

Association of Lipid Profile, Prothrombin Time, INR, and Hepatic Profile with Ultrasonographic Grades of Fatty Liver Disease: A Prospective Observational Study in a Tertiary Care Hospital

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Abstract:

Background: Fatty liver disease (FLD), particularly non-alcoholic fatty liver disease (NAFLD), is a major health problem worldwide and affects 25-38% of the adult population. Ultrasonography is one of the most common non invasive methods to grade hepatic steatosis as Grade I (mild), Grade II (moderate) and Grade III (severe). Correlation of ultrasonographic grades with biochemical parameters including lipid profile and coagulation markers is not well defined in Indian tertiary care settings.

Objectives: To assess the relationship between lipid profile parameters, coagulation parameters (Prothrombin time [PT] and international normalised ratio [INR]), and hepatic biochemical markers with ultrasonographic grades of FLD.

Methods: This prospective observational study enrolled 100 consecutive patients in whom Ultrasonography established a diagnosis of FLD. Steatosis grade was determined by abdominal Ultrasonography and fasting blood samples were analyzed for total cholesterol, triglycerides, HDL, LDL, PT and INR. Clinical histories were collected and biochemical parameters were compared by steatosis grades.

Results: Grade I FLD (72%) was the most common, followed by grade II (21%) and grade III (7%). The most significantly affected age group was 51–65 years (35%). Total cholesterol (139.7, 174.1, 174.4 mg/dL), triglycerides (147.1, 157.4, 238.1 mg/dL), LDL cholesterol (82.0, 96.4, 101.5 mg/dL) and LDL/HDL ratio (2.45, 2.84, 3.16) progressively increased from Grade I to III. HDL levels were low in all grades (35.0-37.4 mg/dL). INR had a significant grade dependent increase (1.50, 2.39, 3.15). PT increased from 18.3 sec in Grade I to 21.1 sec in Grade II, indicating a worsening hepatic synthetic dys-

function. The most severe abnormalities were found in patients with liver failure and alcoholic liver disease.

Conclusion: Triglycerides and INR had the strongest correlation and the severity of FLD on Ultrasonography was associated with progressive dyslipidemia and coagulation impairment. Routine testing of lipids and coagulation may improve risk stratification and clinical management of FLD.

Keywords: Fatty liver disease; NAFLD; Ultrasonography; Lipid profile; Prothrombin time; INR; Hepatic profile; Liver steatosis; Dyslipidemia; Hepatic fibrosis

1. Introduction

Fatty liver disease (FLD) has become one of the most common chronic liver diseases worldwide, from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH), to advanced fibrosis, cirrhosis and hepatocellular carcinoma. Non-alcoholic fatty liver disease (NAFLD) characterized by hepatic fat accumulation > 5% of liver weight in the absence of significant alcohol consumption, viral hepatitis or other secondary causes is now estimated to affect 25-38% of the world's adult population. It is the most common liver disease in the world in both developed and developing countries.^[1]

In India epidemiological data suggest a rapidly increasing burden of NAFLD with prevalence estimates ranging from 9% to 32% in the general population and considerably higher rates among subjects with metabolic comorbidities like obesity, type 2 diabetes mellitus, dyslipidemia and hypertension.^[2] This increase has been driven by urbanization, sedentary lifestyles, calorically dense diets, and the concurrent epidemic of metabolic syndrome.^[3] Tertiary care hospitals are affected more than others as patients are often admitted at advanced stages because of the insidious and largely asymptomatic nature of early stage hepatic steatosis.

The Pathophysiology of NAFLD is complex and not completely understood. The widely accepted “two-hit hypothesis” proposes that insulin resistance causes initial hepatic triglyceride accumulation (first hit), which sensitizes the liver to oxidative stress, mitochondrial dysfunction, lipid peroxidation, and inflammatory cascades (second hit), ultimately leading to NASH and fibrosis.^[4]

More recently, models have invoked a ‘multiple parallel hits’ paradigm in which genetic predisposition, gut dysbiosis, adipokine dysregulation, endoplasmic reticulum stress and innate immune activation synergistically promote disease progression.^[5] Central to this pathogenesis is dyslipidemia especially elevated serum triglycerides, elevated LDL, and reduced HDL which reflects and perpetuates hepatic lipotoxicity.^[6]

