Lipid Profile in Alcoholic and Non Alcoholic Fatty Liver Patients

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Abstract

Background: Fatty liver disease is a common and major chronic liver disease. It has been implicated that patients have disorders of lipid metabolism and involved in the pathogenesis of fatty liver. Lipid profile plays a very important role in diagnosis of liver diseases hence it was designed to observe relationship between lipid profile and fatty liver disease (FLD) based on ultrasonography (USG).

Method and methodology: This Cross-sectional and analytical study was undertaken in the Department of Internal Medicine with collaboration of Department of Radiology and Department of Biochemistry, Universal College of Medical Sciences-Teaching Hospital (UCMS-TH), Bhairahawa, Nepal from March 2019 to February 2020 in total 100 patients diagnosed with FLD by USG.

Result: In 100 cases, the male to female ratio was 1.8:1. 56% of the total cases presented with alcoholic fatty liver disease (AFLD) while remaining 44% with non alcoholic fatty liver disease (NAFLD). The spectrum of lipid abnormality was observed with increased total cholesterol (TC), Low Density Lipoprotein (LDL), increased triglycerides (TG) and Very Low Density Lipoprotein (VLDL) in AFLD cases as compared to NAFLD cases. However, it has been observed that TG/HDL and Non-HDL/HDL were higher in NAFLD as compared to AFLD. There was statistical significant difference in HDL (p-value: 0.019) between alcoholic fatty liver disease grade 1 (AFLG1) and non-alcoholic fatty liver disease grade 1 (NAFLG1). Moreover, it was observed statistical significant difference in HDL between AFLG2 and NAFLG2 (p-value: 0.012).

Conclusion:

Elevated level of TG and decreased HDL has been implicated in the precipitation of the occlusive vascular disease. These parameters in conjunction with Non-HDL/HDL and TG/HDL can be useful in early screening and monitoring of dyslipidemia in the fatty liver patients to prevent cardiovascular diseases.

Background:

Nonalcoholic fatty liver disease (NAFLD) is a condition defined by significant lipid accumulation (5–10%) in hepatic tissue in the absence of significant chronic alcoholic consumption. (1) It includes no more than 30 gram of alcohol per day in men and 20 gram per day in women. (2) Alcoholic fatty liver disease (AFLD), induced by excessive alcohol consumption, and nonalcoholic fatty liver disease (NAFLD), caused by obesity and insulin resistance are the most common diseases associated with hepatic steatosis. (3)

Though liver biopsy is the gold standard method for diagnosis of NAFLD, ultrasonography (USG) which is non-invasive, simple tool, can be used for the early detection of NAFLD in asymptomatic patients. (4) NAFLD is a mild disease which affects both female and male. In the study conducted by Rao BR et al, the raised serum triglycerides (TG), total cholesterol (TC) and low density lipoprotein (LDL) were seen in 82.67%, 60% and 65.33% cases respectively and significantly low HDL in 65.33% of NAFLD patients. (5)

AFLD and NAFLD have similar pathological spectra, ranging from simple hepatic steatosis to steatohepatitis, liver cirrhosis, and hepatocellular carcinoma. Both ALD and NAFLD are frequently accompanied by extrahepatic complications, including cardiovascular disease and malignancy. The survival of patients with ALD and NAFLD depends on various disease-associated conditions. (6) Elevated LDL or TG or low HDL pattern is associated with NAFLD. (7) So the present study attempted to find out answers of some issues such as the spectrum of fatty liver disease who had visited tertiary care hospital UCMS-TH, in the south western region of Nepal. Moreover, the association between fatty liver, hemoglobin and albumin with lipid profile has been observed.

Methods

This cross-sectional and analytical study was undertaken in the Department of Internal Medicine with the collaboration of Department of Radiology and Department of Biochemistry, UCMS-TH, Bhairahawa, Nepal from March 2019 to February 2020.

Study population and sample size was determined as follow:

$$n = \frac{Z^2 PQ}{D^2}$$

n = $(1.96)^2$ ×0.07 × 0.93/ (0.0025) = 100 where, n = sample size, z = critical value = 1.96, P = prevalence of disease = 7%, Q = without disease (1-P), D = allowance error (5%).

