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Serum gamma glutamyl transferase and hs-CRP levels in patients with type 2 diabetes mellitus

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Abstract

Introduction: Type 2 diabetes mellitus and its complications is an important health problem.

As oxidative stress and inflammation appears to play a major role in the pathogenesis of diabetes mellitus and development of its complications; we intend to study the serum GGT activity and hs- CRP levels in type 2 diabetes mellitus without complications, type 2diabetes with complications and age and sex matched normal controls.

Materials and Methods: Study consisted of 75 subjects out of whom 25 subjects were type 2 diabetics without any complications, 25 subjects were type 2 diabetics with complications and 25 were age and sex matched normal controls. Serum GGT, serum hsCRP, FBS and glycated hemoglobin were measured in these subjects.

Results: Levels of serum hs- CRP and GGT is increased in type 2 diabetics without any complications and type 2 diabetics with complications, when compared to controls, which was statistically significant ($p < 0.001$).

Conclusion: Present study showed increase in the levels of hs- CRP and GGT levels in type 2 diabetics without complications and type 2 diabetics with complications when compared to healthy controls. These findings provide evidence that oxidative stress and inflammation plays a role in the pathogenesis of diabetes mellitus and development of its complications.

Keywords: Type 2 diabetes mellitus, Oxidative stress, Inflammation, Gamma glutamyl transferase, High sensitive C- reactive protein.

Introduction

Type 2 Diabetes mellitus because of its increased prevalence and increasing rate of complications has become a challenging health problem[(1)]. It is a metabolic disorder associated with chronic hyperglycaemia resulting from complete or partial decrease in insulin secretion or decrease in biological action of insulin or both. There is also alteration in protein, carbohydrate and lipid metabolism[(2)].

Stress due to oxidation of proteins and lipids and low grade inflammation have been involved in the development of diabetes mellitus and progression of its complications[(3)].

Gamma glutamyl transferase (GGT) is an enzyme that is critical for maintaining adequate levels of reduced glutathione, a major antioxidant. Increase in the levels of gamma glutamyl transferase enzyme may be considered as a hallmark for oxidative stress[(4)].

Obesity and non-alcoholic fatty liver disease (NAFLD) which causes insulin resistance in the liver and contributes to the development of systemic insulin resistance and hyperinsulinemia is associated with increase in the levels of gamma glutamyl transferase (GGT)[(5)].

CRP (C-reactive protein) is strong acute phase reactant that is increased in inflammatory and infectious conditions. It is considered as a marker for "inflammation". It consists of five identical non glycosylated polypeptide subunits and belongs to group of pentraxin family of proteins[(6)].

Highly sensitive assay of C- reactive protein is high sensitive C-reactive protein (hs CRP). Levels of hs-CRP act as a reliable marker of increased inflammation[(7)].

Chronic, systemic, subclinical inflammation has also been identified as a driving force for insulin resistance, metabolic syndrome and type 2 diabetes mellitus[(8)].

As stress due to oxidation of proteins and lipids and inflammation appears to play a major role in the pathogenesis of diabetes mellitus and development of its complications; we intend to study the serum GGT activity and hs- CRP in type 2 diabetes mellitus without complications and type 2diabetes with complications.

Materials and Methods

The study was a hospital based case control study conducted at K.S.Hegde Medical academy, Mangalore between December 2014 to May 2015.

Study population consists of 75 individuals, who were further divided into following groups:

Group I: Diagnosed cases of type 2 diabetics without any complications[(25)]

Group II: Diagnosed cases of type 2 diabetics with any complications[(25)]

Group III: Age and sex matched normal individuals as controls[(25)]

Selection Criteria:

Inclusion Criteria: Known cases of type 2 diabetes mellitus aged more than 40 years and less than 70 years.

Exclusion Criteria: Patients with type 1 diabetes mellitus, chronic alcoholics, known liver or gastrointestinal diseases, liver enzyme concentrations higher than three times the upper limit, systemic drug therapy like corticosteroids, methotrexate, amiodarone, tamoxifen or other hepatotoxic drugs, chronic infections like sarcoidosis, tuberculosis etc., hemolytic anemia and hemoglobin variants.

Ethical considerations: Approval by the institutional ethical committee was obtained. The objectives of the study were explained to all eligible subjects included in the study. Informed consent was sought from all participants.

Sample collection: After obtaining the consent, required data from the patient were obtained. By using aseptic precautions 5mL of blood is collected from anticubital vein after 8-12 hour fasting.

