



ORIGINAL RESEARCH PAPER

General Medicine

STUDY OF PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE IN ASYMPTOMATIC ADULTS PRESENTING WITH HEPATOMEGALY OR UNEXPLAINED LIVER ENZYME ELEVATIONS

KEY WORDS: NAFLD, serum transaminases, hepatomegaly ,cirrhosis

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ABSTRACT

OBJECTIVES: To study the prevalence of hepatic steatosis in non alcoholic asymptomatic adults presenting with hepatomegaly or unexplained elevation of liver enzymes with special reference to nonalcoholic steatohepatitis .

METHODS: A prospective study was conducted in the department of internal medicine in a tertiary care referral centre in New Delhi , India . 500 cases were selected by random sampling in the age group of 20 to 75 years . Patients were divided into three BMI (body mass index) Normal :19-25, Overweight : 25-30, Obese :>30. They were further subjected to liver function tests, ultrasound and liver biopsy.

RESULTS: over all prevalence of Non alcoholic fatty liver disease (NAFLD) found in our study was 15 % . Overall prevalence in males was 58.67% and in females was 41.33%. Prevalence of NASH in patients who underwent liver biopsy was 32% and higher in females as compared to males

CONCLUSION : NAFLD was associated with elevated serum aminotransferases levels in 48.67% of patients . ALT levels were found to be higher than AST levels except in patients with cirrhosis . Out of patients who underwent liver biopsy ,25 in number , 64 % had steatosis, 32% steatohepatitis and 4% had Cirrhosis.

INTRODUCTION : Fatty change (or steatosis) denotes the excess accumulation of lipids within hepatocytes . Non alcoholic fatty liver disease(NAFLD) has a spectrum ranging from simple steatosis to non alcoholic steatohepatitis (NASH), which can progress to cirrhosis liver and hepatocellular carcinoma [1,2]. Two hit theory very well describes the pathogenesis of NASH wherein hepatic steatosis, the first hit is followed up by the second hit , one of which may be reactive oxygen species . Increased oxidative stress due to increased mitochondrial oxidation causes further injury by induction of cytokines, lipid peroxidation and fas ligands and progression from a stage of steatosis to steatohepatitis. The diagnosis rests on the hallmark histological features and rigorous exclusion of significant alcohol consumption . Most patients are asymptomatic, have clinical hepatomegaly, features of fatty liver on imaging and mild to moderate elevations of serum aminotransferases levels. Liver biopsy is essential for positive diagnosis and prognostication of NASH. Histological fat deposition is typically macrovesicular and inflammation of steatohepatitis is predominantly lobular .

NASH has gained more clinical importance recently because it was suggested to be a major cause of cryptogenic cirrhosis [3] and unexplained raised transaminases [4]and can even lead to hepatocellular carcinoma [2]. Even in the absence of significant alcohol intake the liver histology in these patients is indistinguishable from alcoholic hepatitis and the term NASH was introduced by Ludwig et al to describe this entity [5]

METHODS

A prospective study was conducted in the department of internal medicine in a tertiary care referral centre in New Delhi , India . Case selection was done by random sampling in the age group of 20 to 75 years from different social strata presenting with hepatomegaly along with asymptomatic Liver function test derangement or Ultrasound suggestive of fatty liver in the absence of history of alcohol intake . Patients having positive viral markers for hepatitis , on hepatotoxic medications, malignancy , gastrointestinal bypass surgery, pregnancy , bleeding diathesis, portal hypertension or family history of jaundice were excluded.

A detailed history and physical exam were recorded . Patients were divided into three BMI (body mass index) Normal :19-25, Overweight : 25-30, Obese :>30.

ultrasound upper abdomen , biochemical profiling (blood sugar , fasting lipid profile , liver function test , coagulation) and liver biopsy (Maghnum biopsy needle) was done .

RESULTS

500 patients participated in the study out of which there were 284 males and 216 females . Total cases of fatty liver 110, 27 alcoholic liver disease i.e alcohol intake > 40 gm /week , 8 had serum markers of infective hepatitis positive . 75 cases attributed to NAFLD . Thus over all prevalence of NAFLD found in our study was 15 % . Out of 75 cases 44 were males and 31 females . Thus overall prevalence in males was 58.67% and in females was 41.33% . The mean age of distribution in our study was 49.79±8.76 years . The mean age among the males was 50.36±8.38 years . The mean age among females was 48.97±9.35 years . Highest prevalence was seen between 40-50 year age group. (FIG 1)

Mean body weight among study population was 74.45 ± 13.96. Mean body weight in males was 77.45± 13.18 kilograms . Mean body weight in females was 69.71± 13.98 kilograms . Mean BMI of the study population was 26.4± 2.97kg/m². Mean BMI among the males was 26.41± 2.97kg/m². Mean BMI among the females was 26.39± 3.04kg/m².(TABLE 1)

TABLE 1: DISTRIBUTION OF BODY WEIGHT

SEX	NORMAL BMI (n=39)	OVERWEIGHT (n=25)	OBESE(n=11)
MALES	23	15	6
FEMALES	16	10	5

Mean serum aminotransferase (ALT) level in the cohort of histologically proven NAFLD cases was 49.04+25.27 IU/L. mean AST level was 47.8+20.85IU/L . Mean AST/ALT ratio was 0.98 + 0.18.

