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Prevalence and association of non-alcoholic fatty liver disease and insulin resistance among non-diabetic obese, overweight, and metabolically obese normal-weight adult patients attending at a tertiary care hospital in Eastern India

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ABSTRACT

Background: Worldwide, the incidence of obesity, overweight, and metabolic syndrome is dramatically increasing. Non-alcoholic fatty liver disease (NAFLD) is associated with both obesity/overweight and metabolic syndrome. **Aims and Objectives:** The aim of this study is to assess non-invasively the prevalence and association of NAFLD and insulin resistance among non-diabetic obese, overweight, and metabolically obese normal-weight (MONW) adults. **Materials and Methods:** This single-center cross-sectional study included 137 subjects aged more than 18 years, out of which 50 were obese, 22 were overweight, and 31 MONW. All subjects underwent detailed history, complete physical examination, laboratory test, and grading of hepatic fat by ultrasonography. **Results:** The mean age (mean ± standard deviation) of the patients was 36.91 ± 11.01 years with a range of 18–67 years. 53 (38.7%) and 84 (61.3%) of the patients were male and female, respectively. Out of the 137 patients, 73 (53.3%) of patients had NAFLD. The prevalence of NAFLD was significantly higher in the obese group (56.2%) as compared to others ($Z = 5.56$; $P < 0.0001$). The prevalence of NAFLD among overweight, MONW, and normal body mass index (BMI) were 17.8%, 19.2%, and 6.8%, respectively. The proportion of Grade-1 and Grade-2 NAFLD was significantly higher than that of Grade-3 ($Z = 4.16$; $P < 0.0001$). There was a significant association between BMI, insulin resistance measured by homeostasis model assessment-estimated insulin resistance (HOMA-IR), and grade of fatty liver of the patients ($P < 0.0001$). **Conclusion:** NAFLD is more prevalent in obese than other groups. The grade of fatty liver has a significant association with HOMA-IR and BMI.

Key words: Non-alcoholic fatty liver disease; Insulin resistance; Obese; Overweight; Metabolically obese normal weight

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INTRODUCTION

The incidence of obesity and overweight is dramatically increasing globally.[1] Non-alcoholic fatty liver disease (NAFLD) is a spectrum of diseases, which encompasses simple fatty liver, non-alcoholic steatohepatitis, and NAFLD-associated cirrhosis.[2] The diagnosis of NAFLD requires that (a) there is evidence of hepatic steatosis by imaging or histology and (b) there are no causes for secondary hepatic fat accumulation such as the use of

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significant alcohol consumption, use of steatogenic medication or hereditary disorders.[3] In 2020, NAFLD was redefined as metabolic (dysfunction) associated with fatty liver disease.[4]

A correlation among body mass index (BMI), degree of steatosis, and severity of liver injury has been demonstrated.[5] Apart from obesity and overweight, NAFLD may develop in individuals with normal BMI.[6] Non-alcoholic fatty liver has also been found to be associated with insulin resistance and metabolic syndrome.[7] Studies have shown a significant correlation between risk factors for metabolic syndrome, the degree of fatty liver, and weight circumference, thus supporting central adiposity as an independent risk factor for hepatic dysfunction.[8,9]

Aims and objectives

The present study aims to estimate the prevalence of non-alcoholic fatty liver and insulin resistance among non-diabetic obese, overweight, and metabolically obese normal-weight (MONW) adults and find any correlation between non-alcoholic fatty liver and insulin resistance in these subjects.

MATERIALS AND METHODS

This is an observational, single-institutional, cross-sectional study**.** We have included the study population from the patient pool attending our outpatient department, keeping in mind the inclusion and exclusion criteria for the study.

The study population consisted of (I) patients aged more than 18 years old, (II) an obese group with a BMI >25, (III) an overweight group with a BMI between 23 and 24.9 according to consensus guidelines for the Asian Indian population,[10] (IV) MONW group was selected with BMI between 18.5 and 22.9 with three out of five following criteria:

1. Waist circumference >90 cm in males, >80 cm in females
2. Serum triglycerides (TGs) >150 mg/dL
3. High-density lipoprotein-cholesterol (HDL-C) <40 mg/dL in male and <50 mg/dL in female
4. Serum fasting glucose ≥100 <125 mg/dL (without use of insulin or oral antidiabetic medication)
5. Blood pressure ≥130/85 mm of Hg (including the use of antihypertensive medication).[11]

The exclusion criteria were: (I) Other causes of liver diseases, such as viral hepatitis (A-E), malaria, leptospira, hepatotoxins, autoimmune hepatitis, Wilson disease, hemochromatosis, and alpha 1 antitrypsin deficiency were excluded with history and appropriate tests. (II) History of consumption of alcohol and smoking, (III) history of type 1 or type 2 diabetes mellitus and renal disease.

All patients underwent detailed clinical examination including measurement of weight, height, waist circumference, and the following tests:

Fasting venous plasma glucose,2-hour postprandial venous plasma glucose level after 75 gm glucose ingestion, fasting serum insulin, Lipid profile (High density lipoprorein,low-density lipoprotein, Triglyceride, and total cholesterol), liver function test (total bilirubin, conjugated bilirubin, total protein, albumin, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase) and ultrasonography of the abdomen.

