ORIGINAL RESEARCH

Lipid Profile Pattern among Tuberculosis Patients During Anti-Tubercular Treatment Period in A Tertiary Care Hospital at Mandya: Longitudinal Observational Study

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ABSTRACT
Background: Tuberculosis is one of the oldest diseases afflicting humans with significant mortality. Several studies have shown strong association between tuberculosis and hypocholesterolaemia, hypocholesterolaemia can be both consequence of tuberculosis or a risk factor for tuberculosis.
Methods: A longitudinal observational study was conducted inDepartment of Pulmonology of MIMS, Mandya for a period of one year from April 2021 to April 2022 recruiting 107 patients. Data was collected using Pre-tested semi-structured questionnaire including sociodemographic details, diagnostic details, treatment category, lab investigation details.
Results: This study involved 107 newly detected tuberculosis patients. Total cholesterol at the diagnosis being 136.62, at the end of IP being 163.27, which increased to 182.57 at the completion of treatment. The mean triglyceride value at the diagnosis, at the end of IP and at the completion was 115.17, 134.37 and 152.21 respectively. The mean LDL levels showed increasing trend from the point of diagnosis to completion of treatment, the values being 89.71 at the diagnosis, 101.81 at the end of IP and 113.1 at the completion of treatment. It was also found that mean HDL, LDL , VLDL and Triglyceride levels were found to show increasing trend during the course of treatment and pairwise analysis of the lipid profile in different phases of treatment was found to be statistically significant.
Conclusion: Completion of successful tuberculosis treatment is associated with increase in blood lipid levels, the current study adds to the existing literature.
Keywords: Hypocholesterolaemia, Tuberculosis, Anti Tubercular Treatment.

INTRODUCTION
Tuberculosis is one of the oldest diseases afflicting the human race since ancient times.[1]Among communicable diseases, tuberculosis holds second place as a leading cause of death worldwide, killing nearly two million people each year and the risk factors for the disease in less developed and developing country include overcrowding, malnutrition, smoking, depressed immunity etc.[2]According to the WHO report, there were an estimated 8.7 million new cases of tuberculosis.[3]

Many studies have shown relation between blood cholesterol levels and many human diseases including tuberculosis. Specifically, it is reported that hypocholesterolaemiapromotes development of TB where as hypercholesterolemia confers some protection against infection with Mycobacterium tuberculosis. Several studies have shown strong association between tuberculosis and hypocholesterolemia, hypocholesterolemia can be both consequence of tuberculosis or a risk factor for tuberculosis.[2,4]According to an Egyptian study it has been found that hypocholesterolaemia in Tuberculosis is a consequence of the disease rather than being a risk factor andwith regular intake of ATT, there has been increased levels of cholesterol.[1]Despite the existence of such links between cholesterol and TB, it is not known to which extent the treatment of the disease affects lipid indicators in patients with TB.[5]According to a study conducted in Patna, India by Dr.Sushilendu V., et al., the lipid parameters - Total Cholesterol, HDL, LDL, VLDL, TGwere found to be low at the time of diagnosis. It has also been observed that there is significant increase in level of lipid parameters – Total Cholesterol, HDL, LDL and VLDL after completion of Antitubercular treatment.[6]It has also been found that higher baseline cholesterol levels are associated with lower levels of inflammatory markers and low mortality.[7]According to an Egyptian study by MetwallyM et al - Total Cholesterol, HDL, LDL and TG were found to be low at the time of diagnosis and there is significant increase in level of lipid parameters – Total Cholesterol and HDL after completion of Antitubercular treatment.

Thus this study has been undertaken to determine the levels of lipid parameters in tuberculosis patients from initiation till completion of their antitubercular treatment.

MATERIALS AND METHODS
STUDY DESIGN
Longitudinal observational study

STUDY AREA
Department of Pulmonology of Mandya Institute Of Medical Sciences, Mandya.

