

Prospective Study of Correlation between Carotid Intimal Medial Thickness and Non Alcoholic Fatty Liver Disease Along with Its Grades

Dr. Darshana Verma (Md General Medicine)¹, Dr. Vinayak Gour (Md Anaesthesia)²

Abstract: *This study was performed to study correlation between CIMT and NAFLD. This was hospital-based prospective study conducted at the Department of Medicine, Hamidia Hospital and Gandhi Medical College, Bhopal during period of May 2014 to Nov 2014. 100 patients with ultrasonographically proven NAFLD patients from OPD and IPD(45 males and 55 females)AND 100 patients (47 males 53 males) without NAFLD on ultrasonography abdomen were studied. The grade of NAFLD was also taken into correlation for CIMT thickness. After obtaining informed written consent, the general information of patients was recorded on a proforma. After overnight fasting, blood samples was drawn for complete hemogram, blood urea , serum creatinine, lipid profile and serum Mg. Carotid intima media thickness (CIMT) was measured by B mode ultrasound using a 7.5MHz transducer. Descriptive and inferential statistical analyses were performed using SPSS version 20.0.the study shows that average age in NAFLD group was 77.7yrs and was higher than in control group that was 56.33yrs .The study shows that mean BMI is higher in subjects with NAFLD in both males and females as compared to that in non NAFLD group. The study shows that mean Waist/hip ratio is higher in subjects with NAFLD in both males and females as compared to that in non NAFLD group. Serum SGOT and SGPT levels were found to be significantly higher in subjects with NAFLD as compared to that in non NAFLD group.The study shows that CIMT on both sides were higher on NAFLD group as compared to non NAFLD group. We concluded that patients with NAFLD have significant positive correlation, and CIMT (significantly correlated positively with grades of NAFLD as well).It is suggested that since NAFLD along with the grades is associated with inflammation of liver, metabolic syndrome, increased CIMT(which is a proven marker for atherosclerosis and a predictor of CAD and CVA).so now with further research and analysis NAFLD could also be considered as a marker for atherosclerosis and as extended spectrum of metabolic syndrome.*

Keywords: NAFLD non alcoholic fatty liver disease, CIMT- carotid intima medial thickness

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a highly prevalent condition which is characterized by fatty infiltration of liver cells resembling that of alcohol-induced liver injury but occurring in patients who do not abuse alcohol [1]. The incidence of fatty liver is estimated at 14-23%. This figure is 70-90% in obese and type II diabetic people [2]. The prevalence of NAFLD is 20%–30% in the general adult population in Western countries(123) and is now 12%–24% in Asian-Pacific countries.(14) Its prevalence in obese or diabetic patients increases up to 70%–90%.(12) The spectrum of NAFLD ranges from fatty liver alone to steatohepatitis, which histologically is similar to alcoholic hepatitis, and may progress to end-stage liver disease and cirrhosis. That is why the fatty liver, long considered an incidental finding, has received increasing attention [3]. The previous studies have shown that ultrasonographic results are well correlated with histological findings due to fatty infiltration [4, 5]. Therefore, ultrasonography alone can indicate the level of fatty infiltration in liver. On the other hand, NAFLD is strongly associated with obesity, type II diabetes, and dyslipidemia. In addition, the majority of these patients have central obesity and insulin resistance symptoms. Consequently, NAFLD shares many features of the metabolic syndrome, which is a highly atherogenic condition, and its presence is associated with marked cardiovascular risk [1]. It has been shown that intima-media thickness (IMT) of carotid artery, as a reliable index of subclinical atherosclerosis, is a predictor of myocardial infarction and stroke. non- alcoholic steatohepatitis (NASH) represents the more advanced stages of this disease, i.e. the ‘inflammatory’ component in addition

to steatosis, which carries a higher risk of CV disease and mortality than simple steatosis . Insulin resistance and obesity, both key features of the MetS, are strongly associated with NAFLD progression

Definition of non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease is the most common cause of chronic liver disease in the general population and is present when fatty infiltration affects .5% of hepatocytes, in the presence of ,<20 g (2.5 U) of alcohol consumption per day, without evidence of other causes of liver disease

Diagnosis of non-alcoholic fatty liver disease

up to 70% of NAFLD patients may have normal liver enzymes and although alanineaminotransferase (ALT) levels have shown to be the best single biochemical correlate of hepatic steatosis, they do not distinguish between varying stages of NASH and can be normal in histologically severe disease . Furthermore, ultrasound imaging can only detect steatosis when .30% of the liver is affected, but is still recommended as the first-line investigation to ‘confirm’ the presence of fatty liver due to its wide spread availability and low cost, none of the non-invasive modalities can detect inflammation and/or fibrosis, i.e. NASH. Consequently, liver biopsy is at present the ‘gold-standard’ (taking into account potential inaccuracies of sampling variability) for diagnosing NAFLD and staging the degree of NASH and fibrosis by histological assessment, as well as monitoring disease progression

