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Research Article

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Diagnostic utility of gamma glutamyl transpeptidase (γGT) levels in patients with hepatitis and related chronic hepatic abnormalities

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Abstract *Background and Objectives*: γGT is significant Biomarker, has been indicated in screening or determination of chronic hepatic conditions, including suspected HCC. *Aim* Current study described the analysis of γGT levels in Chronic Hepatitis B patients with comorbid of Cirrhosis and X-ray evident suspected development of HCC *Materials and Methods*: Total of 160 patients (males n = 102; females n = 58) within age range of 32-64 years were selected. γGT was analyzed to determine and establish diagnostic utility with hepatitis status. Clinical conditions of patients were classified into four stages I-IV as per criteria and grouped Stage I, n = 31; Stage II, n = 35; Stage III, n = 55 and Stage IV, n = 39. Blood samples were collected for analysis of γGT, ALT (alanine aminotranferase), AST (aspartate aminotranferase), ALP (alkaline phosphatase), Bil (Total bilirubin), albumin, (ALB) Pro-thrombin time (PT), hepatitis profile tests by standard methods via standard methods *Results:* Cumulative data of all 160 patients exhibited 95.75% correlation of with hepatic insufficiency followed by 92.11% for Stage I, 89.41%; Stage II, 97.94% Stage III and 96.37% for Stage IV, depicting highest correlation for Stage III. Conclusion: It is thus suggested that γGT determination in hepatic diseases and suspected HCC is diagnostically significant and has clinical utility to predicts severity of progression of hepatitis and/or HCC, survival and recurrence and in treatment cases, progress of chemotherapy.

Keywords Gamma glutamyl transpeptidase, γGT, hepatitis, Hepatic parameters

Introduction

Bearing nomenclature of EC 2.3.2.2 and responsible for transfer of gamma-glutamyl functional groups [1], located on the cell membrane of various cells but most notably in hepatic cells, the enzyme gamma glutamyl transpeptidase (gGT) is a prominent hepatic enzyme [1]. Since it facilitate the metabolism of extracellular glutathione, elevated levels of γGT signifies adjustment to oxidative stress [2]. It has been reported that since γGT is associated with many metabolic pathways, inclusive of detoxification processes, alteration in its concentration correlates with existing or expecting disease state in liver [3, 4].

Chronic hepatitis B infection (CHBV) is known to develop into cirrhosis and hepatocellular carcinoma (HCC), if remain untreated [1, 5]. It is reported earlier that γGT can predict development of HCC even if patients gets treated

with antiviral therapy and eradicated from CHBV [6,7]. Thus γGT as significant sero-marker or Biomarker, has been indicated in screening or determination of chronic hepatic conditions, including suspected HCC [8]. Therefore current study described the analysis of γGT levels in CHBV patients with comorbid of Cirrhosis and X-ray evident development of HCC.

Material and Methods:

Research protocols and patients selection: Study covers the period of Dec 2019 to Dec 2021 and data gathered, inclusive of hepatic profiles, hepatitis status and laboratory findings, retrospectively, were grouped accordingly as per protocols described earlier [8]. Initial assessments of data was carried out in 670 patients, however further finalized through evaluation and grouping into final number of 160 patients (males n = 102; females n = 58) within age range of 32-64 yrs. To determine and establish diagnostic utility between γGT and hepatitis status, the clinical conditions were classified into four stages I-IV as per description detailed in a study reported earlier [8]. Inclusion and exclusion criteria were also established accordingly, keeping in view related co-morbid and interfering components. Patients were grouped according to their stages as Stage I, n = 31; Stage II, n = 35; Stage III, n = 55 and Stage IV, n = 39.

Sample collection and biochemical analysis: Blood samples were collected for analysis of γGT, ALT (alanine aminotranferase), AST (aspartate aminotranferase), ALP (alkaline phosphatase), Bil (Total bilirubin), albumin, (ALB) Pro-thrombin time (PT), hepatitis profile tests by standard methods Hepatic profile testing was performed on Roche modular e601 (Roche, Basil0 whereas γGT, ALT AST, ALP, Bil and albumin were analyzed by IFCC (international federation of clinical chemists) recommended method on Cobas 6000 c501 (Roche Diagnostics, Basil), where as PT was analyzed on CA-1500 (Sysmex). Normal reference range for ALT is less than 40 IU/L, γGT = 32- 49 IU/L, AST = 35-50 IU/L, ALP = 104-129 IU/L, Bil = less than 1.0 mg/dl, Alb = 3.4-4.8 gm/dl and PT = 8-12 seconds.

