Correlation of BMI and elevated liver enzyme levels with severity of fatty liver infiltration on ultrasound in Sangrur, Punjab

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Abstract
Obesity is a common disorder in our country. It leads to many health risks. Ultrasonography can accurately assess the severity of fatty infiltration in liver. The liver enzymes (AST, ALT) are also altered in triglyceride overload. This study aims to assess the severity of fatty liver on US (Ultrasonography) with increased BMI and to investigate the association of severity of fatty liver with liver enzymes. A comparative prospective study was conducted on 179 patients. Severity of fatty liver was graded on Ultrasonography as follows: Group A- Normal liver, Group B- Grade 1 fatty changes, Group C-Grade 2 fatty changes and Group D-Grade 3 fatty changes. BMI of each patient was calculated. Patients with known liver disease were excluded. Serum liver enzyme levels were recorded. There was significant correlation between value of liver enzymes and increasing BMI. Also, Patients with more BMI have higher grade of fatty infiltration.

Keywords: Obesity, AST, ALT, Ultrasonography.

Introduction
NAFLD has a prevalence of 0-24% in USA. NAFLD occurs when there is accumulation of fat in liver of more than 5-10% by weight. Also, other risk factors such as alcohol abuse, hepatitis etc. should be excluded.¹² Obesity is a world extensive health problem and is increasingly causing an impact on morbidity and mortality. Obesity is a proven predisposing factor of increasing cardio-vascular and neuro-vascular morbidity. Prevalence of obesity is increasing. Hence, it is important to correlate obesity with liver enzymes and USG diagnosis of fatty liver. Early recognition of changes in liver cells would give physicians time to treat the damage process early. Also, the disease could be reversed by the changes of lifestyle by patients. US are a non-invasive and affordable tool for assessing fatty liver and can be done in a clinical setting. The sensitivity of US in detecting fatty infiltration of liver is 60-94% and specificity is 84-95%.³

This study aims to correlate BMI and liver enzymes with severity of fatty liver on ultrasound.

Materials and Methods
The present study was conducted in PGIMER Outreach Center, Sangrur in the Department of Biochemistry and Department of Radiodiagnosis. The study was conducted from September 2018 to January 2019. A total of 179 patients belonging to the age group of 27 to 82 years from both the sexes were selected. Height and weight of each patient was recorded. Patients with known liver disease and with history of alcohol consumption were excluded. Severity of fatty liver was graded on Ultrasonography as follows:

- Group A- Normal liver
- Group B- Grade 1 fatty changes
- Group C-Grade 2 fatty changes
- Group D-Grade 3 fatty changes.

Serum AST, ALT, TP, Albumin, ALP and T. Bil were recorded on cobas c311 Autoanalyser. Grading of fatty liver was done on USG abdomen using machine Mindray DC-60. Liver size was also recorded for each patient.

A data analysis was done using EPI info software. Mean and standard deviation were computed for the variables. The comparison between groups were done by chi square.

Results
Patients were divided into four groups according to severity of fatty liver on USG.

Table 1: Values of liver enzymes - AST and ALT (in U/L) in all four groups

|          | Group A (n=45) | Group B (n=73) | Group C (n=47) | Group D (n=14) | P value |
|----------|---------------|---------------|---------------|---------------|---------|
| AST (in U/L) Mean±SD | 37.35±3.202 | 56.82±50.94 | 36.66±37.52 | 148.43±63.38 | <0.01   |
| ALT (in U/L) Mean±SD | 34.8±28.26 | 59.54±62.28 | 34.19±23.83 | 141.21±48.07 | <0.01   |

Significant correlation was found between liver enzymes and severity of fatty liver (Table 1).