Deranged coagulation parameters, particularly prolonged Prothrombin time (PT) and elevated international normalised ratio (INR), are well recognised sequelae of hepatocellular dysfunction and synthetic failure in advanced liver disease.^[7] However, the association of gut microbiota with early to moderate ultrasonographic grades of fatty liver is an area of active investigation.^[8] Similarly, hepatic biochemical markers such as serum ALT, AST, GGT, ALP, total and direct bilirubin, serum albumin and total protein are surrogate markers of hepatocyte injury and also markers of hepatic functional reserve.^[9]

Abdominal Ultrasonography is the most commonly used, non invasive, cost effective imaging modality in diagnosis and grading of hepatic steatosis. Fatty liver is graded into Grade I (mild), Grade II (moderate) and Grade III (severe) based on echogenicity, hepatorenal contrast, posterior beam

attenuation and diaphragm visualization.^[10] Liver biopsy is the histological gold standard but ultrasonographic grading is a practical alternative especially in resource limited tertiary care settings.^[11] In the Indian tertiary care setting, there is a paucity of prospective studies systematically evaluating the concurrent associations of lipid profile, coagulation parameters (PT, INR), and a complete hepatic biochemical profile with ultrasonographically defined grades of fatty liver disease.^[12] Therefore, this present prospective observational study was planned to assess these associations in patients attending a tertiary care hospital.

LITERATURE REVIEW

2.1 Epidemiology and Global Burden of NAFLD

A landmark systematic review and metaanalysis by Younossi et al. (2016) analyzed 86 studies including more than eight million subjects and reported a global NAFLD prevalence of 25.24% (95% CI: 22.10-28.65%), with the highest estimates in the Middle East (31.79%) and South America (30.45%), and a substantial burden across Asia (27.37%) and North America (24.13%).^[13]

Duseja et al, in India, reported prevalence of NAFLD ranging from about 16-32% in urban adults.^[14] A multicentre Indian study by Amarapurkar et al. (2007) found NAFLD to be present in 28.9% of people undergoing routine ultrasound evaluation.^[15] The INASL consensus statement underscored the rising burden of NAFLD in India and advocated for standardized approaches to diagnosis and management.^[16]

2.2 Ultrasonographic Grading of Hepatic Steatosis

Dasarathy et al. (2009) assessed the diagnostic precision of ultrasound in 200 biopsy-proven NAFLD patients and found a sensitivity of 85% and specificity of 94% for detection of steatosis >30% of hepatocytes ($\kappa = 0.67$).^[17] Ballestri et al. (2022) reiterated the utility of ultrasound in a systematic review of 19 studies, with constraints in identifying mild steatosis below 20-30%.^[18]

2.3 Lipid Profile and Ultrasonographic Fatty Liver Grades

Hypertriglyceridaemia and low HDL were the most consistently elevated lipid abnormalities in NAFLD, independent of diabetes or obesity (Marchesini et al.^[19] Chitturi et al. also demonstrated a positive correlation between serum triglycerides and the grade of histological steatosis.^[20] In a prospective study from India, Bhatt et al. (2017) reported stepwise increase in total cholesterol, LDL and triglycerides across ultrasonographic grades I-III ($p < 0.05$).^[21] Arora et al., (2012) reported that LDL and total cholesterol to HDL ratio were independent predictors of higher ultrasonographic grade.^[22]

2.4 Prothrombin Time, INR, and Hepatic Synthetic Function

Angulo et al. (2007) found that INR was substantially greater in patients with NAFLD who had advanced fibrosis (F3-F4) compared with initial stages of disease.^[23] Shah et al. (2009) demonstrated a significant association of PT prolongation with the degree of hepatocyte ballooning and lobular inflammation on histological assessment.^[24] Patel et al. reported that INR increased stepwise with increasing ultrasonographic grades (Grade I: 1.02 ± 0.06 ; Grade II: 1.08 ± 0.09 ; Grade III: 1.18 ± 0.14 ; $p < 0.01$).^[25]

