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# RESEARCH ARTICLE

# CORRELATION BETWEEN THE NON-ALCOHOLIC FATTY LIVER DISEASE AND COMMON CAROTID ARTERY INTIMAL MEDIAL THICKNESS IN PATIENTS ATTENDING A TERTIARY CARE HOSPITAL

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**ABSTRACT**

***Introduction:*** Non-alcoholic fatty liver disease (NAFLD) is an emerging common non communicable disease, worldwide. It is characterized by accumulation of excess fat within the liver cells which could progress into cirrhosis. Although the gold standard method for diagnosis of this condition is by liver biopsy, the ultrasonography can accurately diagnose it. Atherosclerosis is characterized by the presence of intimal lesions which manifest indirectly as increased intimal medial thickness of an artery. Several studies have shown greater intima-media thickness in patients with NAFLD, but there are no studies reported in Sri Lanka. Hence, this study is done to assess the correlation between the stage of NAFLD and common carotid artery intimal medial thickness (CIMT) in a tertiary care hospital in Sri Lanka. ***Objectives:*** The general objective of this study is to evaluate the correlation between the stage of non-alcoholic fatty liver disease and common carotid artery intimal medial thickness in patients attending Department of Radiology Teaching Hospital Peradeniya. The specific objectives of this study are to describe the socio-demographic profile of the patients with NAFLD, to calculate the body mass index (BMI) of the patients with NAFLD and to determine the correlation between the stage of NAFLD and CIMT of the patients with NAFLD. ***Methods:*** This prospective correlational study was conducted after getting ethical clearance from Faculty of Medicine, University of Peradeniya. 201 patients who fulfill the pre- set exclusion and inclusion criteria were recruited for the study. The main exclusion criteria for this study were patients having chronic illness, communicable diseases and hepatic diseases. Patients who give consent and having any degree of fatty liver were included for the study. Sonographic evaluation of grade of fatty liver and B/L CIMT was done and recorded. Consecutive sampling method was used. Descriptive statistics were used to describe the socio-demographic profile and body mass index. Spearman's rank order correlation test was used to determine the correlation between the stage of NAFLD and CIMT at 95% confidence interval. ***Results:*** The age range of the study population was 23 years to 79 years (Mean = 41.77, SD=12.93) and majority belonged to primary working age group (25- 54 years; 75%). Majority of patients were males (56.2%). Average BMI was 25.18kgm$^{-2}$ (SD=4.37) and 45% of patients were obese. Majority of patients had grade II fatty liver (57.7%). A significant correlation was found between the age and bilateral CIMT.($p$ value <0.001). Average CIMT in right and left side were 0.075 cm (SD= 0.009) and 0.077 cm (SD= 0.01) respectively. Average R/ CIMT in males was 0.074 cm and that of in females were 0.077 cm. Average L/ CIMT in males were 0.076 cm and that of in females were 0.078 cm. A statistically significant difference was found between means of R/ CIMT in male and females ($p$ value 0.045) but no statistically significant difference was found on L/side ($p$ value 0.44). There was no statistically significant correlation between the grade of fatty liver with right CIMT (correlation coefficient= 0.025, $p$ = 0.730) or left CIMT (correlation coefficient = 0.128, $p$ = 0.072). ***Conclusion:*** Majority of patients with NAFLD were males who belonged to primary working age group. 45% of study population were obese. Majority of patients had grade II fatty liver. There is a significant correlation between the age and CIMT. However there was no correlation between the grade of NAFLD and right or left CIMT.

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# INTRODUCTION

**Non-alcoholic fatty liver disease (NAFLD):** Non-alcoholic fatty liver disease (NAFLD) is a very common disorder seen worldwide. It generally refers to a group of conditions where there is accumulation of excess fat in the liver of people who drink little or no alcohol (1). This is a recognized condition that lead to cirrhosis (1%) and hepatocellular carcinoma(2). There are two forms of NAFLD. The most common form of NAFLD is a condition called simple fatty liver. It also called hepatic steatosis. In here fat accumulates in the liver cells. Although having fat in the liver is not normal no obvious inflammation or liver damage occurs. This condition not progress in to more serious complications(3).The other group of the NAFLD is non-alcoholic steatohepatitis (NASH). In here fat accumulate in the liver and it causes inflammation of the liver (hepatitis) and progress to liver cell damage.

The inflammation and the liver cell damage lead to the fibrosis of the liver. This condition may lead to cirrhosis and finally to hepatocellular carcinoma (3). There are many studies done to identify the prevalence of the NAFLD in Srilanka. According to them estimated prevalence of NAFLD in urban population in Srilanka is approximately 32.6 % and that of in rural population is approximately 18 % (4). Risk factors for the NAFLD are obesity, hypertension, Type 2 diabetes mellitus and hyperlipidemia. NAFLD is also considered as liver component of the metabolic syndrome. The main reason for NAFLD at present is due to the sedentary life style of the people(5). Current guidelines recommend utilizing the criteria requiring an alcohol exposure of less than 30 g/d for men and less than 20 g/d for women as safe alcohol consumption as a component of NAFLD diagnosis(6). So patients who take safe level of alcohol belong to the NAFLD category. The diagnosis of the NAFLD is mainly by the ultrasound scan. Current gold standard for diagnosing hepatic steatosis is liver biopsy(7). However due to potential harmful outcomes following biopsy, non-invasive techniques are being used. However biopsy is essential to differentiate NAFLD from the NASH. (7). USS is the currently available non-invasive test for diagnosis of fatty liver. Ultrasonically normal liver is seen with same echogenicity or slightly higher than that of renal cortical or splenic echogenicity. In fatty liver, liver echogenicity is slightly increased when compared to ipsilateral renal cortex and the spleen. Thus fatty liver is graded according to USS findings on echogenicity of liver as summarized below (8).

