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# Anthropometric and Biochemical Findings in Non-Alcoholic Fatty Liver Disease with or Without Diabetes

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**Abstract:** *Background*: Non-alcoholic fatty liver disease (NAFLD) has emerged as a prevalent cause of chronic liver diseases globally in the past decade, posing significant risks to liver health, cardiovascular well-being, and even warranting consideration for liver transplantation. There is limited research on the clinical, anthropometric, biochemical, and metabolic characteristics of NAFLD patients, both with and without diabetes, in Bangladesh. *Aim of the study*: This study aimed to assess the prevalence of diabetes and non-diabetes among a group of NAFLD patients and to investigate the anthropometric, biochemical, and metabolic profiles of NAFLD patients with diabetes compared to those without diabetes. *Methods*: This prospective observational study was conducted at the Department of Gastrointestinal Hepatobiliary & Pancreatic Disorder (GHPD), BIRDEM General Hospital, Dhaka, from April 2014 to April 2015. A total of 111 individuals with ultrasonographically diagnosed NAFLD were included in the study. Participants underwent assessments for various parameters, including anthropometric measurements, biochemical assays (including blood glucose levels, liver function tests, lipid profiles, and HOMA-IR), and the presence of diabetes or metabolic syndrome (as defined by IDF criteria). The patients were categorized and analyzed based on the presence or absence of diabetes. Statistical analysis was performed using SPSS version 16.0. *Results*: Among the 111 NAFLD patients, 71 (63.96%) were diagnosed with diabetes, while 40 (36.04%) did not have diabetes. In comparison to those without diabetes, NAFLD patients with diabetes tended to be older (47.15±10.26 vs. 43.35±10.7 years) and included a higher proportion of females (61.98% vs. 57.50%). They also had a significantly higher prevalence of hypertension (77.47% vs. 40.0%; $p<0.001$), dyslipidemia (64.79% vs. 40.0%; $p=0.01$), and metabolic syndrome (74.64% vs. 30.0%; $p<0.001$). Diabetic NAFLD patients had a higher mean body mass index (BMI) compared to non-diabetic NAFLD patients (27.09±3.98 vs. 25.18±3.58 kg/m2; $p=0.01$). Most patients, both with diabetes (87.32%) and without diabetes (80%), had central obesity. Additionally, diabetic NAFLD patients exhibited higher waist circumference, hip circumference, waist-to-hip ratio, waist-to-height ratio, systolic blood pressure, and diastolic blood pressure when compared to non-diabetic NAFLD patients. Serum levels of ALT, AST, GGT, and ALP were significantly elevated in the diabetic group. While triglyceride levels, total cholesterol, LDL-cholesterol, and fasting insulin levels were also higher in diabetic NAFLD patients, these differences were not statistically significant. However, insulin resistance, as measured by HOMA-IR, was significantly higher in diabetic NAFLD patients. *Conclusion*: NAFLD patients with diabetes exhibit greater metabolic risk factors, including higher BMI, central obesity, hypertension, elevated triglyceride levels, and increased insulin resistance, all of which may contribute to the progression of non-alcoholic steatohepatitis (NASH) and advanced fibrosis. Notably, a substantial proportion of NAFLD patients without diabetes also display metabolic risk factors, highlighting the importance of recognizing NAFLD in individuals without diabetes.

**Keywords:** Non-Alcoholic Fatty Liver Disease (NAFLD), Chronic Liver Diseases

# 1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is characterized by the accumulation of lipids, particularly triglycerides (5-10%), in hepatocytes, constituting more than 5% of total liver weight, without other identifiable causes of liver damage, such as viral hepatitis, alcohol consumption, or metabolic disorders [1]. It was first named and described as nonalcoholic steatohepatitis (NASH) by Ludwig et al. in 1980. NAFLD encompasses a spectrum of liver conditions, ranging from simple steatosis to NASH, NASH-related cirrhosis, and hepatocellular carcinoma, often associated with metabolic syndrome [2]. The typical age range for NASH patients is 40-50 years, increasing to 50-60 years for those with NASH-related cirrhosis [3]. NAFLD has become increasingly prevalent worldwide, initially recognized primarily in industrialized countries but now also diagnosed more frequently in developing nations [4]. Studies conducted in various regions of India have indicated that the prevalence of NAFLD has risen over the past two decades, making it the most common liver disease in India [5]. In countries like China, Japan, and Korea, surveys have reported NAFLD prevalence rates ranging from 10% to 29%, which closely resemble figures from Western studies [6, 7]. While NAFLD was initially associated with obese individuals in affluent societies, this perception has evolved. Lean individuals are now being diagnosed with NAFLD, with 15% of NAFLD patients in developed countries being non-obese, while 65% and 85% are obese and morbidly obese, respectively [8]. Cross-sectional studies of NASH patients have shown that 30-40% present with advanced liver fibrosis, and 10-15% have established cirrhosis [9-11]. It is estimated that NASH is the underlying cause of approximately 80% of cryptogenic cirrhosis cases, accounting for 10%-20% of all cirrhosis cases and progressing to advanced fibrosis in 32%-37% of patients [12]. There is growing recognition that NAFLD is a heterogeneous disease with multiple pathogenic pathways, leading to diverse disease manifestations among patients [13]. Its pathogenesis is believed to involve a multi-hit process, including factors like insulin resistance, oxidative stress, apoptotic pathways, and adipocytokines [14]. Insulin resistance plays a predominant role in NAFLD pathogenesis, even in lean individuals with normal glucose tolerance [15, 16]. The "typical" NAFLD patient is likely to exhibit one or more metabolic disorders linked to insulin resistance, such as central or overall obesity, type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, or metabolic syndrome [17, 18]. Other factors, including drug use (e.g., Amiodarone, Methotrexate, Tamoxifen/synthetic estrogens, Glucocorticoids, Nucleoside analogues, Perhexiline maleate, Calcium channel blockers), specific bariatric surgeries (jejuno-ileal bypass), total parenteral nutrition, and inherited or acquired lipodystrophies, contribute to a small fraction of steatosis or steatohepatitis cases [17]. The incidence of T2DM is on the rise globally, reaching pandemic levels in countries like India and China [19]. Studies have shown that up to 78% of diabetic patients exhibit fatty liver on ultrasound examination [20], often accompanied by elevated serum alanine aminotransferase (ALT) levels [21, 22]. Patients with T2DM are at an increased risk of developing NAFLD, NASH, hepatic fibrosis/cirrhosis, and hepatocellular carcinoma [23-25]. Recent studies have revealed a positive correlation between insulin resistance and the severity of NAFLD, rather than the degree of hyperglycemia, in patients with T2DM [28]. Since metabolic syndrome and NAFLD share similar prevalence patterns, pathogenesis, clinical features, and outcomes [29], they are associated with an elevated risk of cardiovascular diseases, including increased carotid artery wall thickness and lower endothelial flow-mediated vasodilation, which independently predict the risk of future cardiovascular events [30]. Another recent study found that compared to matched Caucasians, Hispanics, Blacks, and Eastern Asians, lean, non-alcoholic, non-diabetic, non-smoking ethnic Asian Indians had a 2- to 3-fold increase in insulin resistance (IR) and a 2-fold increase in hepatic triglyceride content [31]. Recent concepts also suggest that the degree of adipose tissue dysfunction may have a greater metabolic impact than the severity of adiposity [32]. Obesity not only serves as a risk factor for NAFLD but also determines its severity [33]. Genetic factors also play a role in NAFLD predisposition. For instance, there is evidence of a familial component in NAFLD [34]. A recent study from the Dallas group [35] identified ethnic differences in variants of the PNPLA3 (Adiponutrin) gene, which are associated with varying susceptibility to NAFLD and its progression. Various diagnostic methods are available for NAFLD, including a combination of clinical and laboratory tests with imaging methods or liver biopsy [36]. Up to 70% of patients with fatty liver do not exhibit laboratory abnormalities [37]. Elevated serum levels of liver alanine aminotransferase (ALT), which correlates with liver fat independently of adiposity, and, to a lesser extent, aspartate aminotransferase (AST) can be detected [38]. Serum alkaline phosphatase and gamma-glutamyl transferase (GGT) levels are also mildly increased and associated with liver fat, independent of adiposity [39]. However, these markers are not more informative than aminotransferases for diagnosing steatosis or NASH [11]. Among imaging methods (ultrasonography, computed tomography, magnetic resonance imaging), magnetic resonance imaging/magnetic resonance spectroscopy (MRI/MRS) is considered the gold standard for diagnosing fatty liver, but it is cost-prohibitive [9]. Ultrasonography is safer, non-invasive, and more sensitive than computed tomography, providing adequate information about hepatic steatosis [40]. Given the invasive nature of liver biopsy and its limitations, noninvasive and reliable methods, such as the BARD score, the NAFLD fibrosis score, or fibro scan, are necessary for assessing fibrosis [41, 42]. A comprehensive comparative study between diabetic and non-diabetic NAFLD patients, with a specific focus on anthropometric, metabolic, and biochemical characteristics, has not yet been conducted in the Bangladeshi population. It is essential to investigate whether diabetic NAFLD patients experience a more severe form of the disease and are more

