

## Original Research Article

# Carotid intima-media thickness in patients with non-alcoholic fatty liver disease: a study from eastern part of India

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## ABSTRACT

**Background:** Carotid intima-media thickness (CIMT) is a reliable marker of atherosclerosis and cardiovascular events. Association between CIMT with non-alcoholic fatty liver disease (NAFLD) is well known; however, such data are limited from India. This study aimed to assess CIMT in NAFLD patients compared to the healthy control, its relationship with other metabolic covariates, and predictors of increased CIMT.

**Methods:** In an observational study, involving 150 subjects (84 NAFLD and 66 healthy controls), B-mode ultrasound was used for the evaluation of CIMT.

**Results:** The mean CIMT was significantly higher in NAFLD patients compared to the control group:  $0.77 \pm 0.27$  versus  $0.57 \pm 0.11$  mm on left side,  $p < 0.001$  and  $0.79 \pm 0.22$  versus  $0.54 \pm 0.12$  mm on right side,  $p < 0.001$ . The difference was significant even after adjustment of metabolic confounders. Eight NAFLD patients had carotid plaques compared to none in the controls. The mean CIMT did not differ significantly between lean, overweight and obese subjects. A progressive increase in mean CIMT was noted with increasing grades of hepatic steatosis. High CIMT values ( $>95^{\text{th}}$  percentile value in controls, 0.79 mm) were found in 52.3% of NAFLD. On multivariate regression analysis, age [odds ratio (OR) 1.42,  $p < 0.001$ ], serum HDL cholesterol [OR 0.92,  $p = 0.02$ ] and NAFLD [OR: 3.5,  $p < 0.001$ ] were found to be independently associated with high CIMT.

**Conclusions:** NAFLD was significantly associated with CIMT which increased progressively with increasing grades of hepatic steatosis. Over half of NAFLD had increased CIMT, and NAFLD along with higher age and lower HDL-cholesterol independently predicted high CIMT values.

**Keywords:** NAFLD, Carotid, CIMT, Atherosclerosis, Cardiovascular risk

## INTRODUCTION

Cardiovascular disease (CVD) constitutes the leading cause of death worldwide.<sup>1</sup> Therefore, identifying peoples at increased risk of CVD is important to take necessary precautions and to adopt preventive strategies. Most of the CVD starts with the process of atherosclerosis in the arteries. The process of atherosclerosis begins at an early age and progress with time unless the risk factors are controlled. Identification of early atherosclerosis by various methods results in better prediction in cardiovascular risk over and above that offered only by traditional risk factors.<sup>2,3</sup> Among various methods to

identify early atherosclerotic lesions, carotid intima-media thickness (CIMT) measured by ultrasound is the most widely used.<sup>4</sup>

CIMT measurement by B-mode carotid ultrasound is a readily available, safe, fast and real-time imaging tool for assessment of atherosclerosis, particularly in the early stage. Multiple population based and prospective studies have demonstrated a significant association between CIMT and increased CVD events.<sup>5,6</sup> The non-alcoholic fatty liver disease (NAFLD) is currently the most common cause of chronic liver disease worldwide. The prevalence of NAFLD in adult Indian population ranges from 15% to

28%, which is quite comparable to the prevalence in Western world.<sup>7</sup> CVD is among the most important causes of morbidity and mortality in patients with NAFLD.<sup>8,9</sup> Overall deaths from CVD in NAFLD ranges from 13 to 30%. Several studies have found an association between NAFLD and increased CIMT.<sup>10</sup> A systematic review and meta-analysis of seven cross-sectional studies (n=3,497 subjects) has confirmed that NAFLD is strongly associated with increased CIMT and an increased prevalence of carotid atherosclerotic plaques.<sup>11</sup> Thus, by picking up atherosclerotic lesion in asymptomatic stage, sonographic measurement of CIMT can be an acceptable screening tool for the prediction of CVD in NAFLD patients. There is a paucity of data describing association between CIMT and NAFLD across different parts of India. This study was aimed to assess the degree of CIMT in patients with NAFLD compared to that in the healthy controls, and to study the relation between CIMT and other metabolic covariates such as body mass index (BMI), dyslipidemia and diabetes mellitus (DM). In addition, the study was also aimed to determine the predictors of high CIMT.

## METHODS

The study was conducted at department of radiodiagnosis, Narayan Medical College and Hospital, Bihar, between January 2019 and December 2020. The data was collected prospectively from each study subjects in a cross-sectional manner. The study protocol was approved by the institutional ethics committee and was conducted in accordance with the Helsinki declaration (reference no: 0618/18). All subjects provided written consent for participation in the study.

