ASSOCIATION OF γ-GLUTAMYLTRANSFERASES (GGT) WITH AND WITHOUT HYPERTENSIVE RETINOPATHY IN NORTH INDIAN POPULATION

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ABSTRACT

 γ -Glutamyltransferase (GGT) has been extensively studied because it mediates the intracellular uptake of extracellular glutathione, a key component of the antioxidant mechanism. The most common modifiable risk factor for cardiovascular disease is hypertension, and has been found to be associated with serum GGT levels, especially in middle-aged and older adults. Serum GGT is involved in the pathogenesis of hypertension. A case-control study was conducted for 24 months with patients with pre-diagnosed hypertension in the ophthalmology department. Patients were classified into two groups, group 1 with 50

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patients previously diagnosed hypertensive patients aged 40 years without hypertensive retinopathy and group 2 (100 patients) with had hypertensive retinopathy. Serum gamma-glutamyl- transferase was measured using the CORAL Colorimetric Assay Kit. Majority of patients were aged between 40 to 59 years and were females. SBP, DBP and MAP significantly increased in group 2 when compared with group 1. Majority of group 2 patients had GGT levels >40 U/l (89.0%), while the majority of group 1 had her GGT levels less than <40 U/L (62.0%). According to our study, GGT was significantly increased in patients with high blood pressure (SBP and DBP) and a family history of hypertension.

KEYWORDS: GGT, Retinopathy, MAP

INTRODUCTION

The prevalence of hypertension is increasing worldwide due to aging populations and lifestyle changes including unhealthy diet and lack of exercise. ¹In 2010, approximately 1.39 billion adults worldwide had hypertension, and the latest projections show that the prevalence will increase by 30% by the year 2025, exposing nearly 2 billion individuals to risk of hypertension and associated comorbidities.ⁱⁱ Several systems such as cardiovascular, renal, cerebrovascular and retinal are affected by uncontrolled hypertension (HTN). Damage to these systems is called as target organ damage (TOD).ⁱⁱⁱ

 γ -glutamyltransferases (GGTs) have been extensively studied because they mediate the intracellular uptake of extracellular glutathione, a major component of antioxidant mechanisms. Glutathione is produced during normal metabolic processes and plays a crucial role in protecting cells against oxidative stress. Although various contemporary studies have found GGT to be useful as an indicator of liver dysfunction and as a marker of years of alcohol consumption, ^{ivy} but recent documentation found that elevated GGT levels and increased age A positive interaction

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between higher GGT levels and advanced age, , increases in body mass index (BMI), male gender ,smoking, tachycardia, sedentary life style, hypertension, , hyperglycemia, increased LDLcholesterol, and decreased HDL-cholesterol levels, menopause, hypertriglyceridemia, and oral contraceptive use has been reported after exclusion of alcohol consumption vi,viii.

Serum GGT and its role in the developing hypertension and also has a correlation with increased level of arterial stiffness ^{viii,ix}. However it has been established that regardless of the mechanism, younger population with prehypertension exhibit greater serum GGT levels compared with healthy counterparts, but the isolated increase in GGT levels are associated with impaired aortic elasticity in patients with prehypertension.^x Further, hypertension being the primary most common modifiable risk factor for cardiovascular disease, exclusively in middle-age individuals and the elderly has been found to be related to serum GGT levels. Serum GGT is found to

Hypoxia or any other modification in mitochondrial

function, caused by hypertension, are the main conceivable cause of the oxidative stress in hypertensive retinopathy. Disregarding the manner in which hypertension progresses, reactive species of oxygen still remain a leading and fundamental element in the pathogenesis of hypertensive retinopathy. Constantly enhanced levels of hypertension generate an increase in reactive species of oxygen, that, in break the balance in the retina, repercussion, predisposing to cytotoxicity and tissue damage, that are identified on fundoscopy by the ophthalmologist and allow the grading of the qualitative extent and progression of hypertensive retinopathy.^{xiv}

Though literature evaluating association of GGT with hypertensive retinopathy is limited, which can be partly because of the fact that GGT is known to be associated with CVD and Hypertension independently.