The "Insulin resistance" was measured by homeostasis model assessment-estimated insulin resistance (HOMA-IR).[12] It was calculated by multiplying fasting plasma insulin (FPI) by fasting plasma glucose (FPG), then dividing by the constant 22.5, that is,

HOMA-IR=(FPI×FPG)/22.5 (values of FPI and FPG in mmol/L)

= (FPI×FPG)/405 (values of FPI and FPG in mg/dL).

On the ultrasound, the liver shows echogenicity higher than the renal cortex and spleen due to fatty infiltration. The severity of echogenicity was graded as follows:

- Grade-0, normal echogenicity
- Grade-1, slight, diffuse increase in fine echoes in liver parenchyma with normal visualization of diaphragm and intrahepatic vessel borders
- Grade-2, moderate, diffuse increase in fine echoes with slightly impaired visualization of intrahepatic vessels and diaphragm
- Grade-3, marked increase in fine echoes with poor or non-visualization of the intrahepatic vessel borders, diaphragm, and posterior right lobe of the liver.[13]

The study protocol was approved by the institutional ethics committee. Written informed consent was taken from all patients.

Statistical methods

Statistical analysis was performed with the help of SPSS version 23. Using this software, data were expressed as mean±standard deviations that were normally distributed. Basic cross-tabulation and frequency distributions were prepared. A test of proportion (Z-test) was used to test the significant difference between the two proportions. The Chi-square (χ^2) test was used to test the difference between the groups for categorical variables. A corrected Chi-square test was used in case any one of the cell frequencies was found <5 in the bivariate frequency distribution. Significant associations between two variables were tested with

Pearson/Spearman's rho correlation. The t-test was used to test the significant difference between means in two groups for continuous variables. P≤0.05 was considered statistically significant.

RESULTS

The mean age (mean±standard deviation) of the patients was 36.91±11.01 years with a range of 18–67 years, and the median age was 35 years. 53 (38.7%) and 84 (61.3%) of the patients were male and female, respectively. Among the patients, 50 (36.5%), 22 (16.1%), 31 (22.6%), and 34 (24.8%) were obese, overweight, MONW, and having normal BMI, respectively.

Out of the 137 patients, 73 (53.3%) of patients had NAFLD. Among the obese group, 56.2% of patients had NAFLD. The prevalence of NAFLD among overweight, MONW, and normal BMI were 17.8%, 19.2%, and 6.8%, respectively. The Chi-square (χ^2) test showed that there was a significant difference in NAFLD between groups (P<0.0001). The proportion of NAFLD was significantly higher in obese patients (56.2%) (Z=5.56; P<0.0001) (Table 1).

Out of the 73 (53.3%) cases of NAFLD, 33 (24.1%), and 35 (25.5%) were Grade-1 and Grade-2, respectively. Only 5 (3.7%) cases were with Grade-3 NAFLD. Thus, the proportion of Grade-1 and Grade-2 NAFLD was significantly higher than that of Grade-3 (Z=4.16; P<0.0001) (Figure 1).

The Chi-square (χ^2) test showed that there was a significant difference in the grade of fatty liver in different groups of the patients (P<0.0001) (Table 2).

Although the mean HOMA-IR of the patients with NAFLD was higher for obese, overweight, MONWs, and normal BMI than that of the patients without NAFLD, the t-test showed that there were no significant differences between the means (P>0.05) (Table 3).

The mean HOMA-IR of the patients with NAFLD was significantly higher for obese and overweight patients as compared to the patients with normal BMI (P<0.05). However, the mean HOMA-IR of the patients with NAFLD was higher for MONW patients as compared to the patients with normal BMI, but it was not significant (P>0.05) (Table 3).

Tests were performed to assess the strength of association between variables. The grades of NAFLD by USG,

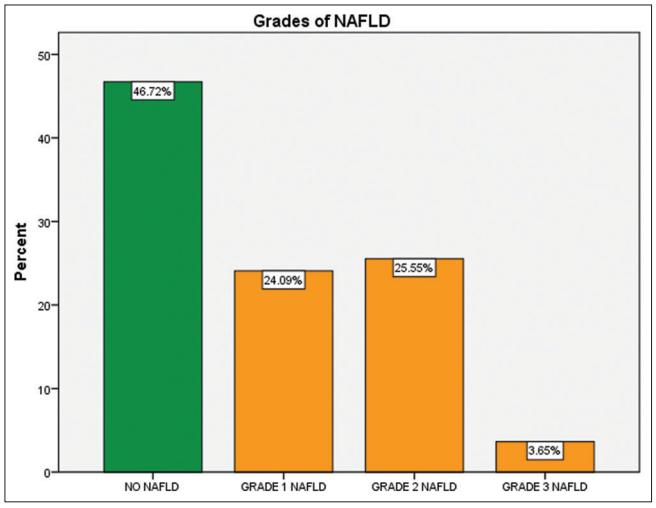

Figure 1: Distribution of grades of NAFLD as per the ultrasonography findings of the patients. NAFLD: Non-alcoholic fatty liver disease, no fatty liver=46.7%, grade 1 fatty liver =24.1%, grade 2 fatty liver=25.5%, grade 3 fatty liver=3.7%

