



A Prospective Study Delineating the Correlation between Non-Alcoholic Fatty Liver Disease and Metabolic Syndrome Using Ncep ATP III Criteria

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Non-alcoholic fatty liver disease (NAFLD), Metabolic Syndrome, NCEP ATP III criteria, correlation, metabolic abnormalities.

ABSTRACT:

BACKGROUND INFORMATION

Non-alcoholic fatty liver disease (NAFLD) and Metabolic Syndrome (MS) exhibit a close association, often co-occurring within individuals. The metabolic syndrome encompasses central obesity, elevated triglycerides, low HDL cholesterol, and impaired fasting glucose, a notable risk factor for NAFLD. Intriguingly, NAFLD can also independently precipitate the onset of MS, indicating a bidirectional relationship between these conditions. Recognizing the intertwined nature of NAFLD and MS is pivotal for formulating effective prevention and treatment strategies. The NCEP ATP III criteria offer a valuable framework for evaluating metabolic health in individuals with NAFLD and have significantly contributed to understanding the interplay between these two conditions.

MATERIALS AND METHODS

A descriptive research approach was adopted for the study, and 120 patients with NAFLD were enrolled. Data were collected on socio-demographic characteristics, clinical profile, and abdominal ultrasound. Participants were evaluated for metabolic syndrome using NCEP ATP III criteria. Data were analyzed to identify the specific components that exacerbate NAFLD. The results were stratified and presented in a detailed report.

RESULT

The study analyzed the relationship between non-alcoholic fatty liver disease (NAFLD) severity and metabolic syndrome (MS) components in 120 patients. A significant proportion of individuals (63.33%) had both conditions, emphasizing their frequent co-occurrence. The prevalence of MS in NAFLD increased with age, particularly in individuals aged 51-60, and 41-50. Also, there is a higher prevalence of MS in non-alcoholic fatty liver disease (NAFLD) in females compared to males, with 60% of females and 40% of males affected. Females had a higher prevalence of overweight and obesity (59.20% and 14.20% in females, respectively, compared to 39.40% and 17.60% in males). As NAFLD grades increased, so did the prevalence of MS components,



particularly elevated fasting blood glucose, hypertension, triglycerides, and waist circumference. Conversely, HDL cholesterol levels decreased with more severe NAFLD.

CONCLUSION

The study successfully demonstrated a strong association between NAFLD and Metabolic Syndrome (MS) using NCEP ATP III criteria. Findings indicate that MS components significantly contribute to NAFLD severity. This study highlights the importance of early identification and management of MS in NAFLD patients to improve clinical outcomes. Future research should explore underlying mechanisms and effective treatment strategies for NAFLD and MS.

INTRODUCTION

Regarding human glands, the liver is both the largest and heaviest. At around 1.5 kg as an adult, it's a bit heavier in men than in women. Among the many vital roles the liver plays are metabolism, digestion, detoxification, and immunity. The gland has dual purposes as an endocrine and exocrine organ. Bile salt production and secretion into the common hepatic duct and bilirubin conjugation and clearance into the gut are also examples of exocrine activity. [1]

Insulin and glucagon secretion regulates blood glucose levels; proteins like fibrinogen, albumin, prothrombin, and many more amino acids are synthesized; proteins are converted into peptide hormones and enzymes; phospholipids, cholesterol, and lipoproteins are produced; gluconeogenesis, glycogen storage, and other processes involving fatty acid metabolism are involved; and the endocrine system stores vitamins and minerals like iron. [2]

OVERVIEW OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Non-alcoholic fatty liver disease (NAFLD) presents as a buildup of fat inside liver cells, even when alcohol use is not a significant contributor. This prevalent liver condition is more frequently observed in individuals who are overweight, have type 2 diabetes, and exhibit elevated cholesterol levels. [3] Non-alcoholic fatty liver disease, a prevalent chronic liver condition, arises when the liver stores excessive fat, generally exceeding 5% of its weight, in individuals who either abstain from heavy alcohol consumption or consume minimal amounts (< 20 g ethanol/d) or possess other identifiable causes for hepatic fat accumulation. This disorder has four separate phases: fibrosis, non-alcoholic steatohepatitis, non-alcoholic fatty liver, and cirrhosis. [4]

STAGES OF NAFLD

Hepatic steatosis, or the buildup of extra fat in liver cells, can lead to oxidative stress and the production of Reactive Oxygen Species (ROS) in non-alcoholic fatty liver disease (NAFLD), however, there is usually little inflammation or damage to the liver cells themselves. While it may not seem like much at first, this seemingly harmless condition can worsen into non-alcoholic steatohepatitis (NASH) and other serious complications such as liver fibrosis and cirrhosis if left untreated. [5]

Non-alcoholic steatohepatitis - ROS and lipid peroxidation products cause hepatocellular injury, resulting in an inflammatory response. Activated Kupffer cells release pro-inflammatory cytokines. It can lead to the development of more serious liver conditions, including fibrosis and cirrhosis. This progression occurs through a series of tangled and complex pathological processes, which highlights the potential severity of NASH. [6]

