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Study of High sensitive C - reactive protein and Gamma-glutamyl transferase in Type 2 Diabetes Mellitus with Hypertension

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ABSTRACT

C-reactive protein (CRP), produced by the hepatocytes is a primary inflammatory marker of T2DM. Higher levels of gamma-glutamyl transferase enzyme (GGT) and Hs CRP (High sensitive CRP)are associated with the complication of poor glycemic control. This study was aimed to find the association of Hs CRP and GGT for cardiovascular risk factors in Type 2 diabetes mellitus (T2DM) and Hypertension in the suburbs of Chennai. This study includes 57 subjects with T2DM and Hypertension (Group A) and 62 subjects with T2DM (Group B) within the age group of 40-60 years. FBS, HbA1C, Hs CRP, GGT and blood pressure were determined. Mean values of FBS, blood HbA1C, Hs CRP and GGT were significantly higher among participants of Group A than Group B. Significant difference of FBS, HbA1C were found between the two groups. In contrast, no significant difference of GGT was found between the groups. Differences were considered statistically significant at two-sided $P < 0.05$. Within the group, Hs CRP shows the significance and positive correlation with FBS, SBP and DBP. Still, GGT does not show any significance in Group A. In contrast, in Group B, both Hs CRP and GGT shows the importance and positive correlation with FBS and HbA1C. It is concluded that high levels of HsCRP are associated with T2DM and Hypertension, indicating increased cardiovascular risk, and it should be included in regular monitoring of type-2 diabetic patients.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global issue, and it is associated with disturbances in protein, carbohydrate and lipid metabolism due to decreased uptake of glucose into muscle and adipose tissue resulting in tissue damage and chronic vascular complications (Wild *et al.*, 2004; Fowler, 2011). Chronic low-grade inflammation with increased production of inflammatory markers has been attributed to the development of T2DM (van Woudenbergh *et al.*, 2011).

Various Prevalence studies have shown that Hyper-

tension is common among patients with T2DM and depends on duration, age, sex, race, glycemic control, and the presence of kidney disease. Furthermore, Hypertension is a risk factor for atherosclerotic cardiovascular disease and microvascular complications. It is the leading cause of morbidity and mortality for individuals with T2DMand is the most significant cause for the direct and indirect effects of diabetes. (Arauz-Pacheco *et al.*, 2003; Ettehad *et al.*, 2016) (Thomopoulos *et al.*, 2017).

C-reactive protein (CRP), produced by the hepatocytes, is considered to be a primary inflammatory marker of T2DM. It markedly increased in both inflammatory, infectious diseases and it is a potential marker of cardiovascular risk in patients with Hypertension. (Blake *et al.*, 2003; Cortez *et al.*, 2016). Serum CRP above 3.0 mg/L is regarded as a worse cardiovascular prognosis, and more than 50% of deaths in diabetic patients are attributed to cardiovascular diseases (Sabatine *et al.*, 2007; Group, 1996). Higher CRP can initiate atherosclerosis and clot formation, so, therefore, it will be advantageous to reduce the plasma levels of CRP (Fowler, 2011). This HsCRP is the most evaluated biomarker for cardiovascular disease (CVD) risk prediction and techniques are available that can detect CRP in a sensitivity range of 0.01 to 10 mg/ l. (Ridker *et al.*, 2007; Rosen *et al.*, 2001).

Gamma-glutamyl transferase (GGT), an enzyme, produced in many tissues, mainly derived from the liver (Iqbal *et al.*, 2010) and it is needed to maintain the levels of reduced glutathione, a major antioxidant. Increase in the levels of gamma-glutamyl transferase is an indicator for oxidative stress (Pleiner *et al.*, 2003) and this leads to chronic inflammation which enhances inflammatory response and associated with complications of poor glycemic control. Studies have already reported that there is an association of Hs CRP as an inflammatory marker and GGT as an oxidative marker in T2DM and Hypertension (van Woudenbergh *et al.*, 2011; Blake *et al.*, 2003; Pleiner *et al.*, 2003). Our objective was to study the association of Hs CRP and GGT for cardiovascular risk factors in T2DM and Hypertension in the suburbs of Chennai.

STUDY SETTINGS

Materials and Methods

This study was conducted for three months among Type 2 Diabetes mellitus and Hypertensive patients who visited the General Medicine Department, ACS hospital, Chennai, institutional ethics committee approved the study protocol.