Adult patients with diagnosis of NAFLD ( $\geq 18$  years) was included in the study. The diagnosis of NAFLD was made on the basis of characteristics features on ultrasonography. Patients with history alcohol consumption ( $>20$  d/day) or secondary cause of fatty liver were excluded. Healthy subjects with normal liver on ultrasonography were taken as control subjects. They were selected from among healthy attendants accompanying patients at our hospital or from the healthy employees of the Institute. An attempt was made to enrol control subjects with demographic profile (i.e. age and gender distribution, and BMI) similar of that of the NAFLD patients.

### Definitions

Grading of NAFLD (grade I, II and III) was based on ultrasonographic hepatorenal echo-contrast, liver brightness, vascular blurring and deep attenuation.

Diabetes mellitus (DM) was diagnosed if the fasting plasma glucose was  $\geq 126$  mg/dl after no calorie intake of at least 8 hours or HbA1C  $\geq 6.5\%$ .

Hypertension was diagnosed based on two separate blood pressure readings of  $\geq 140/90$  mmHg.

Waist circumference was measured using a flexible non-stretchable tape along a horizontal plane at the superior border of the iliac crest. A waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women were considered as marker for abdominal (central) obesity.

BMI categorization was done according to the Asian-Pacific cutoff points.<sup>12</sup> BMI 18.5–22.9 kg/m<sup>2</sup> constituted normal weight, 23–24.9 kg/m<sup>2</sup> overweight and  $\geq 25$  kg/m<sup>2</sup> were labelled as obese.

Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration. Elevated triglyceride values of  $\geq 150$  mg/dl and reduced high-density lipoprotein-cholesterol values ( $<40$  mg/dl in men or  $<50$  mg/dl in women) were considered abnormal.

### Patients' evaluation and procedure

Each patient was evaluated with detailed history and clinical examination. Pertinent history related to metabolic comorbidity was recorded. All the required anthropometric measurements (BMI, and waist circumference) were taken. Relevant blood investigations including fasting plasma glucose, lipid profile, bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total protein, albumin, hemoglobin, and platelet count were done. Then patient was then taken up ultrasonographic measurement of CIMT using Philips A-70 ultrasound machine.

### CIMT measurement

Mean CIMT was determined by high resolution B-mode ultrasonography (USG) with a 7.5 MHz transducer as described in the literature (Figure 1). Scanning was done in patients lying in supine position with neck in slightly hyper-extended position and rotated opposite to the probe direction. The distance between two echogenic lines, separated by echo lucent space in the arterial wall was measured as CIMT. Images of two sides were obtained on CCA, far wall, 2 cm proximal to the dilatation of carotid bulb. The common and internal carotid artery on both sides were imaged for identification of atherosclerotic plaque. In general, 3 values of CIMT were taken from each sides and average value calculated. The mean CIMT represented the average value of CIMT on left and right sides.

### Statistical analysis

Based on previous research, a sample size of 71 was determined, taking into consideration an expected 40% prevalence of high CIMT in NAFLD patients compared to the 25% in the general population. Continuous data with normal distribution were expressed as mean (SD) and those with skewed distribution were mentioned as median (range). Categorical data were represented as the proportions. For the comparison of continuous variables between NAFLD and control subjects, student t-test or

Mann Whitney test were used as applicable. Categorical data were compared using Chi square test or Fisher exact test as applicable. The adjustment for confounders was done by restriction of the analysis. The correlation between CIMT and other relevant variables were assessed using Pearson's correlation coefficients. The upper limit of CIMT was taken as 95<sup>th</sup> percentile of CIMT in control subjects. Univariate and multivariate logistic regression analyses were performed to determine the independent predictors of raised CIMT. Data was analyzed by using statistical package for the social sciences (SPSS) software version 23, and p<0.05 was taken as significant.



