Orginal Article

Demographic Variables and Histological Scoring of Non-Alcoholic Fatty Liver Disease in A Bangladeshi Population

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Abstract

A cross sectional study was carried out in the Department of Pathology, Dhaka Medical College, Dhaka and Department of hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU) during the period of July 2007 to June 2009. Total 55 adult subjects of both sexes were included in this study to evaluate the histological pattern of nonalcoholic fatty liver disease (NAFLD) and its relation with demographic variables including age, sex, BMI, obesity and waist circumference. NAFLD is characterized by macrovesicular deposition of fat in liver. It is now days recognized as a major cause of liver disease and has the propensity for progression to fibrosis and cirrhosis. Study subjects with bright echogenic liver on ultrasonography with no history of alcohol consumption and without having hepatitis B and hepatitis C infections were included. All of them undergone liver biopsy and H&E and Masson's Trichrome stain slides were examined to evaluate the grade and stage of NAFLD. Scoring and semiquantitative assessment of steatosis and NAFLD severity was done according to Kleiner scale known as NAFLD Activity Score (NAS). Among the subjects 24 were male and 31 female. Mean age 41±10.66 years (range 20 - 65 years), BMI 29.13±3.79 kg/m2 (range 24.22 - 39.00 kg/m2), mean of male waist circumference 92.03±6.75 cm (range 88-109 cm) and mean of female waist circumference was 90.17±6.6cm (range 80-102 cm). Only BMI correlated significantly with NAS score whereas age, BMI and waist circumference of male and female subjects correlated significantly with stage of fibrosis. The study concludes that in developing countries like Bangladesh the incidental finding of NAFLD is increasing because of change in life style and food habit.

Key Words: NAFLD, NAS, demographic variables.

Introduction:

Diffuse macrovesicular accumulation of fat in hepatocytes in individuals who do not consume alcohol in quantities considered harmful to liver is referred to as nonalcoholic fatty liver disease (NAFLD).[1] Overall about 5% of patients with NAFLD develop cirrhosis over an average of a seven years period with 1.7% dying from the complications of liver cirrhosis. Although the exact etiology is not clear it could possibly be a part of a metabolic syndrome associated with obesity, hypertension, dyslipidaemia, insulin resistance and diabetes.[2]

In conditions where the supply of free fatty acids becomes excessive, there is accumulation of triglycerides and free radicals. Deposit of fat in the hepatocytes causes fatty degeneration of the liver or steatotic hepatitis which makes affected tissues more sensitive to oxidative stress, enterotoxins and ischemia.[3]

NAFLD has been recognized as a disease of affluent countries and western disease. Approximately 12%-15% of the population is estimated to have NAFLD while 3-4% has NASH.[4] It reaches 25% to 75% in patients with obesity and type 2 diabetes mellitus.[5] In Asia the prevalence of NAFLD are 12% to 24%.[6] In India it varies from 5% to 28%.[7] The prevalence of over weight and obesity is increasing in Bangladesh due to change in dietary habits and a sedentary life style. NAFLD affects all age groups. Its prevalence in the general population ranges from 16 to 25% in adults.[8] The highest prevalence has been described in one study to be between 40 and 49 years of age.[9]

The imaging modalities most often used to identify hepatic steatosis include computerized tomography and ultrasonography. Liver biopsy is considered to be the gold standard for the diagnosis of NAFLD as

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it is the only investigation able to distinguiseh between simple steatosis and NASH or stage the degree of fibrosis. It remains not only the best diagnostic tool for confirming NASH, but also the more sensitive and accurate in specific means of providing important prognostic information in patients with this condition.[10]

In Bangladesh a few studies have been conducted to determine the correlation between demographic variables and histopathological aspect of the disease. Therefore, the aim of this study was to determine histological scoring cellular morphology of patients with bright echogenic liver and to find its relation with demographic variables.

Methods:

Cross sectional study was carried out in the Department of Pathology, Dhaka Medical College, Dhaka and Department of hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU) during the period of July 2007 to June 2009. Total 55 adult subjects with bright echogenic liver on ultrasonography were included in this study purposively with predefined inclusion and exclusion criteria.

Demographic variables were recorded which included age, sex and anthropometric measurements of height, weight, BMI (according to WPRO)[11], central obesity (ATP III)[12] and waist circumference following standard procedure.

The liver biopsy was done by trained hepatologist. The biopsy tissue was preserved in 10% formalin; H&E and Masson's Trichrome stain slides were examined to evaluate the grade and stage of non-alcoholic fatty liver disease. Scoring and semiquantitative assessment of steatosis and NAFLD severity was done according to Kleiner scale.[13]

Individual scores of steatosis, lobular inflammation and hepatocyte ballooning added to produce an overall 'NAFLD Activity Score: (NAS). NAFLD activity score >5: the histological diagnosis will be probable or definite NASH; 3-4: uncertain and 2: not NASH.[13]

The data were evaluated by standard statistical methods using SPSS (Statistical Package for Social Sciences) version 17. Statistical significance was set as 0.05 and $p<0.05$ was considered as significant.

Results:

A total of 55 cases of both sex including 24 male and 31 female study subjects ultrasonographically diagnosed as bright echogenic liver with no history of alcohol consumption, were enrolled in the study to find their histological scoring and cellular involvement. The study was also aimed at assessing the relation between demographic features with the mentioned variables.

