

## Estimation of Serum Cholinesterase in Obese & Non obese type-2 Diabetes mellitus.

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**Abstract:** Serum cholinesterase has been shown to be associated with diabetes mellitus, coronary artery disease, obesity, hypertension and also its role in lipid metabolism where its activity has been positively correlated with serum lipids and lipoprotein level. The objective of the study was to estimate the levels of serum cholinesterase in obese & non-obese type-2 diabetes mellitus patients. To compare the serum levels of cholinesterase with the cardio metabolic risk markers such as BMI, Serum HDL, LDL and Triglycerides. To evaluate serum cholinesterase level / LDL cholesterol ratio in type-2 diabetes mellitus patients. About 120 out patients diagnosed with type 2 DM from KR Hospital, Mysore was selected and was grouped into two groups as obese and non obese based on BMI. 5ml of venous blood was drawn in fasting state for serum cholinesterase and lipid indices by enzymatic method using autoanalyser. Statistical Analysis was done using SPSS 20 version, to see the significance Pearson's correlation and student independent t test was used. In the present study, serum cholinesterase was significantly increased in the obese group as compared to the non obese group, which is  $10105.5 \pm 1040.6$  and  $8640.4 \pm 604.3$  respectively. Serum cholinesterase showed positive correlation with each of lipid indices namely total cholesterol, triglyceride, LDL-C, Total cholesterol to HDL-C ratio, Total cholinesterase to LDL-C ratio, and a negative correlation with HDL-C in obese type-2 DM patients when compared to non obese diabetic patients. The study indicates that serum cholinesterase to LDL-C ratio may serve as a potential risk assessment marker of cardiovascular diseases in obese type-2 diabetic mellitus. Hence obesity in type 2 diabetes mellitus increases the cardiovascular complications. With a relatively low cost and high clinical informative power, serum Cholinesterase assessment should be included in routine clinical diagnostic procedures to evaluate diabetic patient clinical conditions as prognostic & diagnostic parameters in assessing the cardiovascular risk.

**Key words:** Serum cholinesterase, Diabetes, Obesity, Cardiovascular risk, lipid metabolism, Body Mass Index.

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### I. Introduction

**Diabetes mellitus** is a fast-growing global problem with huge social, health, and economic consequences. It is estimated that in 2010 there were globally 285 million people (approximately 6.4% of the adult population) suffering from this disease [1]. Diabetes mellitus is a metabolic disease characterized by hyperglycemia with abnormalities in carbohydrate, fat, and protein metabolism due to defects in insulin secretion, insulin action or both. Many studies have shown that diabetes is consistently associated with changes in plasma lipids and lipoproteins, and these alterations are of interest because of their possible role in the aetiology of the increased cardiovascular disease associated with diabetes. [2] Mortality rates among diabetics are 1.5 to 2.5 times higher than general population. Much of this increased mortality and morbidity is due to cardiovascular complications in diabetic patients. [3]

Cholinesterase represents a group of enzymes that hydrolyze cholinesterase. Serum cholinesterase has been shown to be associated with diabetes mellitus, coronary artery disease, hypertension and also its shown to have a role in lipid metabolism in previous studies where in its activity has been positively correlated with serum lipids and lipoprotein levels. [5] Due to its involvement in lipid metabolism and associated elevated levels in diabetes mellitus patients, cholinesterase gains importance as potential marker for assessing cardiovascular status in diabetic patients. Only few studies have examined the association between serum cholinesterase and risk of cardiovascular disease in type 2 DM patients in relation to body mass index. Thus, this study is undertaken to estimate the level of serum cholinesterase and also to study the lipid profile in diabetic patients and evaluate the possible role of serum cholinesterase level to LDL-C ratio as a biomarker for cardiovascular complications.

