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The estimation of serum gamma glutamyl transferase in fatty liver disease

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Abstract
Background: Fatty liver seems to be common problem among the young and middle aged population. It includes a spectrum of liver disease from simple fatty liver to hepatic steatosis to cirrhosis and hepatocellular carcinoma. Fatty liver disease comprises both alcoholic fatty liver disease to non alcoholic fatty liver disease. Early detection of fatty liver disease helps to prevent these major events of disease progression. The serum gamma glutamyl transferase level rise early in the spectrum of fatty liver disease and returns back to normal in most of the cases. So estimation of the serum gamma glutamyl transferase in fatty liver disease serves as an non invasive biomarker in fatty liver disease.
Aims and Objectives: To evaluate the serum GGT levels in patients with fatty liver and to show that it can be used as a non invasive diagnostic biomarker for the diagnosis of fatty liver disease.
Materials and Methods: The study was a case control study which was done in100 patients. Of the total 100 cases 50 were categorized as case group with ultrasound abdomen finding of fatty liver and the remaining 50 are control group with normal ultrasound abdomen reports. The investigations like, serum gamma glutamyl transferase, liver function test, renal function test, serum random blood sugar, fasting lipid profile, HIV, HbsAg were done with special importance given to serum GGT levels. These parameters between the case and control group were studied based on pearson correlation test and student t-test.
Results: Comparison of GGT values between case and control group, which shows serum GGT level of 69.38 ± 16(IU/L) cases and21.34 ± 5.29(IU/L) controls. The mean serum TGL level was 300 ± 39(IU/L), serum LDL level was 138.5 ± 27(IU/L) in the case (fatty liver) group and the control (normal) group TGL level was 230 ± 35.5(IU/L), LDL level was 138.5 ± 27(IU/L) which was statistically significant and p value was <0.001. The pearson correlation and two tailed student t-test between cases and control group with reference to serum GGT shows a p value of less than 0.001 (p <0.001), which was statistically significant and hence this indicates that serum GGT levels are elevated in majority of cases of fatty liver disease.
Conclusion: Gamma glutamyl transferase levels are significantly elevated above normal in patients presenting with sonographic evidence of fatty liver disease. There is a significant correlation between GGT levels and incidence of asymptomatic fatty liver disease.
The mean value of GGT was significantly elevated in patients with asymptomatic fatty liver disease. Patients with significantly elevated GGT values maybe advised for early life style modifications to prevent further progression of hepatic steatosis. In conclusion, estimation of serum GGT in fatty liver disease serves as non invasive biomarker for diagnosis of fatty liver disease.

Keywords: Serum gamma glutamyl transferase, Fatty liver disease, ultrasound abdomen.

Introduction
Fatty liver disease seems to be a challenging disease to the mankind from the last two decade. Fatty liver seems to be common problem among the young and middle aged population. It includes a spectrum of liver disease from simple fatty liver to hepatic steatosis to cirrhosis and hepatocellular carcinoma. The spectrum of the non alcoholic fatty liver disease seems to be more prevalent, which brings an urge to screen this asymptomatic disease before it gets progressed to complete hepatic steatosis, cirrhosis and hepatocellular carcinoma [11-13]. Most of the patients are asymptomatic till the later stage and even the liver function test seems to be normal. Once the hepatic inflammation and liver cell damage sets in the biochemical profile of liver, serum bilirubin, protein and transaminases like AST, ALT, ALP and GGT starts to rise in blood [1, 13]. The serum GGT level is considered as agood and sensitive index of hepatic inflammation and hepato cellular damage [7]. Serum

GGT is elevated in bile stasis and in alcoholics [5]. Serum GGT is normally found in the tissue membranes of liver, kidney, bile ducts, gall bladder, pancrease and also in the heart muscles. Serum GGT level is significantly elevated in diseases of these organs. Recently may studies on fatty liver proved its relation with further progression leading to major cardiovascular events and diabetes mellitus [2, 3, 8]. It is also raised in patients who are on long term treatment with drugs like anti-epileptics, amiodarone, steroids and calcium channel blockers. The serum gamma glutamyl transferase level rise early in the spectrum of fatty liver disease and returns back to normal in most of the cases. So estimation of the serum gamma glutamyl transferase in fatty liver disease serves as an non invasive biomarker in fatty liver disease

