ORIGINAL ARTICLE

Nonalcoholic Fatty Liver Disease Among Adults Attending Medical Outpatient Clinic Using Ultrasound

Charles U **ODENIGBO**[1]
Ogonna C **OGUEJIOFOR**[1]
Ogochukwu I **EZEJIOFOR**[1]
Nonye N **JISIEIKE-ONUIGBO**[1]
Chibundo U **NWANELI**[1]
Eric O **UMEH**[2]
Ukamaka R **EBUBEDIKE**[2]
Christian E **ONAH**[3]

[1]*Department of Medicine*
[2]*Department of Radiology*
[3]*Department of Chemical Pathology*

Nnamdi Azikiwe University
Nnewi Campus, NIGERIA

Author for Correspondence
Dr Ogochukwu **EZEJIOFOR**
Department of Medicine
Nnamdi Azikiwe University
Nnewi campus, Anambra state
NIGERIA

Phone: +234 803 605 7347
Email:ogoezejiofor@yahoo.com

Received: March 5th, 2019
Accepted: May 14th, 2019

DISCLOSURE
There is no conflict of interest and no external funding

ABSTRACT

Background: Nonalcoholic fatty liver disease (NAFLD) is a common metabolic disorder characterized by accumulation of excess fat in the liver in the absence of significant alcohol consumption. This condition has been linked to certain risk factors such as obesity, Type 2 diabetes, and dyslipidaemia. Data in the developing economies are very scanty, hence the need for this study.

Objectives: To ascertain the frequency and correlates of NAFLD among adult Nigerians and staging this condition using ultrasound. It also aimed at evaluating correlations between NAFLD and possible associated factors such as obesity, type 2 diabetes and dyslipidaemia.

Methodology: Consenting adult patients attending Out Patient Clinic at Nnamdi Azikiwe University Teaching Hospital (NAUTH) who do not have significant alcohol consumption and were serologically negative for Hepatitis B or C infections were recruited for the study. Biodata and other relevant clinical histories were taken and clinical anthropometric measurements obtained. Blood samples were taken from the patients to assess their fasting blood glucose, liver function tests and fasting lipid profiles. An experienced ultra-sonographer performed abdominal ultrasound scan looking for presence of NAFLD and staged it. Data were analysed with statistical package for social sciences software(SPSS), version 17

Results: A total of 102 individuals participated in the study, 46(45.1%) females and 56(54.9%) males. The mean age of the study participants was 53.1±16.4 years (range 22-88 years). Female male ratio was 1:1.2. About thirty-one percent of the patients studied had NAFLD. Both the mean BMI and mean Waist Circumference were higher among subjects with NAFLD compared to those without ultrasonographic evidence of NAFLD, with *p*-values of <0.001 and 0.008 respectively. Diabetes mellitus was significantly present among the participants with NAFLD compared to those participants without evidence of NAFLD (53.1% vs 27.1%, *p*=0.011). Hypertension had a similar relationship, but not significant (p = 0.121).

Conclusion: The prevalence of NAFLD seems to be high in this hospital based study and important correlates are obesity and Diabetes mellitus.

***Key Words*:** *Fatty liver disease, Obesity, Type 2 diabetes, Hyperlipidemia, Metabolic syndrome, Insulin resistance*

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disorders characterized by accumulation of excess fat in the liver in the absence of significant alcohol consumption. The condition ranges from simple excess fat accumulation to steatohepatitis or nonalcoholic steatohepatitis (NASH) with risk of progressive liver damage leading to liver cirrhosis.[1,2] Oxidative stress injury and other factors lead to lipid peroxidation in the presence of fatty infiltration leading to inflammatory changes. Fibrosis enhanced by insulin resistance may occur, which induces connective tissue growth factor. Risk factors for NAFLD are obesity, hypertension, type 2 diabetes and hyperlipidaemia, such that NAFLD is considered the liver component of the metabolic syndrome. Insulin resistance is universal.[2]

Nonalcoholic fatty liver disease is a major public health concern and the most common cause of liver disease in the high-income countries affecting up to 20% of adults; and it is the commonest cause of cryptogenic cirrhosis in the united states.[3]