MATERIALAND METHODS

This Case Control Study was held at Department of Ophthalmology in a tertiary care center of north India, for 24 months with patients pre-diagnosed with hypertension with and without hypertensive retinopathy. Patients were divided into 2 group, Group 1(50 patients) Prediagnosed hypertensives aged above 40 years without hypertensive retinopathy and Group 2 (100 patients) Prediagnosed hypertensives aged above 40 years with hypertensive retinopathy. Patients with co-existing medical illness such as diabetes mellitus, hepatic or/and renal disease, cardiac/cerebral illness, dyslipidemia, recent major surgery or illness, with any ocular media opacity, with history of anti-epileptic drug intake were excluded from the study. Clearance for carrying out the study was obtained from the Institutional Ethical Committee and informed consent was taken from all the participants.

Patients underwent complete ocular examination which included uncorrected vision and the best Corrected vision using the Snellen's Chart, Torch light examination, Distant Direct Ophthalmoscopy, Applanation Tonometry, Slit lamp examination and fundus examination with +90D lens using Zeiss SL 115 Classic Zeiss Style Slit Lamp. Indirect ophthalmoscopy was also done using +20 D lens followed by slit lamp examination using 90D for evaluation of hypertensive retinopathy.

2ml of blood sample was obtained from all study subjects under aseptic conditions and Serum estimation of Gamma-glutamyl transferase was done using CORAL Colorimetric assay kit.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

S.N.	PARAMETER	SUBTYPES	Group 1 (n=50)		Group 2 (n=100)			
			No.	%	No.	%	$\chi^2 = 23.413$	
1.	Age Group	40-49 years	22	44.0	28	28.0	(df=6); p=0.001	
		50-59 years	14	28.0	32	32.0		
		60-69 years	11	22.0	26	26.0		
		\geq 70 years	3	6.0	14	14.0		
2.	Gender	Female	36	72.0	55	55.0	$\chi^2 = 8.158 (df = 2);$	
		Male	14	28.0	45	45.0	p=0.017	
3.	Family H/o HTN		41	82.0	83	83.0	χ^2 =9.204; p=0.010	
4.	Blood Pressure category (mm Hg)	Normal (<120 and <80)	17	34.0	14	14.0	$\chi^2 = 46.706;$	
		Prehypertension (SBP 120-139) (DBP 80-89)	7	14.0	17	17.0	p<0.001	
		High blood pressure (Hypertension) Stage 1 (SBP -140-159) (DBP-90-99)	23	46.0	49	49.0		
		High blood pressure (Hypertension) Stage 2(SBP->=160) (DBP->=100)	3	6.0	20	20.0		

RESULT

Table 1: Age, Gender, Family h/o HTN & Blood Pressure Distribution According JNC 8 Guidelines

Majority of patients in Group 2 (58.0%) were aged between 50 to 69 years, while in Group 1majority were aged between 40 to 59 years (72.0%).On comparing statistically, a significant difference was observed among the groups for age. Majority of patients in Group 1 & Group 2 were females (72.0% & 55.0% respectively). On comparing statistically, a significant difference among the groups was observed for gender. On comparing statistically, a significant difference was observed among the groups for family history of hypertension.

SBP were elevated sharply in Group 2 as compared Group 1 (140.34±17.89 vs. 130.12±15.44 mmHg) also,DBP were elevated in Group 2 as compared Group 1 (89.46±10.94 vs. 83.80±7.53mmHg) therefore, MAP were elevated in Group 2 as compared Group 1 (106.46±12.54 vs. 99.24±8.34 mmHg).

Majority of patients in Group 2 had GGT levels >40 U/l (89.0%), while majority in Group 1 had GGT levels <40 U/l (62.0%) .Statistically, a significant difference was observed among the two groups for GGT levels. A stastifically significant difference was also found between the two groups for GGT levels. Mean difference between the two groups was 7.080, which was also statistically significant.

