Original Article

Dyslipidemia in Patients with Tuberculosis and Diabetes Mellitus

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Aims : To calculate the prevalence of Dyslipidemia in patients with Mycobacterium Tuberculosis infection (Mtb) and Diabetes Mellitus (DM).

Materials and Methods : A study done on 294 patients infected with Mtb were enrolled in the study. Patients infected with Tuberculosis (TB) were selected from Medicine and Pulmonary Medicine Departments in MLN Medical College Prayagraj. Patients were segregated into two groups on the basis of glucose tolerance; Abnormal Glucose Tolerance (AGT) and Normal Glucose Tolerance (NGT).

Results: A total of 294 patients with TB were taken in the study, 143 patients in AGT group and 151 patients in NGT group. The average age of the patients in AGT   group was 47.91 years. Among AGT and NGT, Dyslipidemia was found to be statistically significant among AGT group (p=0.01). Mean Serum Triglycerides (209.8, p<0.004) and LDL Cholesterol (144.3, p<0.0001) in AGT group.

Conclusion : Patient with TB DM are more prone for Dyslipidemia and atherogenicity.

According to The Global Tuberculosis Report 2019, majority of TB cases in 2018 were in the South-East Asian region (44%). Eight countries contributed for two thirds of the Global total: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa (3%)[1].

Insulin Resistance (IR) has been implicated in various diseases, such as Cardiovascular Disease (CVD) [2], Hypertension [3], Polycystic Ovarian Syndrome (PCOS)[4], Type 2 Diabetes (T2DM) [5], Obesity [6], and Metabolic Syndrome (MetS) [3]. The prevalence of MetS in India has been documented to be from 11% to 41% across this vast country with numerous Socio-cultural varieties[7].

The population in both Urban and Rural areas have increase chances of having DM. A recent review found that DM ranged from 3% to 12% across different Rural areas of the country with an expected rate of increase of 2.0 per 1000 population per year[8].

Interestingly, the causative agent of TB, Mycobacterium tuberculosis(Mtb), has been shown to rely heavily on host derived lipids for its survival[9-11]. Mtb induces the formation of lipid-loaded foamy macrophages, similar to atherosclerotic lesions and exploits these cells as its primary niche for replication. Several studies have identified high Cholesterol levels as risk factor for TB[12-14]   and reducing Cholesterol

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> **Editor's Comment :**
> ■ Lipids plays an important role in development of both diabetes and tuberculosis. Hence it may be beneficial to control lipid profile in patients with TB-DM and further research is required to know its effect on treatment in patients with TB-DM.

levels using statins was beneficial in Mtb infected macrophages, mice[15].

MATERIALS AND METHODS

A Total of 294 patients infected with Mtb were enrolled in the study. Patients of TB were selected from Medicine and Pulmonary Medicine Departments in MLN Medical College Prayagraj. All Consecutive adults with TB infection determined Bacteriologically, Histologically, clinically or Radiologically were recruited after informed consent. Patients with serious life threatening TB infection , pregnant women, patients on steroid therapy, those unwilling for study, MDR / XDR TB, HIV, Patient taking lipid lowering agents were excluded.

Informed consent was taken and demographic characteristics, anthropometry and details of the diagnosis of Tuberculosis were obtained. Patients with self-reported history of previous diagnosis of Diabetes and those on treatment with anti-diabetic agents were considered to have DM and no need to have any further testing other than A1C. Patients of DM not previously diagnosed, samples were drawn for A1C and on a subsequent day had an Oral Glucose Tolerance Test (OGTT) on a fasting state. For all the patient's Serum Fasting Lipid Profile was drawn to assess lipid status. Patients were grouped into, either having AGT or NGT. AGT group included patients with Impaired Glucose Tolerance (IGT) and DM.

RESULTS

A total of 294 patients with TB were taken. Of them 143 patients had AGT group, and 151 patients had NGT group. The mean age of the patients in AGT group was 47.91 years while in NGT group was 37.05 years. Majority of patients were male in both the groups.

