CLINICO-BIOCHEMICAL AND HISTOLOGICAL PROFILING OF INDIAN PATIENTS HAVING NON-ALCOHOLIC FATTY LIVER DISEASE

[1]Dr. Uditkumar Agrawal, [2]Dr. Arun Mishra, [3]Dr. Varsha Patel, [4]Dr. Rimjhim Raina
[1]Associate Professor, Department of Biochemistry, NSCGMC, Khandwa, Madhya Pradesh, India
[2]Assistant Professor, Department of Biochemistry, NSCGMC, Khandwa, Madhya Pradesh, India
[3,4]Senior Resident, Department of Pathology, Government Medical College, Satna, Madhya Pradesh, India

Corresponding Author:
Dr. Rimjhim Raina
Email ID: rainarimjhim@gmail.com

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ABSTRACT

Introduction: Non-alcoholic steatohepatitis (NASH) represents a clinicopathological condition characterized by histological alterations akin to those induced by excessive alcohol consumption, despite the absence of alcohol abuse. This investigation aims to assess the clinical, biochemical, and histological characteristics of NASH within a tertiary healthcare facility situated in India.

Materials and Methods: This study adopted an observational, prospective, single-center approach involving patients of varied ages and genders, presenting with heightened liver echogenicity upon routine ultrasound examination. Clinical, biochemical, and histological profiles of the patients were studied.

Results: A cohort of 89 patients participated in the study, comprising 53 males and 36 females. Predominantly, individuals aged between 41 and 50 years constituted the majority. The most prevalent symptom reported was fatigue and malaise, succeeded by right upper abdominal discomfort, jaundice, ascites, and upper gastrointestinal bleeding. Notably, 30 patients remained asymptomatic at the time of diagnosis, with abnormalities detected via sonographic examination and liver function tests conducted during investigations for alternative etiologies. Hyperlipidemia, diabetes mellitus, obesity, and overweight conditions emerged as the leading associated risk factors. Biopsies were performed on 10 patients, majority revealing fatty changes.

Conclusion: This investigation underscores the heightened prevalence of features indicative of the metabolic syndrome among individuals diagnosed with NASH. These findings suggest a significant overlap with systemic disorders associated with insulin resistance syndrome, including hyperlipidemia, hypertension, obesity, type 2 diabetes mellitus, and hepatic steatosis.

Keywords: Hyperlipidemia, hypertension, metabolic syndrome, non-alcoholic steatohepatitis.

INTRODUCTION

Non-alcoholic steatohepatitis (NASH) is a clinical and pathological condition characterized by the development of histological features similar to those seen in individuals with excessive alcohol intake, despite the absence of alcohol abuse. NASH is increasingly acknowledged as a chronic liver ailment due to its potential to progress to end-stage liver disease. Its pathological manifestations resemble those of alcohol-induced liver damage but manifest in obese, diabetic individuals who do not engage in alcohol abuse [1-3].

In the Indian subcontinent, there is a scarcity of literature regarding the prevalence of NASH. However, available reports by Aggarwal et al. [2] and Amarapurkar et al. [4] confirm its prevalence among the Indian population. Progression to cirrhosis has been observed in 7-15% of NASH patients, with a generally slow progression over several years. Ballooning degeneration has been associated with a relatively accelerated advancement to advanced fibrosis [5-8].

Addressing this emerging disease requires multifaceted approaches to mitigate the associated morbidity and mortality. It is imperative for practicing physicians to identify NASH cases promptly to initiate appropriate therapeutic interventions. Recent attention to NASH stems from observations indicating its potential progression to liver cirrhosis and failure over time. Hence, early recognition and intervention to impede and reverse the disease process are recommended. This study aims to assess the clinical, biochemical, and histological characteristics of NASH in a tertiary hospital in India.

MATERIALS AND METHODS

The present investigation was a observational, prospective, single-center study conducted at a tertiary care hospital in India.

