

Grading of Non-Alcoholic Fatty Liver Disease on Ultrasound and Its Correlation with Lipid Profile

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A B S T R A C T

Introduction: The diagnosis and grading of fatty liver on ultrasonography has been frequently observed these days. The objective of the study was to detect different grades of NAFLD on ultrasonography and correlate it with serum lipid abnormalities.

Material and Methods: This was an observational study on 384 patients referred to Bharati medical college and hospital during June 2018 to May 2019. Patients underwent ultrasonography and were considered “cases” if they had fatty liver. Correlation between NAFLD and serum lipid profile was done.

Results: Of 384 patients, 352 (91.7%), 30 (7.8%) and 2 (0.5%) had grade I, II and III fatty liver respectively. Increased total cholesterol, serum triglycerides, LDL and VLDL were seen in 35.2%, 56.8%, 34.9% and 58.9% of cases respectively; while reduced HDL cholesterol levels in 56.5%. Total cholesterol to HDL and LDL to HDL ratio was raised in 37% and 21.1% of cases respectively. The distribution of mean total cholesterol, triglyceride, LDL levels, total cholesterol to HDL ratio and LDL to HDL ratio differed significantly in our study across three grades of NAFLD. The distribution of abnormality of different components of lipid profile did not differ significantly across fatty liver grades.

Conclusion: Significant positive correlation was noted between NAFLD and increasing levels of serum total cholesterol, triglyceride, LDL, total cholesterol to HDL and LDL to HDL ratios. Significant positive correlation between the fatty liver grades and levels of different components of lipid profile was absent. We can thus conclude that dyslipidemia can be predicted in USG diagnosed NAFLD.

Keyword: NAFLD, Dyslipidemia, USG, Grading, LDL, Triglycerides.

INTRODUCTION

Fatty liver is one of the commonest problem worldwide. Its prevalence is around 20%–30% in general population in Western countries and 9% to 32% in India.¹ Initially it was termed as a benign pathology but now it is increasingly been recognized as the primary causes of liver-associated morbidities and mortalities. NAFLD spectrum includes simple steatosis and non-alcoholic steatohepatitis (NASH). Studies have demonstrated that non-alcoholic fatty liver disease (NAFLD) can progress to liver cirrhosis, hepatic failure, and further to hepatocellular carcinoma (HCC) as well.² The diagnosis of NAFLD remains underdiagnosed as most of the patients are asymptomatic till terminal stages of disease.

The sensitivity of USG in detecting hepatic steatosis ranges from 60 to 94% and the specificity from 84 to 95%.^{3,4,5} Although the biopsy is the gold standard tool for diagnosis of NAFLD, its utility is limited by the invasiveness for just the screening. Fortunately, the presumptive diagnosis can

also be made by ultrasound (USG), computed tomography (CT), and magnetic resonance imaging (MRI).

Dyslipidemia is a predisposing factor for complications such as hypertension, atherosclerosis, various heart diseases, renal pathologies, etc. It is possible to correlate ultrasound findings and changes in the dyslipidemia in patients with NAFLD. The objective of the study was to detect different grades of NAFLD on ultrasonography and correlate it with serum lipid abnormalities.

MATERIAL AND METHODS

This was a prospective observational type of study done at Bharati Vidyapeeth medical college and hospital during June 2016 to May 2018. Total 384 patients were scanned with convex probe and Philip HD 11 machine. The examination was performed with the patient in the supine position. Direct contact scanning technique along with acoustic coupling gel was used. Through scanning was done in all possible approaches. The patient's identity was masked and data used purely for the study purpose. All patients diagnosed as fatty

liver on USG of the age more than 18 years were included in the study. While the patients with history of regular alcohol intake more than 30 g/d in males and more than 20 g/d in females were excluded.

Grading of fatty liver was done as –

When the echogenicity was only marginally increased, it was grade I; when the echogenic liver obscured the echogenic walls of portal vein branches, it was grade II, and when the echogenic liver obscured the diaphragmatic outline, it was grade III fatty infiltration⁶

All the subjects in the study diagnosed as NAFLD on ultrasonography were investigated for serum lipid profile –total cholesterol (N< 200 mg/dl), HDL (N> 40 mg/dl for males, >50 for females), triglycerides (N< 150mg/dl), LDL (N< 100mg/dl), VLDL (N< 12-30mg/dl) total cholesterol: HDL ratio (N< 5 for male, < 4.5 for females) and LDL: HDL ratio (N< 3.6 for male, < 3.2 for females). Values outside this range were considered abnormal. Then, a correlation between NAFLD and serum lipid profile was done.

