

A Study of Carotid Intima-Media Thickness and Retinal Artery Changes in Patients with Non Alcoholic Fatty Liver Disease

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Abstract: CONTEXT

Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most common liver diseases reported all over the world and the disease spectrum ranges from simple steatosis to non-alcoholic steato-hepatitis to cirrhosis . Fatty liver, the common term used for NAFLD has strong association with metabolic syndrome. Obesity, type-2 diabetes, dyslipidemia and insulin resistance is therefore evident in most of these patients.

As there is a clear association of fatty liver disease being a part of spectrum of metabolic syndrome, NAFLD , an independent risk factor for atherosclerosis and cardiovascular disease.

The CIMT is considered to be a non-invasive marker for atherosclerosis and the thickness is directly proportional to the presence of atherosclerosis in the coronary vessels and the severity of cardiovascular disease.

AIM OF THE STUDY

1. To measure the thickness of Carotid Intima Media (CIMT) in patients with Non-Alcoholic Fatty Liver Disease (NAFLD) and compare it with Controls, to establish the strong association of NAFLD with increased CIMT and to prove that NAFLD an independent risk factor for cardiovascular morbidity.

2. To look for any associated retinal vascular changes in NAFLD

SETTING AND DESIGN

Analytical Case Control Study.

MATERIALS AND METHODS

This study will be conducted between June 2016 to November 2016, among 50 Patients with non alcoholic fatty liver who are admitted in General Medicine Department Of Government Rajaji Hospital, Madurai and equal number of age matched controls.

Fifty patients with NAFLD confirmed on abdominal ultrasound and 50 controls with normal liver parenchyma underwent carotid artery ultrasonography for measurement of CIMT and detection of atherosclerotic plaque. All the patients will be examined for any associated retinal vascular changes

STATISTICAL ANALYSIS

One way ANOVA, Pearson correlation and Chi square test.

RESULTS

We found the strong association between NAFLD and carotid intima media thickness as p value is 0.001. Mean carotid intima media thickness in NAFLD is 0.9284mm compared to 0.6695 in control group. We also found the strong association between NAFLD and retinal vascular changes as p value is 0.004. 12 patients have retinal changes in NAFLD group compared to 2 patients in control group

CONCLUSIONS

Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most common liver diseases reported all over the world. Carotid Intima Media Thickness (CIMT) is a useful tool for detection of sub-clinical atherosclerosis. In our study, we found that, there is strong association between, NAFLD and 1. Carotid intima media thickness 2. Retinal artery changes .

So all patients with NAFLD should be investigated with carotid Doppler, and they all should be treated with statins and other cardioprotective drugs to prevent cardiovascular complication. They all should get treatment for obesity and with insulin sensitizers to prevent the progression of NAFLD. This simple and non-invasive practice will help in early diagnosis of cardiovascular disease, especially in overt cases

Keywords

Non alcoholic fatty liver disease, Insulin resistance Carotid intima media thickness, Retinal artery changes

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I. Introduction:

Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease. It encompasses a spectrum of conditions associated with lipid deposition in hepatocytes.

It ranges from 1. steatosis (simple fatty liver), 2. nonalcoholic steatohepatitis (NASH–fatty changes with inflammation and hepatocellular injury or fibrosis), 3. advanced fibrosis and cirrhosis.

Studies suggest that although simple fatty liver is a benign condition, NASH can progress to fibrosis and lead to end-stage liver disease. It is strongly associated with obesity and insulin resistance and is currently considered by many as the hepatic component of the metabolic syndrome.

The diagnosis is often made after an incidental finding of elevated liver enzyme levels or due to the clinician's suspicion regarding a patient with obesity or diabetes. Laboratory results or imaging examinations can confirm the diagnosis. However, at present, only a liver biopsy can differentiate simple steatosis from NASH

Because of the consequences of the disease, we emphasize the importance of the detection of NAFLD in high-risk groups, including obese patients, as well as those with evidence of insulin resistance or other components of metabolic syndrome

The diagnosis of NAFLD should prompt management of metabolic risk factors. Weight loss regimens are believed to be helpful, and numerous drugs have been investigated in small studies. Large randomized clinical trials are necessary to determine the real benefit of these agents. Finally, studies on the pathogenesis of NAFLD may not only improve our understanding of the mechanisms involved in NAFLD progression but also may lead to novel therapeutic strategies to treat this condition

CAROTID INTIMA MEDIA THICKNESS

CIMT is a marker of subclinical atherosclerosis. CIMT of > 0.9mm or over the 75 th percentile should be considered as abnormal Carotid ultrasound is the method of choice B mode ultrasonography is used. It is non invasive , easy, cheap, reproducible, sensitive, widely available.

