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Original Article

Internal Medicine Section

Lipid Abnormalities in Tuberculosis Patients with Diabetes Mellitus: A Hospital-based Cross-sectional Study

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ABSTRACT

Introduction: Tuberculosis (TB) is a chronic infectious disease that also causes lipid abnormalities. Limited studies are focusing on metabolic abnormalities in TB patients with Diabetes Mellitus (DM). While studying lipid abnormalities in pulmonary TB patients, there were no marked differences between serum levels of cholesterol, triglycerides, Low Density Lipoprotein (LDL) and High Density Lipoprotein (HDL). However, it was suggested that increased levels of lipoprotein (a) in patients with pulmonary TB may be a risk for atherosclerosis.

Aim: To study the lipid abnormalities in TB patients with DM.

Materials and Methods: This cross-sectional study was conducted in Department of Pulmonary Medicine at a tertiary care teaching Institute {PES Institute of Medical Sciences and Research (PESIMSR} Andhra Pradesh, India, between October 2015 to March 2016 (six months). Four groups were made, Group I included 30 patients with TB and no DM, Group II included 25 patients with TB with DM, Group III had 30 patients with DM only and Group IV was control group with 30 healthy individuals. Lipid profile testing was done for all the participants and the values obtained were compared. Analysis of Variance (ANOVA) test was used to compare the means between the groups and Kruskal-Wallis test when data did not follow the normal distribution. The p-value <0.05 was considered statistically significant.

Results: Total 25 patients in group II had 18 males and seven females with mean age of 48.5±11.12 years. The total cholesterol, triglycerides, Very Low Density Lipoprotein (VLDL) was high in group III (176.33±43.35 mg/dL, 221.733±39.2 mg/dL, 34.8±17.81 mg/dL respectively). The HDL was lowest in group II (27.88±8.03 mg/dL). However, the LDL values showed no significant difference between the groups (p-value=0.162). group I had Low Body Mass Index (BMI) (18.61±3.6 kg/m^2). The atherogenic index was high in group II especially in males.

Conclusion: In patients with TB and DM, screening of lipid profile can provide markers of atherogenicity which may help to predict and prevent cardiovascular events. A good nutritious diet is recommended alongside chemotherapeutics in the treatment for TB patient's management and their lipid profile status should be monitored while managing the patients.

Keywords: Atherogenesis, Cardiovascular risk, Metabolic abnormalities, Nutrition, Oxidative stress

INTRODUCTION

Pulmonary Tuberculosis (PTB) is a chronic infectious disease caused by *Mycobacterium tuberculosis*. Apart from infecting the lungs and extrapulmonary sites in the body, it also affects the nutritional status of the patients. This is often overlooked by the clinician while focusing more on the treatment aspects of the disease. *Mycobacterium tuberculosis* lacks the squalene monooxygenase and oxidizable cyclase that are essential for sterol biosynthesis. Its genome encodes the gene for CYP51B1, a cytochrome P450 enzyme that catalyzes the conversion of lanosterol to 8,14-diene, a key step in cholesterol biosynthesis [1-3]. Therefore, *Mycobacterium tuberculosis* depends on its host lipids for its survival and primarily uses fatty acids as the source of energy rather than carbohydrates, thereby causing hypocholesterolaemia in PTB patients [1,4]. Many other studies have proved hypocholesterolaemia [5-8] and weight loss [6] in PTB patients specifying that serum lipids especially cholesterol affect the overall strength of the immune system and thereby predisposing them to TB infection.

Mycobacterium tuberculosis causes lipid peroxidation by activating the monocytes that generate the free radicals and Reactive Oxygen Species (ROS), thereby lowering levels of antioxidants and lipid profiles in newly diagnosed PTB [7]. Cholesterol is an important nutritional factor because individuals with low cholesterol levels had decreased total T-cells, helper T-cells, and CD8+ cells leading them immunosuppressant and prone to PTB. Moreover, PTB patients on antituberculous drugs were found to have low lipid levels, Therefore, newly diagnosed PTB patients treated with a cholesterol-rich diet, resulted in the sterilisation of sputum culture and suggested that cholesterol be used as a complementary measure in anti-TB treatment [8].

While studying lipid abnormalities in PTB patients, there were no marked differences between serum levels of cholesterol, triglycerides, LDL and HDL. However, it was suggested that increased levels of lipoprotein (a) in patients with PTB may be a risk for atherosclerosis [9,10]. In contrary to the above findings, any inflammatory condition following infection causes the release of free radicals and ROS. This enhances lipid peroxidation causing an increase in bad cholesterol (LDL). Ultimately affecting host lipids in an adverse manner [11].