**Figure 1: CIMT measurement (left panel) as the distance between two echogenic lines separated by echo lucent space in the arterial wall, and carotid plaques (right panel) in a NAFLD patient.**

## RESULTS

### Baseline characteristics of study subjects

A total of 110 patients with NAFLD and 75 controls were evaluated for inclusion into the study. After the detailed evaluation, 26 patients with NAFLD and 09 control subjects were excluded due to various reasons. Finally, 150 subjects (84 NAFLD patients and 66 controls) were included in the final analysis. The baseline demographic, anthropometric and laboratory characteristics of NAFLD patients and control subjects are depicted in Table 1. Among patients with NAFLD, mean age (SD) was 46.2

(15.7) years, 56% (n=47) were male and 20% (n=17) were diabetic. The mean BMI was 25.4 kg/m<sup>2</sup> and 49% (n=41) were obese. The proportion of patients with hypertension, dyslipidemia, hypothyroidism, and smoking history were 35.7%, 38.1%, 7.2% and 8.3%, respectively. The mean age, proportion of patients with hypertension and DM were similar between NAFLD and control. However, mean BMI (25.4±4.7 versus 23.1±4.1 kg/m<sup>2</sup>, p<0.001), proportion of obesity (48.8% versus 24.2%, p=0.002) and dyslipidemia (38.1% versus 22.7%, p= 0.014) were significantly higher among NAFLD as compared to that in the controls. The waist circumference, that represent central or abdominal obesity was significantly higher in NAFLD in compared to the control (87.1±8.4 versus 81.2±11.1 cm, p<0.001). The proportion of female were more in the control group (p=0.04). The level of serum AST was significantly higher in NAFLD than control (p=0.007). Similarly, the levels of serum total cholesterol (200.3±49.7 versus 181.1±18.1, p=0.008), and triglyceride (187.9±81.1 versus 137.6±27.7, p<0.001) were significantly higher among NAFLD than in the control.

### Comparison of CIMT between NAFLD and control

As depicted in the Table 2, the mean CIMT was significantly higher in patients with NAFLD compared to the values in the control group: (0.77±0.27 versus 0.57±0.11 mm on left side, p<0.001) and 0.79±0.22 versus 0.54±0.12 mm on right side, p<0.001). When metabolic confounders (generalized or abdominal obesity, gender, dyslipidemia) were adjusted between the groups by restriction of analysis (58 NAFLD and 46 controls), the difference of CIMT between NAFLD and control remained statistically significant (0.75±0.21 versus 0.62±0.23 mm on left side, p=0.019) and 0.78±0.32 versus 0.61±0.12 mm on right side, p=0.009). In addition, 08 patients with NAFLD were found to have carotid plaques compared to none in control group. A progressive increase in mean CIMT was noted with increasing grades of hepatic steatosis (grade I 0.70±0.17, grade II 0.90±0.22 and grade III 1.02±0.29 mm, p<0.001).

**Table 1: Baseline demographic and anthropometric characteristics of patients and control.**

Parameters	NALD (n=84)	Control (n=66)	P value
Age (years), mean±SD	46.2±15.7	43.2±15.1	0.250
Male: female, n	47:37	26:40	0.044
Height (m), median (range)	1.6 (1.4-1.7)	1.6 (1.4-1.8)	0.868
Weight (kg), mean±SD	68.5±13.7	59.3±11.4	<0.001
BMI (kg/m <sup>2</sup> )	25.4±4.7	23.1±4.1	0.002
Obesity (%)	41 (48.8)	16 (24.2)	0.002
Systolic BP (mm Hg), mean±SD	134.5±19.8	127.1±15.8	0.015
Diastolic BP (mm Hg), mean±SD	83.2±11.9	78.4±9.8	0.010
Waist circumference (cm), mean±SD	87.1±8.4	81.2±11.1	<0.001
Diabetes mellitus (%)	17 (20.2)	22 (33.3)	0.070
Hypertension (%)	30 (35.7)	18 (27.3)	0.271
Dyslipidemia (%)	32 (38.1)	15 (22.7)	0.014
Hypothyroidism (%)	06 (7.2)	10 (15.2)	0.015
Smoking (%)	07 (8.3)	07 (10.3)	0.635

Continued.

Parameters	NAFLD (n=84)	Control (n=66)	P value
Serum total bilirubin (mg/dl)	0.97±0.86	0.7±0.69	0.169
Serum AST (U/l), median (range)	37.7 (11-259)	29.1 (11.6-59)	0.260
Serum ALT (U/l) median (range)	47.5 (13.5-382)	25.6 (12-48)	0.007
Plasting fasting blood sugar (mg/dl)	106.9±38.6	100.1±20.7	0.278
Serum T. cholesterol (mg/dl)	200.3±49.7	181.1±18.1	0.008
Serum HDL cholesterol (mg/dl)	53.4±11.1	55.9±6.9	0.156
Serum LDL cholesterol (mg/dl)	100.3±41.1	88.7±19.2	0.056
Serum TG (mg/dl)	187.9±81.1	137.6±27.7	<0.001
INR, mean±SD	1.17±0.1	1.19±0.9	0.551
Hemoglobin (g/dl), mean±SD	12.7±1.6	11.5±2.0	0.001
TLC /cmm, median (range)	7200 (4000-18200)	7100 (4000-14000)	0.515
Platelet count × 1000/cmm, median	160 (100-290)	170 (50-360)	0.668

