



To Study the Prevalence of Non Alcoholic Fatty Liver Disease among Overweight and Obese Persons Undergoing Preventive Health Checkups in a Tertiary Care Hospital

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ABSTRACT

Introduction: Raised Body Mass Index (BMI) is on an increasing trend nowadays, associated with various complications. The present study was planned to determine the prevalence of Non Alcoholic Fatty Liver Disease (NAFLD) among overweight and obese persons undergoing preventive health checkups and to compare the various risk factors among NAFLD and non-NAFLD population at a tertiary care center in north India.

Methods: A hospital based prospective study was done on 200 persons both male and female with BMI >23 kg/m² according to WHO criteria for the Asians. They underwent a detailed history and clinical examination, blood examination including sugar levels, serum lipid profile and liver function tests along with ultrasonographic (USG) examination for hepatobiliary system.

Results: Out of 200 persons having BMI >23 kg/m², 130 (65%) were males and 70 (30%) were females. Ultrasonography revealed NAFLD in 114 persons (57%) out of which 68.4% were males and 31.5% were females with mean age of male 45.88+/-49 years and of female 46.40+/-11.43 years. NAFLD in overweight category was 50.7% and among obese was 70.9% (p=0.007). Prevalence of risk factors among NAFLD persons

was significantly higher than the non NAFLD group with 50.8% ($p=0.024$) having systolic blood pressure ≥ 130 mmHg, 43.8% ($p=0.002$) having diastolic BP ≥ 85 mmHg, 50.8% ($p=0.001$) had fasting sugar ≥ 100 mg/dl and ALT was found to be elevated in 54.3% ($p=0.006$) of subjects.

Conclusion: It can be concluded from our study, earlier the discovery of fatty liver in routine checkups was considered to have no significance but now it is well established that obesity is a high risk factor for development of NAFLD. Other risk factors like raised blood pressure, elevated fasting sugar and serum triglyceride and low HDL levels may be associated in these patients which may further lead to NAFLD. These risk factors are preventable and reversible.

Key Words: NAFLD, fatty liver, obesity, BMI, overweight

INTRODUCTION

NAFLD is a metabolic disorder characterized by excess accumulation of fat mostly triglycerides within the cytoplasm of hepatocytes more than 5-10% of the liver weight that occurs in people who take little or no alcohol.⁽¹⁾ The term Nonalcoholic Steatohepatitis (NASH) was described by Ludwig et al⁽²⁾. NAFLD exists as a spectrum from simple steatosis without evidence of cell injury to NASH which comprises almost 10-20% of NAFLD. 10-15% of those with NASH progress to cirrhosis of liver⁽³⁾ According to NAS Score (NAFLD Activity Score) NAFLD is categorized into 4 types: 1-simple steatosis 2-steatosis with inflammation 3-steatosis with inflammation and ballooning 4-steatosis with inflammation and fibrosis. Generally the last two types constitute NASH. This division is important in view of prognosis and treatment.

By definition, there is evidence of hepatic steatosis in NAFLD either on imaging or by histology and there should not be any other cause for secondary hepatic fat accumulation like alcohol, hepato toxic drugs or any hereditary disorder. Diabetes, obesity, dyslipidemia and metabolic syndrome are considered to be risk factors of

NAFLD.⁽⁴⁾ The significance of NAFLD has risen as it is now known to be the hepatic manifestation of metabolic syndrome. It is one of the common causes of cirrhosis of liver leading to hepatocellular carcinoma and is the 3rd most common cause of liver transplantation⁽⁵⁾ It is also an independent risk factor for the cardiovascular disease. Any patient with unexplained elevated liver enzymes should be worked up for fatty liver. Elevation of AST and ALT is usually less than two times the normal limits, but more important is the AST: ALT ratio which is usually less than 1, and ratio greater than 1 suggests progression to fibrosis⁽¹⁾ It may however be said that normal values may be associated with more advanced disease.

The incidence and the prevalence of NAFLD has been increasing in both developed and in low and middle income group countries. Overall prevalence of NAFLD is 15-40% in the western world and 9-40% in the Asian population^{(6),(7)} Obesity is a common and well documented risk factor for NAFLD. Both excess BMI and visceral obesity are recognized risk factors⁽⁴⁾ There is an increasing incidence of NAFLD seen among obese children and adults and BMI is used as a useful tool in

distinguishing between NASH and simple steatosis. (8),(9),(10) A study revealed that NAFLD was present in 94% of obese patients (BMI>30kg/m²), 67% in overweight (BMI>25kg/m²) and 24% in normal weight individuals.⁽¹¹⁾ Approximately 90% of patients with NAFLD have more than one feature of Metabolic Syndrome and about 33% have more than 3 criteria.⁽¹²⁾ There is a close relation of high prevalence of NAFLD with T2 diabetes mellitus which has been shown by many studies.^{(13),(14),(15)} Systolic hypertension is an independent predictor of NAFLD as shown in a study in which 64% of NAFLD patients have hypertension.⁽¹⁶⁾

The present study was planned to determine the prevalence of NAFLD among overweight and obese persons who visited us for their preventive health checkups and also to compare the various risk factors among NAFLD and non NAFLD population.

