# EVALUATION OF CARDIOVASCULAR RISK BY CAROTID INTIMA MEDIA THICKNESS IN NON ALCOHOLIC FATTY LIVER DISEASE

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**ABSTRACT**: Non alcoholic fatty liver disease is associated with increased cardiovascular risk. Intima media thickness of common carotid artery is considered to be an excellent non-invasive measure of generalized atherosclerosis. The present study was conducted to evaluate the cardiovascular risk in asymptomatic non alcoholic fatty liver disease (NAFLD) subjects as demonstrated by increased carotid intima media thickness( CIMT) detected by using B-mode ultrasonography. A total of 50 healthy participants, 18 males and 32 females in the age group of 21-50 years of age with incidental finding of fatty liver on ultrasound abdomen, attending hospital outpatient department of Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar were included. The relationship of carotid intima media thickness was observed with various variables. Mean carotid intimal medial thickness was taken on both sides. The result concluded that serum cholesterol >200mg/dl, serum triglycerides >150mg/dl, serum LDL >130mg/dl and increasing grades of fatty liver from grade I to III were significantly associated with increased CIMT. The present study also depicted no significant relationship of age, gender, body mass index (BMI), waist hip ratio (WHR), serum HDL levels with carotid intima media thickness. Fatty changes in liver had direct correlation with carotid intimal medial thickness thereby stressing that asymptomatic NAFLD is an important component/ risk factor and determinant of atherosclerosis.

**KEY WORDS**: Non alcoholic fatty liver disease, carotid intima media thickness, atherosclerosis, cardiovascular risk.

**INTRODUCTION**: Non alcoholic fatty liver disease (NAFLD) represents a spectrum of medical condition in which there is increased infiltration of fats, mostly triglycerides, cholesterol and phospholipids, in excess of 5-10% of liver weight [1, 2]. NAFLD is clinicopathological syndrome that is closely associated with obesity, dyslipidemia, insulin resistance and diabetes mellitus, thus suggesting NAFLD represents another component of metabolic syndrome [3, 4]. It is postulated that NAFLD, like metabolic syndrome is associated with increased risk of atherosclerosis and cardiovascular risk [5, 6].

**MATERIAL AND METHODS**: A total of 50 healthy participants, 18 males and 32 females with incidental finding of non alcoholic fatty liver disease (NAFLD) on ultrasound abdomen, attending the hospital outpatient department of Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar were taken. Informed consent was taken from every participant. Intimal medial thickness of carotid arteries was done by using B-mode ultrasonography, having electrical linear transducer mid frequency of 7-12 MHZ by trained ultrasonologist, in the department of radio-diagnosis, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. Total 6 intimal medial thickness

measurements were taken, 3 on right and 3 on left side and their mean was representative value for each subject.

**EXCLUSION CRITERIA**:

1. Patients of alcoholic liver disease
2. HBsAg positive patients, anti-HCV positive patients, HIV positive patients.
3. Patients with other liver disorders like Wilson's disease, hemochromatosis, autoimmune hepatitis etc.
4. Patients taking drugs known to induce fatty liver like estrogens, valproate, methotrexate, tamoxifen, corticosteroids, amiodarone etc.
5. Obesity with BMI>30 $Kg/m^2$, hypertensive patients, chronic smokers, history of diabetes mellitus
6. Patients having any evidence of arteritis or any evidence of connective tissue disorder.
7. Patients with renal disease, acute illness, thyroid disorder.
8. Patients with weight loss > 3Kg in last 3 months.

**ETHICS**: While performing this study on human subjects, the procedures followed were in accordance with ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975 that was revised in 2000.