NAFLD: non-alcoholic fatty liver disease, BP: blood pressure, SD: standard deviation, BMI: body mass index AST: aspartate aminotransferase, ALT: alanine aminotransferase, HDL: low-density lipoproteins, LDL, high-density lipoproteins, TG: triglyceride, INR: international normalized ratio, TLC: total leucocyte counts, CIMT: carotid intima-media thickness, CVD: cardio-vascular Disease, DM: diabetes mellitus, NASH: non-alcoholic steatohepatitis, CCA: common carotid artery

**Table 2: Comparison of CIMT values between NAFLD and control subjects.**

CIMT	NAFLD (n=84)	Control (n=66)	P value
<b>Left side (cm)</b>			
Mean±SD	0.77±0.27	0.57±0.11	<0.001
Median (range)	0.8 (0.6-1.8)	0.6 (0.3-0.9)	
<b>Right side (cm)</b>			
Mean±SD	0.79±0.22	0.54±0.12	<0.001
Median (range)	0.8 (0.4-1.9)	0.5 (0.3-0.9)	
<b>Average of two sides (cm)</b>			
Mean±SD	0.78±0.22	0.55±0.11	<0.001
Median (range)	0.8 (0.5-1.7)	0.55 (0.35-0.85)	

CIMT: carotid intima-media thickness, NAFLD: non-alcoholic fatty liver disease, SD: standard deviation

**CIMT values as per different demographic and metabolic characteristics**

Taking all study subjects (NAFLD and controls) together, the mean CIMT was significantly higher in subjects with age >40 years as compared to those with <40 years, (0.76±0.22 versus 0.58±0.1.8 mm, p<0.001). Similarly, the mean CIMT values were higher in hypertensive and hyperlipidemic subjects compared to their counterparts (Table 3). The mean CIMT value in diabetic subjects was higher as compared to the non-diabetic ones, with difference being just close to the statistical significance (0.74±0.39 mm versus 0.66±0.18, p=0.052). No significant difference in CIMT values was found between obese and non-obese subjects. A significant positive correlation was noted between CIMT values and age (p<0.001), BMI (p=0.07), systolic BP (p<0.001), waist circumference (p=0.02), fasting plasma glucose (p<0.001), serum cholesterol (p=0.03), serum LDL cholesterol (p<0.001), serum triglyceride (p≤0.001) and grades of hepatic steatosis (p<0.001). However, the strength of correlation was weak to moderate for most variable, the maximus strength was for grade of fatty liver (r=0.64) and age (r=0.49). The CIMT was negatively correlated with serum HDL levels (r=-0.30, p=0.001). There was no significant correlation between CIMT and liver enzymes (Table 4).

**Table 3: CIMT values as per the different characteristics of study subjects.**

Characteristics	N	CIMT (mean±SD)	P value
<b>Age (years)</b>			
>40	83	0.76±0.22	<0.001
<40	67	0.58±0.1.8	
<b>Gender</b>			
Male	73	0.72±0.22	0.059
Female	77	0.77±0.21	
<b>Weight</b>			
Obese subjects	57	0.71±0.24	0.167
Non-obese subjects	93	0.66±0.20	
<b>Diabetes</b>			
Diabetic	39	0.74±0.39	0.052
Non-diabetic	111	0.66±0.18	
<b>Hypertension</b>			
Hypertensive	48	0.78±0.26	0.001
Non-hypertensive	102	0.63±0.13	
<b>Hyperlipidemia</b>			
Hyperlipidemic	47	0.76±0.30	0.013
Non-hyperlipidemic	103	0.64±0.15	

**Table 4: Correlation between CIMT and other relevant variables.**

Variables	Correlation coefficient (r)	P value
Age	0.49	<0.001
BMI	0.14	0.07
Systolic BP	0.41	<0.001
Waist circumference	0.18	0.02
Fasting plasma glucose	0.43	<0.001
Serum total cholesterol	0.20	0.03
Serum triglyceride	0.26	0.005
Serum LDL cholesterol	0.34	<0.001
Serum HDL cholesterol	-0.30	0.001
Serum SGOT	0.009	0.92
Serum SGPT	0.05	0.56
Grade of fatty liver on USG	0.64	<0.001