Patients who have been diagnosed with fatty liver disease based on USG finding of GE LOGIQ6 PRO ultrasound scanner were included in the study. The ethical approval was taken under registration number UCMS/IRC/046/19.

Procedure for patients and grading of fatty liver in USG:

The patients were mostly examined with real-time sonography, after 6–8 hours of fasting period. Mostly supine and right anterior oblique views were obtained. Sagittal, transverse,

coronal, and subcostal oblique views were also performed using both a standard abdominal transducer and a higher frequency transducer. In few cases intercostal views were also needed.

Mild (Grade 1)—Minimal diffuse increase in hepatic echogenicity with normal visualization of diaphragm and intrahepatic vessel borders.

Moderate (Grade 2)—Moderate diffuse increase in hepatic echogenicity with slightly impaired visualization of intrahepatic vessels walls and diaphragm.

Severe (Grade 3)—Marked increase in echogenicity with poor penetration of posterior segment of right lobe of liver and poor or no visualization of hepatic vessels and diaphragm.

The Patients with other causes of liver disease like viral or alcoholic hepatitis, on drugs therapy or any chemotherapy and patient's age less than 1 year and > 80 years were excluded from this study.

Test Procedure:

Serum was separated from the blood sample of the patients diagnosed with fatty liver based on USG and the tests were carried out. In case of delay, the samples were stored in a refrigerator at 4̊C for 2 days at maximum. Within two days, laboratory investigations were performed. A lipid profile test was done which included TG by Glycerol Phosphate Oxidase- Phenol Antipyrine (GPO/PAP method), TC and HDL by Cholesterol Oxidase-Phenol Antipyrine (CHOD-PAP), and calculated LDL by Friedwald's equation. The other tests carried out were total protein by Biuret method, Albumin by Bromo Cresol Green (BCG) dye binding method. The biochemical tests were carried out on fully automated analyzer, Human XL-600 (Germany), and hemoglobin was obtained from hematology analyzer 5 parts (Beckman coulter, DxH 520).

Data Analysis:

All the data from cases were fed in Microsoft office 2007 (MS Excel) and then analyzed by Statistical Package for Social Service (SPSS) for window version; (SPSS 22, Inc., Chicago, IL). All the data were expressed in terms of percentage frequency, median and compared by non-parametric test viz a viz Chi-Square test, Kruskal Wallis-H test, Man Whitney U test, and Spearman's rho correlation etc. P-value < 0.05 was considered to be statistically significant.

Results

Table 1

General demographic characteristics of the study subjects

Characteristics	FLDG1	FLDG2	Total	p-value
Median Age (IQR) in years	44(21-67)	45(24-66)	45(20-80)	0.812
20-40 years n (%)	37 (45.7)	9 (47.5)	46	
41-60 years n (%)	30 (76.9)	9 (47.4)	39	0.384
> 60 years n (%)	14 (93.3)	1 (5.3)	15	
Gender (Male: Female)	1.8:1	5.3:1	1.94:1	
Male n (%)	50 (61.7)	16 (84.2)	66	0.063
Female n (%)	31 (38.3)	3 (15.8)	34	
Alcoholism				
Alcoholics n (%)	42 (51.9)	14 (73.7)	56	0.084
Non-Alcoholics n (%)	39 (48.1)	5 (26.3)	44	
Median Hemoglobin (Hb) IQR	10(5.7-14.3)	10 (7.1-12.9)	10 (3.3-17.7)	0.944
Hb (≤ 10 g/dl) n (%)	56 (69.1)	16 (88.2)	72	0.188
Hb (>10 g/dl) n (%)	25 (30.9)	3 (15.8)	28	
Albumin (Alb) IQR	3.3 (2.8-3.8)	3.2 (2.3-5)	3.2(3.2-3.5)	0.419
Alb (≤ 3.5g/dl)n (%)	62 (76.5)	16 (84.2)	78	0.468
Alb (>3.5 g/dl)n (%)	19 (23.5)	3 (15.8)	22	

Table 1 shows that the median age of the studied subjects was 45 years with interquartile range (IQR) of 20-80 maximum of the patients were between 20-40 years followed by 41-60 years and least were more than 60 years. There was no statistical significance in age distribution in FLDG1 and FLDG2 (p-value: 0.8). Male is to female ratio is 1.8:1 with no statistical significance (p-value: 0.063).

