Original Article

Pattern of Lipid Profile and Blood Pressure in Patients with Non-alcoholic Fatty Liver Disease (NAFLD)

Chowdhury MFK1, Zaman KMU2, Hasan MA3, Amin MA4, Saha KP5, Ashrafuzzaman M6, Islam N7, Ghosh CK8

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is associated with metabolic syndrome (MS) such as hypertension, type 2 diabetes mellitus, dyslipidaemia and obesity. NAFLD is considered as hepatic manifestation of metabolic syndrome (MS).

Objectives: The aim of this study was to see the pattern of lipid profile and blood pressure in NAFLD patients.

Materials and methods: This cross sectional study was carried out in the department of gastroenterology, BSMMU, Dhaka, Bangladesh from October 2016 to March 2017. A total of 100 patients included in this study underwent abdominal ultrasonography after excluding known case of liver disease with other etiology.

Results: The study population were categorized as NAFLD and normal group on the basis of abdominal ultrasonography. NAFLD and normal subjects were 55% and 45% respectively. The mean age was 41.34 ± 10.88 years. Male were 62% and 38% were female. 40% of study subjects were overweight, 23% were obese and 37% had normal bodyweight. Body mass index (BMI) was higher in NAFLD group; 25.10 ± 1.75 vs 21.64 ± 2.62 , P < 0.001). Dyslipidemia was present in 47% of study population. Total cholesterol (TC) (195.5±45.98 vs 140.33±47.86 mg/dl, P < 0.001), Low density lipoprotein-cholesterol (LDL-C) (120.28±43.95 vs 95.15±44.90 mg/dl, P < 0.001) and Triglyceride (TG) (230.50 ± 48.96 vs 148.40±46.43 mg/dl , P < 0.001) was higher and High density Lipoprotein (HDL) (32.69±5.49 vs 39.91±5.74 mg/dl, P < 0.001) was lower in NAFLD group in comparison to normal group. Systolic and diastolic blood pressure (BP) was also significantly higher in NAFLD group (135±12 vs 121±9 mm Hg , P < 0.001) and 82±4 vs 74±3 mm Hg (P < 0.001) respectively.

Conclusion: Higher prevalence of dyslipidemia was found in NAFLD patients. TC, LDL-C , TG and blood pressure was significantly higher in NAFLD patient in comparison to normal group.

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Key Words:
NAFLD, Lipid Profile, Metabolic syndrome, Blood pressure.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) includes a spectrum of disorders ranging from the simple fatty liver to non-alcoholic steatohepatitis (NASH), with increasing fibrosis leading to cirrhosis and ultimately leads to hepatocellular carcinoma (HCC).1 The prevalence of NAFLD is alarmingly growing worldwide in adult and children/adolescent populations, with a bidirectional association between NAFLD and metabolic syndrome.2 Dyslipidaemia, Hypertension, Obesity, insulin resistance, type 2 diabetes mellitus are the most relevant metabolic conditions related to this spectrum of diseases.1,2