Serum is separated and stored at 2- 8^0 C temperature till analysis is done. Following parameters were estimated:

- Serum hs-CRP
- Serum Gamma Glutamyl Transferase
- Fasting blood sugar (FBS)
- Glycated haemoglobin(HbA_1C)

Sample Analysis: Fasting blood sugar was estimated by enzymatic reference method with hexokinase. (Kit: Quantitative determination of glucose by hexokinase method manufactured by roche diagnostics) on cobas c 311 automatic analyzer. Glycated haemoglobin was estimated by Immunoturbidimetric method. (Kit: Quantitative determination of glycated haemoglobin by immunoturbidimetric method manufactured by roche diagnostics) on cobas c 311 automatic analyser. Serum hs- CRP was estimated by measured by immunoturbidimetric method in erba semiautomatic analyzer (Kit: Turbidimetric immunoassay for ultrasensitive determination of C- reactive protein by tulip diagnostics). Serum GGT was estimated by carboxy substrate kinetic method (Kit: Quantitative determination of GGT by enzymatic method manufactured by tulip diagnostics.) in erba semiautomatic analyser.

Statistical Analysis

Statistical analysis was done using the SPSS software. Descriptive and inferential 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. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three groups of patients. p values < 0.05 was considered moderately significant, p values <0.01 was considered strongly significant.

Results

Our study showed significantly higher hs- CRP levels in type 2 diabetics without any complications and type 2 diabetics with complications, when compared to controls. ($p < 0.001$)

Serum GGT levels is also increased in type 2 diabetics without any complications and type 2 diabetics with complications, when compared to controls, which was statistically significant ($p<0.001$).

Table 1: FBS (mg/dl) and glycated haemoglobin (%) levels in three groups of patients studied

Study parameters	Group I DM without complications	Group II DM with complications	Group III Controls	p value
FBS(mg/dl)	185.12±52.40	243.32±58.94	93.88±7.75	<0.001
HbA_1C(%)	8.09±1.21	10.96±1.81	5.69±0.47	<0.001

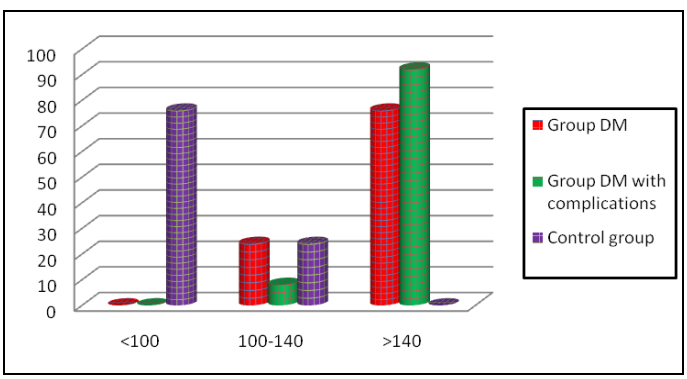

Fig. 1: Comparision of FBS levels between the study groups

Table 2: Comparision of serum hs- CRP between the study groups

Study parameters	Group I DM without complications	Group II DM with complications	Group III Controls	p value
hs- CRP (mg/dl)	0.21±0.07	0.42±0.12	0.07±0.05	<0.001

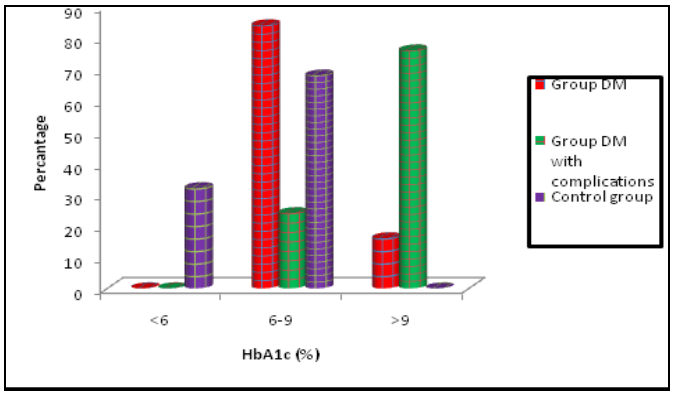

Fig. 2: Comparision of HbA $_1$C between study groups

Table 3: Comparison of serum GGT levels between the study groups

Study parameters	Group I DM without complications	Group II DM with complications	Group III Control	p value
GGT(IU/L)	40.00±8.82	56.34±15.07	20.96±8.14	<0.001

