IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 7 Ser.2 (July. 2022), PP 52-56
www.iosrjournals.org

A Study on Serum Lipids among Patients Undergoing Antitubercular Treatment in a Tertiary Care Hospital in Imphal, Manipur

Nuthan V, Monsang G, Wangkheimayum A, Tongbram C, Swathi TV
Department of Respiratory Medicine, Regional Institute of Medical science, Imphal, Manipur

Abstract:
Background*:Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis (MTB) and it typically affects the lungs but it can affect other organs as well. It has existed for millennia and still continues to be a major global public health problem. Worldwide, TB is the 13th leading cause of death and the second leading infectious killer after COVID-19 (above HIV/AIDS). As per WHO, in 2020, an estimated 10 million people fell ill with tuberculosis worldwide. 5.6 million men, 3.3 million women and 1.1 million children. The ability of Mycobacterium tuberculosis to maintain persistent chronic infection is critically linked to its capacity to use host cholesterol. Multiple abnormalities in lipid metabolism have been reported in TB infected patients. It has been observed that cholesterol depletion has resulted in the derangement in the ability of the macrophages to phagocytose mycobacteria. Reports indicate thathypocholesterolemia promotes the development of TB whereas hypercholesterolemia confers some protection against infection with Mycobacterium tuberculosis. This study has been carried out to estimate serum lipid levels in tuberculosis patients and its temporal changes before and after antitubercular treatment.*
Materials and Methods*: This Observational Analytical Cohort Study was carried out from September 2019 to august 2021. A total of 100 patients were recruited for the study, 50 test subject and 50 control population. The control group were age and sex matched healthy individuals with no complaints and no known disease, non-smokers with normal BMI. Differences between the control group and the cases group was assessed by using the independent student t-test while differences before and after treatment in the same patient was done by using paired student t-test.*
Results*: The mean cholesterol, Triglycerides, HDL-C and LDL-C were low in the study population whereas it was normal in the control population. The differences between the groups were significant for HDL-C and LDL-C with p<0.001 and p<0.01respectively. The mean total cholesterol level, mean triglyceride level, mean HDL-C and LDL-C of the study population before initiation of treatment and after completion of treatment were statistically significant with p<0.001.*
Conclusion:*Hypolipidemia observed in pulmonary tuberculosis patients is a consequence of the disease. It can be corrected by giving ATT and normal diet. The findings of the study are of diagnostic importance in pulmonary TB and could be used to assess the severity of the disease and the progress of the treatment. Recovery from the TB after successful ATT is accompanied by significant improvement of the lipid parameters.*
Key Word*:Pulmonary Tuberculosis; Anti-tubercular treatment (ATT); Total Cholesterol (TC); Triglycerides (TG); Low Density Lipoprotein Cholesterol (LDL-C); High Density Lipoprotein Cholesterol (HDL-C).*

Date of Submission: 03-07-2022 Date of Acceptance: 17-07-2022

I. Introduction

Pulmonary tuberculosis is one of the oldest diseases, afflicting the human race since ancient times. A milestone in therapy was the discovery of drugs with antimycobacterial activity, beginning in 1944 with streptomycin. With the currently available drugs, about 90% of pulmonary tuberculosis cases can be cured.[1] Tuberculosis has existed for millennia and continues to remain a major global public health problem. It typically affects the lungs but can also affect other sites and spreads when a person with TB expels the bacteria into the air while coughing or sneezing.Worldwide, TB is the 13th leading cause of death and the second leading infectious killer after COVID-19 (above HIV/AIDS). As per WHO, in 2020, an estimated 10 million people fell ill with tuberculosis worldwide. 5.6 million men, 3.3 million women and 1.1 million children.[2]According to National Strategic Plan (NSP) 2017-2025, the current focus of Government of India is to achieve rapid decline in TB cases, and morbidity and mortality due to TB, while working towards elimination of TB in the country by