- Grade 0: Normal liver echogenicity
- Grade I: Diffusely increased hepatic echogenicity but periportal and diaphragmatic echogenicity is still appreciable
- Grade II: Diffusely increased hepatic echogenicity obscuring periportal echogenicity but diaphragmatic echogenicity is still appreciable
- Grade III: Diffusely increased hepatic echogenicity obscuring periportal as well as diaphragmatic echogenicity

**Atherosclerosis:** Atherosclerosis is characterized by the presence of intimal lesions called atheroma. Atheromatous plaques are raised lesions composed of soft grumous lipid cores covered by fibrous cap. This can mechanically obstruct the vascular lumen and prone to get rupture resulting in vessel thrombosis. This also can weaken the underlying media and lead to aneurysm formation (9). There are multiple risk factors for the development of atherosclerosis. They are age, sex, obesity, dyslipidemia, smoking, hypertension, family history, diabetes mellitus, high homocystine level and CRP levels(10).

**Common carotid artery as indicator for atherosclerosis:** Left and right Common carotid arteries are major vessels that supply blood to head and neck region. The origin of the left common carotid artery is from the aortic arch and right side from the brachiocephalic trunk. The left CCA has thoracic and cervical course but right CCA has only cervical course. In cervical portion both CCAs follow similar course. It passes upwards from behind the sternoclavicular joint to the level of the upper border of the thyroid cartilage. Both CCAs are within the carotid sheath which is derived from all three layers of deep cervical fascia. It also contain internal jugular vein lateral to the artery and vagus nerve in between two. At the level of C4 the CCAs bifurcate into the external and internal carotid arteries. Carotid intimal – medial thickness (CIMT) has been commonly used as a noninvasive test for assessment of degree of the atherosclerosis(11). Carotid intimal medial thickness is defined as the combined thickness of the CCA medial and intimal layers. This can be reliably assessed using B mode ultrasound. The CIMT is calculated by the measuring the thickness from far wall hyperechoic line which is made by blood-intimal interface to near wall hyperechoic line which is made by and medial-adventitial junction (12). The greater intimal medial thickness of a vessel may indicate the endothelial dysfunction and sub clinical atherosclerosis(13). This conceptcan be used as measurement to diagnose sub clinical atherosclerosis.
Greater intimal medial thickness in carotid arterieshas been found in patients with NAFLD(13).

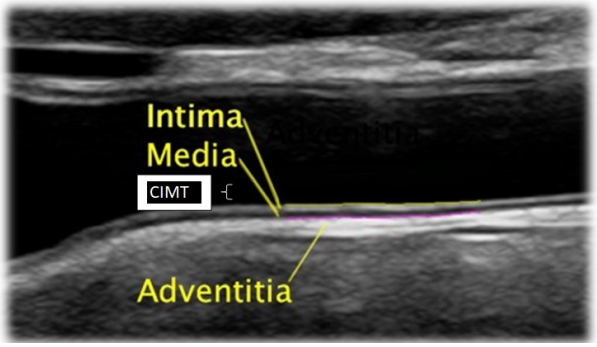


**Fig: 1**

**Literature review**

There are many research studies conducted to find the correlation between nonalcoholic fatty liver diseases and common carotid artery intimal medial thickness. Literature reviews summarized below describe the current research findings. The effect of NAFLD on carotid artery intima-medial thickness as a risk factor for atherosclerosis was conducted by Maryam ZaareNahandi, *et al*, in the gastroenterology ward of Sheykh-Al-raees clinic, Tabriz, Iran, between December 2008 and July 2010.This was a case-control study. 151 subjects were categorized in three groups; group I included 49 patients with NAFLD and DM; group II included 50 non-diabetic NAFLD patients; and group III includes 52 normal subjects as control group. The right and left CIMTs and its maximum reading (CIMTmax) were measured. The median CIMTmax was significantly higher in group I comparing with group II and control group ($p<0.001$). Based on the findings, they found that there is a significant association between the presence of NAFLD and atherosclerosis. This association was independent to the presence of DM. The grade of NAFLD and elevated liver function tests had no effect on severity of atherosclerosis (14).

Another research was conducted on non-alcoholic fatty liver disease as an independent risk factor for carotid atherosclerosis by Abid Rasool, *et al*, 2017; Department of Gastroenterology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India. A total of 200 NAFLD patients and 100 age and sex matched controls were enrolled into the study. Ultrasound was done to document fatty liver and carotid intimal thickness, and relationship between these two was observed. They categorized the subjects according to the grades of the fatty liver and separately calculated the left and right carotid artery intimal medial thickness. The authors concluded that the level of carotid intimal medial thickness was more in cases than in controls and progressively increased with the grade of fatty liver which was statistically significant (15). A study titled non-alcoholic Fatty Liver Disease is Associated with Increased Carotid Intima-Media Thickness in Type 1 Diabetic Patients was carried out by Lei Zhane, *et al*, at the Diabetic Clinic of Shanghai Jiao Tong University from January 2005 to December 2014 . A total of 722 patients (371 men) with T1DM were included in this cross-sectional study. They graded the patients according to the USS appearance of the liver and measured the carotid artery intimal medial thickness. The main outcome measures were detection of NAFLD, CIMT and classical risk factors. The results of the study concluded that NAFLD is associated with elevated C-IMT in T1DM, independent of conventional cardiovascular disease risk factors (16). A study on relationship between carotid artery wall thickness and liver histology in Subjects with nonalcoholic fatty liver disease was done by Giovanni targher MD, *et al*, 2006 in Italy. They compared carotid IMT, as assessed by ultrasonography, in 85 consecutive patients with biopsy-proven NAFLD and 160 age, sex, and BMI-matched healthy control subjects. They concluded that the severity of liver histopathology among NAFLD patients is strongly associated with early carotid atherosclerosis, independent of classical risk factors, insulin resistance, and the presence of metabolic syndrome (17).

A research was conducted on carotid artery intimal medial thickness in nonalcoholic fatty liver disease by Anna LudovicaFracanzani MD *et al*, 2008 in Italy. This is a paired sample case control study. They chose 125 patients with NAFLD and 250 controls who do not have prior diagnosis of diabetes, hypertension and cardiovascular disease. Using B mode ultrasound they evaluated the carotid intima medial thickness and the presence of plaques. A significant difference in mean values of intima medial thickness and prevalence of plaques was observed in NAFLD patients and controls. They concluded the study as patients with NAFLD even with no or mild alterations of liver tests should be considered as high risk for cardiovascular complications (18).