STUDY POPULATION
Newly detected Tuberculosis patientsvisiting Pulmonology department of MIMS Mandya.

INCLUSION CRITERIA
Newly detected cases of tuberculosis who agreed to be a part of the study.

EXCLUSION CRITERIA
Patients with co-morbid conditions like HIV infection, Diabetes Mellitus, known cases of dyslipidemia.

STUDY DURATION
The study was conducted for a period of one year from April 2021 to April 2022.

SAMPLE SIZE

107 Newly detected Tuberculosis cases calculated based on 80% proportion of hypocholesterolaemia as reported in an African study conducted byAkpovi et al[4], with an absolute error of 10% using sample size formula for estimation of single proportion.

STUDY TOOL

Pre-tested semi-structured questionnaire including sociodemographic details, diagnostic details, treatment category, lab investigation details.

DATA COLLECTION

A written informed consent was obtained from the study participants.

Patients were informed about the methodology of the study and reports of lab investigations were noted down.Total cholesterol (TC), high density lipoprotein (HDL) and triglycerides will be assayed by enzymatic methods. Low density lipoprotein (LDL) will be determined by using the Friedwald formula.

DATA ANALYSIS

Data was entered in Microsoft excel and analysed using Epi-info software. Univariate analysis using mean, standard deviation, proportion, median and confidence interval will be done to describe the study variables. Difference in the distribution of variables in different groups were assessed using tests of significance like student t test. Correlation and regression analysis was done for studying various lipid profile variables at two stages of the study.

RESULTS

We recruited 107 patients out of which 80 were males and 27 were females, majority of the patients belonged to 31 to 60 years of age, 28 of them were less than 30 years and 11 patients were above 60 years as shown in Table1. There was no attrition noticed during study period.

Age Category	Gender		Total
	Male	**Female**	
<30yrs	14	14	28
31 to 60 years	59	9	68
>60 years	7	4	11
Total	80	27	107

Table 1 : Age and Gender distribution of sample (N =107)

AGE AND BMI DISTRIBUTION

Maximum age of the sample was 80 and minimum age of the sample 15. The mean age of sample size was found to be 42.63 ± 15.27. The lowest BMI found was 11.93 and highest BMI was found to be 24.18. The mean BMI was 18.87 ± 2.57

Figure1: Distribution of different diagnosis of TB
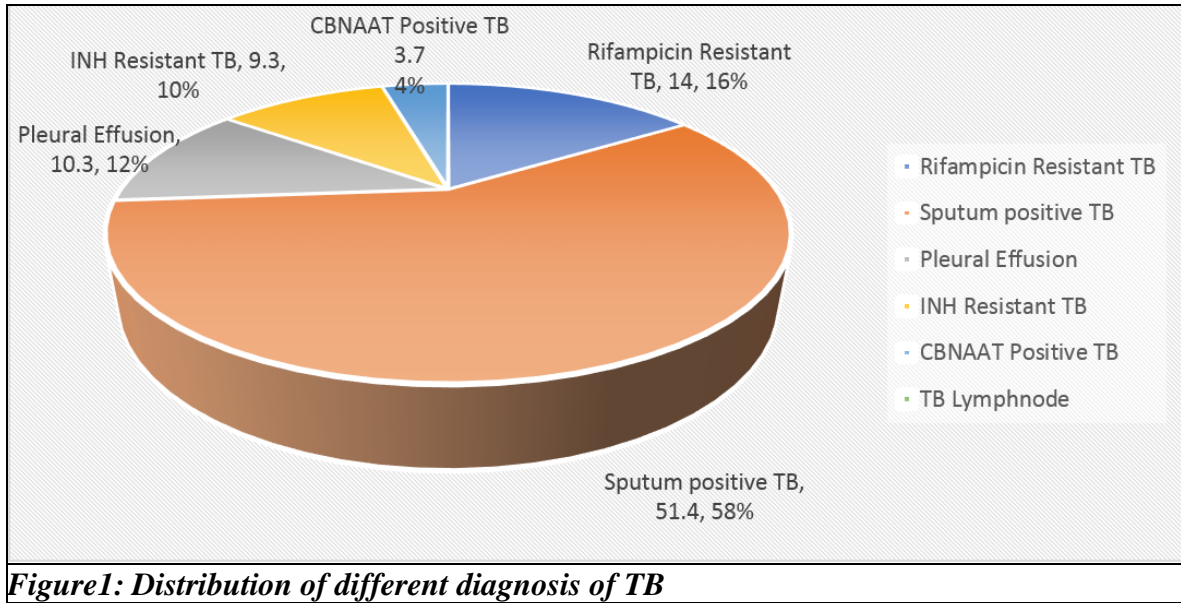
As seen in Figure 1, among different diagnosis of TB, Sputum positive TB accounts for 51.4% of the cases, Rifampicin resistant TB constitutes 14%, Pleural effusion accounts for 10.3%, INH resistant TB were 9.3%, TB Lymphnode cases were 4.7%, Radiologically diagnosed TB were 1.9% and CBNAAT positive TB were 3.7%. There were one case each of MDR TB, CNS TB, Ocular TB, TB tenosynovitis and laryngeal amyloidosis with TB. Among the mode of diagnosis, sputum microscopy was the most commonly used mode of diagnosis – 46.7%, CBNAAT – 32.7%, Chest X ray was used in 10.3%, CT / MRI was used in 5.6%, Histopathology was used in 3.7%, TST was used for 1 patient constituting 0.9% of mode of diagnosis.24% of sample were drug resistant TB and 76% of the sample were drug sensitive TB.

