Original research article

Study of Prevalence of NAFLD and its Associated Risk Factors in Non-Obese and Non-Diabetic Rural Population

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Abstract

Background: NAFLD has become one of the most common health concern Worldwide. Not only the urban population but also the rural population are being commonly diagnosed with NAFLD. Obesity and diabetes are the major risk factors for NAFLD. This study aims to estimate the prevalence of NAFLD and its associated risk factors in rural population of Vikarabad District, other than obesity and diabetes mellitus.

Methods: This is a population-based cross-sectional study on apparently healthy subjects over 18 years and up to 65 years of age. The participants were interviewed for baseline demographic and clinical information. They were subsequently referred for physical examination. NAFLD was diagnosed using abdominal ultrasonography by a single expert radiologist.

Results: Of 906 screened subjects, 300 subjects were non obese, BMI (body mass index) <27 kg/m^2 (According to Joslin Asian American Diabetes Initiative (AADI) BMI criteria for obesity) and non diabetic. The overall prevalence of NAFLD was 18.66% in our study. NAFLD was seen in 25.4% of population who were overweight (BMI 23 – 26.9 kg/m^2) and only in 4.1% of population with normal weight (BMI 18 – 22.9 kg/m^2). The prevalence of NAFLD was 82.1% in subjects with hypertension (BP > 140/90 mm of Hg) and 17.9% in subjects with normal blood pressure. NAFLD prevalence was 67.8% in age group > 45 – 65 years and it was 32.1% in the age group of 18 – 45 years (all $P < 0.01$).

Conclusion: The prevalence of NAFLD in non obese and non diabetic subjects in a sample of Indian rural population is 18.66%. BMI of 23 – 26.9 kg/m^2, hypertension and increasing age are independent risk factors associated with NAFLD in non obese and non diabetic subjects in our study.

Keywords: Non Alcoholic Fatty Liver Disease (NAFLD), Rural population, Body Mass Index (BMI), Obesity, Diabetes, Hypertension.

Introduction

Prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing worldwide, mainly as a result of the global pandemic of obesity.[1] Recent data has proven that the World Health Organization (WHO) cut-off for obesity (body mass index (BMI) > 30 kg/m^2) is not applicable to the Asian population, as they have more body fat at any level of BMI.[2–4] According to Joslin Asian American Diabetes Initiative (AADI) BMI of 23 – 26.9 kg/m^2 is taken as Overweight and BMI ≥ 27 kg/m^2 is considered as obese (Table - 1). Some Asian studies have focused on the prevalence and severity of NAFLD among subjects with normal BMI and found that the prevalence of NAFLD is of great importance.[5–10] Different studies show identical prognosis of NAFLD among lean patients in comparison with obese subject.[5,7,11] But some reports indicate that the severity of nonalcoholic steatohepatitis (NASH) and liver fibrosis is more prominent in non-obese subjects.[12,13] Some studies have shown that human genome has an influence on lean NAFLD and its severity. In this regard, polymorphism in PNPLA3[14,15] and TM6SF2[16,17] genes have been recognized to affect both disease severity and progression in lean patients with NAFLD. These genesaccumulate triglyceride in the liver but do not affect the metabolic panel and thereby, result in NAFLD in lean subjects who do not suffer from the metabolic syndrome. Several studies have estimated the prevalence of NAFLD among Indian general population,[18–22] but few have measured the prevalence and predictors of NAFLD in non obese non diabetic (BMI < 27kg/ m^2) subjects.[23,24] This study aims to estimate the prevalence of non obese and non diabetic NAFLD in the rural population of Vikarabad district and identify the risk factors for this growing health issue.

Study design

This is a population-based cross-sectional study conducted on apparently healthy subjects over 18 years to 65 years of age in Mahavir Institute Of Medical sciences, Vikarabad, in the out patient department of General Medicine. The study period was from 1st February 2020 to 30th November 2020.

Inclusion Criteria

1. Age > 18 years to ≤ 65 years.
2. BMI > 18.5 to < 27 kg/m^2

Exclusion Criteria

1. BMI < 18.5 to ≥ 27 kg/m^2.
2. Diabetes mellitus (Type I and II).
3. HIV, HBsAg & HCV positive patients.
4. Subjects with Alcohol intake > 20 gm/day.
5. Patients with Active malignancy.
6. Patients with Pre-existing chronic liver disease of any etiology.