Fibrogenesis - Stellate Cell Activation: Inflammatory cytokines activate hepatic stellate cells (HSCs), which transform into myofibroblast-like cells. These cells produce Extracellular Matrix (ECM) Components, leading to fibrosis. Collagen Deposition: Excessive deposition of collagen and other ECM proteins disrupts the normal liver architecture, forming fibrous bands around hepatocytes and blood vessels. [6]

Cirrhosis - The fibrous bands become more extensive and interconnected as fibrosis progresses, leading to bridging fibrosis. This stage is characterized by significant scarring and distortion of the liver architecture. In the final stage, the liver becomes cirrhotic, with extensive fibrosis and nodule formation. This results in impaired liver function and can lead to complications such as portal hypertension and liver failure. [7]

GRADES OF NAFLD



Grade I (mild): In this stage, the ultrasound imaging shows a marginal increase in the liver's echogenicity, suggesting a slight rise in fat content compared to a healthy liver. Despite this increase, the sound waves reflect well from the walls of the portal vein branches and the diaphragm. This finding highlights the potential impact of increased liver fat content on ultrasound imaging characteristics while indicating no significant interference with the visualization of important structures within the abdomen. [8]

Grade II (moderate): The echogenicity of the liver appears significantly increased, indicating a denser accumulation of fat within the liver tissue. Consequently, the fatty liver condition obscures the echogenic walls of the portal vein branches, hindering the passage of sound waves through the liver, which in turn affects the clear visualization of these blood vessel walls.

Grade III (severe): In the advanced stage of the condition, the liver exhibits very high echogenicity, indicating a significant buildup of fat. The density of the fatty liver is so pronounced that it not only obscures the portal vein branches but also impedes the clear visualization of the diaphragmatic outline. As a result, the sound waves cannot reach the diaphragm, leading to an indistinct image of its border. [9]

METABOLIC SYNDROME

Metabolic syndrome is distinguished by an array/assortment of metabolic disorders that includes central obesity, insulin resistance, hypertension, and atherogenic dyslipidemia that provoke a significant risk in the development of atherosclerotic cardiovascular disease, type II diabetes mellitus, myocardial infarction, and peripheral vascular diseases. [10]

PREVALENCE OF NAFLD AND METABOLIC SYNDROME

Men exhibit a higher susceptibility to nonalcoholic fatty liver disease (NAFLD) compared to women, with the condition predicted to affect 47 individuals per 1,000 worldwide. Despite a gender imbalance, with men exhibiting a greater prevalence (40%) compared to women (26%), it is projected that 32% of the worldwide population would be affected by NAFLD. [11] Metabolic Syndrome (MS) impacts around 20% to 25% of the Indian population, with a greater prevalence in females compared to males. Metabolic syndrome is prevalent

among older persons, particularly those over 45 years of age, and appears to be worse with advancing age. The overall prevalence of MS was determined to be 6.2% (95% Confidence Interval: 4.9% to 7.7%) using the NCEP-ATP-III criteria. The prevalence rates are significantly changed by gender and age, indicating that a substantial segment of the population is impacted. According to NCEP ATP III criteria, 73% of patients with fatty liver exhibited metabolic syndrome, much higher than the 38% prevalence seen in the control group. [12,13]

PATHOPHYSIOLOGY OF NAFLD AND METABOLIC SYNDROME

Environmental influences can influence gene expression, thereby leading to weight gain. The accumulation of visceral and ectopic fat transpires when subcutaneous adipose tissue approaches its expansion threshold, increasing the mobilization of free fatty acids (FFAs). [14] Muscles may serve as a possible site for this form of ectopic fat accumulation. The accumulation of free fatty acids (FFAs) in the muscles results in insulin resistance (IR), inhibiting the body's ability to absorb glucose in the presence of insulin. Conversely, insulin resistance in adipose tissue promotes lipolysis and elevates the hepatic availability of free fatty acids. [15] Atherogenic dyslipidemia ensues, the liver exhibits insulin resistance, glucose production increases, hepatic fat synthesis occurs, and VLDL is secreted. Lipotoxicity is a phenomenon that transpires when excessive free fatty acids infiltrate the pancreas, leading to the dysfunction of insulin-secreting beta cells. The twin cycle theory posits that this dysfunction results in both increased blood glucose levels and the onset of diabetes. An elevation in hepatic fat accumulation triggers a hormonal response that inhibits the functions of glucagon, which is involved in amino acid metabolism. [16] Hyperacidemia, characterized by elevated blood amino acid concentrations, arises when the liver's ability to synthesize urea is impaired due to this resistance. This resistance stimulates an elevation in glucagon synthesis, thus initiating a continuous feedback loop between the pancreas and liver. The elevated secretion of glucose by the liver is an additional consequence of this cycle of higher glucagon levels. Hypertension is primarily a result of insulin resistance, leading to elevated blood insulin levels, which subsequently enhances sympathetic



nervous system activity and increases salt reabsorption. [17] Inflamed and dysfunctional adipose tissue (AT) exacerbates insulin resistance, diminishes anti-inflammatory adiponectin, and secretes elevated levels of pro-inflammatory adipokines. Lipotoxicity, mitochondrial dysfunction, and endoplasmic reticulum stress induced by triglycerides and toxic metabolites in the liver result in hepatocyte death, apoptosis, and fibrosis. Inflammation of adipose tissue macrophages and insulin resistance is exacerbated by the dipeptidyl peptidase 4 (DPP4) produced and secreted by these dysfunctional hepatocytes. [18]

