Carotid Intima-media Thickness in Patients with Non-alcoholic Fatty Liver Diseases Attending Al-kindy Teaching Hospital.

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بسم الله الرحمن الرحيم

صدق الله العظيم

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Abbreviation	Full Name
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
CVD	Cardiovascular disease
CIMT	Carotid intima-media thickness
BMI	Body mass index
SPSS	Statistical Package For Social Sciences

ABSTRACT:

Background: Non-alcoholic fatty liver disease is one of the most common liver disease. It is caused by fatty infiltration of the liver in the absence of other causes of steatosis .It is strongly associated with central adiposity, high body mass index, insulin resistance states, hypertension and hyperlipidemia, which are features of the metabolic syndrome.

Objectives: To measure the thickness of the carotid intima-media in patients with non-alcoholic fatty liver disease to find out if there is an association between non-alcoholic fatty liver disease and increased carotid intima-media thickness.

Methods: This was a descriptive cross-sectional study carried out at alkindy teaching hospital during the academic year 2022-2023.The data were collected for four months from October 1,2022 to February 1,2023.The sample size was 100 diagnosed cases of non-alcoholic fatty liver disease based on ultrasound findings, which include males and females. The convenience sampling method was used to collect data .Data obtained were entered into the computer using the Microsoft excel program with their statistical analysis and relevant statistical tests, along with the generation of tables using statistical package for social statistics version 26 software.

Results: Out of 100 patients there was 53 one with CIMT >0.08cm , 23 patients of them had grade I fatty liver, 24 had grade II fatty liver and 6 had grade III fatty liver .There were 47 patients with CIMT <0.08cm , 31 patients of them were grade I fatty liver and 16 were grade II fatty liver. The P_ value of chi-square test was 0.015.

Conclusion : This study showed increased carotid intima-media thickness in non-alcoholic fatty liver disease cases.

Key words : Body mass index , fatty liver disease , Ultrasound , Carotid intima-media thickness.

INTRODUCTION:

Nonalcoholic fatty liver disease (NAFLD) is the buildup of extra fat in liver cells that is not caused by alcohol consumption. It is normal for the liver to contain so much fat. However, if more than 5%–10% of the liver's weight is fat, then it is called a fatty liver (steatosis). Steatosis is the first stage of NAFLD when there is a harmless buildup of fat in the liver cells that may only be diagnosed .during tests carried out for another reason.

Steatosis may progress to a more serious form of NAFLD. called non-alcoholic steatohepatitis (NASH), where the liver has become inflamed. Persistent inflammation can cause fibrosis and the formation of scar tissue around the liver and nearby blood vessels, but the liver is still able to function. The fibrosis may progress to cirrhosis after years of inflammation, which is the most severe form of NAFLD, where the liver shrinks and becomes scarred and lumpy; this damage is permanent and can lead to liver failure and liver cancer. [1],[2],[3],[4],[5] .

NAFLD is now recognized as one of the most common causes of chronic liver disease in young people in the developed world. [6] The prevalence of the disease varies in different epidemiological studies and increases with the severity of risk factors [7] and [8]; the majority report an average rate of NAFLD prevalence of 20–30% in Europe [9] [10] and in the Middle East [9] [11], 15% in the Far East [9] [12], and 10–35% in most of the United States [8] studies. However, these rates vary according to the technique used for establishing the diagnosis[8].To simplify the NAFLD diagnosis, several studies have identified demographic and clinical risk factors for NAFLD. such as advanced age [10], male gender [13], Hispanic ethnicity [14], and genetic predisposition(PNPLA3 gene) [15] and the presence of the main features of metabolic syndrome, namely obesity, type 2 diabetes, and hyperlipidemia [10]. However, some people develop non-alcoholic fatty liver disease even if they do not have any risk factors.

Most patients with nonalcoholic fatty liver disease have no symptoms or signs of liver disease at the time of diagnosis, although many patients report fatigue or malaise and a sensation of fullness or discomfort on the right side of the upper abdomen. Hepatomegaly is the only physical finding in most patients [16], [17].

The diagnosis of nonalcoholic fatty liver disease is usually suspected in persons with asymptomatic elevation of aminotransferase levels, radiologic findings of fatty liver, or unexplained persistent hepatomegaly [18]. Abdominal US is currently the most common method employed for qualitative assessment of hepatic steatosis because it is non-invasive, widely available, cheap, and provides useful information. The presence of hepatic steatosis on abdominal US is usually defined based on the presence of at least two of the following findings: increased hepatorenal contrast, liver brightness, deep attenuation, and vascular blurring (Fig. 1). [19]

Fig -1-

Importing studies cannot be used to accurately determine the severity of liver damage. The clinical suspicion of nonalcoholic fatty liver disease and its severity can only be confirmed with a liver biopsy.