The inclusion criteria for this study encompass individuals across all age groups and genders who demonstrate heightened echotexture of the liver during routine ultrasound examinations and express willingness to participate. Conversely, exclusion criteria consist of individuals identified as alcoholics based on the delineation outlined by Powell et al. Additionally, patients diagnosed with viral hepatitis B or C infections are excluded, alongside those presenting with conditions such as sepsis, total parenteral nutrition, jejuno-ileal bypass, or autoimmune disorders. Furthermore, subjects undergoing rapid weight loss and patients using specific drugs including steroids, tamoxifen, hormone replacement therapy, nifedipine, diltiazem, methotrexate, amiodarone, warfarin, pentoxifylline, and chloroquine were also excluded from the study.

All enrolled cases underwent comprehensive clinical, anthropometric, and laboratory assessments subsequent to a screening ultrasound scan of the liver. The extent of fatty infiltration and fibrosis was evaluated based on brightness and posterior attenuation, and appropriately graded by a single radiologist. Patients exhibiting elevated liver enzymes and meeting the criteria for liver biopsy underwent percutaneous liver biopsy subsequent to providing informed consent

during a short-stay hospital admission. Liver biopsy specimens were scored according to the scoring system devised by Brunt et al., performed by a single pathologist. Serum insulin levels, along with fasting blood sugar levels, were measured, and insulin resistance was calculated using a derived formula. Additionally, a correlation between serum ferritin levels and non-alcoholic fatty liver disease was established.

Data compilation was executed using Microsoft Excel, with statistical analysis performed using descriptive statistics methodologies.

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RESULTS

The current investigation enrolled 89 participants, with 40.45% being males and 59.55% females. The majority belonged to the 41 to 50 years age group (Table 1). Fatigability and malaise were the most prevalent symptoms, followed by right upper abdominal discomfort, jaundice, ascites, and upper gastrointestinal bleeding. A notable 33.71% of patients were asymptomatic at diagnosis, with abnormal sonographic findings and liver function test results leading to diagnosis during investigations for other conditions. Hepatomegaly or palpable liver was the most common clinical sign observed (Table 2).

Table 3 outlines the risk factors observed in patients with non-alcoholic fatty liver disease (NAFLD). Dyslipidemia was the most common risk factor in both genders, followed by diabetes mellitus and hypertension.

Blood glucose levels among diabetic and non-diabetic participants are detailed in Table 4, while Table 5 presents the results of liver, kidney, clotting, and lipid profile tests conducted in the study population.

Liver biopsy findings in NAFLD cases are summarized in Table 6, with fatty liver change being the most frequent histological observation.

Table 1: Age and gender wise distribution of cases of NAFLD

Age	Male		Female		Total	
	n	%	n	%	n	%
<20 years	0	0.00	0	0.00	0	0.00
21-30 years	1	1.12	1	1.12	2	2.25
31-40 years	0	0.00	13	14.61	13	14.61
41-50 years	19	21.35	15	16.85	34	38.20
51-60 years	10	11.24	17	19.10	27	30.34
61-70 years	6	6.74	7	7.87	13	14.61
Total	36	40.45	53	59.55	89	100.00
Mean age, years	52.75 ± 8.67		50.44 ± 9.66		51.36 ± 9.27	

Table 2: Signs and symptoms in study population

Symptoms	n	%
Ascites	9	10.11
Asymptomatic	30	33.71
Fatigability	59	66.29
Jaundice	9	10.11
Malaise	59	66.29
Right upper abdominal discomfort	42	47.19
UGI Bleed	6	6.742
Signs		
Abdominal distension	16	17.98
Edema	31	34.83
Hepatomegaly or palpable liver	80	89.89
Icterus	12	13.48
Splenomegaly	15	16.85