NCEP ATP III CRITERIA AND ITS RELATION TO NAFLD AND METABOLIC SYNDROME

All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP III CRITERIA¹⁰ and a relationship between NAFLD and metabolic syndrome was correlated. Metabolic

syndrome was diagnosed as per NCEP ATP 3 criteria (three or more of the following)

1. Elevated waist circumference (asian indian criteria)
 - Men- Equal to or greater than 90 cm
 - Women- Equal to or greater than 80 cm

2. Elevated triglycerides: Equal to or greater than 150 mg/dL (1.7 mmol/L).

Reduced HDL cholesterol:

- Men- Less than 40 mg/dL (1.03 mmol/L)
- Women- Less than 50 mg/dL (1.29 mmol/L)

4. Elevated blood pressure: Equal to or greater than 130/85mmHg or use of medication for hypertension

5. Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycaemia.

Elevated waist circumference (Asian Indian criteria)	Men — Equal to or greater than 90 cm	Women — Equal to or greater than 80 cm
Elevated triglycerides	Equal to or greater than 150 mg/dL (1.7 mmol/L)	
Reduced HDL cholesterol	Men — Less than 40 mg/dL (1.03 mmol/L)	Women — Less than 50 mg/dL (1.29 mmol/L)
Elevated blood pressure	Equal to or greater than 130/85 mm Hg or use of medication for hypertension	
Elevated fasting glucose	Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia.	

Table 1. Metabolic syndrome was diagnosed as per NCEP ATP 3 criteria (three or more of the above)

The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) has defined criteria for diagnosing metabolic syndrome, which is a combination of risk factors that increase the likelihood of developing cardiovascular disease, stroke, and type 2 diabetes. According to these criteria, metabolic syndrome is identified when three or more of the following components are present in an individual.

Abdominal obesity: This is determined by an increased waist circumference relative to height. Excess abdominal fat, also known as visceral fat, is a crucial aspect of metabolic syndrome and is associated with a heightened risk of cardiovascular disease and type 2 diabetes.

High triglycerides: Elevated levels of triglycerides in the blood indicate high triglycerides, which are a significant component of metabolic syndrome. Having

high triglyceride levels is associated with an increased risk of atherosclerosis and heart disease. [19]

Low HDL cholesterol: Reduced levels of "good" cholesterol, also known as high-density lipoprotein (HDL) cholesterol, characterize metabolic syndrome. Low levels of HDL cholesterol are associated with an increased risk of heart disease and may indicate abnormal lipid metabolism.

High blood pressure: Elevated blood pressure, meeting the criteria for hypertension, is another key component of metabolic syndrome. Hypertension is a major risk factor for cardiovascular disease and is known to lead to complications such as heart attack, stroke, and kidney failure. **Insulin resistance:** Insulin resistance is often indicative of impaired fasting glucose or the presence of type 2 diabetes. This means that the body's cells are not



effectively responding to insulin, leading to high blood sugar levels. Insulin resistance plays a fundamental role in metabolic syndrome and is associated with an increased risk of cardiovascular disease and type 2 diabetes. [20]

MATERIALS AND METHODS

It is a prospective Observational study on “the correlation between non-alcoholic fatty liver disease and metabolic syndrome using NCEP ATP III criteria” conducted at the Department of Radiology at Malla Reddy Hospital, Suraram, Hyderabad, Telangana. The study was carried out for 6 months and the sample size was 120 patients. The study procedure was explained to the subject and informed consent was obtained from patients individually. After obtaining ethical clearance, all required information was collected using a patient data collection form. Information was obtained regarding sociodemographic characteristics, clinical profile, and USG of the abdomen considering NAFLD, then the patient was evaluated for the presence of metabolic syndrome through NCEP ATP III criteria if they meet

any three or more parameters which include Elevated waist circumference, Elevated triglycerides, Reduced HDL cholesterol, Elevated blood pressure, and Elevated fasting glucose. Samples were collected based on inclusion and exclusion criteria, followed by collecting baseline demographic data for all participants. The inclusion criteria include patients who are >18 years & < 65 years, gender Male and female, patients diagnosed as NAFLD based on abdominal ultrasonography, and patients who are willing to participate in the study. The exclusion criteria include patients who are <18 years & >65 years, patients with a history of alcohol intake, patients with a history of any chronic liver disease Patients with a history of following drug intake -steroids, synthetic estrogens, heparin, amiodarone, valproic acid, antiviral agents and pregnant women. The data was noted in the data collection form and analyzed through MSEXCEL to identify the specific component exacerbating NAFLD. IBM SPSS Software will be utilized for further analysis by a statistician to conclude. Thereafter, the results will be stratified and the detailed project report will be prepared and submitted.

RESULTS

Table 2. Frequency of Grades in NAFLD Patients

GRADES	FREQUENCY	PERCENTAGES
Grade I	67	55.8 %
Grade II	43	35.8 %
Grade III	10	8.3 %
Total	120	100 %

The frequency and percentage distribution of 120 distinct individuals in three Grades- Grades I, II, and III are displayed. Grade I is the most prevalent grade,

accounting for 55.8% of the total population. At 8.3%, Grade III is the least prevalent followed by Grade II at 35.8%.