Cardiovascular disease (CVD), especially atherosclerosis , is one of the most common complications of NAFLD, and it increases the rate of liver-related mortality. This association is not surprising since NAFLD has been

considered a part of the metabolic syndrome, which can cause cardiovascular diseases. Moreover, both NAFLD and metabolic syndrome present similar pathophysiological mechanisms, such as increased visceral adiposity, altered lipid metabolism, increased oxidative stress, and systemic inflammation, that could explain their association with CVD [20].

Several studies have been conducted to establish NAFLD as an independent risk factor for atherosclerosis and cardiovascular disease. Most of these studies used carotid artery intima-media thickness (IMT) as a noninvasive marker of subclinical atherosclerosis [21], [22].

Increased CIMT caused by old age, high cholesterol , smoking, high blood pressure, diabetes , obesity and sedentary lifestyle . It may lead to atherosclerosis and it is associated with an increased risk of cerebrovascular disease by formation of plaque that lead to narrowing or blocking of the main arteries that supply the brain and this will lead to stroke formation.[23]

So if we found a relation between NAFLD and increased CIMT this will make us able to make an early diagnosis of atherosclerosis and treat them properly, thereby decreasing the rate of morbidity and mortality associated with these conditions.[24]

IMPORTANCE OF THIS STUDY:

Non-alcoholic fatty liver disease (NAFLD) is considered a potential independent risk factor for carotid atherosclerosis. The clinical findings suggest that the detection of fatty changes in the liver in abdominal ultrasonography should warn us about the probability of the presence of increased carotid intima-media thickness, which is a sign of atherosclerosis and is linked to an increased risk of myocardial infarction, stroke, and peripheral vascular disease.This will make us able to make an early diagnosis of these conditions and treat them properly, thereby decreasing the rate of morbidity and mortality associated with them.

OBJECTIVES:

1.Find the association between non-alcoholic fatty liver disease and cardiovascular diseases.

2. To measure the thickness of the carotid intima media (CIMT) in patients with non-alcoholic fatty liver disease (NAFLD).

3. Find a way for early diagnosis of atherosclerosis to decrease the rate of morbidity and mortality associated with it.

METHODS:

Study design: This was a descriptive cross-sectional study carried out at Alkindy Teaching Hospital during the academic year 2022–2023.

Data collection time: The data were collected for fourth month from October 1, 2022 to February 1, 2023.

The sample size: The sample size was 100, which included males and females. Convenience sampling was used to collect the data.

Inclusion and Exclusion criteria: Patients that were included in this study were between 21 and 60 years of age with an ultrasonic finding of fatty liver and a negative history of alcoholic abuse (the diagnosis of NAFLD requires the exclusion of alcoholic abuse as a cause of liver disease).Patients with chronic liver disease and a history of hepatitis were excluded from this study.

Data collection: Data obtained were entered into the computer using the Microsoft Excel program with their statistical analysis and relevant statistical tests, along with the generation of tables using Statistical Package for Social Statistics (SPSS) version 26 software.

Method of data collection: During the US imaging of a patient diagnosed with NAFDL, also the radiologist check if there is an increase in the carotid artery intima-media thickness (IMT) to determine the relationship between NAFLD and CIMT. It is considered an increase in the CIMT if it is greater than 0.08 cm and a normal if it is less than 0.08 cm.

Diagnosis of fatty liver disease was made on the basis of presence of fatty liver on abdominal ultrasonographic examination and graded as follows: Grade 1: slight diffuse increase in the fine echoes. Liver appears bright compared to the cortex of the kidney. Normal visualization of diaphragm and intra hepatic vessel border.

Grade 2: moderate diffuse increase in the fine echoes. Slightly impaired visualization of the intra hepatic vessels and diaphragm.

Grade 3: marked increase in the fine echoes. Poor or no visualization of intra hepatic vessel borders, diaphragm and the vessels.

ETHICAL COSIDERATION:

Verbal permission was taken from each patient preceding data collection and the details were kept anonymous.

RESULTS:

Out of 100 cases, there were 44 males and 56 females. The age group with the most NAFLD cases (≥50) had 37 cases, followed by 34 cases in the age group (41-50), 17 cases in the age group (21-30), and 12 cases in the age group (31-40). 48 were obese, 22 were overweight, and 30 were normal with respect to their BMI. About the carotid intima thickness, 53 patients were >0.08cm and 47 patients were <0.08cm. About 54 patients were Grade I NAFLD, 40 patients were Grade II, and 6 patients were Grade III. In 100 cases, 56 patients had hepatomegaly and 44 had normal liver size. 55 patients were smokers, and 45 were non-smokers are shown in table 1.