Aims and Objectives

To evaluate the serum GGT levels in patients with fatty liver and to show that it can be used as a non invasive diagnostic biomarker for the diagnosis of fatty liver disease

Materials and Methods

Thestudy was a case control study which was done in 100 patients admitted in RMMCH, Chidambaram, Tamil Nadu, India. All the100 participants were between the age group of 20-70 years. The hundred participants were divided into 2 groups, which includes 50 controls and remaining belong to the 50 case group.

The 50 cases were selected based on the patients admitted with ultrasoundabdomen finding of fatty liver disease who are asymptomatic or does not have any clinical symptom of liver disease on presentation to hospital and also includes patient with vague abdominal pain.

The control group of study population includes 50 patients of healthy volunteers with ultrasound abdomen showing normal reports. The control group was further selected by excluding:

- Patient clinically presented with icterus.
- The patients with known history suggestive of renal, pancreas, respiratory, cardiac and neurological diseases, who presented with icterus.
- Patients who were on drugs like anti epileptics, amiodarone, tamoxifen, synthetic oestrogens, heparin, calcium channel blockers, valproic acid, antiviral agents and steroids.
- Patients who had undergone biliopancreatic surgeries were excluded from the study by taking a proper history and by doing a proper examination and investigations.
- Pregnant patients were excluded from the study.

Both the case and control group were made to undergo blood chemistry analysis like serum random blood sugar, serum gamma glutamyl transferase, liver function test, renal function test, fasting lipid profile, HIV, HbsAg.

Patient with ultrasound finding of fatty liver were categorized as cases. The grading of fatty liver was done into 3 groups namely, Grade I fatty liver, Grade II fatty liver, Grade III fatty liver.

The reference serum GGT level of cases were compared with control group. The normal level of GGT 9-40 IU/L. The diabetes mellitus was diagnosed with random blood sugar more than 180 mg/dl. Triglyceride level of more than 150mg/ dl was taken as reference range above the normal value, for HDL values between 40 mg/dl or higher and for LDL values less than 130 mg/dl is taken as normal reference range. ALT level of 7-50 U/L was taken as reference range above the normal value. AST 8-40 U/L was taken as reference range above the normal value. ALP 40 -129 U/L was taken as reference range above the normal value.

The Ethical clearance was obtained from the ethical committee of Rajah Muthiah Medical College, Chidambaram, India. Written consent was obtained from all the patients after explaining them about the study in their own language.

Statistical methods

The correlation test, chi square test and ANOVA test were used to study distribution of the various parameters involved in the study. Chi square test and the student t test were used to find the significance of proportions of study parameters between cases and control.

Statistical software

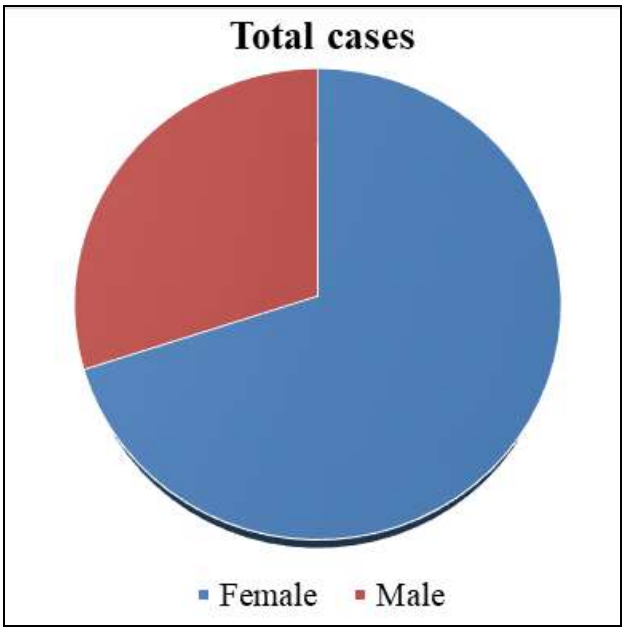
The statistical data was analysed using SPSS software version 28.0.1.0. All the data was entered using MS Excel and MS Word and the tables were generated using MS excel.