High triglyceride (TG) and low high-density lipoprotein cholesterol (HDLC) levels predisposes patients to artherosclerosis3. About 20–80% of NAFLD patients also have dyslipidemia.4 A Common change in the metabolic
profile among patients with T2DM, MS, and obesity is dyslipidemia, suggesting a close relationship between T2DM, MS, and obesity and NAFLD. NASH significantly raises the level of oxidized low-density lipoprotein cholesterol (LDL-C). High LDL-C is a well-established risk factor for atherosclerosis. The most common form of dyslipidemia in NAFLD patients is atherogenic dyslipidemia, which is characterized by hypertriglyceridemia, low HDL-C levels, and high LDL-C levels. Long standing dyslipidemia may increase the expression and activity of sterol regulatory element binding protein-1c, a transcription factor, which adversely affects the profiles of lipid and lipoprotein synthesis in the liver, including increased TG, LDL, and very low-density lipoprotein (VLDL) levels and decreased HDL-C levels. There is a strong link between insulin resistance and metabolic dyslipidemia in T2DM. The increase of free fatty acid (FFA) flux occurs if insulin resistance develops. The increased FFA level boosts TG and VLDL production as well as triggers oxidative stress and lipid peroxidation, all of which are closely associated with the development of NAFLD. Consequently, this physiological dysfunction also increases the risk for atherogenesis, thereby predisposing patients to cardiovascular diseases (CVDs). In addition, circulating adipokines and cytokines as well as associated lipotoxicity, mitochondrial dysfunction, oxidative stress, and endoplasmic reticulum stress are involved in steatosis. Hypertension is one of the most common cardiovascular diseases (CVD) with increasing prevalence around the worldwide. Non-alcoholic fatty liver disease has been considered as a pathological change of the liver which could be a risk factor for CVD and metabolic syndrome. As an important component of the metabolic syndrome, hypertension is prevalent in patients with NAFLD. The development of NAFLD is associated with key components of the metabolic syndrome both in adults and children. Individuals with NAFLD typically have high level of blood pressure, body mass index (BMI), waist circumference, and insulin resistance. Non-alcoholic fatty liver disease (NAFLD) not only promotes the development of severe liver diseases but also the increase of blood pressure. Several studies reported that NAFLD is associated with hypertension or prehypertension among different kinds of population in various regions. Hypertension, a multifactorial disorder resulting from the interplay between genetic predisposition and environmental risk factors, is a growing public health problem that affects about 30% of the general population. Emerging epidemiological evidence has demonstrated that about 49.5% of patients with hypertension have NAFLD, and the prevalence of hypertension is significantly higher in individuals with NAFLD than the general population. NAFLD may induce multiple systemic adverse effects including inflammation, renin-angiotensin system (RAS) – sympathetic nervous system (SNS) activation and insulin resistance (IR), which are critical pathophysiological mechanisms leading to the development of hypertension. Several studies have shown that NAFLD seems to be independently associated with an increased risk of prehypertension and hypertension.

This study was designed to see the pattern of lipid profile and blood pressure level among the NAFLD patients attending at a tertiary level hospital. This will help us to know the association of lipid profile abnormalities and blood pressure level, which help us for the earlier identification of dyslipidemia and hypertension and better management at early period.

**Methods**

This cross-sectional study was carried out in the department of gastroenterology, BSMMU, Dhaka, Bangladesh, who underwent abdominal ultrasonography during the period of October 2016 to March 2017. A total of 100 patients attended at inpatient and outpatient department of gastroenterology of BSMMU were selected for the study. Body weight, height, Body mass index (BMI) was calculated for every patient. Blood pressure was measured with maintaining appropriate method. Abdominal ultrasonography, Viral markers including HBsAg, Anti HCV, abdominal ultrasonography, liver biochemical tests including ALT, AST, GGT, Serum Albumin, TSH and serum creatinine was done. Those with serological markers of hepatitis B or C virus, alcohol consumption greater than 140 g/week, known liver disease because of another etiology, history of cancer / taking chemotherapy, pregnant women, the patients taking diuretics, low dose aspirin, cyclosporine, pyrazinamide, ethambutol, allopurinol, febuxostat, known case of renal failure or gout were excluded in this study. Written informed consent were obtained from all participants.

The definition of NAFLD requires that:

a. There is evidence of hepatic steatosis by ultrasonography and
b. There is no causes for secondary hepatic fat accumulation such as significant alcohol consumption.

Body mass index (BMI) is the Weight in kilograms divided by the height in metres squared.

<table>
<thead>
<tr>
<th>Normal reference range</th>
<th>18.5-24.9 kg/m²</th>
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<tbody>
<tr>
<td>Over Weight</td>
<td>25-29.9 kg/m²</td>
</tr>
<tr>
<td>Obese</td>
<td>&gt; 30 kg/m²</td>
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</tbody>
</table>
For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline has been referred.

According to NCEP-ATP III guidelines

a. hypercholesterolemia is defined as total cholesterol > 200mg/dl

b. high LDL:
   When value > 100 mg / dl,

c. hypertriglyceridemia as TG > 150 mg/dl

d. low HDL: when value < 40 mg/dl.

