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Original Research Paper

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STUDY ON ELEVATED SERUM GAMMA-GLUTAMYL TRANSFERAGE (GGT) LEVEL TO EVALUATE ITS CLINICAL RELEVANCE IN PATIENTS FROM DIFFERENT INDIGENOUS COMMUNITIES IN A TERTIARY CARE CENTRE, RIMS RANCHI JHARKHAND INDIA

Neelam Kumari	Senior Resident, in Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi.
Chandra Bhushan Sharma	Professor, in Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi.
Rishi Tuhin Guria	Associate Professor, in Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi.
Sanjay Kumar*	Associate Professor, Department of Forensic Medicine and Toxicology, Rajendra Institute of Medical Sciences(RIMS),Ranchi. *Corresponding Author
Piyush Kumar	Junior Resident, in Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi.
Vikram	Junior Resident, in Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi.
Tapan	Junior Resident, in Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi.

ABSTRACT

Very few studies have examined the interaction between various environmental and life style factors on elevated serum GGT concentration. Such studies especially in tribal dominated Jharkhand is further rare. Whereas the present study has been done to elucidate the interaction between overweight/obesity and alcohol intake on liver enzyme concentrations and results of instant study have been found to be very useful for better clinical practice. In the instant study, it has been found that higher Body Mass Index (BMI) of patients were associated with elevated Serum GGT level, which in turn associated with hypertension, incident diabetes, metabolic syndrome, cardiovascular disease etc., which increases the morbidity and mortality.

Aims & Objectives-

The aim of this study is to examine the association between various environmental and lifestyle factors on elevated serum GGT level in a community based indigenous population in Eastern part of India and its clinical relevance.

Material And Methods

The present study enrolled a total of 404 patients either through outdoor or indoor patients coming to Department of Medicine, RIMS, Ranchi, Jharkhand. Patients with serum GGT concentrations > 38 IU/L and aged 18 years or above from all different communities were included for the study. Additionally, we excluded patients with Serum GGT level < 38 IU/L, yielding a final sample of 193 patients (75 women) for the present study. All patients provided written consent, and the study protocol was approved by the Institution Review Board of the Rajendra Institute of Medical Sciences, Ranchi, Jharkhand. Participants' age, gender, religion followed by community, occupation with annual per capita income, BMI were recorded. Retrospectively participants' dietary habits were also recorded.

Strengths And Limitations

The present study has several strengths including the community based sample of men and women, their religion, occupation, income which indirectly affect their life style like physical activity. However, there are several limitations that must be noted like small sample size, localized population of Eastern India, which limits the generalizability of our result to other ethnic groups.

KEYWORDS :

BACKGROUND

Serum GGT is not the only marker of chronic liver disease, it does predict future diabetes, coronary heart disease, stroke (1,2). In clinical practice, serum GGT is measured as a marker of excessive alcohol consumption or of hepatic disease. GGT is secreted by liver as well as other tissues including the kidneys, vascular pericytes in the brain (3,4). GGT has a primary role in Glutathione metabolism, and acts as an antioxidant in the metabolism of amino acids to maintain intracellular Glutathione levels (5). GGT may also have a pro-oxidant activity by promoting the generation of free radical species in presence of free metal ion (6). Evidence from epidemiologic studies show that higher serum GGT Concentration are associated with greater risk of hypertension (7), incident diabetes (8,10), metabolic syndrome (10,11), cardiovascular disease(11,14) and all cause mortality including CVD mortality(17) including CVD mortality (15,16). These associations of GGT with adverse sequelae were independent of alcohol consumption (9).

RESULTS

A total number of 193 patients, from different indigenous communities, aged 18 years and above (mean age-43.52 years, 38.9 % women) with elevated Serum GGT level 38 IU/L and above coming to tertiary health care centre, Department of Medicine (both indoor and outdoor) Rajendra Institute of Medical Science (RIMS), Ranchi, Jharkhand, India were included in this study. Overall 47.77% patients had Serum GGT ≥ 38 IU/L. Measures included serum GGT, BMI, self reported physical activity, alcohol intake along with patient's occupations, religion, dietary habits and other co-morbid conditions (like Chronic liver disease, hypertension, diabetes etc.) prevalent in community were.

Measurement of GGT and other environmental and life style factors

Serum GGT was measured in the morning sample after 8 hours of overnight fast. Patients underwent phlebotomy, the blood was immediately centrifuged, plasma and serum

separated and stored under -20 ^{0}C until assessed. GGT activity was measured in plasma using Kinetic Photometric procedure with Cobra Integra 800. The inter assay coefficient of variation for GGT using this method is less than 4% (18).