Table 1: *Demographical and clinical characteristics of patients with NAFLD.*

Variable		No.	%	Total
Gender	Male	44	44	44
	Female	56	56	56
Age	21-30	17	17	17
	31-40	12	12	12
	41-50	34	34	34
	≥50	37	37	37
BMI	Normal	30	30	30
	Over Weight	22	22	22
	Obese	48	48	48
IMT	> 0.08	53	53	53
	< 0.08	47	47	47
Fatty Grade	I	54	54	54
	II	40	40	40
	III	6	6	6
Smoking	Yes	55	55	55
	No	45	45	45
Liver Size	Normal	44	44	44
	Enlarge	56	56	56

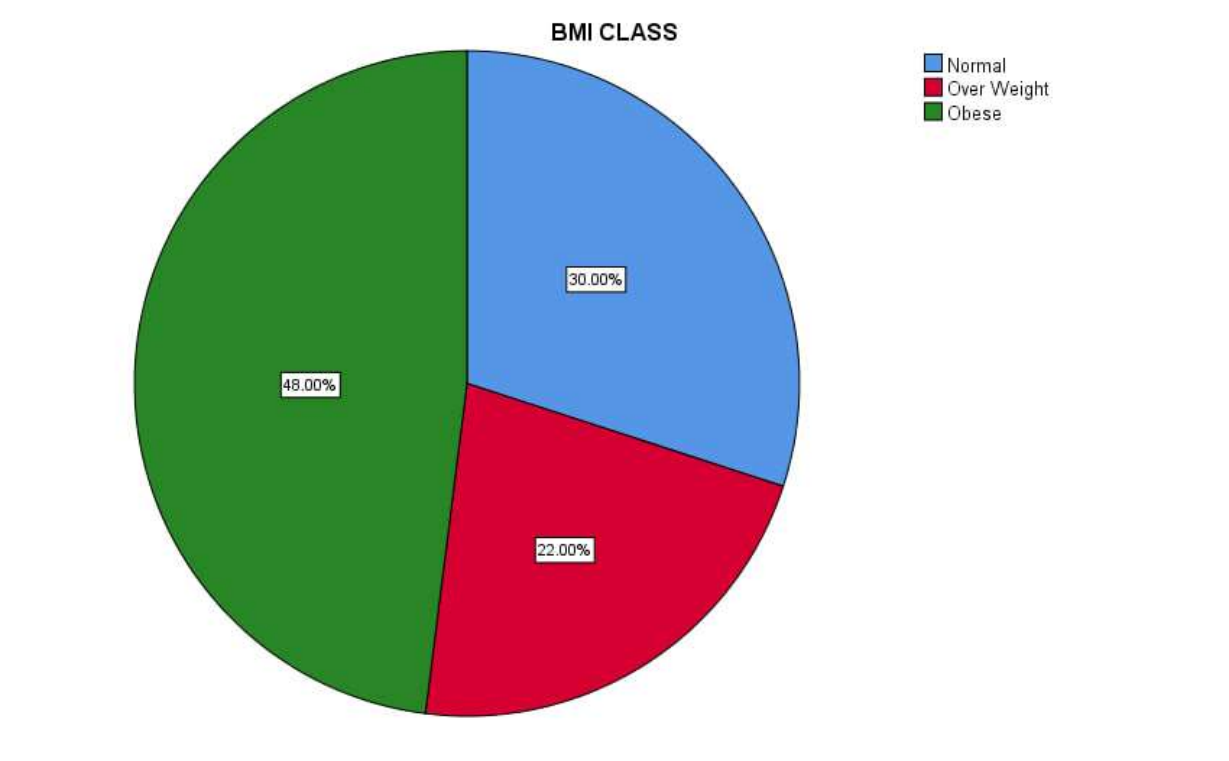

Fig-2-

The percent of each BMI class in our sample.