The pathophysiology of dyslipidemia in type 2 DM results from metabolic disturbances in glucose and lipid metabolism which is mediated through insulin resistance. Very few studies have focussed on serum lipid levels in PTB with DM. In the present study, authors would like to describe the pattern of lipid profile among newly diagnosed TB patients with DM and without DM. By doing so, present study could find out lipid abnormalities early that helps to recommend adjuvant nutrient therapy or oral hypolipidemic drugs. Moreover, measuring lipid profile and other nutritional parameters in these patients regularly helps to prevent oxidative stress and predict the prognosis.

The objectives of the present study was to compare the lipid profile and related factors among newly diagnosed TB patients with DM and those without DM.

MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Pulmonary Medicine at a tertiary care teaching Institute {PES Institute

of Medical Sciences and Research (PESIMSR}, Andhra Pradesh, India, between October 2015 to March 2016 (six months). The study was conducted after prior approval from the Institutional Ethical Committee {(PESIMSR/IREC/35/2015) Dated: 17.04.2015}. Informed consent were taken from the participants before enrolling in the study.

Inclusion criteria: All patients with TB confirmed by sputum examination attending the Department of Pulmonary Medicine, of either gender and having age above 18 years were included in the study.

Exclusion criteria: Patients with retroviral disease, renal diseases, cardiac diseases, neoplasm, patients on oral hypolipidemic drugs, pregnant women, lactating women, and other endocrine disorders were excluded from the study.

Sample size calculation: The sample size was calculated by using the standard sample size calculator software OpenEpi supported by Centre of Disease Control and Prevention, Atlanta (www.openepi.com). A total of 115 patients were selected and were further divided into four groups:

Group I (n=30): Newly diagnosed TB patients, confirmed by sputum examination without DM.

Group II (n=25): Newly diagnosed TB patients with pre-existing DM (Duration of DM varied among subjects from 3 months to 10 years and they were on medications). Fasting blood sugar ≥126 mg/dL and Post Prandial Blood Sugar (PPBS) ≥200 mg/dL or Glycated haemoglobin (HbA1c) ≥6.5%.

Group III (n=30): Only DM patients (Newly diagnosed and pre-existing).

Group IV (n=30): This was control group and included healthy subjects without the disease who came for a routine health check-up.

Participant's height, weight, waist circumference, and hip circumference were measured. Body Mass Index (BMI) was calculated by using the formula weight (kg) divided by the square of height (m^2). Random Blood Sugar (RBS) was taken from patient records.

Procedure

A 5 mL of blood sample was collected in these patients in 12 hour fasting state and after centrifugation the following tests were done in Vitros 250 autoanalyser.

- **Triglyceride (tgl):** L-α-glycerol-phosphate oxidase and peroxidase method was used for estimation of triglyceride.
- **Total Cholesterol (TC):** Cholesterol oxidase peroxidase method was used for estimation of TC.
- **High-Density Lipoprotein (HDL):** Enzymatic method was used for estimation of HDL.
- **Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL):** Calculated method using Freidman's calculation was used for estimation of LDL and VLDL.

VLDL=TGL/5

LDL=TC (HDL+VLDL).

This formula cannot be used if TGL levels are ≥450 mg/dL.

STATISTICAL ANALYSIS

Data were entered into Microsoft office 2019. Statistical Package for the Social Sciences (SPSS) statistics software version 15.0 was used for statistical analysis. Descriptive statistics was represented using percentages and proportions. ANOVA was used for parametric tests and non parametric tests (Kruskal-Wallis test) when data did not follow the normal distribution curve. In all analyses, the p-value <0.05 was considered statistically significant.

RESULTS

Out of 55 confirmed cases of TB, 25 patients with DM had a mean age of 48.5±11.12 years and 30 patients without DM had a mean age of 37.13±12.4 years. In comparison with these two groups, 30 patients with diabetes mellitus and 30 healthy individuals had a mean age of 46.93±10.39 years and 56.93±10.80 years, respectively. All groups had equal gender distribution except group II, which had more number of males. The BMI, waist circumference, and hip circumference were lowest in group I. The highest BMI, waist circumference and hip circumference were seen in group III and were overweight. Patients in group II were having normal BMI but less than in comparison with group III (p-value <0.05).

