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Short Communication

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The Relation Between Elevated Liver Enzymes and Nonalcoholic Fatty Liver Disease

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ABSTRACT

Non alcoholic fatty liver disease has a broad spectrum ranging from pure steatosis to steatohepatitis and it is a common condition which is a fast assuming importance as a possible precursor of serious liver disorders including cirrhosis and hepatocelluler carcinoma.

The present study was aimed to assess the role of elevated aminotranseferase levels as a prerequisite to suspect nonalcoholic steatohepatitis (NASH) in patients with nonalcoholic fatty liver disease.

Thirty patients with ultrasonographic finding of fatty liver were enrolled in this study which was started in June 2007, all patients were negative for HBsAg, anti HCV, HIV.

By liver biopsy mild steatosis and mild ballooning of hepatocytes was diagnosed in 33.4%, moderate in 30%, and sever in 36.6%, acute lobular inflammation was present in 26.6%, chronic in 73.4%. Seventeen patients had pericellular fibrosis, focal in 66.7% and extensive in 33.3%. Periportal fibrosis was present in 56.6%, focal in 50% and extensive in 6.6%. No evidence of bridging fibrosis and no cirrhosis.

The mean Aspartate amino transferase (AST) was 27.8%, only eight patients (5 females and 3 males) had high AST (26.6%) and twenty-two patients had normal AST (73.4%). The mean Alanine aminotransferase (ALT) was 42.5%, nine patients (4 females and 5males) had high ALT (30%) and twenty-one patients had normal ALT (70%). The mean AST/ALT ratio was 0.65, twenty patients (66.6%) with AST/ALT ratio < 1and ten patients (33.4%) with AST/ALT ratio ≥ 1.

Conclusion: Non Alcoholic steatohepatitis can be associated with normal ALT or AST and a liver biopsy is the golden standard method in diagnosis. However, liver biopsy is not being justified if the patient has normal enzymes.

Keywords *- Fatty;Liver; Steatohepatitis; Steatosis; Aminotransferase; Biopsy.*

INTRODUCTION

Fatty liver is characterized by a diffuse accumulation of fat in hepatocytes. When fatty liver occurs in an individual who does not consume alcohol in quantities considered to be harmful to the liver (less than 20 gm of ethanol per week), it is referred to as non alcoholic fatty liver disease (NAFLD).[1] It has broad spectrum ranging from pure steatosis (fatty liver alone) to steatohepatitis (NASH), cirrhosis and hepatocellular carcinoma.[2]

Prevalence of NASH is not well defined among patients who had liver biopsies NASH is seen in approximately 7-9% in western countries and 1.2 % in Japan.[3]

It is an important public health problem as it may progress to fibrosis and cirrhosis in 10-25% of affected subjects.[1]

There are different conditions associated with steatohepatitis including Insulin resistance (Syndrome X, Lipoatrophy); Disorders of lipid metabolism (Abetalipoproteinemia, Hypobetalipoproteinemia, Andersen's disease, Weber-Christian syndrome); Total parenteral nutrition; Chronic inflammatory conditions as Rheumatoid arthritis and SLE.[4] Severe weight loss due to Jejeno-ileal bypass, Gastric bypass, Severe starvation, Small bowel bacterial overgrowth, also associated with steatohepatitis. Exposure to some drugs as Amiodarone, Diltiazem, Tamoxifen, Steroids and environmental toxic exposure play role.[4]

Ultrasonography is an important non-invasive diagnostic tool for NAFLD. It has a sensitivity of 82-90% for detecting fatty liver. Liver biopsy is confirmatory in diagnosing NAFLD, related fatty liver, inflammation and fibrosis.[5]

A specific and effective treatment for NAFLD does not exist, but treatment of associated condition like hyperlipidemia and obesity are helpful. Potential therapeutic medications include metformin, ursodeoxycholic acid, vitamin E, betaine, etc.[6]

The objective of this study was to assess the role of elevated aminotransferase levels as a prerequisite to suspect NASH in patients with NAFLD.

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MATERIALS AND METHODS

A case series study was conducted in University of Tripoli Hospital at Gastroenterology department unit C, from June 2007 to July 2012, where thirty patients with ultrasonographic findings of fatty liver disease were enrolled in this preliminary study.

