ORIGINAL RESEARCH

Non-alcoholic fatty liver disease: prevalence and predictive factors- Experience of a tertiary care centre

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Received: 18 November, 2023 Accepted: 07 January, 2024

ABSTRACT

Background& Objectives: Non-alcoholic fatty liver disease or NAFLD is a liver condition which is highly prevalent, yet underappreciated and under-reported. As a spectrum of disease, this condition is characterized by accumulation of fat or steatosis in liver cells in the absence of other identifiable causes such as excessive alcohol consumption. Early intervention before the onset of fibrosis presents an excellent prognosis as the condition is largely reversible at this stage. However, if the treatment is delayed, fibrosis sets up that may further progress to end-stage liver disease or hepatocellular carcinoma which have a very poor outcome. It is therefore prudent that all efforts should be made to diagnose this condition early and the risk factors specifically targeted. Based on this background this study was conducted to study demography and predictive factors of this condition.**Methods:**This hospital based cross sectional study was conducted in medicine department of our hospital over 2 years from December 2021 to November 2023 targeting relatives of patients who didn't give history of previous liver disease. Those who gave history of even occasional alcohol intake, diagnosed case of HBV or HCV, suffering from other known liver disease and those taking medications with a potential to cause chronic liver disease were excluded. Relevant demographic, anthropometric and medical data were recorded and focused laboratory investigations were done. All such participants underwent ultrasonography of liver to look for hepatic steatosis.**Result:**Over the study period 329 subjects were analysed. Among them 67 had evidence of NAFLD on USG and the rest 262 were apparently normal, thus giving a prevalence of 25.6% for NAFLD. The two groups didn't differ significantly in terms of age, gender, dietary preference or hypertension. But patients with NAFLD had a significantly higher BMI as well as higher incidence of diabetes mellitus, ischemic heart disease and metabolic syndrome. Among the laboratory parameters, fasting blood sugar, total cholesterol, triglycerides and total cholesterol to high density lipoprotein ratio (TC/HDL) was significantly higher in NAFLD group as compared to the normal group.**Conclusion:**The prevalence of NAFLD is strikingly high in the general population. There is higher occurrence of increased BMI, diabetes mellitus and metabolic syndrome as well as increased fasting blood sugar total cholesterol and serum triglycerides in these patients.

Key words:NAFLD, risk factors, steatosis, ultrasonography.

INTRODUCTION

Non-alcoholic fatty liver disease or NAFLD is a liver condition which is highly prevalent, yet underappreciated and under-reported. As a spectrum of disease, this condition is characterized by accumulation of fat or steatosis in liver cells in the absence of other identifiable causes such as excessive alcohol consumption.[1,2] Clinical presentation of this condition ranges from non-alcoholic fatty liver (NAFL) which is a seemingly benign condition to non-alcoholic steatohepatitis (NASH) which is associated with inflammation and liver injury.[3] Left untreated, NAFLD has the potential to progress to fibrosis and cirrhosis.[4] The true burden of this condition is not clearly known but available literature does suggest that NAFLD is now the commonest cause of liver disorder in western population, affecting 25-30% of their adult population.[5] Recent studies also indicate that this condition is on the rise among people of developing countries, particularly in the Asia-Pacific region.[6] It is now known that there exists a close relationship between type 2 diabetes mellitus, central obesity, hyperlipidaemia and metabolic syndrome, so these have a respective prevalence of 23%, 51%, 69% and 43% in NAFLD.[7] Not surprisingly, the prevalence of NAFLD has

increased from 15% in 2005 to 25% in 2010 in parallel to rising rates of obesity. Studies have revealed that cardiac and vascular diseases are the most frequent cause of mortality in these patients. However, it is not well known to researchers as which pathophysiological mechanisms connect cardiovascular disease and NAFLD.[8] It is believed that release of proinflammatory mediators in NAFLD damages vascular endothelium that contributes to the cardiovascular disease seen in this condition.