Maximum patients of AGT and NGT group had a BMI in normal range value ie, 46.8% and 52.3% respectively. On comparison the odds of Glucose intolerance were less in underweight patients (OR=0.45; 95% CI 0.20-1.01; p=0.05) whereas Obese patients had higher odds of Glucose Intolerance (OR = 4.20; 95% CI 0.86-20.4; p=0.05).

Among AGT and NGT, Dyslipidemia was found to be statistically significant among AGT group (p=0.01). Correlation between age and Dylipidemia was calculated and was found to be equal in both the groups(correlation coefficient 0.28 in AGT and 0.27 in NGT group; p<0.001) suggesting age as a non-confounding variable in our study. Mean Serum Triglycerides was 209.8 mg/dl in AGT group and 170.93 mg/dl in NGT group (p <0.004). The LDL Cholesterol in AGT group was 144.3 mg/dl and 97.03 mg/dl in NGT group(p<0.0001) (Tables 1&2 and Figs 1&2).

DISCUSSION

A total of 294 TB patients with DM were taken up for study and status of Lipid Profile was determined at
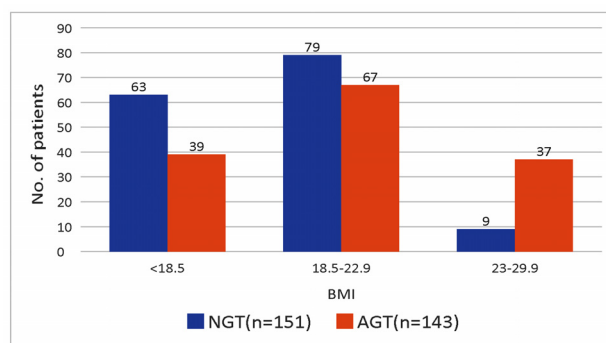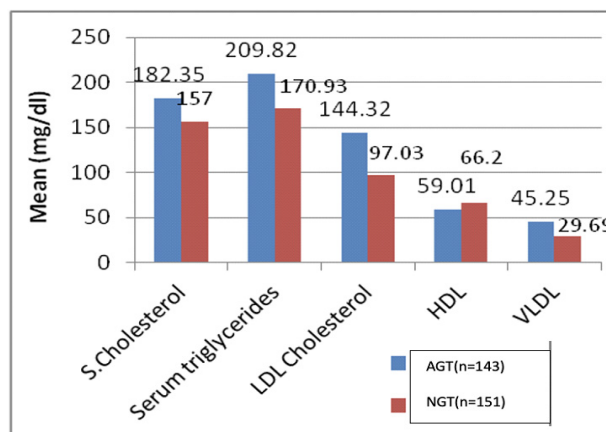

Fig 1 — BMI and glucose intolerance

Fig 2 — Association of dyslipidemia in patients with TB and DM

the time of admission. It was found out that mean age in patients with TB and AGT group was significantly higher (47.91 years) as compared to those with TB alone (37.05years, p=0.0001). Gadallah, et al [16] in a nationwide population-based study found that screening for DM among 1435 TB patients with no history of DM detected 30 new cases of DM, with a case detection rate of 2.09%. It was found out that majority of patients in AGT group had Dyslipidemia as compared to NGT group which was statistically significant (p=0.01). Mean Serum Triglycerides level and LDL Cholesterol were (209.82 ± 68.03, p<0.004) and (144.32± 24.83, p<0.0001) respectively in AGT group. In this study HDL values were lower and VLDL values were higher in AGT group even though they were not statistically significant. In a similar study done by Vrieling, et al[17] on 177 patients it was observed that DM patients had Dyslipidemia as evidenced by high levels of VLDL, Triglycerides and low HDL Cholesterol. They concluded that TB-DM patients possess a distinctive Plasma Lipid Profile with pro-atherogenic properties. Several studies conducted in the past showed