Hypertension defined as

a. Grade 1 hypertension (mild) : Systolic BP 140-159 mmHg/Diastolic BP 90-99 mmHg

b. Grade 2 hypertension (moderate) : Systolic BP 160-179 mmHg/Diastolic BP 100-109 mmHg

c. Grade 3 hypertension (Severe) : Systolic BP > 180 mmHg/Diastolic BP >110 mmHg

Statistical Analysis

Numerical variables were presented as mean ± SD. Gender was expressed in male female ratio. Categorical variables were expressed in percentage. All statistical analyses were performed using SPSS version 23. Distribution of the data were tested with Shapiro Wilk test with a significance level of d” 0.05. Only Age was normally distributed. All other numerical variables were non-normally distributed. During comparison of two independent numerical variable, student’s t test and Mann Whitney U test were used for normally and non-normally distributed data respectively. Two set of categorical variables were tested using Chi-Square test and Fisher’s exact test. A 2-tailed value of P d” 0.05 was considered statistically significant for all analysis.

Results

A total of 100 patients were studied. Of them NFALD was diagnosed in 55% by abdominal ultrasonography (Figure 1). Mean age of the study participants was 41.34 ±10.88 years. Number of male was 1.63 times higher than female. Demographic parameters are shown in Table I. Forty seven percent of study population had one or more abnormal serum lipid parameters. BMI was higher in NAFLD group (P < 0.001). 39% of participants in NAFLD group was dyslipidemic whereas only 8% of normal group was dyslipidemic (Table II). Total cholesterol (TC), triglyceride (TG) and low density lipoprotein (LDL) was significantly higher in NAFLD group (P < 0.001). High density lipoprotein (HDL) was lower in NAFLD patients in comparison to normal group (p < 0.001) (Table III). Both the systolic and diastolic blood pressure were also higher in NAFLD group in comparison with normal group (p < 0.001) (Table IV).

### Table-I

<table>
<thead>
<tr>
<th>Demographic parameters (n=100)</th>
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<tbody>
<tr>
<td>Age (years)</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Male: female</td>
</tr>
<tr>
<td>BMI</td>
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</table>

BMI- body mass index

### Table-II

<table>
<thead>
<tr>
<th>Distribution of subjects according to serum lipid profile across NAFLD (n=55) and normal group (n=45).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid profile status</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration

According to liver ultrasonography findings patients were categorized as Non Alcoholic Fatty Liver Disease-NAFLD (fatty liver) and normal liver

<table>
<thead>
<tr>
<th>Table-III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison of means of BMI and lipid profile parameters between NAFLD (n=55) and Normal group (n=45)</td>
</tr>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>-------------------------------</td>
</tr>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
</tr>
<tr>
<td>Lipid profile parameters(mg/dl)</td>
</tr>
<tr>
<td>TC</td>
</tr>
<tr>
<td>TG</td>
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<tr>
<td>LDL-C</td>
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<td>HDL-C</td>
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</tbody>
</table>

According to liver sonography findings patients were categorized as Non Alcoholic Fatty Liver Disease-NAFLD (fatty liver) and normal liver

BMI : Body Mass Index expressed in kg/m²
TC : Total cholesterol
TG : Triglyceride
LDL-C: Low Density Lipoprotein Cholesterol.
HDL-C: High Density Lipoprotein Cholesterol.

P value d” 0.05 was considered statistically significant. Data was analyzed by 2 tailed t test

*Student’s t-test was used
Table IV

Comparison of means of systolic BP and diastolic BP between NAFLD (n=55) and Normal group (n=45)

<table>
<thead>
<tr>
<th>Variables</th>
<th>NAFLD (mmHg)</th>
<th>Normal (mmHg)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>135±12</td>
<td>121±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>82±4</td>
<td>74±3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P value ≤0.05 was considered statistically significant. Data was analyzed by 2 tailed t test

*Student’s t-test was used

Discussion

This hospital based observational study was undertaken to see the pattern of lipid profile and blood pressure level in NAFLD patients. A total number of 100 patients who fulfilled the inclusion and exclusion criteria attended at department of Gastroenterology during the period of October’2016 to March’2017 were enrolled in this study.

The present study findings were discussed and compared with previously published relevant studies. Most of the study subjects hailed from different districts of Bangladesh.