Patients with NAFLD are mostly asymptomatic but some may present with fatigue, right upper quadrant discomfort, hepatomegaly, acanthosis nigricans, and lipomatosis. Most commonly it comes to light as an abnormal liver function test such as elevated serum aminotransferases (ALT and AST) or incidental finding of hepatic steatosis on abdominal ultrasonogram. Treatment and outcome of this condition is dependent on a number of factors, especially stage of the disease. This emphasises the importance of careful risk stratification while planning the management of NAFLD in a patient.[9] A four-pronged strategy is commonly employed which focusses on: lifestyle modification, targeting the components of the metabolic syndrome, liver-directed pharmacotherapy for high-risk patients and managing the complications of cirrhosis.

Researchers have established without doubt that early intervention before the onset of fibrosis presents an excellent prognosis as the condition is largely reversible at this stage. However, if the treatment is delayed, fibrosis sets up that may further progress to end-stage liver disease or hepatocellular carcinoma which have a very poor outcome. It is therefore prudent that all efforts should be made to diagnose this condition early and the risk factors specifically targeted which may require involvement of a multidisciplinary team. Based on this background this study was conducted at our tertiary care centre to study demography and predictive factors of this condition.

MATERIALS AND METHODS

Study Setting:OPD and IPD of department of Medicine, NSMCH, Bihta, Bihar, India.

Study duration: 2 years, from December 2021 to November 2023.

Study design: hospital based cross sectional study.

Inclusion criteria: In this study all relatives accompanying patients in O.P.D and I.P.D of our Medicine department were screened for eligibility. Those who didn't give history of a previous liver disease were considered as potential participants and explained about the study. Those who consented were finally included in this study.

Exclusion criteria: Relatives who gave history of even occasional alcohol intake, diagnosed case of HBV or HCV, suffering from other known liver disease and those taking medications with a potential to cause liver disease were excluded from the study.

Study technique: Information regarding baseline characteristics such as age, sex, anthropometry, comorbidities, duration of any disease (if known) was collected and entered in a structured proforma. Detailed history taking and physical examination were undertaken on each subject and relevant laboratory investigations were sent as per standard protocols. USG of liver was performed on all participants and fatty liver was defined by the presence of at least two of three abnormal findings on abdominal ultrasound: (1) diffusely increased echogenicity (bright) liver with liver echogenicity greater than kidney with (2) vascular blurring and (3) deep attenuation of ultrasound signal.[10]Steatosis of liver was further categorised into three grades of severity as per follows: Grade 1 for normal visualization of diaphragm/ intrahepatic vessels, Grade 2 for impaired visualization of diaphragm/ intrahepatic vessels and Grade 3 for poor visualization of diaphragm/ intrahepatic vessels.[11]Careful anthropometric measurements were done to record height, weight, waist and hip circumference. BMI was calculated using Quetelet's index. Anthropometric parameters were classified into normal or abnormal as per WHO guidelines.[12] Metabolic syndrome was defined as a waist circumference of > 90 cm for men and > 80 cm for women plus any two of the following: a) Blood pressure > 130/85 mm Hg b) Serum triglycerides > 150 mg/dL c) Serum HDL < 40 mg/dL for men and < 50 mg/dL for women d) Fasting blood sugar > 100mg/dL.

Statistical analysis: Information obtained was recorded, tabulated and entered in Microsoft excel sheet and then analyzed by using statistical software "SPSS ver.20®. Variables were expressed as mean, standard deviation, proportions and percentiles as appropriate. We used Pearson's chi-square test for categorical parameters and independent samples' t test for continuous parameters. P-value <0.05 was taken as significant.

RESULT

Total 381 relatives gave initial consent for enrolment in the present study. Among them 52 were excluded (15 withdrew consent, 3 had HBV infection, 1 had HCV infection, 15 had evidence of other chronic liver disease, 18 were taking hepatotoxic drugs). So, final analysis was done on 329 subjects. 67 had evidence of NAFLD on USG and the rest 262 were non-NAFLD, thus giving a prevalence of 25.6% for NAFLD. Table 1 depicts the demographic and anthropometric parameters of the two groups. The two groups didn't differ significantly in terms of age, gender, dietary preference or hypertension. But subjects with NAFLD had a significantly higher BMI as well as significantly higher incidence of diabetes mellitus, ischemic heart disease and metabolic syndrome as shown in the table below.