2025.[3]The ability of Mycobacterium tuberculosis to maintain persistent chronic infection is critically linked to its capacity to use host cholesterol.[4] Macrophages upon infection with virulent MTB had been frequently observed to accumulate lipid bodies to become foamy macrophages and are essential for allowing the pathogen to establish chronic infection.[5]In addition, the cellular lipids found in foamy macrophages play a crucial role in reactivation of latent tuberculosis.[4]Changes in blood lipids occur naturally during the course of tuberculosis infection, with decrease in early phase of the infection in both total cholesterol and HDL-C and increases in triglycerides in later stages.[6]A clear derangement of the ability of the macrophage to phagocytose mycobacteria was observed when they were depleted of cholesterol.[7] Various studies have shown the importance of cholesterol in the maintenance of cellular immunity and potential destructive effects of low cholesterol levels on the lymphocytes.[7,8] In the present study, an attempt has been carried out to estimate serum lipid levels in tuberculosis patients and its temporal changes before and after antitubercular treatment in the population of Manipur.

II. Material And Methods

This Observational Analytical Cohort Study was carried out on the population of Manipur presenting to Department of Respiratory Medicine, Regional Institute of Medical Sciences, Imphal, Manipur from September 2019 to August 2021.

Study Design: Observational Analytical Cohort Study

Study Location: Department of Respiratory Medicine, Regional Institute of Medical Sciences, Imphal, Manipur

Study Duration: September 2019 to august 2021

Sample size: 100 (50 case and 50 control). The control population were age and sex matched healthy individuals with no complaints and no known disease who were non-smokers with normal BMI.

Sample size calculation: Sample size was calculated using the formula;

$k=n_2/n_1=1$

$n1=(\sigma_1^2+\sigma_2^2/K)\ (z_1-\alpha/2+z_1-\beta)^2/\Delta^2$

In which $\sigma_1=40$, $\sigma_2=40$, $K=1$, $\alpha=0.001$, $\beta=0.2$, respective values taken from the study Vibha Sushilendu et al.[9]

$n_1=(40^2+40^2/1)\ (3.29+0.84)^2/33^2$

$n_1=50$

$n_2=k\times n_1=50$

Group 1 includes 50 patients and Group 2 includes 50 patients.

So, the calculated sample size is equal to 100.Therefore, a total of 100 patients were taken up for the present study.

$\Delta=|\mu_2-\mu_1|$=absolute difference between two means

σ_1,σ_2=variance of mean #1 and #2

n_1=sample size for group #1

n_2= sample size for group#2

α= probability of type 1 error

β= probability of type 2 error

z= critical Z value for a given α or β

k= ratio of sample size for group #2 to group #1

Inclusion criteria:

1. Newly diagnosed pulmonary and extrapulmonary tuberculosis patients.
2. Patients >12 years of age

Exclusion criteria:

1. HIV-TB coinfected patients.
2. Patients who underwent incomplete TB treatment or relapse cases of TB.
3. Multidrug resistant TB.
4. Diabetes, endocrine or genetic disorder. Pregnant or lactating women.
5. Patients who were on antilipidemic medications.
6. Patients unwilling to participate in the study

Procedure methodology

The study was conducted under some variables, in which the independent variables are age, sex, religion, marital status, personal habits like smoking, residential area, socio-economic status and BMI of the patient. Dependent variables are outcome in antitubercular treatment with changes in serum total cholesterol, LDL, HDL-C, LDL-C and triglyceride levels. After due written informed consent was obtained, a detailed clinical history and complete clinical examinations were done for all the participants. Routine investigations

were done including complete hemogram, LFT, KFT, Urine routine examination, random blood sugar, fasting and post prandial blood sugar (if required), ECG, Chest X-ray and Mantoux test. Anthropometric measurements like height, weight and BMI were recorded. On the basis of signs and symptoms, two sputum samples were collected in two consecutive days to be examined for Acid Fast Bacilli at DMC RIMS, Imphal. In order to determine Smear positivity index, the number of Acid-Fast Bacilli (AFB) was counted and analyzed using Lohman EM.[10]After an overnight fasting, fasting blood sample were collected from patients to measure lipid by enzymatic method using Randox kit at Clinical Biochemistry laboratory. Fasting lipid profile were done on two occasions, one before ATT initiation and one after 6 months of ATT treatment. Ethical approval was obtained from the Institutional ethics committee, RIMS, Imphal.