RESULTS

Age distribution

Of total 384 subjects included in this study, 34 cases (8.9%) were between 20.0 - 29.0 years age group, 108 cases (28.1%) had their age between 30.0 – 39.0 years, 95 cases (24.7%) had their age between 40.0 – 49.0 years, 100 cases (26.0%) had their age between 50.0 – 59.0 years, 36 cases (9.4%) had their age between 60.0 – 69.0 years, 11 cases (2.9%) were between 70.0 – 79.0 years age group (table-1).

So, the mean ± SD of age of cases studied in the entire study group was 45.5 ± 11.8 years. The minimum – maximum range of age was 23 – 76.0 years.

Sex distribution

Of 384 cases studied, 261 cases (68.0%) were males and 123

Age (Years)	No of cases	Percentage
20 – 29	34	8.9
30 – 39	108	28.1
40 – 49	95	24.7
50 – 59	100	26
60 – 69	36	9.4
70 – 79	11	2.9

Table-1: Age distribution of cases studied (n= 384).

	No of cases	Percentage
Male	261	68
Female	123	32

Table-2: Sex distribution of cases studied (n= 384)

Grade of fatty liver	No of cases	Percentage
I	352	91.7
II	30	7.8
III	2	0.5

Table-3: Distribution of cases studied according to fatty liver grades on USG (n= 384).

cases (32.0%) were females. The male to female sex ratio in the entire study group was 2.12: 1.00 (table-2).

Distribution of fatty liver grades on ultrasound

Of total 384 cases, 352 (91.7%) had Grade I fatty liver, 30 (7.8%) had Grade II fatty liver and only 2 cases (0.5%) had Grade III fatty liver (table-3).

Distribution of grades of fatty liver according to age

The distribution of grades of fatty liver did not differ significantly across various age groups of cases studied (P-value>0.05) (table-4).

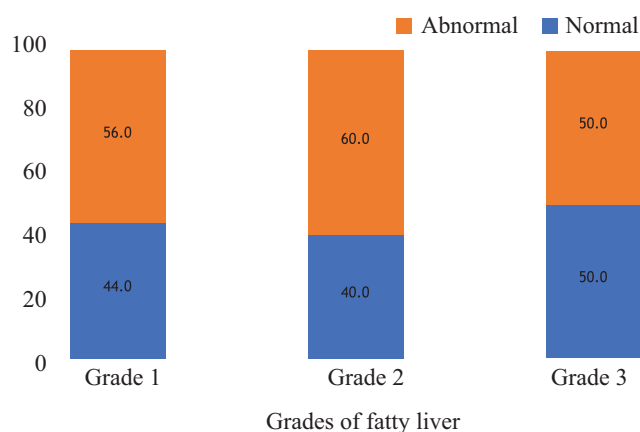


Figure-1: Distribution of prevalence of abnormality of HDL cholesterol according to the grades of fatty liver (n=384).

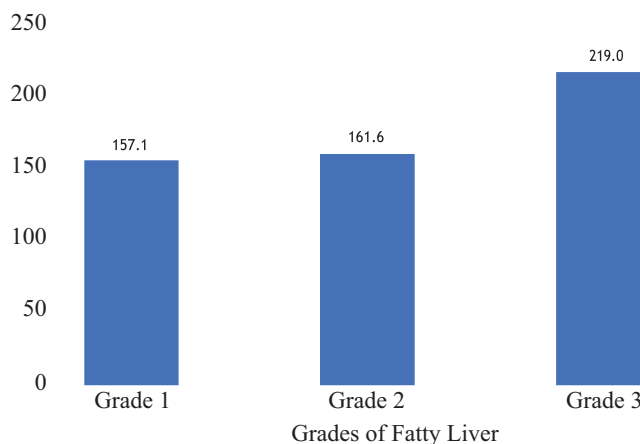


Figure-2: Distribution of mean Triglycerides according to the grades of fatty liver (n=384).

