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High Resolution Ultrasound Evaluation Of Mean Carotid Intima-Media Thickness Of Patients With Moderate To Severe Non-Alcoholic Hepatic Steatosis.

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Abstract
Background*: This Study Aims To Compare The Mean Carotid Artery Intima Media Thickness, A Marker Of Atherosclerosis, Between Patients With Moderate To Severe Nonalcoholic Fatty Liver Disease And, A Control Group, In Order To Investigate The Association Of This Condition With Obesity, Type II Diabetes, And Dyslipidemia, Which Are Highly Prevalent Factors.*
Materials And Methods*: For This Study, A Total Of Nonalcoholic Hepatic Steatosis Patients And 50 Control Subjects Were Selected From The General Population In Guntur. Measurements Of Mean Common Carotid Artery Intima-Media Thickness (CCIMT) And Other Cardiovascular Risk Factors Were Obtained. The Collected Data Were Then Analyzed Using X2 And Independent T-Tests.*
Results*: The Analysis Of Data Revealed Significant Difference Between Nonalcoholic Hepatic Steatosis Patients And The Control Group. Specifically, The Nonalcoholic Hepatic Steatosis Patients Exhibited Significantly Higher Values In Common Carotid Intima Media Thickness, Waist Circumference, Waist/Hip Ratio, Body Mass Index, Triglyceride, Total Cholesterol (P=0.001), As Well As ALT (P=0.04), And ALP (P=0.047) Levels Compared To The Control Group.*
Conclusion*: Giving Significantly Higher Risk For Atherosclerosis And Cardiovascular Disease Observed In Nonalcoholic Hepatic Steatosis Patients, It Is Imperative To Assess Common Carotid Intima Media Thickness And Other Cardiovascular Risk Factors In All Individuals Affected By This Condition.*

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I. Introduction:

Nonalcoholic fatty liver disease (NAFLD) is a commonly encountered condition characterized by the accumulation of fat in liver cells, similar to the fatty infiltration seen in alcohol-induced liver injury. Notably, NAFLD occurs in individuals who do not engage in alcohol abuse [1]. The incidence of fatty liver is estimated to range from 14% to 23%. However, in individuals who are obese or have type II diabetes, this prevalence increases significantly, reaching rates between 70% and 90% [2].

NAFLD encompasses a spectrum of conditions, ranging from simple fatty liver to steato-hepatitis which exhibits histological similarities to alcoholic hepatitis. In some cases, NAFLD can progress to advanced stages of liver disease and eventually lead to cirrhosis. Due to these potential consequences, fatty liver, once considered an incidental finding, has gained significant attention in recent years [3].

Liver biopsy is considered the gold standard diagnostic test for NAFLD, although its use may be limited in patients due to ethical and medical considerations [4]. While elevated liver enzyme levels are commonly observed in NAFLD patients, these tests have low specificity. Therefore, clinical evaluation of NAFLD typically involves a combination of ultrasound findings and laboratory tests. Previous studies have demonstrated a strong correlation between ultrasonographic results and histological findings, specifically related to fatty infiltration [4, 5]. Thus, ultrasonography alone can provide an indication of the degree of fatty infiltration.

Moreover, NAFLD is closely associated with obesity, type II diabetes, and dyslipidemia. A significant proportion of NAFLD patients exhibit central obesity and symptoms of insulin resistance. Consequently, NAFLD shares several characteristics with the metabolic syndrome, which is a highly atherogenic condition, leading to a significant cardiovascular risk.

Extensive research has demonstrated that carotid artery intima-media thickness (IMT), serving as a reliable indicator of subclinical atherosclerosis, can predict the likelihood of myocardial infarction and stroke. Recent studies have highlighted the association between nonalcoholic fatty liver and atherosclerosis, particularly

in healthy men. These findings reflect the complex and contradictory effects of metabolic syndrome, including insulin resistance and increased visceral fat, on the development of both conditions [6, 7].

To explore atherosclerosis, B-mode ultrasound imaging provides a non-invasive method for directly vitalizing the arterial wall. The technique allows for the measurement of carotid intima-media thickness (CIMT), which serves as a reliable indicator of the extent of atherosclerosis. Importantly, CIMT assessment through ultrasound has shown to be more sensitive in detecting early stages of atherosclerosis compared to angiography, making it a valuable tool for early detection and monitoring of the disease [8].

In various cross-sectional studies, the presence of carotid atherosclerosis has been observed in patients with nonalcoholic fatty liver disease (NAFLD). Additionally, a recent recognition has been made regarding the association between carotid intima-media thickness (IMT) and the severity of liver injury [9]. Long term cohort studies on patients with NAFD, spanning up to 18 years, have revealed mortality rates from coronary heart disease (CHD) equivalent to those attributed to cirrhosis [1].