**RESULTS**: In the present study total of 50 healthy subjects were taken among whom, 18 (36%) were males and 32 (64%) were females. Out of 18 males, 9 (50%) were having normal CIMT and 9 (50%) were having increased CIMT. Among 32 females, 23 (71.9%) were having normal CIMT and 9 (28.1%) were having increased CIMT. The gender has no relationship with increased CIMT in NAFLD subjects. According to BMI, 4 (8%) of subjects were overweight and 46 (92%) were of grade I obesity. Among 4 overweight subjects, 1 (25%) hade normal CIMT and 3 (75%) had increased CIMT. Similarly out of 46 subjects having grade I obesity, 31 (67.4%) had normal CIMT and 15 (32.6%) had increased CIMT. The relationship between obesity and CIMT was not significant. As respect to WHR, 33 (66%) had normal WHR and 17 (34%) had abnormal WHR. Out of these 17 subjects, 11 (64.7%) had normal CIMT and 6 (35.3%) had increased CIMT. Abnormal WHR had no correlation with increased CIMT in NAFLD subjects in the present study. As per serum cholesterol levels, 33 (66%) subjects had serum cholesterol levels <200mg/dl and 17 (34%) had levels > 200mg/dl. Out of 17 subjects having serum cholesterol levels >200mg/dl, 2 (11.8%) had normal CIMT while 15 (88.2%) had increased CIMT. The study revealed that increased serum cholesterol was associated with increased CIMT in NAFLD patients and the relationship was statistically significant ($p<0.001$). With regards to serum triglycerides levels, 38 (76%) had levels <150mg/dl and 12 (24%) had levels >150mg/dl. Among 12 subjects having increased serum triglycerides levels, 3 (25%) had normal CIMT and 9 (75%) had increased CIMT. These findings in the present study concluded that increased serum triglycerides levels are significantly related to increased CIMT in NAFLD subjects ($p=0.001$). As respect to serum LDL levels, 40 (80%) subjects had levels <130mg/dl and 10 (20%) had levels >130mg/dl. Out of 10 subjects having increased serum LDL, 1 (10%) had normal CIMT and 9 (90%) had increased CIMT. The study concluded that increased serum LDL levels are associated with increased CIMT in NAFLD subjects which was highly significant ($p<0.001$).

According to serum HDL levels, 14 (28%) had normal serum HDL levels (i.e. > 40mg/dl) and 36 (72%) had abnormal serum HDL levels. Among 36 having abnormal serum HDL levels (i.e. <40mg/dl), 21 (58.3%) had normal CIMT and 15 (41.7%) had increased CIMT. The result showed that decreased serum HDL levels are not significantly associated with increased CIMT in NAFLD subjects. With regards to increasing grades of fatty liver from grade I to III on ultrasound,15 (30%) had grade I fatty liver, 30 (60%) had grade II fatty liver and 5 (10%) had grade III fatty liver changes. Out of 15 subjects having grade I changes, 11 (73.3%) had normal CIMT and 4 (26.7%) had increased CIMT. Out of 30 subjects having grade II changes, 21 (70%) had normal CIMT and 9 (30%) had increased CIMT. Out of 5 subjects having grade III fatty changes, all 5 (100%) had increased CIMT. These findings suggested that with increasing grades of fatty liver there was significant increase in CIMT which was statistically significant (p=0.007).