prone to developing NASH/fibrosis compared to non-diabetic NAFLD patients. The objective of this study was to examine the anthropometric, metabolic, and biochemical features of NAFLD patients with and without diabetes.

# 2. Objective

### *2.1. General Objective*

The objective of this study was to investigate the anthropometric, biochemical, and metabolic characteristics of individuals with non-alcoholic fatty liver disease (NAFLD), both with and without diabetes.

### *2.2. Specific Objectives*

1) To assess height, weight, waist circumference, and hip circumference.
2) To compute the Body Mass Index (BMI), waist-to-hip ratio, and waist-to-height ratio.
3) To measure the blood pressure of study population.
4) To determine fasting blood sugar levels, measure blood sugar levels two hours after consuming a 75-gram glucose solution, and assess HbA1C.
5) To measure the fasting serum insulin and calculate the insulin resistance index.
6) To diagnose DM according to WHO.
7) To diagnose the metabolic syndrome.

# 3. Methodology

This was a hospital based observational prospective study. For this study a total of 111 patients including male and female were selected by purposively, those are with ultra-sonographic evidence of fatty liver attending and those who are GHPD outpatient. The study was conducted at the department of Gastrointestinal Hepatobiliary, BIRDEM General Hospital, Dhaka, Bangladesh from April, 2014 to April, 2015.

### *3.1. Inclusion Criteria*

Patients were ultrasonographycally diagnosed as fatty liver without alcohol use or occasional use (< 30gram alcohol per day in men, and < 20 gram in women).

### *3.2. Exclusion Criterias*

1) Patients with chronic liver disease (e.g.: Hepatitis B and C, hemochromatosis, Wilson’s disease, autoimmune disease etc.).
2) Patients who take hepatotoxic drugs (e.g.; estrogens, amiodarone, methotrexate, tamoxifen, neucloside analogue) during the past 6 months.
3) Patients with systemic comorbidities (e.g.; COPD, renal failure, cardiac failure), neoplastic disease, hypothyroidism, hypogonadism and polycystic ovarian syndrome.
4) Patients with raised ALP by bone disease (e.g.; Renal osteodystrophy, fractured bone, osteomalacia, vitamin-D deficiency, Paget's disease).
5) Patients with <18 and >70 years of age.

### *3.3. Study Procedure*

Comprehensive medical histories were obtained for each patient, including details about diabetes mellitus, hypertension, dyslipidemia, metabolic syndrome, smoking habits, alcohol consumption, medications, and family history of diabetes mellitus and obesity. Exclusion criteria involved the following: significant alcohol misuse (defined as < 30 grams of alcohol per day in men and < 20 grams in women), evidence of hepatitis B and C, indications of drug-induced fatty liver or other specific liver conditions such as hemochromatosis, Wilson's disease, or autoimmune liver disease. Additional diseases like coronary artery diseases, chronic kidney diseases, cerebrovascular and peripheral vascular disease, hypothyroidism, chronic and acute inflammatory conditions, asthma, and chronic bronchial diseases were also excluded from the study. Patients underwent a physical examination, during which various anthropometric measurements were taken, including height, weight, body mass index (BMI), waist circumference (WC), and hip circumference (HC). The waist-to-height ratio was also calculated by dividing the waist measurement by the height measurement, with values greater than 0.53 for males and 0.50 for females considered as indicative of overweight. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after 15 minutes of resting in a seated position using an appropriately sized cuff and sphygmomanometer. The mean value of the two blood pressure measurements was recorded. Blood samples were collected from the antecubital vein of all participants after a 12-hour fast. These samples were placed in vacuum tubes with anticoagulant and gel, allowed to clot for 30 minutes, and then centrifuged for 15 minutes at 2000 x g at room temperature. All biochemical measurements were conducted on the same day. Enzymatic colorimetric methods were used to measure blood glucose, triglycerides (TG), total cholesterol, high-density lipoprotein (HDL-C) cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma glutamyl transpeptidase (GGT). Low-density lipoprotein-cholesterol (LDL-C) levels were calculated using Friedewald's formula [LDL = TC - HDL - TG/5 (mg/dL)]. Insulin levels were assessed using an indirect solid-phase chemiluminescence immunoassay. Diabetes mellitus was diagnosed according to WHO criteria. Insulin resistance (IR) was determined using the homeostatic model assessment (HOMA) score, which involves a mathematical model based on fasting blood glucose and fasting plasma insulin [fasting serum insulin (μunits/ml) × fasting plasma glucose (mmol/l)]/22.5, as described by Matthews et al. in 1985. Individuals with a HOMA-IR value greater than 2.0 were considered to have insulin resistance in this study.