Table 2: Distribution of lipid profile in different phases of treatment						
LIPID PROFILE	**Mean**	**Std. Deviation**	**Wilk's lambda**	**p value**	**Effect size**	**Pairwise difference**
TC at diagnosis	136.62	46.27	0.45	<0.001	0.54	all <0.001
TC at the end of IP	163.27	44.07				
TC at treatment completion	182.57	50.45				
TG at diagnosis	115.17	55.22	0.68	<0.001	0.31	all 0.001
TG at the end of IP	134.37	68.64				
TG at treatment completion	152.21	74.80				
LDL at diagnosis	89.71	33.80	0.61	<0.001	0.38	all <0.001
LDL at the end of IP	101.81	35.29				
LDL at treatment completion	113.10	40.13				
VLDL at diagnosis	22.97	10.96	0.68	<0.001	0.31	all <0.001
VLDL at the end of IP	27.66	14.95				
VLDL at treatmentcompletion	32.70	16.96				
HDL at diagnosis	28.10	10.77	0.451	<0.001	0.549	all <0.001
HDL at the end of IP	36.15	11.43				
HDL at treatment completion	42.42	13.24				

As shown in table 2, the mean total cholesterol value showed increasing trend during the course of treatment Total cholesterol at the diagnosis being 136.62, at the end of IP being

163.27, which increased to 182.57 at the completion of treatment. Pairwise analysis showed statisticallysignificant differencein mean total cholesterol values at diagnosis, end of IP and at completion phase with p value of <0.001 . The mean triglyceride value at the diagnosis, at the end of IP and at the completion was 115.17, 134.37 and 152.21 respectively. There was statistical significant difference observed between pairwise analysis of triglyceride values in different treatment phases with p value of <0.001. The mean LDL levels showed increasing trend from the point of diagnosis to completion of treatment, the values being 89.71 at the diagnosis, 101.81 at the end of IP and 113.1 at the completion of treatment, there was statistical significant difference observed in pairwise analysis using of mean LDL values in different phases of treatment with p value of <0.001. It was observed that there was constant rise in mean values of both VLDL and HDL during the course of treatment and pairwise analysis of mean VLDL and HDL in different phases of treatment showed statistical significance with p value of <0.001.