Table 3: Risk factors in NAFLD patients

Risk Factors	Male		Female		Total	
	n	%	n	%	n	%
Obesity	16	17.98	25	28.09	42	47.19
Overweight	19	21.35	25	28.09	45	50.56
Diabetes Mellitus	25	28.09	27	30.34	52	58.43
Hypertension	22	24.72	25	28.09	47	52.81
Dyslipidemia	25	28.09	30	33.71	55	61.8
Coronary Artery Disease	16	17.98	19	21.35	36	40.45

Table 4: Blood glucose levels in study participants

Blood Glucose	FBS (Mean ± SD)	PP2BS (Mean ± SD)
Diabetic	169.25 ± 73.20	263.70 ± 68.50
Non Diabetic	86.95 ± 20.80	113.45 ± 44.60

Table 5: Laboratory parameters in study population

Parameter	Mean ± SD
Renal function tests	
Blood urea	27.50 ± 7.00 mg/dl
Serum creatinine	1.91 ± 1.00 mg/dl
Liver function tests	
Alkaline phosphatase	236.00 ± 115.00 IU/L

Conjugated bilirubin	0.20 ± 0.40 mg/dl
Serum albumin	3.70 ± 0.70 gm/dl
Serum glutamate oxaloacetate transferase (SGOT)	47.00 ± 130.00 IU/L
Serum glutamate pyruvate transferase (SGPT)	58.00 ± 150.00 IU/L
Total bilirubin	1.20 ± 1.00 mg/dl
Total serum protein	6.50 ± 0.80 gm/dl
Clotting tests	
Prothrombin time (PT)	14.10 ± 2.30 sec
Partial thromboplastin time (APTT)	33.90 ± 7.00 sec
Serum Lipid Profile	
HDL	35.00 ± 13.00 mg/dl
LDL	110.00 ± 40.00 mg/dl
Total cholesterol	190.00 ± 90.00 mg/dl
Triglyceride level	210.00 ± 110.00 mg/dl
VLDL	40.00 ± 35.00 mg/dl

Table 6: Liver Biopsy Findings in NAFLD cases

Liver Biopsy	n=10	%
Cirrhosis	3	30.00
No specific changes	3	30.00
Normal liver biopsy	3	30.00
Simple fatty change	6	60.00
Steatohepatitis	1	10.00

DISCUSSION

The majority of our patient cohort comprised females, mirroring the findings of Aggarwal et al. in 2001 [2], suggesting a potential reflection of local social attitudes or a referral bias. Various complaints or symptoms were reported among the patients. Fatigability and malaise were the most prevalent symptoms, followed by right upper abdominal discomfort. These observations contrasted with the findings of Lee RG [9] and Aggarwal et al. [2]. Notably, the predominance of females in our study population may indicate a higher prevalence of associated nutritional anemia, a common issue among females in India, although this aspect was not further analyzed.

Non-alcoholic steatohepatitis (NASH) often presents without symptoms or signs of liver disease. At presentation, 50% were asymptomatic, contrasting with the 9% reported by Aggarwal et al. [2]. Hepatomegaly, was the most common clinical sign, while other typical signs such as oral/mucosal candidiasis, skin pigmentation, or gynecomastia were absent, aligning with the findings of Vuppalanchi et al. [6].

In our study, obesity, overweight, hyperlipidemia, and diabetes mellitus were the most prevalent associated risk factors for NASH development. Truncal obesity emerged as a significant risk factor. These results echoed those of Agarwal et al. [2] and Marchesini G et al. [10]. Additionally, 52 were diabetic, consistent with the findings of Marchesini G et al. [10].

Elevated serum levels of SGOT, SGPT, or both are common in NASH patients. In our study, mean SGPT mean SGOT elevated levels observed. These results were akin to those reported by Mathieson NL et al. [11]. Serum alkaline phosphatase levels werealso elevated in patients, similar to findings by Pinto TK et al. [12]. Liver ultrasonography revealed hepatomegaly in 90% of patients, while cirrhosis was present in 10%. Steatosis grading showed moderate to severe levels in the majority of cases, consistent with Vuppalanchi ngulo P et al. [6].