Hepatitis staging I to IV, Inclusion and Exclusion criteria: The stages were designated according to clinical and lab profile data. Stage I = Hepatitis C or B reactive + fatty liver seen, stage II = hepatitis C or B reactive + cirrhosis [non-invasive]; stage III = hepatitis C or B highly reactive + with CT/X ray described cirrhosis progression; stage IV = Hepatitis C or B highly reactive + highly progressive/ proliferative cirrhosis or/and hepatoma. Patients with previous history of surgery, immuno-compromised, known alcoholics, steroidal therapies, below 20 years and above 80 yrs were excluded from the study.

Statistical analysis: Data were statistically analyzed by Pearson's correlation, multivariate analysis with level of significance $P< 0.05$ and regression R2 analysis by SPSS version 22 (USA).

Results

A total of 160 patients (males = 102 and females 58) were assessed for determination of diagnostic utility of γGT levels with hepatic anomalies, more specifically, four stages of progression of hepatitis. Results are summarized in Fig 1 to Fig 4. Cumulative data of all 160 patients exhibited 95.75% correlation of with hepatic insufficiency (Fig 1: $y = 5.917x + 48.247$; $R^2 = 0.9575$); followed by 92.11% for Stage I (Fig 2: $y = 3.0649x + 120.25$, $R^2 = 0.9211$); 89.41%; Stage II (Fig 3: $y = 2.9485x + 296.5$ $R^2 = 0.8941$); 97.94% Stage III (Fig 4: $y = 5.4143x + 385.07$ $R^2 = 0.9794$) and 96.37% for Stage IV (Fig 5: $y = 3.6622x + 874.42$ $R^2 = 0.9637$), depicting highest correlation for Stage III.

Discussion

Earlier and recently reported studies regarding γGT argued its diagnostic significance in hepatitis, hepatic anomalies and even hepatoma [1-7]. In presented study, patients (n = 160; Males = 102 and females = 50) with known hepatic pathology were selected, their liver function tests (mentioned in materials and methods) were done and γGT was

designated to be analyzed via regression correlation against stage of hepatic pathology. R^2 regression analysis of all patients exhibited 95.75% correlation of with hepatic insufficiency (y = 5.917x + 48.247; R^2 = 0.9575); followed by 92.11% for Stage I (y = 3.0649x + 120.25, R^2 = 0.9211); 89.41%; Stage II (y = 2.9485x + 296.5 R^2 = 0.8941); 97.94% Stage III (y = 5.4143x + 385.07 R^2 = 0.9794) and 96.37% for Stage IV (y = 3.6622x + 874.42 R^2 = 0.9637).

Fig 1: Cumulative correlation of gGT levels at Stages I to IV of Hepatitis in general hepatic abnormalities (Total patients n = 160)

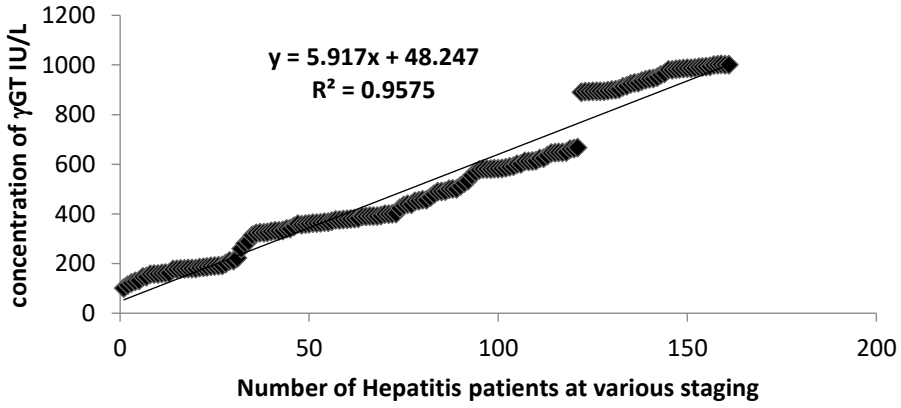
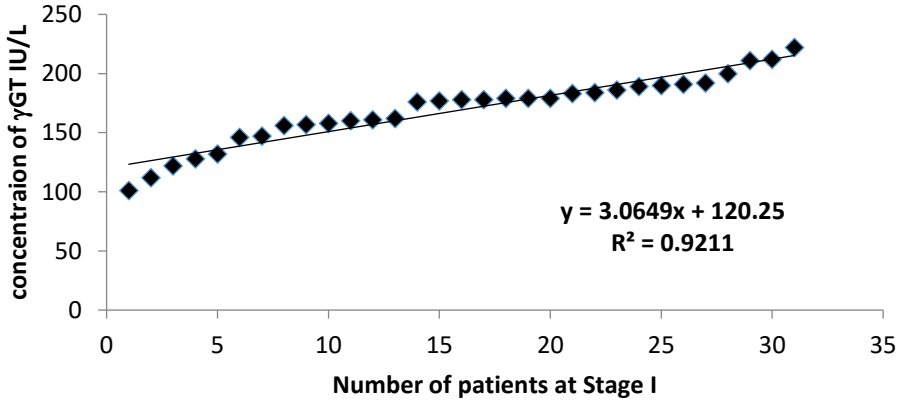