DISCUSSION

Among the 107 patients studied, 80 were males and 27 were females, majority of the patients belonged to 31 to 60 years of age, 28 of them were less than 30 years and 11 patients were above 60 years. The age of the patients was similar to previous studies – In a Ukrainian study of pro-atherogenic lipid profile in pulmonary tuberculosis patients with concurrent insulin resistance, the age group range of patients was from 20 – 55 years,[8] In an African study by Akpovi et al., the age group of patients ranged from 12 to 62 years.[5]

The mean age of sample size was found to be 42.63 ± 15.27, which was similar to the mean age of case in an African study by Akpovi et al.[5] The mean BMI was 18.87 ± 2.57. Among different diagnosis of TB, Sputum positive TB accounts for 51.4% of the cases, Rifampicin resistant TB constitutes 14%, Pleural effusion accounts for 10.3%, INH resistant TB were 9.3%, TB Lymphnode cases were 4.7%, Radiologically diagnosed TB were 1.9% and CBNAAT positive TAB were 3.7%. There were one case each of MDR TB, CNS TB, Ocular TB, TB tenosynovitis and laryngeal amyloidosis with TB. 24% of sample were drug resistant TB and 76% of the sample were drug sensitive TB. According to Metwally M, et al., study Pulmonary TB constituted 53%, TB Lymphnode and Pleural effusion patients were around 17% each followed by TB peritonitis patients – 13%, which is almost similar to our study population.[1]

In our study, at the time of diagnosis, the mean total Cholesterol was 136.62, the mean triglyceride was 115.17, the mean LDL was 87.71, the mean VLDL was 22.97 and mean HDL was 28.10. The baseline lipid profile in the current study was found to be within normal range unlike several previous studies which have shown low baseline cholesterol levels – According to an Egyptian study by Metwally M et al., the mean lipid levels at the diagnosis were - Total Cholesterol - 120±26 , HDL - 42.6 ± 15.1, LDL - 77.16±24.9, Triglycerides - 80.1 ± 23.5 ; According to an Indian study by Sushilendu V et al., lipid levels at the time of diagnosis were as follows : Total cholesterol -130 ± 25 mg/dl and HDL - 34 ± 7 mg/dl, LDL - 70 ± 14 mg/dl and TG -134 ± 39 mg/dl. According to a study conducted by Chidambaram et al., in Taiwan the Serum Total Cholesterol and Triglyceride levels, HDL, LDL were found to be reduced at the time of diagnosis; which indirectly indicates hypocholesterolaemia to be a major predisposing factor in the development of tuberculosis or a sequelae of tuberculosis.[1,6,7] According to anEgyptian study by Metwally M et al., it is hypothesized that the low lipid levels in tuberculosis patients is found to be due to sequelae of the disease rather than being a risk factor, as it was observed that all the lipid parameters got corrected with stabilisation of the disease, if hypocholesteraemia would have been a risk factor, it would have persisted both before the onset of disease and post treatment completion.[1]The possible

explanation for normal lipid levels in the present study could be due to early diagnosis of Tuberculosis before manifestation of the disease sequelae due to increased NTEP awareness. In the current study, the follow up lipids levels in end of IP and treatment completion were : mean Total Cholesterol - 163.27 and 182.57, mean Triglycerides - 134.37 and 152.21, mean LDL levels - 101.81 and 113.1, mean VLDL - 27.66 and 32.1, mean HDL levels – 36.15 and 42.42 respectively.In our study we have found increasing trend in all lipid parameters with statistically significant increase in the lipid parameter values in end of IP and treatment completion. In previous studies,it was also found that mean Total Cholesterol and HDL were found to show increasing trend during the course of treatment and pairwise analysis of the lipid profile in different phases of treatment was found to be statistically significant.[1,5–7,9] The pairwise analysis mean LDL levels at the diagnosis and after treatment completion was not found to be statistically significant in previous studies, [1,5,7,9] but in the present study there has been statistically significant increase mean LDL levels in pairwise analysis at different phases of treatment. The mean Triglyceride levels also has shown statistically significant increasing trend unlike the older studies.[1,6,7]. In our study we have also found significant increase in VLDL levels during the course of ATT like in previous study, [9] however no such statistical significance was observed in Ukrainian study by Shvets O et al.[8]

CONCLUSION
Completion of tuberculosis treatment is associated with increase in all blood lipid parameter levels, which is a crucial finding and also adds to the existing literature. Hence assessment of lipid levels at different phases of treatment is prudent.