MATERIAL AND METHODS

The study included 200 overweight and obese persons both male and female aged 18-65 years who visited our hospital for routine health checkup from 1st January 2014 till 31st December 2014. A detailed history was taken including history of hypertension, diabetes, smoking and alcohol intake and a general physical and systemic examination was done as a part of preventive health checkup. All persons taking alcohol > 20gm/ day, using any drug especially hepato toxic drugs or history of jaundice or any other liver ailment were excluded from the study. Detailed history also included any past ailments, blood transfusion or any surgical treatment. Blood pressure of each individual was

measured in right arm supine position and height, weight and waist circumference of each individual was measured by a trained attendant while the subject was barefooted and was wearing light clothes. BMI was calculated as: weight (kg)/ height (m²).

Biochemical testing was performed after overnight fasting and test for blood sugar, lipid profile (triglyceride and HDL) along with ALT, AST levels were done. Viral markers were sent for patients with past history of jaundice. All the biochemical testing was done in the same pathology lab using the standard laboratory methods and pathologist was not aware of the clinical finding of the patients. Abdominal ultrasound was done in all the patients by a trained radiologist. There after the patient was subjected to counseling which was done by the physician.

Data Analysis: All data analysis was done using SPSS software data and expressed as the mean \pm standard deviation and as percentage. The comparison of parameters and the risk association between each parameter was performed using Pearson Chi- square test. Values <0.05 were taken as significant.

Definitions: Overweight and obesity were defined as BMI = 23.0-24.9 kg/m² and BMI = 25.0-30.0 kg/m² respectively according to the WHO (modified) guidelines for Indo Asian patients. Patients with morbid obesity (BMI>30kg/m²) were not included in our study. Blood pressure, fasting sugar levels, dyslipidemia and abdominal obesity were defined using the modified ATP III criteria⁽¹⁷⁾ of metabolic syndrome in which raised systolic and diastolic blood pressure were taken as \geq 130mmHg

and ≥ 85 mmHg respectively. Impaired fasting glucose level was taken as ≥ 100 mg/dl and dyslipidemia was defined as TG levels ≥ 150 mg/dl and HDL as <40 mg/dl in males and < 50 mg /dl in females. Central obesity was taken as waist circumference ≥ 90 cm in men and ≥ 80 cm in women. Presence of three out of these five risk factors determined metabolic syndrome. AST and ALT were taken as per our laboratory normal values which were 46IU/L and 49 IU/L respectively. Diagnosis of NAFLD was made by looking at the diffuse increase in the echogenicity of liver on USG.

RESULTS

Out of 200 subjects, 130 (65%) were males and 70 (35%) were females with mean age of males 45.8 ± 11.49 years and of female 45.9 ± 11.43 years. Ultrasonography revealed NAFLD in 57% out of which 68.4% were males and 31.5% were females (M:F ratio 2:1). (Table-1)

Table 1: Prevalence of NAFLD in our study

Total no of patients =200

	NAFLDn (%)	Non NAFLDn (%)	p value
Male (130)	78(68.4%)	52(60.4%)	
Female (70)	36(31.5%)	34(39.5%)	0.242
Total	114(57%)	86(43%)	
	Overweight n=138	Obese n=62	
NAFLD	70(50.7%)	44(70.9%)	
Non NAFLD	68(49.2%)	18(29.1%)	0.007

Mean BMI of persons with NAFLD was higher in contrast to non NAFLD group. (Table 2) Subjects were further divided into overweight (n=138) and obese(n=62) categories and it was found that50.72%

of overweight and 70.96% obese persons had NAFLD (p=0.007) thereby showing a positive correlation with increase in BMI.