Eligible subjects of either gender of all ages, who agree to participate in the study, were included.

There are four sonographic findings of diffuse fatty changes in the liver:-Diffuse hyperechoic echo texture (bright liver), increased liver echo texture compared with the kidneys, Vascular blurring and Deep attenuation.

Subjects who had not consumed alcohol were further tested to have negative serological test markers for viral hepatitis, autoimmune chronic hepatitis, primary biliary cirrhosis, Wilson's disease and alpha1 antitrypsin deficiency.

Known diabetics and subjects taking lipid lowering agents, subjects with history of gastric bypass or jejeno-ileal bypass, extensive small bowel resection and biliopancreatic disease were excluded.

Detailed clinical examination of each subject was done including blood pressure measurement to note presence or absence of hypertension.

AST, ALT and AST/ALT ratio and fasting blood glucose were obtained for each subject.

Each subject underwent liver biopsy in a standard way after getting informed consent and necessary investigations like hemoglobin level, platelets count, prothrombin time and blood group. Decision to perform liver biopsy in each subject was done on individual basis i.e. for exclusion of other causes of liver disease, assessment of degree of fibrosis and determination of long term prognosis; subjects were included in this decision. Liver biopsy was taken under ultrasound guide with aseptic precautions and sent to histopathology to assess the staging and grading of steatohepatitis.

Data was analyzed using statistical programme (SPSS) version 16, Descriptive statistics were used as mean, SD, and %. *Chi square* test was used for categorical data, $P<0.05$ considered significance

RESULTS

The study results revealed that among 30 NAFLD patients 23(76.7%) were females and seven (23.3%) were males, male to female ratio was 1:3.3; and mean age of patients was 40 ± 15 years.

Table 1 showed that most of the cases were symptomatic 23(76.7%) complaining of vague right hypochondrial pain, 3(10%) were hypertensive, 24(80%) subjects were overweight or obese, 3(10%) subjects were newly discovered diabetics, 11(36.7%) had hypertriglyceridemia and 26.7 (n = 8) had hypercholesterolemia. Eight patients (26.6%) had high AST (5 females and 3 males), and the other twenty-two patients had normal AST values; nine patients (30%) had high ALT and twenty-one (70%) patients had normal ALT; AST\ALT ratio <1 in twenty patients (66.6%) and AST\ALT ratio ≥1 in ten patients (33.4%); ALT levels in most of the patients higher than AST level (Table 1).

The mean AST level was 27.8 ± 13.9 U\L, mean ALT level was 42.5 ± 20.2 U\L and the mean AST\ALT ratio was 0.65.

By liver biopsy, mild steatosis and mild ballooning of hepatocytes was diagnosed in 33.3%, moderate in 30% and severe in 36.7%; Acute lobular inflammation was present in 26.7%, chronic in 73.3%. Seventeen patients had pericellular fibrosis, focal in 66.7% and extensive in 33.3%. Periportal fibrosis was present in 56.7%, focal in 50% and extensive in 6.6%, no evidence of bridging fibrosis and no cirrhosis.

Table 1: Clinical and biochemical features of NAFLD

Character	No.	%
Symptomatic	23	76.7
Co-morbidity:		
Hypertension	3	10
Diabetes	3	10
Overweight or obese	24	80
Hypertriglyceridemia	11	36.7
Hypercholesterolemia	8	26.7
AST level:		
High AST	8	26.7
Normal AST	22	73.3
***ALT** level:*		
High ALT	9	30
Normal ALT	21	70
AST\ALT ratio:		
AST\ALT ratio <1	20	66.6
AST\ALT ratio ≥1	10	33.4
Steatosis		
Mild	10	33.3
Moderate	9	30
Sever	11	36.7
lobular inflammation		
Acute	8	26.7
Chronic	22	73.3
Pericellular fibrosis	17	56.7

NASH was diagnosed in 16 patients (53.3%), 9 patients (56.2%) with normal ALT and 7 patients (43.7%) of those with increased ALT; and simple steatosis in 14 patients (46.7%), 11 patients (78.6%) with normal ALT and 3 patients (21.4%) with increased ALT. There was non-significant difference in ALT level in both groups, (P=0.617) (Figure 1).