### *3.4. Statistical Analysis*

Statistical analyses were conducted using SPSS version 16.0.

Normally distributed continuous variables were presented as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. Differences in continuous variables were assessed using Student's t-test, and for comparisons involving three or more means, an Analysis of Variance (ANOVA) test was employed to determine statistical significance. Categorical variable differences were analyzed using Pearson's Chi-square (X^2) test. The threshold for statistical significance was set at a p-value of < 0.05, with a confidence interval of 95%.

### *3.5. Ethical Considerations*

This study received approval from the Ethical Review Committee of BIRDEM General Hospital. The study's objectives, procedures, alternative diagnostic methods, risks, and benefits were explained to the patients in a clear and easily understandable local language. Informed consent was obtained from each patient, with an assurance of maintaining confidentiality of all records. Patients were also informed that the procedure would be beneficial for both the physician and patients in guiding the management of the case.

## 4. Results

All 111 patients with ultrasonographic evidence of fatty change in liver (NAFLD) were included in this study. NAFLD patient after attending at GHPD OPD with certain inclusion criteria were selected in this study as study subjects. Frequency of NAFLD with and without DM and correlation with clinical, laboratory and radiological findings were obtained. Among 111 study population 71 (63.96%) patients were diabetics and 40 (36.04%) patients were non-diabetics based on blood glucose values.

***Table 1.*** *Age distribution of the patients. (N=111).*

| Age in years | Study group | | Total |
|---|---|---|---|
| | DM (n=71) | Non DM (n=40) | |
| 21-30 yrs. | 4 | 3 | 7 |
| 31-40 yrs. | 21 | 15 | 36 |
| 41-50 yrs. | 24 | 15 | 39 |
| 51-60 yrs. | 15 | 6 | 21 |
| > 60 yrs. | 7 | 1 | 8 |
| Mean ±SD | 47.15±10.26 | 43.35±10.7 | 45.8±10.5 |
| Duration of DM (Year) | 7.56±4.3 | | |

Table 1 showed the mean age of the sample was 45.8±10.5 years. Relative to patients without DM, patients with DM were older (47.15±10.26 vs. 43.35±10.7 years) and most of the affected individuals were aged 31 to 50 years (63.38% vs. 75%) and the remainder were aged <31 years (5.71% vs. 7.5%) and aged >60 years (9.8% vs. 2.5%). In diabetic patients, mean duration of diabetes was 7.56±4.3 years.

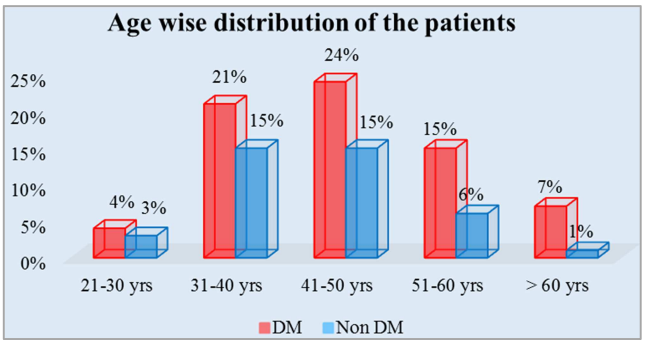


***Figure 1.*** *Column chart showed group wise age distribution of the patients (N=111).*

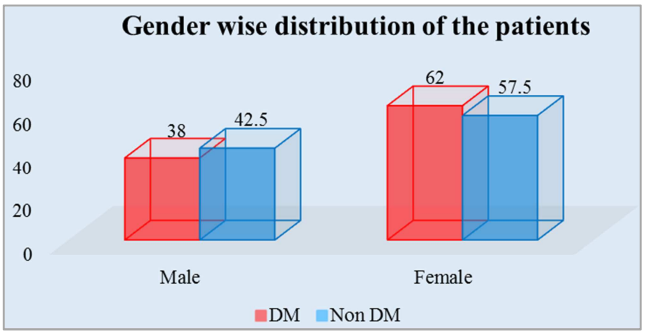


***Figure 2.*** *Column chart showed gender wise distribution of patients. (N=111).*

Figure 2 showed out of 111 cases, 67 were females (60.36%) and 44 were males (39.63%). Female to male ratio was 1.52. Relative to patients without DM, patients with DM had higher proportion of females (62.0% vs. 57.50%).

***Table 2.*** *Co-morbidities of the study groups (N=111).*

| Co-morbidity | Study group N=111 | | Total | p value |
|---|---|---|---|---|
| | DM (71) | Non-DM (40) | | |
| Hypertention, n (%) | | | | |
| Yes | 55 (77.47) | 16 (40.0) | 71 | <0.001 |
| No | 16 (22.53) | 24 (60.0) | 40 | |
| Dyslipidaemia, n (%) | | | | |
| Yes | 46 (64.79) | 16 (40.0) | 62 | 0.01 |
| No | 25 (35.21) | 24 (60.0) | 49 | |
| Metabolic syndrome, n (%) | | | | |
| Yes | 53 (74.64) | 12 (30.0) | 65 | <0.001 |
| No | 18 (25.36) | 28 (70.0) | 46 | |

Table 2 showed co-morbidities like hypertension, dyslipidaemia and metabolic syndrome were present in (71, 63.96%), (62, 55.86%) and (65, 58.56%) respectively of the total patients. Relative to patients without DM, patients with

DM had higher prevalence of hypertension (55, 77.47% vs. 16, 40%; p < 0.001), dyslipidaemia (46, 64.79% vs. 16, 40%; p=0.01) and metabolic syndrome (53, 74.64% vs. 12, 30%; p < 0.001) respectively and this differences were statistically significant.

***Table 3.*** *BMI of the study population (N=111).*

| Body mass index-BMI (Kg/m$^2$) | Study group | | Total | p value |
|---|---|---|---|---|
| | DM | Non DM | | |
| Normal | 15 | 19 | 34 (30.63%) | 0.01* |
| Over weight | 20 | 09 | 29 (26.13%) | |
| Obese | 36 | 12 | 48 (43.24%) | |
| Total | 71 | 40 | 111 | |
| Mean±SD | 27.09±3.98 | 25.18±3.58 | 26.40±3.92 | 0.01** |

Table 3 showed the normal BMI were (34, 30.63%), overweight were (29, 26.13%) and obese were (48, 43.24%) of the total patients, according to the criteria for Asians population. The mean body mass index (BMI) of diabetic patients were significantly higher than non-diabetic patients (27.09±3.98 vs. 25.18±3.58 kg/m$^2$; p=0.01).