Table 1: Characteristics of study population in the two groups

Parameters	Non-NAFLD (n=262)	NAFLD (n=67)	P value
Age in years (Mean ± SD)	46.28 ± 11.39	48.51 ± 11.94	0.16
Male gender (percentage)	52.3%	56.7%	0.50
BMI in Kg/m^2 (Mean ± SD)	23.08 ± 4.23	25.72 ± 6.74	**<0.001**
Waist-hip ratio (Mean ± SD)	0.93 ± 0.089	0.95 ± 0.094	0.10
Hypertensive (percentage)	27.4	39.1	0.06
Diabetes mellitus (percentage)	22.1	43.3	**<0.001**
Ischemic heart disease (percentage)	8.4	19.4	**0.009**
Non-vegetarian diet (percentage)	62.9	70.1	0.27
Metabolic syndrome (percentage)	14.1	31.3	**0.001**

Important laboratory investigations were conducted on all study participants as depicted in table 2 below. On comparison of these parameters, we found that fasting blood sugar, total cholesterol, triglycerides and total cholesterol to high density lipoprotein ratio (TC/HDL) was significantly higher in NAFLD group as compared to the normal group.

Table 2: Important laboratory parameters in the two groups

Laboratory parameters	Non-NAFLD (n=262)	NAFLD (n=67)	P value
Fasting blood sugar (mean ± SD)	108.2 ± 33.8	121.6 ± 46.9	**0.008**
AST (mean ± SD)	35.2 ± 21.9	39.1 ± 23.4	0.20
ALT (mean ± SD)	39.1 ± 23.3	43.6 ± 25.3	0.17
AST: ALT (mean ± SD)	1.09 ± 0.32	1.01 ± 0.29	0.06
Total cholesterol (mean ± SD)	155 ± 31.3	166 ± 38.9	**0.01**
Triglycerides (mean ± SD)	118.4 ± 35.3	135.4 ± 44.5	**0.001**
HDL cholesterol (mean ± SD)	45.3 ± 15.4	41.8 ± 14.2	0.09
LDL cholesterol (mean ± SD)	86.1 ± 31.5	89.4 ± 34.3	0.45
Total cholesterol: HDL cholesterol(mean ± SD)	3.81 ± 1.12	4.13 ± 1.21	**0.04**
LDL:HDL (mean ± SD)	2.23 ± 0.42	2.31 ± 0.44	0.17

Patients with NAFLD were further subclassified according to the severity of NAFLD and important demographic and laboratory parameters were studied in individual groups and compared with non-NAFLD group as shown in table 3 below. Using one-way ANOVA test, we compared different study parameters across the four groups and found significant difference in ALT level among the three grades of severity of NAFLD (P value: 0.001).

Table 3: Demographic and laboratory parameters in different grades of severity.

Parameters	Non-NAFLD (n=262)	Grade 1 NAFLD (n= 41)	Grade 2 NAFLD (n=18)	Grade 3 NAFLD (n=8)
Age in years (Mean ± SD)	46.28 ± 11.39	47.2 ± 12.1	48.1 ± 11.8	49.4 ± 12.3
Male gender (percentage)	52.3%	51.7	55.4	56.9
BMI in Kg/m^2 (Mean ± SD)	23.08 ± 4.23	24.9 ± 6.1	25.2 ± 6.4	28.3 ± 7.1
Waist-hip ratio (Mean ± SD)	0.93 ± 0.089	0.94 ± 0.091	0.96 ± 0.095	0.98 ± 0.098
Hypertensive (percentage)	27.4	31.3	38.1	42.6
Diabetes mellitus (percentage)	22.1	28.1	43.7	47.8
Ischemic heart disease (percentage)	8.4	15.2	19.7	21.5
Non-vegetarian diet (percentage)	62.9	64.4	70.4	72.3
Metabolic syndrome (percentage)	14.1	21.3	30.1	33.1
Fasting blood sugar (mean ± SD)	108.2 ± 33.8	121.4 ± 35.3	130.6 ± 44.7	152 ± 45.1
SGOT (mean ± SD)	35.2 ± 21.9	36.9 ± 22.3	38.9 ± 23.1	40.1 ± 24.9
SGPT (mean ± SD)	39.1 ± 23.3	40.7 ± 24.6	42.2 ± 24.8	85.4 ± 28.9
SGOT: SGPT (mean ± SD)	1.09 ± 0.32	1.07± 0.31	0.96 ± 0.29	0.92± 0.27
Total cholesterol (mean ± SD)	155 ± 31.3	159.3 ± 33.8	164 ± 37.4	167 ± 38.9
Triglycerides (mean ± SD)	118.4 ± 35.3	123.5 ± 37.2	144.4 ± 43.5	178.3 ± 45.1
HDL cholesterol (mean ± SD)	45.3 ± 15.4	44.2 ± 15.1	42.2 ± 14.7	40.3 ± 13.9
LDL cholesterol (mean ± SD)	86.1 ± 31.5	87.2 ± 31.9	88.6 ± 33.8	89.1 ± 34.9
Total cholesterol: HDL cholesterol	3.81 ± 1.12	3.9 ± 1.1	4.5 ± 1.2	4.6 ± 1.4