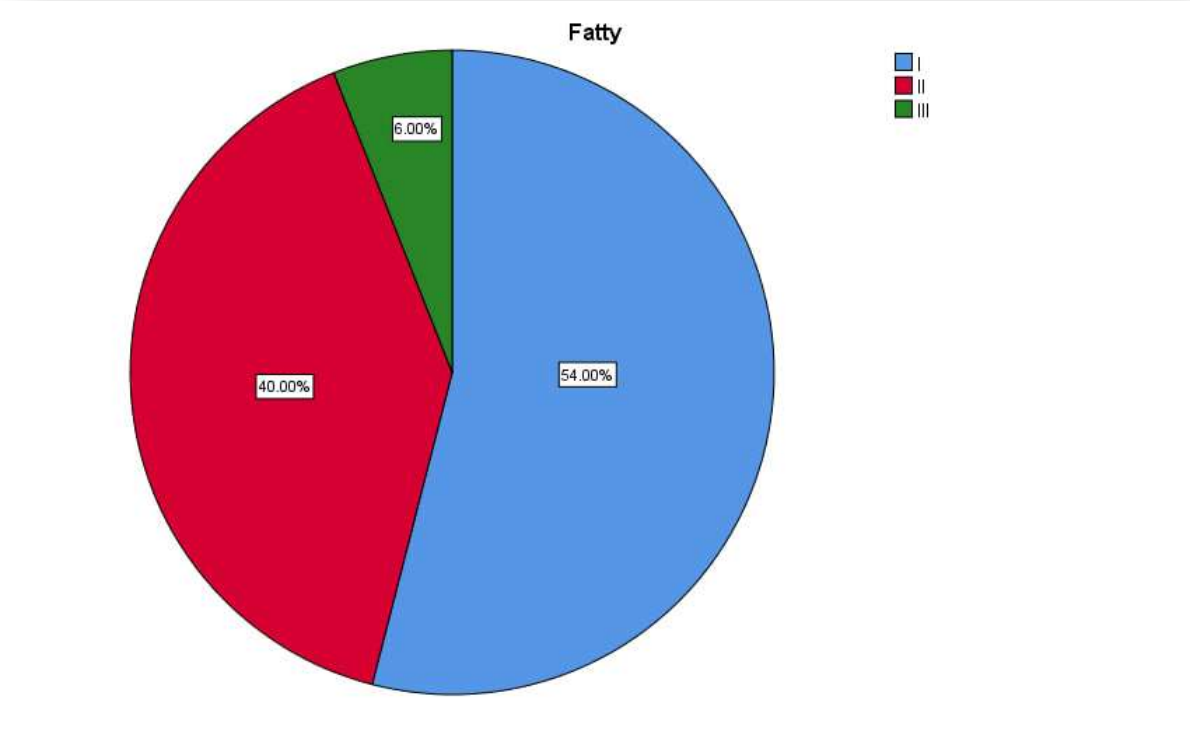

Fig-3-

The percent of cases in each NAFLD Grade in our sample.