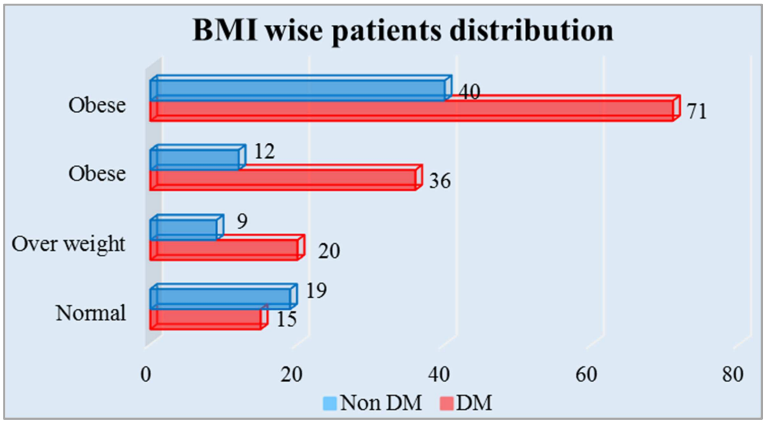


***Figure 3.*** *Bar chart showed BMI status of the patients (N=111).*

***Table 4.*** *Central obesity of the study groups (N=111).*

| Variable | Study group | | Total | p value |
|---|---|---|---|---|
| | DM | Non DM | | |
| | Mean±SD | Mean±SD | | |
| Waist circumference (cm) | 94.47±8.61 | 92.35±8.21 | 93.71±8.5 | 0.30 |
| Hip circumference (cm) | 98.28±8.8 | 97.6±8.4 | 98.1±8.6 | 0.72 |
| Waist/hip Ratio | 0.95±0.02 | 0.92±0.80 | 0.94±0.05 | 0.01 |
| Waist /height Ratio | 0.70±0.28 | 0.60±0.17 | 0.66±0.25 | 0.03 |
| Central obesity | | | | |
| Central obesity absent | 09 (12.68%) | 08 (20%) | 17 | |
| Central obesity present | 62 (87.32%) | 32 (80%) | 94 | |
| Total | 71 | 40 | 111 | |

Table 4 illustrates that the prevalence of central obesity was higher in patients with diabetes (62, 87.32%) compared to those without diabetes (32, 80%). This was evident in the significantly greater measurements of waist circumference, hip circumference, and waist-to-hip ratio, with values of (94.47±8.61 vs. 92.35±8.21 cm; p=0.20), (98.28±8.8 vs. 97.6±8.4 cm; p=0.72), and (0.95±0.02 vs. 0.92±0.80; p=0.01), respectively. Additionally, another indicator of visceral obesity, namely the waist-to-height ratio, was also significantly higher in the diabetic group, with values of (0.70±0.28 vs. 0.60±0.17; p=0.03).

***Table 5.*** *Blood pressure of the study groups (N=111).*

| Blood pressure | Study group | | Total | p value |
|---|---|---|---|---|
| | DM (71) | Non DM (40) | | |
| | Mean±SD | Mean±SD | | |
| Systolic blood pressure (mm of Hg) | 139.76±15.89 | 135.0±15.23 | 138.04±15.76 | 0.01 |
| Diastolic blood pressure (mm of Hg) | 85.0±10.31 | 83.50±11.10 | 84.45±10.58 | 0.03 |

Table 5 presents the mean systolic and diastolic blood pressure values for the study sample, which were recorded as

138.04±15.76 mm Hg and 84.45±10.58 mm Hg, respectively. Notably, when comparing diabetic patients to non-diabetic patients, it was evident that the diabetic group had significantly higher systolic and diastolic blood pressure readings, with values of [(139.76±15.89; 135.0±15.23 mm Hg; p=0.01)] as opposed to [(85.0±10.31; 83.50±11.10 mm Hg; p=0.03)] in the non-diabetic group.

***Table 6.*** *Liver enzymes of the study population (N=111).*

| Liver enzymes | Study group | | Total | p value |
|---|---|---|---|---|
| | DM (71) | Non DM (40) | | |
| | Mean±SD | Mean±SD | | |
| ALT (IU/L) | 81.45±58.27 | 69.65±52.73 | 48.72±32.34 | 0.001 |
| AST (IU/L) | 57.84±41.82 | 50.89±38.54 | 38.55±28.38 | 0.01 |
| GGT (IU/L) | 39.39±13.29 | 36.08±13.72 | 30.20±12.59 | 0.001 |
| Alkaline phosphatase (IU/L) | 114.64±27.96 | 112.26±26.34 | 108.02±22.93 | 0.20 |
| ALT/AST Ratio | 1.40±0.38 | 1.34±0.37 | 1.24±0.32 | 0.02 |
| AST/ALT Ratio | 0.77±0.26 | 0.76±0.22 | 0.75±0.14 | 0.76 |

Table 6 showed liver enzymes like ALT, AST, GGT, ALP levels, ALT/AST ratio and AST/ALT ratio were (81.45±58.27 vs. 48.72±32.34 U/L; p=0.001), (57.84±41.82 vs. 38.55±28.38 U/L; p= 0.01), (39.39±13.29 vs. 30.20±12.59 U/L; p=0.001), (114.64±27.96 vs. 108.02±22.93 U/L; p= 0.02), (1.37±0.39 vs. 1.24±0.28; p=0.07), (0.76± 0.26 vs. 0.81±0.18; p=0.24) respectively. Among them ALT, and GGT were significantly higher in NAFLD diabetic group.

***Table 7.*** *Metabolic parameters of study population (N=111).*

| Metabolic profile | Study group | | Total | p value* |
|---|---|---|---|---|
| | DM | Non DM | | |
| | Mean±SD | Mean±SD | | |
| S. Triglyceride (mg/dl) | 246.64±143.93 | 229.80±143.11 | 240.6±143.2 | 0.55 |
| S. Total cholesterol (mg/dl) | 187.67±49.22 | 175.12±48.03 | 183.2±48.9 | 0.19 |
| S.HDL-cholesterol (mg/dl) | 36.05±6.14 | 35.75±5.85 | 35.9±6.0 | 0.79 |
| S.LDL-cholesterol (mg/dl) | 97.64 (±27.18) | 94.15±28.37 | 96.5±27.5 | 0.55 |
| Fasting insulin (µU/ml) | 19.52±19.19 | 14.79±11.0 | 17.8±16.8 | 0.15 |
| Insulin resistance index (HOMA-IR) | 2.98±1.85 | 2.0±0.85 | 2.63±1.6 | 0.002 |

Table 7 presents the metabolic parameters, such as triglyceride levels (246.64±143.93 vs. 229.80±143.11 mg/dl; p=0.55), which were relatively higher in the NAFLD diabetic group. Conversely, low HDL-cholesterol levels were equally prevalent (36.05±6.14 vs. 35.75±5.85 mg/dl; p=0.79) in both diabetic and non-diabetic patients with NAFLD. Total cholesterol (187.67 ± 49.22 vs. 175.12±48.03 mg/dl; p=0.19), LDL-cholesterol (97.64±27.18 vs. 94.15±28.37 mg/dl; p=0.55), and serum fasting insulin (19.52±19.19 vs. 14.79±11.0 µU/ml; p=0.15) were relatively higher in diabetic NAFLD patients, although these differences did not reach statistical significance. However, insulin resistance, as measured by HOMA-IR, was notably higher in the NAFLD group with diabetes (2.98±1.85 vs. 2.0±0.85; p=0.002), and this difference was statistically significant.