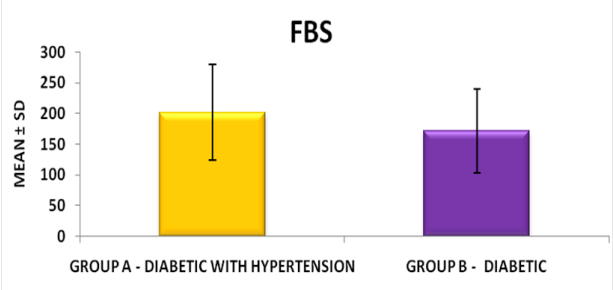

Figure 1: Graphical representation of mean ± standard deviation (FBS)

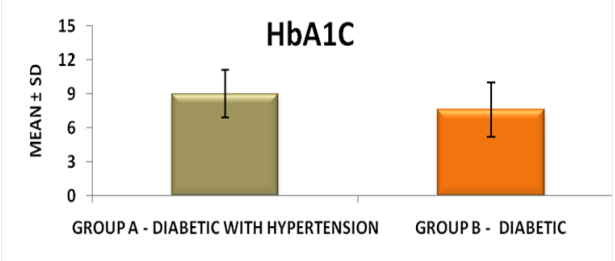

Figure 2: Graphical representation of mean ± standard deviation (HbA1C)

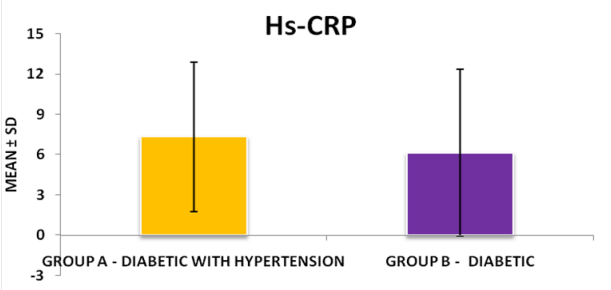

Figure 3: Graphical representation of mean ± standard deviation (Hs-CRP)

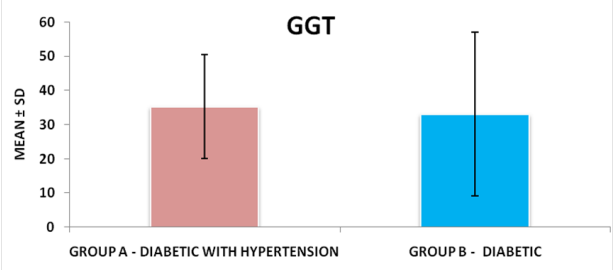

Figure 4: Graphical representation of mean ± standard deviation (GGT)

Inclusion criteria

The study population included 119 patients with Type2 diabetes mellitus. The age group of the study participants was 40-60 years, consists of 57 subjects with T2DM and Hypertension (Group A)and62 subjects with T2DM (GroupB). All the participants were provided with an information sheet, and informed written consent was obtained. A structured questionnaire including the demo-

Table 1: Gender Distribution

			GROUP		Total
			GROUP A - DIABETIC WITH HYPERTENSION	GROUP B - DIABETIC	
GENDER	MALE	Count	30	26	56
		% within GROUP	52.6%	41.9%	47.1%
	FEMALE	Count	27	36	63
		% within GROUP	47.4%	58.1%	52.9%
TOTAL		Count	57	62	119
		% within GROUP	100.0%	100.0%	100.0%

Table 2: Mean ± standard deviation of FBS, HbA1C, Hs CRP, and GGT

	GROUP	N	Mean	Std. Devaiation	Sig
FBS	GROUP A - DIABETIC WITH HYPERTENSION	57	201.9154	78.43414	
	GROUP B - DIABETIC	62	172.1811	68.38599	0.029*
HbA1C	GROUP A - DIABETIC WITH HYPERTENSION	57	9.000	2.1335	
	GROUP B - DIABETIC	62	7.568	2.3788	0.001*
Hs-CRP	GROUP A - DIABETIC WITH HYPERTENSION	57	7.347	5.5656	
	GROUP B - DIABETIC	62	6.145	6.1944	0.050*
GGT	GROUP A - DIABETIC WITH HYPERTENSION	57	35.212	15.1873	
	GROUP B - DIABETIC	62	33.095	23.9820	0.101

*p< 0.05, *** p< 0.001

Table 3: Group A -Hs CRP Correlation with FBS, HbA1C, GGT, SBP, DBP

	FBS	HbA1C	GGT	SBP	DBP
Correlation Coefficient	.179*	.028	.162	.341***	.325**
Sig. (2-tailed)	.050	.762	.078	.000	.001
N	57	57	57	57	57

*p< 0.05, *** p < 0.001

Table 4: Group A - GGT Correlation with Hs CRP, FBS, HbA1C, SBP, DBP

	HsCRP	FBS	HbA1C	SBP	DBP
Correlation Coefficient	.162	.118	.083	.012	.074
Sig. (2-tailed)	.078	.195	.367	.901	.423
N	57	57	57	57	57

*p< 0.05, *** p < 0.001

Table 5: Group B Correlation of Hs CRP with FBS, HbA1C, GGT

	FBS	HbA1C	GGT
Correlation Coefficient	.247**	.240**	.037
Sig. (2-tailed)	.005	.006	.675
N	62	62	62

**p<0.01

Table 6: Group B- Correlation of GGT with Hs-CRP, FBS and HbA1C

	Hs-CRP	FBS	HbA1C
Correlation Coefficient	.037	.183*	.210**
Sig. (2-tailed)	.675	.037	.017
N	62	62	62

*p<0.05, ** p< 0.01

graphic details, present and past medical history, surgical history, any recent infections, drug history and intake of steroids was obtained.