Pseudo-cholinesterase or serum cholinesterase or butyl cholinesterase (BChE) BChE plays a role in lipid metabolism, either directly or through a synergistic action with cholesterol esterase[6] It regulates the degradation of butyrylcholine, an intermediate of lipid metabolism, as demonstrated also by the close relation between serum BChE levels, cholesterol, and triacylglycerols.[7] The hypothesis that LDL-cholesterol is formed from very-low density lipoproteins (VLDL-cholesterol) in the presence of BChE (8) is supported by the fact that increased BChE activity is associated with abnormal lipid metabolism in humans. This suggests that BChE was specifically involved in the synthesis of lipoproteins (9,10)

**BChE in diabetes and CVD-** High BChE activities correlate with cardiovascular risk factors like hypercholesterolemia, hypertension, and obesity and Type I or Type II diabetes [11] In two other studies on diabetic patients, BChE was found to be significantly correlated with serum insulin, C-peptide, and free fatty acid.[12] Circumstantial evidence was provided demonstrating that insulin resistance and an increased flux of free fatty acids from adipose tissue to the liver stimulated the hepatic synthesis of serum BChE; these results suggest the involvement of BChE in the pathophysiology of the metabolic syndrome. Other functions of BChE involve the maintenance of endothelial integrity both directly and indirectly. Blood pressure might be influenced by BChE because its substrate acetylcholine induces vasodilatation by triggering nitric oxide release via endothelial muscarinic cholinergic receptors.[13] An excess of cholinesterase activity in the metabolic syndrome could also adversely affect endothelial function and ultimately increase blood pressure in turn, The positive correlation between lipid peroxidation and BChE help in establishing the relationship between increased serum acetyl cholinesterase and vascular complications in diabetes[14,15]

From the various studies made on BChE and its co-relation with lipid metabolism in the human body, it's clear that BChE is very closely involved in development of obesity. However, not much research is done regarding their co-relation with diabetes, BMI and its involvement in atherogenesis, thus this study was taken up to address this issue.

## **II. Aim And Objectives**

1. To estimate the levels of serum cholinesterase in obese & non-obese Type-2 diabetes mellitus patients.
2. To compare the serum levels of cholinesterase with the cardio metabolic risk markers such as BMI, Serum HDL, LDL and Triglycerides.
3. To evaluate serum cholinesterase level / LDL cholesterol ratio in type-2 diabetes mellitus patients.

## **III. Materials And Methods**

Is a Cross sectional study. The study was conducted over a span of 2 months. Study population was taken from patients admitted to K.R Hospital, Mysore with type-2 diabetes mellitus. The diabetic patients were diagnosed on the basis of the WHO criteria. All patients have a history of duration of disease for more than one year and no one of them had hypertension.

**Inclusion criteria:** Patients admitted to K.R Hospital, Mysore between 30-60 years of age of either sex with type -2 diabetes mellitus, with a mean age of  $44.75 \pm 7.97$  yr. **Exclusion criteria:** Patients with Gestational diabetes, Liver dysfunction, renal dysfunction & other systemic diseases were excluded.

**Study design:** The study population was divided into 2 groups based on BMI.

Group 1: Obese diabetic patients with BMI >25

Group 2: Non-obese diabetic patients with BMI <25

**Sample size calculation:** Sample size has been calculated with confidence level of 95% and allowable error of 10%, the sample size in each group was 60.

**Data collection:** Data regarding age, sex, occupation, diet, physical activity, BMI, Blood pressure and others was extracted from the patient. Ethical clearance was taken from the Institutional Research Committee. A written informed consent was taken from the subjects.

**Sample Collection procedure:** The studied samples were collected from 120 patients who reported to KR Hospital, Mysore medical college and research institute. About 5ml of fasting venous sample was collected from

the patient in a plain vacutainer under aseptic precautions. The serum was then analyzed for lipid profile and serum cholinesterase by enzymatic method using fully automated chemistry analyzer Cobas 6000.