2.5 Hepatic Biochemical Profile and Fatty Liver Grading

Mofrad et al. (2003) showed that up to 59% of patients with biopsy proven NAFLD had normal serum aminotransferase, prompting questions regarding the efficacy of enzyme based screening.^[26] Guha et al. (2006) reported correlation between ALT and ultrasonographic steatosis grade ($r = 0.43$, $p < 0.001$), plateauing at Grade III, possibly reflecting reduced hepatocyte mass.^[27] In a north Indian tertiary centre, Verma et al. (2013) reported progressively lower serum albumin levels with increasing ultrasonographic grades.^[28]

2.6 Metabolic Syndrome and Comorbid Associations

Eckel et al. (2005) and NCEP-ATP III criteria have shown that hepatic steatosis is a consequence and an independent promoter of insulin resistance and cardiovascular risk.^[29] NAFLD patients with more severe grades in Ultrasonography had increased carotid intima media thickness independent of traditional cardiovascular risk factors, showed Targher et al.^[30] Mishra et al. emphasised the exceptionally high burden of NAFLD in Asian Indians due to greater visceral adiposity at lower BMI, atherogenic dyslipidemia and early onset of type 2 diabetes.^[31]

MATERIALS & METHODS

3.1 Study Design and Setting

This study was designed as a hospital based analytical, prospective, observational, and descriptive study conducted in the Departments of Gastroenterology, Biochemistry, and Radio diagnosis & Imaging at Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University (BHU), Varanasi.

3.2 Study Duration

The study was carried out over 02 years, during which patients meeting the eligibility criteria were consecutively enrolled.

3.3 Study Population and Sample Size

In the present analysis, 103 patients were evaluated from Eastern Uttar Pradesh. Patients of all Ultrasonography grades of fatty liver (Grade 1, Grade 2, and Grade 3) were included.

Fatty liver disease was diagnosed:

- ❖ Clinically, based on history and examination
- ❖ Radiologically, using Ultrasonography (USG) of the liver
- ❖ Biochemically, supported by lipid profile and liver function tests (LFTs)

Both alcoholic and non alcoholic cases were initially considered, but only eligible patients fulfilling inclusion criteria were enrolled.

Inclusion Criteria

- ❖ Patients of either sex, aged 20-80 years
- ❖ Non alcoholic patients
- ❖ Patients with Ultrasonography confirmation of fatty liver
- ❖ Patients with supportive lipid profile findings
- ❖ Patients with liver function test (LFT) confirmation

Exclusion Criteria

- ❖ Patients with conditions affecting lipid metabolism or liver status, including:
 - History of liver failure
 - History of liver cirrhosis
- ❖ Alcoholic patients

Data Collection

After obtaining informed consent, the following data were collected:

Demographic Data

- ❖ Age
- ❖ Sex

Laboratory Parameters

- ❖ Coagulation Profile:
 - Prothrombin Time (PT)
 - International Normalized Ratio (INR)
- ❖ Haematological Parameters:
 - Haemoglobin (Hb.)
 - Total Leukocyte Count (TLC)
 - Differential Leukocyte Count (DLC)
 - Platelet Count
 - Mean Corpuscular Volume (MCV)
- ❖ Glycaemic Parameters:
 - Random Blood Sugar (RBS)
 - Glycated Haemoglobin (HbA1c)

Radiological Assessment

- ❖ Ultrasonography (USG) was used to grade fatty liver into:
 - Grade 1 (Mild)
 - Grade 2 (Moderate)
 - Grade 3 (Severe)

Ethical Considerations

The study was conducted following approval from the Institutional Ethics Committee. An informed written consent was obtained from all participants.

- ❖ Consent forms were provided in both Hindi and English to ensure clear understanding.
- ❖ In cases where participants were unable to consent, consent was obtained from legally acceptable relatives.

Statistical Analysis

Data were entered and analyzed using appropriate statistical software (SPSS-24).

- ❖ Descriptive statistics were used to summarize demographic and clinical variables.
- ❖ Mean values of laboratory parameters were compared across different grades of fatty liver.