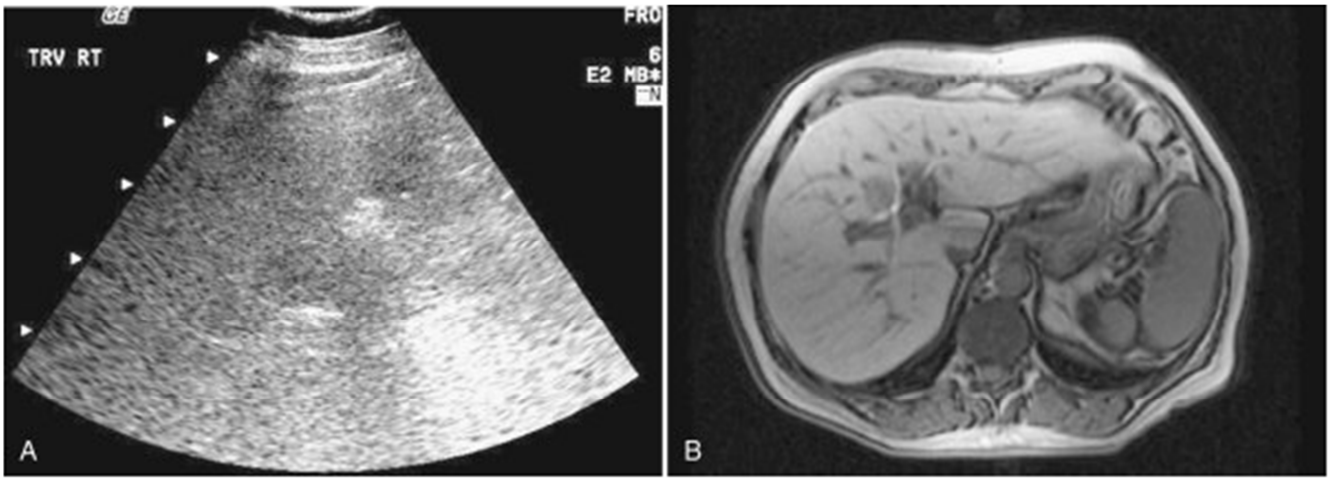


***Figure 4.*** *Diagram: A, Ultrasound revealing elevated echogenicity. B, Magnetic resonance image on T1-weighted sequence displaying a highly illuminated fatty liver.*

# 5. Discussion

Certainly, here is the revised passage with the reference number included:

"Non-alcoholic fatty liver disease (NAFLD) has emerged as the most common liver disease in the 'Western' economies. Prevalence of nonalcoholic fatty liver disease is rising in the Asia-Pacific region as the society becomes affluent and traditional lifestyles change (increasing fat in the diet, less physical activity, increasing prevalence of type 2 diabetes) [43]. BIRDEM hospital is a tertiary care 'center of excellence for both diabetic and non-diabetic care' hospital, and the patients are referred from all across the country. The anthropometric, biochemical and metabolic differences in non-alcoholic fatty liver disease with or without diabetes had not been previously examined in Bangladesh. Non-alcoholic fatty liver disease (NAFLD) represents a continuum of disease, characterized histologically by excessive accumulation of hepatic fat in the absence of significant alcohol consumption; with or without inflammation, varying degree of fibrosis, and cirrhosis. A number of studies have found a positive relationship between NAFLD and abnormal glucose tolerance. A total of 111 patients with ultra-sonographic evidence of fatty change in liver (NAFLD) were included in this study. Among them 71, (63.96%) were diabetics and 40, (36.04%) were non-diabetics. This is quite high as compared to a previous large population-based Indian study from Coastal Eastern India where the prevalence has been reported to be round 24.08% and 23.00% respectively [43]. Most of our NAFLD patients were between 31 and 50 years of age; this result is similar to that of several reports from Asia [45-48]."

Compared with NAFLD patients without diabetes, patients with diabetes were older (47.15 years vs. 43.35 years). However, age does not affect the development of NAFLD/NASH. The female predominance in NAFLD contrasts with reports from developed countries. The female predominance (60.36%) observed in this study may be a result of socially conservative attitudes that led many women in my study to stay at home and participate in household chores without no job, which leads to a sedentary life. Female predominance was also observed in a population study conducted in India (49). NAFLD is more common in people with a sedentary lifestyle. Based on occupation, the majority of our patients, both DM and non-DM, were housewives (45.04%), but also businessmen (26.12%), military personnel (19.81%). and retirees (7.20%). This figure is quite on par with previous research based on the Bangladeshi population, where housewives, service workers and entrepreneurs were (53.1%), (14.6%), (13,0%) [45]. When NAFLD patients with diabetes were compared with NAFLD patients without diabetes, components of the metabolic syndrome such as central obesity, increased triglyceride levels, and hypertension were more common. in the previous group. This finding is not surprising because diabetes is a manifestation of the metabolic syndrome, which is closely related to NAFLD. This supports the fact that there is a strong association between the different components of the metabolic syndrome, but it is difficult to determine whether diabetes is a risk factor for developing fatty liver and its characteristics. different scores of metabolic syndromes or not after this study. This study observed that hypertension, dyslipidemia and metabolic syndrome appeared in (71, 63.96%), (62, 55.86%) and (65, 58.56%) respectively. of the total number of patients. Compared with patients without diabetes, patients with diabetes had a higher rate of hypertension (55, 77.47% vs. 16, 40%; $p < 0.001$), dyslipidemia (46, 64.79% vs. 11.2). 16.40%; $p = 0.01$) and metabolic syndrome (53, 74.64% vs. 12, 30%; $p < 0.001$). A similar result has been observed in population studies [43, 50]. Prashanth et al 2009 [51] found a high prevalence of NAFLD and NASH (nonalcoholic steatohepatitis) in patients with type 2 diabetes, which increased with many components of metabolic syndrome. chemistry. Banerjee et al. In 2008 [52] observed that, histologically, there was only fatty changes in 43%, NASH in 40% and more advanced disease in 23% of diabetic NAFLD patients. Obesity, especially central obesity, has been described as one of the most important risk factors for NAFLD and fibrosis, with NASH prevalent in 18.5% of obese patients [9].