LIMITATIONS
1. Details of pharmacological management was not considered in the study.
2. The effect of nutrition on lipid profile has not been studied.

STRENGTHS
1. No attrition noted during the period of study.

FUTURE RECOMMENDATIONS
Research on mechanism of change in the lipid profile at cellular level will be of great value to substantiate the current results available.

BIBLIOGRAPHY
1. Metwally M, Metwally MM, Raheem HA. Lipid Profile in Tuberculous Patients: A Preliminary Report Neurophysiology of COPD View project Lipid Profile in Tuberculous Patients: A Preliminary Report [Internet]. 2012. Available from: http://www.lifesciencesite.comhttp//www.lifesciencesite.com.103
2. Iyamu O.A, Ugheoke J.E, Ozor M.O, Airhomwanbor K.O, Eidangbe A.P et al. The Effect of Nutritional Supplementation on Serum Lipid Levels and Effectiveness of Antitubercular Chemotherapy. American Journal of Biochemical research. 2014; 2(2):36-4-Google Search [Internet]. [cited 2022 Oct 19];Available from: https://www.google.com/search?client=safari&rls=en&q=2.+Iyamu+O.A,++Ugheoke+J. E,+Ozor+M.O,+Airhomwanbor+K.O,+Eidangbe+A.P+et+al.+The+Effect+of+Nutritional +Supplementation+on+Serum+Lipid+Levels+and+Effectiveness+of+Antitubercular+Che motherapy.+American+Journal+of+Biochemical+research.+2014;+2(2):36-4&ie=UTF-8&oe=UTF-8

3. World health organization. Global Tuberculosis report 2021. [Internet]. 2021. Available from: https://www.who.int/teams/global-tuberculosis-programme/tb-reports

4. Pérez-Guzmán C, Vargas MH, Quiñonez F, Bazavilvazo N, Aguilar A. A cholesterol-rich diet accelerates bacteriologic sterilization in pulmonary tuberculosis. Chest [Internet] 2005;127(2):643–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15706008

5. AKPOVI DC, GBAGUIDI LHS, ANAGO E nie, AFFOLABI D, DOUGNON T gnon V, FAIHUN F, et al. Tuberculosis treatment raises total cholesterol level and restores high density lipoprotein cholesterol (HDL-C) in patients with pulmonary tuberculosis. African J Biotechnol 2013;12(41):6019–24.

6. Sushilendu DV. Study of Lipid profile in pulmonary TB cases: pre and post anti-tuberculosis treatment. J Med Sci Clin Res [Internet] 2019;7(2). Available from: http://jmscr.igmpublication.org/v7-i2/40 jmscr.pdf

7. Chidambaram V, Zhou L, Ruelas Castillo J, Kumar A, Ayeh SK, Gupte A, et al. Higher Serum Cholesterol Levels Are Associated With Reduced Systemic Inflammation and Mortality During Tuberculosis Treatment Independent of Body Mass Index. Front Cardiovasc Med 2021;8.

8. Shets O, Shevchenko O, Piskur Z, Stepanenko H, Pohorielova O. Pro-atherogenic lipid profile in pulmonary tuberculosis patients with concurrent insulin resistance. Inter Collegas 2021;8(2):111–4.

9. Jyothi ., Chandana G, Kumar BP. Lipid Abnormalities in Tuberculosis Patients with Diabetes Mellitus: A Hospital-based Cross-sectional Study. J Clin DIAGNOSTIC Res 2022;