Original Article

Non-Alcoholic Fatty Disease of Liver

Does Ultrasonically Measured Subcutaneous Abdominal Fat Relate with Grades of Non-Alcoholic Fatty Disease of Liver (NAFDL)?

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ABSTRACT

Objective: This study was designed to assess the relationship of SAFT and the presence of NAFDL along with its severity grade in T2DM and Obesity.

Study Design: Observational / cross section study

Place and Duration of Study: This study was conducted at the Department of Medicine, Rai Medical College Sargodha from January to December, 2021.

Materials and Methods: This study was carried out on the patients presenting in medical OPD, from 40 to 70 years of age, both genders. Obesity was assessed by the simplest and most practiced parameter of obesity as "Looking Obese" or having a "sacking or protuberant tummy". T2DM was confirmed on the basis of available blood sugar and HbA1c record. After applying inclusion (obesity and T2DM) and exclusion criteria, volunteering participants were asked to get an abdominal ultrasound (USG) examination for grading of Hepatic Parenchymal Echogenicity (HPE) in NAFDL and to measure Subcutaneous Abdominal Fat Thickness (SAFT) through the same acoustic window. Subcutaneous Abdominal Fat Thickness (SAFT) measured in mm during USG examination was divided into 4 grades, G1 (0 – 25), G2 (25.01 – 50), G3 (50.01 – 75) and G4 (75.01 – 100) for the convenience of evaluation.

Results: 420 females and 186 males were included in this study. Among the 420 females, 270 had G1 HPE, out of these 13% had G1 SAFT, 82% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. There were 150 females exhibiting G2 HPE, out of these 92% had G1 SAFT, 4% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. No female had G3 HPE. Out of 186 males, 102 males had G1 HPE, out of these 47% had G1 SAFT, 53% had G2 SAFT and none had G3 or G4 SAFT. There were 84 males exhibiting G2 HPE, out of these 29% had G1 SAFT, 71% had G2 SAFT and none had G3 or G4 HPE.

Conclusion: The relationship between upper quadrant and lower quadrant can be the subject of some future studies. The organizations can invite opinion for the recommendation of standard points of window.

Key Words: T2DM, NAFDL, Subcutaneous abdominal fat thickness, CLD.

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INTRODUCTION

Obesity though known to exist from pre-historic times but recently the number of patients suffering from obesity has increased alarmly. Since 1980 the prevalence of being overweight and obese has risen 39% by 2015 as defined by Body Mass Index (BMI) in epidemiological studies. It is projected to rise to 57.8% by 2030 if present trends continue. In economically under developed societies higher prevalence is seen in middle-aged adults from wealthy and urban strata especially among females. On the contrary in high-income countries, there is not much a difference in gender or age groups but is disproportionately greater in disadvantaged groups. Psychosocial and personal cost of obesity are well known. Initially thought to be an evolutionary defense against unpredictable famines and times of shortage of food in different catastrophic events as subcutaneous fat depots, new data has produced abundant evidence of its health hazards highlighting the importance of the selective fat deposition around the viscera and its relationship with increased cardiovascular diseases (CVD). Recently focus has shifted to its deposition in the liver because of its

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metabolic consequences and potential to cause cirrhosis. Paralleling this trend, over the past three decades the increasing incidence of T2DM and prediabetes are observed among children, adolescents and younger adults, it has more than doubled globally. The causes are embedded in a very complex group of genetic and epigenetics interacting within an equally complex societal framework that determines behavior and environmental influences. By 2010 estimates 285 million, 90% had T2DM. It is expected to rise to 439 million, 7.7%, by 2030, Asia being the epicenter, we are among the top 10.[1-3]

Grey scale USG is widely available and used parameter for estimation of both the SAFT and HPE change grades. USG of the liver is the reference for the detection of fatty liver. A multifactorial intervention approach on the risk factors can bring remission and prevent more severe complications.[4,5]