RESULT

4.1 Age Distribution of Study Participants

A total of 100 patients with confirmed fatty liver disease on Ultrasonography were enrolled. The participants were divided into four age groups: 20 to 34, 35 to 49, 50 to 64, and ≥ 65 years. The largest percentage of the study cohort was the 51-65 year age group at 35% of the cohort, followed by the 36-50 year group (32%), then the 20-35 year group (21%), and then those above 65 years (12%). Age wise distribution is shown in Table 1. These results suggest that fatty liver disease is a disease of middle-aged to older adults, consistent with the knowledge that older age, metabolic deterioration and hepatic steatosis are interrelated.

Table 1: Age Group Distribution of Study Participants (n = 100)

Age Group	Frequency (n)	Percent (%)	Valid Percent (%)
20–35 years	21	21.0	21.0
36–50 years	32	32.0	32.0
51–65 years	35	35.0	35.0
>65 years	12	12.0	12.0

4.2 Distribution of Fatty Liver Grades by Clinical History

The distribution of patients across ultrasonographic grades of fatty liver disease (Grade 1 mild, Grade 2 moderate, Grade 3 severe) stratified by clinical history is summarized in Table 2. The majority of patients were in the Grade 1 category (78 out of 100), Grade 2 and Grade 3 consisted of 21 and 7 patients respectively.

In patients without significant clinical history, 60 had Grade 1, 13 had Grade 2, and 5 had Grade 3 fatty liver, indicating that subclinical or de novo hepatic steatosis predominates in the absence of underlying liver disease. Hepatitis patients had 3 cases in Grade 1 and 1 case in Grade 2, with no Grade 3 cases, indicating relatively intact liver architecture at this stage. Similarly, patients with cirrhosis were distributed as 3 in Grade 1 and 1 in Grade 2, with no patients in Grade 3 probably because of exclusion of advanced cirrhotic patients as per study protocol.

Notably, patients with a history of liver failure (n = 2) were exclusively in Grade 1, which may be reflective of the inclusion of patients presenting at an early compensated stage. The alcoholic subgroup showed a different distribution with a relatively higher prevalence of Grade 2 (6 patients) and Grade 3 (2 patients) compared to the other clinical subgroups, emphasizing the role of ongoing hepatotoxic alcohol exposure in accelerating steatosis progression.

Table 2: Distribution of Fatty Liver Grade by Clinical History

Clinical History	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)
No Clinical History	60	13	5
Hepatitis	3	1	0

Clinical History	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)
Liver Failure	2	0	0
Cirrhosis	3	1	0
Alcoholic	4	6	2

4.3 Biochemical Parameters across Ultrasonographic Grades of Fatty Liver

Table 3: Mean values of lipid profile parameters, coagulation indices and other biochemical markers according to ultrasonographic grade.

Total cholesterol: Mean total cholesterol progressive increase across grades from 139.73 mg/dL in Grade 1 to 174.07 mg/dL in Grade 2 and 174.43 mg/dL in Grade 3 was observed. This progressive increase reflects a worsening of hepatic lipid dysregulation with increasing severity of steatosis.

Triglycerides: Mean triglyceride levels showed the most striking grade dependent increase among all lipid parameters 147.1 mg/dL in Grade 1, 157.4 mg/dL in Grade 2 and 238.1 mg/dL in Grade 3. Hypertriglyceridaemia as a hallmark of advanced hepatic steatosis is underlined by the near 90 mg/dL increase between Grade 2 and Grade 3.

HDL Cholesterol: Low levels of HDL were consistent and persistent in all three grades 36.3 mg/dL (Grade 1), 37.4 mg/dL (Grade 2), and 35.0 mg/dL (Grade 3) suggesting chronic HDL suppression independent of the grade of steatosis and most likely related to underlying insulin resistance and dyslipidemia.

LDL Cholesterol: The mean LDL cholesterol showed a consistent stepwise rise from 82.04 mg/dL in Grade 1, 96.36 mg/dL in Grade 2, and 101.50 mg/dL in Grade 3. This progressive elevation is in parallel with the increasing severity of steatosis and associated hepatocellular lipotoxicity.

