

# Hepatic Steatosis

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## ABSTRACT

**OBJECTIVE:** To determine the frequency of hepatic steatosis by ultrasonography in diabetics and compare with non-diabetics.

**MATERIAL AND METHODS:** This case-control study was carried out in a private clinic at Hyderabad, Sindh - Pakistan, on 100 patients out of which 50 were known diabetics and 50 were controls. Liver ultrasound findings were studied in both study groups.

**RESULTS:** Bright liver was shown in 20 (40%) diabetics out of which 12 were females and 8 were males. Control group showed bright liver in 15 (30%) out of which 6 were males and 9 were females. Focal/patchy infiltration was seen in 4 (16%) of diabetic men and 5 (20%) of diabetic women, whereas control group showed patchy infiltration in 10 (20%) patients, equals in males and females. In addition peri-portal fibrosis was found in 4 males and 6 females in the diabetic group. Liver biopsy/CT-scan confirmed the sonographic findings.

**CONCLUSION:** Ultrasonography is a cost effective and non-invasive procedure to diagnose steato-hepatitis. It is readily available and the results are comparable to other invasive and or expensive diagnostic tools.

**KEY WORDS:** Steatosis, Steatohepatitis, Diabetes, Obesity, Ultrasonography.

## INTRODUCTION

Lipid metabolism takes place mainly in liver. This is defined as accumulation of fat, mainly triglycerides, exceeding 5% of liver weight. It is caused by failure of normal hepatic fat metabolism either due to defect within the hepatocyte or to delivery of excess fat, fatty acid or carbohydrate beyond the secretory capacity for lipid of the liver cell<sup>1</sup>. Non-Alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH) may accompany obesity, diabetes, parenteral nutrition, jejuno-ileal bypass and chronic inflammatory bowel disease<sup>2</sup>. Non-alcoholic fatty liver disease (NAFLD) encompasses both simple steatosis and non-alcoholic setatohpatitis, which may ultimately lead to cirrhosis of liver.

NASH can lead to liver related death in 12-25%<sup>3</sup>. It can develop into sub-acute liver failure and hepatocellular carcinoma<sup>4</sup>.

These facts were barely recognized before 1981 but now 17-33% Americans are found to have NAFLD<sup>5</sup>. In other studies, the prevalence of 10-51% has been quoted involving all ages<sup>5</sup>. It has a worldwide distribution, and parallels the frequency of central adiposity, obesity, insulin resistance, metabolic syndrome and type-II diabetes. NASH could be present in one third of NAFLD cases. Age, activity of steatohepatitis and established fibrosis predispose to cirrhosis with a 7-10 year liver related mortality of 12-15%<sup>4</sup>. Many cases of cryptogenic cirrhosis are likely end-stage NASH. Pathogenic concepts for NAFLD/NASH must account for strong links with over-nutrition and under-activity, insulin resistance and genetic factors. Lip-toxicity,

oxidative stress, cytokines, and other inflammatory mediators may each play a role in transition of steatosis of NASH<sup>3,5</sup>. Chronic hepatitis-C with steatosis has shown less response to anti-viral therapy.

Awareness of this relatively benign condition that leads to ultimate liver injury and cirrhosis has often been gone unnoticed in our practice<sup>5</sup>.

NAFLD/NASH can best be diagnosed on liver biopsy, but patients usually refuse this procedure for various reasons. Non-invasive methods like CT-scan and ultrasonography are the next choice to detect staetosis/fibrosis. CT-scan facility is not easily available, is expensive and time consuming. Ultrasonography is the cost effective and easily available method for prompt diagnosis. Comparing diagnostic efficacy on ultrasound versus CT-scan, it was shown that the overall accuracy of ultrasonography for the detection of FIL (fatty infiltration liver) was 85%, with 100% sensitivity, and 56% specificity. The sonographic/CT correlation in grading the severity of FIL was particularly good for grade II (moderate) and grade III (severe) FIL<sup>6</sup>.

This study was aimed to determine the frequency of NAFL/NASH in our population on ultrasound and compare the findings between diabetics and non-diabetics.