MATERIALS AND METHODS

This Observational / cross section study was carried out on patients presenting to Medical OPDs of RMCS, between the ages of 40-70 years, both genders, with obesity and T2DM from January, 2021 to December, 2021. Obesity was assessed by the simplest and most practiced parameter of obesity as "Looking Obese" or with "sacking or protuberant tummy" as the entry point into the study. T2DM was confirmed on the basis of available blood sugar and HbA1c record as per standard. (1)

After applying inclusion and exclusion criteria, volunteering participants were asked to get an abdominal USG examination by the participating Radiologists using standard 2-5MHz convex transducer and parameters for grading the HPE characteristic of NAFDL and SAFT through the same acoustic window as per standard.(6) SAFT measured in millimeters (mm) during USG examination was divided into 4 grades, G1 (0 – 25), G2 (25.01 – 50), G3 (50.01 – 75) and G4 (75.01 – 100) for the convenience of evaluation.

Inclusion Criteria:

40-70 years age, both sexes,
Obesity as defined.
T2DM as defined

Exclusion Criteria:

Seriously sick patient or terminally ill patient.
Untreated Chronic HBV and HCV disease
Established cirrhosis of liver
Regular alcohol use in last 3 Months
Any other metabolic cause of hepatomegaly or CLD
Pregnancy
Ascites of any etiology
Major end organ disease, liver, kidney, heart, lungs
Active steroid use in last 6 months
Hypothyroidism

Sample Size and Sampling Technique: A minimum sample size of 385 patients was calculated as minimum required to maintain a 5 % margin of error, a 95% confidence interval and a 75% response distribution, using a raosoft sample size calculator.

Statistical Analysis: Data analysis was done using Microsoft Excel version 2016 and Statistical Package for Social Sciences (SPSS) software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) were the primary analytical methods used to relate NAFLD severity score with the subcutaneous abdominal fat pad thickness.

RESULTS

420 females and 186 males were included in this study. There were 270 females exhibiting G1 hepatic parenchymal changes (HPE), out of these 13% had G1 SAFT, 82% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. There were 150 females exhibiting G2 HPE, out of these 92% had G1 SAFT, 4% had G2 SAFT, 4% had G3 SAFT and none had G4 SAFT. No female had G3 HPE. (table 1)

Out of 186 males, 102 males had G1 HPE, out of these 47% had G1 SAFT, 53% had G2 SAFT and none had G3 or G4 SAFT. There were 84 males exhibiting G2 HPE, out of these 29% had G1 SAFT, 71% had G2 SAFT and none had G3 or G4 HPE. (table 2).

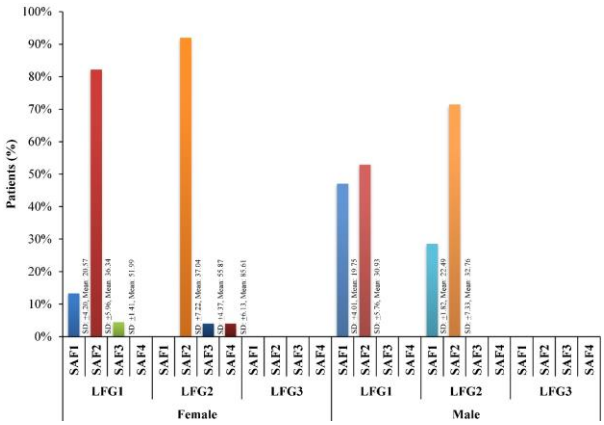
Table No.1: Subcutaneous Abdominal Fat Thickness (SAFT), females. N 420

Liver Fat Grade		SAFT			
		Grade 1 (0 – 25)	Grade 2 (25.01 – 50)	Grade 3 (50.01 – 75)	Grade 4 (75.01 – 100)
Grade 1	270	13.33% (SD: +4.20, Mean: 20.57)	82.22% (SD: +5.96, Mean: 36.34)	4.44% (SD: +1.41, Mean: 51.99)	0 (SD: + 0.00, Mean: 0.00)
Grade 2	150	92.00% (SD: +7.22, Mean: 37.04)	4.00% (SD: +4.37, Mean: 55.87)	4.00% (SD: +6.13, Mean: 85.61)	0 (SD: + 0.00, Mean: 0.00)
Grade 3	0	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)