LDL/HDL Ratio: The LDL/HDL ratio, a well-established marker of atherogenic dyslipidemia, increased progressively from 2.451 in Grade 1 to 2.839 in Grade 2 and 3.156 in Grade 3, reinforcing the increasing cardiovascular risk burden with advancing steatosis.

Prothrombin Time (PT): The mean PT elevated from 18.3 seconds in Grade 1 to 21.1 seconds in Grade 2. However, the mean PT for Grade 3 (19.7 seconds) was slightly lower than Grade 2, perhaps reflecting the small sample size (n = 7) of Grade 3, or confounders concurrent with this subset. However, PT prolongation through the grades indicates progressive hepatic synthetic dysfunction.

INR: INR increased in a clinically significant and incremental manner across grades from 1.50 in Grade 1, 2.39 in Grade 2, and 3.15 in Grade 3. This monotonic increase is the most evident trend observed across all biochemical parameters and is highly suggestive of a sequential impairment of hepatic coagulation factor synthesis with increasing ultrasonographic steatosis grade.

Table 3: Mean Biochemical Parameters by Ultrasonographic Fatty Liver Grade

Lab Parameter	Grade 1 Mean	Grade 2 Mean	Grade 3 Mean
Total Cholesterol (mg/dL)	139.73	174.07	174.43
Triglycerides (mg/dL)	147.1	157.4	238.1

Lab Parameter	Grade 1 Mean	Grade 2 Mean	Grade 3 Mean
HDL Cholesterol (mg/dL)	36.3	37.4	35.0
LDL Cholesterol (mg/dL)	82.04	96.36	101.50
LDL/HDL Ratio	2.451	2.839	3.156
Prothrombin Time (s)	18.3	21.1	19.7
INR	1.50	2.39	3.15

4.4 Biochemical Parameters across Age Groups

The mean biochemical parameters stratified by age group are presented in Table 4. The highest total cholesterol was in the youngest (20-35 years: 161.76 mg/dL) and oldest (>65 years: 169.67 mg/dL) age groups, while the lowest value was in the 36-50 year group (132.47 mg/dL). Triglyceride levels were highest in the 20-35 year group (193.8 mg/dL) indicating early onset Hypertriglyceridaemia in younger patients with fatty liver disease.

HDL cholesterol showed a decreasing trend with increasing age 40.5 mg/dL (20-35 year group) falling to 33.3 mg/dL (51-65 year group) before a slight recovery to 38.8 mg/dL (>65 year group). LDL cholesterol was significantly higher in the >65 year group (110.00 mg/dL) than other age groups, indicating an increasing atherogenic burden in the elderly subgroup. Similarly, the LDL/HDL ratio was highest in the >65 year group (3.063) followed by the 51-65 year group (2.635).

The Prothrombin time was significantly prolonged in the 36-50 year group (22.5 seconds) and the INR was highest in this same group (2.65), suggesting a possibly greater prevalence of significant hepatic synthetic dysfunction or comorbid conditions (such as alcoholic liver disease) in this middle aged cohort. The lowest INR values were found in the youngest and oldest groups (1.40 and 1.24, respectively).

Table 4: Mean Biochemical Parameters by Age Group

Lab Parameter	20–35 yr	36–50 yr	51–65 yr	>65 yr
Total Cholesterol (mg/dL)	161.76	132.47	150.42	169.67
Triglycerides (mg/dL)	193.8	140.3	139.6	176.5
HDL Cholesterol (mg/dL)	40.5	36.4	33.3	38.8
LDL Cholesterol (mg/dL)	92.24	79.80	80.87	110.00
LDL/HDL Ratio	2.408	2.457	2.635	3.063
Prothrombin Time (s)	16.8	22.5	18.3	15.8
INR	1.40	2.65	1.46	1.24

4.5 Biochemical Parameters across Clinical History Subgroups

The mean biochemical parameters according to subgroups of clinical history are shown in Table 5. Mean total cholesterol was 155.39 mg/dL, triglyceride was 159.9 mg/dL and INR was 1.73 in patients with no clinical history representing the baseline biochemical profile of primary NAFLD cohort.

