a major public health burden globally with its risk management playing an important role in primary care. On the other side, tuberculosis (TB), even today continues to be a major public health problem in much of the developing world. Tuberculosis has been linked with CVD, and its potential role to CVD was not surprising as many infections contribute to the pathogenesis of CVD [1]. Individuals with diabetes mellitus (DM) have three times the risk of developing TB and there are now more individuals with TB-DM co-morbidity than TB-HIV co-infection [2]. The DM-TB patients have more severe infections, higher mycobacterial loads, higher treatment failure rates and longer delayed clearance of mycobacterium than the TB patients. They require longer treatment and are more likely to develop multidrug resistance tuberculosis (MDR -TB) than are patients with TB alone [3].

The relationship between TB and DM is not well understood. However, literatures state that the connecting bridge between TB and CVD is found to be cytokines. Normally when organisms enter our body they are taken up by the macrophages and degraded within the lysosomal compartment but *Mycobacterium tuberculosis* diverts this by inhibiting the fusion of phagosomes with lysosomes and by inhibiting the process of autophagy. The T-helper cells which are known to have protective effect in TB patients has an opposite effect on heart since Th-1 causes increased release of IFN-gamma which plays an important role in the formation of fibrous cap around the plaque in atherosclerosis [4].

Determining the CVD risk level in patients with PTB will be beneficial in the future delivery of health care services. Very limited studies are reported in finding the CVD risk in TB patients. To the best of our knowledge, no study is conducted among the South Indian patients. Therefore, the present study is aimed to estimate 10-year risk of a major CVD event in TB patients with and without DM in a tertiary care hospital.

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Methodology

A cross-sectional study was conducted in the Department of Pulmonology department of Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, from November 2019 to March 2020. Human Institutional Ethics Committee approval was obtained prior to the starting of the study (Ethical Clearance Number: CSP/19/NOV/81/402).

Patients aged 40 to 80 years, both gender, either pulmonary or extra-pulmonary TB with not less than 3 months were included for the study. Patients with any cardiovascular comorbidities were excluded from the study. The study was conducted retrospectively. Demographic details such as age, gender, education, occupation, family monthly income, smoking status, history of DM, types of TB, duration of infection, types of treatment, blood pressure value and plasma glucose levels were taken from patient's medical record.

For assessing CVD risk we used WHO/ISH risk prediction chart. As the study was conducted in Tamil Nadu, India, we used WHO/ISH risk prediction charts for South East Asian Region without diabetes mellitus (SEAR D) to assess the prevalence of cardiovascular risk over 10 years. The risk level ranged from <10%, 10%to 19%, 20% to 29%, 30% to 39% and ≥40%.

The data were analysed by Statistical Package for Social Sciences (SPSS) software, version 16.0. Frequency distributions and percentages were computed for different study variables. The association between various study categorical variables was calculated by using Chi-Square test. All *p*-values were statistically significant when values were less than 0.05.

Results

A total 136 patients filled the selection criteria and their data were included for the analysis. Majority of the patient were male (84%) and aged between 40 to 49. About 69% of the study patients were non-smokers and 62% of them had DM. Pulmonary TB was the most common type of TB (79%). The socio-demographic and other baseline characteristics of study patients are shown in Table 1.

96% of the study patients belong to low-risk category according to WHO/ISH risk. The association between the study variables and WHO/ISH risk is shown in Table 2. Statistically significant difference is observed with respect to age ($p<0.001$), SBP ($p<0.001$), type of treatments ($p<0.05$).

Discussion

The co-existence of communicable and non-communicable diseases are increasing in low and middle income countries. This increase in incidence is mainly due to the change in day-to-day lifestyle of people. TB remains the major cause of disability adjusted life years in many regions of low and middle income countries for which the world health assembly has implemented many policies to reduce the incident cases by 90% in the year of 2030 [5].

In this study, the results indicated a low CVD risk level in terms of age, sex, presence or absence of diabetes, smoking status, and mean systolic blood pressure, the category of PTB and history of previous PTB treatment except for respondents aging 70 to 79 years old with moderate risk. This finding has been supported by the study of Emilio et al. [1] and Hinkle et al. [6] who explained that normal anatomic and functional changes lead to decreased myocardial contractility, prolonged systole, and delayed conduction, thus, stressful physical and emotional conditions especially that occurs suddenly may have adverse events on the aged person. However, it has been observed that respondents with the pre-determined risk factors obtained higher mean scores than other respondents. Sex impacts the developmental programming of blood pressure and cardiovascular risk as emphasized in the study of Intapad et al. [7], Wei-YC et al. [8]. Although the incidence of CVD in women is usually lower than in men, women have higher mortality and worse prognosis after acute cardiovascular events as emphasized in the study of ZujieGao et al. [9]. Among the 22 female patients observed there is 18.1% risk for CV event as opposed to 9.6% among men. In our study only 4 female patients were found to have high risk in contrast to 11 high risk male patients as emphasized by Bhaskaran Dhanaraj et al. [10], who conducted a survey in the metropolitan city of South-India in which higher prevalence of PTB disease among men aged ≥55 years was found to be more. Malnutrition among the patient population is found to impair immune functions in individuals leading to higher sensitivity towards infectious diseases as emphasized by RS Kashyap et al. [11]. In contrast to this our study has no correlation between the patient's socioeconomic class and risk of cardiovascular event among TB patients. Respondents who have smoked obtained higher scores than those who haven't smoked which is supported by the study of Messner et al. [12] that smoking plays an active role not only in the initiation of CVD but also contributes significantly to cause disease progression and fatal cardiovascular outcomes. It was also found that smoking has an impact on the development of active TB in LTBI patients