Table I: Descriptive analysis of statistics

Statistics	Range	Mean ± SD
Age (years)	20 -65	41.00 ±10.66
BMI (kg/m2)	24.22 -39.00	29.13 ± 3.80
Male waist (cm)	80.00 - 109.00	92.04 ± 6.75
Female waist (cm)	80.00 - 102.00	90.17 ± 6.66

Table I shows analysis of descriptive statistics of study subjects. Age distribution of the study subjects shows that the mean age was 41±10.66 years (range 20-65 years). Mean BMI was 29.13±3.79 kg/m2 (range 24.22 - 39.00 kg/m2). The mean of male waist circumference was 92.03±6.75 cm (range 88-109 cm) and the mean of female waist circumference was 90.17±6.6cm (range 80-102 cm).

Table II: Distribution of study subjects by obesity status (n=55)

BMI (kg/m2)	Frequency	Percentage
Normal	1	1.8
Over weight	35	63.6
Obese	19	34.5

Table-II shows the distribution of study subjects according to the obesity status. Thirty five of the subjects (63.6%) were over weight, 19 (34.5%) were obese and only 1 (1.8%) was with normal BMI.

Table III: Distribution of subjects by waist circumference

Sex of the subjects	Normal waist (cm) Frequency (%)	Raised waist (cm) Frequency (%)
Male (n = 24)	8 (33.3%)	16 (66.7%)
Female (n = 31)	3 (9.7%)	28 (90.3%)

Table III shows the distribution of male & female subjects according to the waist circumference respectively. Out of 24 male subjects 16 (66.7%) exhibited raised and 8 (33.3%) normal waist circumference. Of 31 female subjects 28 (90.3%) exhibited raised and 3 (9.7%) exhibited normal waist circumference.

Table IV: Distribution of patients according to NAS Score (n=55)

NAS score	Frequency	Percentage
≥5	39	70.9
3-4	8	14.5
2	8	14.5

Table IV shows distribution of study subjects according NAFLD activity scores (NAS). 70.9% subjects had NAS score 5 i.e definite NASH; 14.5% had score 3-4 i.e uncertain NASH and 14.5% had NAS score >2 i.e not NASH.

Table V: Distribution of patients according to Fibrosis (n=55)

Fibrosis	Frequency	Percentage
1. Perisinusoidal or Periportal	31	56.4
2. Perisinusoidal and portal/Periportal	7	12.7
3. Bridging	6	10.9
4. Cirrhosis	3	5.5

Table V shows distribution of subjects according to Fibrosis staging. 56.4% cases were stage 1; 12.7% cases were stage 2; 10.9% cases were stage 3 & the rest 5.5% were stage 4.

Table VI: Correlation between NAS score and demographic variables

NAS Score vs. Independent variable	r	p
BMI (kg/m2)	.337	.012*
Male Waist (cm)	.198	.354ns
Female Waist (cm)	-.064	.732ns
Age of the Patient (years)	.104	.450ns

Pearson's correlation coefficient
* = Significant
ns = Not significant

Table VI shows correlation between NAS score and the demographic variables. It reveals that BMI correlated significantly with NAS score. The other variables are not correlated with NAS score.

Table VII: Correlation between Fibrosis stage and demographic variables

Fibrosis vs. Independent variable	r	12 pt
BMI (kg/m2)	.580	.000*
Male Waist (cm)	.577	.010*
Female Waist (cm)	.387	.042*
Age of the Patient (years)	.299	.041*

Spearman rank correlation coefficient
* = Significant
ns = Not significant

Table VII shows correlation between fibrosis stage and demographic variables. It reveals that BMI, waist circumference of male and female, and age of the patients correlated with stage of fibrosis.

Discussion:

In the Aisa-Pacific region NAFLD is common due to the major risk factors like obesity; T2DM and its prevalence ranging from 5% to 40%.[14] At the same time obesity, dyslipidaemia, diabetes mellitus are closely associated disease, have been shown to be rapidly increasing in prevalence.[15] In developing countries like Bangladesh the incidental finding of NAFLD is increasing because of change in life style, food habit and lack of conciousness. A significant number of cases of "cryptogenic cirrhosis" are found which may represent end stage of NAFLD.

In outpatient hospital of Bangladesh, we encounter many patients having bright echogenic liver on ultrasonography especially who are dyslipidaemic and diabetic. If hepatitis B and hepatitis C infection and history of alcohol consumption are excluded, these patients are presumed to have NAFLD.

The mean age of the studied population was 41 years (reange 20-65 yrs), 31 were female and 24 were male. Harrison et al. studied a total 22 patients where the mean age was 50.6 years (range 33-64 yrs).[16] Malik et al. in his study in Malaysia found 47.0 ± 12.2 years in his 75 NAFLD cases.[17]

Prevalence of NAFLD increases by a fraction of

4.6 in obese people. Truncal obesity is an important risk factor for development of NAFLD in subjects with even normal BMI. Up to 74% prevalence of NAFLD has been noted in obese persons.[18] In various studies 39 to 90% of NAFLD patients were found to be obese.[19] Our results correspond with these studies; we found that almost all of our patients (98.1%) were either overweight (63.6%) or obese (34.5%) with a mean BMI of 29.13.

We attempted to find the correlation of possible risk factors like BMI, central obesity, age and sex with histological scoring system.

Among the studied variables only BMI significantly correlated with NAS score. On the other hand BMI, central obesity and age significantly correlated with staging of fibrosis.

However, studies involving a large number of patients and repeated determination of these parameters should be performed for a better evaluation of their prognostic value in NAFLD.

Conclusion:

This study revealed that subjects presented with bright echogenic liver on ultrasonography without having hepatitis B and hepatitis C infections and history of alcohol consumption are almost certainly have nonalcoholic fatty liver disease (NAFLD) associated with over weight, obesity and age. However, studies involving a large number of patients and repeated determinations of these parameters should be performed for a better evaluation of their prognostic value in NAFLD.

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