Table 3. Distribution of NAFLD GRADES by Gender

GRADES	MALE		FEMALE	
	Frequency	Percentages	Frequency	Percentages
GRADE I	29	43.30%	38	56.70%
GRADE II	15	34.90%	28	65.10%
GRADE III	4	40%	6	60.00%
TOTAL	48	100%	72	100%

The table presents a comparative analysis of gender distribution across NAFLD grades - Grade I, Grade II, and Grade III, a noteworthy observation is that there are

a majority of female subjects (38,28,6 respectively) in all three grades. While Grade I exhibits a relatively equitable gender ratio, Grade II and Grade III



demonstrate a significantly higher proportion of females when compared to males.

Table 4. Distribution of Age by NAFLD Grades

AGE (in years)	GRADE I	GRADE II	GRADE III	TOTAL	Age percentages
18-30	4	2	0	6	5.0%
31-40	9	1	0	10	8.3%
41-50	23	16	4	43	35.8%
51-60	29	20	6	55	45.8%
61-65	3	2	1	6	5.0%
TOTAL	68	41	11	120	100%

Age distribution of individuals appear in the above-given table across three grades: Grade I, Grade II, and Grade III. The majority of individuals in all grades fall within the 51-60 (total -55 subjects), and 41-50 age range (total 43 subjects), while fewer individuals are in the younger age groups. Age-related declines in the overall number

of participants indicated a higher prevalence of older individuals in the higher grades. These results illustrate potential age-related trends or patterns in the population under investigation. The oldest age group (61-65) is relatively small (6), representing fewer participants in all grades.

Table 5. Gender-Specific Distribution of BMI Categories

BMI	MALE		FEMALE		BMI-Total	
	FREQUENCY	PERCENT AGES	FREQUENCY	PERCENT AGES	FREQUENCY	PERCENT AGES
NORMAL (21.5-24.9 kg/m ²)	17	53.10%	15	46.90%	32	26.70%
OVER Wt. (25.0-29.9 kg/m ²)	28	39.40%	43	60.60%	71	59.20%
OBESE (30.4-35.1 kg/m ²)	3	17.60%	14	82.40%	17	14.20%
GENDER TOTAL:	48	40%	72	60%	120	100%

The table above presents a comparative analysis of BMI distribution among males and females. It categorizes individuals into three BMI groups: normal, overweight, and obese. The observation is that, compared to the prevalence of overweight (39.40%) and obese (17.60%) in males, there is a larger prevalence of overweight

(60.60%) and obese people (82.40%), in females. These findings underscore the significant health implications of overweight and obesity within the population and guide public health campaigns that encourage healthy lifestyles and lower the incidence of these diseases.

Table 6. Frequency of Metabolic Syndrome in NAFLD

NAFLD	FREQUENCY	PERCENTAGES
NAFLD W MS	76	63.33%
NAFLD W/O MS	44	36.67%
TOTAL	120	100%



The table represents a comprehensive analysis of NAFLD prevalence and its association with Metabolic Syndrome (MS) within a given population. Of the 120 individuals included in the study, a significant proportion of NAFLD had MS (63.33%), underscoring a robust correlation between the two conditions. The smaller

proportion of individuals with NAFLD did not have MS (36.67%). These findings underscore the prevalence of NAFLD and its frequent co-occurrence with MS within the studied population, suggesting the importance of screening for both conditions in individuals with either diagnosis.

Table 7. Gender distribution in NAFLD patients with and without Metabolic Syndrome

GENDER	NAFLD W MS (n=76)	NAFLD W/O MS (n=44)	TOTAL (n=120)
MALE	27 (35.53%)	23 (52.27%)	48 (40%)
FEMALE	49 (64.47%)	21 (47.73%)	72 (60%)

The graphical representation demonstrates a significant gender disparity in the prevalence of non-alcoholic fatty liver disease (NAFLD). Females exhibited a notably higher rate of NAFLD (60%) compared to males (40%). Moreover, females with NAFLD were more likely to

present with Metabolic Syndrome (64.47%). In contrast, males with NAFLD were without MS (52.27%). These findings highlight the importance of early detection, particularly in females, to address the potential co-occurrence of MS and mitigate disease progression.

Table 8. Frequency of Metabolic Syndrome in NAFLD by age group

Age-Group	NAFLD W MS	NAFLD W/O MS	Age-Group-Total
18-30	0 (0.0)	6 (100.0)	6(5%)
31-40	5 (50.0)	5 (50.0)	10(8.4%)
41-50	30 (69.8)	13 (30.2)	43(35.8%)
51-60	38 (69.1)	17 (30.9)	55(45.8%)
61-65	3 (50.0)	3 (50.0)	6(5%)
NAFLD-TOTAL	76 (63.3%)	44 (36.7%)	120(100%)

The table shows a comprehensive analysis of NAFLD prevalence and its association with Metabolic Syndrome (MS) across different age groups. The age range of 51–

60 (45.8%) has the highest frequency of MS in NAFLD, followed by the 41–50 age group (35.8%).