Results

Thiswas a case control study which includes equal number of cases and the results were compared between them. Of the total 100 cases 50 were categorized as case group with ultrasound abdomen finding of fatty liver and the remaining 50 are control group with normal ultrasound abdomen reports.

Table 1: Distribution of study group based on gender

	Cases		Control	
	Frequency (n)	**Percent (%)**	**Frequency (n)**	**Percent (%)**
Female	35	70	36	72.0
Male	15	30	14	28.0
Total	50	100	50	100.0



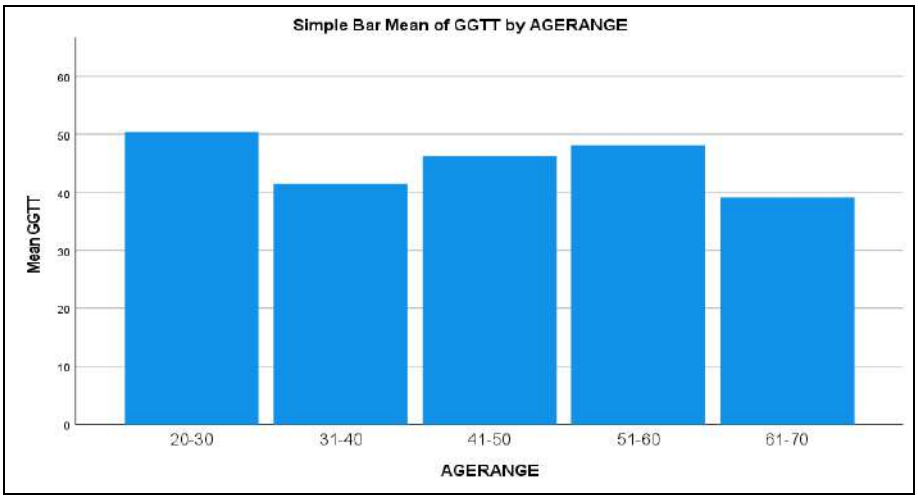
Graph 1: Distribution of study group based on gender

Table and Graph 1 and 2: Out of the hundred study population 71% were female and remaining 29% were male. In the case group about 35 (70%) are female, 50 (30%) are

males and in the control group about 36 (72%) are female, 14 (28%) are males. Most of the study group were between the ages of 51 – 60 years (28%) followed by 61-70 years (22%) and others are between the age group 20-30 years (21%).

Table 2: Distribution of study group based on age

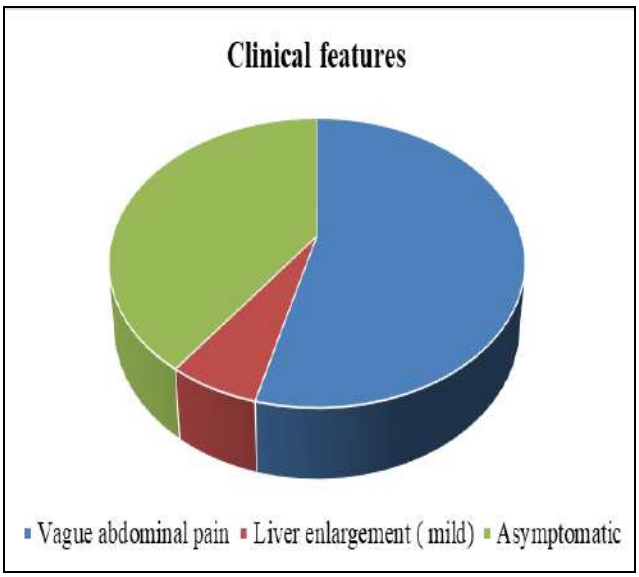
Age (in years)	Frequency (N)	Percent (%)
20-30	21	21.0
31-40	15	15.0
41-50	14	14.0
51-60	28	28.0
61-70	22	22.0
	100	100.0