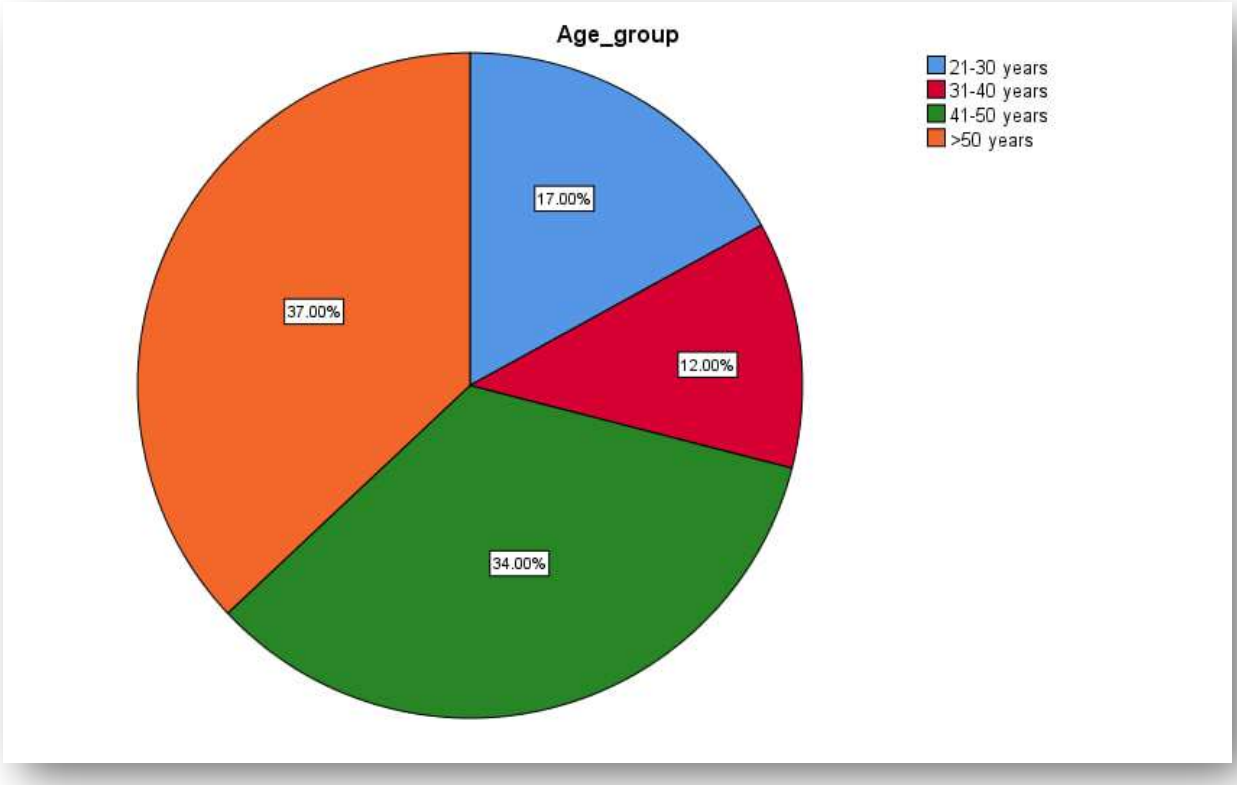

Fig-4-

The percent of each age groups in our sample.

Table 2 shows the relationship between carotid intima-media thickness (CIMT) and nonalcoholic fatty liver disease (NAFLD) grading. In patients with IMT >0.08cm, 23 patients had grade I fatty liver, 24 had grade II fatty liver, and 6 had grade III fatty liver. Patients with IMT< 0.08 cm (31 were Grade I fatty liver, and 16 were Grade II fatty liver .For the comparison between CIMT and fatty grades, the chi-square test was used to determine the statistical significance of differences in qualitative variables. p-value(0.015) Less than 0.05 is considered statistically significant. These results suggest that CIMT values increase with advanced fatty grades.

Table 2: *The relation between carotid intima -media thickness(CIMT)and nonalcoholic fatty liver disease (NAFLD) grading.*

IMT	Fatty Grade			Total	P_ Value
	I	II	III		
<0.08	31	16	0	47	0.015**
>0.08	23	24	6	53	
Total	54	40	6	100	

