

Effect of Dietary modification and regular physical exercise on liver function tests in Patients with Non-alcoholic Fatty Liver Disease

Research Article

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Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) describes a spectrum of clinicopathological changes in liver extending from simple steatosis through non-alcoholic steatohepatitis (NASH) to fibrosis. NAFLD is an increasingly prevalent disease, there is a lack of approved therapies for it. Dietary modification and regular physical activities help in weight reduction, which is main principle of treatment in fatty liver diseases.

Objectives: To evaluate the efficacy of exercise and reduction of fatty food intake in NAFLD patients.

Methods: This was sixmonths randomized open level clinical trial. Study was done in Department of Hepatology BSMMU from June 2017 to September 2018. 50 patients with sonographic evidence of Fatty liver, who fitted the inclusion & exclusion criteria were enrolled by lottery method. All the included patients were advised to do regular physical exercise and diet restrictions. The liver function tests were done in all patients. After six months of follow up patients underwent biochemical tests of liver function test again in follow up. All data was presented as mean $\pm$ SD & analyzed by SPSS (version 23). Qualitative data was analyzed by Chi-square test & quantitative data was analyzed by student's t-test. A statistically significant result was considered when P value was less than 0.05.

Results: In Comparative analysis of anthropometric, biochemical; ALT, AST, GGT improvement was observed but the improvement was not statistically significant.

Conclusion: Supplementation of pharmacological therapy should be added with non pharmacological therapy in patients with NAFLD to achieve improvement of liver function test.

Keywords: Effectiveness, Implementation, Community-Based Scholarship Program, Tesda Scholarship Program.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is considered as the hepatic manifestation of metabolic syndrome and is currently the most common cause of liver disease in many developed countries. The

definition of NAFLD requires that there must be (1) evidence of hepatic steatosis, either by imaging or by histology and (b) lack of secondary causes of hepatic fat accumulation, such as significant alcohol consumption, long term use of steatogenic medications or monogenic hereditary disorders.

NAFLD is histologically further categorized into non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH) (AASLD Guide line 2017). NAFLD and NASH were recognized as distinct entities when Ludwig et al. in 1980 described liver lesions commonly associated with alcohol abuse (i.e. fatty change, lobular hepatitis and pericellular fibrosis) that were found in patients who did not have a history of excessive drinking.

The histological spectrum of NAFLD includes non-alcoholic fatty liver (NAFL; steatosis without hepatocellular injury), steatohepatitis (NASH; steatosis with inflammation and hepatocyte ballooning degeneration), fibrosis and ultimately cirrhosis (Chalasani et al. 2017). Those patients who progress to cirrhosis are at risk of potentially life threatening liver-related complications such as portal hypertension, hepatic failure and hepatocellular carcinoma (Liu et al. 2014).

NAFLD is strongly associated with insulin resistance and other components of the metabolic syndrome, like Type 2 Diabetes Mellitus, central obesity, hyperlipidemia, hypertension and with other conditions associated with insulin resistance such as atherosclerosis, hyperuricaemia and PCOS (Clark JM et al. 2003). Although NAFLD is more common in subjects with obesity and Diabetes Mellitus (DM), it also occurs in lean (7%) and non-diabetic subjects (Younossi et al. 2012).

Worldwide prevalence of NAFLD ranges from 17% to 46% in the general population, assessed by ultrasonography. On the other hand, the estimated prevalence of NASH is lower, ranging from 3 to 5% (Vernon G et al. 2011).

There is a very high prevalence of NAFLD in individuals with type 2 Diabetes Mellitus (T2DM). An ultrasonographic study of patients with T2DM showed a 69 % prevalence of NAFLD (Leite et al. 2009).

The prevalence of NAFLD in India above 20 years of age was 18.9% and increasing secondarily to an increase in burden of Diabetes Mellitus (DM), metabolic syndrome and changing in lifestyle (Amarrapuker et al. 2007). The average age for NASH patients is 40-50 years and that for NASH-related cirrhosis is 50-60 years.