Graph 2: Distribution of study group based on age

Table 3: Distribution of case group based on clinical features

Clinical features	Cases
Asymptomatic	27(58%)
Liver enlargement	3 (1.5%)
Vauge abdominal pain	20 (40.5)



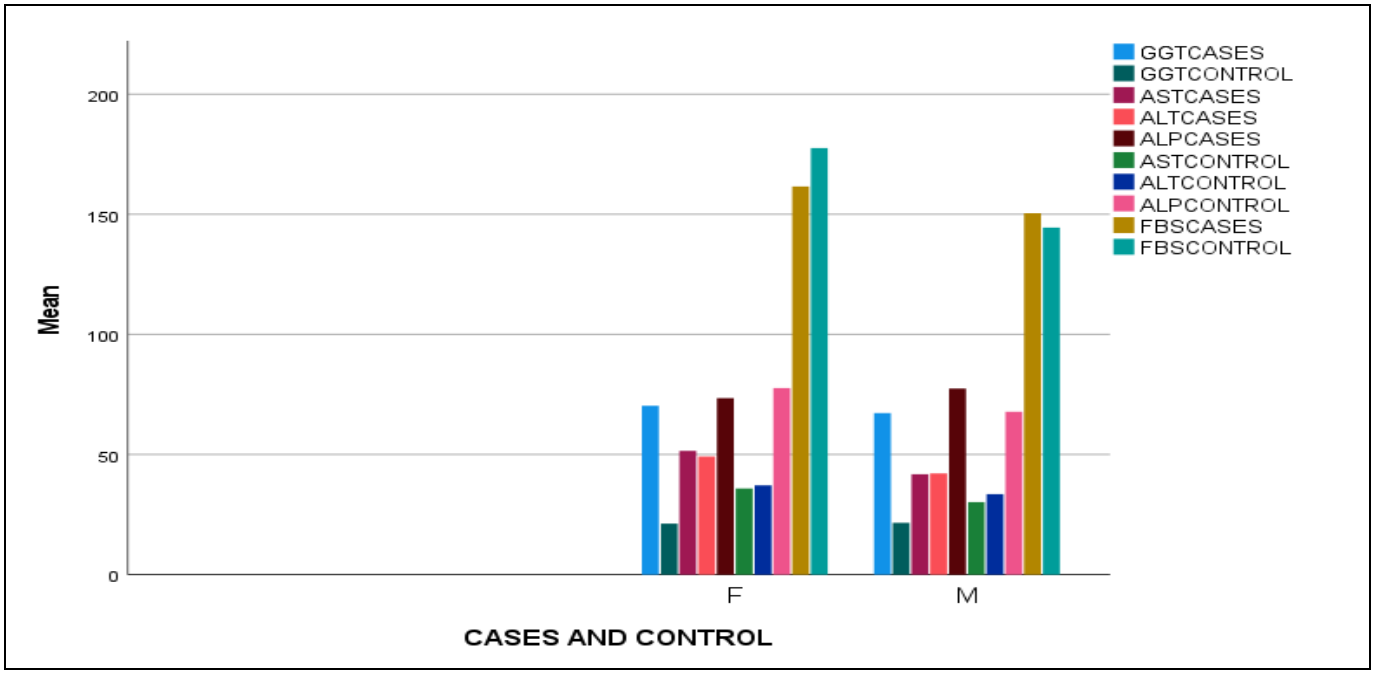
Graph 3: Distribution of case group based on clinical features

Table and graph 3: Most of the cases had no symptom of liver disease they were categorized into asymptomatic group with 27 cases (58%), and those with mild liver enlargement are 3 cases (1.5%) and the remaining 20 (40.5%) cases had vague abdominal pain.