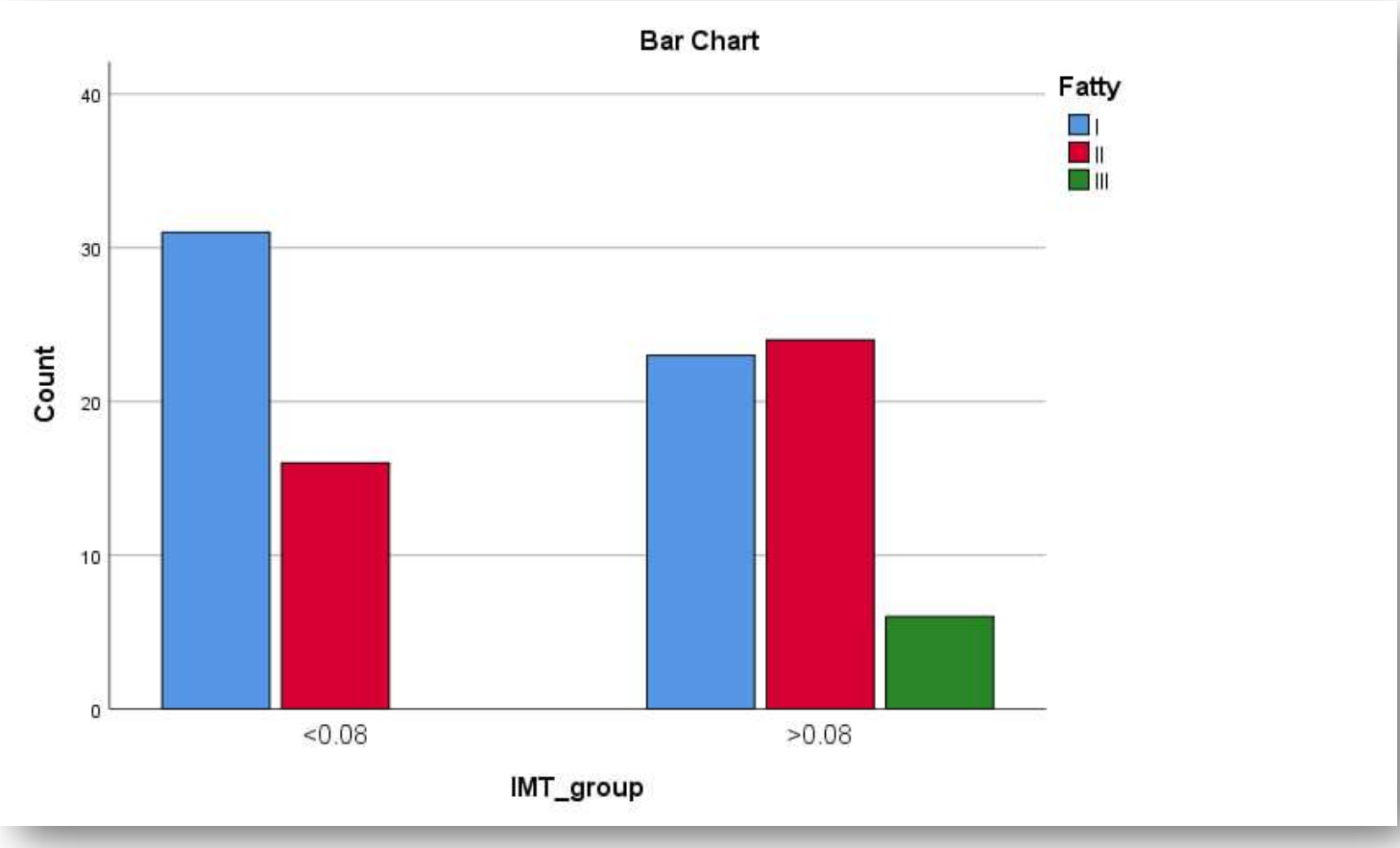

fig-5-

The relation between carotid intima -media thickness(CIMT)and nonalcoholic fatty liver disease (NAFLD)grading.

Table 3 represents the relationship between CIMT and BMI in patients with NAFLD. There are increased CIMT values in obese (BMI ≥30 kg/m2) as compared to normal (BMI ≤ 25) and overweight (BMI >25 kg/m2 and< 30 kg/m2) cases. Likewise, there were increased CIMT values in overweight cases as compared to normal BMI cases. p-value(0.004) Less than 0.05 is considered statistically significant .These results suggest that CIMT values are increased in high BMI cases.

Table 3: *carotid intima-media thickness (CIMT) as per BMI in NAFLD patient.*

IMT	BMI			Total	P_ Value
	Normal	Overweight	Obese		
<0.08	21	11	15	47	0.004**
>0.08	9	11	33	53	
Total	30	22	48	100	