BP: blood pressure, BMI: body mass index, AST: aspartate aminotransferase, ALT: alanine aminotransferase, HDL: high-density lipoproteins, LDL, high-density lipoproteins, USG: ultrasound

### Normal upper limit of CIMT

In control subjects, CIMT was 0.60 mm at 75<sup>th</sup> percentile and 0.79 mm at 95<sup>th</sup> percentile. The value at 95<sup>th</sup> percentile (0.79 mm) was taken as upper limit of normal CIMT in this study. Therefore, a CIMT value >0.79 mm was defined as high CIMT. The proportion of subjects with high CIMT was 52.3% (n=44) in NAFLD, while it was only 6.06% (n=04) in control subjects (p<0.001). Moreover, among patients with high CIMT, the proportion of NAFLD was 91.7% (n=44).

### Factors associated with high CIMT

Univariate and multivariate logistic regression analyses were performed to identify factors associated with high CIMT in the entire study cohort. On univariate analysis, presence of NAFLD (p<0.001) age (p=0.001, male (p=0.02), hypertension (p<0.001), waist circumference (0.008), and serum lipid were significantly associated with high CIMT. On multivariate logistic regression analysis, only age [OR 95% CI: 1.42 (1.06-1.22), p<0.001], HDL cholesterol [OR 95% CI: 0.92 (0.82-0.98), p=0.02] and NAFLD [OR 95% CI: 3.5 (2.5-38.2), p<0.001] were found to be independently associated with high CIMT (Table 5).

**Table 5: Variables associated with increased CIMT (>0.79 mm).**

Parameters	Univariate analysis			Multivariate analysis		
	High CIMT (mm) (n=48)	Normal CIMT (mm) (n=102)	P value	OR	95% CI	P value
Age (year),	55.9±13.9	39.7±13.1	<0.001	1.142	1.06-1.22	<0.001
Male gender, n (%)	30 (62.5)	43 (42.2)	0.020			
BMI (mg/kg <sup>2</sup> )	25.3±5.0	23.9±4.3	0.097			
Obesity n (%)	21 (43.8)	36 (35.3)	0.320			
Hypertension n (%)	26 (54.2)	22 (21.6)	<0.001			
Waist circumference cm	87.7±8.4	83.1±10.6	0.008			
Diabetes mellitus n (%)	16 (33.3)	23 (22.5)	0.160			
Hypothyroidism n (%)	02 (4.2)	12 (11.8)	0.051			
NAFLD n (%)	44 (91.7)	40 (39.2)	<0.001	3.5	2.5-38.2	<0.001
Smoking n (%)	05 (10.4)	09 (8.8)	0.754			
Serum total cholesterol (mg/dl)	20.9±47	184.8±31.6	0.020			
Serum triglyceride (mg/dl)	190.1±80.1	149.5±52.5	0.002			
Serum LDL cholesterol, (mg/dl)	110.1±43	87.7±23.5	0.001			
Serum HDL cholesterol, (mg/dl)	49.3±10.6	57.0±7.4	<0.001	0.92	0.82-0.98	0.023
Serum SGOT, U/l, (mg/dl)	49.3±43.4	44.6±10.7	0.579			
Serum SGPT (U/l) (mg/dl)	58.1±67.7	45.6±12.6	0.212			

CIMT: carotid intima-media thickness, NAFLD: non-alcoholic fatty liver disease, BMI: body mass index, AST: aspartate aminotransferase, ALT: alanine aminotransferase, HDL: low-density lipoproteins, LDL, high-density lipoproteins

## DISCUSSION

The results of our study revealed that the mean CIMT in NAFLD was significantly higher than non-NAFLD healthy subjects. The upper limit of normal CIMT was 0.79 mm in healthy control. Using this cut-off as surrogate marker of atherosclerosis, the prevalence of carotid atherosclerosis in NAFLD was 52.3%, which was much higher than that in non-NAFLD control (6.6%). The

factors independently predicted high CIMT were presence of NAFLD, high age and low serum HDL-cholesterol. Because high CIMT is a reliable predictor of increased cardiovascular risk, its measurement should be strongly considered in all NAFLD patients in order to recognize the cardiovascular risk at early stage, so that the corrective measures can be taken. CIMT measurement by ultrasound is a readily available tool for assessment of atherosclerosis and prediction of CVD risk. Multiple studies have found

