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*International Journal of Current Research*
*Vol. 7, Issue, 12, pp.23904-23907, December, 2015*

**INTERNATIONAL JOURNAL OF CURRENT RESEARCH**

**ISSN: 0975-833X**

## RESEARCH ARTICLE

# SERUM CHOLINESTERASE IN RELATION TO LIPID INDICES AS CARDIO-VASCULAR RISK ASSESSMENT MARKER IN TYPE 2 DIABETES MELLITUS

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**ARTICLE INFO**

***Article History:***
Received 04th September, 2015
Received in revised form
19th October, 2015
Accepted 05th November, 2015
Published online 30th December, 2015

***Key words:***

Serum Cholinesterase,
Type 2 Diabetes mellitus,
Fasting blood glucose,
Cardiovascular disease,
Lipid indices{total cholesterol,
HDL-C(high density lipoprotein-cholesterol, LDL-C(low density Lipoprotein- cholesterol),
Triglycerides,
Total cholesterol to HDL ratio}.

**ABSTRACT**

**Introduction:** Serum cholinesterase has been shown to be associated with DM, coronary artery disease, hypertension and also its shown to have role in lipid metabolism in previous studies where in its activity has been positively correlated with serum lipids and lipoprotein levels. However, 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 and their findings are not consistent.

**Aim**: a) To measure serum cholinesterase levels in diagnosed type 2 Diabetes mellitus patients.
b) To assess the correlation between serum cholinesterase and lipid indices in the above patients with respect to their BMI.

**Method:** Data of 30 out-patients with diagnosed type 2 DM (cases) and 30 age and sex matched healthy individuals from general population (controls) were collected and their blood drawn for serum cholinesterase, Fasting blood glucose (FBG) and lipid profile analysis in Beckman coulter Biochemistry auto analyser.

**Results:** Serum Cholinesterase was higher in cases compared to controls. Serum cholinesterase in cases was 9480.7 ± 1439.04 and in controls was 7092.9 ± 985.46 with t score of 7.4986 with P value of 0.0001 which is statistically very significant. Serum cholinesterase showed positive correlation with each of lipid indices namely total cholesterol (r score:0.8542 p:0.00001), triglycerides (r score:0.4334 p:0.05), LDL-C(r score:0.6939 p:0.0069), total cholesterol to HDL-C ratio (r score:0.4513 p:0.045) and negative correlation with HDL-C (r score:-0.447 p:0.0481) in the over-weight and obese patients of Type 2 DM as compared to their levels in the controls.

**Conclusion:** The results of this study indicate that serum cholinesterase may serve as a potential risk assessment marker of cardiovascular disease in type 2 Diabetes Mellitus.



***Citation:*** **Roopa, R., Maruthi Prasad, B. V. and Vishwanath, H. L. 2015.** "Serum cholinesterase in relation to lipid indices as cardio-vascular risk assessment marker in type 2 diabetes mellitus", *International Journal of Current Research,* 7, (12), 23904-23907.

## INTRODUCTION

Diabetes mellitus (DM) is a group of disorders characterized by chronic hyperglycaemia associated with disturbance of carbohydrate, fat and protein metabolism due to absolute or relative deficiency of insulin secretion or its action. Type 2 DM is a heterogeneous disease characterized by variable degrees of insulin resistance and increased glucose production. Insulin resistance occurs when the cells become less sensitive to the effects of insulin (Peter H. Bennett and Williams C. Knowles, 2005). Diabetes causes long term dysfunction of various organs like heart, kidneys, eyes, nerves and blood vessels. Age adjusted mortality rates among diabetics is 1.5 to 2.5 times higher than general population. Much of this increased mortality and morbidity is due to cardio vascular complications in diabetic patients (Park *et al*., 2013). 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 (Hanachi *et al*., 2009; Howard *et al*, 1993; Pryor and Squandrito, 1995). Cholinesterase represents a group of enzymes that hydrolyze acetylcholine and other choline esters.

**Two types of cholinesterase based on biochemical properties:**

**1. True or specific cholinesterase or acetylcholinesterase**

It is found in all excitable tissues (central and peripheral nervous system and muscles) and in erythrocytes. It is a high turnover enzyme with high affinity for acetylcholine, inhibited at high concentrations of acetylcholine, and with low affinity for non-choline esters (Davis *et al*., 1997).

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**2. Nonspecific or pseudo-cholinesterase or serum cholinesterase or butyrylcholinesterase (BChE) which hydrolyses both choline and aliphatic esters**

(BChE) is an αglycoprotein synthesized in liver. Found in the central and peripheral nervous system, in most tissues and in the liver. It has lower affinity for acetylcholine and is not inhibited by high concentrations of acetylcholine (Davis *et al*., 1997). BChE half-life is about 12 days (Ostergaard *et al*., 1988; Pan *et al*., 2009).