Overall, the liver failure subgroup showed the highest degree of metabolic abnormalities with significantly low total cholesterol (65.00 mg/dL) and HDL cholesterol (25.0 mg/dL) levels consistent with end stage hepatocyte dysfunction affecting lipoprotein synthesis. The liver failure group had the highest LDL/HDL ratio (3.415), which suggests a highly atherogenic lipid profile, even though the absolute cholesterol levels were low. PT was prolonged (29.9 seconds) and INR was highest among all groups (2.23) confirming severe coagulopathy secondary to hepatic synthetic failure.

Alcoholic subgroup had significantly higher PT (26.5 seconds) and INR (2.16) indicating ongoing hepatocellular injury from alcohol. Total cholesterol (133.79 mg/dL) and triglycerides (146.0 mg/dL) were slightly lower than the no history group, consistent with alcohol-induced changes in hepatic lipid metabolism.

The patients with cirrhosis had a low mean total cholesterol (130.00 mg/dL), a low HDL (30.5 mg/dL) and a significantly low LDL/HDL ratio (2.168), which is in agreement with the hypercholesterolemia of advanced chronic liver disease. Both PT (21.3 sec) and INR (1.90) were high, indicating a deficiency of coagulation factors in hepatic fibrosis. Moderate hepatocellular impairment was observed in patients with hepatitis with mild derangements total cholesterol 140.25 mg/dL, INR 1.87.

Table 5: Mean Biochemical Parameters by Clinical History Subgroup

Lab Parameter	No Clinical History	Hepatitis	Liver Failure	Cirrhosis	Alcoholic
Total Cholesterol (mg/dL)	155.39	140.25	65.00	130.00	133.79
Triglycerides (mg/dL)	159.9	165.3	120.0	110.0	146.0
HDL Cholesterol (mg/dL)	37.0	36.3	25.0	30.5	36.8
LDL Cholesterol (mg/dL)	90.21	82.50	82.50	67.00	70.13
LDL/HDL Ratio	2.607	2.295	3.415	2.168	2.513
Prothrombin Time (s)	17.4	21.2	29.9	21.3	26.5
INR	1.73	1.87	2.23	1.90	2.16

DISCUSSION

The present prospective observational study was conducted to evaluate the association of lipid profile, Prothrombin time (PT) and INR with ultrasonographic grades of fatty liver disease in 100 patients at a tertiary care center in Eastern Uttar Pradesh. The results show biochemical abnormalities that are consistent and grade dependent in all the parameters studied.

5.1 Age Distribution

The 51-65 year age group was most affected (35%), consistent with the well established predilection of NAFLD for middle aged adults due to progressive insulin resistance and metabolic deterioration.^[32] Notably, 21% of patients were in the 20-35 year group, reflecting the rising trend of early onset fatty liver disease in young Indian adults, attributed to increasing visceral adiposity at lower BMI thresholds, sedentary lifestyles, and the metabolic transition in this population.^[33]

5.2 Lipid Profile and Ultrasonographic Grade

Total cholesterol, triglycerides, LDL cholesterol and LDL/HDL ratio increased stepwise from grade 1 to grade 3. HDL cholesterol remained persistently low in all grades. These results are in agreement with the previous literature. The most constant lipid abnormalities in NAFLD independent of obesity and diabetes are Hypertriglyceridaemia and low HDL as shown by Marchesini et al.^[19]. Similarly, Indian subjects in ultrasonographic grades I-III showed gradual increase in total cholesterol, LDL and triglycerides ($p < 0.05$) as reported by Bhatt et al.^[21] and directly substantiate our findings. Chitturi et al.^[20] reported a positive correlation between serum triglycerides and histological grade of steatosis.

Triglycerides exhibited the most striking grade dependent increase in the present study from 147.1 mg/dL (Grade 1) to 238.1 mg/dL (Grade 3) reflecting accelerating hepatic lipotoxicity, consistent with the pathophysiological framework proposed by Tilg and Moschen.^[34] At Grade 3, the LDL/HDL ratio was > 3.0 , indicating a significantly atherogenic lipid profile at this stage, as described by Eckel et al.^[29] and Targher et al.^[30], who linked higher grades of ultrasonographic steatosis with increased cardiovascular risk. The consistent suppression of HDL in all the grades without any significant grade dependent trend, is in line with Ramesh et al. (2022),^[35] who reported a uniform HDL suppression in Indian NAFLD patients independent of steatosis severity and indicative of chronic insulin resistance driven HDL catabolism rather than a grade progressive phenomenon.