**Justification of study:** Carotid intimal – medial thickness (CIMT) has been commonly used as a noninvasive test for the assessment of degree of atherosclerosis. Due to sedentary life style of the people now a days NAFLD has become a common disease. Many studies are found regarding the NAFLD and CIMT. Most of them are combined with the type 2 diabetes, NAFLD and CIMT. There is lack of studies that correlate with the pure NAFLD and the CIMT. There are no researches that are found in the literature regarding CIMT and NAFLD in Sri Lanka, hence this research is planned, to assess the atherosclerosis in people with NAFLD in Sri Lanka. The correlation between the NAFLD and common carotid artery intimal medial thickness of patients who come for routine ultra sound scans to Department of Radiology at TH Peradeniya is evaluated in this study.TH Peradeniya is a major tertiary care hospital in the central province which has a large draining area with variety of patients.

**Objective of the study**

**General Objective**

•To determine the correlation between the stage of non-alcoholic fatty liver disease and common carotid artery intimal medial thickness in patients attending Department of Radiology Teaching Hospital Peradeniya

**Specific Objectives**

- To describe the socio-demographic profile of the patients with NAFLD attending Radiology Department of Teaching Hospital Peradeniya
- To calculate the BMI of the patients with NAFLD attending Radiology department of Teaching Hospital Peradeniya
- To determine the correlation between the stage of NAFLD and the CIMT of the of the patients with NAFLD attending Radiology department of Teaching Hospital Peradeniya

# METHODOLOGY

**Design:** This study is a prospective correlational study.

**Ethical consideration:** Ethical clearance was obtained from Ethical review committee, Faculty of Medicine, University of Peradeniya.

**Study Setting:** This study was carried out in patients who were attending routine ultra sound scans at Radiology Department, TH Peradeniya

**Study period:** From 2020 June to 2021 December

**Study Population:** Patients attending for routine ultra sound scan of the abdomen to radiology department TH Peradeniya

**Inclusion criteria**

- Patients who are having any degree of NAFLD.
- Patients who consume safe level of alcohol or non-alcoholics

**Exclusion criteria**

- Patients who are severely ill or having acute illness.
- Patients who are mentally unsound, deaf and blind.
- Patients with type 1or 2 diabetes mellitus, coronary artery diseases and hypertension.
- Patients who are having cirrhosis, evidence of chronic liver diseases or known hepatic diseases.
- Patients with biliary diseases. ( Obstructive jaundice)
- Patients who underwent hepatic surgery.
- Patients with malignancy.
- Patients who are having history of ischemic stroke/TIA.
- Chronic alcoholic patients.
- Pregnant women.
- Patients who underwent endarterectomy.

**Sample size and sample techniques:** The sample size was calculated for this correlational study as follows (19)

- $\alpha$ (two-tailed) = 0.05 (Threshold probability for rejecting the null hypothesis. Type I error rate)
- $\beta$ = 0.2 (Probability of failing to reject the null hypothesis under the alternative hypothesis. Type II error rate.)
- r = 0.2 (The expected correlation coefficient.)

The standard normal deviate for $\alpha = Z_\alpha = 1.9600$
The standard normal deviate for $\beta = Z_\beta = 0.8416$
$C = 0.5 * \ln[(1+r)/(1-r)] = 0.2027$

Total sample size = $N = [(Z_\alpha+Z_\beta)/C]^2 + 3 = 194$

The sampling method is consecutive sampling. (Subjects who give consent and meet inclusion and exclusion criteria)
Sample size of this study was 201

**Method**

Data collection tool was an investigator administered standard and validated data collection sheet. The informed written consent was obtained by the principal investigator prior to sonographic examination after explaining about the study. Data collection sheet was administered by the same investigator to eliminate the interviewer bias. Explanations about the study setting was done to the study participants where necessary. Demographic details of the patients who gave consent for the study were collected by the principal investigator. Same scale was used to measure the height and weight of the patients to minimize the instrumental bias. The ultrasound scan of the liver was performed by using Philips Affinity 70 gray scale USS machine using low frequency (5MHz) curved array probe. All the scans were done using the same machine to eliminate the instrumental bias. All the scans was done by the principal investigator (Second year Radiology Registrar) which was supervised by a Consultant Radiologist at TH Peradeniya. The patient was kept in supine position and the abdomen was adequately exposed. The size of the liver, margin of the liver and echogenicity and echo texture of the liver was recorded. Size of the liver was measured in sagittal plane in the mid clavicular line from the diaphragm to the inferior border on B mode image. Also looked for the edges of the liver. If the edge is rounded or above measurement is > 15 cm taken as hepatomegaly.

**If the patient had fatty liver; it was graded as follows.**

- **Grade 0:** Normal liver echogenicity
- **Grade I:** Diffusely increased hepatic echogenicity but periportal and diaphragmatic echogenicity is still appreciable
- **Grade II:** Diffusely increased hepatic echogenicity obscuring periportal echogenicity but diaphragmatic echogenicity is still appreciable
- **Grade III:** Diffusely increased hepatic echogenicity obscuring periportal as well as diaphragmatic echogenicity.

After that USS of the bilateral common carotid artery was performed by Philips gray scale USS machine using high frequency linear array (10Mz) probe. The scan was done in supine position with head slightly extended and turned to the opposite side of the common carotid artery being examined.Both side of the CCA imaged at three places. (Proximal part, mid part and at the level of carotid bulb)

**Following Sonographic features were recorded**

- In longitudinal view of the CCA anterior (near) and posterior (far) wall of the CCA seen as two echogenic lines separated by the hypo echoic space. Carotid intimal medial thickness is defined as the combined thickness of the CCA medial and intimal layers. The measurement is made between the two hyperechoic lines made by blood-intimal interface and medial-adventitial junctions as far and near-wall respectively.
- The mean of three maximum right and left posterior (far) wall measurements were calculated for each CCA.
- If atheromatous plaque is present the size of the plaque, type of plaque, degree of luminal stenosis and nature of calcification of the plaque.
- Types of the plaques are classified as follows
  - Type 1 is thin rim over the surface; predominantly anechoic
  - type II is < 25% echogenic components
  - type III is< 25% hypo echoic component
  - type IV predominantly echogenic

**Statistical analysis and plan of presentation of results:** Data was entered and analyzed using SPSS version 23. Descriptive statistics was used for the analysis and presentation of the socio-demographic profile of the participants. Graphical methods like pie charts and bar charts and tabular formats were used to present the demographic profile in descriptive manner. The stage of NAFLD is categorized in to categorical ordinal data. The CIMT are of numerical continuous data. Hence, Spearman's rank order correlation test was used to determine the correlation between those two variables at 95% confident interval, placing the *p* value at 0.05.

