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THE CORRELATION BETWEEN UTRASOUND FINDINGS AND LIVER FUNCTION TEST VALUES IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Gastroenterology

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ABSTRACT

Objective: To detect and compare Liver Function Test abnormalities in patients diagnosed with different grades of Non Alcoholic Fatty Liver disease diagnosed on ultrasonography. **Methods:** A total of 90 cases diagnosed using Ultrasonogram were investigated with Liver Function Test parameters. Then a comparison of liver function test abnormalities with different grades of ultrasound was done. P value <0.05 was considered statistically significant **Results:** Out of 90 cases of NAFLD diagnosed using USG grade 1 cases were 54.4%, grade 2 cases were 24.4%,grade 3 cases were 21.1% . Average age of the patient was 45.82. Male to female ratio was 3:1. Upon statistical analysis it was found that increasing grades of NAFLD diagnosed by Ultrasonogram was significantly associated with LFT value abnormalities. **Conclusion:** Even though liver biopsy is the gold standard for diagnosing NAFLD, Ultrasonogram which is a simple and non-invasive method can be used for early detection of NAFLD.

KEYWORDS

1. INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) includes a spectrum of diseases ranging from nonalcoholic steatosis to nonalcoholic steatohepatitis and finally to cirrhosis. Hepatic steatosis describes accumulation of fat mostly as triglycerides, cholesterol and phospholipids, in excess of 5-10% of liver weight. For many years the discovery of fatty liver during routine evaluation was not thought to have clinical significance. However it was known that obese and diabetic patient could develop histological steatohepatitis similar to that seen with alcohol induced liver diseases[1]. NAFLD was first described by Ludwig *etal*.in1980 as a condition with histological similarity to alcoholic liver disease but observed in patience without a history of significant alcohol intake[1]. Now the diagnostic criteria for NAFLD have an upper limit for alcohol consumption, which are 20 and 30 gram/day for women and men respectively[4,5]

NAFLD is now increasingly recognized as a major health problem. In a population based study by Browning et al in 2004 it was determined that 1/3 of general population in US has excessive accumulation of lipids in liver[2].Prevalence of NAFLD in India is comparable to that in West. In a study conducted by Amarapurkar *et al* prevalence of NAFLD based on USG was 18.9%[3].Incidental detection of NAFLD was considered of no importance in the past. But now it has been proved that some of these cases can progress gradually to fibrosis, cirrhosis and liver failure.

Most patients with NAFLD have no symptoms or signs of liver failure. They usually present with asymptomatic elevation serum aminotransferases or detected incidentally on routine ultrasound examinations. However some patients report fatigue or malaise or sensation of fullness in the right side of upper abdomen. Majority of patients are overweight and likely to have elevated waist hip ratio.Other features of metabolic syndrome are present. Hepatomegaly is the only physical finding in most patients[7].

As mentioned earlier, clinical suspicion of NAFLD is commonly triggered by abnormal aminotransferases[6]. The degree of aminotransferase levels are usually less than 1.5 times the upper limit of normal, ranging up to 4 times the normal. However aminotransferases are not helpful in distinguishing between fatty liver alone and NASH. Usually ALT is elevated more and AST/ALT ratio of more than 2 is almost never seen in NAFLD. In a study conducted by Georgie kirvosky *et al* the sensitivity and specificity of NALD was 44 and 80% respectively[8]

Ultrasonogram is easily available, safe, radiation free and cost effective way for diagnosing fatty liver. More over the degree of involvement can be quantified using a semi quantitative scale depending up on the degree of hepatic involvement. Thus echogenicity of liver can be graded to 3 different grades.

Liver biopsy can confirm a diagnosis of NAFLD and determine its severity. However liver biopsy is a painful and invasive procedure[9]. Rarely it can cause potentially life threatening complications like bleeding[10]. In addition it is financially impractical in huge number of cases.

In a study by Chun-Hsien Hsu it was shown that both elevated ALT and abnormal echogenicity of liver have been linked to metabolic syndrome[11]. In this study it was also established that abnormal liver echogenicity of liver is more significantly associated with metabolic syndrome than elevated ALT. In an another study by Dhumal Uttareswar Mahaling *et al* a comparison of different grades of USG with lipid profile was done which showed increasing grades of fatty liver was significantly increasing values of total cholesterol, LDL and VLDL[11]. No significant association was found between increasing grades of sonography and triglyceride levels.