Table 4: Demographic profile and baseline characteristics between the cases and control group

Parameters	Cases (Mean ± Sd value)	Controls (Mean ± Sd value)	p Value
GGT (IU/L)	69.3 ± 16	21.34 ± 5.29	<0.001
AST (IU/L)	48 ± 13.43	34.14 ± 8.03	<0.001
ALT (IU/L)	47.08 ± 9.69	36 ± 5.95	<0.001
ALP (IU/L)	74.68 ±17.2	74.72 ± 15	<0.3
RBS (mg/dl)	178 ± 59.1	167 ± 50.8	<0.001
TGL (mg/dl)	300 ± 39	230 ± 35.5	<0.001
LDL (mg/dl)	138.5 ± 27	120 ± 20.2	<0.001

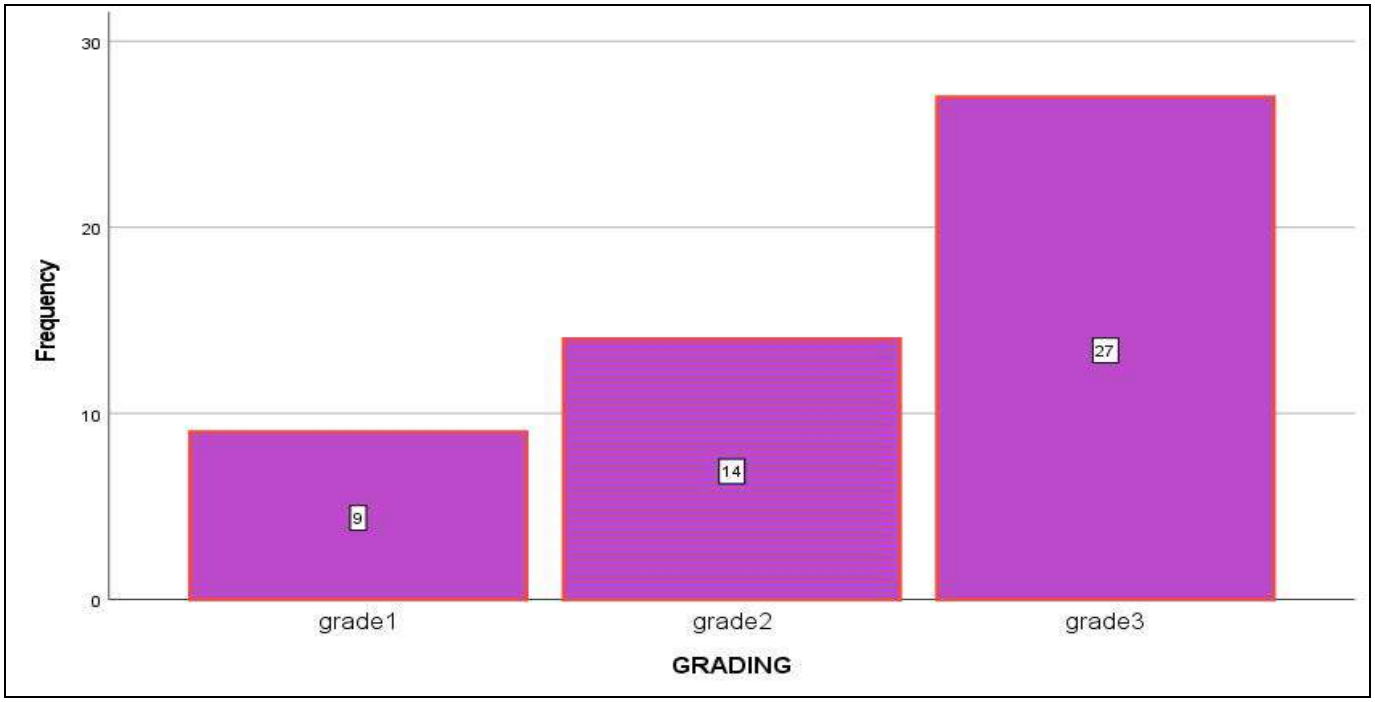
Table and graph 4: The serum GGT level was 69.3 ± 16 (IU/L) in the case and the control group was 21.34 ± 5.29(IU/L) which was statistically significant and p value was <0.001.The serum AST level was 48 ± 13.43 (IU/L) in the case and the control group was34.14 ± 8.03 (IU/L) which was statistically significant and p value was <0.001. The serum ALT level was 69.3 ± 16 (IU/L) in the case and the control group was 21.34 ± 5.29 (IU/L) this was also statistically significant and p value was <0.001.The serum ALP level was 74.68 ±17.2 (IU/L) in the case and the control group was 74.72 ± 15 (IU/L)this was not statistically significant and p value was <0.3.The serum RBS level was 178 ± 59.1(IU/L) in the case and the control group was 167 ± 50.8 (IU/L) which was statistically significant and p value was <0.001.The serum TGL level was 300 ± 39 (IU/L), serum LDL level was 138.5 ± 27 (IU/L) in the case and the control group TGL level was 230 ± 35.5(IU/L),LDL level was 138.5 ± 27 (IU/L) which was statistically significant and p value was <0.001.