Exclusion criteria

Smokers, alcoholics and patients with chronic liver diseases, renal diseases, recent surgeries were excluded from the study.

Methodology

The recruited subjects were asked to visit the hospital after an overnight fast of 10 – 12 hours, 5mlof the Blood sample was collected in EDTA tube. It was used to estimate the fasting blood glucose by glucose oxidase peroxidase enzymatic endpoint method, HbA1c by resin exchange method, Hs CRP by immunoturbidimetry (Rifai *et al.*, 1999) and GGT by modified IFCC method (Schumann *et al.*, 2002). Liver enzymes, lipid profile, renal function test and blood parameters were also determined by using standard laboratory procedures.

Systolic pressure and diastolic pressure were determined by using digital sphygmomanometer in the sitting position on the left arm. Three recordings were taken after at least 10–15 min of rest. Then, the average of the three readings was obtained.

RESULTS

A total of 119 subjects between the ages of 40 – 60 years, and it includes 56 males and 63 female Table 1. Data were presented as mean ± standard deviation, differences among groups were calculated using t-test or Mann-Whitney test for parametric and nonparametric variables, respectively. Chi-square test was used. Mean values of FBS, blood HbA1C, Hs CRP and GGT were significantly higher among participants of Group A than Group B (Figure 1, Figure 2, Figure 3 and Figure 4). A significant difference of FBS, HbA1C were found between the two groups, whereas no significant difference of GGT was found between the groups Table 2. Differences were considered statistically significant at two-sided $P < 0.05$. Statistical analysis was performed using Statistical Package for the SPSS 17 version.

The correlation analysis was performed by Kendall's tau method for nonparametric variables respectively. Hs CRP shows significance and positively correlated with FBS, SBP and DBP but GGT does not show any significance in Group A, whereas in Group B both Hs CRP and GGT shows significance and positive correlation with FBS and HbA1C. (Table 3, Table 4, Table 5 and Table 6).

DISCUSSION

In our study serum, Hs CRP Levels are significantly associated with T2DM in both Group A (T2DM and Hypertension) and Group B (T2DM) and shows a positive correlation with FBS, HbA1C, SBP and DBP. It was found that diabetic patients had a significantly elevated median of HbA1c, HsCRP and GGT as compared to controls (Khan and Qayyum, 2009; Sharma *et al.*, 2010). Suhadbahijri (2018) shows that high levels of Hs-CRP and GGT are associated with Hypertension and poor glycemic control, indicating increased cardiovascular risk. There was an elevated and significantly higher Hs CRP among hypertensive when compared with Normotensive, and a similar correlation was found in HsCRP with pre-hypertension with age-matched groups (Sinha *et al.*, 2014). Elevated HsCRP and Hypertension-leads to Increased cardiovascular risk. The combination of greatly increases the (Jiménez *et al.*, 2015; Hui-Liu *et al.*, 2019). Similar results were found in Group A of our study where Hs CRP shows the significance and positively correlated with SBP and DBP.

On analysis of GGT values, there was a mean difference of GGT between the groups (Group A 35.2U/I and Group B 33U/I), but it does not show any significant differences in-between the Groups. Low-grade hepatic inflammation induced by hepatic steatosis results in increased production of GGT; this could cause oxidative stress. This increase in GGT synthesis can lead to over utilization of glutathione. (Kunutsor *et al.*, 2015). Similarly, in this study also Hs CRP and GGT were significant and shows a positive correlation with FBS and HbA1C in Group B. Elevated serum GGT could be a cardiometabolic risk factor either as a mediator of low-grade systemic inflammation and oxidative stress results from elevated serum GGT could be a car-

diometabolic risk factor due to transport of glutathione into the cells. (Alissa, 2018). Statistical significance and correlation were not found for GGT within the various variables of T2DM and Hypertension.

CONCLUSION

It is concluded that increased levels of hs-CRP are associated in T2DM with Hypertension, which could lead to increased cardiovascular risk, and it should be included in the regular monitoring of diabetic patients. Further studies are needed to find the effect of GGT in diabetic and hypertension subjects using a bigger sample size.

ABBREVIATIONS

T2DM- Type 2 Diabetes Mellitus, FBS-Fasting blood sugar HbA1C –Glycated haemoglobin, Hs CRP-High sensitive C-Reactive protein, GGT-Gamma-glutamyl Transferase, SBP-Systolic Blood Pressure, DBP-Diastolic blood pressure.

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Conflict of Interest

There is no conflict of interest among authors.

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