Table 9. Prevalence of Metabolic Syndrome in NAFLD

GRADES	METABOLIC SYNDROME				TOTAL
	PRESENT		ABSENT		
	Frequency	Percentages	Frequency	Percentages	
GRADE I (n=67)	43	64.17%	24	35.82%	67 (100%)
GRADE II (n=43)	26	60.46%	17	39.53%	43 (100%)
GRADE III (n=10)	7	70%	3	30%	10 (100%)



We found that Metabolic Syndrome is higher in grade I (64.17%), Whereas the Absence of metabolic syndrome in grade III was found the least (30%).

Table 10. Comparison of Variables of NCEP ATP III Criteria for the presence of MS in NAFLD Patients

Variables	NAFLD W MS			NAFLD W/O MS			P value
	n (%)	MEAN	SD	n (%)	MEAN	SD	
Fasting Blood Glucose (\geq 100mg/dL) (n=69)	53(76.8)	114.1	10.3	16(23.2)	105.2	5.6	0.002
Hypertension (SBP \geq 130mmHg) (n=49)	32(65.3)	140.3	5.3	17(34.7)	135.7	2.4	0.002
Hypertension (DBP \geq 85mmHg) (n=49)	32(65.3)	94.3	4.7	17(34.7)	88.4	1.8	<0.001
Waist Circumference (M \geq 90cm) (n=24)	19(79.2)	96.5	7.4	5(20.8)	90.8	0.4	0.106
Waist Circumference (F \geq 80cm) (n=46)	36(78.3)	93.8	7.5	10(21.7)	84.4	5.5	<0.001
HDL (\geq 150Mg/dL) (n=83)	63(75.9)	172.8	22.1	20(24.1)	156.8	0.5	0.048
HDL (M<40Mg/dL) (n=23)	16(69.6)	36.1	2.8	7(30.4)	38.4	0.5	0.048
HDL (F<50Mg/dL) (n=37)	30(81.1)	41.5	6.4	7(18.9)	47.6	2.3	0.021

The table indicates significant associations between variables of metabolic syndrome (MS) in individuals with non-alcoholic fatty liver disease (NAFLD). While waist circumference in males did not exhibit a significant difference (p-value <0.106) between the two groups,

variables such as fasting blood glucose, hypertension, triglycerides, waist circumference in females, and HDL levels have shown significant association with and without metabolic syndrome in NAFLD.

Table 11. Frequency of variables of NCEP ATP III criteria in NAFLD patients with and without Metabolic Syndrome

Variables with frequency	GRADE I NAFLD		GRADE II NAFLD		GRADE III NAFLD	
	Metabolic syndrome		Metabolic syndrome		Metabolic syndrome	
	Present	Absent	Present	Absent	Present	Absent
Fasting Blood Glucose (\geq 100mg/dL) (n=69)	27	8	22	7	4	1
Hypertension (\geq 130/85mmHg) (n=49)	15	9	13	7	4	1
Waist Circumference (M \geq 90cm) (n=24)	11	3	6	1	2	1
Waist Circumference (F \geq 80cm) (n=46)	20	6	13	4	3	0
Triglycerides (\geq 150mg/dL) (n=83)	35	13	23	6	5	1



HDL (M<40mg/dL) (n=23)	10	4	5	3	1	0
HDL (M<50mg/dL) (n=37)	14	3	13	3	3	1

The table represents the frequency of NCEP ATP III criteria variables in NAFLD patients with and without MS associated with different grades, where

Triglycerides(>150mg/dL) at grade I NAFLD were found to maximum (35).

Table 12. Mean Comparison of the variables of NCEP ATP III criteria in association with NAFLD severity with Metabolic Syndrome

VARIABLES	GRADE I W MS			GRADE II W MS			GRADE III W MS			P VALU E
	n (%)	MEA N	SD	n (%)	MEA N	S D	n (%)	MEA N	SD	
Fasting Blood Glucose(=/>100mg/dl) (n=53)	27 (50.9%)	105.85	3.1	22 (41.6%)	120.1	3.5	4 (7.5%)	136.5	10.9	<0.000
Hypertension (SBP=/>130mmHg) (n=32)	15 (46.9%)	137.6	2.89	13 (40.6%)	139.8	2.35	4 (12.5%)	152	3.6	<0.000
Hypertension (DBP=/>85mmHg) (n=32)	15 (46.9%)	90.13	2.7	13 (40.6%)	98.1	2.6	4 (12.5%)	97.5	2.9	<0.000
Waist Circumference(M=/>90cm) (n=19)	11 (57.9%)	92.6	1.4	6 (31.6%)	97.2	3.3	2 (10.5%)	115.5	4.95	<0.000
Waist Circumference(F=/>80cm) (n=36)	20 (55.6%)	88.9	3.23	13 (36.1%)	97.5	4.12	3 (8.3%)	110.7	4.04	<0.000
Triglycerides(=/>150mg/ dl) (n=63)	35 (55.6%)	156.1	3.3	23 (36.5%)	187.4	8.4	5 (7.9%)	222	19.8	<0.000
HDL(M<40mg/dl) (n=16)	10 (62.5%)	37	2.31	5 (31.3%)	35.6	2.61	1 (6.3%)	30	NA	0.044



HDL(F<50mg/dl) (n=30)	14 (46.7%)	45.9	3.6 1	13 (43.3%)	38.8	5.8	3 (10%)	33	4.6	<0.000
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It demonstrates the significance of the association of all the variables at different grades (I, II, III) with the presence of metabolic syndrome at p-value <0.05, whereas HDL decreases with an increase in NAFLD severity grades.