NAFLD has been associated with insulin resistance and hyperinsulinaemia, even in lean subjects with normal glucose tolerance. Genetic environmental factors also interact to determine disease progression. PNPLA3 gene was strongly associated with hepatic fat content (Pan et al. 2014). NASH most likely causes approximately 80% of the cases of cryptogenic cirrhosis, which accounts for 10%-20% of all cirrhosis cases (Grattagliano et al. 2007). Among patients diagnosed with NASH related cirrhosis, the risk of developing portal hypertension is 17%, 23% and 52% at 1, 3 and 10 years, respectively. Among patients with early-stage NASH, the overall mortality over 10-15 years is approximately 10%-12%, being significantly higher in the NASH patients, compared to the general population. The risk of developing decompensated cirrhosis is 5%-10%, and that of hepatocellular cancer is 1%-2% (Hui et al. 2003).

PREVALANCE OF NAFLD

The prevalence of NAFLD is rapidly increasing worldwide in parallel with the increase in obesity and type 2 diabetes. The overall global prevalence of NAFLD diagnosed by imaging is around 25.24%. The highest prevalence of NAFLD reported in the Middle East is 31.79% and South America 30.45%, whereas the lowest prevalence rate reported in Africa is 13.48%. The prevalence of NASH among NAFLD patients who had liver biopsy for a clinical indication is 59.1%. The prevalence of NASH in the general population ranges between 1.5% to 6.45% (Younossi et al. 2016). The prevalence of NASH is about 3% but could be more than 25% in obese individuals (Vernon, Baranova and Younossi 2011). In Asia, similar prevalence of NAFLD has been found in the range of 15% to 30% in the general population and over 50% in patients with diabetes and metabolic syndrome (Wong et al. 2013). The overall prevalence of NAFLD in Bangladesh range from 4 to 33.86% in both genders. Individuals from rural areas had a higher prevalence of 36.95% of NAFLD than the individuals from urban areas - 33.00%. NAFLD prevalence was 71.18%, 62.8%, and 40.77% among diabetic, hypertensive, and individuals with family history of liver disease, respectively. Overweight and obese individuals had a prevalence of NAFLD of 44.05% and 63.55% respectively. The highest prevalence was (73.21%) among rural obese women

than any other BMI classifications (Alam et al. 2018). The prevalence of NASH among NAFLD patient is high (42.4%). Females are predominant sufferer of NAFLD in Bangladesh (Alam et al. 2014). The prevalence of NAFLD is the most frequently recorded liver disease and is most common among Bangladeshi patients (Alazawi et al. 2014).

NATURAL HISTORY OF NAFLD

NAFLD patients fall into two broad categories: NASH and non-NASH. The non-NASH subtype of NAFLD includes all patients with simple steatosis as well as patients with steatosis and nonspecific changes. Although NASH can follow a potentially progressive course for liver disease, the non-NASH subtype does not progress or progresses very slowly. Hepatic injury induced by NASH is similar to that caused by alcohol induced liver disease; however, NASH seems to progress more slowly and is histologically less severe than steatohepatitis caused by alcohol. NAFL has largely been considered benign, but recent cohort studies show a high risk for progression to NASH in up to 44% on serial biopsies at 5 years (McPherson et al. 2015). Pooled data suggest that about 21% of patients with NASH will have some regression of fibrosis while 38% of patients will progress over 5.3 years' of follow-up (Argo and Caldwell 2009). NASH causes progressive fibrosis that can lead to cirrhosis and hepatocellular cancer (HCC).