The diagnosis of NAFLD is made using ultrasound and liver biopsy as patients with NAFLD may present with "normal" liver biochemistry.[4,5,6,7,8] Also, at least 20% of people with persistently abnormal alanine aminotransaminase values have an alternative diagnosis. Ultrasound demonstrate fatty infiltration of the liver, with the exclusion of other causes of liver injury, such as alcohol. Liver biopsy allows staging of the disease but when this should be performed is unclear as there are no definitive guidelines.[9] Many researchers recommend biopsy if the value of alanine transferase(ALT) is up to twice the normal limit.[9]

Although liver biopsy is the gold standard method for diagnosing and staging NAFLD, majority of patients can be affectively diagnosed non-invasively with ultrasound.[10] A diagnosis of NAFLD requires that there is evidence of hepatic steatosis on imaging or histology, and other causes of liver disease or steatosis have been excluded.[11]

This condition however has not been particularly studied in our environment despite the predominance of the associated risk factors, hence the need for this study.

The objectives of the study were to determine the frequency of NAFLD among adult outpatient attendees, to document the stages of NAFLD using ultrasound and to evaluate the correlation between NAFLD and associated risk factors such as obesity, hypertension, type 2 diabetes, hyperlipidaemia and metabolic syndrome.

METHODOLOGY

This is a prospective descriptive study involving the recruitment of consecutive adult patients (18 years and above) attending the medical outpatient clinic of Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi. A written informed consent was obtained from the patients. Ethical approval was obtained from NAUTH Ethics and Research Committee (approval number – NAUTH/CS/Vol 10/176/2017/083) Exclusion criteria include existing liver disease, abnormal liver enzymes, significant alcohol consumption (>21units/week and 14units/week for males and females, respectively), and Hepatitis B and C infection.

Structured questionnaires were administered to all patients recruited for the study to obtain history on relevant biodata, history of risk factors of NAFLD and others. Clinical examinations such as blood pressure measurement, height, weight, waist and hip circumference were carried out on all recruited patients and body mass index was calculated.

The blood pressure was measured after five minutes of sitting with Accoson® mercury Sphygmomanometer. Palpation method was first used to estimate the systolic blood pressure before a stethoscope was used to identity Korotkoff sound for the exact systolic and diastolic blood pressure.

The height in meter was measured using a stadiometer (Seca 213-Portable stadiometer) while the weight of each participant was measured using a standardized weighing scale (Movel scientific instrument Co. Ltd). The Basal Metabolic Index (BMI) was calculated using height and weight i.e. square of the height in meter divided by weight in kilogram(H^2/Wt).

Ten milliliter of venous blood were collected from all participant after an overnight fast and sent to the laboratory in a plain bottle for the measurement of fasting blood glucose, fasting lipid profile, and liver function test. Glucose was assayed colourimetrically using the glucose oxidase method of Trinder.[12] Total bilirubin was assayed using the method of Jendrassik and Grof.[12] Aspartate transferase(AST) and Alanine transferase(ALT) were determined using the spectrophotometric method of Bergermeyer while Alkaline Phosphate was assayed using the spectrophotometric method of Schlebusch.[13,14]

The serum Total Cholesterol level was estimated by enzymatic colourimetric method described by Naito.[15] The serum High density lipoprotein-cholesterol (HDL-C) level was estimated by Cholesterol oxidase-Peroxidase (CHOD-POD Method) enzymatic colourimetric reaction, according to the method as described by Grove and Naito.[16] Serum TG level was estimated by Phosphate oxidase-Peroxidase (GPO-POD) enzymatic colourimetric reaction according to the method as described by Fossati.[17] The Low density lipoprotein-cholesterol(LDL-C) was estimated by computation, according to the methods by Friedewald.[18]

Ultrasound Technique

All participants were scanned by two radiologists using a Mindray Real time ultrasound machine with 3.5MHz ultrasonic transducer manufactured by Shenzhen Mindray Bio-medical Electronics Co. LTD.

The examination was performed with the participants in the supine and left lateral decubitus positions to obtain an optimal view. Coupling ultrasound gel was applied over the right upper quadrant and epigastric regions of the abdomen. The transducer was placed over the same area and a detailed examination of the liver carried out. The liver was scanned in multiple planes (Sagittal, transverse and oblique).