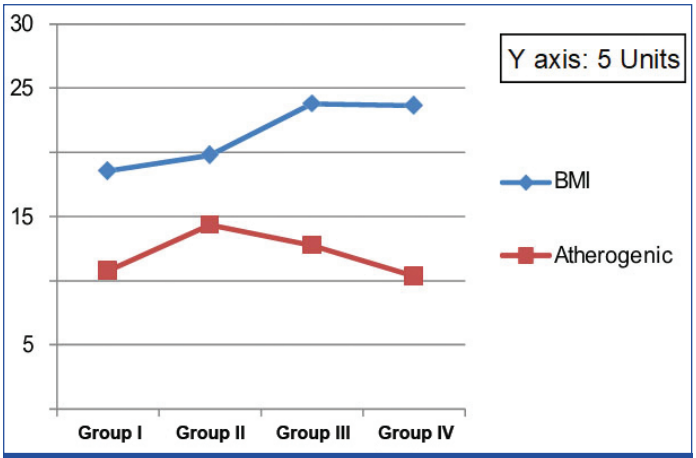
The total cholesterol, triglycerides, VLDL was high in Group III as compared to patients in group II with TB (p-value <0.05). The HDL was lowest in group II as compared to the other groups (p-value <0.05). The LDL values showed no significant difference between the groups p-value=0.162 [Table/Fig-1].

Atherogenic Index of Plasma (AIP) was calculated by log10 (TGL/HDL) and a non parametric test (Kruskal-Wallis test) used for comparison of BMI with AIP as the data did not follow the normal distribution curve p-value <0.05. The values of AIP were measured in decimals to get the graph we had multiplied its values with factor 20; group I: 0.53±0.26; group II: 0.71±0.24; group III: 0.62±0.30; group IV: 0.59±0.10 [Table/Fig-2].

There were no significant differences among lipid profiles in various age groups in TB patients [Table/Fig-3] the genders in group I and group II patients [Table/Fig-4,5]. [Table/Fig-4] shows that there was overall cardiovascular risk in male, both in group I and group II, but the risk was less in both males and females in group I than in group II. Although the AIP index fell under high risk among all groups, but was found to be highest in group II patients.

Characteristics	Group I (n=30)	Group II (n=25)	Group III (n=30)	Group IV (n=30)	p-value (ANOVA)
Male	18 (60%)	18 (72%)	12 (40%)	18 (60%)	-
Female	12 (40%)	7 (28%)	18 (60%)	12 (40%)	-
Age (years)	37.13±12.4	48.5±11.12	46.93±10.39	56.93±10.80	<0.001
Body mass index (kg/m^2)	18.61±3.6	19.8±3.7	23.83±3.46	23.71±3.2	<0.001
Waist circumference (cm)	77.55±10.8	81.44±11.88	89.5±5.16	80.32±3.2	<0.001
Hip circumference (cm)	82.00±10.33	86.11±11.49	92.34±5.6	83.51±22.1	<0.001
Random blood sugar (mg/dL)	100.8±21.28	205.2±92.54	239.63±78.79	153.4±33.13	<0.001
TC (mg/dL)	134.56±31.11	140.88±46.71	176.33±43.35	153.6±27.15	<0.001
Triglycerides (mg/dL)	109.93±42.09	149.2±59.2	221.733±39.2	135.9±26.5	0.009
HDL (mg/dL)	32.63±12.8	27.88±8.03	34.13±4.57	44.53±20.64	<0.001
LDL (mg/dL)	79.16±23.29	80.76±42.46	95.63±41.07	92.28±22.90	0.162
VLDL (mg/dL)	23.66±9.04	30.16±11.69	34.8±17.81	27.18±5.30	0.004

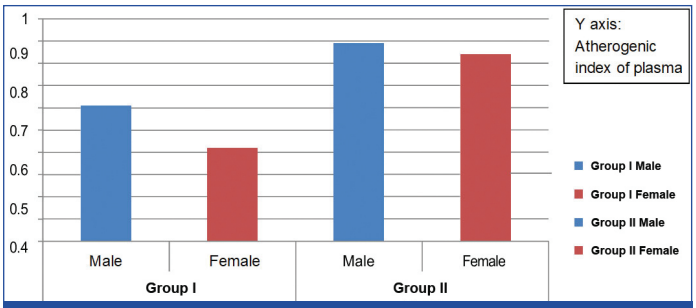
[Table/Fig-1]: General characteristics and biochemical parameters between groups.
TB: Tuberculosis; DM: Diabetes mellitus; BMI: Body mass index; TC: Total cholestrol; HDL: High density Lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; (p-value <0.05 was considered statistically significant)



[Table/Fig-2]: Comparison of BMI and Atherogenic index in the groups.