**Statistical Analysis:** The results are expressed as Mean  $\pm$  Standard deviation.  $p < 0.05$  was considered statistically significant. Statistical analysis was performed using Epi info software and for test of significances student 't' test was used.

#### IV. Result

In the present study the baseline characteristics of the subjects are shown below. The mean age of participants was  $44.75 \pm 7.97$  yr.

**Table 1:** Age distribution of both group

Age group (in years)	BMI <25	BMI $\geq$ 25	Total
30-40	19	21	40
40-50	27	20	48
50-60	14	18	32

**Table 2:** Gender distribution of both groups.

Gender	BMI <25	BMI $\geq$ 25	Total
Male	32	33	65
Female	28	27	55

**Table 3:** Shows the statistically significant increase in Serum cholinesterase levels in obese individuals when compared with non-obese individuals:

Group	Number	Mean $\pm$ Std. Deviation	P value
Obese	60	10105.5 $\pm$ 1040.6 mg/dl	<0.001
Non obese	60	8640.4 $\pm$ 604.3 mg/dl	

p value <0.001 statistically significant

**Figure 1:** Serum cholinesterase levels in obese and non-obese individuals:

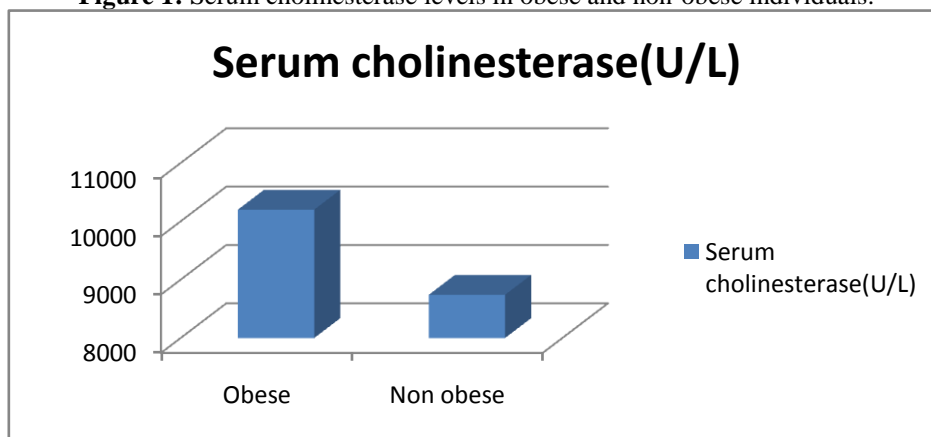
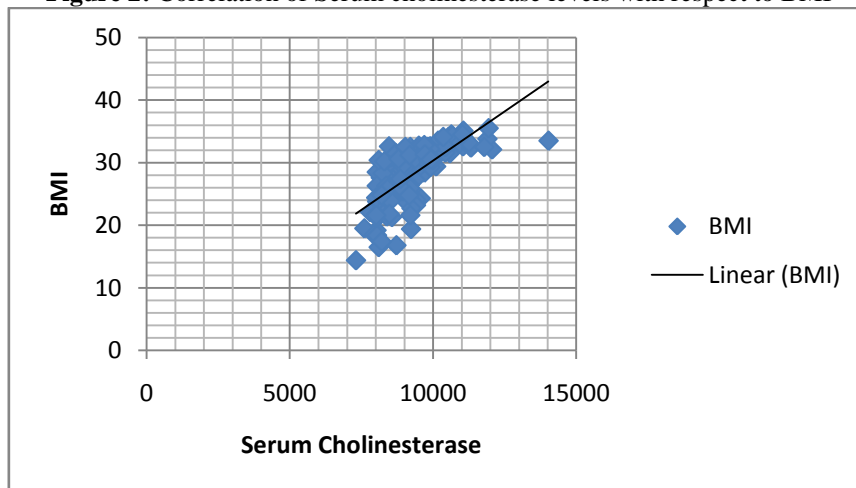


Figure 2 shows positive correlation of Serum cholinesterase levels with respect to BMI, where serum cholinesterase increases with increase in Body Mass Index with r value of 0.67.