Graph 4: Demographic profile and baseline characteristics between the cases and control group

Table 5: Ultrasound grading of fatty liver (Cases)

	Frequency (N)	Percent (%)
Grade1	9	18.0
Grade2	14	28.0
Grade3	27	54.0
Total	50	100.0

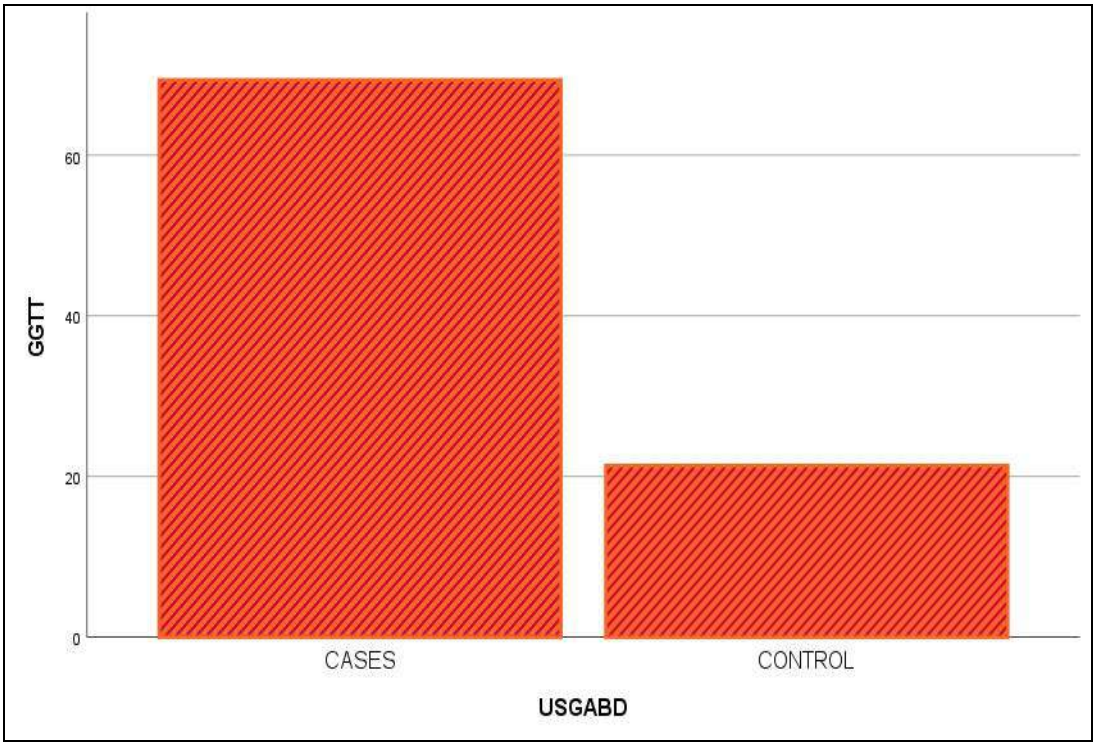


Graph 5: Ultrasound grading of fatty liver

Table and graph 5: Of the total 100 patients 50 (50%) had fatty liver [FLD] and 50 (50%) had no fatty liver [normal ultrasound]. Among the FLD patients 18%, had grade I, 28% had grade II and 54% had grade III fatty liver as diagnosed by ultrasound.