Parameters	18-30 years	31-40 years	>40 years	p-value (ANOVA)
RBS (mg/dL)	103.18±27.6	93.10±14.32	106.44±18.47	0.36
TC (mg/dL)	140.64±26.47	145.10±40.93	115.44±12.1	0.07
Triglycerides (mg/dL)	113±32.6	113±60.55	102.67±29.81	0.83
HDL (mg/dL)	37.09±14.59	34.90±12.54	24.67±7.31	0.07
LDL (mg/dL)	81±25.9	88±25.4	67.11±11.3	0.14
VLDL (mg/dL)	24.55±7.9	11.90±3.7	7.51±2.50	0.89

[Table/Fig-3]: Comparison of RBS and lipid profile as per age groups in tuberculosis (TB) patients.
*TB: Tuberculosis; DM: Diabetes mellitus, BMI: Body mass index; TC: Total cholestrol; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low-density lipoprotein; RBS: Random blood sugar



[Table/Fig-4]: Comparison of the Atherogenic Index of Plasma (AIP) with gender in TB and TB+DM groups.

Biochemical parameters	Male (Group I)	Female (Group I)	p-value	Male (Group II)	Female (Group II)	p-value
RBS (mg/dL)	102.16± 19.16	98.75± 24.87	0.67	203.44± 94.94	209.86± 93.18	0.88
TC (mg/dL)	132.16± 30.80	138.117± 32.59	0.61	150.83± 49.53	115.29± 26.75	0.08
Tgl (mg/dL)	111.83± 45.61	107.68± 37.95	0.76	158.67± 63.2	124.6± 43.53	0.20
HDL (mg/dL)	30.38± 11.80	36.00± 14.20	0.25	28.56± 9.11	26.14± 4.22	0.51
LDL (mg/dL)	77.6± 21.3	81.5± 26.7	0.66	88.72± 44.11	64.57± 11.27	0.19
VLDL (mg/dL)	23.94± 9.31	23.25± 9.02	0.84	32.33± 12.52	26.86± 6.86	0.28

[Table/Fig-5]: Comparison of RBS and lipid profile with gender in TB and TB+DM.
*TB: Tuberculosis; DM: Diabetes mellitus; BMI: Body mass index; TC: Total cholestrol; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low-density lipoprotein; Student's t-test

DISCUSSION

The present study findings were similar to the study of Oyedeji SO et al., pertaining to the TB patients without DM [12]. The study showed that patients with TB were predisposed to oxidative stress and presented with low lipid profile levels. Similar findings were seen in Taparia P et al., and Musharaf MS et al., [5,13]. Both studies concluded that parameters of lipid profile were deranged in PTB cases.

About patients with TB and DM, similar findings were seen in Vrieling F et al., which showed that TB patients presented with wasting disease [14], represented by decreased amino acid levels including histidine and alanine in contrary to lipid profile levels. However, diabetic patients are evidenced by high levels of VLDL, triglycerides and LDL cholesterol. The TB-DM patients displayed metabolic characteristics of both wasting and dyslipidemia and concluded that TB-DM patients possessed a distinctive plasma lipid profile with pro-atherogenic properties.

The AIP is considered as a superior predictive power in identifying dyslipidemia atherosclerosis and Cardiovascular Diseases (CVD) studies than by investigating conventional lipid levels [15,16]. The risk of CVD according to AIP values can be classified as: Low risk: <0.11 is associated with low risk of CVD; Intermediate Risk: 0.11 to 0.21 the values between and upper than High Risk: >0.21. [17,18].

The BMI increased in patients with DM and patients with TB and DM. TB patients had low BMI. AIP was high in patients with TB and DM. Atherogenic findings were seen in Vrieling F et al., which concluded that TB+DM patients possessed pro-atherogenic properties [14].

Limitation(s)

Larger sample size is required for establishing significant results in PTB patients concerning lipid profiles in various age groups and gender. Apart from measuring lipid profile other pro-atherogenic markers can provide a better picture of risk for CVD in tuberculosis patients with DM patients.

CONCLUSION(S)

Lipid levels were low in PTB patients thereby recommending a good nutritious diet alongside chemotherapeutic management. Lipid profile status should be monitored while managing these patients. Authors found high lipid levels in TB and DM patients which suggests that the screening of lipid profiles in them can help to assess and prevent cardiovascular events. These findings support further research on the benefits of improved blood lipid control in the treatment of TB and DM. Authors suggest further biomarkers of oxidative stress and atherogenicity to support the cardiovascular risk diseases in patients with TB and DM.

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