2. MATERIALS & METHODS

A hospital based cross sectional study was conducted using 90 patients who were found to have at least grade 1 fatty liver changes on USG. Approval from institution ethics committee was obtained prior to the study. Informed consent from each patient was taken. Patients with alcohol intake more than 20 gram /day in females and 30 gram/day in males were excluded from the study.

Patients with serological evidences for chronic hepatitis, diagnosed cases of Wilson's disease and haemochromatosis, patients using drugs which are supposed to cause elevations in liver enzymes were also excluded.

Subjects were considered as patients if they have at least grade 1 fatty liver in accordance with standard criteria by American gastroenterology association. The diagnosis of fatty liver was made on basis of hepatic echogenicity and is classified in to 3 grades with a standardized semi quantitative scale

Grading of non-alcoholic fatty liver disease on USG

Grade1:

Mild increase in fine echoes. Compared to cortex of kidney liver appears bright. Visualization of intrahepatic vessel borders and diaphragm is normal.

Grade2:

Moderate diffuse increase in fine echoes. Impaired visualization of intrahepatic vessel borders with preserved visualization of diaphragm.

Grade3:
Marked increase in fine echoes. Both intrahepatic vessels and diaphragm are poorly visualized. There is poor penetration of right lobe posterior segments.

All patients diagnosed as NAFLD on USG were investigated with liver function tests. Then a relationship between NAFLD and Liver Function Tests were compared

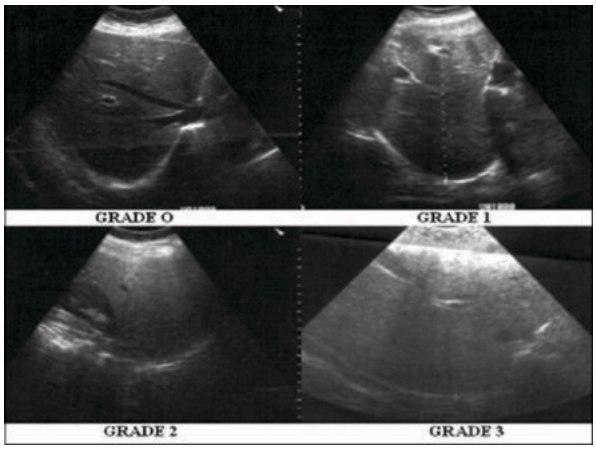


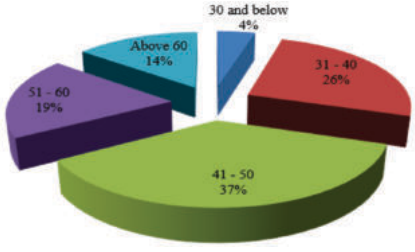
Diagram showing normal liver and liver NAFLD three grades.

RESULTS

A total of 90 ultrasonographically diagnosed NAFLD cases were included in the study. Mean age of the patients was 45.82. Mean age in males was 46.59. Mean age in females was 41.44. Most of the patients belonged to fourth and fifth decades.

Table 1
Showing age distribution

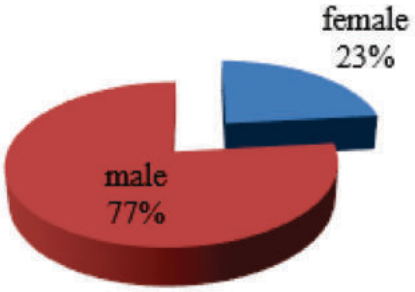
		Frequency	Percent
	30 and below	4	4.4
	31 - 40	23	25.6
	41 - 50	33	36.7
	51 - 60	17	18.9
	Above 60	13	14.4
	Total	90	100.0



Most of the patients were males. Male to female ratio was 3:1

Table showing sex distribution
Table 2

		Frequency	Percent
	female	21	23.3
	male	69	76.7
	Total	90	100.0



On ultrasonography Grade 1 NAFLD cases were seen in 54.4%, Grade 2 in 24.4 % and grade 3 in 19% patients.

