An Observational Study to Assess Fasting Lipid Profile Parameters among Drug Sensitive Pulmonary Tuberculosis Patient with Type2 Diabetes Mellitus

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Abstract: *Background and Objectives: Mycobacterium tuberculosis, can remain in the human body for decades by evading elimination by the host's immune system. Type 2 diabetes mellitus (DM) increases risk for development of tuberculosis by weakening the immune. Now, there is growing evidence towards tuberculosis linked with dyslipidaemia. We aim to compare the fasting lipid profile parameter in drug sensitive pulmonary tuberculosis patients with and without diabetes. Methods: An observational, cross - sectional and comparative study was conducted at the Department of Pulmonary Medicine, SRN Hospital, MLN Medical College, Prayagraj, from October 2022 and December 2023. Patients of pulmonary tuberculosis were split into two groups: diabetic and non - diabetic—and lipid profile was assessed. Results: The results were found to be statistically significant when comparing DM and non - DM thresholds, which showed that the fraction of DM patients of S. TC (p = 0.00) and S. TG (p = 0.00) was statistically greater as compared to NON - DM group. Conclusion: Our study suggest that low lipid levels are associated with high incidence of tuberculosis and severity of disease. And low level of high - density lipid in diabetic patient are associated with extensive radiological lesion and severity of disease.*

Keywords: Pulmonary tuberculosis, Diabetes mellitus, S. TC (Serum total cholesterol), S. TG (Serum triglyceride).

1. Introduction

The infection with Mycobacterium tuberculosis is the cause of tuberculosis disease, which is spread from patient suffering from active pulmonary tuberculosis who expel bacteria into the air (e. g. by coughing, sneezing, laughing and talking). About 25% of the world population is estimated to be infected with tuberculosis bacilli [1]. After infection, the chance of developing active tuberculosis disease is highest during the first two years is 5% and after that risk of infection reduces [2]. It is evident that while the frequency of tuberculosis has decreased due to current therapeutic and preventive measures against its spread, the issue is still very much alive. It is well known fact that uncontrolled diabetes mellitus is very important risk factor in development and progression of tuberculosis disease. It is also now come up that the uncontrolled lipid profile in patient of tuberculosis with diabetes and without diabetes has very important role in disease control and progression.

Hyperglycemia has been linked to compromised immune responses to M. TB, in several studies. It's interesting to observe that monocyte derived macrophages (MDMs) from patients with a "chronic" history of DM had a reduced ability to destroy intracellular M. TB [3]. Individuals with uncontrolled diabetes have a higher susceptibility to infections and tend to experience more severe illnesses due to their immuno - compromised status. They are more likely to have reactivation of previous tuberculosis (TB) sites rather than new infections, and they commonly show lower lobe involvement more frequently than those without diabetes [4].

The current evidence suggests that there is association of more infection in case of low serum cholesterol. As, serum cholesterol regulates body hormones and basic cellular metabolism in form of various enzymes and in function of phagocytosis and cell growth [5].

The cytotoxic action of lymphocytes is dependent on cholesterol in their cell membrane [6]. T cells, CD4+, CD8+, and other activated lymphocyte types attract to macrophages and produce chemicals like tumour necrosis factor and interferon that increase the macrophages' ability to destroy M. TB [7]. One of the primary weaknesses in the host defense mechanism against tuberculosis may be the macrophages' lower - cholesterol in cell membrane, which prevents them from destroying M. TB [8]. Pulmonary TB was found to have a harmful impact on the level and function of the lipid profile [9]. Low cholesterol levels in a malnourished individual can weaken the immune system, increasing the risk of latent tuberculosis progressing to active disease [10].

Pulmonary TB causes various pathological mechanisms involving lipid peroxidation and depletion of antioxidants. *Mycobacteria* make active forms of oxygen (reactive oxygen species [ROS]) and active nitrogen gene production (reactive nitrogen species [RNS]) by activating both mononuclear and polymorphic nuclear phagocytes [11]. Evidence suggests that

increased levels of free radicals for pulmonary TB patients have been found to reduce the body's response to antioxidant energy and contribute to the formation of lung function abnormalities [12].

2. Materials and Methods

It was an observational, comparative, cross - sectional study that was conducted at the Department of Pulmonary Medicine, SRN Hospital, MLN Medical College, Prayagraj. All the pulmonary tuberculosis patients attending the OPD and IPD in the Department of Pulmonary Medicine were eligible for getting enrolled in this study, between October 2022 and December 2023. The methods used in this investigation agreed with the institutional committee on human experimentation's ethical guidelines.

This is an observational study to determine lipid profile among tuberculosis patient with and without type - 2 diabetes mellitus. Patients were enrolled in this study as per inclusion and exclusion criteria. Diagnosis of tuberculosis according to sputum AFB, clinic - radiological findings.