Fig 2: Correlation analysis of γGT levels in Hepatic abnormalities viz Hepatitis Stage I (n = 31)



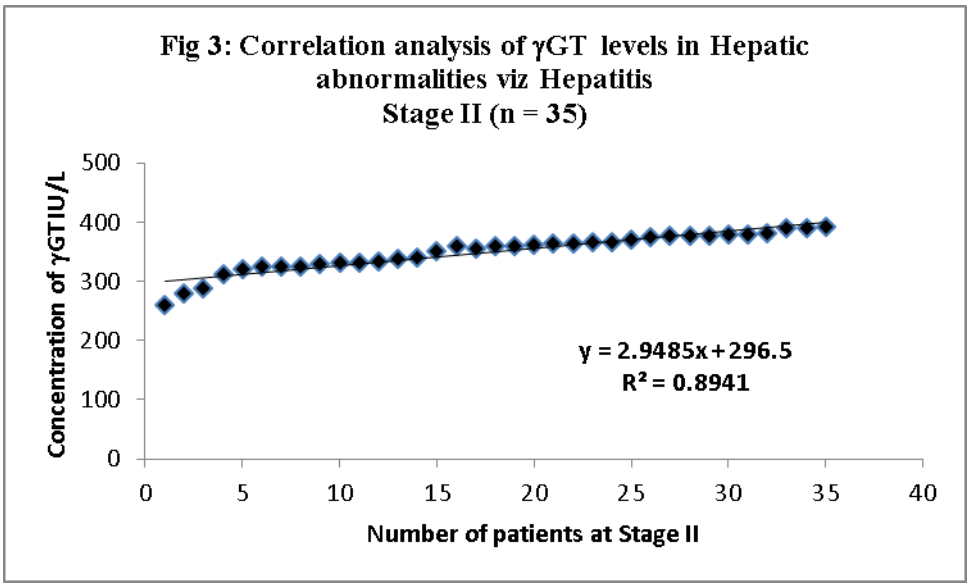


Fig 3: Correlation analysis of γGT levels in Hepatic abnormalities viz Hepatitis
Stage II (n = 35)
Concentration of γGTIU/L
500
400
300
200
100
0
0
5
10
15
20
25
30
35
40
Number of patients at Stage II
y = 2.9485x+296.5
R² = 0.8941