Statistical analysis

Statistical data was analyzed using SPSS software version 21 (IBM). Before analysis, data was checked for consistency and completeness. Differences between the control group and the cases group was assessed by using the independent student t-test while differences before and after treatment in the same patient was done by using paired student t-test. Quantitative data was expressed as MEAN±SD. Data was evaluated by using Student's t-test. P value of <0.05 was taken as significant. Correlation between various parameters was studied by Pearson correlation.

III. Result

The mean age of the participants were 47.6±14.3 years. 24 of them were male and 76 were females (Figure 1). Out of the 50 case group, 42 were positive for sputum study of both direct AFB stain and CBNAAT (Cartridge based nucleic acid amplification test), while remaining 8 patients sputum study was negative for both direct smear and CBNAAT but were positive on Mantoux test (Table 1). The mean total cholesterol, Triglycerides, HDL-C and LDL-C were low for all the case group in comparison with the control group, however it was statistically significant only for HDL-C and LDL-C (Table 2). On using the Wilcoxon-signed-rank test for comparison of the mean total cholesterol level, mean triglyceride level, mean HDL-C and mean LDL-C levels before initiation of ATT and after 6 months of ATT, there was statistically significant diffenrence with p<0.001. (Table 3).

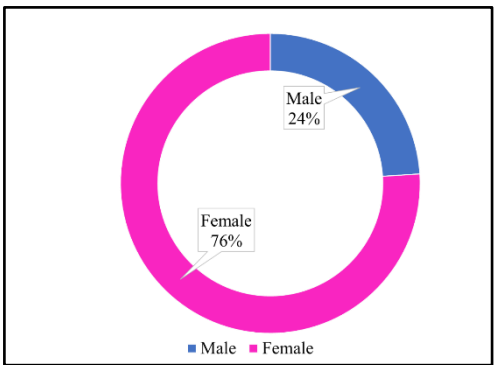

Figure 1: Gender distribution of the participants.

Test	Category	Frequency	Percentage
Sputum AFB	Positive	42	84.0 %
	Negative	8	16.0 %
Sputum CBNAAT	Positive	42	84.0 %
	Negative	8	16.0 %
Mantoux test	Positive	50	100.0 %
	Negative	0	-

Table 1: Findings of tuberculosis related tests among the case group (N=50)

Lipid profile parameters	Cases (N = 50)	Controls (N = 50)	P value
Total Cholesterol (mg/dL)	142.64 (38.94)	152.94 (23.39)	0.11
Triglycerides (mg/dL)	114.84 (41.17)	122.02 (27.63)	0.31
High Density Lipoproteins (mg/dL)	30.48 (12.42)	40.40 (6.06)	**< 0.001***
Low Density Lipoproteins (mg/dL)	85.26 (37.63)	100.58 (16.91)	**0.01***

Table 2: Lipid profile among study participants (cases before ATT v/s controls). The table shows the Mean±SD of which both HDL-C and LDL-C values were statistically significant. P value: Independent samples t-test; *p value significant at < 0.05

Mean lipid profile parameters	Before initiation of ATT	After 6 months of ATT	P value
Total cholesterol level	142.64 (38.94) mg/dL	164.30 (31.84) mg/dL	<0.001
Triglyceride level	114.84 (41.17) mg/dL	126.42 (38.28) mg/dL	<0.001
HDL-C level	30.48 (12.42) mg/dL	41.82 (7.35) mg/dL	<0.001
LDL-C level	85.26 (37.63) mg/dL	98.82 (34.35) mg/dL	<0.001

Table 3: Changes in the mean values of the lipid profile parameters before initiation and after six months of ATT is shown to be statistically significant with p<0.001.