In this current study it was observed that the mean age was found 41.34±10.88 years with range from 20-70 years (Table-1). The majority of population were found between 36-45 years (33%). Out of this 100 subjects 62% were male and 38% were female (Figure-1). A large study (N=1320) was conducted by Kurata et al in 2005 showed that the majority of population between 35-48 years there were 60% male and 40% were female. In this study out of 100 study patients 55% were found to have fatty liver on ultrasound scan of liver and they were grouped as NAFLD. 45% of respondents were normal on ultrasound scan of liver and fall in another group, termed as normal group. Among NAFLD people 35 patients (63.63%) were male and 20 patients (36.37%) were female. Among Normal subjects 27 patients (60%) were male and 18 patients (40%) were female. In a recent study Colleredo et al in 2003 showed 53% of study population were NAFLD and 47% of study population were normal groups. 60% were male and 40% were female.

Most of the study population (40%) had BMI between 25-29.9 kg/m²; 23% of study population had BMI ≥30 kg/m². The mean BMI of NAFLD group was 25.10 ± 1.75 kg/m² and in normal group it was 21.64 ± 2.62 kg/m² (Table-3). The difference between these two groups was statistically significant (p value<0.001). Western pacific regions of WHO states that BMI>23 kg/m² in Asian population is associated with adverse metabolic outcome. In one study Baba et al in 2007 showed mean BMI of NAFLD patients were 28.30±2.96 kg/m2. Another study done by Zelber-sagiS et al in 2006 showed strong association between BMI and NAFLD.

In this study, 53% had normal serum lipid profile and 47% had dyslipidemia. In NAFLD group, dyslipidemia and normal serum lipid profile status was 70.91% and 29.09%% respectively. In normal group, dyslipidemia was 17.78% and normal serum lipid profile was 82.22% (Table-2).

Result of this study showed that the level of LDL-C, total cholesterol and TG were significantly higher in NAFLD group than normal group. The mean TG level in NAFLD group was 230.50±48.96 mg/dl and in normal group the mean TG level was 148.40±46.43 mg/dl. The mean HDL-C level in NAFLD group was 32.69±5.49 mg/dl in normal group the mean HDL-C level was 39.91±5.74 mg/dl. The difference of mean between two groups was statistically significant (P value<0.001). Statistically significant difference of mean of LDL-C and total cholesterol was
also found in NAFLD group compared to normal group (Table-3). This finding was in agreement with the previous study conducted by Bugianes et al in 2004.

In a study conducted by Santhoshakumari et al patients with NAFLD had higher TC, LDL, and TG and lower HDL as compared to the control group. In another study, again mean LDL and TC was higher than the normal range among NAFLD subjects. Further, Novakovic et al., in Servia, compared chemical parameters with NAFLD and found that there is significant relationship between TG, LDL, TC and inverse relationship with HDL in the group. The study done by Pardhe as well as Jain et al indicated similar result.

In this study the mean systolic blood pressure in NAFLD group was 135±12 mm hg and mean diastolic blood pressure was 74±3 mm hg (Table 4). The difference between these two groups was statistically significant (P value<0.001). In the present study, the mean SBP and DBP in the NAFLD group was higher than that of normal group, where individuals with higher systolic and diastolic blood pressure indicated higher risk of developing NAFLD and a significant relationship was observed between BP and NAFLD. These findings were consistent with previous studies conducted by Kleiner et al. 2005. This result was in accordance with the findings of a number of studies.

Limitations:

In this study only the ultrasonography was used to diagnose NAFLD where liver biopsy is the gold standard for this purpose. Liver biopsy was not done because of its invasiveness, risk of complications and high cost. On the other hand, abdominal ultrasonography is a non-invasive, low risk, simple, relatively low-cost, and easily available method.

Conclusion:

Our study showed, NAFLD patients are more dyslipidemic and having higher systolic and diastolic blood pressure compared to normal population. Thus, implementation of therapeutic strategy for dyslipidemia and hypertension with lipid lowering and antihypertensive agents may mitigate the risk of CVD in NAFLD patients.

References


characteristics of patients with nonalcoholic fatty liver


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