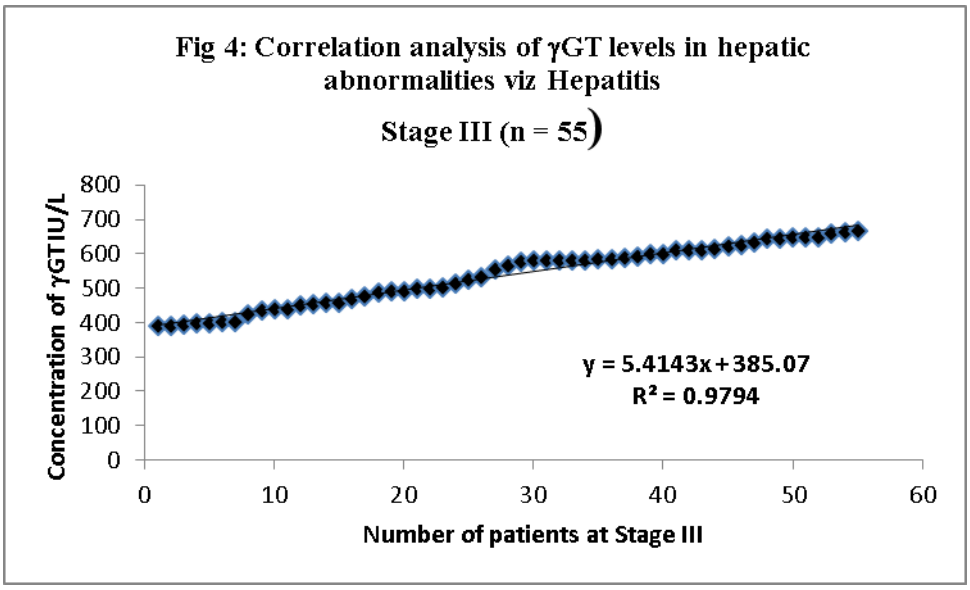
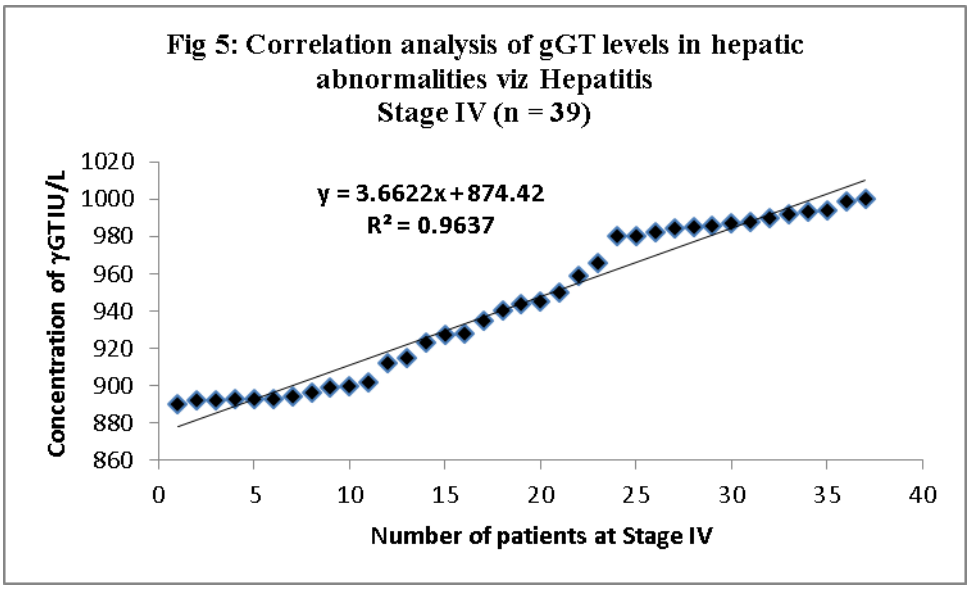


Fig 4: Correlation analysis of γGT levels in hepatic abnormalities viz Hepatitis
Stage III (n = 55)
Concentration of γGTIU/L
800
700
600
500
400
300
200
100
0
0
10
20
30
40
50
60
Number of patients at Stage III
y = 5.4143x+385.07
R² = 0.9794



Highest correlation of gGT depicted for Stage III of hepatic anomalies inclusive of hepatitis C or B highly reactive + with CT/X ray described cirrhosis progression.

It is widely accepted that γGT is a significant marker of liver injury [1-7]. Working as facilitator in glutathione metabolism in cells, γGT enabling lowering of oxidative stress [2]. Since higher levels of GGT is an indicator of pro-oxidant activity and cellular insufficiency, it is also suggested to be significant tool to asses other systemic diseases, such as cardiovascular, metabolic and pre-post hepatic injuries [9-11]. Recent and past studies also reported correlation of elevated levels of γGT with progression of malignancies such as HCC, Colorectal (CRC), bile duct and indicator of increased risk of cancer in larynx, stomach and oesophagus [7, 12]. Hepatitis B and C patients positivity and its severity scale has also been noted in selected population, graded for non-invasive methods of diagnostic selectivity and utility of γGT [13, 14]. Furthermore, normalization of gGT levels and predicament of Hepatitis antigen also seems to be associated and clinically correlated [14]. Diagnostic utility of γGT levels and HCC has also been documented and argued that γGT levels predicts severity of progression of HCC, survival and recurrence and in treatment cases, progress of chemotherapy [15,16]. A study reported earlier that high γGT concentration even in patients which has now free of HCV, can still develop HCC and at a high risk of malignancies [7].

Conclusion

Current study correlated γGT levels of 160 patients, grouped as per four stages of Hepatic abnormalities, with diseased state both cumulatively and individually. Data of all patients exhibited 95.75% correlation of with hepatic insufficiency, followed by 92.11% for Stage I, 89.41%; Stage II, 97.94% Stage III and 96.37% for Stage IV Highest correlation of γGT depicted for Stage III of hepatic anomalies inclusive of hepatitis C or B highly reactive + with CT/X ray described cirrhosis progression.

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