IV. Discussion

Lipids and its metabolites have beneficial effects on tuberculosis resistance through the immune system. Extensive research on lipids has been carried out in various disease conditions especially cardiovascular and diabetes mellitus. However, there is paucity of information on the role of lipids in immune system to fight against infections. The findings in this study could therefore serve to evaluate the pattern of lipid profile in relation to prevalence of pulmonary tuberculosis. Lipids are essential factors that determine our nutritional status. Low lipid level leads to increased susceptibility to various infections, including TB.[11,12]Cholesterol is the most studied lipid in this direction. It constitutes 30% of lipid content of plasma membranes and affects its fluidity.[13]Secretory process of phagocytic cells,like macrophages, requires cholesterol (such as for cell motility, exocytosis and endocytosis). Their phagocytic activity was found to be deranged in cholesterol deficiency.[7]It is also required for bacterial entry into host macrophages and for growth and multiplication in host. MTB preferentially uses fatty acids than carbohydrates as primary carbon source during chronic infection.[14]In this study, the level of TC was significantly lower in patients with TB. Similar observations were reported by Deniz et al[11]and Perez-Guzman et al[15]. It supports the assertion by the study Metwally MM[16], that patients with pulmonary TB have hypocholesterolemia that prove to be a consequence of the disease itself rather than a risk factor. It is also found that serum cholesterol increased significantly to a level more than that of control after six months of regular intake of ATT. If hypocholesterolemia is being corrected during ATT, then the patient would have had normal serum cholesterol value before being decreased and consequently, hypocholesterolemia would be considered as consequence of the disease rather than a risk factor, as risk factors should be present before, during and after treatment.

We also assessed the level of lipids in response to ATT. We showed that the concentration level of TC, TG, HDL-C and LDL-C were significantly increased in treated TB patients at six months of ATT compared to baseline, which is consistent with the findings from Akpovi DC et al[17] and Iyamu OA[18]. The increment of lipid profile concentration after taking ATT treatment in TB patient might be due to the nutritional status and immune function improving[19]and the cleaning ofcirculating of bacilli in the blood.[20] It was found in this study that HDL-C level was decreased significantly in non-treated TB patients compared to controls, and increased significantly after treatment. Similar results were obtained by Akpovi DC et al.[17] During inflammations, catabolism of HDL-C increases and there is overexpression of inflammatory proteins such as phospholipase A2 and circulating amyloid A, during acute phase of TB. This overexpression is in response to inflammation, which stimulates HDL-C catabolism. Therefore, in successfully treated TB patients, HDL-C level is supposed to increase after ATT.[21]

V. Conclusion

It is observed that patients with pulmonary tuberculosis have hypolipidemia which is a consequence of the disease. Hypolipidemia can be corrected by regular intake of antitubercular drugs and normal diet. The findings of the study are of diagnostic importance in pulmonary TB infection and could be used to assess the severity of the disease and progress of treatment. Recovery from TB after successful ATT is accompanied by significant improvement of lipid parameters such as total cholesterol, triglycerides, LDL-C and HDL-C. additional research is required to fully assess the link between TB treatment and levels of total cholesterol and other lipid components in patients with pulmonary TB. It would be interesting to study the effectiveness of cholesterol supplement in TB patient care.

References

[1]. Rieder, H. L., & International Union against Tuberculosis and Lung Disease IUATLD. (2002). *Interventions for tuberculosis control and elimination* (pp. 15-93). Paris: International Union Against Tuberculosis and Lung Disease.

[2]. https://www.who.int/news-room/fact-sheets/detail/tuberculosis

[3]. Central TB Division Directorate General of Health Services. (2018). India TB report 2018, revised national TB control programme annual status report.

[4]. Catron, D. M., Lange, Y., Borensztajn, J., Sylvester, M. D., Jones, B. D., &Haldar, K. (2004). Salmonella enterica serovar Typhimurium requires nonsterol precursors of the cholesterol biosynthetic pathway for intracellular proliferation. *Infection and immunity*, *72*(2), 1036-1042.

[5]. Prabakaran, J. J., Efrem, B., Araya, M., Mebrahtu, M., Zeraburuk, H., Yemane, M., ... & Ghebreyesus, A. (2017). Association of Dietary and Serum Cholesterol with Active Pulmonary Tuberculosis: A Hospital Based Study. *Int. J. Curr. Microbiol. App. Sci*, *6*(12), 4056-4073.

[6]. Yagi, T., Yamagishi, F., Sasaki, Y., Itakura, M., Fujikawa, A., Kuga, M., & Ishimaru, G. (2004). STUDY ON CASES DEVELOPED PULMONARY TUBERCULOSIS AFTER RECEIVING GASTRECTOMY. *Kekkaku (Tuberculosis)*, *79*(5), 355-359.

[7]. Gatfield, J., & Pieters, J. (2000). Essential role for cholesterol in entry of mycobacteria into macrophages. *Science*, *288*(5471), 1647-1651.