# RESULTS

**Socio-demographic profile:** Out of the 201 study subjects, most of the patients were males (n = 113; 56.2%) and majority belonged to primary working age group (age 25-54y) (n=151; 75%).

**Table 1. Age distribution of study population**

| Age Group | Frequency | Percentage (%) |
|---|---|---|
| 1 Elderly (65 and over) | 9 | 5% |
| 2 Mature working age (55-64) | 19 | 9% |
| 3 Primary working age (25-54) | 151 | 75% |
| 4 Young | 22 | 11 % |
| Total | 201 | 100% |

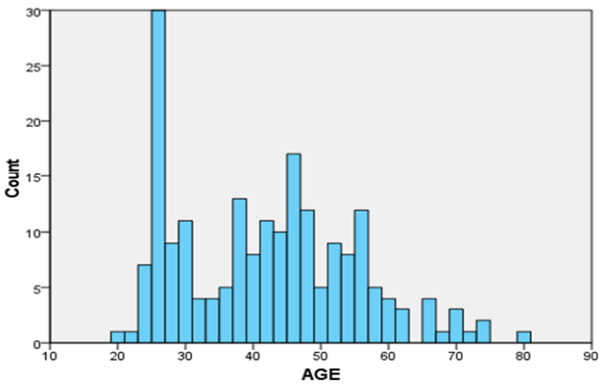


**Fig. 2.**

**Table 2. Sex distribution of study population**

| | Frequency | Percentage |
|---|---|---|
| Female | 88 | 43.8 % |
| Male | 113 | 56.2 % |
| Total | 201 | 100 % |

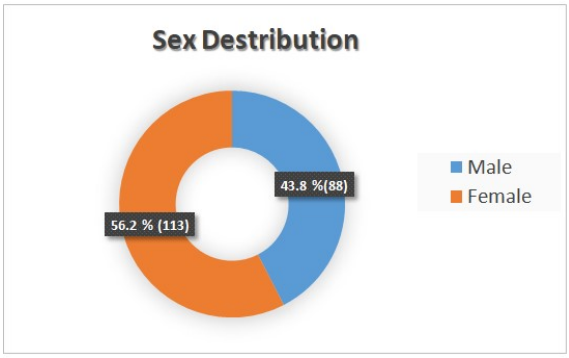


**Fig: 3**

The mean age of study population was 41.77 (SD1=12.93). Minimum age was 23 and maximum age was 79 years. Majority of the patients are non-smokers (171; 85.1%) and the study population belonged to non-alcoholics or who consume safe level of alcohol.

**Table 3. Distribution of smoking among study population**

| Smoking | Frequency | Percentage |
|---|---|---|
| Yes | 30 | 14.9 % |
| No | 171 | 85.1 % |
| Total | 201 | 100 % |

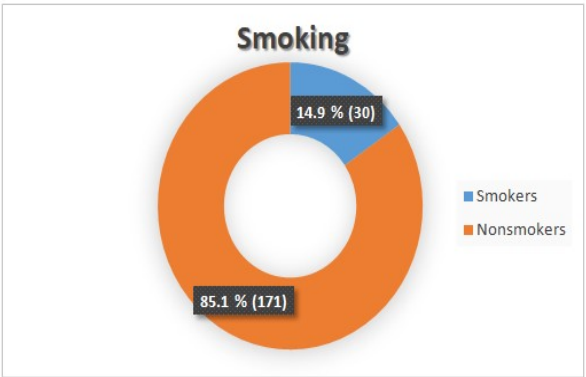


**Fig: 4**

When considering BMI of the study population most of the patients were obese (n=90 ; 45%) and over weight (n= 47 ; 23%). Mean BMI was 25.1 kg/m$^2$ (SD = 4.37)

**Table 4. BMI distribution of study population**

| BMI category | Frequency | Percentage (%) |
|---|---|---|
| Underweight (< 18.5) | 4 | 2 % |
| Normal ( 18.5 – 22.9) | 60 | 30 % |
| Overweight (23 – 24.9) | 47 | 23 % |
| Obese (> 25) | 90 | 45 % |
| Total | 201 | 100% |

**USS finding analysis:** The mean size of the liver in study population was 14.67 cm (SD = 1.18). Majority of patients had normal size liver (n=139; 69%).Majority of the study population had grade II fatty liver (n=116 ; 57.7%). Mean value of the right side CIMT was 0.075 cm (SD = 0.009) and that of left side was 0.077 cm (SD = 0.010). There values are within the normal range when compared with the values of other studies.

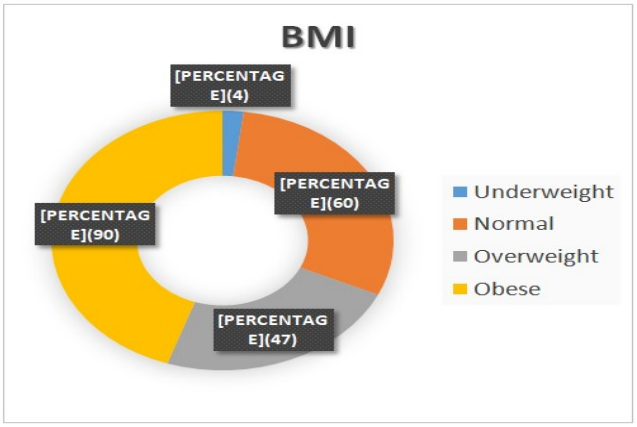


**Fig. 5.**

**Table 5. Liver size distribution in study population**

| | Frequency | Percentage (%) |
|---|---|---|
| Hepatomegaly | 62 | 31% |
| No hepatomegaly | 139 | 69% |
| Total | 201 | 100% |