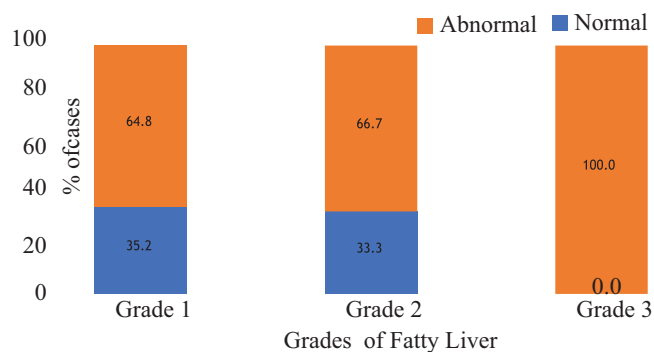


Figure-9(B): Distribution of prevalence of abnormality of LDL cholesterol according to the grades of fatty liver (n=384).

Age groups (years)	Fatty liver (Grades)						Total	
	Grade I		Grade II		Grade III			
	n	%	n	%	n	%	n	%
20 – 29	32	94.1	2	5.9	0	0	34	8.9
30 – 39	102	94.4	6	5.6	0	0	108	28.1
40 – 49	82	86.3	11	11.6	2	2.1	95	24.7
50 – 59	91	91.0	9	9.0	0	0	100	26
60 – 69	35	97.2	1	2.8	0	0	36	9.4
70 – 79	10	90.0	1	9.1	0	0	11	2.9
Total	352	91.7	30	7.8	2	2.1	384	100

Table-4: Distribution of cases studied according to age and fatty liver grades on USG (n= 384).

Grades of fatty liver	Total cholesterol (mg/dl)				
	N	Mean	S.D.	Minimum	Maximum
I	352	188.6	39.6	73	358
II	30	178.9	44.0	101	258
III	2	249.5	34.7	225	274

Table-5(A): Distribution of mean total cholesterol according to the grades of fatty liver (n=384).

Grades of fatty liver	N	Total cholesterol (mg/dl)			
		Normal		Abnormal	
I	352	226	64.2%	126	35.8%
II	30	23	76.7%	7	23.3%
III	2	0	0%	2	100%

Table-5(B): Distribution of abnormality of prevalence of total cholesterol according to the grades of fatty liver (n=384)

Grades of fatty liver	N	HDL cholesterol (mg/dl)			
		Mean	S.D.	Minimum	Maximum
I	352	42.7	9.3	22	72
II	30	40.8	9.4	28	58
III	2	37.7	8.1	32	44

Table-6(A): Distribution of mean HDL cholesterol according to the grades of fatty liver (n=384).

Grades of fatty liver	n	HDL cholesterol (mg/dl)			
		Normal		Abnormal	
I	352	155	44%	197	56%
II	30	12	40%	18	60%
III	2	1	50%	1	50%

Table-6(B): Distribution of prevalence of abnormality of HDL cholesterol according to the grades of fatty liver (n=384)

Grades of fatty liver	n	Triglycerides (mg/dl)			
		Normal		Abnormal	
I	352	203	57.7%	149	42.3%
II	30	15	50%	15	50%
III	2	0	0%	2	100%

Table-7(B): Distribution of prevalence of abnormality of Triglycerides according to the grades of fatty liver (n=384).

Grades of fatty liver	n	LDL cholesterol (mg/dl)			
		Mean	S.D.	Minimum	Maximum
I	352	114.3	33.7	11.2	247.6
II	30	105.7	35.1	34.6	162.2
III	2	164.5	36.1	139	190

Table-8(A): Distribution of mean LDL cholesterol according to the grades of fatty liver (n=384)

LDL cholesterol (mg/dl)

Grades of fatty liver	n	Normal		Abnormal	
I	352	124	35.2%	228	64.8%
II	30	10	33.3%	20	66.7%
III	2	2	0%	2	100%

Table-8(B): Distribution of prevalence of abnormality of LDL cholesterol according to the grades of fatty liver (n=384).

Grades of fatty liver	n	VLDL cholesterol (mg/dl)			
		Mean	S.D.	Minimum	Maximum
I	352	31.3	15.8	4.0	112.2
II	30	32.3	16.2	9.4	72.0
III	2	47.1	6.9	42.3	52.0

Table-9(A): Distribution of mean VLDL cholesterol according to the grades of fatty liver (n=384).