(mean ± SD)				
LDL:HDL (mean ± SD)	2.23 ± 0.42	2.09 ± 0.48	2.28 ± 0.61	2.35 ± 0.73

DISCUSSION

The present study was aimed to study demography and related factors of NAFLD. Very few Indian researchers from non-metro cities have focused on the occurrence of NAFLD. In this study, we found its prevalence to be of 25.6%. Prevalence of NAFLD in Asian countries ranges between 9 to 40 %[13] which correlates with our study. A lower prevalence of 18% was reported by Das et al[14] on nonobese adults in Indian setting. Difference in disease prevalence estimation can be attributed to the lack of uniformity of the populations studied and study designs. Perhaps the prevalence is under-reported due to the absence of early clinical features and lack of a highly sensitive, easily available and cost-effective diagnostic modality. NAFLD is slightly more prevalent in males as compared to females as reported by many researchers including Amarapurkar et al.[15] In the present study 57% of patients were males but there was no significant sex difference among NAFLD patients. However, some researchers have reported male sex to be an independent predictor of NAFLD. This might be attributed to undisclosed alcoholism by males. Mean BMI of patients with NAFLD in this study was 25.72 ± 6.74 which is significantly higher than those without this condition which is comparable to the findings of Misra et al.[16] In this study we didn't find any significant difference in central obesity in the two groups. Bajaj et al[17] also reported that there is no significant association between central obesity and NAFLD in Indians. However, some other researchers including that of Amarapurkar et al[15] have shown contradictory results. This can be partly explained by the fact that Asians have a higher tendency for intraabdominal fat accumulation and that degree of adipose tissue dysfunction is more important than the degree of adipose tissue accumulation in increasing the risk of NAFLD. The present study showed that NAFLD was more significantly associated with metabolic syndrome which is in agreement to the findings of Sivapackianathan et al.[18]

In this study, we also found that fasting blood sugar level, serum cholesterol and triglycerides were significantly higher in NAFLD patients as compared to their counterparts. Similar association has been reported by Amarapurkar et al[15] and Kumar et al.[19] ALT level was comparable between NAFLD patients and their counterparts, but ALT level rose drastically with the increasing grade of severity of the disease. Similar finding was noted with BMI, fasting blood sugar level as well as serum triglyceride level. However, as there were only 8 patients with grade 3 NAFLD in this study, it can't be estimated as how good such increase in value of these parameters would correlate with the disease severity.

CONCLUSION

To conclude, this study has found that the prevalence of NAFLD is strikingly high in the general population. There is higher occurrence of increased BMI, diabetes mellitus and metabolic syndrome as well as increased fasting blood sugar total cholesterol and serum triglycerides in these patients. Owing to its ease of doing and availability, Ultrasonography proves to be a vital diagnostic modality in the diagnosis of such patients.

6.Limitation: First, the present study is a single centre study. Second, it is a hospital-based study and so the findings may not be representative of the general community. Third, risk factors were not estimated as per severity of the grade of steatosis.

7. Conflict of interest: None to declare

8. Financial disclosure: The authors declare that this study has not been done under financial assistance of any sort.

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