The combination of diabetes and obesity may pose an additional risk. In a study of severely obese diabetic patients, 100% had at least mild steatosis, 15% had steatohepatitis, and 19% had cirrhosis [53]. In this study, BMI was in the normal range in patients (34, 30.63%), overweight (29, 26.13%), and obese (48, 43.24%), according to European population criteria. ASIAN. This result is different from the population study conducted in Bangladesh, where normal, overweight, and obese BMI were 13.5%, 8.1%, and 75.1%, respectively [45]. The mean body mass index (BMI) of diabetic patients was significantly higher than that of nondiabetic patients (27.09 ± 3.98 vs. 27.09 ± 3.98). 25.18 ± 3.58 kg/m2). These were quite similar in patients (26.6 ± 3.9 vs. 26.3 ± 3.9 $kg/m^2$) to a previous large-scale study based on the east coast of India and were quite low. in the United States, reported at 37 versus 35 kg/m2 [54]. Most patients showed central obesity (94, 84.68%). The presence of central obesity was higher in diabetic patients (62, 87.32%) than in non-diabetic patients (32, 80%) because they had waist circumference, hip circumference, waist/hip ratio and waist/height ratio were significantly higher (94.47 ± 8.61 vs. 92.35 ± 8.21 cm; $p = 0.20$), (98.28 ± 8, 8 vs. 97.6 ± 8.4 cm; $p=0.72$), (0.95±0.02 vs. 0.92±0.80; $p=0.01$), (0.70±0.28 vs. 0.60 ±0.17; $p=0.03$) respectively. According to a Japanese report, the incidence of NAFLD is higher after increasing BMI or abdominal circumference. Liver enzymes are usually only mildly elevated, usually hepatocellular, in NAFLD patients and in the most common presentation in patients. NAFLD accompanied by elevated liver enzymes is associated with a risk of developing clinically significant end-stage liver disease (57). In this study, the average liver enzyme concentrations ALT, AST, GGT, ALP, ALT/AST and AST/ALT ratio were 69.65 ± 52.73, 50.89 ± 38.54, 36, respectively. 0.08 ± 13.72, 112.26 ± 26.34, 1.34 ±.37, and.76

±.22. Similar results were observed in a study performed in Linköping, Sweden, where the mean ALT, AST, ALP, and AST/ALT ratios were 76 ± 43 U/L, 45 ± 50 U/L, respectively. 23 U/L, 61 ± 33. U/ L, 0.6 ± 0.2. [57] and a study from Bangladesh, where mean ALT, AST, and GGT levels were 56.7 ± 35.9 U/L, 46.6 ± 50.5 U/L, and 46.2 ± 28, respectively. 0.6 U/L [45]. In this study conducted on diabetic and non-diabetic patients, the results of liver enzyme measurements such as ALT, AST, GGT, ALP concentrations, ALT/AST ratio and AST/ALT ratio were respectively (81.45±58.27 vs. 48.72±32.34 U/L; p=0.001), (57.84±41.82 vs. 38.55±28.38 U/L; p=0, 01), (39.39±13.29 vs. 30.20±12.59 U/L; p=0.001), (114.64±27.96 vs. 108.02±22.93 U/L; p=0.02), (1.37 ± 0.39 vs. 1.24 ± 0.28; p = 0.07), (0.76 ± 0.26 vs. 0.81 ± 0.18; p = 0.24). Among them, ALT and GGT were significantly higher in the diabetic NAFLD group. A similar result was observed in a US population study that reported ALT, AST/ALT as (64.18 ± 49.21 vs. 78.49 ± 60.09 U/L; p = 0.004), (0.92 ± 0.35 vs. 0.79 ± 0.37; p < 0.001). corresponding. Alanine aminotransferase has been observed to be more than twice normal in 20% of children with T2DM and this in most cases is due to NAFLD [2].

In the case of simple steatosis and steatohepatitis, triglycerides are known to be the main type of lipid that accumulates in the liver. Therefore, lipid profile is necessary to understand the pathogenesis of NAFLD. Our study observed relatively higher triglyceride levels (246.64 ± 143.93 vs. 229.80 ± 143.11 mg/dl; p = 0.55) in the NAFLD group with diabetes. road. Low HDL cholesterol levels were also present (36.05 ± 6.14 vs. 3.05 ± 6.14). 35.75 ± 5.85 mg/dL; p = 0.79) persisted in diabetic and non-diabetic patients. Total cholesterol (187.67 ± 49.22 vs. 175.12 ± 48.03 mg/dl; p = 0.19), LDL cholesterol (97.64 ± 27.18 vs. 94.15 ± 28.37 mg/dl; p = 0.55) and fasting serum insulin (19.52 ± 7:19 p.m. vs. 12:19 p.m.). 14.79 ± 11.0 μU/ml; p = 0.15) was relatively higher in NAFLD diabetic patients, but not statistically significant. This result is similar to that of a previous study based on an Indian population from the east coast of India, where triglycerides and total cholesterol were reported to be round (218.40 ± 17.60 vs. with 192.00 ± 9.00 mg/dl), (183.80 ± 65.00 vs. 186.50 ± 49.00 mg/dl), respectively [43]. NAFLD is strongly associated with insulin resistance (IR) and other components of the metabolic syndrome, such as type 2 diabetes, central obesity, hyperlipidemia, and hypertension [50]. NAFLD has also been shown to be associated with IR independently of BMI, and studies have reported that IR is commonly present in non-obese NAFLD patients, even in the absence of metabolic disorders other [58, 59]. The pathogenesis of NASH appears to be a multifactorial process. The initial insult is the development of large vesicular steatosis with accumulation of fat in the liver due to reduced hepatic oxidation of free fatty acids and/or increased hepatic denovo lipogenesis and /or reduced lipid export from the liver. Although IR can contribute to dysregulation of lipid metabolism, once fatty liver develops, it can exacerbate hepatic IR and diabetes, contributing to a vicious cycle [60]. In this study, insulin resistance measured by HOMA-IR was naturally higher in the diabetic NAFLD group (2.98 ± 1.85 vs. 2.98 ± 1.85). 2.0 ± 0.85; p=0.002) and this difference is statistically significant. This result is comparable to that of a previous large Indian population-based study in which HOMA-IR was (2.6 ± 0.36 vs. 1.84.0 ± 0.20; p = 0.000) [43]. In a Bangladeshi population-based study, HOMA-IR was compared with obese and non-obese individuals and the results were not significant [44].

# 6. Limitations of the Study

1) The study focused on a specific hospital in Dhaka city, so the findings may not accurately represent the entire country.
2) Due to time limitations associated with conducting this study as part of a thesis, it was challenging to gather a sufficient number of samples within a short timeframe.

# 7. Recommendations

Additional research is warranted, including larger sample sizes and long-term, biopsy-controlled prospective cohort studies.

# References

[1] Neuschwander-Tetri BA and Caldwell SH, 2003. Nonalcoholic Steatohepatitis: Summary of an ASLD Single Topic Conference. Hepatology 37: 1202-1219.