RISK FACTORS

The etiology of NAFLD are not clearly known, but there are some group of risk factors associated with NAFLD: nutritional (starvation, obesity, bariatric surgery, parenteral nutrition, celiac disease), metabolic (insulin resistance, dyslipidemia, pregnancy), drugs (glucocorticoids, tamoxifen, amioderone, valproic acid, zidovudine), genetic predisposition and others (inflammatory bowel disease etc). So genetic predisposition,

overabundance of calorie rich food and lack of physical activity contribute to development of obesity. Obesity is a pro-inflammatory state that leads to insulin resistance (IR) which is closely associated with NAFLD development and progression. There is also some emerging risk factors such as polycystic ovary syndrome, hypothyroidism, hypogonadism, hypopituitarism, obstructive sleep apnoea in NAFLD.

PATHOEGNESIS

The pathophysiology of NAFLD is multifactorial and not completely understood. According to the "two-hit" hypothesis (Day & James. 1998), insulin resistance and obesity promote the synthesis of fatty acids from glucose and inhibit β -oxidation of fatty acids. The excess of fatty acids lead to triglyceride synthesis and to their intrahepatic accumulation (first hit). The increased levels of fatty acids and triglycerides are associated with the production of free radicals which causes lipid peroxidation and activating proinflammatory and fibrogenic cytokines lead to NASH (second hit) (Chitturi and Farrell 2001)

Multiple hit pathogenesis: The traditional 'two-hit' pathophysiological theory has now been challenged as knowledge of the interplay between insulin resistance, adipokines, adipose tissue inflammation and other less recognized pathogenetic factors have increased over the last few years. More recently it has been argued that multiple hits from adipose tissue and gut occur at the same time and promote liver inflammation.

Distinct hit hypothesis: A more recent model proposed that development of simple steatosis and NASH follows distinct pathways. There are many other factors that promote the activation of the pathways that leads to the development of steatosis and NASH. Most important among those factors include genetic factors (Alam et al. 2016).

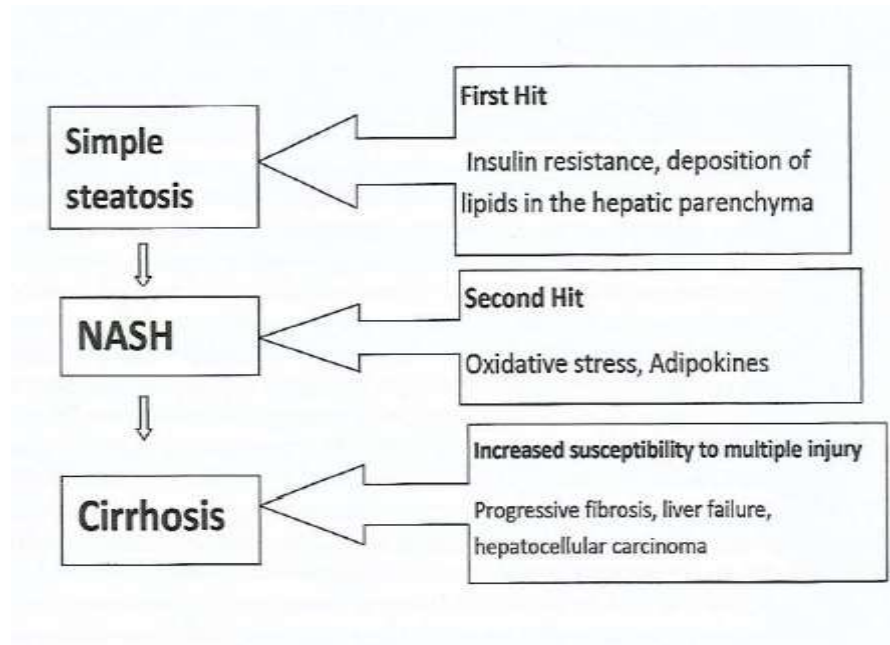


FIGURE 1- Pathogenesis of NAFLD

CLINICAL FEATURES

TABLE 1- Symptoms, Signs, and Laboratory Features of NAFLD

Symptoms	Signs	Laboratory Features
Common		
None (48%-100% of patients)	Hepatomegaly	2- to 4-fold elevation of serum ALT and AST levels AST/ALT ratio < 1 in most patients Serum alkaline phosphatase level slightly elevated in one third of patients Normal serum bilirubin, serum albumin, and prothrombin time Elevated serum ferritin level
Uncommon		
Vague right upper quadrant pain Fatigue Malaise	Splenomegaly Spider telangiectasias Palmar erythema Ascites	Low-titer (<1:320) antinuclear antibodies