**Table 6. Grade of fatty liver distribution among study population**

| Grade of the fatty liver | Frequency | Percentage |
|---|---|---|
| Grade I | 81 | 40.3 % |
| Grade II | 116 | 57.7 % |
| Grade III | 4 | 2.0 % |
| Total | 201 | 100 % |

**Table 7.Values of R/ CIMT**

| Right side average CIMT | Values (cm) |
|---|---|
| Mean | 0.075 cm |
| Minimum | 0.053 cm |
| Maximum | 0.125 cm |

**Table 8. Values of L/ CIMT**

| Left side average CIMT | Values (cm) |
|---|---|
| Mean | 0.077 cm |
| Minimum | 0.049 cm |
| Maximum | 0.129 cm |

**Correlational analysis:** When considering correlation between the age and the average right and left CIMT; there is a statistically significant correlation. ($p$ value <0.001) (positive)

**Table 9. Correlation between the age and bilateral CIMT**

| | P value | Significance |
|---|---|---|
| Age and right CIMT | < 0.001 | Significant |
| Age and left CIMT | < 0.001 | Significant |

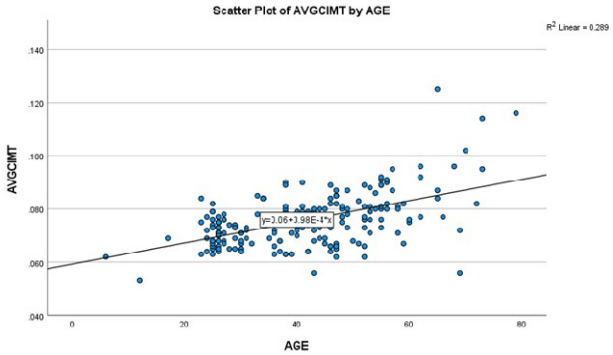


**Fig. 6. Correlation between age and R/ CIMT**

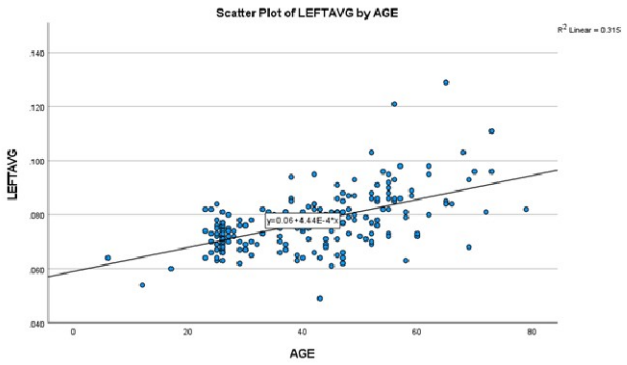


**Fig. 7. Correlation between age and L/ CIMT**

When analyzed the gender and CIMT; Mean values of right and left CIMT in male and female are 0.074cm, 0.077 cm and 0.076 cm, 0.078 cm respectively. When comparing the mean values between male and females, statistically significant difference was found on right side CIMT.

**Table 10. Mean values of CIMT with gender**

| CIMT | Sex | Mean |
|---|---|---|
| Right | M | 0.074 cm |
| | F | 0.077 cm |
| Left | M | 0.076 cm |
| | F | 0.078cm |

**Table 11. Significance of means in B/L CIMT and gender**

| CIMT | *p* value | Significance |
|---|---|---|
| Right | 0.045 | Significant |
| Left | 0.448 | Non-significant |

No statistically significant difference was found on left side. No correlation was found between the Grade of the fatty liver and the average CIMT of right and left CCA.

**Table 12. Grade of fatty liver and average values of bilateral CIMT**

| Grade of fatty liver | I | II | III |
|---|---|---|---|
| Mean right side CIMT | 0.076 cm | 0.075 cm | 0.077 cm |
| Mean left side CIMT | 0.076 cm | 0.071 cm | 0.077 cm |

Spearman's rank order correlation test was used to determine the correlation between Grade of the fatty liver and bilateral CIMT at 95% confident interval, placing the $p$ value at 0.05. ($p$ values were 0.730 and 0.072 in right and left respectively).

**Table 13. Correlation between fatty liver grade and CIMT**

| | P value | Significance |
|---|---|---|
| Fatty liver grade and average right side CIMT | 0.730 | Not significant |
| Fatty liver grade and average left side CIMT | 0.072 | Not significant |

# DISCUSSION

Nonalcoholic fatty liver disease is an emerging health problem at present due to sedentary life style. In this study we evaluated the presence of sub clinical atherosclerosis among the NAFLD patients, taking,CIMT as the indicator. The average CIMT value on right side was 0.075 cm and on left side was0.077 cm in this study group.

When compared with other studies which evaluated NAFLD patients, these values were within the normal range. According to the cross sectional descriptive study done in Nepal, National Academy of Medical Sciences, Bir Hospital from July 2018 to June 2019 by Bom BC et al. among 70 diagnosed cases of non-alcoholic fatty

liver; mean carotid intima-media thickness was 0.7140±0.1796mm on right and 0.7161±0.1828mm on left side.(20)So these findings are tally with our study. Astatistically significant difference in mean values of R/ CIMT between male and female groups was found in our study but therewas no such difference in L/ CIMT between them. However higher mean CIMT values were seen in female group than males on both sides. But such correlation was not found in other similar studies. A cross sectional retrospective study done in South Korea by Hyun-jim et al. the study concluded as out of a total of 1121 patients, the men had more fatty liver disease than the women. The mean CIMT of the men was significantly higher than that of the women, and the men had more plaque than the women. The women with fatty liver disease had a significantly higher mean CIMT value and more plaque than the women with normal livers.(21)This finding in our study may need to be reconfirmed with a bigger sample size.
Most of the patients of the study population were males (n=113; 56.2%) and majority of the study population belonged to primary working age group (age 25-54) (n=151; 75%). The cause for this finding likely to be that the NAFLD is more common in men than in women in reproductive age group. (22)