Cases were selected in this study among patients according to the inclusion and exclusion criteria, diagnosis of tuberculosis according to sputum AFB smear examination as per NTEP criteria, pulmonary TB (diagnosed by physician on clinical and radiological ground) inclusion criteria. Exclusion criteria were comorbid patient except diabetes mellitus, Patients with liver diseases, glycogen storage disease, lipid storage disorders, female taking oral contraceptive pills, patient on lipid lowering agents, patient on long term steroid patient, patients not giving consent. All tuberculosis patients are divided into two groups: diabetes non - diabetic and compared with LIPID Profile between groups. Measurement of Haematological parameters investigation is - Hb, TLC, DLC, FBS, PPBG, HbA1C, S. TC, S. LDL, S. HDL, S. VLDL, S. TG, LFT, KFT.

Statistical analysis
It was performed using student T - test and χ2 test to data obtained. To convey quantitative data, measurements such as mean and standard deviation were applied: if p value was < 0.05, it was considered to be statistically significant. Correlation between various parameter was studied by Pearson correlation. As a result, we discovered a link between pulmonary tuberculosis and lipid profile parameter in diabetics and non - diabetics.

3. Results

The baseline characteristics including demographics and clinical and biochemical features of the study population are shown in [Table 1]. As it can be seen, when we compared subjects fasting lipid profile parameter in diabetes mellitus and without diabetes mellitus in pulmonary tuberculosis patients. Patient with type2 Diabetes mellitus had higher fasting blood glucose, glycated haemoglobin, serum cholesterol, low - density lipoprotein and triglyceride levels but lower high - density lipoprotein cholesterol levels.

In this study we included a total of 200 pulmonary tuberculosis patient of whom 60 cases were diabetics and 140 were non - diabetics. The lipid profiles of every participant were tested. In diabetic group 38 were males and 22 were females, while in non - DM 93 males and 47 were females. The majority of participants (71) were between the ages 18 - 35years in non - DM and average age in DM was around 46 - 65 years. The mean BMI of the study population was found to be 19.17 in DM and were 16.94 in non - DM [table 1]. Compared to DM, there were noticeably decreased lipid parameters in non - DM, particularly in the form of total cholesterol (TC), HDL, and LDL.

**Table 1:** Characteristics of the study on Tuberculosis patient with Type2 Diabetes Mellitus

Parameters	Variable	DM (Total No.60)	%age	NON - DM (Total No.140)	%age
Gender	Male	38	63.33	93	66.43
	Female	22	36.67	47	33.57
Age	18 - 35	1	1.67	71	50.71
	36 - 45	14	23.33	23	16.43
	46 - 55	22	36.67	14	10.00
	56 - 65	18	30.00	21	15.00
	66 above	5	8.33	11	7.86
Weight (Kg)	Mean	46.35	+8.739	41.84	+8.387
Height (cm)	Mean	158.30	+10.490	156.49	+8.509
BMI (Kg/m2)	Mean	19.17	+3.786	16.94	+2.836
Blood sugar profile	HbA1C (%)	8.74	+2.081	5.09	+0.440
	FBS	187.22	+38.169	89.86	+9.799
	PPBG	292.12	+59.706	112.48	+17.433

The comparisons of mean S. TC, S. TG, S. LDL, S. HDL, S. VLDL and LDL: HDL between the DM groups with NON - DM are displayed in Table 2 and Fig.1. The managed group's mean S. TC, S. TG, S. LDL, S. HDL, S. VLDL and LDL: HDL were 131.100+24.34, 172.883+38.98, 71.800+15.36, 37.067+10.96, 25.283+9.087 and 2.015+0.605, whereas the NON - DM group's mean values were 112.58+20.83,

108.41+19.27, 65.74+11.05, 35.11+8.55, 22.66+26.35 and 1.90+0.41. We observed reduced HDL level in both the groups DM and non - DM. And we observed elevated level of cholesterol, triglycerides and LDL level in DM group when compared to non - DM group. In comparison to the Pairwise t - Test was used to explore the association between 'Lipid profile' with DM and NON - DM (Diagnosis).

Table 2: Lipid profile comparisons of mean S. TC, S. TG, S. LDL, S. HDL, S. VLDL and LDL: HDL in between DM and NON - DM