Table 2: Demographic and metabolic profile of patients in NAFLD and Non NAFLD group (mean \pm standard deviation)

	NAFLD (n=114)	Non NAFLD (n=86)
Age in yrs	45.8 \pm 11.4	45.7 \pm 11.4
BMI kg/m2	27.04 \pm 3.4	26.98 \pm 3.0
Waist circumference cm	91.4 \pm 10.9M 88.5 \pm 8.8F	90.3 \pm 9.1M 84.4 \pm 6.7F
SBP mmHg	136.2 \pm 18.2	136.18 \pm 18.1
DBP mmHg	89.1 \pm 14.07	87.6 \pm 11.9
TG mg/dl	177.8 \pm 110.6	178.62 \pm 111.5
HDL mg/dl	39.7 \pm 18.23	39.3 \pm 18.7
FBS mg/dl	114.51 \pm 35.1	109.6 \pm 33.3
AST IU/L	45.2 \pm 28.9	41.7 \pm 33.3
ALT IU/L	51.9 \pm 37.6	48.1 \pm 35.3
H/O diabetes	30	16
H/O hypertension	48	28
H/O smoking	10	10

Table 3: Prevalence of various risk factors in NAFLD and Non NAFLD categories

Parameters	NAFLD (n=114) n (%)	Non NAFLD (n=86)n(%)	p value
Waist circumference >90cmM,>80cmF	62(54.3%)	40(46.5%)	0.270
SBP ≥ 130 mmHg	58(50.8%)	30(34.8%)	0.024
DBP ≥ 85 mmHg	50(43.8%)	20(23.2%)	0.002
TG ≥ 150 mg/dl	64(56.1%)	42 (48.6%)	0.305
HDL<40 mg/dl M,<50mg/dl F	76(66.6%)	54(62.7%)	0.569
FBS ≥ 100 mg/dl	58(50.8%)	24(27.9%)	0.001
AST>46 IU/L	52(45.6%)	36(41.8%)	0.596
ALT >49IU/L	62(54.3%)	30(34.8%)	0.006

50.8% of total NAFLD subjects had systolic pressure ≥ 130 mmHg in contrast to 34.8% in non NAFLD group ($p=0.024$). Similarly, diastolic pressure above ≥ 85 mmHg was seen in 43.8% NAFLD persons in contrast to 23.25% among non NAFLD ($p=0.002$) (Table 3) clearly showing a close association of high blood pressure with NAFLD. Mean systolic and diastolic blood pressure were high in NAFLD group as compared to non NAFLD (Table 2). Fasting blood sugar level ≥ 100 mg/dl was seen among 50.87% in NAFLD in comparison to 27.9% among non NAFLD group ($p=0.001$). Mean fasting values were 114.51 ± 35.13 mg/dl and 109.63 ± 33.3 mg/dl among NAFLD and non NAFLD groups respectively. 56.1% of patients had raised triglyceride levels and 66.6% had low HDL level in NAFLD group in comparison to 48.8% and 62.7% in non NAFLD group respectively.

We also compared the AST and ALT values among the two groups and it was seen that AST was in normal range in both the groups but the mean values were higher in NAFLD in contrast to non NAFLD group (Table 2). However ALT was raised in NAFLD subjects (51.94 ± 37.6 IU/L) compared to the non NAFLD group (48.11 ± 35.3 IU/L). AST /ALT ratio was < 1 . It was also seen that NAFLD group had raised ALT compared to non NAFLD group ($p=0.006$) (Table 3). Similarly, 45.6% had raised AST in NAFLD group in contrast to 41.8% in non NAFLD group clearly indicating that significant patients had raised AST/ALT values among NAFLD group in our study population.

DISCUSSION

Prevalence of NAFLD is increasing both in developed and developing countries. In a study done in the USA, the prevalence of hepatic steatosis and NAFLD was found to be 21.4% and 19.0% respectively by USG.⁽¹⁸⁾ In Dallas heart study the prevalence of NAFLD as determined by MR spectroscopy was 31%.⁽¹⁹⁾ Earlier the discovery of fatty liver in routine checkups was considered to have no significance but now it is well established that even diabetics and obese patients can develop steatohepatitis similar to that seen in alcohol liver disease which can later on develop into cirrhosis of liver. Obesity is one of the major risk factors of development of NAFLD. BMI is a widely used parameter to measure obesity primarily because it's a simple, inexpensive, and noninvasive test, the results from which can be used at the population level by public health professionals. Obesity is now no longer an epidemic just in USA but is becoming a global phenomenon. There has been a recent increase in the prevalence in countries like China and Japan probably due to increase in obesity. A study in Taiwan showed the prevalence of NAFLD on USG to be 48.4% with males having a greater prevalence than females (57.8% vs 32.4%). The study also revealed that old age, male gender, higher BMI, AST and ALT levels, presence of hypertension, hyperuracemia, hypercholesterolaemia, high FBS and hypertriglyceridaemia as significant risk factors of NAFLD.⁽²⁰⁾ Another study on employees of Shanghai revealed the prevalence of NAFLD about 38.17% on ultrasound and also BMI a better index for diagnosing NAFLD.⁽²¹⁾ Study conducted in Mumbai on the residents of 2 railway

colonies revealed the prevalence of NAFLD around 18.9% on ultrasound, more in males (24.6% vs 13.6%).⁽²²⁾ Similar study done in coastal regions of India showed 24.5% healthy attendants of patients having evidence of fatty liver on USG with males >females (27% vs 14%). The study also revealed that patients with fatty liver had a higher BMI (mean 25.9kg/m²).⁽²³⁾