Normal value of BChE ranges between 4,900 and 11,900 U/L. An increased activity of BChE has been reported in obesity, diabetes, uremia, hyperthyroidism, and in hyper-lipidemic subjects (Acetylcholinesterase activity changes on visceral organs of VMH lesion-induced obese rats, 2006; Cucuianu *et al*., 2002; Kutty and Payne, 1994). BChE serum level decreases in many clinical conditions such as acute and chronic liver damage, inflammation, injury and infections and malnutrition.

## MATERIALS AND METHODS

Study was done on randomly selected 30 diagnosed type 2 DM out patients attending Victoria Hospital attached to BMC & RI. The study also included age and sex matched 30 healthy individuals from general population. Patients with liver dysfunction, renal dysfunction, essential hypertension, neoplastic diseases and on its treatment, also, Pregnant and lactating mothers were excluded from the study. After written informed consent, 5 ml of venous blood was obtained by venepuncture under aseptic conditions, centrifuged and the separated serum was used for estimation of serum cholinesterase, Fasting Blood Glucose (FBG) and lipid profile in Beckman coulter Biochemistry auto analyser.

### Study design

A case control study to measure serum cholinesterase levels in diagnosed type 2 Diabetes mellitus patients and to assess the correlation between serum cholinesterase and lipid indices in the above patients with respect to their BMI was undertaken.

### Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%).

Significance is assessed at 5 % level of significance. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups.

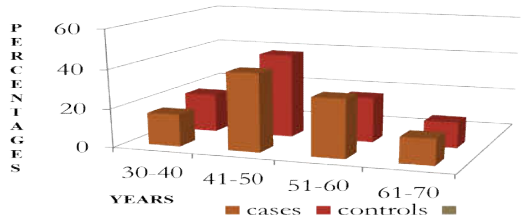
### Statistical software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

**Statistical analysis I. age distribution of cases and controls studied**

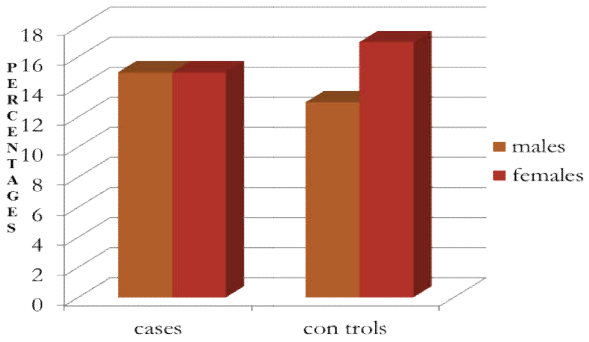
| Age group (in years) | Cases | Controls | Total |
|---|---|---|---|
| 30-40 | 05(16.67%) | 06(20%) | 11(18.33 %) |
| 41-50 | 12(40%) | 13(43.33%) | 25(41.67%) |
| 51-60 | 09(30%) | 07(23.33%) | 16(26.67%) |
| 61-70 | 04(13.33%) | 04(13.33%) | 08(13.33%) |
| **TOTAL** | **30** | **30** | **60** |
| Mean ± SD | 49.8±9.91 | 48.9±9.06 | |

**t score:0.3809 P value: 0.7047 not significant**




**II. GENDER DISTRIBUTION**

| Gender | Cases | Controls | Total |
|---|---|---|---|
| Male | 15(50%) | 13(43.33%) | 41(68.33%) |
| Female | 15(50%) | 17(56.67%) | 19(31.67%) |
| **Total** | **30** | **30** | **60** |

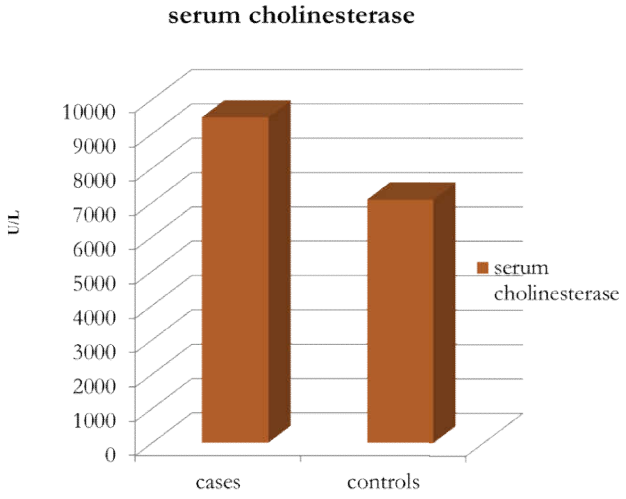



**P value: 0.604, chi square value :0.2679 not significant**

**III. Comparison of means of fasting blood glucose (FBG) and Serum Cholinesterase in two groups studied**

| Subjects | Total no. | Mean ± SD | |
|---|---|---|---|
| | | FBG | Serum Cholinesterse |
| Cases | 30 | 199.2 ±100.1 | 9480.7±1439.04 |
| Controls | 30 | 60.6 ± 11.1 | 7092.9±985.46 |

| | | |
|---|---|---|
| t score | 7.5378 | 7.4986 |
| P value | 0.0001** | 0.0001** |




