Journal of Cardiovascular Disease Research

ISSN:09758309762833. VOL14, ISSUE 08, 2023

Study of Atherogenic Index in Tuberculosis Patients, before and after Anti-Tubercular Chemotherapy in a Tertiary Care Hospital in Mandya: Longitudinal Observational Study

Dr. Mohankumar C.K.[1], Dr. Anjali G.[2], Dr. Vaishak K M.[3], Dr. Bindiya J.[4]

[1]Associate Professor, Department of Pulmonology, Mandya Institute of Medical Sciences, Mandya, Karnataka, India.
[2]Senior Resident, Department of Pulmonology, Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India.
[3]Senior Resident, Department of General Medicine, Mandya Institute of Medical Sciences, Mandya, Karnataka, India.
[4]Lady Medical Officer, Department of Community Medicine, Mandya Institute of Medical Sciences, Mandya, Karnataka, India

Corresponding Author:Dr. Bindiya J

Article History: **Received:** 13.05.2023 **Revised:**07.07.2023 **Accepted:** 01.08.2023

ABSTRACT

Background: Tuberculosis is the leading cause of death, due to single infectious agent in the world. Tuberculosis patients have increased risk of both cardiovascular and cerebrovascular disorders. The role of lipids in pathogenesis of tuberculosis and atherosclerosis is crucial. Atherogenic index is a strong predictor of atherosclerosis and coronary heart disease. Though studies in the past have shown the atherogenic index changes in tuberculosis patients , studies showing its relation with anti tubercular treatment is very sparse and this necessitated the need for our current study.
Method: A longitudinal observational study was conducted in Department of Pulmonology, 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. **Atherogenic index** was calculated by using the following formula AIP = log(TG/HDL).
Results: This study involved 107 newly detected tuberculosis patients. The mean Atherogenic index of Plasma (AIP) was found to be 0.6 at diagnosis, 0.55 at end of IP treatment and 0.54 at completion phase of treatment. There was statistically significant difference between AIP at the time of diagnosis and completion phase in pairwise analysis.
Conclusion: Atherogenic index of plasma is robust biomarker of dyslipidaemia and atherosclerosis. Tuberculosis patients showed higher AIP and completion of Antitubercular treatment showed decrease in AIP. This study paves the way for further scope of research in the field of molecular changes in host lipid with tubercular chemotherapy.

Keywords : Atherosclerosis, Dyslipidaemia, Atherogenic index.

INTRODUCTION

Being an age old disease, Tuberculosis is also the leading cause of death, due to single infectious agent in the world.[1] Tuberculosis patients have increased risk of both cardiovascular and cerebrovascular disorders. The role of lipids in pathogenesis of tuberculosis and atherosclerosis is crucial. Few preclinical studies also suggest the manipulation of host lipids in several ways[2] A logarithmically transformed ratio of triglyceride (TG) / high-density lipoprotein cholesterol (HDL-C) is called Atherogenic index. Being a strong predictor of atherosclerosis and coronary heart disease, it also reflects the true relationship between protective and atherogenic lipoprotein.[3] Being a chronic infectious disease tuberculosis causes lipid abnormalities. It is found that tuberculosis has no effect on total cholesterol and triglycerides, but has effect on LDL, HDL and VLDL. In tuberculosis patients, there has been increase in Lipoprotein A, which is also suggested to be a risk factor for atherosclerosis. In a study done in Andhra Pradesh, it was found that, patients with tuberculosis and Diabetes had high atherogenic index compared patients groups which had either of them alone.[4] Though studies in the past have shown the atherogenic index changes in tuberculosis patients, studies showing its relation with anti tubercular treatment is very sparse and this necessitated the need for our current study.

MATERIALS AND METHODS: The present Longitudinal observational study was conducted for a period of 1 year, April 2021 to April 2022 on Newly detected Tuberculosis cases registered in Mandya District.

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Inclusion Criteria: Newly detected cases of tuberculosis who agree to be part of the study.

Exclusion Criteria: Patients with co-morbid conditions like HIV infection, diabetes mellitus, known cases of hypercholesterolemia were excluded from the study.
Study Tool: Pre-tested semi-structured questionnaire. Tools used for Standardised diagnostic procedures used in RNTCP.

Data Collection: A written informed consent was obtained from the study participants. 5ml of 12 hours fasting venous Blood samples was systematically collected from the participants by trained technicians, at diagnosis before initiating the treatment and after completion of Intensive phase and after completion of full treatment
Total cholesterol (TC), high density lipoprotein (HDL) and triglycerides was assayed by enzymatic methods. Low density lipoprotein (LDL) was determined by using the Friedwald formula.
Atherogenic Index was calculated by using the following formula
AIP = log(TG/HDL).[5]
Sample Size: 107 (64) Newly detected Tuberculosis cases was calculated based on 80% proportion of hypocholesterolaemia as reported in Akpovi et al study[4], with an absolute error of 10%.
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 continuous study variables. Difference in the distribution of variables in different groups will be assessed using tests of significance like student t test. Correlation and regression analysis will be used for studying various lipid profile variables at two stages of the study.