Grades of fatty liver	n	Total cholesterol to HDL ratio			
		Mean	S.D.	Minimum	Maximum
I	352	4.58	1.26	1.4	8.9
II	30	4.59	1.46	1.8	7.4
III	2	6.88	2.37	5.2	8.6

Table-10(A): Distribution of mean Total cholesterol to HDL ratio according to the grades of fatty liver (n=384).

Grades of fatty liver	n	Normal		Abnormal	
		I	352	223	63.4%
II	30	19	63.3%	11	36.7%
III	2	0	0%	2	100%

Table-10(B): Distribution of prevalence of abnormality of Total cholesterol to HDL ratio according to the grades of fatty liver (n=384).

Grades of fatty liver	n	LDL to HDL ratio			
		Mean	S.D.	Minimum	Maximum
I	352	2.78	0.98	0.20	6.37
II	30	2.73	1.06	0.61	4.61
III	2	4.55	1.91	3.2	5.9

Table-11(A): Distribution of mean LDL to HDL ratio according to the grades of fatty liver (n=384).

Grades of fatty liver	n	Normal		Abnormal	
		I	352	277	78.7%
II	30	25	83.3%	5	16.7%
III	2	1	50.0%	1	50%

Table-11(B): Distribution of prevalence of abnormality of LDL to HDL ratio according to the grades of fatty liver (n=384).

Distribution of mean total cholesterol according to grades of fatty liver

The distribution of mean total cholesterol levels differs significantly across three grades of fatty liver (P-value<0.05) (table-5a).

Distribution of abnormality of total cholesterol according to grades of fatty liver

The distribution of prevalence of abnormality of total cholesterol levels did not differ significantly across three grades of fatty liver (P-value>0.05) (table-5b).

Distribution of mean HDL cholesterol according to the grades of fatty liver

The distribution of mean HDL cholesterol did not differ

significantly across three grades of fatty liver (P-value>0.05) (table-6a).

Distribution of prevalence of abnormality of HDL cholesterol according to the grades of fatty liver

The distribution of prevalence of abnormality of HDL cholesterol levels did not differ significantly across three grades of fatty liver (P-value>0.05) (table-6b)

Distribution of mean Triglycerides according to the grades of fatty liver

The distribution of mean Triglycerides did not differ significantly across three grades of fatty liver (P-value>0.05) (fig-1).

Distribution of prevalence of abnormality of Triglycerides according to the grades of fatty liver

The distribution of prevalence of abnormality of Triglyceride levels did not differ significantly across three grades of fatty liver (P-value>0.05) (fig-2), (table-7b).

Distribution of mean LDL cholesterol according to the grades of fatty liver

The distribution of mean LDL cholesterol differs significantly across three grades of fatty liver (P-value<0.05) (table-8a).

Distribution of prevalence of abnormality of LDL cholesterol according to the grades of fatty liver:

The distribution of prevalence of abnormality of LDL cholesterol levels did not differ significantly across three grades of fatty liver (P-value>0.05) (table-8b).

Distribution of mean VLDL cholesterol according to the grades of fatty liver

The distribution of mean VLDL cholesterol did not differ significantly across three grades of fatty liver (P-value>0.05) (table-9a).

Distribution of prevalence of abnormality of VLDL cholesterol according to the grades of fatty liver

The distribution of prevalence of abnormality of VLDL cholesterol levels did not differ significantly across three grades of fatty liver (P-value>0.05) (fig-3).

Distribution of mean Total cholesterol to HDL ratio according to the grades of fatty liver

The distribution of mean total cholesterol to HDL ratio differs significantly across three grades of fatty liver (P-value<0.05) (fig-4).

Distribution of prevalence of abnormality of Total cholesterol to HDL ratio according to the grades of fatty liver

The distribution of prevalence of abnormality of Total cholesterol to HDL ratio did not differ significantly across three grades of fatty liver (P-value>0.05) (table-10b).

Distribution of mean LDL to HDL ratio according to the grades of fatty liver

The distribution of mean LDL to HDL ratio differs significantly across three grades of fatty liver (P-value<0.05) (table-11a).

Distribution of prevalence of abnormality of LDL to HDL ratio according to the grades of fatty liver

The distribution of prevalence of abnormality of LDL to HDL ratio did not differ significantly across three grades of fatty liver (P-value>0.05) (table-11b).