**IV. Correlation between serum cholinesterase and Fasting blood glucose in type 2 diabetic patients studied**

| Parameter | | Fasting blood glucose |
|---|---|---|
| serum cholinesterase | r score | 0.4658 |
| | P value | 0.0094** |

**V. Correlation between serum cholinesterase and lipid indices in overweight and obese type 2 diabetic patients studied**

| Parameter | | Total cholesterol | Triglycerides | HDL-C | LDL-C | CHO/HDL |
|---|---|---|---|---|---|---|
| serum cholinesterase | r score | 0.8542 | 0.4334 | -0.447 | 0.6939 | 0.4513 |
| | P value | 0.00001** | 0.05+ | 0.0048* | 0.0069* | 0.045* |

**VI. Correlation between serum cholinesterase and lipid indices in normal BMI type 2 diabetic patients studied**

| Parameter | | Total cholesterol | Triglycerides | HDL-C | LDL-C | CHO/HDL |
|---|---|---|---|---|---|---|
| serum cholinesterase | r score | 0.2505 | 0.3343 | 0.1722 | 0.1667 | 0.1365 |
| | P value | 0.4851 | 0.3451 | 0.6342 | 0.6453 | 0.7069 |

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value:0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01)

**VII. Summary**

| Parameter | Mean ± SD | | t score | P value |
|---|---|---|---|---|
| | CASES | CONTROLS | | |
| FBG | 199.2 ±100.1 | 60.6 ± 11.1 | 7.5378 | 0.0001** |
| Serum cholinesterase | 9480.7±1439.04 | 7092.9±985.46 | 7.4986 | 0.0001** |
| Total cholesterol | 194.3±45.21 | 163.5±31.1 | 3.0743 | 0.0032** |
| Triglycerides | 272.7±216.9 | 119.5±50.4 | 3.7697 | 0.0004** |
| LDL-C | 109.6±41.6 | 106.2±22.5 | 0.3938 | 0.6952 |
| HDL-C | 36.4±9.94 | 42±13.6 | 1.8208 | 0.0738 |
| CHO/HDL ratio | 5.5±1.86 | 4.1±1.33 | 3.3535 | 0.0014** |

## DISCUSSION

In the present study, it was observed that the serum cholinesterase of cases was significantly higher than that of controls ($p<0.001$). It was also observed that when a correlational analysis was made between the serum cholinesterase and FBG, there was a positive correlation ($r= 0.4658$) which was statistically significant ($p< 0.01$). BchE may be involved in the pathogenesis of type 2 DM either by 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 (Johansen *et al*., 2004). In the present study, 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 respect to total cholesterol, moderate positive correlation with LDL-C and total Cholesterol to HDL-C ratio and also negative correlation with HDL-C which was statistically significant ($p< 0.05$) in overweight and obese type 2 diabetic patients compared to normal BMI type 2 diabetic patients.

The results of the present study is in accordance with a study done by Tomoyuki *et al*. (2007) who had reported that serum butyrylcholinesterase is strongly associated with adiposity, the serum lipid profile and insulin resistance. The results of the present study can also be compared with study done by Alcantara *et al*. (2002) who had shown that but yrylcholinesterase activity was positively correlated with age, sex, body mass index, hypertension and diabetes, as well as with albumin, triglycerides, total cholesterol, low-density lipoprotein cholesterol and apoprotein B (Apo B), and measures of overweight, obesity and body fat distribution, the traditional risk factors of coronary artery disease. Few of the studies like 'Serum but yrylcholinesterase in type 2 diabetes mellitus: a biochemical and bioinformatics approach' by Sridhar *et al*. (2005) showed but yrylcholinesterase enzyme was inversely related to serum cholesterol and Mauro M. Cwiertnia *et al*. (2010) suggested that the positive correlation of the BChE activities to diabetes mellitus and to insulin resistance may depend on the CHE2 locus variability which is not in accordance with the present study.

### Conclusion

This case control study showed that serum cholinesterase is seen increased in type 2 DM patients and suggests that serum

cholinesterase very much correlates with serum lipid indices in overweight and obese type 2 diabetic patients.

Hence, a easily available biochemical parameter, SERUM CHOLINESTERASE can be used as a potential RISK ASSESSMENT MARKER of cardiovascular disease in type 2 diabetes mellitus.

**Limitation**

Limitation of the current study is that community based study comprising large group of representatives is necessary to generalize serum cholinesterase as more specific tool in type 2 DM.

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