RESULTS: The mean age of sample size was found to be 42.63 ± 15.27. Maximum and minimum age of the sample was 80 and 15 respectively. Majority of the patients belonged to age group of 31 to 60 years, 28 of them were found to be less than 30 years of age and 11 patients were above 60 years of age. Total of 107 patients were recruited for the study, out of which 80 were males and 27 were females, as shown in Table 1. The lowest BMI found was 11.93 and highest BMI was found to be 24.18. The mean BMI was 18.87 ± 2.57. 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 : Participants Age and Gender distribution (N =107)

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 treatment completion	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				

Table 2: Distribution of lipid profile in different phases of treatment

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As shown in table 2, there has been an increasing trend in mean total cholesterol value during the course of treatment - Total cholesterol at the diagnosis, at the end of IP and at the completion of treatment being 136.62, 163.27 and 182.57 respectively. There was statistically significant difference in pairwise analysis of 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 was 115.17, at the end of IP was 134.37 and at the completion was 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 which increased to 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.

Atherogenic Index of Plasma (AIP)	Mean	Std. Deviation	Wilk's Lambda	p Value	Effect Size	Pairwise Difference
AIP at diagnosis	0.60	0.23	0.941	0.041	0.059	significant between diagnosis and completion
AIP at end IP	0.55	0.25				
AIP at completion	0.54	0.25				

Table 3: Comparison of Atherogenic Index of Plasma in different phases of treatment

As shown in Table 3, the mean Atherogenic index of Plasma was found to be 0.6 at diagnosis, 0.55 at end of IP treatment and 0.54 at completion phase of treatment. There was statistically significant difference between AIP at diagnosis and completion phase in pairwise analysis.

DISCUSSION

The mean age of sample size was found to be 42.63 ± 15.27. Maximum and minimum age of the sample was 80 and 15 respectively. Majority of the patients belonged to age group of 31 to 60 years, 28 of them were found to be less than 30 years of age and 11 patients were above 60 years of age. Total of 107 patients were recruited for the study, out of which 80 were males and 27 were females. 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,[6] In an African study by Akpovi et al., the age group of patients ranged from 12 to 62 years.[7] In our study, there has been an increasing trend in mean total cholesterol value during the course of treatment and there was statistically significant difference in pairwise analysis of mean total cholesterol values at diagnosis, end of IP and at completion phase with p value of <0.001 . The mean triglyceride value also showed statistical significant difference observed between pairwise analysis of triglyceride values in different treatment phases with p value of <0.001. 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. The 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 an Indian study by Sushilendu V et al.,[8] which was similar to our current study findings. In a Taiwan study conducted by Chidambaram et al.,[2] it was also found that there were reduced levels of Serum Total Cholesterol and Triglyceride levels, HDL, LDL at the time of diagnosis like in our study; which indirectly indicates hypocholesterolaemia to be a major predisposing factor in the development of tuberculosis or a sequelae of tuberculosis. In our study we made an attempt to measure the mean Atherogenic index of Plasma during different phases of treatment, which was found to be 0.6 at diagnosis, 0.55 at end of IP treatment and 0.54 at completion phase of treatment. There was statistically significant difference between AIP at diagnosis and completion phase in pairwise analysis. This finding is suggestive of High atherogenic index in Tuberculosis patient which in turn indicates higher risk of atherosclerosis in tuberculosis patient as suggested by Chidambaram et al. study in Taiwan. The study also has taken an initiative to find the changes of atherogenic index during different phases of treatment, which is also showed statistically significant reduction in the Atherogenic index at the time of diagnosis to treatment completion. This indicates successful completion of tuberculosis treatment will reduce the risk of atherosclerosis and also paves the way for further molecular research in the field of effect of antitubercular treatment on host lipid levels.

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CONCLUSION

Tuberculosis is a potential risk factor for atherosclerosis. Successful completion of tuberculosis treatment is associated with decrease in atherogenic index which indicates reduction in risk of atherosclerosis. Hence it is crucial to measure atherogenic index in all phases of antitubercular treatment.

LIMITATIONS

1. The effect of co morbidities like diabetes and hypertension has not been studied, as they are in exclusion criteria.
2. The effect of nutrition and food intake on lipid profile has not been studied.

STRENGTHS

1. No attrition noted during the period of study.
2. This study has compared the AIP in different phases of antitubercular treatment, unlike in other studies were only lipid levels are studied.

FUTURE RECOMMENDATIONS

The study paves the way for further molecular research in the field of effect of antitubercular treatment on host lipid levels which can substantiate the current results.

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