that identification of early atherosclerosis give better prediction in cardiovascular risk over and above that offered only by traditional risk factors.<sup>2,3</sup> In general, a CIMT value at 75<sup>th</sup> or 95<sup>th</sup> percentile for a given normal population or an absolute thickness >10 mm is considered abnormal.<sup>4,5,13</sup> In our study, the 75<sup>th</sup> percentile of CIMT in control subjects was only 0.60 mm which was too low to be considered as upper limit of normal. As many studies have found that 95<sup>th</sup> percentile of CIMT is better cut-off for defining upper limit of normal, we took 95<sup>th</sup> percentile corresponding to 0.79 mm as upper limit.<sup>13</sup> Even the 95<sup>th</sup> percentile cut-off value was lesser than the 75<sup>th</sup> percentile cut-off values in many Western studies. Therefore, Indian may be at risk of CVD at lower CIMT cut-off. In a study on Indian population, the maximum normal CIMT was 0.7 mm.<sup>14</sup>

NAFLD is currently the commonest cause of chronic liver disease worldwide. The prevalence of NAFLD in India not less in the Western world.<sup>7</sup> In NAFLD it is not the liver disease but CVD that constitutes the most important causes of morbidity and mortality.<sup>8,9</sup> Patients with NAFLD have atherogenic dyslipidemia, oxidative stress, pro-inflammatory internal milieu, insulin resistance, and hypertension, which render them at high risk for atherosclerosis.<sup>15</sup> Several studies have found an association between NAFLD and increased CIMT even after adjusting for metabolic variables.<sup>10</sup> In our study too, NAFLD was independent predictor of high CIMT [OR 95% CI: 3.5 (2.5-38.2),  $p < 0.001$ ]. Moreover, among patients with high CIMT, the proportion of NAFLD was as high as 91%.

The relationship between CIMT and NAFLD was assessed by Sookoian et al in a meta-analysis by summarising 7 studies, including 1427 patients and 2070 healthy subjects. They concluded that NAFLD and CIMT correlated strongly.<sup>11</sup> However, there is a paucity of data describing association between CIMT and NAFLD in India. This is the first study involving CIMT assessment in NAFLD from the eastern part of India. In our study too, the mean CIMT value was significantly higher in patients with NAFLD compared to the controls, even after adjusting the metabolic confounders. Moreover, carotid plaques were also detected in eight NAFLD patients compared to none in the control group. Mishra et al have described a higher CIMT in NAFLD patients than non-NAFLD controls (0.56±0.10 versus 0.48±0.13 mm,  $p < 0.001$ ).<sup>16</sup> Another small study from India has demonstrated a significant association between NAFLD and increased CIMT.<sup>17</sup> Our study found a progressive increase in mean CIMT with increasing grades of hepatic steatosis. Similarly, in study by Rasool et al, the value of CIMT was found to be increased progressively with the increasing grades of fatty liver.<sup>18</sup>

Few studies have assessed the relationship between the value of CIMT and the liver enzyme, as well as NAFLD severity. Petit et al have found no significant association between CIMT and the severity of liver involvement,

including liver enzymes.<sup>19</sup> In our study also, there was no significant correlation between CIMT and liver enzymes. We also did not find a significant difference in CIMT values between obese and non-obese subjects. This observation is quite interesting and pertinent for our population as lean NAFLD is not so uncommon in India.<sup>20</sup> This also suggest that the CVD risk in lean subjects can be assessed by measuring CIMT. Generation of such data from the eastern part of India makes it a novel study; however, it has several limitations too.

### Limitations

One of the limitations of our study is being a single centre hospital-based study which limits the generalizability of the results. It is a cross-sectional analysis, so it was not possible to determine the actual occurrence of CVD in patients with elevated CIMT levels. There was no liver biopsy to confirm both the diagnosis and the severity of NAFLD. Therefore, it was not possible to study the relationship between severity of NAFLD and CIMT.

### CONCLUSION

In conclusion, our study found a significant association between CIMT and NAFLD. The mean CIMT was significantly higher in NAFLD patients compared to the matched controls. The CIMT values did not differ between BMI categories; however, it increased with the grades of fatty liver. The normal upper limit of normal CIMT (0.79 mm) was lesser than the cut-offs in the Western population but was comparable to the cut-off in found in the previous Indian studies. Over half of NAFLD subjects were found to have high CIMT and one tenth of them had carotid plaques. High age, presence of NAFLD and low HDL-cholesterol were found to be independently associated with high CIMT.

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