DISCUSSION

The findings of the study show that NCEP ATP 3 (National Cholesterol Education Program Adult Treatment Panel III) criteria served as a valuable framework for assessing the presence of MS in NAFLD patients. NCEP ATP III criteria determine the relationship between NAFLD and MS. NCEP ATP III criteria has also shown components of MS that individually exacerbate the severity of NAFLD which is detected by liver ultrasonography. NAFLD is strongly associated with metabolic abnormalities including central obesity, type 2 diabetes mellitus, hypertension, and dyslipidemia. NCEP ATP III criteria facilitate better clinical decision-making and patient management in the presence of MS. The criteria offer a fastidious understanding of NAFLD severity by better diagnosis.

The study included a total of 120 patients, with varying demographic and clinical characteristics. The study revealed that there is a higher prevalence of metabolic syndrome in NAFLD patients with 63.33% which is assessed by NCEP ATP III criteria and statistical significance is found in diabetes mellitus, triglycerides, HDL, and hypertension. Our present study shows that there is an association between NAFLD and MS by NCEP ATP III criteria which is very similar to a study which was conducted by **Rakesh Gaharwar**, our study also shows components of MS of NCEP ATP III criteria that exacerbate NAFLD severity. [21]

The present study demonstrated a higher prevalence of non-alcoholic fatty liver disease (NAFLD) in females compared to males. Specifically, 60% of females had NAFLD, while only 40% of males were affected. While our findings align with previous studies indicating a higher prevalence of non-alcoholic fatty liver disease (NAFLD) in females compared to males, their study did not observe a statistically significant difference in the

prevalence of NAFLD between genders in the study conducted by **Dr. P.Asati1, Dr. P.Kukrele, Dr. Sarita Jalodiya** in the dept of medicine NSCB MCH Jabalpur. [22]

Furthermore, our analysis revealed a gender-specific association between NAFLD and metabolic syndrome (MS). Females were more likely to exhibit MS in NAFLD (64.47%), whereas males were more prone to NAFLD without MS (52.27%). This suggests that MS may play a more significant role in the development or progression of NAFLD in females compared to males. [23]

The distribution of patients based on age groups revealed that most of the patients have a higher prevalence of metabolic syndrome in NAFLD between the age group of 51-60(45.8%) and 41-50(35.8%), where the mean age group was found to be 49 years. In the total study population, females (n=72) were found to be more than males(n=48). Additionally, the gender-specific distribution of BMI categories shows a large group of patients from both males (39.40%) and females (60.60%) belonging to the overweight category followed by normal and obese respectively. This study shows that age, gender, and BMI distribution are crucial for understanding potential differences in disease prevalence and severity. A similar report was found in a study conducted by **Julie Ann Thomas, Sourya Acharya2, Samarth Shukla** in the Department of Medicine, Maharashtra India. [24]

Our study shows 55.8%,35.8%, and 8.3% of cases had grade I, II, and III fatty liver respectively. 76(63.33%) of cases of NAFLD have metabolic syndrome according to the NCEP ATP III criteria. A similar study was found by **Pradeep Nigam, and Ravi Prakash Pandey** in the Department of Medicine, SSMC and SGMH, Rewa, Madhya Pradesh, reported 55%, 36% and 8.5% of cases had grade I, II, and III fatty liver respectively. Pande A and Pande V11 found in their study that 49%, 38%, and 13% had grade I, II, and III fatty liver disease respectively.

The study included 76 patients with metabolic syndrome (MS) in non-alcoholic fatty liver disease (NAFLD) and



44 patients without MS in NAFLD. According to the NCEP ATP III criteria, 69 (90.8%) patients had impaired fasting glucose levels, out of which 53 (76.8%) are with metabolic syndrome in NAFLD and 16 (23.2%) are without metabolic syndrome respectively. 49 (64.5%) patients exhibited hypertension, out of which 32 (65.3%) were with metabolic syndrome in NAFLD and 17 (34.7%) were without metabolic syndrome respectively. 70 (92.1%) patients had increased waist circumference, among males 19 (79.2%) were with MS, and 5 (20.8%) were without MS respectively. In females, 36 (78.3%) are with MS in NAFLD and 10 (21.7%) are without MS respectively. 83 (109.2%) patients had elevated triglyceride levels, 63 (75.9%) were with metabolic syndrome in NAFLD and 20 (24.1%) were without metabolic syndrome respectively. Low HDL levels were observed in 60 (78.9%) NAFLD patients. Among males, 16 (69.6%) are with MS and 7 (30.4%) are without MS respectively. In females, 30 (81.1%) are with MS and 7 (18.9%) are without MS. The study found that all variables of the NCEP ATP III criteria, except for waist circumference in males, were statistically significant, suggesting a strong association between NAFLD and MS. A similar report was found by **Pradeep Nigam, Ravi Prakash Pandey** in the Department of Medicine, SSMC and SGMH, Rewa, Madhya Pradesh. This study resulted Comparison of the Prevalence of variables in NAFLD Patients with and without Metabolic Syndrome. [25]