2. Methods

100 patients with diagnosis of NAFLD and 100 patients without NAFLD attending opd or ipd to medicine department of Hamidia Hospital and GMC Bhopal were taken for the study from a period of collection of data: MAY 2013 – DEC 2014. The patient excluded were 1) those with a history of known liver disease, Hep B, Hep C positivity. 2) those who consume more than 20 g alcohol daily or abuse alcohol, and 3) those with ultrasonic-proven liver disease other than fatty liver. 4) those with other known co-morbid conditions like hypothyroidism, History of carotid surgery, Malignancy, Significant illness. Information was collected through prepared proforma for each patient and informed consent was obtained from each participant. The study protocol was approved by Institutional Ethics Committee of Gandhi medical college, Bhopal. History of smoking, DM, hypertension. Cardiovascular event, hyperlipidemia were evaluated. A complete clinical examination was done. Hypertension was defined as blood pressure >140/90 mm Hg or if patient is already on antihypertensive drug. The morning urine sample and blood samples were collected after 8 hours of overnight fasting for complete hemogram, blood urea levels, serum creatinine levels, FBS, serum electrolytes and lipid profile (Total cholesterol, Triglycerides and HDL). All the biochemical parameters were measured by standard laboratory technique. Carotid intima media thickness was measured by B mode ultrasound using a 7.5MHz transducer. Intima Media Thickness was defined as distance between leading edge of first echogenic line (Lumen – Intima interface) and second echogenic line

(Media – Adventitia interface) of far wall. Three measurements were taken 0.5, 1 and 2 cm below carotid bifurcation of common carotid artery on each side. The arithmetical averages of these were taken. The IMT of both sides (right and left) was calculated CIMT measurement was always performed by single radiologist in plaque free arterial segments.

3. Observations

NAFLD	CIMT thick	Normal	Total
gr 1	36	27	63
	57.1%	42.9%	100.0%
gr2	33	0	33
	100.0%	0.0%	100.0%
gr3	4	0	4
	100.0%	0.0%	100.0%
Total	73	27	100
	73.0%	27.0%	100.0%

	NAFLD gr1	NAFLD gr2	NAFLD gr3	NAFLD absent
AGE < 50	9	2	0	24
AGE > 50	54	31	4	76
total	63	33	4	100

Variables	Cases Overall	Cases Males	Cases Females	Control Overall	Control Males	Control Females
AGE	77.7 yrs	66.49yrs	62.66yrs	56.33yrs	56.1	56.25
CIMT Right	0.813	0.77	0.86	0.591	0.57	0.62
CIMT left	0.827	0.794	0.866	0.59	0.586	0.629

CIMT/NAFLD	NAFLD GRADE1	NAFLD GRADE2	NAFLD GRADE3	NO NAFLD	TOTAL
CIMT R < 0.8	51	7	0	92	150
CIMT R > 0.8	12	26	4	8	50
TOTAL	63	33	4	100	200
NAFLD/CIMT	NAFLD GRADE1	NAFLD GRADE2	NAFLD GRADE3	NO NAFLD	TOTAL
CIMT L < 0.8	52	5	0	91	148
CIMT L > 0.8	11	28	4	9	52
TOTAL	63	33	4	100	200

CIMT RIGHT	CIMT < 0.85	42%	8%	< 0.0001
	CIMT > 0.85	58%	92%	
CIMT LEFT	CIMT < 0.85	43%	9%	< 0.0001
	CIMT > 0.85	57%	91%	
SEX	MALE	45%	47%	0.5621
	FEMALE	55%	53%	

Variable	Limits	Cases	Control	P Value
AGE	AGE < 50	89%	76%	< 0.013
	AGE > 50	11%	24%	

4. Discussion

Out of 100 cases 55 were males and 45 were females. and in control group 52 were males and 48 were females. and so sex matched cases and control group were selected. There was no statistically significant relationship exists between the two groups (P VALUE - 0.526). Based on the Data from other Asian countries show that the prevalence of fatty liver was higher in males being 13.3% and 2.7%, respectively, in

males and females in China, 21.6% and 11.2%, respectively. (11)

Among cases CIMT right side was 0.813 mm on average and in males was 0.772 mm on average and in females was 0.868 mm on average. 0.591 and among control group it was 0.813 mm on average and in males was 0.588 mm on average and in females it was 0.628 mm on average which was statistically significant (P VALUE < 0.0001) (P VALUE < 0.0001) Targheret al^[7] studied a population of 200 diet-controlled type 2 diabetic subjects, reported that NAFLD patients had a markedly greater carotid IMT. In contrast IMT values were found to be significantly higher in diabetic patients regardless of the degree of steatosis by Cakiret al^[8]. Similarly other two studies performed in diabetic population reported that hepatic steatosis was not associated with carotid atherosclerosis and suggested that the association of hepatic steatosis and cardiovascular disease might be just an epiphenomenon^[9,10]. Targheret al^[6] compared carotid IMT in 85 patients with NAFLD and 160 age-, sex-, and BMI-matched healthy control subjects and found that the severity

of liver histopathology in NAFLD patients was strongly associated with early carotid atherosclerosis. Also Kucukazmanet al^[15] in a recent study showed a significant positive correlation between ultrasonographic steatosis grade and mean IMT ($r = 0.376$, $P < 0.001$).

5. Conclusion

Herewith the end of our study it is concluded that NAFLD along with its grades is significantly positively correlated with CIMT on both sides (P value < 0.0001).and with age (P value < 0.013).NAFLD is not related to sex (P value 0.56).so it is concluded that NAFLD is correlated with many of the markers for cardiovascular risksindependently of classical risk factors, insulin resistance, and the presence of metabolic syndrome, suggesting that the severity of liver damage could play a role in atherosclerosis development The prevalence of NAFLD in subjects with MetS is increased four-fold compared with those without the disease and 30% of NAFLD subjects have MetS. Despite MetS itself conferring an approximate doubling of CV mortality risk,¹⁵ there is still abundant evidence linking NAFLD to increased CV disease risk over and above that associated with the MetS criteria, suggesting that NAFLD per se contributes to atherosclerosis.

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