Table 3
Showing distribution of NAFLD grades

		Frequency	Percent
	Grade 1	49	54.4
	Grade 2	22	24.4
	Grade 3	19	21.1
	Total	90	100.0

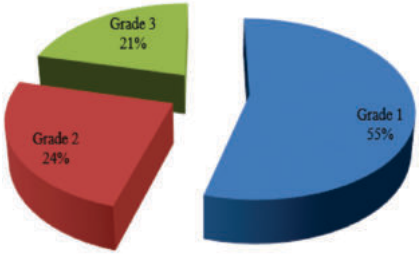
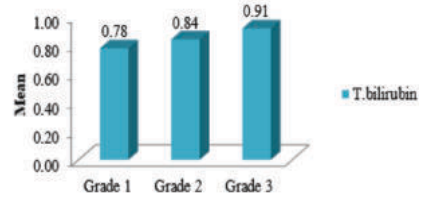


Table 4 shows comparison of total bilirubin changes in different grades of NAFLD analyzed statistically by analysis of variance (ANOVA). P value was found to be 0.124.It was observed increasing grades of NAFLD were not significantly associated with total bilirubin

Table 4
Showing distribution total bilirubin in different USG grades

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	.7759	.23587	.7082	.8437	2.135	.124
Grade 2	22	.8377	.28507	.7113	.9641		NS
Grade 3	19	.9147	.25596	.7914	1.0381		
Total	90	.8203	.25592	.7667	.8739		



Graph showing mean values of total bilirubin in different grades of NAFLD.

Direct Bilirubin:
Table 5 shows comparison of direct bilirubin changes with different grades of NAFLD analyzed statistically by ANOVA. It was observed that increasing grades of NAFLD were significantly associated with direct bilirubin.

Table 5
Showing distribution of direct bilirubin in different USG grades

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	.2300	.06341	.2118	.2482	5.877	.004
Grade 2	22	.2473	.10425	.2011	.2935		HS
Grade 3	19	.3011	.07117	.2667	.3354		
Total	90	.2492	.08084	.2323	.2662		

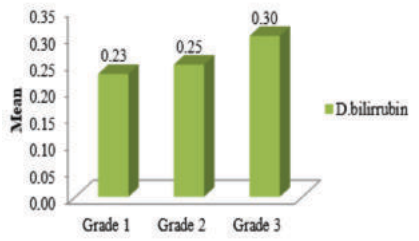


Table 6 shows comparison of SGOT with increasing grades of NAFLD. It was found that increasing grades on NAFLD were significantly associated with SGOT. P value was found to be 0.0001

Table 6
Showing distribution of SGOT in different ultrasound grades.

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	49.94	17.382	44.95	54.93	55.747	.000
Grade 2	22	67.05	19.048	58.60	75.49		HS
Grade 3	19	95.47	3.935	93.58	97.37		
Total	90	63.73	23.963	58.71	68.75		

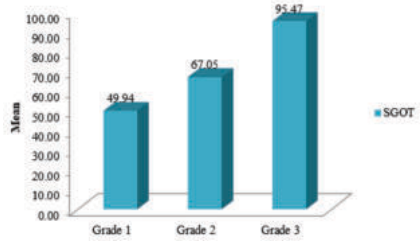


Table 7 shows comparison of SGPT with increasing grades of NAFLD. It was found increasing grades of NAFLD were significantly associated with SGPT. P value was found to be 0.0001

Table 7
Showing distribution of SGPT in different NAFLD grades.

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	55.71	20.256	49.90	61.53	82.427	.000
Grade 2	22	89.77	30.234	76.37	103.18		HS
Grade 3	19	129.74	11.229	124.32	135.15		
Total	90	79.67	36.589	72.00	87.33		

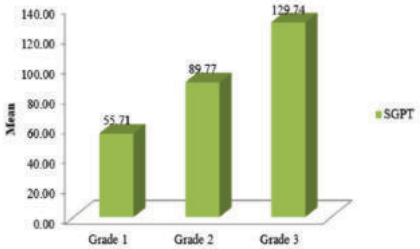


Table 8 shows comparison of ALP with increasing grades of NAFLD. It was found that increasing grades of NAFLD is not significantly associated with ALP