Written informed consent was obtained from all subjects.

Data collection

Participants were recruited in an 8-hour fasting status to Mahavir General Hospital. They were re-interviewed for baseline demographic and clinical information. They were subsequently referred for physical examination, blood sampling and abdominal ultrasonography.

Physical examination

All participants underwent general physical examination. Weight was measured in upright position using a digital well-calibrated scale on hard ground while the participants wore light clothes without shoes. Height was measured to the nearest 0.1 cm with a standard ruler on a wall with the participants standing upright, the feet paired and their back to the ruler. Blood pressure was measured using a calibrated sphygmomanometer following 10 minutes of relaxation and the measurement was repeated 2 minutes later. The average was documented as the systolic blood pressure (SBP) and diastolic blood pressure (DBP) of the participants. Subjects taking antihypertensive medications or those with SBP ^{3} > 140 mmHg or DBP ^{3} > 90 mmHg were considered hypertensive.

Blood sampling

Venous blood sample was taken for FBS, PLBS, HbA1C, and Viral markers. Subjects meeting the American Diabetes Association criteria for Diabetes mellitus and those positive for viral markers were excluded from the study.

Abdominal sonography

NAFLD or simple steatosis was diagnosed using abdominal ultrasonography by a single expert radiologist who was blind to previous records of participants. GE LOGIQ P9 scanner with curvilinear probes of frequency 1 – 5 MHz was used. Steatosis was defined as poor penetration of the posterior segment of the right lobe of the liver, increase in hepatic echogenicity, and poor or no visualization of the hepatic vessels and diaphragm.[28]

Table 1: Joslin Asian American Diabetes Initiative (AADI)

BMI Cut off for Asians and Asian – Americans (kg/m^2)	NIH BMI Cut off (kg/m^2)	Comments
< 18.5	< 18.5	Under weight
18.5 – 22.9	18.5 – 24.9	Normal
23 – 26.9	25 – 29.9	Over weight
≥ 27	≥ 30	Obese

Table 2: Sex wise distribution of participants

Male	Female
190	110
63%	37%

Table 3: BMI of study participants

BMI	Total	Male	Female
18.5 - 22.9	96	68	28
23 - 26.9	204	122	82

Table 4: Blood pressure levels in study group

Age group	Total	Number of subjects with Average blood pressure ≥ 140/90 mm of Hg
18 – 25	36	1
26 – 35	45	3
36 – 45	64	16
46 – 55	86	28

56 – 65	69	33
Total	**300**	**81**

Table 5: Age wise distribution of study participants

Age group	Number of subjects
18 – 25	36
26 – 35	45
36 – 45	64
46 – 55	86
56 – 65	69
Total number of subjects	**300**

Results

Of 906 participants who were screened, 300 were eligible who were non obese (BMI < 27 kg/m^2), non diabetic. Among the study population males were 190 (63%) and females were 110 (37%)(Table - 2). The total number of participants with NAFLD were 56, and the overall prevalence of NAFLD among the study population was 18.66% (95% exact confidence interval (CI) 13.48%–22.18%). The prevalence of NAFLD was seen in 25.4% of population who were overweight (BMI 23 – 26.9) and only in 4.1% of population with normal weight (BMI 18 – 22.9) (P < 0.01) (Table – 6). The prevalence of NAFLD was 82.1% in subjects with hypertension (BP > 140/90) and 17.9% in subjects with normal blood pressure (P < 0.01)(Table – 8). NAFLD prevalence was 67.8% in age group > 45 – 65 years and it was 32.1% in the age group of 18 – 45 years (P < 0.01)(Table – 10).

There was no significant difference in the prevalence of NAFLD between male (19.4%) and female (17.2%) subjects (P > 0.01)(Table – 11).