Parameters	DM (Total No.60)	NON - DM (Total No.140)	Welch - t test	P. values
S. TC	131.100+24.34	112.58+20.83	5.14	<0.001*
S. TG	172.883+38.98	108.41+19.27	12.19	<0.002*
S. LDL	71.800+15.36	65.74+11.05	2.76	<0.01*
S. HDL	37.067+10.96	35.11+8.55	1.23	0.22
S. VLDL	25.283+9.087	22.66+26.35	1.04	<0.30*
LDL: HDL	2.015+0.605	1.90+0.41	1.37	0.17
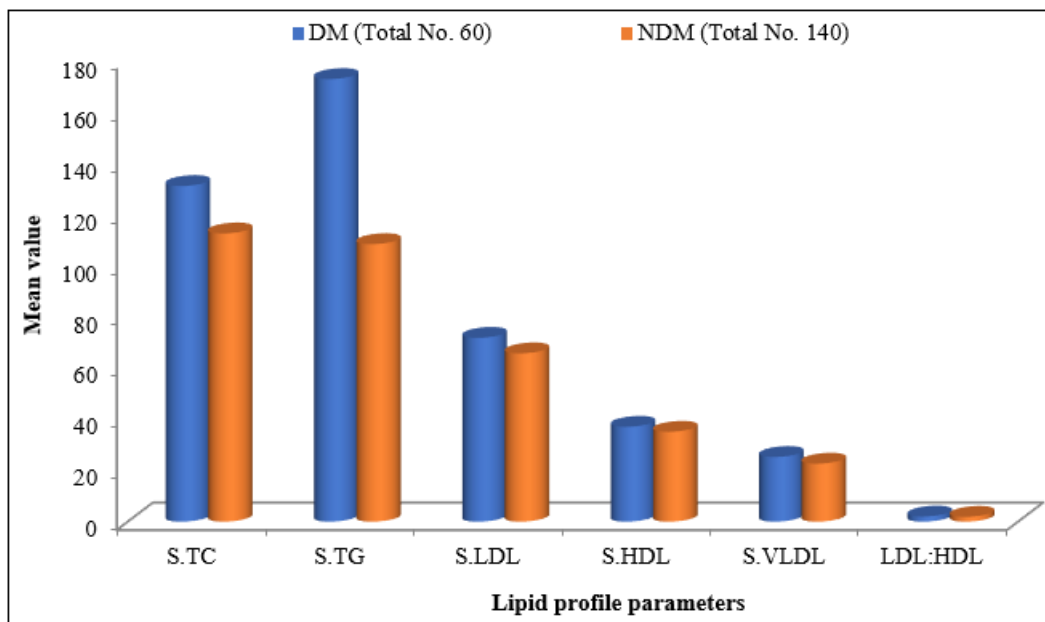
Figure 1: Bar chart shows the mean S. TC, S. TG, S. LDL, S. HDL, S. VLDL and LDL: HDL in between group DM and non - DM

4. Discussion

In our study, independent T - test showed that the mean and standard deviation of S. TC, S. TG, S. LDL, S. HDL, S. VLDL and LDL: HDL were statistically significantly higher in DM patients than in NON - DM (P <0.05). This was in concurrent findings reported in various studies [13, 14]. The results were found to be statistically significant when comparing DM and NON - DM groups, which showed that the fraction of DM patients of STC (p < 0.05) and STG (p = 0.00) was statistically significantly higher compared to NON - DM group in male (Table 2). In case of female STC (p = 0.00), STG (p = 0.00), S. LDL (p = 0.00), S. VLDL (p = 0.01) and LDL: HDL (p = 0.01) was statistically significantly higher compared to NON - DM group. The study shows low level of HDL in DM patient mostly in uncontrolled HbA1C. An association of low HDL was unique the TB - DM subgroup. HDL cholesterol modulates innate and adaptive immunity through interactions with lipid rafts on myeloid and lymphoid cells [15]. The low HDL cholesterol associated with type 2 DM and pre - diabetes might be a glucose - independent factor contributing to TB susceptibility.

Our study revealed an association between TB patients and dyslipidaemia in diabetes mellitus (DM) and non - diabetes mellitus (NON - DM). According to the study, oxidative stress and the severity of disease were greater in patients with low lipid levels. A large portion of the lipid composition of cell membranes is of cholesterol. The membrane's fluidity needs to be preserved. Cholesterol is also necessary for

macrophage phagocytic processes as endocytosis, exocytosis, and cell motility. Low level of cholesterol causes interruption in its phagocytic activity [16].

Pérez - Guzmán et al. suggested that hypocholesterolaemia was established as a risk feature in the case of PTB progression [17], as patients with low lipid levels may experience more severe inflammation compared to those with normal lipid levels. A previous study that reported that serum TC was lower in the TB group than in the TB - T2DM group [18]. An adequate level of cholesterol is necessary for the proper functioning of the immune system.

Another study revealed that pulmonary tuberculosis patients of non - DM group have lower - level lipid parameters than DM - TB group [19], which was also shown in this study. And the study suggests that lipid profile of each individual may be different because of chronicity of T2DM and period of TB - DM comorbidity.

The limitations of this study were the sample size and single - centre data. The study also had a few other limitations as we did not consider the effect of other medical conditions, lifestyle factors, medications or treatments, dietary habits, or physical activity on lipid profiles, thus limiting the ability to draw meaningful conclusions about the differences between the two groups.

5. Conclusion

We observed dyslipidaemia in both group of DM and NON - DM patients of pulmonary tuberculosis. Hypocholesteraemia was seen in NON - DM group which results in increase severity of disease. Pulmonary tuberculosis patients with DM have normal range of S. Cholesterol, TGs, LDL levels but have low HDL level, as HDL modulates innate and adaptive immunity which increases severity of disease with poor outcome. So, lipid levels should be corrected while treating TB for a better response to treatment. More studies at larger scale and multicentre to be done to implement lipid profile test as a routine diagnostic investigation mainly in tuberculosis with diabetes patient and their treatment outcome.

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