**Figure 2:** Correlation of Serum cholinesterase levels with respect to BMI



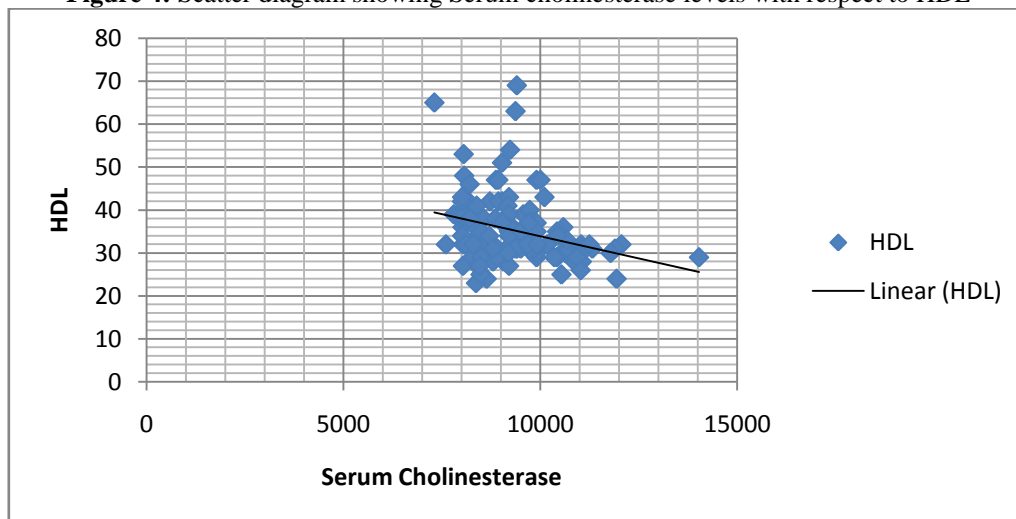
**Table 4:** Comparison of the serum levels of cholinesterase of both groups with the lipid indices

Group	Cholesterol	HDL	LDL	Triglyceride	Serum cholinesterase
Non obese	185.5±14.2	38.1±9.1	111.9±10.7	176.4±27.4	8640.4±604.3
Obese	195.3±17.1	32.2±3.8	120.9±12.7	210.5±47.5	10105.5±1040.6

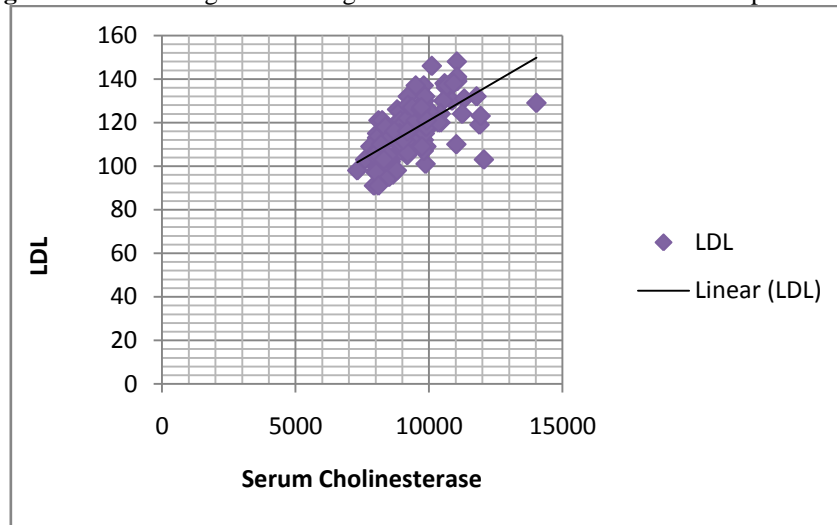
Test of significance: Students t test, p value <0.05 is significant. Pearson correlation coefficient for HDL is -0.295. Pearson correlation coefficient for LDL is 0.640. Pearson correlation coefficient for triglycerides is 0.591

As observed in table 4, serum cholinesterase decreased significantly with increase in HDL whereas serum cholinesterase was increases significantly with increase in LDL and triglycerides.