Table 1 — Baseline characteristics				
Characteristics	AGT(n=143)	NGT(n=151)	2	p -Value
Age :				
<50 years	70(48.9%)	123(81.45%)	34.41	<0.001
>50 years	73(51.1%)	28(18.54%)		
Gender :				
Male	100(69.9%)	92(60.9)	2.6	0.11
Female	43(30.1%)	59(39.1%)		
Residence :				
Rural	100(69.9%)	64(42.4%)	22.59	<0.001
Urban	43(30.1%)	87(57.6%)		
Education :				
Below High school	124(86.7%)	110(72.8%)	8.69	0.003
Above High school	19(13.3%)	41(21.2%)		
Age (Years)	47.91 ± 15.32	37.05 ± 13.58		0.0001
Hb (g/dl)	10.66± 1.61	10.53 ± 1.58		0.08
Serum creatinine				
(mg/dl)	1.28 ± 0.52	0.95 ± 0.29		0.0001

Table 2 — Association of dyslipidemia in patients with TB and DM (Values in mg/dl)			
Lipid profile	AGT(n=143)	NGT(n=151)	p value
S Cholesterol (mean ± SD)	182.35 ±32.26	157 ± 42.37	0.15
S Triglycerides (mean ± SD)	209.82 ± 68.03	170.93 ±85.19	0.004
LDL Cholesterol (mean ± SD)	144.32 ±24.83	97.03 ±41.69	0.0001
HDL Cholestrol (mean ±SD)	59.01 ± 27.94	66.20 ± 26.03	0.18
VLDL (mean ±SD)	45.25 ± 51	29.69 ± 11.89	0.23

the benefits of using statin therapy for decreasing the incidence of TB in elderly population with DM. A study done by Lee, *et al*[18] among 27,958 patients age >65 years and were followed up from 1998 to 2009. A total of 13,981 Type 2 diabetic patients were chosen. Calcium channel blocker, beta blocker, and statin users exhibited a reduced independent association after controlling for age, sex, other co-morbidities, and medications, with risk ratios of 0.76 (95 percent CI, 0.58-0.98), 0.72 (95 percent CI, 0.58-0.91) and 0.76 (95 percent CI, 0.60-0.97), respectively. Calcium channel blocker, beta blocker, and statin medication may reduce TB infection in older Taiwanese patients with Type 2 Diabetes, according to the researchers. Lai, *et al*[19] did another trial with 8098 new TB cases and 809 800 control individuals. Statin users had a lower chance of active Tuberculosis, according to the researchers. Statin use for more than 90 days in a year was linked to the lowest unadjusted risk of Tuberculosis (RR 0.74; 95 percent CI 0.63 to 0.87). After correcting for individual confounders (RR 0.66; 95 percent CI 0.56 to 0.78) and DRS adjustment, the protective effect of active TB persisted (RR 0.66; 95 percent CI 0.56 to 0.78) (RR 0.62; 95 percent CI 0.53 to 0.72). The result of their study showed that patients with Dyslipidemia had reduced chances of infection with active Tuberculosis who were on stations, and the duration of stations offered prevention from Tuberculosis. In a similar study by Liao, *et al*[20] to identify 8,236 patients above 20 years with recent infection of Pulmonary Tuberculosis. Odds Ratio (OR) of Pulmonary Tuberculosis was 0.67 for patients who had been taking statins (95% CI 0.59, 0.75). The adjusted ORs of Pulmonary Tuberculosis were 0.87 (95% CI 0.69, 1.10) for patients with total duration of statins use <3 months, 0.77 (95% CI 0.58, 1.03) for 3-6 months, and 0.59 (95% CI 0.51, 0.68) for ≥6 months, compared with subjects who never used statins. They concluded statins use correlates with a small but statistically significant risk reduction of Pulmonary Tuberculosis. The protective effect is stronger for prolonged use of statins.

CONCLUSION

In this study it was observed that patients with TB-DM are more prone for Dyslipedimia as compared to patients with TB alone.

Limitation : This was a small population study.

REFERENCES

1 World Health Organization. Global tuberculosis report 2019. Available from: https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf?ua=1.

2 Ginsberg HN — Insulin resistance and cardiovascular disease. *J Clin Invest* 2000; **106:** 453-8.

3 Natali A, Ferrannini E — Hypertension, insulin resistance, and the metabolic syndrome. Endocrinol Metab *Clin North Am* 2004; 33: 417-23.

4 Park KH, Kim JY, Ahn CW, Song YD, Lim SK, Lee HC — Polycystic ovarian syndrome (PCOS) and insulin resistance. *Int J Gynaecol Obstet* 2001; **74:** 261-7.