When the variables of metabolic syndrome, were observed about the grades of NAFLD, the fasting blood glucose showed a mean of 105.85, 120.1, and 136.5 in grades I, II, and III, respectively ($p < 0.05$ for all comparisons). The systolic blood pressure showed means of 137.6, 139.8, and 152 in grades I, II, and III, respectively ($p < 0.05$ for all comparisons). The diastolic blood pressure showed means of 90.13, 98.1, and 97.5 in grades I, II, and III, respectively ($p < 0.05$ for all comparisons). Waist circumference (≥ 90 cm) in males showed means of 92.6, 97.2, and 115.5 in grades I, II, and III, respectively ($p > 0.05$ for all comparisons). Waist circumference (≥ 80 cm) in females showed means of 88.9, 97.5, and 110.7 in grades I, II, and III, respectively ($p < 0.05$ for all comparisons). Triglycerides showed a mean of 156.1, 187.4, and 222 in grades I, II, and III, respectively ($p < 0.05$ for all comparisons). HDL in males showed a mean of 37, 35.6, and 30 in grades I, II,

and III, respectively ($p < 0.05$ for all comparisons). HDL in females showed a mean of 45.9, 38.8, and 33 in grades I, II, and III, respectively ($p < 0.05$ for all comparisons). These findings indicate that the severity of NAFLD is associated with a significant increase in all the variables studied, except for HDL. As NAFLD progresses from Grade I to III, there is a significant rise in fasting blood glucose, systolic and diastolic blood pressure, waist circumference (females), and triglycerides, while HDL levels decrease. This suggests that the metabolic abnormalities associated with NAFLD worsen with increasing disease severity. A similar study is conducted by **Zahaan Vakil, Kiran Ahire** Department of General Medicine, Seth G. S. Medical College, and KEM Hospital, Mumbai, Maharashtra, India. They showed a higher prevalence of all components of metabolic syndrome in cases of NAFLD, our study also showed a mean of all components of NCEP ATP III criteria in patients with NAFLD with MS. [26]

CONCLUSION

This study provides compelling evidence that the NCEP ATP III criteria are a reliable and effective tool for identifying metabolic syndrome in patients with non-alcoholic fatty liver disease (NAFLD). Among the 120 participants, a significant proportion (63.33%) exhibited metabolic syndrome in NAFLD underscoring the critical need for lifestyle interventions to mitigate the severity of NAFLD in these individuals. Conversely, the remaining 36.67% presented with NAFLD alone, suggesting the potential influence of additional factors beyond MS, such as genetic predisposition (including family history and genetic variants) and lifestyle choices, including sedentary behavior and unhealthy dietary patterns.

The study revealed a notable association between the severity of non-alcoholic fatty liver disease (NAFLD) and key metabolic syndrome (MS) components, such as fasting blood glucose levels, triglyceride levels, and blood pressure measurements. Obesity and overweight were prevalent among a large proportion of female participants. Implementing lifestyle modifications, such as regular physical activity, a balanced diet, stress management, and caloric restriction, could be instrumental in reducing weight and maintaining a normal BMI, potentially mitigating the risk factors associated with metabolic syndrome. The severity of NAFLD is linked to worsening metabolic abnormalities



and vice versa. There was a significant increase in blood glucose, blood pressure, waist circumference, and triglycerides as NAFLD progressed from Grade I to III, while HDL levels decreased. This study highlights the importance of considering NCEP ATP III criteria when evaluating NAFLD patients. Early identification and management of MS components can potentially improve clinical outcomes and slow down NAFLD progression. Future research should delve into the underlying mechanisms connecting the severity of non-alcoholic fatty liver disease (NAFLD) to specific metabolic abnormalities, as well as evaluate the effectiveness of various treatment approaches for managing NAFLD and its associated metabolic complications. Clinical pharmacists can play a pivotal role in mitigating NAFLD severity by providing comprehensive patient counseling on lifestyle modifications.