[8]. Dabrowski, M. P., Peel, W. E., & Thomson, A. E. (1980). Plasma membrane cholesterol regulates human lymphocyte cytotoxic function. *European journal of immunology*, *10*(11), 821-827.

[9]. Sushilendu, V., Kumar, N., & Kumar, U. (2019). Study of Lipid profile in pulmonary TB cases: pre and post anti-tuberculosis treatment. *J Med Sci Clinic Res*, *7*, 211-215.

[10]. Lohmann, E. M., Koster, B. F. P. J., Le Cessie, S., Kamst-van Agterveld, M. P., Van Soolingen, D., &Arend, S. M. (2012). Grading of a positive sputum smear and the risk of Mycobacterium tuberculosis transmission. *The International Journal of tuberculosis and lung disease*, *16*(11), 1477-1484.

[11]. Deniz, O., Tozkoparan, E., Yaman, H., Cakir, E., Gumus, S., Ozcan, O., ... &Ekiz, K. (2006). Serum HDL-C levels, log (TG/HDL-C) values and serum total cholesterol/HDL-C ratios significantly correlate with radiological extent of disease in patients with community-acquired pneumonia. *Clinical biochemistry*, *39*(3), 287-292.

[12]. Volpato, S., Palmieri, E., Fellin, R., &Zuliani, G. (2000). Acute phase markers are associated with reduced plasma lipid levels in a population of hospitalized elderly patients. *Gerontology*, *46*(1), 22-27.

[13]. SALUNKHE, V. S., PATIL, V. W., & RAI, P. (2020). Lipid Profile as a Nutritional Status Marker in Tuberculosis. *Journal of Clinical & Diagnostic Research*, *14*(12).

[14]. Miner, M. D., Chang, J. C., Pandey, A. K., Sassetti, C. M., & Sherman, D. R. (2009). Role of cholesterol in Mycobacterium tuberculosis infection.

[15]. Pérez-Guzmán, C., Vargas, M. H., Quiñonez, F., Bazavilvazo, N., Aguilar, A., & Team, O. S. (2005). A cholesterol-rich diet accelerates bacteriologic sterilization in pulmonary tuberculosis. *Chest*, *127*(2), 643-651.

[16]. Metwally, M. M., & Raheem, H. A. (2012). Lipid profile in tuberculous patients: A preliminary report. *Life Science Journal*, *9*(1), 719-722.

[17]. Akpovi, D. C., Gbaguidi, L. H. S., Anago, E., Affolabi, D., Dougnon, T. V., Faihun, F., &Anagonou, S. (2013). Tuberculosis treatment raises total cholesterol level and restores high density lipoprotein cholesterol (HDLC) in patients with pulmonary tuberculosis. *African Journal of Biotechnology*, *12*(41).

[18]. Iyamu, O. A., Ugheoke, J. E., Ozor, M. O., Airhomwanbor, K. O., Eidangbe, A. P., Idehen, I. C., ... &Akpede, N. (2014). The effect of nutritional lipid supplementation on serum lipid levels and effectiveness of antitubercular chemotherapy. *American Journal of Biomedical Research*, *2*(2), 36-41.

[19]. El- Sadr, W. M., Mullin, C. M., Carr, A., Gibert, C., Rappoport, C., Visnegarwala, F., ... & Raghavan, S. S. (2005). Effects of HIV disease on lipid, glucose and insulin levels: results from a large antiretroviral- naive cohort. *HIV medicine*, *6*(2), 114-121.

[20]. Cliff, J. M., Lee, J. S., Constantinou, N., Cho, J. E., Clark, T. G., Ronacher, K., ... &Dockrell, H. M. (2013). Distinct phases of blood gene expression pattern through tuberculosis treatment reflect modulation of the humoral immune response. *The Journal of infectious diseases*, *207*(1), 18-29.

[21]. Taparia, P., Yadav, D., Koolwal, S., & Mishra, S. (2015). Study of lipid profile in pulmonary tuberculosis patients and relapse cases in relation with disease severity-A pilot study. *Indian J Sci Appl Res*, *2*, 41-50.

Nuthan V, Monsang G, et. al. "A Study on Serum Lipids among Patients Undergoing Antitubercular Treatment in a Tertiary Care Hospital in Imphal, Manipur." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(07), 2022, pp. 52-56.