Table 6: Comparison of GGT between cases and controls

Parameters	Cases (Mean ± Sd value)	Controls (Mean ± Sd value)	p Value
GGT (IU/L)	69.38 ± 16	21.34 ± 5.29	<0.001
Ultrasound Abdomen	50 ± 0	50 ± 0	<0.001



Graph 6: Comparison of GGT values between control and cases group

Table and graph 6: Comparison of GGT values between case and control group, which shows serum GGT level of 69.38 ± 16 (IU/L) cases and 21.34 ± 5.29 (IU/L) controls. The pearson correlation and two tailed student test between cases and control group with reference to serum GGT shows a p value of less than 0.001 ($p<0.001$), which was statistically significant and hence this indicates that serum GGT levels are elevated in majority of cases of fatty liver disease. Hence estimation of serum GGT can be used as a non invasive diagnostic biomarker for the diagnosis of fatty liver disease.

Discussion

In this case control study, the serum gamma glutamyl transferase level is compared between the cases and the control groups of patients who were selected based on the ultrasound findings of presence of fatty liver disease and the normal ultrasound abdomen reports. In this study the comparison of cases and controls are done in reference with serum GGT, which revealed a significant rise in serum GGT in cases with fatty liver ($p <0.001$) [6]. This study also proved these seems to be consistent rise in the level of AST, ALT, TGL, LDL, and FBS [1, 4]. The serum GGT values between case 69.38 ± 16 (IU/L) with a p value of <0.001, which is significantly higher than the controls. This indicates that serum GGT is the sensitive in detecting fatty liver disease even in non alcoholic cases. There are various other studies that support the correlation of serum GGT with fatty liver disease. This study was compared with that of Franzini M-*et al*., according to that study, the total GGT was elevated in the nonalcoholic liver disease cases as compared to that in the controls, with values of 39.4 U/L vs. 18.4 U/L respectively, ($p < 0.001$) [7]. Another study was done by Giovanni Targher *et al*., the GGT level in nonalcoholic liver diseases was 38±16IU/L and it was 27± 14IU/L in the cases and controls respectively, which was statistically significant, ($p <0.001$) [10]. The GGT level was compared to the alanine trans aminase (ALT) level in the cases, where there was no significant difference between their levels. This meant that the GGT level was equally and significantly elevated as compared to the ALT level. Again, the GGT levels were compared with the AST levels, where the GGT levels were found to be more significantly raised as compared to the AST levels. This was correlated with the findings of the study of Christi A Matteoni *et al*., where the GGT level was more significantly elevated than the ALT level in chronic non alcoholic liver diseases [9, 10]. According to the study of Giovanni Targher *et al*., the elevated GGT levels were similar to the ALT levels and they were more elevated than the AST levels in chronic non alcoholic liver diseases[10]. In contrast, in alcoholic liver diseases, it was confirmed that the aspartate transaminase (AST) level was more significantly raised than the GGT and the ALT levels. In this study the serum GGT was found to be significantly elevated than other biomarkers of hepatocyte injury like AST and ALT with p value of less than 0.001. Serum GGT was consistently elevated along with the other markers of hepatic steatosis like elevated triglycerides and LDL levels. Hence serum GGT serves as a good sensitive marker of early detection of fatty liver disease.

Conclusion

Gamma glutamyl transferase levels are significantly elevated above normal in patients presenting with sonographic evidence of fatty liver disease. There is a significant correlation between GGT levels and incidence of asymptomatic fatty liver disease. The mean value of GGT was significantly elevated in patients with asymptomatic fatty liver disease. Patients with significantly elevated GGT values maybe advised for early life style modifications to prevent further progression of hepatic steatosis. In conclusion, estimation of serum GGT in fatty liver disease serves as non invasive biomarker for diagnosis of fatty liver disease.

Limitations of the study

This study included only 100 participants who were randomly accessed based on the ultrasound finding of fatty liver and GGT. The participants were need to be followed for longer period of timeto follow up persistent elevation of serum GGT.

Source of support – Nil

Conflict of interest – None

Ethical Committee Clearance Obtained from Institution - Yes

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