(Sleisenger and Fordtran's Gastrointestinal and liver disease)

LABORATORY FEATURES

In patients with suspected NAFLD, the serum aminotransferases are usually abnormal; however, the combination of imaging consistent with hepatic steatosis and an elevated alanine aminotransferase (ALT) raises concern for NASH. The degree of liver enzyme elevation does not predict the degree of hepatic inflammation nor fibrosis, and a normal ALT level does not exclude clinically important histologic injury.

The alkaline phosphatase and gamma glutamyl transpeptidase (GGT) levels may be elevated, but the serum bilirubin level, prothrombin time, and serum albumin level typically are normal, except in patients with NAFLD associated cirrhosis level. Up to one fourth of patients with NAFLD may have antinuclear antibodies (ANA) in low titres (less than 1:320) (Adams and Talwalkar 2006). Antimitochondrial

antibodies (AMA) and hepatitis B surface antigen are not detected. Antibody to hepatitis C virus (anti-HCV) must be absent to implicate NAFLD as the sole cause of abnormal liver biochemical test levels; however, steatosis, often in association with visceral obesity, frequently accompanies HCV infection and may be associated with a more aggressive course.

IMAGING FEATURES

Abdominal ultrasound is widely used for the diagnosis of NAFLD. Increased hepatic echogenicity compared to the kidneys or the spleen. It is the best non-invasive tests for the diagnosis of steatosis are the imaging ones. US should be the first method to be used in a clinical setting. It is inexpensive, non invasive, widely available and it has 60–94% sensitivity and 66-97% specificity for hepatic steatosis (Saverymattu et al. 1986).



FIGURE 3- (Left) - Diffuse fat accumulation in the liver at USG. The echogenicity of the liver is greater than that of the renal cortex. Intrahepatic vessels are not well depicted. The ultrasound beam is attenuated posteriorly, and the diaphragm is poorly delineated.

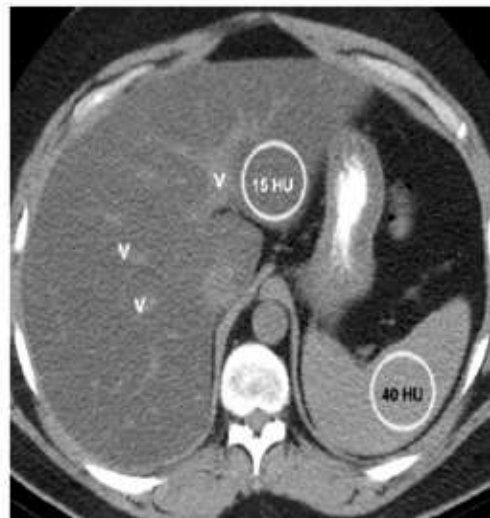


FIGURE 3- (Right) - Diffuse fat accumulation in the liver at unenhanced CT. The attenuation of the liver (15HU) is markedly lower than that of the spleen (40 HU). Intrahepatic vessels (v) also appear hyper attenuated in comparison with the liver.

CT- has similar accuracy for NAFLD as US, being superior only for focal steatosis (Fierbinteanu-Braticevici et al. 2010). CT has several limitations, has radiation hazards not suitable for screening of steatosis.

MRI is superior to US in detecting and quantifying minor fat infiltration, being able to detect down to 3% of steatosis, no radiation exposure, but expensive (Fishbein et al. 2005).