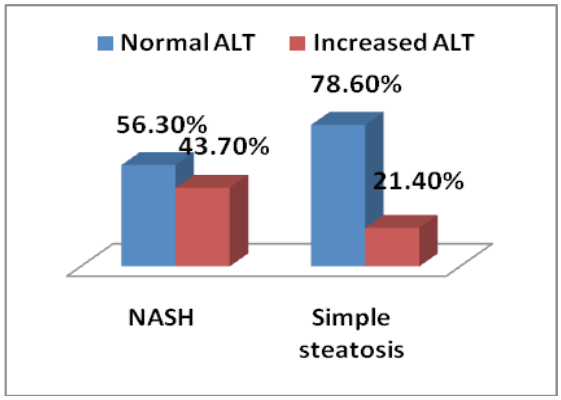

Figure 1: Distribution of patients by ALT enzyme level and type of steatosis

NASH was diagnosed in 16 patients (53.3%), the mean AST value was 31.8 while the mean ALT value was 59.3; and simple steatosis in 14 patients (46.7%), the mean AST value was 26.2 and the mean ALT value was 26.4 (Figure 2).

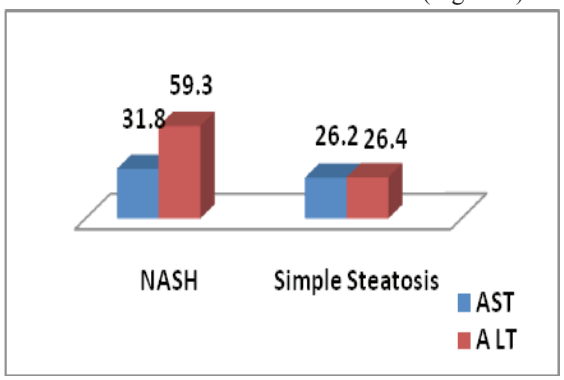

Figure 2: Distribution of the patient according to the type of steaosis and mean value of ALT and AST level.

DISCUSSION

Increasing age, diabetes, obesity and hypertriglycidemia are generally associated with advanced form of NAFLD.[6,7] Ultrasound diagnosis of fatty liver in this study showed that 100% of the cases corresponded with histopathological findings. And all patients met the all criteria for ultrasound diagnosis of fatty liver, Ultrasound has 82-90% sensitivity and 77% specificity in detecting fatty liver[8], it is however unable to distinguish between NASH and other forms of NAFLD.[9]

The serum ALT value has long been used as a surrogate marker of liver injury, it is however, well known that the ALT values does not correlate well with the severity of liver disease noted on liver biopsy in subjects with chronic liver disease. This is particularly true when one considers the stage of fibrosis present in an individual patient; the present study confirms this to be true also for NAFLD.

Several published studies have provided detailed information on the histological and clinical spectrum of findings in patients with NAFLD. The majority of subjects in these studies were identified by the presence of elevated liver enzymes, it is however, known that both fatty liver and NASH may exist without elevation of ALT.[10]

An important question is the following:

To identify subjects with clinically significant NAFLD in the absence of symptoms, signs or abnormal ALT values, it is clearly both unreasonable and impractical to perform routine liver biopsies for this purpose, although much work need to be done to determine who should be evaluated, the current study suggest that those with hepatomegaly or ultrasonographic feature of fatty liver are more likely to have significant underlying pathology.

This proved that patients with normal ALT may also have NASH and severe fibrosis, our study expands their observation to patients who are commonly referred to out patients clinic for steatosis and or metabolic alterations, being representative of much larger group of NAFLD patients, in the general population the data by Mofrad et al[11] were only partially confirmed in a recent study limited to potential liver donors in which the prevalence of NASH in patients with or without increased ALT was only 3.4% and 2.1% respectively[12]; similar results were also reported by Machado et al.[13,14]

CONCLUSION

Non Alcoholic steatohepatitis{NASH} can be associated with normal Alanine aminotransferase{ALT}or Aspartate aminotransferase{AST} and a liver biopsy is the golden standard method in diagnosis however, liver biopsy is not be justified if the patient has normal enzymes.

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