Given the high prevalence of fatty liver in the society and the feasibility of diagnosing it noninvasively using ultrasound, the objective of this study is to investigate ultrasound measurement of carotid intima media thickness (CIMT) as compared to a control group. CMIT serves as a non-invasive marker for atherosclerosis and provides insight into cardiovascular risk associated with non-alcoholic fatty liver disease.

II. Materials and Methods:

This case-control study included a total of 100 subjects who were divided into two groups. The first group comprised individuals with a sonographically determined moderate to severe degree of fatty liver, while the second group consisted of non-fatty liver controls. The study population was selected from individuals aged 25 years and above residing in Guntur city. To ensure compatibility, age and sex-matched controls were chosen from the same geographical area. All participants underwent liver ultrasound examination, using Mylab X6 Esoate, performed by a single radiologist. Additionally, evaluation of intima media thickness of right common carotid artery was conducted by the same radiologist.

Before being included in the study, all the subjects provided informed consent. Detailed demographic information, including age, gender, ethnicity, marital status, smoking or passive smoking, and alcohol consumption, was recorded for each participant. Blood pressure measurements were taken twice, with a 30 minute interval, using a mercury thermometer. Height and weight measurements were taken to calculate body mass index (BMI). Waist circumference, measured at the midpoint between the lowest rib cage and the iliac crest after exhalation. As well as hip circumference at the widest point between the hips and bottom, were also recorded. Additionally, the waist/hip ratio was calculated.

Furthermore, a series of examinations were conducted by accredited laboratories. These examinations included fasting venous blood samples to measure glucose levels, triglycerides, total cholesterol, High density lipo-protein (HDL), low density lipo-protein (LDL), and liver enzymes such as aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP).

Exclusion criterion:

1) Individuals with documented history of liver disease,
2) Individuals who consume more than 20gms of alcohol per day or engage in alcohol abuse.
3) Individuals with liver disease other than fatty liver that have been confirmed through ultrasound imaging.

The diagnosis of non-alcoholic fatty liver disease (NAFLD) relies on two key factors: the presence of hepatic steatosis or steatohepatitis and confirmation that the disease is non-alcoholic origin.

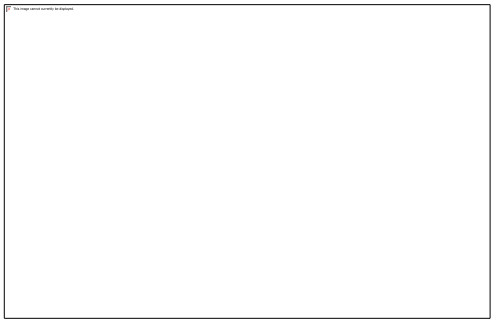
Radiological imaging techniques such as ultrasonography, CT scan, and MRI, either individually or in combination, have been found to have a suitable threshold for diagnosing fatty infiltration of the liver. Among these methods, ultrasonography is the most accessible and cost-effective [10]. The criteria for diagnosing fatty liver using abdominal ultrasonography with a 3.5MHz probe are as follows

-**Grade I (mild):** There is a slight increase in liver echogenicity, but the visualization of the liver is still normal.

-**Grade II (moderate):** There is a moderate increase in liver echogenicity, and there is a slight impairment of visualization of the intrahepatic vessels.

-**Grade III (severe):** There is a marked increase in liver echogenicity, and there is poor or no visualization of the diaphragm, intrahepatic vessels, and posterior part of the right lobe of the liver.

To calculate the mean carotid intima media thickness (CIMT) using 7.5-MHz ultrasound probe, the mean thickness of intima and media layers in the right common carotid artery, proximal to the bulb, and the wall of the artery distal to the probe were measured (Fig. A). Subsequently, these two groups were analyzed using statistical software such as SPSS-16, with independent t-tests and χ 2 tests being employed.



III. Results:

In this study, a total of 50 patients who had moderate to severe fatty liver disease were included, along with 50 healthy controls who were matched in terms of age and sex. Among the subjects, 48% were men, and 52% were women. The mean age of the fatty liver group was 55±10 years, which was similar to the mean age of the control group, which was 55±8years.

In the fatty liver group, 6% of the subjects were smokers, while in the control group, 4% were smokers. Additionally, 18% of the fatty liver group and 8% of the control group were passive smokers. These percentages indicate that there was no significant difference in smoking habits between the two groups.

When it comes to carotid intima thickness (CMIT), the fatty liver group had an average IMT of 0.75±0.14 mm, while the control group had an average IMT of 0.54±0.1mm. The significant difference between the two groups (p=0.001) indicates that the fatty liver group had a significantly higher IMT compared to the control group.