The percentage of alcoholic and nonalcoholic patients with FLDG1 were 51.9% and 48.1% respectively and with FLDG2 were 73.7% and 26.3% respectively with no statistical significance (p-value: 0.084). The median hemoglobin concentration is 10 with IQR of 3.3–17.7 g/dl overall. Among the studied cases, 72%

were anemic and 28% were having normal hemoglobin concentration. FLDG2 was observed anemic with frequency 88.2% whereas FLDG1 with 69.1%. The median serum albumin level was 3.2 with IQR of 3.2–3.5 g/dl. In total 78% of the cases were having a lower levels of serum albumin while 22% had normal levels. FLDG2 was observed low albumin level with frequency 84.2% whereas FLDG1 was observed low albumin with 76.1%. However, there was no statistical significance in distribution of hemoglobin concentration and serum albumin with different FLDG1 and FLDG2 (p-value: 0.419 and 0.468) respectively.

Table 2
Status of lipid profile in the study subjects

Lipid profile	status	FLD Type		Total	p-value	FLD Grade		Total	p-value
		Alc.	Non-Alc.			1	2		
TC	Normal	30	41	71	0.58	58	13	71	0.78
	High	14	15	29		23	6	29	
TG, VLDL	Normal	12	24	36	0.1	30	6	36	0.6
	High	32	32	64		51	13	64	
HDL	Normal	14	25	39	0.1	29	10	39	0.1
	Low	30	31	61		52	9	61	
LDL	Normal	35	50	85	0.1	70	15	85	0.4
	High	9	6	15		11	4	15	

Table no 2 shows the association of lipid profile variables with different types and grades of FLD. The FLD with alcoholics were found maximum with increased TG in 32 (72.72%), decreased HDL 30 (68.18%), increased TC in 14 (31.81%), increased LDL in 9 (20.45%) as compared to non alcoholics with TG in 32 (57.14%), decreased HDL in 30 (68.18%), increased LDL in 50 (10.71%) respectively. The FLDG2 were found maximum with increased TG in 13 (68.42%), increased TC 6 (32.57%), increased LDL 4 (21.05%) as compared to FLD G1 with TG in 51 (62.96%), increased LDL in 11 (13.38%), increased in TC 23 (28.39%) respectively. On contrary, the decreased HDL was maximum in FLD Grade 1 with frequency 52 (64.19%) as compared to FLD Grade 2 with 9 (47.36%). However, there was no significant association in the frequency of TC, TG, VLDL, HDL and LDL with types of FLD (p-values: 0.58, 0.1, 0.1 and 0.1 respectively) and with FLD grades (p-values: 0.78, 0.6, 0.1 and 0.4 respectively).

Table 3: Association of Median Lipid profile value with different grades and types of FLD

Lipid	AFLDG1	AFLDG2	NAFLDG1	NAFLDG2	Total	p-value
TC	165.51	187.0	172.0	146	172	0.646
TG	161	173.5	197.0	238.0	191	0.583
VLDL	32.2	34.7	39.4	47.6	38.10	0.583
HDL	37.5*[a]	42*[b]	39.0*[a]	36.0*[b]	39.0	0.107
LDL	165.0	187.0	172.0	146.0	84.6	0.697
NHDL/HDL	3.12	3.24	3.46	3.08	3.33	0.838
TG/HDL	4.19	4.25	5.07	6.80	4.56	0.506

Man Whitney U test p-value: *[a]0.019 (AFLDG1 vs NAFLDG1) , *[b]0.012 (AFLDG2 vs NAFLDG2)

There was statistical significant difference in HDL (p-value: 0.019) between AFLDG1 and NAFLDG1, HDL between AFLDG2 and NAFLDG2 (p-value: 0.012). However, Non-HDL is to HDL ratio and TG is to HDL ratio were increased in NAFLD as compared to AFLD.