S.N.	Blood	Group 1 (n=50)		Group	2 (n=100)	ANOVA	
	Pressure (mm Hg)	Mean	SD	Mean	SD	F	ʻp'
1	SBP	130.12	15.44	140.36	17.89	20.861	<0.001
2	DBP	83.80	7.53	89.46	10.94	11.871	<0.001
3	MAP	99.24	8.34	106.46	12.54	18.686	<0.001

 Table 2: Mean Blood pressure Distribution

S.N.	PARAMETER		Group 1 (n=50)		Group 2(n=100)		
			No.	%	No.	%	
1	GGT levels	≤40	31	62.0	11	11.0	χ2=113.164; p<0.001
		>40	19	38.0	89	89.0	
2	Mean±SD		39.46±2.77		46.54 ± 6.48		F=339.93p<0.001
3	Mean Diff			7.080			<0.001

Table 3: Distribution of GGT Levels and GGT Mean

DISCUSSION

Hypertension is the most common preventable risk factor for cardiovascular disease Chronic Kidney Disease (CKD) and the leading single cause of death and disability among all causes worldwide ^{xv} It also increases the risk of developing and progressing diabetes retinopathy, glaucoma, and age-related macular degeneration. Successful prevention and treatment of hypertension is key to reducing the disease burden and promoting longevity for the world's population.

GGT plays a role in the pathophysiological processes which includes oxidative stress and lipid peroxidation, which are crucial to the pathogenesis and development of insulin resistance and the metabolic syndrome ^{xvi} Increased serum levels of GGT is seen in individuals who consume excessive alcohol, but apart from that a number of studies have shown that serum levels of GGT also directly correlates with elevated risk of hypertension, diabetes, and metabolic syndrome ^{xvii}

A total of 150 patients were enrolled in this study. The

age of the study population ranged from 40 to 85 years, with a mean age of 53.51 ± 9.60 years. The majority of patients were female, (56.5%). Besharat et al. (2006)^{xviii} conducted a study of patients aged 25–85 years, mean age 64.47 ± 10.66 years. Ebnik et al. (2007)^{xix} included patients aged between 30 to 74 years in the study. Omotoso *et al.* (2016)^{xx} reported in their study a majority of women (77.7%) with a mean age of 58.9 years.

This study was conducted to assess the relevance of her GGT levels in patients with and without hypertensive retinopathy. In our study, SBP, DBP, and MAP were elevated in patients with retinopathy (140.36 ± 17.89 mmHg, 89.46 ± 10.94 mmHg and 106.46 ± 12.54 mmHg respectively) as compared to hypertensive patients with no retinopathy (130.12 ± 15.44 mmHg, 83.80 ± 7.53 mmHg, 99.24 ± 8.34 mmHg respectively). A similar finding was made by Valizadeh et al. (2018) ^{xxi} they reported higher SBP & DBP in patients with retinopathy compared to patient without retinopathy. Although they did not identify a mean difference between the and groups.

GGT was found to be significantly increased in patients with hypertensive retinopathy (46.54 \pm 6.48 U/L) compared to hypertensive patients without retinopathy (39.43 \pm 2.78 U/L). Karaka et al. (2013) ^{xxii} reported similar findings that her GGT level was significantly elevated in the three groups after comparing her GGT between grade I and grade II retinopathy and controls. Divia et al. (2019) ^{xxiii} also reported that her GGT was significantly increased in patients with retinopathy compared with those without retinopathy.

The results of the current study, conducted during the COVID-19 pandemic, made it more interesting and allowed us to document the association between serum GGT and hypertensive retinopathy.

CONCLUSION

A diagnosis of COVID-19 is generally associated with SARS which includes dry cough, fever, and breathing difficulties. However, studies suggest that hepatobiliary complications (high GGT) are prevalent in COVID-19 patients . Even though none of the COVID positive patients were taken for the study but COVID history was not taken before enrolling the patients which might affect the results.

According to our study ,GGT was significantly increased in patients with higher blood pressure (SBP and DBP) levels and with a positive family history of hypertension. It was also observed that GGT was directly proportional with hypertensive retinopathy. Mean GGT was maximally raised in patients of hypertensive retinopathy as compared to hypertensives without retinopathy. Therefore, GGT levels are associated with the disease and therefore we might used it as one of the biomarkers for early diagnosis of hypertensive retinopathy.

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