AVAILABLE THERAPY

Weight loss generally reduces hepatic steatosis, achieved either by hypocaloric diet alone or in

conjunction with increased physical activity. Loss of at least 3-5% of body weight appears necessary to improve steatosis, but up to 10% may be needed to improve necroinflammation. Pharmacotherapy should be considered for patients with NASH and or fibrosis to halt or reverse disease progression. Metformin has no significant effect on liver histology and is not recommended as a specific treatment for liver disease in adults with NASH. Pioglitazone can be used to treat steatohepatitis in patients with biopsy-proven NASH. It improves insulin resistance, biomarkers, steatosis and inflammation. Side effects like weight gain, bone fracture in women, congestive heart failure are concern. Long term safety and efficacy of pioglitazone in patients with NASH is not established (Frohnert, Hui and Bernlohr 1999). Vitamin E administered at daily dose of 800 IU/day improves liver histology in non-diabetic adults with biopsy-proven NASH. Vitamin E is not recommended to treat NASH in diabetic patients, NAFLD without liver biopsy, NASH cirrhosis or cryptogenic cirrhosis (Guy et al. 2015). Long term use may cause prostate cancer and haemorrhagic stroke. Ursodeoxycholic acid showed some biochemical but no histological improvement. Pentoxifylline may improve liver enzymes and histology (Alam et al. 2017). A synthetic farnesoid X receptor agonist Obeticholic acid improves insulin resistance in type 2 DM. In phase 11b FLINT trial 72 week treatment with Obeticholic acid in non-cirrhotic NASH patients improved all NASH. Main issues with safety and tolerability were increased LDL cholesterol and pruritus (Mudaliar et al. 2013). Elafibranor is a dual PPAR α and PPAR δ agonist that improves insulin sensitivities and have been shown to reduce steatosis, inflammation, pro-inflammatory gene expression in dietary induced NASH (Staels et al. 2013). LEAN trial is the first multicentered double blind placebo controlled RCT showed Liraglutide is safe and shown improvement of liver histology in obese NASH patients (Armstrong et al. 2016). Omega 3 fatty acid supplementation has significant benefits in NAFLD.

MATERIALS AND METHODS

Type of Study: Observational study.

Place of Study: Department of Hepatology, Bangabandhu Sheikh Mujib Medical University.

Duration of Study: From 03-06-2017 to August 2018

Study population: Patients of NAFLD attended at outpatient Department of Hepatology, BSMMU.

Sampling technique: Simple randomization.

Sample size determination: Sample size was determined using following formula-

Sample size for hypothesis testing of the difference between two mean

$$n = \frac{(Z_{\alpha} + Z_{\beta})^2 \times (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

3.2 SELECTION OF PATIENTS

Inclusion criteria:

1. Patients with ultrasonographic evidence of fatty liver with raised ALT.
2. Patients from 18 years to 70 years of age.

Exclusion criteria:

1. Patient with significant alcohol intake (more than 30 gm/day in case of male and more than 20 gm/day in case of female)
2. History of taking drugs –
 - a. Drugs that may cause fatty liver (i.e. tamoxifen, valproate, amiodarone, MTX)
 - b. Concomitant drugs-Vitamin E, Statin, Metformin, Silymarin.
3. Chronic viral hepatitis (HBV, HCV).
4. Known and overt case of any other liver diseases, Wilson's disease, Autoimmune liver diseases, Hemochromatosis, Cirrhosis of liver (other than NASH).
5. Pregnancy
6. Psychiatric disorders.
7. Patients with recent MI, Liver failure, hypothyroidism.
8. Co-morbid conditions (COPD, CKD, cardiac failure etc)

3.3 STUDY PROCEDURE

Patients attending in outpatient Department of Hepatology, BSMMU with sonological evidence of fatty liver (Ultrasonography done in Radiology department of BSMMU) was assessed by history taking and physical examination. After considering the inclusion and exclusion criteria, he/she was

initially selected. Then the patients were explained about the aims, objectives of the study and necessity of the investigations. After obtaining informed written consent, he was enrolled finally in my study. The patients were given a dietary list which contain low fatty foods and advised to increase physical exercise, including at least 30 minutes walking, like life style modification, management of diabetes, hypertension, dyslipidaemia. Close liaison was maintained between all groups of patient. Permanent address, present address including phone number of all patients was kept. To avoid confounding variable and improve patients compliance telephone survey was done. All patients were advised to contact immediately if any need arises. Each patient was advised for follow up monthly for three months and then at 6 months.