BMI was calculated from baseline measurement using the formula Weight in Kilogram/ (height in meter)^{2}.

Physical activity were measured using a 7-days recall method in which patients were asked to report daily physical activities of at least 30-minutes duration of moderate intensity and categorized as Sedentary (little or no exercise), moderately active (construction workers or person running one hour daily), vigorously active (agricultural worker or person swimming 2 hours daily) and extremely active (competitive cyclist).

Alcohol consumption was collected by recall diary and converted to number of standard drinks per week and categorized as light drinker (≤ 3 drinks per week on average over past year or at least 12 drinks in past year), moderate drinker (3-7 drinks per week for female, 3-14 drinks per week for male) and heavy drinker (≥ 8 drinks per week for female, ≥15 drinks per week for male).

Dietary habit was measured on recall method, whether vegetarian or non vegetarian and number of nonvegetarian servings taken per week were recorded.

Liver Function Test, Renal Function Test, Random Blood Sugar, lipid profile and ultrasound abdomen along with other relevant clinical investigations were done in all the patients and accordingly study inference and conclusion were drawn.

Statistical Analysis

For statistical analysis we used SPSS Model 16. Data are presented as mean ± SD unless indicated otherwise. We built adjusted models with age, gender, religion (Tribal, Nontribal or Mohammedan), occupation with their annual income per capita (Low, Low Middle, Upper Middle, High), dietary habits, alcohol consumption, physical activity, BMI, presence of co-morbidities. A two sided P value <0.05 was considered statistically significant. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

RESULTS

Demographic characteristics of study patients are displayed in Table 1. In our study clinical correlates of circulating Serum GGT included age, gender, alcohol consumption, religion followed by social communities, dietary habits, Body Mass Index (BMI), Physical activity and co-morbidities prevalent in community.

Table-1baseline Characteristics Of Study Participants

Characteristics	Category	Numbers	Percentage
Age (Years)	15-30	53	27.50
	31-45	60	31.10
	46-60	44	22.80
	61 and above	36	18.70
Gender	Male	118	61.10
	Female	75	58.90
Occupation	Farmer	36	18.70
	Housewife	64	33.20
	Office worker	09	04.70
	Self employed	70	36.30
	Unemployed	14	07.30
Social Community	Tribal	71	36.80
	Non tribal	100	51.80
	Mohammedan	22	11.40
Dietary Habit	Non vegetarian	177	91.70
	Vegetarian	16	08.30
Alcohol Consumption	Yes	133	68.90
	No	60	31.10
Physical Activity	Sedentary	137	71.00
	Moderate activity	56	29.00
BMI	<20	04	02.10
	20-24	177	91.70
	25 and above	12	06.20
Co-morbidities (prevalent in community)	Hepatorenal	112	58.00
	Cardio/ Cerebro-	33	17.10
	Endocrine	08	04.10
	Infectious	21	14.00
	Others	13	06.70

We first calculated prevalence of elevated Serum GGT levels with age. With mean age of patients 43.52 (Range- 61, SD-16.12,Variance-260.053), we found some association with elevated Serum GGT level (P value-0.072),but statistically not significant (Table 2).

Table- 2 Association of Age with elevated Serum GGT level.

Age	Range	Mean ± SD	Chi-Square Value	df	P Value
	61	43.52 ± 16.12	19.769	12	0.072

Statistical Analysis for gender (58.9% women) also showed association with elevated Serum GGT level (Chi Square value-7.903, df-4,P Value-0.095), but statistically not significant.

For Body Mass Index (BMI) 91.70% patients had BMI between 20-25 with mean 22.76 which was significantly associated with elevated Serum GGT level (Variance-2.63) (Table3).

Table- 3 Association Of BMI With Elevated Serum GGT Level.

Body Mass Index (BMI)	Range	Mean ± SD	Chi-Square Value	df	P Value
	10.0	22.76 ±16.12	24.062	08	0.002*

* Significant Association.

In dietary habits 91.7% patients were Non vegetarian with mean number of servings of Non Vegetarian food was 1.44 per week, SD-0.276 and variance 1.43. It has not shown any statistically significant association with elevated Seum GGT level (Table 4).

Table- 4 Association Of Dietary Habit With Elevated Serum GGT Level.