Table 1: Distribution of NAFLD among different groups of patients

BMI	With NAFLD n (%)	Without NAFLD n (%)	Total	Chi-square	P-value
Obese	41 (56.2)	9 (14.1)	50 (36.5)	38.01	P<0.0001
Overweight	13 (17.8)	9 (14.1)	22 (16.1)		
Metabolically obese normal weight	14 (19.2)	17 (26.6)	31 (22.6)		
Normal BMI	5 (6.8)	29 (45.3)	34 (24.8)		
Total	73 (100.0)	64 (100.0)	137 (100.0)		

NAFLD: Non-alcoholic fatty liver disease, n: Number, BMI: Body mass index

Table 2: Distribution of different grades of fatty liver in different groups of patients

Grade of fatty liver as per USG finding	Obese (n=50) (%)	Overweight (n=22) (%)	MONW (n=31) (%)	Control (n=34) (%)	Total (%)	Chi-square	P-value
Grade-0	9 (18.0)	9 (40.9)	17 (54.8)	29 (85.3)	64 (46.7)	40.02	P<0.0001
Grade-1	16 (32.0)	7 (31.8)	6 (19.4)	4 (11.8)	33 (24.1)		
Grade-2	23 (46.0)	5 (22.7)	6 (19.4)	1 (2.9)	35 (25.5)		
Grade-3	2 (4.0)	1 (4.5)	2 (6.5)	0 (0.0)	5 (3.6)		
Total	50 (100.0)	22 (100.0)	31 (100.0)	34 (100.0)	137 (100.0)		

MONW: Metabolically obese normal weight, USG: Ultrasonography, n: Number

Table 3: Distribution of HOMA IR (mean±SD) with and without NAFLD patients among different groups

BMI classification	HOMA IR (mean±SD)				t-test	P-value
	n	With NAFLD	n	Without NAFLD		
Obese (n=50)	41	3.73±1.94	9	3.01±2.50	t_{48}=0.81	0.44
Overweight (n=22)	13	3.34±2.06	9	2.16±1.18	t_{20}=1.70	0.10
Metabolically obese normal weight (n=31)	14	1.48±0.72	17	1.30±0.46	t_{29}=0.81	0.41
Normal (n=34)	5	1.24±0.25	29	1.11±0.64	t_{32}=0.79	0.42

HOMA-IR: Homeostasis model assessment-estimated insulin resistance, SD: Standard deviation, n: Number, BMI: Body mass index, P<0.05 Statistically Significant

Table 4: Association of variables: Grades of NAFLD, HOMA-IR, and BMI

Variable	Variable	Correlation coefficient	P-value
HOMA-IR	BMI (kg/m^2)	0.538**	P<0.0001
Grades of NAFLD (by USG)	BMI (kg/m^2)	0.467**	P<0.0001
Grades of NAFLD (by USG)	HOMA-IR	0.361**	

**Correlation is significant at the 0.01 level (2-tailed). NAFLD: Non-alcoholic fatty liver disease, HOMA-IR: Homeostasis model assessment-estimated insulin resistance, BMI: Body mass index, USG: Ultrasonography

HOMA-IR, and BMI were positively correlated with each other (Table 4).

DISCUSSION

Our study compared insulin resistance and fatty liver among obese, overweight, MONW non-diabetic adults. This study showed a higher prevalence of NAFLD in the obese group (56.2%) compared to other groups.

A recent systemic review and meta-analysis showed a 28.2–40.8% prevalence of NAFLD in India.[14]

This study also showed that the proportion of Grade-1 (24.1%) and Grade-2 fatty liver (25.5%) was higher than Grade-3 fatty liver (3.7%). Insulin resistance, a key factor in metabolic syndrome, is prevalent in NAFLD.[15]

Studies showed that HOMA-IR is independently associated with the risk of NAFLD in the non-diabetic and non-obese population.[16]

In this study, there was no significant difference in mean HOMA-IR in patients with NAFLD as compared to those without NAFLD in all groups. However, HOMA-IR was positively correlated with fatty liver and BMI.

Limitations of the study

There were certain limitations in this study. This is a single-center study with a small sample size. For diagnosis of NAFLD, we solely depend on USG. We could not perform fibro-scan or liver biopsy.

Despite these limitations, the present study showed a high prevalence of NAFLD in non-diabetic obese as well as overweight and patients with features of metabolic syndrome with normal weight.

CONCLUSION

The prevalence of NAFLD is higher in obese than in other groups. The grade of fatty liver has a significant association with HOMA-IR and BMI. NAFLD has become one of the common non-communicable diseases in India not only in obese but also in overweight and even normal-weight populations. Therefore, people should have regular screening to rule out fatty liver disease.

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SP, LV, JB, and SR- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, and manuscript preparation; **SR-** Submission of article; **SP and SR-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **SP, JB, and SR-** Design of study, statistical analysis and interpretation; **SP, JB, LV, and SR-** Review manuscript.

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