Clinical evaluation:

After taking history, blood pressure, height and weight (BMI), waist circumference was measured. BMI was calculated using the formula: weight (in Kg) / height (in meter²).

Metabolic syndrome was defined according to Asian criteria and three of five listed criteria was considered: waist circumference ≥ 80 cm for women and ≥ 90 cm for men, serum triglyceride ≥ 150 mg/dl, serum high density lipoprotein (HDL) cholesterol < 50 mg/dl for women and < 40 mg/L for men, elevated blood pressure (systolic blood pressure ≥ 130 and or diastolic blood pressure ≥ 85 mmHg or drug treatment for hypertension) and plasma glucose ≥ 100 mg /dl (5.6mmol/l) or drug treatment for diabetes. BMI (kg/m²) was measured according to WPRO (2000): Underweight: < 18.5 , normal: $18.5 - 22.9$, overweight: $23 - 24.9$, obese1: $25 - 29.9$, obese 2: ≥ 30 . Sonographic feature of NAFLD based on presence of bright hepatic echotexture (compare with kidney), blurring of intrahepatic vasculature, deep attenuation either singly or in combination.

Biochemical evaluation:

Collection of blood from each study participant for following investigations:

- a. Alanine aminotransferase (ALT)
- b. Aspartate aminotransferase (AST)
- c. Gamma-glutamyl transferase (GGT)
- d. Fasting blood sugar (FBS)
- e. Blood sugar 2hrs after breakfast

- f. Fasting lipid profile
- g. Serum Thyroid stimulating hormone (TSH)
- h. Serum free Thyroxine (FT₄)
- i. Viral markers – HBsAg, Anti HBc(T), Anti-HCV
- j. Serum ferritin
- k. Serum ceruloplasmin
- l. ANA
- m. HOMA-IR

Biochemical evaluation was done in department of Biochemistry of BSMMU, USG was done in department of Radiology, Viral markers were investigated in department of Virology of BSMMU.

Study schedule, surveillance parameters, data collection:

After screening, the included patients were followed up monthly for three months, then at 6 months. Each visit was taken between 12 to 2 pm & consisted of clinical examination, blood pressure measurement & BMI determination and a questionnaire. Serum was collected for FBS, 2HABF, ALT, AST, GGT, FLP, HOMA-IR was done in first and last visit after six months. All informations and records of the patients were kept confidential. Study compliance was strictly monitored. FBS, 2HABF & HbA_{1c}, Lipid profile for diabetic & dyslipidemic patients was done accordingly. The primary parameters were recorded that were compared between first and last visit are BP, WC, BMI, ALT, AST, GGT, TC, TG, HDL, LDL, FBS, 2HABF, HOMA-IR.

STATISTICAL ANALYSIS

- All data was presented as mean $\pm$ standard deviation (SD) & analyzed by statistical package SPSS (version 23.0 IBM Corp: Armonk NY USA).
- Qualitative data was analyzed by Chi-square test.
- Quantitative data was analyzed by student's t-test.
- To observe effect of intervention, paired T test was done in both groups between before and after intervention.
- A statistically significant result was considered when p value was less than 0.05.

ETHICAL CONSIDERATION

Prior to commencement of the study, the aim and objectives of the study along with its procedure, risk and benefit of the study was explained to the patients. All informations and records were kept confidential. Omega 3 Fatty Acid drug was taken from a single company named Drug International Bangladesh. Ethical clearance for the study was taken from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh in it's 139 th meeting held on 3rd June 2017, prior to the commencement of this study. Patients had all rights to withdraw him/her from this study at any level of this study period.