Findings suggestive of NAFLD included liver parenchymal echogenicity, liver to kidney contrast, attenuation of the diaphragm and

loss of bright vessel walls. The echogenicity of the liver was determined in comparison to the right kidney. A diffuse increase in liver echogenicity was defined as echogenic liver

Data were analyzed using statistical package for social sciences (SPSS) version 17. Mean BMI and Waist circumference were compared among the different sexes and also among participant with and without NAFLD and the level of significance determined. Also, the mean values for fasting blood glucose, total cholesterol, low density lipoprotein cholesterol, triglycerides and high-density lipoprotein cholesterol were obtained and compared among the two group and the level of significance determined. Results were presented in tables that showed percentages, mean and *p* values.

RESULTS

A total of 102 individuals participated in the study, forty-six (45.1%) females and fifty-six (54.9) males (Table 1). The mean age of the participants in the study was 53.11±16.41 years (range= 22-88years). Female to male ratio was 1:1.2. Nonalcoholic fatty liver disease was found in 31.2% of participants. Other participants' general characteristics such as educational status and anthropometry were also captured in the table.

Table 2 shows the general comparison of anthropometric and metabolic parameters such as basal metabolic index and waist circumference among participants with sonographic evidence of fatty liver disease and those without such evidence. The basal metabolic index and waist circumference are the great contributors of fatty liver disease with p values of < 0.001 and 0.008, respectively

Table 3 shows the relationship between NAFLD and some risk factors. Diabetes Mellitus was significantly present among the participants with NAFLD compared to those participants without evidence of NAFLD (53.1% vs 27.1%, *p*=0.011). Hypertension had a similar relationship, but not significant (*p* = 0.121).

The distribution of NAFLD among different sexes according to variables such as educational status, body mass index, waist circumference and the metabolic parameters such as blood glucose and lipids is as shown in Table 4

DISCUSSION

NAFLD was seen among 31.2% of the participants in this study which is comparable to the reported prevalence in the United States(US) general population. The reported prevalence when defined by liver ultrasound in the US ranged between 17% and 46% depending on the population studied.[19] Therefore, it can be said that NAFLD is not restricted to a particular geographic area but can be seen in any part of the world where risk factors for its development are present.

In the general United States population, the prevalence of NAFLD was reported to be 25% average with an incidence rate of two new patients per 100 people per year.[20,21] This general prevalence rate is comparable to the findings in our study, although our sample size is small.

Table 1. General characteristics of the participants

Variable	**Male**	**Female**	**Total**	***p*-value**
N	56(54.9)	46(45.1)	102(100)	
Educational status				0.504
None	1(100)	0(0)	1(100)	
Primary	17(63.0)	10(37.0)	27(100)	
Secondary	11(45.8)	13(28.3)	24(100.0)	
Tertiary	27(54.0)	23(46.0)	50(100.0)	
BMI (kg/m^2), mean	25.70±4.11	30.51±7.41		<0.001
Normal	21.85±2.19	22.22±2.32		0.679
Overweight	27.10±1.08	27.41±1.41		0.416
Obese	33.11±1.77	37.36±6.28		0.094
Waist circumference(cm) Mean	93.71±12.7	101.62±16.18		0.010

Table 2. General relationship between NAFLD and Anthropometric/Metabolic parameters

	Fatty Liver	**No Fatty Liver**	***p*-value**
BMI (kg/m^2)	31.28± 8.00	26.31± 4.60	<0.001
Normal	6(20.7%)	23(79.3)	
Overweighed	13(29.3%)	31(70.5)	0.059
Obese	13(50%)	13(50%)	
WC (cm)	102.77± 15.74	94.54± 13.70	0.008
FBS (mmol/l)	7.70± 4.13	6.08±2.29	0.069
Tchol (mmol/l)	5.11± 1.43	4.88±1.76	0.650
LDL-c (mmol/l)	3.20± 1.02	3.01±1.13	0.571
HDL-c (mmol/l)	1.32± 0.51	1.37±0.46	0.743
TG (mmol/l)	1.90± 2.72	2.02±2.72	0.880

FBS=fasting blood suga Tchol=Total cholesterol; LDL-c= Low density lipoprotein cholesterol
HDL-c =High density lipoprotein cholesterol TG=Triglyceride.