**Figure 4:** Scatter diagram showing Serum cholinesterase levels with respect to HDL



**Figure 5:** Scatter diagram showing Serum cholinesterase levels with respect to LDL



**Figure 6:** Scatter diagram showing Serum cholinesterase levels with respect to Triglycerides

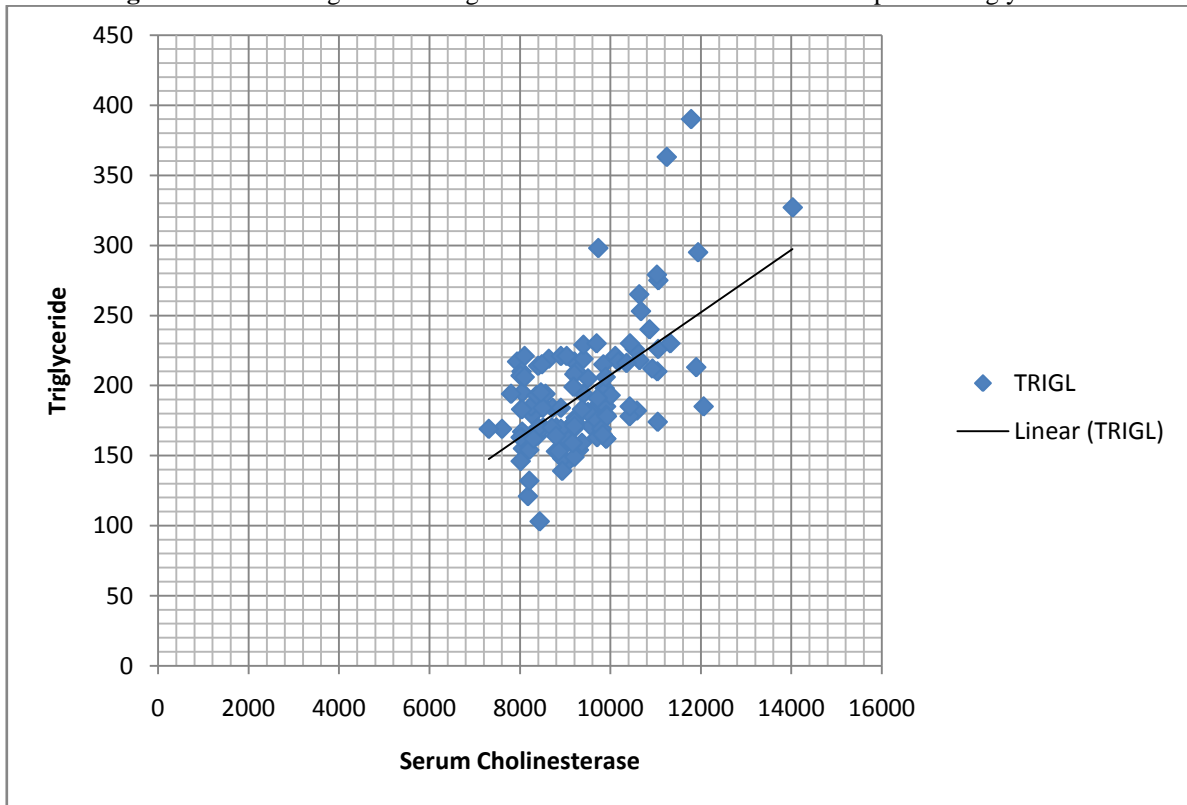


Table 5 shows the cholesterol/HDL ratio was significantly higher in the obese when compared to the non-obese individual.