RESULT

Demographic characteristics:

Mean age of the study population is 38.57 ± 9.2 years and minimum age was 18 years and maximum was 67 years. Female preponderance was observed.

Demographic variable of the sample population (50)

Age	39.7 ± 9.8
Sex	
Male	14(28.0)
Female	36(72.0)
Occupation	
Student	1(2.0)
Service	6(12.0)
Business	7(14.0)
Housewife	31(62.0)
Others	5(10.0)
Education	
Illiterate	9(18.0)
Primary	14(28.0)
Secondary	12(24.0)
Higher secondary	7(14.0)
Graduate plus	8(16.0)
Monthly income (Taka)*	
Up to 5000	31(62.0)
5000-15000	4(8.0)
Above 15000	15(30.0)

Distribution of clinical and biochemical variables:

Mean BMI was 27.7 ± 3.4 kg/m². Mean waist circumference was 95.2 ± 6.9 cm. The number of Increased waist circumference present in the study subjects were 44 in. Mean Systolic Blood Pressure was 121.8 ± 9.8 mm Hg; Mean Diastolic Blood Pressure was 76.2 ± 8.1 mm Hg. SGPT of was 51.4 ± 32.7 U/L. SGOT was 39.4 ± 36.5 U/L. GGT was 41.5 ± 32.2 U/L. Fasting Blood sugar was 5.9 ± 2.3 mmol/L and the Two Hours after Breakfast was 8.8 ± 3.4 mmol/L. HbA1c was $6.9 \pm 1.5\%$. Insulin resistance Index (HOMA-IR) was 2.8 ± 3.3 . Total cholesterol was 193.3 ± 44.6 mg/dl. HDL was 41.4 ± 12.0 mg/dl. LDL was 112.6 ± 45.9 mg/dl. Triglyceride was 194.5 ± 98.9 mg/dl.

Baseline Clinical and Biochemical characteristics-

Variables#	(n = 50)
Clinical variables	
BMI (kg/m ²)	27.7 ± 3.4
Waist circumference (cm)	95.2 ± 6.9
Systolic BP (mmHg)	121.8 ± 9.8
Diastolic BP (mmHg)	76.2 ± 8.1
Biochemical variables	
ALT (U/L)	51.4 ± 32.7
AST (U/L)	39.4 ± 36.5
Gama GT (U/L)	41.5 ± 32.2
Fasting Blood Sugar (mmol/L)	5.9 ± 2.3
2 hours after breakfast (mmol/L)	8.8 ± 3.4
HbA1c (%)	6.9 ± 1.5
Insulin resistance index	2.8 ± 3.3
Serum Cholesterol Total (mg/dl)	193.3 ± 44.6
HDL (mg/dl)	41.4 ± 12.0
LDL (mg/dl)	112.6 ± 45.9
Serum Triglyceride (mg/dl)	194.5 ± 98.9

Changes in clinical and biochemical variables after 6 months-

BMI remained almost static: at baseline 27.7 ± 3.4 kg/m² and 6 months after intervention it was 27.6 ± 3.4 kg/m². Mean waist circumference was decreased significantly from 95.2 ± 6.9 cm to 94.8 ± 6.9 (p = 0.005). Mean systolic and diastolic pressure was not

decreased significantly. Mean serum ALT decreased from 51.4 ± 32.7 U/L at baseline to 41.3 ± 36.4 U/L after 6 months of intervention. Serum ALT did not respond statistically significant ($p = 0.098$). However, Mean AST was static; at baseline 39.3 ± 36.8 U/L and 39.0 ± 44.3 U/L. Gamma GT also decreased from 41.5 ± 32.2 U/L at baseline to 38.9 ± 23.1 U/L after 6 months but not significantly ($p = 0.412$). Mean Fasting blood sugar at baseline 5.9 ± 2.3 mmol/L and increased to 6.1 ± 2.2 mmol/L after 6 months whereas 2 hrs after breakfast at baseline was 8.8 ± 3.4 mmol/L and it decreased to 8.2 ± 3.7 mmol/L. Mean HbA1c at baseline was 6.9 ± 1.5 % and it was decreased to 6.6 ± 1.7 %. Insulin resistance index (HOMA-IR) were increased in both before and