Table 4
Association of Lipid profile with Hemoglobin and Albumin Status

Lipid profile		Hemoglobin status		p-value	Albumin status		p-value
		Normal	Anemic		Normal	Low	
		28	72		22	78	
TC	Normal	19	52	0.66	15	56	0.7
	High	9	20		7	22	
HDL	Normal	12	27	0.62	5	34	0.07
	Low	16	45		17	44	
LDL	Normal	23	62	0.61	19	66	0.83
	High	5	10		3	12	
TG	Normal	8	28	0.33	9	27	0.5
	High	20	44		13	51	

Table 4 shows that the association of Lipid profile was non-significant with hemoglobin status and albumin status with TC, HDL, LDL and TG p-value (0.66, 0.62, 0.61 and 0.33) and p-value (0.7, 0.07, 0.83 and 0.5) respectively.

Table 5
Spearman's rho Correlation of Study variables

Lipid Non-HDL/HDL		TG/HDL	Hb	Alb
S. TC (mg%)	.538**	.316**	.060	− .010
	.000	.002	.555	.924
HDL (mg%)	− .340**	− .299**	.068	− .172
	.001	.003	.499	.087
LDL (mg%)	.616**	.050	.047	.071
	.000	.621	.640	.481
VLDL (mg%)	.517**	.891**	0.027	− .085
	.000	.000	.791	.403
Non-HDL/HDL	1	.657**	.079	0.085
		.000	.436	.398
TG/HDL	.657**	1	.006	0.013
	.000		.949	.029
** Correlation is significant at the 0.01 level (2-tailed)				
* Correlation is significant at the 0.05 level (2-tailed)				

Table 5 shows the Spearman's correlation of the lipid profile results with different variables. Serum TC and HDL have significant correlation with non-HDL is to HDL ratio and TG is to HDL ratio with p-value of 0.001 and 0.002 respectively. Similarly, LDL shows significant correlation with non-HDL is to HDL ratio with p-value of 0.001. VLDL shows significant correlation with non-HDL is to HDL ratio and TG is to HDL with p-values 0.001 each. TG is to HDL ratio showed significant correlation with non-HDL is to HDL ratio with p-value of 0.001.

Discussion

AFLD represents a broad range of histological changes ranging from simple steatosis to heavier forms of liver injury, including alcoholic hepatitis (AH), cirrhosis, or the parallel development of hepatocellular carcinoma (HCC). (8) NAFLD is emerging as the most common chronic liver condition in the Western

world. It is associated with insulin resistance and frequently occurs with features of the metabolic syndrome.

Paik YH et al included a total of 186 patients in their study, out of that 106 cases were NAFLD and 80 were AFLD. There was no significant difference between the NAFLD and ALFD groups (p = 0.635) (9). In our study, we studied a total of 100 patients which included 44 with NAFLD and 56 with AFLD and similar to their study there was no significant difference between the NAFLD and AFLD groups (p-value = 0.8).

Mahaling DU et al, in their study out of 70 cases which were diagnosed as NAFLD on USG, NAFLDG1 cases were 47.15%, NAFLDG2 were 42.85% and NAFLDG3 were 10%. The mean age of the patients was found to be 49.14 years. Male to female ratio was 3:4. Serum TG, TC, LDL and VLDL levels were raised in 67.14%, 45.71% 34.28%, 25.71% of cases respectively. Low serum HDL levels were seen in 62.85% of patients. Their study has shown increasing grades of NAFLD were significantly associated with increasing values of TC. (4) In our study, NAFLDG3 and AFLDG3 cases were not present. The male to female ratio was 1.8:1. The median age of the patients was found to be 45.90 years which is similar to their study. TC, TG and VLDL and LDL were raised in 29%, 64% and 15% of the cases respectively. Some variables of the lipid profile showed a significant elevation of TG (85%) ($p < 0.05$) and significant raised TC levels (82.5%). ($p < 0.01$) (10) Similar to their study, Low serum HDL levels were seen in 61% of the cases. The significant association was only observed in median HDL level between AFLDG1 and NFLDG1 (p-value: 0.019) and AFLDG2 and NAFLDG2 (p-value: 0.012). Unlike their study, no significant association was seen between other lipid profiles except HDL with fatty liver disease.