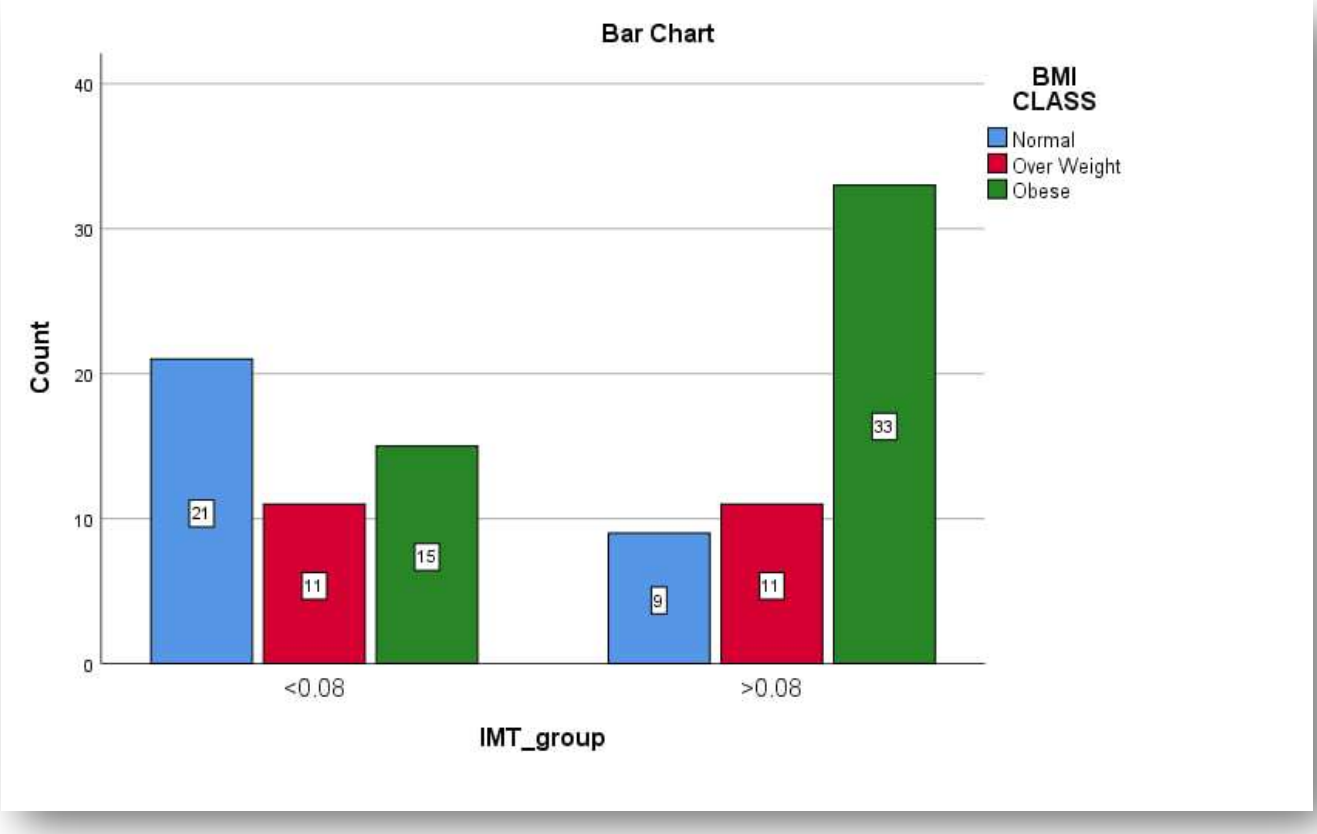

Fig-6-

The relation between carotid intima-media thickness (CIMT) and BMI in NAFLD patients.

Table 4 shows patients with IMT< 0.08 cm, and their ages (21–30) were 15,(31-40) were 10, age (41-50) were 7 , and age (≥50) were 15.Patients with IMT >0.08cm and their age (21–30) were 2, age (31–40) were 2,age(41–50) were 27 and older (≥50) were 22.P_Value (0.0003) less than 0.05 is considered statistically highly significant. These results suggest that IMT values are increasing with age.

Table 4: *The relation between carotid intima-media thickness(CIMT) and age.*

IMT	Age				Total	P _Value
	21-30	31-40	41-50	>50		
<0.08	15	10	7	15	47	0.0003**
>0.08	2	2	27	22	53	
Total	17	12	34	37	100	