Table No.2: Subcutaneous Abdominal Fat Thickness (SAFT), males. N186

Liver Fat Grade		SAFT			
		Grade 1 (0 – 25)	Grade 2 (25.01 – 50)	Grade 3 (50.01 – 75)	Grade 4 (75.01 – 100)
Grade 1	102	47.06% (SD: +4.01, Mean: 19.75)	52.94% (SD: +5.76, Mean: 30.93)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)
Grade 2	84	28.57% (SD: +1.82, Mean: 22.49)	71.43% (SD: +7.33, Mean: 32.76)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)
Grade 3	0	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)	0 (SD: + 0.00, Mean: 0.00)

Same is graphically depicted as Graph 1.



Graph No.1: Subcutaneous Abdominal Fat Thickness (SAFT), females and males

DISCUSSION

NAFDL is an umbrella term to cover spectrum from non-alcoholic fatty liver or steatosis (NAFL), a benign, non-progressive clinical entity to non-alcoholic steatohepatitis (NASH), fibrosis and CLD.[7,8] Diagnosis of NAFDL prevalence is based on hepatic steatosis diagnosed by histology or imaging modalities in nonalcoholic subjects (alcoholic liver disease occurs when daily alcohol consumption exceeds 20 g in women or 30 g in men) and appropriate exclusion of other liver diseases. The assessment of hepatic steatosis is typically based on observations of the liver echotexture, echo penetration, visibility of the diaphragm, and clarity of liver vessel structures.[9,10]

The pathophysiologic feature of NAFDL include abnormal glycemic and Lipemic axis, altered amino acid and hepatic Iron homeostasis with increased bile acid production in a complex dynamic multistage interaction between diet, genetics, environment and metabolism.[11] IR and elevated levels of circulating free fatty acids (FFAs) leads to excessive accumulation of triglycerides in liver cells.[12] The resulting lipotoxicity mediated by oxidative stress and exaggerated inflammatory response predispose to progressive hepatic injury.[13] IR links abundant but inefficiently processed glucose to lipids metabolism, NAFDL often exhibits both hyperinsulinemia and IR leading to TG accumulation and T2D, respectively. Amino acids simultaneously regulate both glucose and lipid metabolism. Bile acid plays its role through choline. Excess Iron accumulation in the liver fuels inflammation and oxidative stress. Oxidative stress in turn augments lipid accumulation by adding fatty acids and cholesterol, a vicious circle is activated, all contributing and influencing each other.[14]

The obesity must be prioritized for intervention due to high potential for prevention and reversal. Overweight or obese NAFDL patients are more likely to develop steatohepatitis and severe forms of liver disease. Obesity (excessive BMI and visceral obesity) is the most common and well documented risk factor for NAFLD. This bidirectional association between NAFDL and components of MetS has been strongly established. T2DM and NAFDL can develop almost simultaneously in patients with confounding effect on prevalence statistics of both conditions. Similarly the prevalence of NAFDL in individuals attending lipid clinics has been estimated to be 50%.[15]

Liver biopsy, though still is gold standard, has limitations due to small sample size subject to sampling errors, chances of bleeding and being an invasive procedure. Ultrasonography of the liver is the most widely used investigation in epidemiological studies due to its wide availability, cost-effectiveness, real time evaluation capability and reliability, however due to subjective nature of the test inter-observer agreement is relatively poor. CT assesses fatty liver on the degree of attenuation of parenchyma, steatosis appearing hypodense due to reduction in liver attenuation with sensitivity and specificity of 82% and 100% respectively of moderate-severe hepatic steatosis. However, both CT and USG have limited diagnostic accuracy for detecting mild steatosis. The Proton magnetic resonance spectroscopy (MRS) has emerged as most reliable non-invasively tool to quantify the fat

content in liver with sensitivity of (80-91%) and specificity of (80.2- 87%). [16]

CONCLUSION

In this study we couldn't find any relationship of SAFT with HPE grades in both sexes. This clearly implies that hepatic fat deposition is under multiple metabolic and hemostatic influences. Moreover we couldn't find any recommendation for any particular point of reference in the literature, we decided to take right upper quadrant, a standard point for the liver, for our study. In most cases of obesity the maximum subcutaneous fat deposition is below the umbilicus. The relationship between upper quadrant and lower quadrant can be the subject of some future studies. The organizations can invite opinion for the recommendation of standard points of window.