Among the201study population most of the patients belonged to the obese (45%) or overweight (23%) BMI category. Obesity directly contributes to the development of NAFLD and this fact was proved in this study as well. This study showed a correlation between the age and bilateral CIMT (p value <0.001). Many other studies also have shown the similar correlation.(23),(24),(25). No correlation between the grade of the fatty liver and CIMT was found in our study, but many other research had shown a correlation between these two. Mean values of CIMT on right side in grade I, II, and III NAFLD are 0.076 cm, 0.075 cm, 0.077 cm respectively. Mean values of CIMT on left side in grade I, II, and III are 0.076 cm, 0.071 cm, 0.077 respectively. A research conducted on non-alcoholic fatty liver disease as an independent risk factor for carotid atherosclerosis by Abid Rasool, et al, 2017; in India showed that patients with Grade 1 fatty liver had left intima-media thickness (IMT) in the range of 0.4–0.6 mm (mean IMT - 0.69 mm) and right IMT in the range of 0.5–0.8 mm (mean IMT - 0.71 mm). In patients with Grade 2 fatty liver, left IMT was in the range of 0.6–1.0 mm (mean IMT - 0.80 mm) and right IMT in the range of 0.7–1.0 mm (mean IMT - 0.84 mm), while in patients with Grade 3 fatty liver, left IMT was in the range of 0.8–1.2 mm (mean IMT - 0.93 mm) and right IMT in the range of 0.9–1.4 mm (mean IMT - 0.99 mm). (15). But these findings are not tally with our study which shows no correlation between the grade of NAFLD and CIMT.

A case control study was conducted by Maryam et al. (2008) by using 151 patients who were categorized in to three groups, group I includes 49 patients with NAFLD and DM; group II includes 50 non-diabetic NAFLD patients; and group III includes 52 normal subjects as control group. In this study maximum CIMT was measured and they concluded the study as there is a significant association between the presence of NAFLD and atherosclerosis. This association was independent to the presence of DM. (12) Another case control study done by Giovanni et al. (2006) using 85 consecutive patients with biopsy-proven NAFLD and 160 age, sex, and BMI-matched healthy control subjects, concluded the severity of liver histopathology among NAFLD patients is strongly associated with early carotid atherosclerosis (26). The above described research were case control studies, which showed increase CIMT in patients with NAFLD when compared to control group, whereas our study was done only in patients with NAFLD to evaluate the correlation between the thickness of CIMT and grade of NAFLD. However a study done by Bom et al. (2019) in Nepal using 70 diagnosed patients with NAFLD to assess the grade of fatty liver and the CIMT(20) concludedthat there is correlation between the grade of the fatty liver and CIMT.
In the above study there were no grade III fatty liver patients and only grade I and II patients were included intothe study population Our study population is much higher and included the grade III fatty liver as well. A study done by Abid Rasool et al. (2017) in Indiausing a total of 200 NAFLD patients and 100 age and sex matched controls,concluded that the level of carotid intimal medial thickness was more in NAFLD patients than in controls and progressively increased with the grade of fatty liver which was statistically significant. (15).However in this study the presence of diabetes mellitus, hypertension or any other non-communicable disease in the NAFLD patients were not excluded, which may have been a contributing factor for the increase in CIMT other than the NAFLD. In contrast in our study, the patients with other non-communicable disease such as diabetes mellitus, hypertension, and coronary artery disease were excluded and the study was done in patients with NAFLD without any other risk factors that contribute to atherosclerosis

**Conclusion**

Majority of patients with NAFLD were males who belonged to primary working age group and obeseor overweight. Majority of patients had grade II fatty liver. A significant correlation was found between the age and CIMT. There was no correlation between the grade of NAFLD and right or left CIMT.

**Limitations:** The detailed clinical examination and relevant laboratory investigations were not carried out. The diagnosis of NAFLD was exclusively based on ultrasound findings although liver biopsy is the gold standard to diagnose NAFLD.

**LIST OF ABBREVIATION**

**AbbreviationDescription**

| | |
|---|---|
| BMI | Body mass index |
| CCA | Common carotid artery |
| CIMT | Carotid intimal medial thickness |
| CRP | C- reactive protein |
| DM | Diabetes mellitus |
| Hx | History |
| L/ CIMT | Left side Carotid intimal medial thickness |
| NAFLD | Nonalcoholic fatty liver disease |
| NASH | Nonalcoholic steatohepatitis |
| MHz | Megahertz |
| R/ CIMT | Right side Carotid intimal medial thickness |
| T1DM | Type 1 diabetes mellitus |
| TH | Teaching Hospital |
| TIA | Transient ischemic attack |

# REFERENCES

Non-alcoholic Fatty Liver Disease (NAFLD) [Internet]. American College of Gastroenterology. [cited 2021 Jan 19]. Available from: https://gi.org/topics/fatty-liver-disease-nafld/

Klein S, Dufour JF. Nonalcoholic fatty liver disease and hepatocellular carcinoma. Hepatic Oncol. 2017 Jul;4(3):83–98.

Definition & Facts of NAFLD & NASH | NIDDK [Internet]. National Institute of Diabetes and Digestive and Kidney Diseases. [cited 2021 Jan 19]. Available from: https://www.niddk.nih.gov/health-information/liver-disease/nafld-nash/definition-facts

Matthias AT, Fernandopulle ANR, Seneviratne SL. Survey on knowledge of non-alcoholic fatty liver disease (NAFLD) among doctors in Sri Lanka: a multicenter study. BMC Res Notes. 2018 Aug 3;11(1):556.

Kumar And Clarks Clinical Medicine, 8th Edition 2012 [Internet]. [cited 2021 Jan 19]. Available from: http://archive.org/details/KumarAndClarksClinicalMedicine8thEdition2012_201803

Delker E, Brown Q, Hasin DS. Alcohol Consumption in Demographic Subpopulations: An Epidemiologic Overview. Alcohol Res Curr Rev. 2016;38(1):7–15.