Table 3. Contribution of Diabetes and Hypertension on the presence of NAFLD

		Fatty Liver Disease		**p-value**
History of Diabetes Mellitus		Yes (%)	No (%)	
	Yes	17 (53.1)	19 (27.1)	0.011
	No	15(46.9)	51(72.9)	
	Total	**32 (100)**	**70(100)**	
History of Hypertension	Yes	23(71.9)	39(55.7)	0.121
	No	9(28.1)	31(44.3)	
	Total	**32(100)**	**70(100)**	

Table 4. Distribution of NAFLD among different sexes and related parameters

Variable	Male	Female	Total	*p*-value
Educational status				
None	0(0)	0(0)	0(0)	
Primary	4(40.0)	6(60.0)	10(100.0)	
Secondary	2(28.6)	5(71.4)	7(100.0)	0.859
Tertiary	6(40.0)	9(60.0)	15(100.0)	
BMI, mean				
Normal	22.42±2.49	22.20±0.79		0.913
Overweight	27.58±1.06	27.83±1.09		0.690
Obese	33.60±1.83	39.94±6.85		0.234
Waist circumference Mean	96.54±14.29	106.50±15.71		0.083
FBS mean	8.63±5.15	7.29±3.76		0.521
TC mean	5.15±2.53	5.09±0.86		0.935
LDL-C	2.99±1.39	3.28±0.89		0.614
HDL-C	1.31±0.60	1.32±0.50		0.983
TG	3.61±5.04	1.24±0.54		0.099

FBS=fasting blood sugar Tchol=Total cholesterol LDL-c= Low density lipoprotein cholesterol
HDL-c =High density lipoprotein cholesterol TG=Triglyceride

Also a study carried out in Brooke Medical Centre, showed that Hispanics had the highest prevalence rate of NAFLD (58.3%), then Caucasians (44.4%) and African Americans (35.1%).[22] Other studies showed prevalence of 45% in Hispanics, 33% in whites and 24 % in blacks.[23] Reports from India estimated the prevalence of NAFLD to be around 9 to 32% of the general Indian population with a higher incidence rate amongst obese and diabetic patients.[24]

This apparent high prevalence for NAFLD may be attributed to the global rise in incidence of obesity and its associated metabolic abnormalities of which the developing countries is not exempt from. Once considered a high-income country problem, overweight and obesity are now on the rise in low- and middle-income countries particularly in urban settings. Close to 35 million overweight children are living in developing countries and 8 million in developed countries.[16]

Our finding of high prevalence of NAFLD is similar to reports from the developed economies. It could be explained by the adoption of westernized diet, rapid technological changes leading to reduced physical activity and sedentary lifestyle that is associated with urbanization.[24] There is paucity of data on the prevalence of NAFLD in the general Nigerian population, however a study carried out in a diabetic clinic in South-West Nigeria, reported a prevalence of NAFLD to be 8.7% in the study population while the prevalence rate among diabetic patients was 9.5%.[25] Among the non-diabetic patients the prevalence rate was 4.5% and the difference was not statistically significant.[1]

The overall prevalence in the above study reported in 2011 was generally low when compared with the prevalence of our study. The low prevalence rate reported may be due to the study location and the rapid urbanization changes that may have occurred in the interval between both studies (more than 7 years' interval). An earlier report from the same region among a cohort of HIV patients on highly active anti-retroviral therapy (HAART) known to increase the risk of NAFLD was documented as 13.3%.[26]

It is unclear if NAFLD occurs more in men than women with previous studies reporting contradicting gender prevalence; some studies have shown that middle aged women are more affected,[27,28,29] while others have found a higher prevalence in males.[30,31] Our study showed a higher prevalence of NAFLD in females (43.5%) compared to males (21.4%), agreeing with earlier reports indicated above.

The ages of NAFLD subjects ranged between 22 to 88 years with a mean age of 53.11±16.41years. This is in keeping with earlier reports that NAFLD occurs at all ages with incidence increasing as body size increases with age.[16] The increase in body size that occur with age could also result in increase in the parameters such as body mass index and waist circumference that are recognized risk factors for NAFLD.