Author's Contribution:

Concept & Design of Study:	Mohammad Mohsin Rana
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. Hepatol 2016;64:73–84.
2. Perseghin G. Lipids in the wrong place: visceral fat and nonalcoholic steatohepatitis. Diabetes Care 2011;34 (Suppl. 2):S367–S370.
3. Hwang JH, et al. Increased intrahepatic triglyceride is associated with peripheral insulin resistance: in vivo MR imaging and spectroscopy studies. Am J Physiol Endocrinol Metab 2007;293:E1663–E1669.
4. Abougazia AS, Alnuaimi AS, Mahran AS, et al. Prevalence and risk factors of nonalcoholic fatty liver disease in primary health care centers among subjects examined by abdominal ultrasound in Qatar: A case-control study. World Family Med 2020; 18(9): 34-44.
5. Ejaz S, Mukhtar S, Uzair M, Farooq MY, Sajjad S, Muzaffar F. Correlation Between Ultrasonographic Grading of Fatty Liver and Lipid Profile. Am Scientific Res J Engineering, Technology, Sciences (ASRJETS).ISSN (Print) 2313-4410, ISSN (Online) 2313-4402, © Global Society of Scientific Research and Researchers
6. Hegazy M, Mostafa A. Liver ultrasound scanning in the detection of hepatic steatosis and fibrosis in NASH patients. Egypt J Int Med 2012;24(2): 27–31.
7. Vanni E, Bugianesi E, Kotronen A, De Minicis S, Yki-Järvinen H, Svegliati-Baroni G. From the metabolic syndrome to NAFLD or vice versa? Dig Liver Dis 2010;42:320-330.
8. Rinella ME: Nonalcoholic fatty liver disease: A systematic review. JAMA 2015;313:2263-2273.
9. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and Management of Nonalcoholic Fatty Liver Disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatol 2017;67:328.
10. Chen J, Chao Y, Tsai Y, Chan H, Wan Y, Tai D, Po-Hsiang Tsui. Clinical Value of Information Entropy Compared with Deep Learning for Ultrasound Grading of Hepatic Steatosis. Entropy 2020;22:1006 doi:10.3390/e22091006. www.mdpi.com/ journal/entropy
11. Marchisello S, Di Pino A, Scicali R, Urbano F, Piro S, Purrello F, Rabuazzo AM. Pathophysiological, molecular and therapeutic issues of nonalcoholic fatty liver disease: An overview. Int J Mol Sci 2019;20:1948.
12. Bessone F, Razori MV, Roma MG. Molecular pathways of nonalcoholic fatty liver disease development and progression. Cell Mol Life Sci 2019;76: 99-128.
13. Shao M, Zixiang Ye, Qin Y, Tao Wu. Abnormal metabolic processes involved in the pathogenesis of non-alcoholic fatty liver disease (Review). Experimental Therapeutic Med 2020;20:26.
14. Hashimoto E, et al, editor. Diagnosis of Liver Disease. 2nd Edition. Springer Nature Singapore Pte Ltd;2019.p.79-84.
15. Chalasani N, Younossi Z, Lavine JE, et al. Practice Guidance. The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance from the American Association for the Study of Liver Diseases. Hepatol 2018;67(1): 328-57.
16. Ejaz S, Mukhtar S, Uzair M, Farooq MY, Sajjad S, Muzaffar F. Correlation Between Ultrasonographic Grading of Fatty Liver and Lipid Profile. American Scientific Research Journal for Engineering, Technology, and Sciences (ASRJETS). ISSN (Print) 2313-4410, ISSN (Online) 2313-4402.