Dyson JK, Anstee QM, McPherson S. Non-alcoholic fatty liver disease: a practical approach to diagnosis and staging. Frontline Gastroenterol. 2014 Jul;5(3):211–8.

Singh D, Das CJ, Baruah MP. Imaging of non alcoholic fatty liver disease: A road less travelled. Indian J Endocrinol Metab. 2013 Nov 1;17(6):990.

Robbins Basic Pathology 9th Edition (Download PDF) | CME & CDE | Medical textbooks, Pathology, Free medical [Internet]. Pinterest. [cited 2021 Jan 19]. Available from: https://www.pinterest.com/pin/831266043694139866/

Fruchart Jean-Charles, Nierman Melchior C., Stroes Erik S. G., Kastelein John J. P., Duriez Patrick. New Risk Factors for Atherosclerosis and Patient Risk Assessment. Circulation. 2004 Jun 15;109(23_suppl_1):III–15.

Kota SK, Mahapatra GB, Kota SK, Naveed S, Tripathy PR, Jammula S, et al. Carotid intima media thickness in type 2 diabetes mellitus with ischemic stroke. Indian J Endocrinol Metab. 2013 Jul 1;17(4):716.

Gamage PJ. Intima-media thickness | Radiology Reference Article | Radiopaedia.org [Internet]. Radiopaedia. [cited 2022 May 18]. Available from: https://radiopaedia.org/articles/intima-media-thickness-3

Wójcik-Cichy K, Koślińska-Berkan E, Piekarska A. The influence of NAFLD on the risk of atherosclerosis and cardiovascular diseases. Clin Exp Hepatol. 2018 Mar;4(1):1–6.

Nahandi MZ, Khoshbaten M, Ramazanzadeh E, Abbaszadeh L, Javadrashid R, Shirazi KM, et al. Effect of non-alcoholic fatty liver disease on carotid artery intima-media thickness as a risk factor for atherosclerosis. Gastroenterol Hepatol Bed Bench. 2014;7(1):55–62.

A R, W D, M L, I D, N S, Ma K. Nonalcoholic fatty liver disease as an independent risk factor for carotid atherosclerosis. Brain Circ. 2017 Jan 1;3(1):35–40.

Zhang L, Guo K, Lu J, Zhao F, Yu H, Han J, et al. Nonalcoholic Fatty Liver Disease is Associated with Increased Carotid Intima-Media Thickness in Type 1 Diabetic Patients. Sci Rep [Internet]. 2016 May 26 [cited 2021 Jan 19];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4880892/

Targher G, Bertolini L, Padovani R, Rodella S, Zoppini G, Zenari L, et al. Relations between carotid artery wall thickness and liver histology in subjects with nonalcoholic fatty liver disease. Diabetes Care. 2006 Jun;29(6):1325–30.

Fracanzani AL, Burdick L, Raselli S, Pedotti P, Grigore L, Santorelli G, et al. Carotid artery intima-media thickness in nonalcoholic fatty liver disease. Am J Med. 2008 Jan;121(1):72–8.

Kohn JS Michael. Correlation sample size | Sample Size Calculators [Internet]. [cited 2021 Jan 21]. Available from: https://sample-size.net/correlation-sample-size/

BC B, Jaiswal RK, Gupta PK, Paudel R, Subedi RK. Carotid Intima-media Thickness in Patients with Non-alcoholic Fatty Liver Disease Attending a Tertiary Care Center: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2021 May;59(237):454–9.

Kim HJ, Lim CW, Lee J hyuk, Park HB, Suh Y, Cho YH, et al. Gender-based differences in the relationship between fatty liver disease and atherosclerosis. Cardiovasc J Afr. 2016;27(5):281–6.

Lonardo A, Nascimbeni F, Ballestri S, Fairweather D, Win S, Than TA, et al. Sex Differences in NAFLD: State of the Art and Identification of Research Gaps. Hepatol Baltim Md. 2019 Oct;70(4):1457–69.

Beşir FH, Yazgan S, Celbek G, Aydın M, Yazgan O, Erkan ME, et al. [Normal value correlates of carotid intima- media thickness and affecting parameters in healthy adults]. Anadolu Kardiyol Derg AKD Anatol J Cardiol. 2012 Aug;12(5):427–33.

Saxena Y, Saxena V, Mittal M, Srivastava M, Raghuvanshi S. Age-Wise Association of Carotid Intima Media Thickness in Ischemic Stroke. Ann Neurosci. 2017;24(1):5–11.

Diaz A, Bia D, Zócalo Y, Manterola H, Larrabide I, Lo Vercio L, et al. Carotid Intima Media Thickness Reference Intervals for a Healthy Argentinean Population Aged 11–81 Years. Int J Hypertens. 2018 Feb 14;2018:e8086714.

Sookoian S, Pirola CJ. Non-alcoholic fatty liver disease is strongly associated with carotid atherosclerosis: A systematic review. J Hepatol. 2008 Oct 1;49(4):600–7.

# ANNEXURES

# ANNEXURES; 01

***Data collection sheet***

1. Date: …….. Serial number: ……..

2. Age: …… Sex: ……..

3. Occupation: ……..
4. Past medical history:
   - Hx of Stroke/ TIA Y/N
   - Hx of CAD Y/N
   - Dyslipidemia Y/N
   - Hypertension Y/N
   - Diabetes mellitus Y/N
   - Any kind of hepatic disease Y/N

5. Smoking Y/N

6. Consume alcohol Y/N

7. If Yes; Is it safe limit Y/N

8. Past surgical Hx: ……..
9. Body weight: ..... height: …… BMI: ……

10. USS findings

- Liver
  - ✓ Size : …….
  - ✓ Edge : ……
  - ✓ Margin : …….
  - ✓ Echogenicity : ……..
  - ✓ Echo texture : ……..
  - ✓ Grade of fatty liver : ……

- R/ CCA
  - ✓ CIMT
    - ➢ Proximal CIMT : …….
    - ➢ Mid CIMT : ……
    - ➢ Bulb level CIMT : ……
    - ➢ Average CIMT : …….
    - ➢
  - ✓ Atheromatous plaques : Y/N
    - ➢ Height of the plaque : ……
    - ➢ Type of the plaque : type ……
    - ➢ Degree of luminal narrowing : ……