## MATERIALS AND METHODS

This case-control study was conducted at a private clinic in Hyderabad, Sindh – Pakistan, where beside the Hyderabad city, patients are presented from rural areas as well. Patients were enrolled for this study from January 2006 to December 2006. Fifty known

diabetics with duration of diabetes >5-years were paired for age, sex and BMI>30-kg/m<sup>2</sup> with non-diabetics who were mostly presented with acid-peptic disease. After obtaining an informed consent, all subjects underwent detailed history and physical examination. Patients with history of cholecystectomy, alcoholism, liver disease due to other etiology, hypertension, ischemic heart disease, prolonged history of diarrhea, or use of hypotoxic drugs were excluded from the study. Height, weight, waist circumference, and body mass index of each subject were recorded. Plasma glucose (random), SGPT, triglyceride were carried out in all subjects. Serum HbA1c level was recorded in diabetics. Ultrasonography was performed with Aloka, using 3.5 MHz transducer. Liver biopsy was performed in 10 diabetics and 5 controls. CT scan was performed in 5 subjects of each group. Frequencies and proportions were calculated and ultrasonographic findings were evaluated by the author (AH).

**RESULTS**

In each study groups 25 males and 25 females were enrolled. Seventy percent were obese in both groups, as detailed in (Table I).

Diffuse fatty infiltration (bright liver) showed enlarged liver, with diffuse increase in echogenicity. Bright walls of portal vein wre blurred as against the bright parenchyma of liver. Focal infiltration was interpreted as white hyper-echoic rounded areas that were sharply defined by straight lines as to give them a local or focal appearance.

They were multifocal with intervening areas of normal liver (Figure I).

Echogenicity was more in areas of FIL, as compared to kidneys. Data revealed that bright liver was shown in 20 (40%) diabetics out of which 12 were females and 8 were males. Control group showed bright liver in 15 (30%) out of which 6 were males and 9 females. Focal/patchy infiltration was seen in 4 (16%) of diabetic men and 5 (20%) of diabetic women, whereas control group showed patchy infiltration in 10 (20%) patients with equal males and females. In addition, peri-portal fibrosis was found in 4 males and 6 females in the diabetic group. All these findings were co-related with duration, and poor control of diabetes, obesity and lipid levels. Fibrosis was found in cases with bright liver along with elevation of SGPT. In the control group, focal fibrosis in 2 of each males and females had raised liver enzymes (Figure II). Liver biopsy done in 15 patients proved sonographic findings showing infiltration of lymphocytes, bridging fibrosis and periportal fibrosis, macro-micro vesicular fat deposits. CT-scan findings confirmed ultrasound findings, showing increased echogenicity with attenuation of 30 HU unenhanced and 50 HU with enhancement.

In cases of bright liver fat content was estimated about 10% of the liver mass.

**TABLE I:  
CHARACTERISTICS OF BOTH STUDY GROUPS**

	Diabetic (n=50)		Control (n=50)	
	Male	Female	Male	Female
Obese (BMI>30-kg/m <sup>2</sup> )	15 (60%)	20(80%)	15 (60%)	20(80%)
Blood sugar (Random<200-mg/dL)	20 (80%)	20(80%)	25 (100%)	25 (100%)
HbA1c (<7.5%)	15 (60%)	20(80%)	25 (100%)	25 (100%)
SGPT (Raised ≥60)	10 (40%)	15(60%)	05 (20%)	08(32%)
S. Triglyceride (<150-mg/dL)	15 (60%)	20(80%)	10 (40%)	15(60%)

**FIGURE I:  
BRIGHT LIVER**



**DISCUSSION**

Non-alcoholic fatty liver disease (NAFLD) is an increasingly recognized form of chronic liver injury. It encompasses a wide spectrum of fat-induced liver injury ranging from relatively benign steatosis to steatohepatitis, advanced fibrosis and cirrhosis of liver<sup>7,8</sup>. It is frequently associated with obesity and visceral fat. Both the prevalence and severity are related to BMI, waist circumference ratio, hypertriglyceridemia and type-2 diabetes. The pathogenesis of NAFLD is very complex. There is mitochondrial, morphological and functional alteration, as well as high sensitivity to inju-

**FIGURE II:  
FOCAL FATTY INFILTRATION AS SEEN ON  
ULTRASOUND**



rious stimuli, an increased inflammatory activity and modification in cellular metabolism at post receptor level<sup>9</sup>. Lipid peroxidation/oxidative stress and/or endotoxin induced cytokine release are implicated<sup>10</sup>.