Several other clinical variables were also examined. The fatty liver group had a significantly higher body mass index (BMI) than the control group (30.6±5.7 versus 25.7±4.2; p=0.001). There were also significant differences (p=0.0001) observed in waist circumference and waist/hip ration between the fatty liver and control groups (102±11 versus 88±10, and 0.92±0.04 versus 0.86±0.04, respectively).

These results suggest that individuals with fatty liver disease had higher IMT, BMI, waist circumference, and waist/hip ratio compared to the control group, indicating potential associations between fatty liver disease and cardiovascular risk factors.

Despite the differences observed in certain clinical variables, there were no significant differences between the fatty liver group and the control group in terms of systolic and diastolic blood pressure, ethnicity, and marital status.

Regarding blood pressure, no significant difference was found between the fatty liver and control groups. The average systolic blood pressure was 137 ± 30mm of Hg in the fatty liver group and 85±12 mm of Hg in the control group. Similarly, the average diastolic blood pressure was 136±17 mm of Hg in the fatty liver group and 79 ±8 mm of Hg in the control group.

In the laboratory analysis, although the fatty liver group and higher levels of fasting blood glucose and AST compared to the control group (104±38 versus 96± 44mg/dL and 27±18 versus 25±10IU/L, respectively), these differences were not statistically significant.

However, the fatty liver group did show significant differences in the levels of total cholesterol, triglycerides, ALT, and ALP compared to the control group. The fatty liver group had higher levels of total cholesterol (205±47 versus 174±38mg/dL, p=0.001), triglycerides (193±102 versus 111±52 mg/dL, p=0.001), ALT (243±78 versus 213±51 IU/L, p=0.048) compared to the control group.

These findings suggest that individuals with fatty liver disease exhibited significant differences in lipid profile and liver enzyme levels compared to the control group, indicating potential metabolic and liver function abnormalities associated with fatty liver disease.

IV. Discussion:

In the conducted study, the comparison of carotid intima-media thickness (IMT) between patients with moderate to severe fatty liver and the control group revealed a significant increase in IMT in the fatty liver group. These findings are consistent with previous studies that have linked non-alcoholic fatty liver disease (NAFLD) with elevated IMT, suggesting the presence of early generalized atherosclerosis [12-14]. The results indicate that individuals with fatty liver disease are at higher risk of developing early atherosclerosis and are also more susceptible to cardiovascular complications. These findings emphasize the importance of recognizing the association between NAFLD and cardiovascular risk, highlighting the need for comprehensive management and preventive measures for these patients.

As mentioned earlier, abdominal ultrasonography, is a cost-efficient and easily accessible method of screening and diagnosing fatty liver disease. However, it is worth noting that the diagnosis of mild fatty liver

disease (Grade I) may require more expertise and experience, and there can be a higher level of disagreement among observers when reporting Grade-I fatty liver [15]. To mitigate this potential issue, the study specifically included moderate to severe cases of fatty liver (grade II and III) in the fatty liver group to reduce the potential variability in the diagnosis and ensure more consistent inclusion criteria for the study.

Non-alcoholic fatty liver disease (NAFLD) is a prevalent condition, affecting up to one third of the general population. It is particularly common among individuals with cardio-metabolic risk factors, including abdominal obesity, type II diabetes, and other components of metabolic syndrome (MetS). As the understanding of NAFLD continues to grow, its association with MetS has received increasing recognition. This recognition has prompted greater attention to the potential risk of NAFLD in the development of cardiovascular disease [12].

Metabolic syndrome is a cluster of risk factors that contribute to the development of cardiovascular disease and type II diabetes. The risk factors include abdominal obesity, dyslipidemia, high blood pressure, insulin resistance or glucose intolerance, prothrombotic condition or proinflammatory states.

The results of the study demonstrated significant differences between the fatty liver group and the control group in several parameters. Specifically, individuals with fatty liver disease had significantly higher waist circumference, waist/hip ratio, BMI, triglyceride levels, and total cholesterol values compared to control group. These findings indicate a higher prevalence of abdominal obesity and dyslipidemia in individuals with fatty liver disease.

Additionally, there were significant differences observed in the levels of liver enzymes, specifically alanine aminotransferase (ALT) and alkaline phosphatase (ALP), between the two groups. Elevated ALT levels, in particular are indicative of liver inflammation, which is commonly associated with non-alcoholic fatty liver disease (NAFLD).

However, it is important to note that mean diastolic blood pressure and fasting glucose levels were higher in the control group, but these differences did not reach statistical significance. This suggest that there may not be a substantial difference in these parameters between these two groups within the context of this study.