Table 6: NAFLD prevalence in relation to BMI

BMI (kg/m^2)	Total subjects	Subjects with NAFLD
Normal weight (18.5 – 22.9)	96	4 (4.1%)
Over Weight (23 – 26.9)	204	52 (25.4%)

Table 7: NAFLD prevalence and blood pressure

Age	No. of subjects with Hypertensi-on	NAFLD subjects with Hypertension	Total NAFLD subjects in Age group
18 – 25	1	1	2
26 – 35	3	2	4
36 – 45	16	9	12
46 – 55	28	12	14

56 – 65	33	22	24
Total	**81**	**46**	**56**

Table 8: NAFLD prevalence according to blood pressure

Blood pressure	**Total no. of subjects**	**NAFLD (%)**
Normal (<140/<90 mm of Hg)	**219**	**17.9%**
Hypertension (>140/>90 mm of Hg)	**81**	**82.1%**

Table 9: NAFLD prevalence according to age in study group

Age	**No. of NAFLD subjects**	**Male**	**Female**
18 – 25	02 (5%)	2	0
26 – 35	04 (8%)	3	1
36 – 45	12 (18.7%)	8	4
46 – 55	14 (16.2%)	9	5
56 – 65	24 (34.7%)	15	9
Total	**56**	**37**	**19**

Table 10: Overall prevalence of NAFLD in Younger and Older age groups

Age in Years	**NAFLD prevalence**
> 45	**67.8%**
≤ 45	**32.1%**

Table 11: Sex wise prevalence of NAFLD in study subjects

Sex	**Total No. of participants**	**Number of participants with NAFLD**	**NAFLD (%)**
Male	190	37	19.4
Female	110	19	17.2

Higher BMI even in the range of less than 27 kg/m^2, high blood pressure and increasing age, were independent predictors of NAFLD in non obese and non diabetic participants.
The prevalence of NAFLD increase according to age in men and women. Overall, sex difference was not associated with increasing or decreasing prevalence of NAFLD ($P > 0.01$).

Discussion

Generally, it has been estimated that the prevalence of lean NAFLD ranges from 20–40% in the United States and Europe[30] to 12–42% in the Asian general population,[8,31–34] which is significantly lower than the prevalence among obese subjects. Cho[9] reported prevalence of NAFLD in non diabetic, non obese subjects as 12.4%, and NALFD subjects were significantly older and predominantly male. Recent world health organization expert consultation pronounced that the body-mass index (BMI) criterion is not suitable for Asian populations since the relation between BMI and metabolic syndrome is ethnic-specific.[35] They report that

Asians have a higher percentage of body fat compared age, sex, and BMI-matched white individuals. Also, Asians have a greater number of risk factors to develop type 2 diabetes mellitus and cardiovascular disease even when BMI is < 25 kg/m^2.
In this study, both systolic and diastolic blood pressures were higher in NAFLD subjects. Others have reported this finding and also demonstrated an association between hypertension and a greater risk of NAFLD in the general population.[48,49] In our study, both systolic and diastolic blood pressure was an independent factor of developing NAFLD in non obese subjects. Whether hypertension has a causal effect on developing NAFLD remains unknown.
Traditionally, two pathogenetic pathways are described for development of NASH: Visceral fat deposits causing an increased influx of free fatty acids to liver; and insulin resistance causing increased secretion of very low-density lipoprotein (VLDL).[52] More recent studies propose that although dyslipidemia and dysglycemia are two components of fatty liver disease, this condition is independent of fat deposits, including visceral adipose tissue.[53] In our study we didn't tested for lipid profile abnormalities as it has been well established as a risk factor for NAFLD in many previous studies.
One of the frequently used indices for assessing insulin resistance is the homeostasis model assessment of insulin resistance (HOMA-IR).[57] Few studies have assessed the role of HOMA-IR in non obese patients with NAFLD and have confirmed higher levels of insulin resistance in non obese NAFLD patients.[34,58,59] In our study we didn't measured HOMA-IR.

Our study being a cross-sectional one it precludes a conclusion regarding natural course of NAFLD and causal relationships. Although ultrasonography is the main diagnostic modality in epidemiological studies of NAFLD and it has acceptable sensitivity for detection of hepatic steatosis, the fact that it is operator based limits the results.

Conclusion

The prevalence of NAFLD in non obese and non diabetic subjects in Vikarabad district was 18.66%. Higher BMI, higher blood pressure, and Increasing age are independent factors associated with the presence of NAFLD in non obese and non diabetic subjects. Our results indicate that the Indian rural population may develop NAFLD even though their BMIs are in non obese range. This is a rather high prevalence, and has implications for health studies in Indian NAFLD patients who are non obese and non diabetic.

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