In our study, bright liver was found in 40% of diabetics and 30% in the control group, with female preponderance. This is explainable with change of life-style, obesity, uncontrolled diabetes, and high lipid profile especially hypertriglyceridemia.

Liver biopsy is the most accurate method for diagnosis of steatosis but in our set up it is difficult to convince the patients for invasive procedures. CT-scan is not available in every institution and is a costly procedure that an average person cannot afford. Sonography has been recognized as a reliable and easy procedure that does not involve much cost. Hyperlipidemia is a known risk factor for fatty infiltration of liver, a condition that can progress to cirrhosis and liver failure. Out of 95 patients in a study 55% had hypercholesterolemia, 26% had severe hypertriglyceridemia and obesity and diabetes were present in 36% and 12% cases respectively. Sixty-four percent patients had elevated liver enzymes. Ultrasound findings revealed diffuse fatty liver in 50%. Hypertriglyceridemia and mixed hyperlipidemia were more associated with fatty liver than simple hypercholesterolemia. It was further more common among diabetics<sup>11</sup>.

In our study 40% cases had bright liver in the diabetic group and 30% in the control group. Focal infiltration was found in 36% of diabetic group and 20% in the control group. This clearly shows close correlation with obesity and hyperlipidemia. Further rise in diabetic group suggests that fatty infiltration is part of metabolic syndrome. Raised serum enzymes, which were found in 50% of diabetics, and 26% of control group suggests progression from FIL, to steato-

hepatitis.

In a prospective study on 187 patients, 91.4% sonographic findings of fatty infiltration of liver were confirmed on liver biopsy<sup>12</sup>. In other study CT-scan and ultrasound findings were compared with fat and fibrous contents of liver biopsy specimen, where it was estimated that patients with bright liver findings had 10% or higher fat content<sup>13</sup>.

Another study revealed 100% sensitivity of ultrasound findings of liver steatosis on liver biopsy. Increased echogenicity and hypoechoic focal changes are reliable indicators of fatty infiltration<sup>6,14</sup>. In other study CT scan/ultrasound findings were compared in six cases. CT-scans demonstrated multiple round areas of low attenuation within both lobes of liver. In all cases ultrasound studies showed hyperechoic foci in three cases and diffuse inhomogeneous hyper-echogenicity in the rest cases. Follow up after therapy the lesions disappeared within two months, thus excluding liver neoplasms<sup>15</sup>. Live-kidney echo levels with ultrasound findings can also be useful in the diagnosis of fatty liver disease<sup>16</sup>. Ultrasound can also predict the degree of fibrosis<sup>17</sup>. Hepatic steatosis, fibrosis and inflammation has also been evaluated by some researchers in chronic hepatitis-C and found ultrasound a useful non-invasive tool<sup>18</sup>. In other study liver biopsy was evaluated retrospectively in 155 patients. Relative high echoes of the liver as compared with kidney were observed in all 33 patients whose fatty infiltration occupied more than 10% of each lobule irrespective of etiology. Among such patients, loss of echoes from the gallbladder wall was additionally found in 18 of 19 patients uncomplicated with hepatic fibrosis, but only 3 of 14 cases with this complication. They concluded that fatty infiltration without fibrosis in the liver can be differentiated from that with fibrosis by ultrasonic examination<sup>19</sup>. Hyper-echogenicity of liver relative to kidney ultrasound beam attenuation, and poor visualization of intrahepatic structures is comparable with CT in perivascular fatty infiltration<sup>20</sup>.

## CONCLUSION

Ultrasonography is a cost effective and non-invasive procedure to diagnose steato-hepatitis. It is readily available and the results are comparable to other invasive and or expensive diagnostic tools.

NAFLD is very common in our society but often ignored by us, although it is reversible by changing life style, with control of risk factors like management of obesity, strict control of diabetes, hyperlipidemia, and drugs like antioxidants, and other drugs such as ursodeoxycholic acid, etc. Awareness of this condition can prevent mortality and morbidity.

When unnoticed it may progress to steato-hepatitis, and fibrosis, and ultimately liver cirrhosis, and hepato-

cellular carcinoma. This study aimed to invite attention of general practitioners, as well as clinicians to this problem, that can be easily diagnosed by an expert sonologist, which itself is highly specialized subject.

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