The findings of the study highlight several important comorbidities in patients with fatty liver disease. The higher waist to hip ratio observed in fatty liver group indicates a higher incidence of central obesity in these individuals. Furthermore, the elevated lipid profile, specifically increased levels of triglycerides and total cholesterol, suggests that patients with fatty liver are at a higher risk for cardiovascular diseases.

However, no significant differences were observed between two groups in terms of blood pressure or diabetes. This indicates that, while these metabolic syndrome components were not significantly different between the two groups of the study. The focus should still be on the easy diagnosis of fatty liver through ultrasound examination and its association with metabolic syndrome components such as central obesity, triglycerides, and high cholesterol. Consequently, it is crucial to evaluate patients with fatty liver disease for carotid intima media thickness (IMT) and other metabolic syndrome components.

In summary, the study suggests that the patients with fatty liver disease should undergo comprehensive assessment, including evaluation of carotid artery IMT, to identify and manage potential cardiovascular risks. By incorporating this evaluation into routine examinations, health care providers can facilitate early detection and intervention, which can significantly reduce the cardiovascular complications associated with fatty liver disease and metabolic syndrome.

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References

[1]. Brea A, Mosquera D, Martin E, Et Al. Nonalcoholic Fatty Liver Disease Is Associated With Carotid Atherosclerosis: A Case-Control Study. Arterioscler Thromb Vasc Biol 2005; 25(5): 1045-1050.
[2]. Acikel M, Sunay S, Koplay M, Et Al. Evaluation Of Ultrasonographic Fatty Liver And Severity Of Coronary Atherosclerosis, And Obesity In Patients Undergoing Coronary Angiography. Anadolu Kardiyol Derg 2009; 9(4): 273-9.
[3]. Younossi Z, Diehl AM, Ong JP. Nonalcoholic Fatty Liver Disease: An Agenda For Clinical Research. Hepatology 2002; 35(4): 746-752.
[4]. Kim HC, Kim DJ, Huh KB. Association Between Nonalcoholic Fatty Liver Disease And Carotid Intima-Media Thickness According To The Presence Of Metabolic Syndrome. Atherosclerosis 2009; 204(2): 521-5.
[5]. Joy D, Thava VR, Scott BB. Diagnosis Of Fatty Liver Disease: Is Biopsy Necessary? Eur J Gastroenterol Hepatol 2003; 15(5): 539-43.
[6]. Fracanzani AL, Burdick L, Raselli S, Et Al. Carotid Artery Intima-Media Thickness In Nonalcoholic Fatty Liver Disease. Am J Med 2008; 121(1): 72-8.
[7]. Aygun C, Kocaman O, Sahin T, Et Al. Evaluation Of Metabolic Syndrome Frequency And Carotid Artery Intimamedia Thickness As Risk Factors For Atherosclerosis In Patients With Nonalcoholic Fatty Liver Disease. Dig Dis Sci 2008; 53(5): 1352-1357.
[8]. Bots ML, Grobbee DE. Intima Media Thickness As A Surrogate Marker For Generalised Atherosclerosis. Cardiovasc Drugs Ther 2002; 16(4): 341-51.

[9]. Targher G, Bertolini L, Padovani R, Et Al. Relations Between Carotid Artery Wall Thickness And Liver Histology In Subjects With Nonalcoholic Fatty Liver Disease. Diabetes Care 2006; 29(6): 1325-1330.
[10]. Choudhury J, Sanyal AJ. Clinical Aspects Of Fatty Liver Disease. Semin Liver Dis 2004; 24(4): 349-362.
[11]. Suhas G, Parulekar L, Robert L. Bree. Liver. In: Mcgaham JP, Goldberg BB. Diagnostic Ultrasound. 2nd Ed. New York: Informa Health Care; 2008: 390-392.
[12]. Targher G, Arcaro G. Non-Alcoholic Fatty Liver Disease And Increased Risk Of Cardiovascular Disease. Atherosclerosis 2007; 191(2): 235-40.
[13]. Sookoian S, Pirola CJ. Non-Alcoholic Fatty Liver Disease Is Strongly Associated With Carotid Atherosclerosis: A Systematic Review. J Hepatol 2008; 49(4): 600-7.
[14]. O'Leary DH, Polak JF. Intima-Media Thickness: A Tool For Atherosclerosis Imaging And Event Prediction. Am J Cardiol 2002; 90(10C): 18-21.
[15]. Scatarige JC, Scott WW, Donovan PJ, Et Al. Fatty Infiltration Of The Liver: Ultrasonographic And Computed Tomographic Correlation. J Ultrasound Med 1984; 3(1): 9- 14.