5 Reaven GM — Banting lecture role of insulin resistance in human disease. *Diabetes* 1988; **37:** 1595-13.

6 Kahn BB, Flier JS — Obesity and insulin resistance. *J Clin Invest* 2000; **106:** 473-8.

7 Khan Y, Lalchandani A, Gupta AC, Khadanga S, Kumar S — Prevalence of metabolic syndrome crossing 40% in Northern India: Time to act fast before it runs out of proportions. *Journal of Family Medicine and Primary Care* 2018; **7(1):** 118-5.

8 Misra P, Upadhyay RP, Misra A, Anand K — A review of the epidemiology of diabetes in rural India. *Diabetes Res Clin Pract* 2011; **92:** 303-8.

9 Russell DG, Cardona PJ, Kim MJ, Allain S, Altare F — Foamy macrophages and the progression of the human tuberculosis granuloma. *Nat Immunol* 2009; **10(9):** 943-8.

10 Lee W, VanderVen BC, Fahey RJ, Russell DG — Intracellular Mycobacterium tuberculosis exploits host-derived fatty acids to limit metabolic stress. *J Biol Chem* 2013; **288(10):** 6788-800.

11 Kim MJ, Wainwright HC, Locketz M, Bekker LG, Walther GB, Dittrich C, *et al* — Caseation of human tuberculosis granulomas correlates with elevated host lipid metabolism. *EMBO Mol Med* 2010; **2(7):** 258-74.

12 Soh AZ, Chee CB, Wang YT, Yuan JM, Koh WP — Dietary cholesterol increases the risk whereas PUFAs reduce the risk of active tuberculosis in Singapore Chinese. *J Nutr* 2016; **146(5):** 1093-100.

13 Martens GW, Arikan MC, Lee J, Ren F, Vallerskog T, Kornfeld H — Hypercholesterolemia impairs immunity to tuberculosis. *Infect Immun* 2008; **76(8):** 3464-72.

14 Martens GW, Vallerskog T, Kornfeld H — Hypercholesterolemic LDL receptor-deficient mice mount a neutrophilic response to tuberculosis despite the timely expression of protective immunity. *J Leukoc Biol* 2012; **91(6):** 849-57.

15 Parihar SP, Guler R, Khutlang R, Lang DM, Hurdayal R, Mhlanga MM, *et al* — Statin therapy reduces the mycobacterium tuberculosis burden in human macrophages and in mice by enhancing autophagy and phagosome maturation. *J Infect Dis* 2014; **209(5):** 754-63.

16 Gadallah M, Amin W, Fawzy M, Mokhtar A, Mohsen A — Screening for diabetes among tuberculosis patients: a nationwide population-based study in Egypt. *African Health Sciences* 2018; **18(4):** 884-7.

17 Vrieling F, Ronacher K, Kleynhans L, van den Akker E, Walzl G, Ottenhoff THM, *et al* — Patients with Concurrent Tuberculosis and Diabetes Have a Pro-Atherogenic Plasma Lipid Profile. *E Bio Medicine* 2018; **32:** 192-9. Available from https://doi.org/10.1016/j.ebiom.2018.05.011.

18 Lee MY, Lin KD, Hsu WH, Chang HL, Yang YH, Hsiao PJ, *et al* — Statin, Calcium Channel Blocker and Beta Blocker Therapy May Decrease the Incidence of Tuberculosis Infection in Elderly Taiwanese Patients with Type 2 Diabetes. *Int J Mol Sci* 2015; **16(5):** 1369-16.

19 Lai CC, Lee MTG, Lee SH, Hsu WT, Chang SS, Chen SC, *et al* — Statin treatment is associated with a decreased risk of active tuberculosis: an analysis of a nationally representative cohort. *Thorax* 2016; **71(7):** 646-6.

20 Liao KF, Lin CL, Lai SW. Population-Based Case-Control Study Assessing the Association between Statins Use and Pulmonary Tuberculosis in Taiwan. Front. *Pharmacol* 2017; **8:** 597. Available from:doi: 10.3389/fphar.2017.00597.