**Table 5 :** Cholesterol/HDL ratio in obese and non-obese individuals:

Group	Number	Mean+ Std. Deviation	p Value
Obese	60	7.2±1.3	<0.05
Non obese	60	5.1±1.1	

p value <0.05 significant

Table 6 shows, serum cholinesterase /LDL level is significantly higher in the obese when compared to the non-obese individual with mean standard deviation 84.1±8.5 .

**Table 6** Serum cholinesterase/LDL levels in obese and non-obese individuals:

Group	Number	Mean± Std. Deviation	p Value
<b>Obese</b>	60	84.1±8.5	<0.05
<b>Non obese</b>	60	77.5±5.3	

p value <0.05 significant

## V. Discussion

In the present study, it was observed that the serum cholinesterase of obese individuals was significantly higher than that of non obese type-2 diabetes mellitus patients with mean standard deviation 10105.5±1040.6 mg/dl, which is in agreement to the study conducted by Roop et al [6]. This suggests that probably BChE may be involved in the pathogenesis of type-2 DM either by the way of amyloid fibrils or by modifying other risk factors of insulin resistance. Amyloid fibrils in pancreatic islets produce excessive superoxide radicals, lipid peroxidation and nitric oxide inactivation, contributing to apoptosis of beta cells [16]. Furthermore, the result suggests that obesity also increases the activity of BChE. This might be because of the association between rough endoplasmic reticulum and enzyme BChE, as confirmed by electron microscopic studies [17]. When protein intake is high, as observed in obese individuals, the subsequent increased activity of rough endoplasmic reticulum results in increased production of BChE. Increased BChE activity further promotes the pathogenesis of type-2 diabetes mellitus. It was also observed that when a correlational analysis was made between the serum cholinesterase and lipid indices, there was a strong positive correlation with cholesterol & triglyceride and moderate positive correlation with LDL-C and total cholesterol to HDL-C ratio and a negative correlation with HDL, which was statistically significant in obese type-2 diabetic patients when compared to normal type-2 diabetic patients. The results of the present study can be compared with study done by Alcantara et al [18] had shown that butyrylcholinesterase activity was positively correlated with age, sex, body mass index, hypertension and diabetes, as well as with albumin, triglycerides, total cholesterol, low lipoprotein cholesterol and apoprotein B, and measures of overweight, obesity, the traditional risk factors of coronary artery disease. These changes suggest that lipid concentrations seem to form the basis for vascular complications seen in diabetics. The hypertriglyceridemia seen in the diabetics in this study is a common metabolic aberration of diabetes. The elevation of serum triglyceride may be the result of increased endogenous production of very low-density lipoproteins and chylomicron, or a defective removal of circulating triglyceride, or a combination of both these mechanisms [19]. The result also showed that the cholesterol to HDL-C ratio was significantly higher in obese when compared to non obese type-2 diabetes mellitus patients, which is in accordance with the study conducted by Aryal M. et al [20]. Furthermore, it was also observed that the risk factor for heart diseases increases with increase in BMI. Thus confirming that obesity is an added risk factor for heart diseases. Furthermore, the cholinesterase to LDL-C ratio showed positive correlation with the cholesterol HDL ratio, suggesting that it is intimately related to obesity, type-2 diabetes mellitus and heart diseases. Thus the cardiac risk represented by the cholinesterase to LDL-C ratio is in accordance and as significant as the cholesterol to HDL-C ratio.

## VI. Conclusion

The study showed that serum cholinesterase is increased in type 2 DM patients and suggests that serum cholinesterase very much correlates with serum lipid indices in obese type 2 diabetic patients. Due to its mutual involvement in obesity, diabetes and atherogenesis, the **cholinesterase to LDL-C ratio** can be used as a potential **RISK ASSESSMENT MARKER** of cardiovascular disease in type 2 diabetes mellitus and used to assess the cardiovascular changes in diabetic patients.

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