[2] Angulo P. 2002. Nonalcoholic Fatty Liver Disease. N Engl J Med 346: 1221-1231.

[3] Sheth M, Riggs M, Patel T. Utility of the Mayo End-Stage Liver Disease (MELD) score in assessing prognosis of patients with alcoholic hepatitis. BMC Gastroenterol. 2002; 2:2. doi: 10.1186/1471-230x-2-2. Epub 2002 Jan 22. PMID: 11835693; PMCID: PMC65516.

[4] Cotter TG, Rinella M. Nonalcoholic Fatty Liver Disease 2020: The State of the Disease. Gastroenterology. 2020 May; 158 (7): 1851-1864. doi: 10.1053/j.gastro.2020.01.052. Epub 2020 Feb 13. PMID: 32061595.

[5] Singh, S. P., Nayak, S., Swain, M., Rout, N., Mallick, R. N., Agarwal, O., Meher, C. and Rao, M. 2004. Prevalence of Nonalcoholic Fatty Liver Disease in Coastal Eastern India: A Preliminary Ultrasonographic Survey. Tropical Gastroenterology. 25 (2): 76-9.

[6] Fan JG, Zhu J, Li XJ et al. 2005. Fatty liver and the metabolic syndrome among Shanghai adults. J. Gastroenterol. Hepatol. 20: 1825-32.

[7] Fan JG, Saibara T, Chitturi S, Sung JJY, Kim BI, Chutaputti A, 2007. The Asia–Pacific working party for NAFLD. What are the risk factors and settings for non-alcoholic fatty liver disease in Asia–Pacific? J. Gastroenterol. Hepatol. 22: 794-800.

[8] Younossi ZM, Stepanovo M, Fang Y, Younossi Y, Mir H, Shrishard M. 2011. Changes in prevalence of the most common causes of chronic liver disease in United States from 1988 to 2008. Clin Gastroenterol Hepatol. 9 (6): 524-30.

[9] Sanyal AJ. 2002. AGA technical review on nonalcoholic fatty liver disease. Gastroenterology; 123: 1705-25.

[10] Fassio, E, Alvarez, E, Dominguez, N, Landeira, G. and Longo, C, 2004. Natural history of nonalcoholic steatohepatitis: a longitudinal study of repeat liver biopsies. Hepatology 40: 820-826.

[11] Angulo P, Lindor KD, 2002. Non-alcoholic fatty liver disease. J Gastroenterol Hepatol 17 (Supp-1): S186-S190.

[12] Grattagliano I, Portincasa P, Palmieri VO, Palasciano G, 2007. Managing nonalcoholic fatty liver disease: recommendations for family physicians. Can Fam Physician, 53: 8.

[13] Z. M. Younossi, M. J. Reyes, A. Mishra, R. Mehta, L. Henry. 2014. Systematic review with meta-analysis: non-alcoholic steatohepatitis- a case for personalised treatment based on pathogenic targets Aliment. Pharmacol. Ther. 39 (1): 3-14.

[14] Hui JM, Hodge A, Farell GC, Kench JG, Kriketos A, George J, 2004. Beyond Insulin resistance in NASH; TNF alpha or adiponectin. Hepatology. 40: 46-54.

[15] E. Bugianesi, A. J. McCullough, G. Marchesini, 2005. Insulin resistance: a metabolic pathway to chronic liver disease. Hepatology, 42 (5), pp. 987–1000.

[16] Marchesini G, Bugianesi E, Forlani G, Cerrelli F, Lenzi M, Manini R, et al. 2003. Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. Hepatology. 37: 917-923.

[17] Chitturi S, Farrell GC, 2001. Etiopathogenesis of nonalcoholic steatohepatitis. Semin. Liver Dis. 21: 27-41.

[18] Chitturi S, Farrell G, Frost L, et al. 2002. Serum leptin in NASH correlates with hepatic steatosis but not fibrosis: a manifestation of lipotoxicity? Hepatology 36 (2): 403-409.

[19] Wild S, Roglic G, Green A, Sicree R, King H. 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care; 27, 1047-53.

[20] Stone BG, Van Thiel DH. 1985. Diabetes mellitus and the liver. Semin Liv Dis. 5: 828.

[21] Foster KJ, Griffith AH, Dewbury K, et al. 1980. Liver disease in patients with diabetes mellitus. Postgrad Med J. 56: 767–772.

[22] Silverman JF, Pories WJ, Caro JF. 1989. Liver pathology in diabetes mellitus and morbid obesity. Clinical, pathological, and biochemical considerations. Pathol Annu. 24: 275-302.

[23] H. B. El-Serag, T. Tran, J. E, 2004. Everhart. Diabetes increases the risk of chronic liver disease and hepatocellular carcinoma. Gastroenterology, 126 (2) pp. 460–468.

[24] Hossain N, Afendy A, Stepanova M, Nader F, Srishord M, Rafiq N, et al. 2009. Independent predictors of fibrosis in patients with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol. 7 (11): 1224-9.

[25] Neuschwander-Tetri, B. A, Clark, J. M, Bass, N. M, Van Natta, M. L, Unalp-Arida, A, Tonascia, J. et al. 2010. Clinical, laboratory and histological associations in adults with nonalcoholic fatty liver disease. Hepatology 52: 913-924.

[26] Tolman KG, Fonseca V, Tan MH, Dalpiaz A. 2004. Narrative review: hepatobiliary disease in type 2 diabetes mellitus. Ann Intern Med 21; 141: 946-56.

[27] Roberto De Marco, Francesca Locatelli, Giacomo Zoppini, Giuseppe Verlato, Enzo Bonora, Michele Muggeo. 1999. Cause -Specific Mortality in Type 2 Diabetes- The Verona Diabetes Study. Diabetes Care. 22: 756-61.

[28] Das, S, Singh, S. P, Parida, P. K. and Mallick, R. N, 2010. Non-Alcoholic Fatty Liver Disease in Subjects with Type 2 Diabetes Mellitus and Non-Diabetics with Special Reference to Insulin Resistance and Hepatic Histopathological Changes. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 4, 226-229.

[29] Loria P, Lonardo A, Carulli L, Verrone AM, Ricchi M, Lombardini S, et al. 2005. Review article: the metabolic syndrome and non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 22 (Suppl-2): 31-6.

[30] Targher G, Arcaro G. 2007. Non-alcoholic fatty liver disease and increased risk of cardiovascular disease. Atherosclerosis. 191 (2): 235-40.

[31] Petersen KF, Dufour S, Feng J, Befroy D, Dziura J, Man CD, et al. 2006. Increased prevalence of insulin resistance and nonalcoholic fatty liver disease in Asian-Indian men. Proc Nat Acad Sci. 103: 18273-27.

[32] Succurro E, Marini MA, Frontoni S, Hribal ML, Andreozzi F, Lauro R, et al. 2008. Insulin secretion in metabolically obese, but normal weight, and in metabolically healthy but obese individuals. Obesity (Silver Spring). 16: 1881-6.