Table 8
Showing distribution of ALP in different USG grades

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	82.69	15.254	78.31	87.08	.375	.688
Grade 2	22	83.23	23.360	72.87	93.58		NS
Grade 3	19	87.32	26.247	74.67	99.97		
Total	90	83.80	19.924	79.63	87.97		

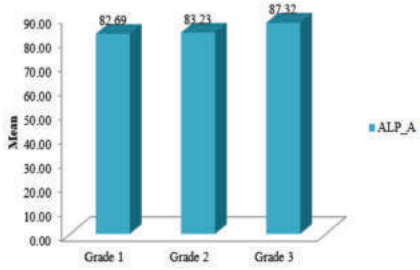


Table 9 shows comparison of Total protein with increasing grades of NAFLD. It was found that increasing grades of NAFLD was not significantly associated with total protein. P value was found to be 0.503

Table 9
Showing distribution of total protein in different USG grades

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	7.344	.3992	7.229	7.459	.692	.503
Grade 2	22	7.241	.2806	7.117	7.365		NS
Grade 3	19	7.289	.2726	7.158	7.421		
Total	90	7.307	.3485	7.234	7.380		

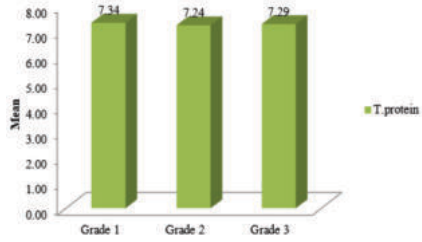
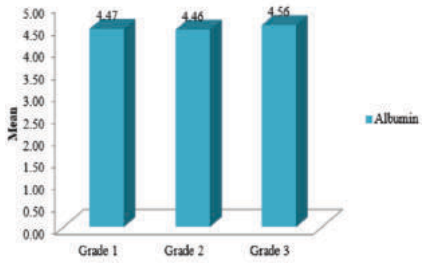


Table 10 shows comparison of serum albumin with increasing grades of NAFLD. It was found that increasing grades of NAFLD is not significantly associated with albumin. P value was found to be 0.488

Table 10
Showing distribution of serum albumin in different USG grades

	N	Mean	Std. Deviation	95% Confidence Interval for Mean		ANOVA F	p
				Lower Bound	Upper Bound		
Grade 1	49	4.473	.3103	4.384	4.562	.723	.488
Grade 2	22	4.459	.3202	4.317	4.601		NS
Grade 3	19	4.563	.2813	4.428	4.699		
Total	90	4.489	.3060	4.425	4.553		



DISCUSSION

NAFLD has been emerged as one of the most common cause of liver disease in Europe and America. In India and other Asian countries also, due to increasing prevalence of obesity and metabolic syndrome, the incidence of NAFLD is increasing recently. It is estimated that approximately 20% obese and 5% over weight patients have NAFLD. Our present study was intended to understand the extent of LFT changes in different grades of NAFLD, diagnosed by noninvasive methods, thus replacing liver biopsy, which is an invasive and painful procedure.

In our study patients age ranged from 27 to 68.mean age was 45.8. Mean age in males were 46.59 and mean age in females were 41.44. In an Indian study conducted by amararapurkar *et al*the mean age was 55.4.

In NAFLD most of the patients are asymptomatic. Usually the disease is diagnosed incidentally by routine USG or incidental detection of elevated transaminases.

Liver biopsy is considered as the gold standard investigation for diagnosing NAFLD. But liver biopsy is painful, invasive and associated with complications also. So it is not possible to perform liver biopsy in each and every cases of NAFLD. So ultrasonography is

an important investigation for diagnosing NAFLD. This is once again emphasized in our study by demonstrating significantly increased transaminase levels in different grades of NAFLD diagnosed by Ultrasonogram

Ultrasonography can be used as a tool for detecting NAFLD in early stages. NAFLD grades diagnosed by sonography showed significant association with serum direct bilirubin, SGOT and SGPT. So it is possible to say USG is an inexpensive, simple and radiation free modality for early detection of NAFLD.

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