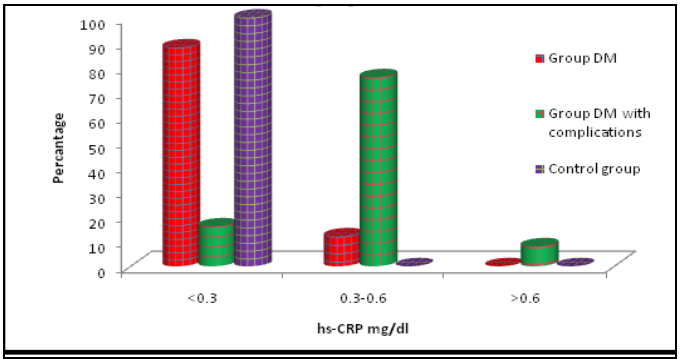

Fig. 3: Comparision of serum hs- CRP between the study groups

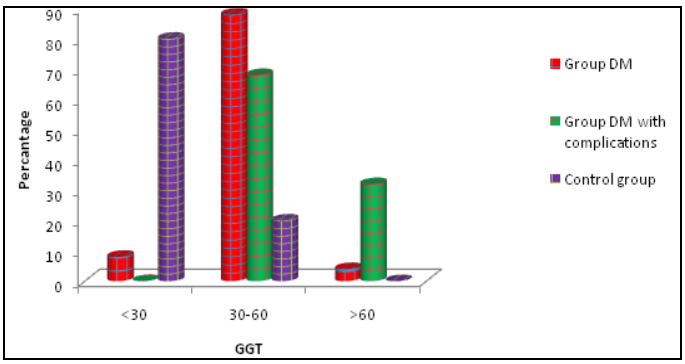

Fig. 4: Comparison of serum GGT between study groups

Our study showed significantly higher hs- CRP levels in type 2 diabetics without any complications and type 2 diabetics with complications, when compared to controls. ($p < 0.001$)

Serum GGT levels is also increased in type 2 diabetics without any complications and type 2 diabetics with complications, when compared to controls, which was statistically significant ($p<0.001$).

Discussion

In the present study a significantly high ($p<0.001$) increase in the levels of serum hs – CRP was observed in diabetics without complications and diabetics with complications when compared to healthy controls. These observations are in accordance to the findings of Baig MSA et. al[9].

Chronic subclinical inflammation is associated with resistance to the actions of insulin which favours the pathogenesis of type 2 diabetes mellitus and its complications[10]. Cytokines that induce inflammation - tumour necrosis factor alpha (TNF- α), interlukin-1 (IL-1), and interlukin - 6 (IL-6) are released by the adipose tissue in type 2 diabetes mellitus. They are involved in multiple metabolic pathways relevant to insulin resistance, including regulation of insulin secretion, free radical production, lipoprotein lipase action and adipocyte function[11].

Our study showed an increase in the levels of hs – CRP in diabetics with complications than without complications. hs- CRP activates complement system. It also produces recruitment of monocytes and enhances entry of LDL into macrophages. Increased endothelial production of E- selectin, ICAM- 1, and VCAM -1 which produces abnormal vascular reaction, decreased insulin transport and insulin resistance in the peripheral tissue[12].

Present study showed a significantly high ($p<0.001$) increase in the levels of serum GGT in type 2 diabetics without complications and type 2 diabetics with complications when compared to controls which is in accordance to the findings of Sharma R et. al[13]. Elevated GGT may be due to excess fat deposition in the liver. Hepatic insulin resistance can be due to fatty liver which in turn contributes to systemic insulin resistance[14].

Beta cells of pancreas and vascular endothelium are poor in scavenging the free radicals. Therefore beta cells are prone to oxidative stress. Defense against oxidative stress may produce increased GGT[15].

As oxidative stress may have a role in chronic inflammation, elevated hs - CRP and the oxidative stress would give rise to further inflammatory response[16].

Conclusion

Present study showed that serum GGT and hs - CRP levels are increased in type 2 diabetic without complications and type 2 diabetics with complications when compared to healthy controls. Serum GGT and hs - CRP also showed a positive correlation. These findings suggest that inflammation and stress due to oxidation of proteins and lipids may play a role in pathogenesis of type 2 diabetes mellitus and progression of its complications.

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