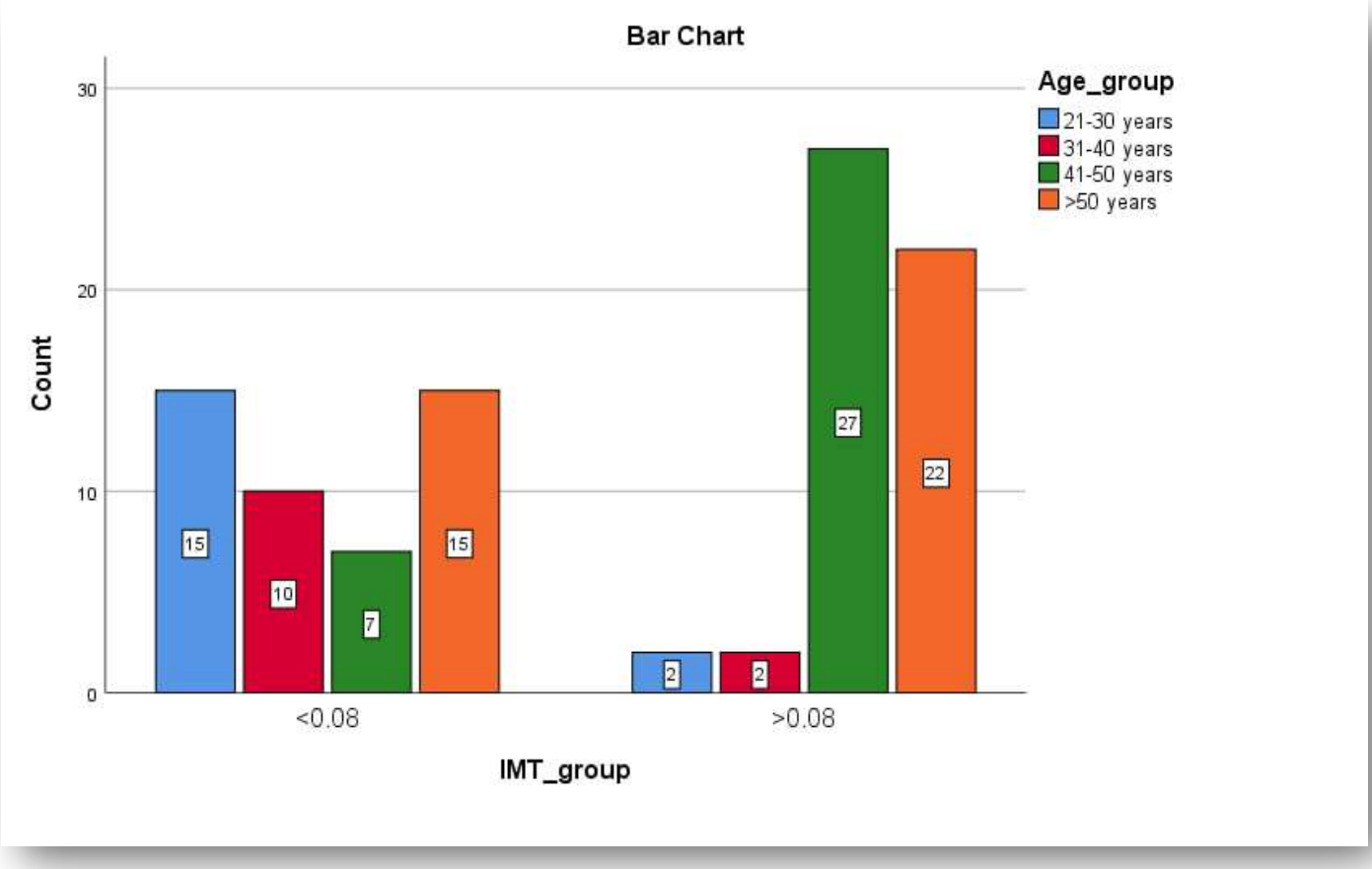

Fig-7-

The relation between carotid intima-media thickness(CIMT) and age.

Table 5 showed that from 53 patients with CIMT > 0.08cm, 36 of them had hepatomegaly and 17 had normal liver size, and from 47 patients with CIMT < 0.08 cm, 20 of them had hepatomegaly and 27 had normal liver size. A P_ value (0.011) less than 0.05 is considered statistically significant. These results suggest that liver size increases with increased carotid intima-media thickness.

Table 5: *The relation between the carotid intima-media thickness(CIMT) and the liver size.*

Liver Size	IMT		Total	P _Value
	<0.08	>0.08		
Normal	27	17	44	0.011**
Enlarge	20	36	56	
Total	47	53	100	

As shown in table 6 , out of the patients who were found to have hepatomegaly, 31 were grade I, 19 were grade II, and six were grade III. For patients with normal liver size, 23 patients were grade I, and 21 patients were grade II. P _Value was not statistically significant because of the sample's small size, but since all our grade III patients showed to have hepatomegaly, it means that liver size increases with advanced fatty liver grade.

Table 6: *The relation between the liver fatty grade and liver size.*

Liver Size	Fatty Grade			Total	P _Value
	I	II	III		
Normal	23	21	0	44	0.052
Enlarge	31	19	6	56	
Total	54	40	6	100	

DISCUSSION:

Our results suggest that patients with NAFLD showed signs of increased CIMT. Besides, the degree of carotid intimal thickness was significantly associated with the grade of fatty liver. This association was statistically significant (p-value = 0.015).Our results are supported by a study carried out by Rasool et al.(23) which found that the level of CIMT was higher in patients with NAFLD and progressively increased with the grade of fatty liver, which was statistically significant (p-value =0.0001).Study by Cai et al.(25[)

We also detected an association between BMI and CIMT and 48% of our NAFLD cases had BMI ≥ 30, while 52% of them had BMI ≤30. Our results showed increased CIMT values in obese (BMI ≥30 kg/m2) as compared to normal (BMI≤ 25 kg/m2) and overweight (BMI > 25 kg/m2 and < 30 kg/m2) cases. Our findings were similar to the findings of Riaz et al.(26) (2013), who stratified CIMT with respect to BMI into groups of BMI≤ 30 kg/m2 and BMI ≥ 30 kg/m2, where 55.96% and 44.04% of NAFLD cases had BMI ≤30 kg/m2 and BMI ≥30 kg/m2, respectively. Their results showed a statistically significant association between NAFLD and raised CIMT in BMI ≥30 kg/m2.

In a study carried out by Khanal (27) liver size increases with advanced fatty liver grade .In our study, although the P _ value was not statistically significant, this was because of our sample size, but since all patients with grade III fatty liver showed to have hepatomegaly, it means that liver size increase with advanced fatty liver grades .

CIMT was also found to increase with advanced age, and the relation between them was statistically highly significant, with a p-value of 0.0003, and these results are similar to those carried out by Chouhan et al.(28)

As the most important result, we showed an association between the presence of NAFLD and an increase in the value of CIMT that was similar to other studies (sookoian , guleria et al.) (29) (30)

CONCIUSION:

This study concluded that the frequency of raised carotid intima-media thickness is higher in patients with non-alcoholic fatty liver disease and shows the positive association between non-alcoholic fatty liver disease and(NAFLD) and raised carotid intima-media thickness.

RECOMMENDATIONS:

-Study the relationship between fatty liver and its grade with HBA1c and lipid profile.

-We recommend that CIMT screening be implemented in all NAFLD patients, and patients with increased carotid IMT could be aggressively treated not only for liver disease but also for underlying CVD risk factors, which will ultimately reduce the morbidity and mortality of these high-risk patients.

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