- L/ CCA
  - ✓ CIMT
    - ➢ Proximal CIMT : …….
    - ➢ Mid CIMT : ……
    - ➢ Bulb level CIMT : ……
    - ➢ Average CIMT : …….
  - ✓ Atheromatous plaques : Y/N
    - ➢ Height of the plaque : ……
    - ➢ Type of the plaque : type ……
    - ➢ Degree of luminal narrowing : ……%

# ANNEXURES 02

**Correlation between the non-alcoholic fatty liver diseases and common carotid artery intimal medial thickness of patients attending Department of Radiology Teaching Hospital Peradeniya, Sri Lanka.**

**Information sheet**

**PART I**

**Introduction**

I am Dr.R.M.M.S.K.Kumara, working at Teaching Hospital Peradeniya as a Registrar in Radiology. I am doing a research on, correlation between the non-alcoholic fatty liver diseases and common carotid artery intimal medial thickness of patients attending Department of Radiology Teaching Hospital Peradeniya, Sri Lanka.

I am going to give you information and invite you to be part of this research. You do not have to decide today whether to participate in this research or not. Before you decide, you can talk to anyone you feel comfortable about the research.
There may be some words that you do not understand. Please ask me to stop as we go through the information sheet and I will take time to explain. If you have questions later, you can ask them from me.

**1:1 Title of the research**:
Correlation between the non-alcoholic fatty liver diseases and common carotid artery intimal medial thickness of patients attending Department of Radiology Teaching Hospital Peradeniya, Sri Lanka.

**1:2 Purpose of the research:**
Non-alcoholic fatty liver disease (NAFLD) is a very common disorder seen in worldwide. It generally refers to a group of conditions where there is accumulation of excess fat in the liver of people who drink little or no alcohol. There are many risk factors for NAFLD such as age, sex, obesity, dyslipidemia, smoking, hypertension, family history, diabetes mellitus, high homocystine level and CRP levels
Carotid intimal – medial thickness (CIMT) has been commonly uses as a test for assessment of degree of the atherosclerosis. It is a noninvasive method.
Due to sedentary life style of the people in now a days NAFLD is a common disease. So it is important to investigate correlation between NAFLD and sub clinical atherosclerosis in this patients.

No researches have done in Sri Lanka addressing above matter.
So the aim of this study is to find out whether there is any correlation between the NAFLD and the CIMT by using patients that attending radiology department, TH Peradeniya which is a tertiary care hospital in Sri Lanka.

**Type of Research:** If you found to be having fatty liver during your routing ultrasound scan; you are eligible for the study when you doesn't give history of diabetes mellitus, Hypertension or any other exclusion criteria. After your consent, routing ultrasound scan of the abdomen is performed. Then asses the grade of the fatty liver and documented by the investigator.
Then your neck region scan to determine the CIMT at the same time and documented.
Finally your height, weight will measure and documented.

**Participant selections:** Participants will be selected during routing ultrasound scan at radiology department after considering inclusion and exclusion criteria. Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this unit/hospital will continue and nothing will change. If you choose not to participate in this research project, you will be offered all the treatment that is routinely offered in this unit/hospital. You may change your mind later and stop participating even if you agreed earlier.

**Risks:** There is no risks by undergoing ultrasound scan of the abdomen and neck. No obvious side effects. During the scan we gather information about your liver and carotid arteries will documented. Privacy of the information will be secured. When disseminating the findings of the research, it will be done as a group.

**Benefits:** There are number of benefits you will get. One is that you can have information regarding whether you are having the fatty liver or not. If you having fatty liver you have to have a proper follow up at clinic level and life style modification. Other one is you can have information about CIMT. Whether there are any athermanous plaques, luminal stenosis etc. If you having those things you have to get treatments and need follow up. Those things will beneficial for your health. If those things are present you have to modify your life style. This will lead to better healthy future. Future generations are likely to benefit from final outcome of this research.

**Reimbursements:** You will not be given any other money or gifts to take part in this research.

**Confidentiality:** The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with lock and key. It will not be shared with or given to anyone.

**Right to Refuse or Withdraw:** You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this ward in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you wish without losing any of your rights as a patient here. Your treatment at the clinic will not be affected in any way.
.
**Who to Contact:** If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

Name: Dr. R.M.M.S.K. Kumara.

Address: "Madhumina" house, Wadawala, Karandagolla
T/P and e-mail: 0710553004/ kasunkumarakd@gmail.com

**PART II**

**Certificate of Consent:**

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Name of Participant……
Signature of Participant ……
Date ……..

**If illiterate:**

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.
Print name of witness…….AND Thumb print of participant
Signature of witness ……
Date …….

# ANNEXURES 03

**Correlation between the non-alcoholic fatty liver diseases and common carotid artery intimal medial thickness of patients attending Department of Radiology Teaching Hospital Peradeniya, Sri Lanka.**

**CONSENT FORM**

**Part A - To be filled by the participant**

The participant should complete the whole of this sheet herself.

1. Have you read the information sheet? (Please keep a copy for yourself) YES/NO
2. Have you had an opportunity to discuss this study and ask any questions? YES/NO
3. Have you had satisfactory answers to all your questions? YES/NO
4. Have you received enough information about the study? YES/NO
5. Who explained the study to you? ……
6. Do you understand that you are free to withdraw from the study at any time, YES/NO
   without having to give a reason and without affecting your future medical care?
7. Information held by the investigators relating to your participation in this
   study may be examined by other research assistants. All personal details
   will be treated as STRICTLY CONFIDENTIAL.
   Do you give your permission for these individuals to have access to your records? YES/NO
8. Have you had sufficient time to come to your decision? YES/NO
9. Do you agree to take part in this study? YES/NO

Participant's signature: …… Date:……
Name (BLOCK CAPITALS):
……
……

**Part B - To be filled by the investigator**

I have explained the study to the above volunteer and she has indicated her willingness to take part.

Signature of investigator: ……..... Date: ……

Name (BLOCK CAPITALS):
……
……

*******