Liver biopsy was performed in 25 patients (14 males and 11 females) Thus the prevalence of NASH was 32% and higher in females as compared to males.

Table 2 : RESULTS OF LIVER BIOPSY

	Steatosis	Steatohepatitis	Cirrhosis
Total	16(64%)	8(32%)	1(4%)
Males	10(71.4%)	3(21.4%)	1(7.1%)
Females	6(54.5%)	5(45.5%)	0

DISCUSSION

Non alcoholic fatty liver disease (NAFLD) is being increasingly recognized as a common liver disorder that contributes significantly to liver related morbidity and mortality. NAFLD is said to be the hepatic manifestation of metabolic syndrome a variably defined aggregate of disorders related to obesity, type 2 diabetes

mellitus, hypertension and hyperlipidemia . Spectrum of NAFLD ranges from simple steatosis to steatohepatitis and cirrhosis with risk of hepatocellular carcinoma . the gold standard for diagnosis is the clinicopathologic correlation of steatosis on liver biopsy and exclusion of other causes of fatty liver clinically. In our study histological confirmation of steatosis was possible in only 25 cases.

In our study using ultrasound as the primary diagnostic modality in patients who had insignificant (< 40 gm/wk) or no alcohol intake and who were negative for viral markers of hepatitis , the prevalence of fatty liver which would be attributed to NAFLD was 15%.

Singh SP et al, 2004[6] in a preliminary ultrasound based survey has reported the prevalence of fatty liver in 24.5% of population in coastal eastern india which is close to the results of our study. The analysis of the Dionysos Nutrition and Liver study by Bedogni G et al , 2005[7] with prevalence and risk factors of NAFLD reported a prevalence of 20% in those not suspected with liver disease and 25% in those with suspicion of liver disease . This study was also based on detection of fatty liver by ultrasound with exclusion of other causes of fatty liver by clinical measures . The prevalence in males was 58.67% of the study population while the prevalence in females was found to be 41.33% . Thus in our study the prevalence in male was found to be greater than females . studies by Ludwig J et al,1980[5] and Diehl AM et a, 1988[8] reported higher prevalence in females . However , Bacon et al ,1994[9] , reported a higher prevalence in males

In our study the mean age was 49.78+ 8.75 years . The mean age in males was 50.36 + 8.38 years while the mean age in females was 48.97+ 9.35 years . Singh SP et al , 2004 [6] in a study of prevalence of fatty liver in coastal eastern India that person with ultrasonographic fatty liver had a higher BMI , mean 25.9 + 4.17 kg/m² than persons without fatty liver , mean 22.1+ 3.27 kg/m² . (p < 0.001). In our study the prevalence of obesity and overweight (defined by BMI > 25) was reported to be 48% (36 cases) which coincides with the data reported earlier in the literature . Of this group 11 cases (14.67%) had BMI > 30 .

In the cohort in which liver biopsy was possible (25 patients) steatohepatitis was found in 54.54% in obese individuals , while cirrhosis was present in 9.09% as compared to 32 % cases of steatohepatitis and 4% cases of cirrhosis overall thus obesity is associated with increased risk of progression to severe forms of NAFLD and cirrhosis.

NAFLD is the most common cause of abnormal liver function tests among adults (Mandez – Sanchez et al , 2003[10]) . A population based survey in a 'Mediterranean town', Pendino GM et al , 2003 [11] concluded that in 24 % of individuals with abnormal LFTs , the probable cause was NAFLD . In this subgroup, increased body weight , hypercholesterolemia, and hyperglycemia were common , and 63,3% of them had a bright liver on ultrasonography. In our study 44 cases (58.67%) of the total had elevated ALT levels . In the subgroup group of histological proven cases of NAFLD the mean AST/ALT ratio correlated with the histological severity . In patients with simple steatosis AST/ALT ratio was 0.99 while in cases of NASH AST/ALT ratio was 0.93 . In Case of cirrhosis AST/ALT ratio was 1.0 .

CONCLUSION

NAFLD seems to be a common problem in Indian patients with the prevalence around 15%. Disease tends to occur more commonly in males than in females . The prevalence in males was 58.67% while the prevalence in females was 41.33%. The peak incidence tends to occur in the 4th decade . The mean age was 49.79 years . There was no differences in the age groups between two sexes . NAFLD was associated with elevated serum aminotransferases levels in 48.67% of patients . ALT levels were found to be higher than AST levels except in patients with cirrhosis . out of patients who underwent liver biopsy (25) , 64 % had steatosis, 32% steatohepatitis and 4% had Cirrhosis.

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