DISCUSSION

In our study mean \pm SD of age of cases studied in the entire study group was 45.5 ± 11.8 years. The minimum – maximum range of age was 23 – 76.0 years. Most of the western studies have reported the mean age of NAFLD between 41-45 years. In Indian studies mean age was reported to be (42.90+10.54) years by Roli Agarwal et al⁷ 55.4 years by Amarapurkar et al⁸⁰, (49.14+9.65) years by Mahaling et al¹⁰

So, age distribution in our study was comparable to other studies for international and Indian population.

Among the 384 patients included in the study, 352 (91.7%), 30 (7.8%) and 2 (0.5%) had grade I, II and III fatty liver respectively. This is similar to 83%, 17% and 0% for grade I, II and III respectively in a study by Bhusal et al.⁸ Similar distribution was seen in study by Sen et al.⁹ However, studies by Mahaling et al¹⁰ and Roli Agarwal et al⁷ had higher percentages of grade II and III cases.

In our study, distribution of cases was studied according to age and fatty liver grades on USG by Chi-Square test. It was found statistically insignificant (P>0.05) Thus the 61 distribution of grades of fatty liver did not differ significantly across various age groups of cases studied.

In our study raised total cholesterol, serum triglycerides, LDL and VLDL were seen in 35.2%, 56.8%, 34.9% and 58.9%. Raised total cholesterol, serum triglycerides, LDL and VLDL were seen in 45.71%, 67.14%, 34.28% and 25.71% of cases respectively by Mahaling et al.¹⁰ Roli Agrawal et al⁷ reported hypercholesterolemia in 21.8% patients, hypertriglyceridemia in 63.7%, elevated LDL in 25% of patients and elevated VLDL in 56.5% of patients. Bhusal et al⁸ reported total cholesterol, serum triglycerides, LDL, were raised in 53%, 59%, and 72% respectively.

In our study decrease in HDL cholesterol was seen in 56.5%. Mahaling et al¹⁰, Roli Agrawal et al⁷ and Bhusal et al⁸ reported low HDL in 62.8%, 45.1% and 57% respectively. In addition to these, total cholesterol to HDL ratio and LDL to HDL ratio was raised in 37% of cases and 21.1% of cases respectively. Data for these ratios was not available in similar studies for comparison. The distribution of mean total cholesterol, triglyceride, LDL levels, total cholesterol to HDL and LDL to HDL ratios differs significantly in our study (P<0.05) across three grades of fatty liver using the same test. In Mahaling et al study¹⁰, serum total cholesterol, serum HDL, serum LDL and VLDL showed statistical significance with increasing grades of NAFLD. Serum triglyceride showed no statistical significance with increasing grades of NAFLD. In Bhusal et al⁸ study there was significant positive correlation of presence of NAFLD with increasing levels of serum total cholesterol, LDL and triglyceride and significantly decreasing HDL.

Distribution of prevalence of abnormality of different components of lipid profile did not differ significantly across three grades of fatty liver. Similar results were found by Bhusal et al⁸ Therefore, Ultrasonography is a cheap, fast, and widely available imaging technique for applications in fatty liver. US has been reported to have a sensitivity ranging from 60% to 94% and a specificity of 66% to 95%⁷⁵; lower sensitivities are frequently observed in patients with mild disease.¹¹ Limitations of US include it being subject to interobserver variability, difficulty in obese patients, and the high proportion of NAFLD patients with coexisting obesity.

CONCLUSION

Study thus concluded that the fatty liver was more common in male sex with the commonest age group affected being of 20–30 years. Almost three quarters of fatty liver patients had normal liver size while one quarter had increased size of

the liver. Majority of patient with NAFLD had dyslipidemia. There was significant positive correlation of presence of NAFLD with increasing levels of mean serum total cholesterol, triglyceride, LDL levels, total cholesterol to HDL and LDL to HDL ratios. There was no significant positive correlation of presence of NAFLD with increasing level of mean serum VLDL and decreasing level of mean serum HDL. Ultrasound is a 1st line imaging tool to diagnose and subsequently grade the steatosis. It is cheap, widely available. However, it has drawbacks such as observer dependency. From the study, it was shown that increasing grades of fatty liver had significant association with deranged lipid profile. Deranged lipid profile is associated with cardiovascular problems. Hence, increasing grades of fatty liver has indirect relationship with cardiovascular problems.

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