Our study has revealed the prevalence of NAFLD to be around 57% among which 68.42% were males and 31.57% were females. Further it was seen that NAFLD was more prevalent among obese subjects (70.9%) in comparison to overweight (50.7%). Similar results were shown by Hamaguchi et al⁽²⁴⁾ who showed that among obese patients NAFLD was prevalent in 67.3% of males and 45.8% of females. Another study done by Hu et al⁽²¹⁾ showed prevalence of NAFLD as 38.17% in general population. Same study also revealed presence of obesity in 22.4% of NAFLD and 8.19% of non NAFLD patients. Various studies in India have compared the body mass indices with NAFLD. Vishwna than et al⁽²⁵⁾ showing as high as 85.3% of obesity in NAFLD patients, Uchil et al⁽²⁶⁾ showed the presence of overweight in 52.8% of NAFLD, frank obesity in 24.8% and normal BMI in 21.7% of NAFLD patients and study by Ramesh et al⁽²⁷⁾ showed presence of obesity in 68.8%, overweight in 18% and lean in 13.2% of NAFLD patients.

Obesity as very well understood is associated with liver abnormality, known as nonalcoholic fatty liver disease (NAFLD), characterized by an increase in intrahepatic triglyceride (IHTG) content (i.e. steatosis) with or without inflammation and fibrosis (i.e. steatohepatitis). Steatosis which is the hallmark

of NAFLD, occurs when the rate of hepatic fatty acid uptake from plasma and fatty acid synthesis is greater than the rate of fatty acid oxidation and export (as triglyceride within VLDL).⁽²⁸⁾ So, the excessive amount of intrahepatic triglyceride represents an imbalance between complex interactions of metabolic events. The presence of steatosis is associated with a constellation of adverse alterations in glucose, fatty acid and lipoprotein metabolism and abnormalities in fatty acid metabolism, in conjunction with adipose tissue, hepatic, and systemic inflammation, leads to the development of insulin resistance, dyslipidemia and other cardio metabolic risk factors associated with NAFLD. The prevalence of steatosis is over 90% in severely obese patients (BMI >35kg/m²) in a series of patients undergoing bariatric surgery.⁽²⁹⁾ Other studies also showed the presence of increased steatosis and steatohepatitis among obese NAFLD patients as much as 65% and 20% in class 1 and 11 obesity⁽³⁰⁾ and 84% and 40% among morbid obese patients⁽³¹⁾ respectively.

Various risk factors were also studied among NAFLD group and there was a positive correlation between presence of raised blood pressure (systolic /diastolic) and high fasting blood sugar levels with NAFLD. Our results were comparable to the study done by Hamaguchi et al⁽²⁴⁾ which has compared the risk factors among obese and non-obese population. The study showed the prevalence of impaired fasting sugar in 48.9%, hypertension in 39.9%, elevated triglyceride in 33.6%, low HDL in 45.4% and increased waist circumference among 48.8% of obese male NAFLD patients in comparison to 28.9%, 16.5%, 13.2%, 24.8% and 2%

in non-obese male NAFLD patients. However in our study we could not demonstrate a positive correlation with raised triglyceride levels. Similar study also revealed 46.5% rise of ALT among obese male patients in comparison to 13.7% among non-obese population comparable to raised ALT of 54.3% in our study.

Most common presentation of NAFLD is mildly raised aminotransferase levels. Kalra et al⁽¹⁵⁾ have tried to record the prevalence of NAFLD in T2 DM patients on the basis of elevated aminotransferase levels, with elevated AST in 19% and ALT in 15.9% of NAFLD population in contrast to our study where AST/ALT were raised in 45.6% and 54.3% of NAFLD patients respectively. This has been very well shown in study done by Ruhl et al⁽³²⁾ which shows that in absence of other causes, overweight and obesity increases the risk of liver disease. Elevated ALT levels were found among 2.8% in a large national population based study and the proportion increased to 65% among overweight and obese (BMI >25 kg/m²) thereby suggesting central adiposity as one of the major determinants of elevated serum ALT levels.

CONCLUSION

It can be said that obesity is not only a risk factor for development of T2 DM, coronary artery disease or metabolic syndrome but also a risk factor for the development of NAFLD. Recognition of obesity on the basis of BMI remains a simple and inexpensive measure and detecting fatty liver on ultrasound in these persons done during health checkups can prevent its progression to end stage liver disease.

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