**DISCUSSION**: In the present study 50 subjects with incidental finding of NAFLD were evaluated for carotid intima media thickness using colour doppler of carotids. Out of 50 subjects, 18 (36%) were males and 32 (64%) females. In the present study, 17 (34%) NAFLD patients had serum cholesterol levels >200mg/dl, out of which 15 (88.2%) were having increased intima media thickness and this relationship was highly significant (p<0.001). These findings were consistent with the findings of study done by Giovanni Targher and colleagues who also demonstrated a significant relation of nonalcoholic hepatic steatosis with increased carotid intima media thickness in healthy men having increased serum cholesterol (p<0.01)[7]. Nicolla Villanova and associates similarly depicted that increased serum cholesterol levels were associated with increased CIMT and this relationship was highly significant (p<0.001)[8]. In the present study, 12 (24%) NAFLD subjects had serum triglycerides level >150mg/dl, out of which 9 (90%) were associated with increased intima media thickness which was also significant (p=0.001). These findings were in line with the findings of Giancula Perseghin, who published an article stating increased serum triglycerides deposit in the liver may cause direct damage and endothelial dysfunction leading to increased intima media thickness, which was significant (p<0.01) [9]. In the present study, 10 (20%) NAFLD subjects had serum LDL levels >130mg/dl, out of which 9 (90%) had increased CIMT which was highly significant (p<0.001). These findings were in consistent with the findings of study done by Nimmer Assy and colleagues who showed a significant relationship (p<0.001) of higher degree of carotid calcification even without metabolic syndrome in NAFLD patients having increased levels of serum LDL [10]. Stafeno Ramilli also demonstrated high degree of carotid lesions in NAFLD patients with high serum LDL levels and the relationship was highly significant (p<0.001) [11]. In the present study, 15 (30%) NAFLD subjects had grade I fatty liver on ultrasound out of which 4 (26.7%) had increased CIMT. 30 (60%) subjects had grade II fatty liver on ultrasound, out of which 9 (30%) had increased CIMT. 5 (10%) subject had grade III fatty liver on ultrasound and all 5 (100%) subjects had increased CIMT. Increasing grades of fatty liver was associated with increased carotid intima media thickness and this relationship was significant (p=0.007). These findings were in consistence with the findings of study performed by ML Thakur and associates that evaluated that NAFLD is associated with subclinical atherosclerosis, independent of obesity and metabolic syndrome in Asian Indians, and the relationship was statistically significant (p<0.050)[12]. It emphasizes that hepatic fat also participates in the progression of atherosclerosis other than visceral fat as seen from the increased CIMT in all the 5 (100%) subjects having grade III fatty liver as compared to 9 (30%) subjects having

grade II fatty liver and 4 (26.4%) subjects having grade I fatty liver on ultrasonography. The present study did not show any significant relationship of gender, BMI, WHR, serum HDL levels with increased CIMT in NAFLD subjects.

**CONCLUSION**: The present study concludes that nonalcoholic fatty liver disease is associated with atherosclerosis in healthy subjects, having dyslipidemia. This stresses the need for early evaluation of cardiovascular risk factors and adequate control measures to prevent the acceleration of atherosclerosis, if NAFLD is incidentally found on ultrasonography of abdomen.

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| Serum Cholesterol | Normal CIMT (<0.8) | Abnormal CIMT (>0.8) | Total |
|---|---|---|---|
| S. Cholesterol < 200mg/dl | 30 (90.9%) | 3 (9.1%) | 33 |
| S. Cholesterol > 200 mg/dl | 2 (11.8%) | 15 (88.2%) | 17 |
| Total | 32 | 18 | 50 |

Table 1: Relationship of Serum Cholesterol with CIMT

$X^2 = 30.504$; df=1; $p < 0.001$; Highly significant.

| Serum Triglyceride | Normal CIMT (< 0.8) | Abnormal CIMT (> 0.8) | Total |
|---|---|---|---|
| S. Triglyceride < 150 mg/dl | 29 (76.3%) | 9 (23.7%) | 38 |
| S. Triglyceride > 150 mg/dl | 3 (25%) | 9 (75%) | 12 |
| Total | 32 | 18 | 50 |

Table 2: Relationship of Serum Triglycerides with CIMT

X2 =10.424; df =1; p = 0.001; Significant

| Serum LDL | Normal CIMT (< 0.8) | Abnormal CIMT (> 0.8) | Total |
|---|---|---|---|
| S. LDL < 130 mg/dl | 31 (77.5%) | 9 (22.5%) | 40 |
| S.LDL > 130 mg/dl | 1 (10%) | 9 (90%) | 10 |
| Total | 32 | 18 | 50 |

Table 3: Relationship of Serum LDL with CIMT

X2 = 15.820; df = 1; p < 0.001; Highly Significant

| Grade of Fatty Liver | Normal CIMT (< 0.8) | Abnormal CIMT (>0.8) | Total |
|---|---|---|---|
| Grade I | 11 (73.3%) | 4 (26.7%) | 15 |
| Grade II | 21 (70%) | 9 (30%) | 30 |
| Grade III | 0 (0%) | 5 (100%) | 5 |
| Total | 32 | 18 | 50 |

Table 4: Relationship of Grades of fatty liver with CIMT

X2 = 9.923; df = 2; p = 0.007; Significant

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