Liver biopsy remains the gold standard for diagnosing NASH. However, only 10 patients underwent biopsy in our study, revealing varying histopathological findings. Treatment strategies for NASH typically involve addressing associated metabolic conditions, improving insulin resistance, and utilizing hepatoprotective agents, as outlined in the literature [13-16].

Limitations of our study include a limited number of liver biopsies, unavailability of serum insulin levels for all patients, and challenges in long-term patient follow-up to assess treatment responses effectively. These limitations underscore the need for further research in this field.

CONCLUSION

This study underscores the prevalence of features indicative of the metabolic syndrome among patients diagnosed with NASH. Patients with NASH commonly exhibit systemic disorders characteristic of insulin resistance syndrome, including hyperlipidemia, hypertension, obesity, type 2 diabetes, and hepatic steatosis. These findings highlight the importance of considering NASH in patients presenting with abnormal transaminase levels, particularly in cases where serological tests for hepatitis B virus (HBV) and hepatitis C virus (HCV) are negative, and there is no history of alcoholic liver disease.

REFERENCES

1. McCullough AJ. The epidemiology and risk factors of NASH. In: Farrell GC, George J, Hall P, McCullough AJ, editors. Fatty Liver Disease: NASH and Related Disorders. Oxford: Blackwell Publishing; 2005:23–37.
2. Agarwal AG. A technical review on nonalcoholic fatty liver disease. Gastroenterology. 2001;123:1705–1725.
3. Falck-Ytter Y, Younossi ZM, Marchesini G, Mc Cullough AJ. Clinical features and natural history of nonalcoholic steatosis syndromes. Semin Liver Dis. 2001;21:17–26.
4. Gupte P, Amarapurkar D, Agal S, et al. Non-alcoholic steatohepatitis in type 2 diabetes mellitus. J Gastroenterol Hepatol. 2004;19:854–8.

5. Musso G, Gambino R, Cassader M, Pagano G. Meta-analysis: Natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Ann Med. 2010;43(8):1–33.
6. Vuppalanchi R, Chalasani N. Non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: Selected practical issues in their evaluation and management. Hepatology. 2009;49(1):306–31.
7. Naik AP, Shareef MMA. Study of clinical, biochemical, histological profile of patients with non-alcoholic fatty liver disease. Eur J Mol Clin Med. 2022;9(1):1640-1648.
8. Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated aminotransferase levels in the United States. Am J Gastroenterol. 2003;98:960–7.
9. Lee RG. Nonalcoholic steatohepatitis: a study of 49 patients. Hum Pathol. 1989;20:594–598.
10. Marchesini G, Brizi M, Bianchi G, et al. Nonalcoholic fatty liver disease. A feature of the metabolic syndrome. Diabetes. 2001;50:1844–1850.
11. Mathieson NL, Franzen LE, Fryden A, Fuberg U, Bodenar G. The clinical significance of slightly to moderately increased liver transaminase values in asymptomatic patients. Scand J Gastroenterol. 1999;34:55–91.
12. Pinto, Falck-Ytter Y, Younossi ZM, Marchesini G, et al. Clinical features and natural history of nonalcoholic steatosis syndromes. Semin Liver Dis. 1990;21:17–26.
13. Singh DK, Sakhuja P, Malhotra V, Gondal R, Sarin SK. Independent predictors of steatohepatitis and fibrosis in Asian Indian patients with non-alcoholic steatohepatitis. Dig Dis Sci. 2008;53:1967–76.
14. Al Knawy B, Shiffman M. Percutaneous liver biopsy in clinical practice. Liver Int. 2007;27:166–73.
15. Kadayifci A, Merriman R, Bass N. Medical treatment of non-alcoholic steatohepatitis. Clin Liver Dis. 2007;11:119–40.
16. Luyckx FH, Desaiva C, Thiry A, et al. Liver abnormalities in severely obese subjects: effect of drastic weight loss after gastroplasty. Int J Relat Metab Disord. 1998;27:166–73.