NAFLD has been associated with many aetiological risk factors and this could either be primary or secondary.[32] Primary factors are related to insulin resistance and the metabolic syndrome which include obesity, type 2 diabetes mellitus and dyslipidemia which frequently coexist in many patients.[32] The reported prevalence of obesity in several series of patients with NAFLD varied between 30 and 100 percent, the prevalence of type 2 diabetes mellitus varied between 10 and 75 percent, and the prevalence of hyperlipidemia varied between 20 and 92 percent. The prevalence of NAFLD increases by a factor of 4.6 in obese people, with body-mass index greater than or equal to 30. Regardless of body-mass index, the presence of type 2 diabetes mellitus significantly increases the risk and severity of NAFLD.[33]

Truncal obesity seems to be an important risk factor for NAFLD, even in patients with a normal body-mass index.[34,35] Subjects with NAFLD in this study have significantly higher values of waist circumference and BMI compared to those without NAFLD and the greater percentage was observed among females. This may be attributed to the fact that females have a higher percentage of body fat compared to men because they require fewer calories per pound of body weight daily.[35] The role of central adiposity seems crucial because visceral fat is an important source of triglycerides leading to steatosis. Fifty percent of our study subjects with NAFLD were found to be obese (BMI > 30) while 29.5% were overweight. History of Diabetes mellitus was significantly associated with NAFLD in this study. This is not surprising as DM is a risk factor for NAFLD. However, hypertension was not significantly associated with NAFLD.

The characteristic lipid findings in literature in NAFLD include increased cholesterol (VLDL and LDL-C), increased triglyceride and low HDl.[36] The findings in this study showed higher mean values of TC and LDL

(5. 11 ±4.13 and 3.2 ± 1.02 respectively), lower value of HDL and TG (1. 32±0.51 and 1.90±2.72, respectively) among those with NAFLD. There was no statistically significance difference in the lipid variables between the subjects with NAFLD and those without. The lower mean TG level observed in this study is contrary to the expectation in NAFLD. This could be due to the relatively small size of our study population which is a limitation of this study.

CONCLUSION

The prevalence of NAFLD is high at 31.2% in this study. Obesity is a significant risk factor. A community based study is needed to further ascertain the exact prevalence in our environment

REFERENCES

1. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis. *Mayo Clin Proc* 1980; 55:434-438.
2. Chitturi S, Farrell GC. Etiopathogenesis of nonalcoholic steatohepatitis. *Semin Liver Dis* 2001; 21:27-41.
3. Clark JM, Diehl AM. Non-alcoholic fatty liver disease: an under recognized cause of cryptogenic cirrhosis. *JAMA* 2003;289(22):3000–3004.
4. Bianchi L. Liver biopsy in elevated liver function tests? An old question revisited. *J Hepatol* 2001; 35:290–294.
5. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, *et al*. The utility of radiological imaging in non-alcoholic fatty liver disease. *Gastroenterology* 2002; 123:745–750.
6. Mofrad P, Contos M, Haque M, Sargeant C, Fisher RA, Luketic VA, *et al*. Clinical and histologic spectrum of non-alcoholic fatty liver disease with normal ALT values. *Hepatology* 2003; 37:1286–1292.
7. Clark JM, Diehl AM. Defining non-alcoholic fatty liver disease: implications of epidemiological studies. *Gastroenterology*. 2003; 124:248–250.
8. Yu AS, Keefe EB. Elevated AST or ALT to non-alcoholic fatty liver disease: accurate predictor of disease prevalence? *Am J Gastroenterol* 2003; 98:955–956.
9. Dyson JK, Anstee QM, Mcpherson S. Non-alcoholic fatty liver disease; a practical approach to diagnosis and staging. *Frontline Gastroenterology* 2014; 5:211-218.
10. Chedasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K *et al*. The diagnosis and management of non-alcoholic fatty liver disease; Practice guideline by American Association for Study of Liver Disease and American College of Gastroenterology. *Gastroenterology* 2012;1592-1609.
11. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Annals of Clinical Biochemistry* 1969; 6: 24-27.
12. Jendrassik L, Grof P. Colorimetric Method of Determination of bilirubin. *Biochemische Zeitschrift* 1938; 297: 81-82.
13. Bergmeyer HU, Scheibe P, Wahlefeld AW. Methods for aspartate and alanine amino transferase. Clinical Chemistry 1979; 125 :1487.
14. Schlebusch H, Rick W, Lang H, Knedal M. Standards in the activities of clinically important enzymes. *Deutsche Medizinische Wochenschrift* 1974; 99: 765-766.
15. Naito HK. Cholesterol. In: Kaplan A. Clinical Chemistry. Toronto Princeton: The CV Mosby Co St. Louis; 1984. p.1194-1206.
16. Naito HK, Kaplan A. High-density lipoprotein (HDL) cholesterol. Clinical Chemistry. Toronto: C. V. Mosby; 1984. p.1207-1213.
17. Fossati P, Prencipe L, Lorenzo P. Serum triglycerigle determination colourimetrically with an enzyme that produces hydrogen peroxide. *Clinical Chemistry* 1982;28: 2077 – 2080.
18. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultra-