Dietary Habit	Range	Mean ± SD	Chi-Square Value	df	P Value
	61	43.52 ± 16.12	7.549	4	0.110

In our study sample, 36.3% patients were self employed, followed by 33.2% housewife and 18.27 % farmers. They again showed no statistically significant association with serum GGT level (Table 5).

Table- 5 Association Of Occupations With Elevated Serum GGT Level.

Occupations	Chi-Square Value	df	P Value
Farmer	16.892	16	0.393
Housewife			
Office Worker			
Self employed			
Unemployed			

In Socio-community analysis, 51.8% patients were non-tribal, 36.8% tribal and 11.4% mohammedan. However, our study did not reveal any statistically significant association with elevated serum GGT level (Table-6).

Table- 6 Association Of Social Community With Elevated Serum GGT Level.

Social Community	Chi-Square Value	df	P Value
	4.954	8	0.763

About 68.9% patients were alcoholic with 1.5 drinks per day without significant association with elevated Serum GGT level

(Table-7).

Table-7 Association Of Alcohol Consumption With Elevated Serum GGT Level.

Alcohol Consumption	Chi-Square Value	df	P Value
	7.269	4	0.122

In this study, 71% patients were sedentary having only mild physical activity with no significant association with elevated serum GGT level (Table-8).

Table-8 Association Of Physical Activities With Elevated Serum GGT Level.

Physical Activities	Chi-Square Value	df	P Value
	2.319	4	0.677

Among 193 patients, 58% patients are having either chronic liver disease, chronic kidney disease or hepatorenal syndrome without statistical significant association with elevated serum GGT level (Table-9).

Table-9 Association Of Chief Diagnosis With Elevated Serum GGT Level.

Chief Diagnosis	Chi-Square Value	df	P Value
	17.750	16	0.339

CONCLUSION

In our observational study of community based sample, higher BMI was associated with higher serum GGT concentrations, which in turn were associated with increased morbidity and mortality. Community interventions need to target BMI of patients to reduce the risk of elevated Serum GGT level.

DISCUSSION

Principal Findings

Our study showed association of BMI with elevated serum GGT. In prior studies,higher GGT levels has been associated with alcohol consumption, metabolic risk incident diabetes (10).

Mechanism

It is at present unclear the mechanism underline the association between BMI and Serum GGT level. An increase in concentration of serum GGT is conventionally interpreted as a marker of alcohol abuse, insulin resistance and/or Liver damage (26). However, neither of these interpretations explain the observed association in the current study of GGT with BMI. GGT and BMI has been shown to positively correlate with Markers of Chronic Inflammations such as CRP and Fibrinogen (6), which on the other hand closely Correlate with the obesity (8,9). As a primary function ectoenzyme GGT maintain intracellular concentration of Glutathione, the most important non-protein antioxidant of the cell (11). Increased GGT activity can be a response to oxidative stress facilitating increased transport of Glutathione precursor into cell (11).Also, ectoplasmatic GGT may be involved in the generation of reactive oxygen species, particularly in the presence of Fe^{3+} and CU^{2+25}. Recently oxidative stress was shown to induce obesity (28) and a GT mediated oxidative stress was reported to be capable of inducing oxidation of lipids (11). GGT plays an important role in homeostasis of plasma cysteine as well (13) which similar to GGT induces oxidative stress mainly in the presence of Copper ion (29). Cysteine has been related with body fat in both men and women, independent of GGT (13). Furthermore, GGT levels have been reported to correlate with adipokines such as adiponectin (30) which play an important role in obesity by different pathways i.e, increased energy expenditure, insulin sensitivity or fatty acid oxidation (28).

CONCLUSION

In our community based sample, higher Body Mass Index (BMI) of patients were associated with elevated Serum GGT level, which in turn associated with hypertension, incident diabetes, metabolic syndrome, cardiovascular disease etc., which increases the morbidity and mortality.

Therefore, in clinical practice, the working clinician should keep an alert if any of the patients found to have higher BMI with elevated serum GGT level. These patients should be certainly worked up to prove or disprove any associated co-morbidities and accordingly clinical management protocol should be taken to reduce the patients' BMI and subsequent elevated serum GGT level, so that patients' co-morbidities and mortalities of the patients be reduced. Since, in our study, sample size was small, further additional studie with large sample size are needed to confirm our findings and to elucidate the underlined pathogenetic mechanisms.

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