Pradhan B et al in their study which included a total of 1,500 patients, they found that 447 patients had AFLD. Chronic liver disease (CLD) was detected in 144 patients (9.6%). On multivariate analysis, they found the following variables to be significantly associated with CLD: male sex (odds ratio [OR]: 1.81; 95% confidence interval [CI]: 1.12–2.94; P = 0.02) (11). Similar to the study male predominance was found in our study as well.

Bhusal K, Simkhada R, Nepal P had shown mild NAFLD in 83%, moderate in 17% and severe in none of the participants which is similar finding in our study. Age of the participants ranged from 26 to 79 years with mean being 45 ± 11.99 years. Similar to their study, the present study has shown TG, TC and LDL levels were raised in 57.14%, 26.78%, 10.71% of the NAFLD cases respectively and High density lipoprotein level was decreased in 55.35% of cases. Similarly, TG, TC and LDL levels were raised in 72.72%, 31.87%, 20.45% of the AFLD cases respectively and High density lipoprotein level was decreased in 68.18% of cases. In contrast to their study NAFLDG1 was observed in 48.1% and 26.3% in NAFLDG2. We studied patients with AFLD too in whom 51.9% were having grade 1 and 73.7% had grade 2 FLD. This indicates alcoholism and chronicity progresses with the FLD grade. The increasing grades of non-alcoholic fatty liver disease weren't significantly associated with increasing level of lipid abnormalities. (12) Unlike their study, we found no association between the presence of dyslipidemia and either type of the fatty liver disease. Similar to their study, no significant association of different grades of FLD was observed with increasing lipid abnormalities.

Khalil F et al, in their study, found that the largest group of patients (38%) was in the fifth decade of life. followed by 30% in the sixth decade of life. As the grade of NAFLD increased, there was associated significant increase in levels of serum TC (p-value 0.005), TG (p-value 0.002) LDL (p-value 0.001) and VLDL (p-value 0.003) and associated significant decrease in HDL (P-value 0.001). (13) Unlike their study, most of the patients were in their third to fourth decade of life (46%) followed by fifth to sixth decade (39%) and lowest number of patients were older than 60 years of age (15%) and there was no association between dyslipidemia and FLD.

Khanal U et al had found that the mean age of fatty liver in males was 44.3 years and in females was 51.9 years. 22.9% of patients with NAFLD had increased liver size. Significant association with increasing grades of fatty liver was found with increasing levels of TC (p = 0.028), LDL (p = 0.017), liver size (p = 0.001), and body mass index (BMI) (p = 0.045) in patients diagnosed with NAFLD. No significant association with increasing grades of FLD was found with increasing levels of TG (p = 0.32) and high density lipoprotein (p = 0.25). (14) (15) In contrast our study has shown strong association with median HDL level and there was no significant association with TG, TC and LDL. This difference in the lipid abnormality spectrum might have arisen due to wide distribution of lipid level values and pattern of alcohol consumption and USG grading of FLD.

Conclusion

Constellations of dyslipidemia pattern and frequency of fatty liver disease in alcoholic and nonalcoholic patients may become cumbersome and can be indicated for cardiovascular diseases.

Abbreviations

AFLD:alcoholic fatty liver disease, AH:alcoholic hepatitis, BCG:bromo cresol green, CHOD-PAP:Cholesterol Oxidase-Phenol Antipyrine, CI:confidence interval, CLD:chronic liver disease, FLD:fatty liver disease, G1:Grade 1, G2:Grade 2, GPO/PAP:Glycerol Phosphate Oxidase- Phenol Antipyrine, HCC:hepatocellular carcinoma, HDL:high density lipoprotein, LDL:low density lipoprotein, NAFLD:non alcoholic fatty liver disease, OD:odd ratio, TC:total cholesterol, TG:triglycerides, USG:Ultrasonography, VLDL:very low density lipoprotein

Declarations

Ethical approval and consent to participate

Ethical approval was taken from the Institutional Review Board, UCMS-TH registration number UCMS/IRC/046/19 and oral as well as written consent was taken from all the patients for their enrolment into the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

Authors' contributions

AS and NG were involved in conception, design, data collection, literature review, manuscript preparation and data analysis. SR was involved in drafting the manuscript and critical revision for intellectual content. US, AJ were involved in literature review and manuscript preparation. All authors have equally contributed for the research. All authors have read and approved the final manuscript.

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Availability of data and materials

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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