5.3 Coagulation Parameters and Ultrasonographic Grade

The highest increase with increasing grade that was found to be of clinical importance and monotonically increasing was INR: 1.50 (Grade 1), 2.39 (Grade 2), and 3.15 (Grade 3). PT also increased from 18.3 s (Grade 1) to 21.1 s (Grade 2). These findings suggest progressive hepatic synthetic dysfunction with increasing steatosis. Angulo et al.^[23] reported a significant increase of INR in NAFLD patients with advanced fibrosis, and Shah et al.^[24] showed that PT prolongation correlated with histological hepatocellular injury. Jachs M et al.^[37] confirmed INR elevation as a reliable predictor of hepatic decompensation. Bozic D and Babic A^[36] characterized coagulopathy as an integral marker of progressive chronic liver disease. The INR values in the present cohort were higher than the reported values by Patel et al.^[25] (Grade I: 1.02; Grade III: 1.18). This may be because the present study population was a tertiary referral population, with a wider spectrum of clinical history, and the phenotypic characteristics of Indian NAFLD patients as discussed by Siddiqui and Bhatt.^[38] The

relatively mild attenuation of Grade 3 PT (19.7 s) versus Grade 2 is probably due to the small size of the Grade 3 subgroup (n=7) and other confounding variables and should be interpreted with caution.

5.4 Clinical History Subgroup Analysis

Patients with liver failure had the most severe derangements total cholesterol 65.0 mg/dL, HDL 25.0 mg/dL, PT 29.9 s, and INR 2.23 consistent with end stage hepatocellular synthetic failure as described by Méndez-Sánchez et al.^[40] and Bozic D and Babic A.^[36] Alcoholic patients similarly showed elevated PT (26.5 s) and INR (2.16), reflecting alcohol mediated coagulation factor impairment. Cirrhotic patients exhibited characteristic hypocholesterolaemia (130.0 mg/dL) with elevated coagulation indices, consistent with hepatic synthetic failure of advanced fibrosis, as documented by Verma et al.^[28]

5.5 Limitations

The study has sample size of 100 patients limits subgroup statistical power; histological confirmation by liver biopsy was not performed, with Ultrasonography serving as the grading surrogate acknowledging its limitations for mild steatosis (<20-30%) as noted by Ballestri et al.,^[40] and formal inferential statistical testing with multivariate adjustment for BMI, diabetes, and medication history was not performed. Future larger studies with histological correlation and multivariate analysis are warranted.

CONCLUSION

The present study demonstrates a consistent, grade dependent escalation in total cholesterol, triglycerides, LDL cholesterol, LDL/HDL ratio, PT, and INR with increasing ultrasonographic severity of fatty liver disease, with triglycerides and INR showing the most pronounced increases. HDL cholesterol remained persistently suppressed across all grades, reflecting a chronic atherogenic milieu irrespective of steatosis severity. The highest biochemical burden was observed in the 51- 65 and >65 year groups, while liver failure and alcoholic liver disease patients exhibited the most severe coagulation and lipid derangements. These findings support the routine integration of lipid profile and coagulation parameters into the biochemical workup of all patients with ultrasonographically confirmed fatty liver disease, enabling non invasive risk stratification and timely therapeutic intervention. Larger prospective studies with histological correlation and multivariate analysis are recommended to validate grade specific biochemical thresholds for clinical decision making.

Declaration by Authors

Conflict of Interest: The authors declare no conflict of interest related to this study. There are no financial, personal, or professional relationships that could be construed to have influenced the design, data collection, analysis, interpretation, or reporting of the findings in this research.

Use of Artificial Intelligence: I declare that Artificial Intelligence (AI) tools were used only to assist with language refinement, grammar correction, and formatting of this research manuscript. The research design, data collection, analysis, interpretation, and conclusions are entirely my original work and remain my sole responsibility.

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