centrifuge. *Clinical Chemistry* 1972;18: 499–502.
19. Vermon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non- alcoholic fatty liver disease and non- alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther* 2011; 34:274-285.
20. Loria P, Adinolfi LE, Bellentani S, Bugianesi E, Grieco A, Fargion S, *et al*. Practice guidelines for the diagnosis and management of NAFLD: A decalogue from the Italian association for the study of the Liver (AISF) expert committee. *Digestive and Liver disease* 2010; 42(4): 272-282.
21. Obesity and overweight. World Health Organization website. Available at http://www.who.int/dietphysicalactivity /publications/facts/obesity/en/. [Accessed June 21, 2012].
22. Willians CD, Stengel J, Asike ML. Prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: A prospective study. *Gastroenterology* 2011; 140(1): 124-131.
23. Kaira S, Vithhalani M, Gulati G, Kulkarni CM, Kadam Y, Pallivathukkal J, *et al*. Study of prevalence of Nonalcoholic fatty liver disease (NAFLD) in type 2 diabetes patients in India (SPRINT). *JAPI* 2013; 61: 448-453.
24. Torres DM, Harrison SA. Diagnosis and therapy of nonalcoholic steatohepatitis. *Gastroenterology* 2008; 134(6):1682-1698.
25. Onyekwere CA, Ogbera AO, Balogun BO. Nonalcoholic fatty liver disease and the metabolic syndrome in an urban hospital serving an African community. *Annals of Hepatology* 2011; 10(2): 119-124.
26. Lesi OA, Soyebi KS, Eboh CN. Fatty liver in a cohort of HIV positive Africans on HAART. *J Natl Med Assoc 2009*; 101(2): 151-155.
27. Powell EE, Cooksley WG, Hanson R, Searle J, Halliday JW, Powell LW. The natural history of nonalcoholic steatohepatitis: a follow-up study of forty-two patients for up to 21 years. *Hepatology* 1990; 11(1): 74-80.
28. Nomura H, Kashiwagi S, Hayashi J, Kajiyama W, Tani S, Goto M. Prevalence of fatty liver in a general population of Okinawa, Japan. *Jpn J Med* 1988; 27(2):142-149.
29. Luyckx FH, Desaive C, Thiry A, Dewé W, Scheen AJ, Gielen JE, *et al*. Liver abnormalities in severely obese subjects: effect of drastic weight loss after gastroplasty. *Int J Obesity Relat Metab Disord* 1998; 22(3):222-226.
30. Clinical practice committee AGA. AGA Technical review on NAFLD. *Gastroenterology* 2002; 123:1705-1725.
31. Jacob M. Kneeman, Joseph Misdraji, Kathleen E. Corey. *Therap Adv Gastroenterol* 2012;5(3):199-207.
32. Ruderman N, Chisholm D, Pi-sunyer X, Schneider S. The metabolically obese normal- weight individual revisited. *Diabetes* 1998; 47:699- 713.
33. Assy N, Kaita K, Mymin D, Levy C, Rosser B, Minuk G. Fatty infiltration of liver in hyperlipidemic patients. *Dig Dis Sci* 2000; 45: 1929-1934.
34. Jerry R. Balentine, Melissa Conrad Soppler. Medicinenet.com. obesity centre 2018; 5:1-18.
35. Obesity and overweight. World Health Organization website. Available at http://www.who.int/dietphysicalactivity /publications/facts/obesity/en/. [Accessed June 21, 2012].
36. Klementina FT, Damjana R. NAFLD: focus on lipoprotein and lipid deregulation. *Hindawi J Lipids* 2011; 2011:1-14.