REFERENCES

1. Bazira, P. J. (2023). Anatomy of the liver. *Surgery*, 41(6), 313–318.
2. Song, X., Hou, K., Zhou, H., Yang, J., Cao, T., & Zhang, J. (2024). Liver organoids and their application in liver cancer research. *Regenerative Therapy*, 25, 128–137.
3. Argo, C. K., & Caldwell, S. H. (2009). Epidemiology and natural history of non-alcoholic steatohepatitis. *Clinics in Liver Disease*, 13(4), 511–531.
4. Niu, X., Zhu, L., Xu, Y., Zhang, M., Hao, Y., Ma, L., Li, Y., & Xing, H. (2023). Correction: Global prevalence, incidence, and outcomes of alcohol related liver diseases: a systematic review and meta-analysis. *BMC Public Health*, 23(1), 1380.
5. Seitz, H. K., & Neuman, M. (2022). Narrative review on alcoholic liver disease: from fibrosis to cancer. *Digestive Medicine Research*, 5, 15–15.
6. Loomba, R., & Sanyal, A. J. (2013). The global NAFLD epidemic. *Nature Reviews. Gastroenterology & Hepatology*, 10(11), 686–690.
7. Abdelmalek, M. F. (2021). Nonalcoholic fatty liver disease: another leap forward. *Nature Reviews. Gastroenterology & Hepatology*, 18(2), 85–86.
8. Steen Pedersen, J., & Bendtsen, F. (2018). *Adult Non-alcoholic Fatty Liver Disease (NAFLD)*. 23–46.
9. Pouwels, S., Sakran, N., Graham, Y., Leal, A., Pintar, T., Yang, W., Kassir, R., Singhal, R., Mahawar, K., & Ramnarain, D. (2022). Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. *BMC Endocrine Disorders*, 22(1), 63.
10. Papatheodoridi, M., & Cholongitas, E. (2018). Diagnosis of non-alcoholic fatty liver disease (NAFLD): Current concepts. *Current Pharmaceutical Design*, 24(38), 4574–4586.
11. Giannopoulos, C. K., Tzima, I. G., Tentolouris, N. K., & Vasileiadis, I. A. (2023). Common pathogenetic pathways of non-alcoholic fatty liver disease and type 2 diabetes mellitus. *Current Diabetes Reviews*, 19(9), e160223213720.
12. Huang, P. L. (2009). A comprehensive definition for metabolic syndrome. *Disease Models & Mechanisms*, 2(5–6), 231–237.
13. Khatiwada, S., Sah, S. K., Kc, R., Baral, N., & Lamsal, M. (2016). Thyroid dysfunction in metabolic syndrome patients and its relationship with components of metabolic syndrome. *Clinical Diabetes and Endocrinology*, 2(1), 3.
14. Teng, M. L., Ng, C. H., Huang, D. Q., Chan, K. E., Tan, D. J., Lim, W. H., Yang, J. D., Tan, E., & Muthiah, M. D. (2023). Global incidence and prevalence of nonalcoholic fatty liver disease. *Clinical and Molecular Hepatology*, 29(Suppl), S32–S42.
15. Goyal, A., Arora, H., & Arora, S. (2020). Prevalence of fatty liver in metabolic syndrome. *Journal of Family Medicine and Primary Care*, 9(7), 3246–3250.
16. Godoy-Matos, A. F., Silva Júnior, W. S., & Valerio, C. M. (2020). NAFLD as a continuum: from obesity to metabolic syndrome and diabetes. *Diabetology & Metabolic Syndrome*, 12(1), 60.



17. Wainwright, P., & Byrne, C. D. (2016). Bidirectional relationships and disconnects between NAFLD and features of the metabolic syndrome. *International Journal of Molecular Sciences*, 17(3), 367.
18. Rochlani, Y., Pothineni, N. V., Kovelamudi, S., & Mehta, J. L. (2017). Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. *Therapeutic Advances in Cardiovascular Disease*, 11(8), 215–225.
19. Herman, R., Kravos, N. A., Jensterle, M., Janež, A., & Dolžan, V. (2022). Metformin and insulin resistance: A review of the underlying mechanisms behind changes in GLUT4-mediated glucose transport. *International Journal of Molecular Sciences*, 23(3), 1264.
20. Radu, F., Potcovaru, C.-G., Salmen, T., Filip, P. V., Pop, C., & Fierbințeanu-Braticievici, C. (2023). The link between NAFLD and metabolic syndrome. *Diagnostics (Basel, Switzerland)*, 13(4), 614.
21. Gaharwar, R., Trikha, S., Margekar, S. L., Jatav, O. P., & Ganga, P. D. (2015). Study of clinical profile of patients of non alcoholic fatty liver disease and its association with metabolic syndrome. *The Journal of the Association of Physicians of India*, 63(1), 12–16.
22. Asati, D. P., & Asst. Professor, DM Gastroenterology, Dept of Medicine NSCB MCH Jabalpur. (2017). Study of Patients with Non Alcoholic Fatty Liver Disease and its Association with Metabolic Syndrome in tertiary centre. *Journal of Medical Science and Clinical Research*, 05(06), 22901–22904.
23. Pardhe, B. D., Shakya, S., Bhetwal, A., Mathias, J., Khanal, P. R., Pandit, R., Shakya, J., Joshi, H. O., & Marahatta, S. B. (2018). Metabolic syndrome and biochemical changes among non-alcoholic fatty liver disease patients attending a tertiary care hospital of Nepal. *BMC Gastroenterology*, 18(1), 109.
24. Thomas, J., Acharya, S., Shukla, S., Thomas, J., Pratapa, K., & Hulkoti, S. (2020). Liver Disease (NAFLD) in Metabolic Syndrome (MetS)-A case control study. *Medical Science*, 2020(103), 1490–1499.
25. Nigam, P., Prakash Pandey, R., Pawar, M., & Indurkar, M. (2018). Clinical profile of nafld patients and its correlation with metabolic syndrome. *Journal of Evolution of Medical and Dental Sciences*, 7(04), 433–436.
26. Vakil, Z., & Ahire, K. (2023). Clinical profile of nonalcoholic fatty liver disease and its correlation with metabolic syndrome and cardiovascular risk. *International Journal of Applied & Basic Medical Research*, 13(4), 234–239.