Table 2: Values of BMI (in kg/m2) in all four groups

|          | Group A (n=45) | Group B (n=73) | Group C (n=47) | Group D (n=14) | P value |
|----------|---------------|---------------|---------------|---------------|---------|
| BMI      | 24.22±3.65   | 27.1±3.83    | 32.19±5.06    | 38.27±4.87    | <0.01   |

Significant relation was formed between increasing BMI and grade of fatty liver change on ultrasound with p values of <0.01 (Table 2).
**Discussion**

Day et al proposed a “two hit theory” for progression of simple statuses to NASH. The first hit is peripheral insulin resistance which leads to triglyceride accumulation in hepatocytes. This increases fatty acid beta oxidation. At this point, without a “Second Hit”, statuses remain stable. However, in the presence of a second hit (e.g., Diabetes mellitus, mitochondrial abnormalities etc.) there is increased production of reactive oxygen species which leads to cell injury, inflammation and fibrosis.1

Although, histopathology is the gold standard to detect fatty liver changes but US is a cheap, non-invasive method and can be performed on OPD basis. Also, US can detect the severity of statuses and grading of fatty infiltration can be done. Therefore, US is a reliable tool in the determination of fatty liver infiltration with high sensitivity and specificity. In the present study (Table 2) the severity of fatty liver on ultrasound was significantly associated with increased BMI and increased liver enzymes. This information is very useful for physicians as patients whose livers are vulnerable for second hits can be identified and lifestyle modifications can be initiated soon.

Also, in our study increased BMI was found to be the most important factor related to the severity of fatty liver. Increased BMI was found to be directly associated with grade of fatty liver on US. This means that the measures to halt the progression of fatty liver should begin as early as possible. We also concluded that there is significant association between increasing BMI and increased liver enzymes (Table 1).

Ruhl et al in their large, national population based study, found that 65% of the patients had elevated ALT activity due to increased BMI.2 Stranges S et al evaluated the relationship between indices of abdominal fat accumulation and biochemistry of liver cases. Central adiposity was assessed by abdominal height and BMI. Abdominal height was concluded to be powerful predictor of increased ALT and increased GGT.3 Sull JW examined the association with BMI and S. Aminotransferase levels in the Korean population and found that S. liver enzymes are strongly associated with BMI. Liver enzymes are also raised in heavy alcohol drinkers than in non-drinkers.4

Fan R et al did a study that showed that higher BMI was significantly associated with fatty liver in a nonlinear fashion and the risk of fatty liver is 3.55 times higher in overweight population than in normal population and 7.59 times higher in obese population. They concluded that higher BMI is an independent dose dependent risk factor for fatty liver and prevention of fatty liver focusing on continuous changes in BMI should be noted.5

Choi JW did a study to determine association between obesity and serum liver enzymes. They concluded that mean activities of serum liver enzymes were significantly higher in both men and women with high fatness. Also a high prevalence of fatty liver is seen in patients with high total body fat.6 Marchesini G et al did a study to find out the association between insulin resistance and hepatocellular necrosis. Median ALT and AST increases with increasing obesity class and exceeded normal limits in 21% of the cases. They concluded that in obesity, insulin resistance is a risk factor for raised Liver enzymes.7 Strauss et al measured serum ALT and GGT levels in 2450 children between 12-18 years of age. 60% of children with increased ALT were obese or overweight. 6% of overweight children have increased ALT and 10% of obese children had increased ALT. They concluded that overweight and obesity are most common findings in adolescents with increased ALT levels.8

The frequency of metabolic syndrome obesity, HTN, glucose intolerance and hypertriglyceridemia were found to be significantly higher in patients with severe fatty liver changes on USG than in normal patients in a study done by Hsiac PJ.9 Therefore, we conclude that the severity of fatty infiltration has a significant correlation with increased BMI and elevated liver enzymes. This information is very helpful to the physician as it tells them about the threshold to oxidative stress and the risks of developing cardiovascular disease. We suggest that all patients with elevated BMI should undergo US and if fatty liver is present, immediate steps should be taken to reduce weight. Patients should be counselled regarding the consequences and the need to implement lifestyle modifications to reduce morbidity.

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**Conflict of interest**

None.

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