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and it was emphasized that the highest risk of smoking for LTBI was noted in patients aged from 65-74 years by Jia-Yih Feng et al. [13]. The age standardized prevalence of diabetes and HTN in India was found and compared with the most developed country Unites States in which we found that the age standardized prevalence of DM in India had no significant difference to that of US but HTN ratio was found to be more prevalent in India and was supported by Pascal geldsetzer et al. [14], It was also emphasized in a study by Reaven et al. [15] that hyper-insulinemia has a direct link to the development of essential HTN which may lead to CVD by increasing the TG levels and by decreasing the HDL-C level which was found to be contrary to the study done by Jeppesen et al. [16]. But in our study both the glucose tolerance as well as blood cholesterol level were not taken into account. A survey of 26,000 adults for HTN was done and the prevalence was found to be 20% but it was found that the prevalence was nearly 67% which often goes undiagnosed as they are asymptomatic which was supported by the data studied by Mohan V et al. [17], in which Chennai was found to be the city with higher prevalence rate. It was also emphasized in the study of Bundy et al. that reducing systolic blood pressure to levels below currently recommended targets significantly reduces the CVD risk and all-cause mortality [18]. The study of Chen et al, also presented that elevated glycosylated hemoglobin (HbA_{1C}) levels were associated with increased risks of CVD and death caused by early endothelial dysfunction and progressive vascular inflammation that lead to cardiovascular events [19]. Haffner et al. [20] reported death rates due to cardiovascular causes over a 7-year period in patients with and without T2DM in which risk of developing MI was more among patients with DM and in our study there is greater number of patients with DM. It was also found that anti-diabetic treatments are associated with a lower risk of CVD and has a cardio-protective effect as emphasized by Marso SP et al. [21]. Respondents undergoing treatment with category IV DOTS have higher risk of developing cardiovascular disease among the three categories of PTB wherein a study conducted by Atif et al. [22] presented that relapse of PTB (category IV) might be due to poor glycemic control due to interaction of certain PTB drug interactions and malnutrition, contributing to a higher risk of developing CVD. These studies support the implication that patients with predetermined risk factors have a higher risk of developing CVD. Glucose tolerance is found among TB patients with DM leading to elevated HbA1c level and also anti-TB drugs like rifampicin is known to interact with anti-diabetic class of drugs like sulfonylurea's decreasing its action as emphasized by Bloomgarden ZT et al. [23] and NiemiM et al. [24]. Chemotaxis of monocytes is also impaired in TB patients with DM leading to higher cardiovascular risk as emphasized by Wang CH et al. [25].

CONFLICT OF INTEREST

None

Table 1

Socio-demographics and baseline characteristics of the study patients

Variables	N	Percentage
Gender		
Male	114	83.82
Female	22	16.18
Age (In years)		
40-49	59	43.38
50-59	39	28.68
60-69	28	20.59
70-79	9	6.62
≥80	1	0.74
Smoking		
Yes	42	30.88
No	94	69.12
Diabetes		
Absent	52	38.24
Present	84	61.76
SBP(in mmHg)		
120-139	111	81.61
140-159	21	15.44

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160-179	4	2.94
Types of TB		
PTB	108	79.41
Extra-PTB	11	8.09
MDR-TB	6	4.41
Post-TB Sequelae	5	3.68
Old-PTB	2	1.47
PTB relapse	4	2.94
Duration of infection		
<12months	109	80.15
12-120months	22	16.18
120-240months	2	1.47
240-360months	2	1.47
≥360months	1	0.74
Types of treatment		
CAT-1	94	69.12
AKT-4	18	13.24
2FDC	2	1.47
3FDC	1	0.74
CAT-2	7	5.15
Modified ATT	12	8.82
CAT-4	2	1.47
Socioeconomic		
Lower	93	69.38
Upper lower	35	25.73
Lower middle	8	5.88

[SBP-systolic blood pressure, PTB- pulmonary tuberculosis, MDR- Multi drug resistance tuberculosis, CAT- category, ATT- Anti-tubercular treatment, FDC- Fixed drug combination]

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Table 2. Association between study variables and risk score

Study variables	WHO/ISH risk		Pears on Chi-square value	P value
	Low	High		
Age (In years)				
40-49	58	1		
50-59	37	2		

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60-69	21	7	38.76	<0.001
70-79	4	5		
≥80	1	0		
Gender				
Male	103	11	1.368	0.242
Female	18	4		
Smoking				
Yes	86	8	9.115	0.058
No	18	7		
Diabetes				
Absent	48	4	0.955	0.323
Present	73	11		
SBP(in mmHg)				
120-139	107	4	1.213	<0.001
140-159	14	7		
160-179	0	4		
Types of TB				
PTB	96	12	2.240	0.815
MDR-TB	6	0		
Extra-PTB	10	1		
Post-TB Sequelae	4	1		
Old PTB	2	0		
PTB relapse	3	1		
Duration of infection				
<12months	99	10	4.536	0.338
12-120months	17	5		
120-240months	2	0		
240-360months	2	0		
≥360months	1	0		
Types of treatment				
CAT-1 and daily regimen ATT in FDC	85	9	7.952	<0.05
CAT-2	4	3		
Modified ATT	11	1		
CAT-4	2	0		
Socio economic class				
Lower(V)	85	8	2.528	0.238
Upper lower(IV)	30	5		
Lower Middle(III)	6	2		

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