[33] Fabbrini E, Sullivan S, Klein S, 2010. Obesity and nonalcoholic fatty liver disease: Biochemical, metabolic, and clinical implications. Hepatol. 51: 679-89.

[34] Osterreicher C. H. and D. A. Brenner, 2007. The genetics of nonalcoholic fatty liver disease. Ann Hepatol. 6 *(2)*: 83-*8.*

[35] Romeo S*,* Kozlitina J*,* Xing C*,* Pertsemlidis *A,* Cox D*,* Pennacchio LA*,* Boerwinkle E*,* Cohen JC*,* Hobbs HH. *2008.* Genetic variation in PNPLA3 confers susceptibility to nonalcoholic fatty liver disease. Nat Genet. 40 (12): 1461-5.

[36] Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, Charlton M, Sanyal AJ, Jun 2012. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 55 (6): 2005-23.

[37] Browning, J. D, Szczepaniak, L. S, Dobbins, R, Nuremberg, P, Horton, J. D, Cohen, J. C. et al. 2004b. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. Hepatology 40: 1387-1395.

[38] Kotronen A, Westerbacka J, Bergholm R, Pietilainen KH, Yki-Jarvinen H, 2007. Liver fat in the metabolic syndrome. J Clin Endocrinol Metab 92: 3490–3497.

[39] Thamer C, Tschritter O, Haap M, Shirkavand F, Machann J, Fritsche A, Schick F, Haring H, Stumvoll M 2005. Elevated serum GGT concentrations predict reduced insulin sensitivity and increase intrahepatic lipids. Horm Metab Res 37: 246-251.

[40] Di Lelio A, Cestari C, Lomazzi A, Beretta L, 1989. Cirrhosis: diagnosis with sonographic study of the liver surface. Radiology. 172 (2): 389–92.

[41] Dowman, J. K, Tomlinson, J. W. and Newsome, P. N. 2011. Systematic review: the diagnosis and staging of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. Aliment Pharmacol Ther 33: 525-540.

[42] Wong, V. W., Vergniol, J., Wong, G. L., Foucher, J., Chan, H. L., Le Bail, B. et al. 2010. Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. Hepatology 51: 454-462.

[43] Shivaram Prasad Singh, Ayaskanta Singh, Girish Kumar Pati, Bijay Misra, Debasis Misra, Sanjib Kumar Kar, et al. 2014. A Study of Prevalence of Diabetes and Prediabetes in Patients of Non-Alcoholic Fatty Liver Disease and the Impact of Diabetes on Liver Histology in Coastal Eastern India. Journal of Diabetes Mellitus. 4, 290-296.

[44] Shahinul Alam & Utpal Das Gupta & Mahbubul Alam & Jahangir Kabir & Ziaur Rahman Chowdhury & A. K. M. Khorshed Alam. 2014. Clinical, anthropometric, biochemical, and histological characteristics of nonobese nonalcoholic fatty liver disease patients of Bangladesh. Indian Society of Gastroenterology. 33 (5): 452-7.

[45] Shahinul Alam, Sheikh Mohammad Noor-E-Alam, Ziaur Rahman Chowdhury, Mahabubul Alam, Jahangir Kabir. 2013. Nonalcoholic steatohepatitis in nonalcoholic fatty liver disease patients of Bangladesh. World J Hepatol. 5 (5): 281-287.

[46] Sheth SG, Gordon FD, Chopra S. 1997. Nonalcoholic steatohepatitis. Ann Intern Med 126 (2): 137-145.

[47] Li H, Wang YJ, Tan K, Zeng L, Liu L, Liu FJ, Zhou TY, Chen EQ, Tang H, 2009. Prevalence and risk factors of fatty liver disease in Chengdu, Southwest China. Hepatobiliary Pancreat Dis Int; 8: 377-382.

[48] Park SH, Jeon WK, Kim SH, Kim HJ, Park DI, Cho YK, et al. 2006. Prevalence and risk factors of non-alcoholic fatty liver disease among Korean adults. J Gastroenterol Hepatol. 21: 138-143.

[49] Mohan V, Farooq S, Deepa, M, et al. 2009. Prevalence of Nonalcoholic Fatty Liver Disease in Urban South Indians in Relations to Different Grades of Glucose Intolerance and Metabolic Syndrome. Diabetes Research and Clinical Practice, 84: 84-91.

[50] Clark JM, Brancati FL, Diehl AM, 2003. The prevalence and etiology of elevated aminotransferase levels in the United States. Am J Gastroenterol; 98: 960-967.

[51] Prashanth M, Ganesh HK, Vima MV, John M, Bandgar T, Joshi SR, et al. 2009. Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus. J Assoc Physicians India. 57: 205-10.

[52] Banerjee S, Ghosh US, Dutta S, 2008. Clinic pathological profile of hepatic involvement in type-2 diabetes mellitus and its significance. J Assoc Physicians India. 56: 593-9.

[53] Adams LA, Lymp J. F, St Sauver J, Sanderson S, Lindor, K. D, Feldstein A. et al. 2005a. The natural history of nonalcoholic fatty liver disease: A population-based cohort study. Gastroenterology 129: 113-121.

[54] Juanwen, Zhang, Zhao Ying, Xu Chengfu, Hong Yani, Lu Huanle, Wu Jianping, et al. 2014. "Association between serum free fatty acid levels and nonalcoholic fatty liver disease: a cross-sectional study." Scientific reports 4: 5832. doi: 10.1038/srep05832.

[55] Hamaguchi M, Takeda N, Kojima T, Ohbora A, Kato T, Sarui H, Fukui M, Nagata C, Takeda J, 2012. Identification of individuals with non-alcoholic fatty liver disease by the diagnostic criteria for the metabolic syndrome. World J Gastroenterol. 18 (13): 1508–1516.

[56] Manco M, Bedogni G, Marcellini M, Devito R, Ciampalini P, Sartorelli MR, Comparcola D, Piemonte F, Nobili V, 2008. Waist circumference correlates with liver fibrosis in children with non-alcoholic steatohepatitis. Gut; 57: 1283-1287.

[57] Ekstedt, M, Franzen, L. E, Mathiesen, U. L, Thorelius, L, Holmqvist, M, Bodemar, G. et al. 2006. Long-term follow-up of patients with NAFLD and elevated liver enzymes. Hepatology 44: 865-873.

[58] Marchesini G, Brizi M, Bianchi G, et al. 2001. Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes. 50: 1844-50.

[59] Kim HJ, Kim HJ, Lee KE, et al. 2004. Metabolic significance of nonalco- holic fatty liver disease in nonobese, nondiabetic adults. Arch Intern Med. 164: 2169-75.

[60] Edmison J, McCullough AJ, 2007. Pathogenesis of non-alcoholic steatohepatitis: human data. Clin Liver Dis. 11: 75-104.