after 6 months; at baseline 2.8 ± 3.3 and it increased to 3.8 ± 8.5 after 6 months. Mean Serum cholesterol at baseline 193.6 ± 45.0 mg/dl and after 6 months increased to 196.3 ± 46.0 mg/dl. Mean Serum HDL at baseline was 41.6 ± 12.0 mg/dl and after 6 months it improved to 42.8 ± 9.6 mg/dl. Mean Serum LDL before treatment was 112.4 ± 46.4 mg/dl and after 6 months it was 119.2 ± 38.6 mg/dl. Mean Serum Triglyceride at baseline was 196.0 ± 99.3 mg/dl and after 6 months it decreased to 181.0 ± 73.6 mg/dl. The life style modification, dietary restriction and increase physical exercise has no significant effect on liver function test as the reduction of ALT, AST, GGT, Blood sugar, Insulin resistance is not statistically significant.

Changes in clinical and biochemical variables before and after intervention

Variables	Control		p-value
	Baseline (n = 50)	After 6 months (n = 50)	
Clinical variables			
BMI (kg/m²)	27.7 ± 3.4	27.6 ± 3.4	0.818
Waist circumference (cm)	95.2 ± 6.9	94.8 ± 6.9	0.005 ^s
Systolic BP (mmHg)	121.8 ± 9.8	120.1 ± 9.3	0.103
Diastolic BP (mmHg)	76.2 ± 8.1	74.0 ± 6.3	0.004
Biochemical variables			
ALT (U/L)	51.4 ± 32.7	41.3 ± 36.4	0.098
AST (U/L)	39.3 ± 36.8	39.0 ± 44.3	0.971
Gamma GT (U/L)	41.5 ± 32.2	38.9 ± 23.1	0.412
Fasting blood sugar (mmol/l)	5.9 ± 2.3	6.1 ± 2.2	0.709
B. sugar 2 hrs. after breakfast (mmol/l)	8.8 ± 3.4	8.2 ± 3.7	0.205
HbA1c (%)	6.9 ± 1.5	6.6 ± 1.7	0.316
Insulin resistance index	2.8 ± 3.3	3.8 ± 8.5	0.270
Serum cholesterol (mg/dl)	193.6 ± 45.0	196.3 ± 46.0	0.658
Serum HDL (mg/dl)	41.6 ± 12.0	42.8 ± 9.6	0.529
Serum LDL (mg/dl)	112.4 ± 46.4	119.2 ± 38.6	0.212
Serum TG (mg/dl)	196.0 ± 99.3	181.0 ± 73.6	0.234

Data were analyzed using **Paired t-Test** and were presented as **mean $\pm$ SD**.

SUMMARY

This observational study has assessed the effects of dietary change, increase physical exercise, life style modification on NAFLD patients. We evaluated 50 NAFLD patients coming to Hepatology department, BSMMU with nonspecific symptoms with USG findings of fatty liver, by anthropometric features, biochemical test. These patients received no drug. In

this study 6 months the liver function test; ALT, AST, GGT, waist circumference, lipid profile and BMI was not significantly improved irrespective of diabetic status. In summary, this study demonstrated that the only life style change, increase physical activities, decrease fatty food intake in NAFLD patients not enough to improve liver function test. As there is no significant body

weight and BMI reduction the LFT was not improved.

CONCLUSION

NAFLD and NASH are well recognized causes of progressive chronic liver disease leading to cirrhosis and hepatocellular carcinoma. To date, no therapy provided evidence of significant efficacy, and as a consequence, no approved therapeutic options are available worldwide. This study has demonstrated that only non pharmacological therapy for NAFLD patient is not enough. It should be added by suitable pharmacological therapy. Further large RCT studies are necessary to confirm and expand these findings.

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