CIMT is measured in the common carotid , just before the bifurcation . CIMT is measured between lumen - intima and media – adventitia. In the latest ESH/ESC hypertension guidelines (2013) carotid IMT > 0.9 mm is considered as marker of asymptomatic organ damage,

II. Materials And Methods:

Study Population: This study will be conducted between June 2016 to November 2016, among Patients with non alcoholic fatty liver who are admitted in General Medicine Department Of Government Rajaji Hospital, Madurai and equal number of age matched controls.

Inclusion Criteria: 1. Sonographically proven fatty liver. 2. Age – adults > 30 3. Gender – both male and female 4. Non alcoholic or alcoholic with < 20g/day consumption

Exclusion Criteria: 1. Patients who have problems for abdominal ultrasonography, 2. Those who are using steroid in diseases such as bronchial asthma, rheumatoid arthritis and Intestinal Bowel Disease (IBD) and 3. Those who are being treated with drugs affecting laboratory results, for example, aspirin, statins, fibrates and metformin, 4. those who have a history of liver disorders such as HBV or HCV, infection 5. Those who are consuming more than 20gm/ day of alcohol were excluded

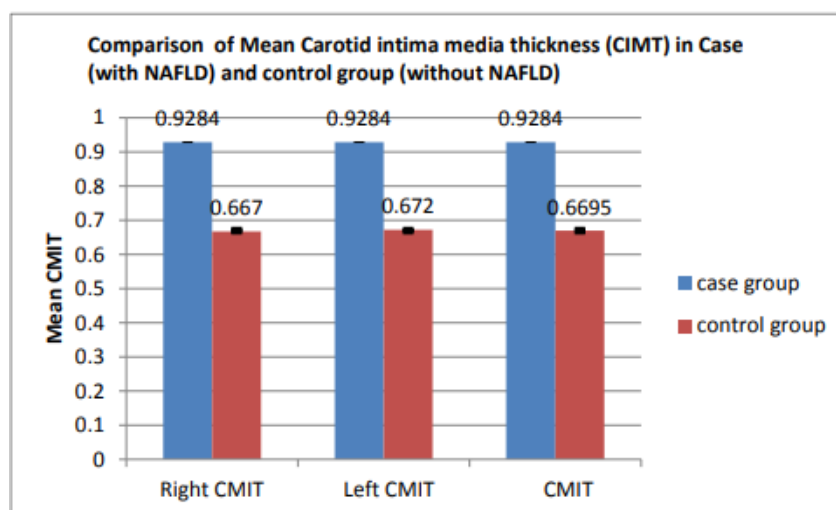
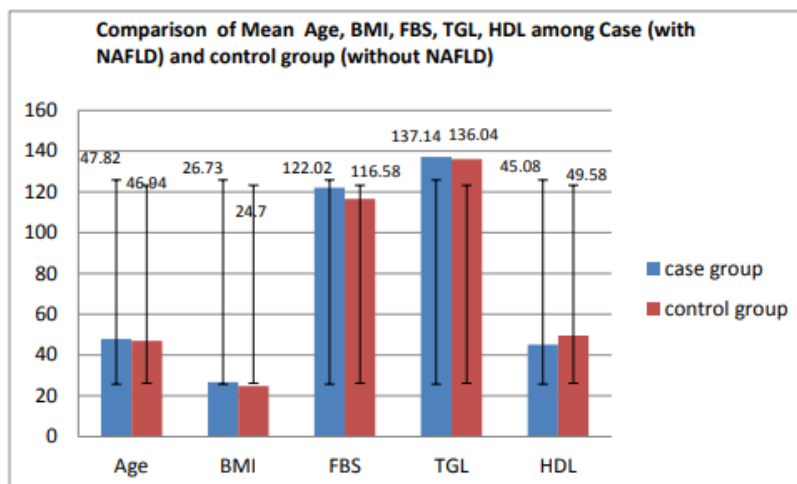
Ethical Committee Approval: Obtained.

Study Protocol: Fifty patients with NAFLD confirmed on abdominal ultrasound and 50 controls with normal liver parenchyma satisfying the inclusion and exclusion criteria are evaluated with 1. Complete history regarding presenting complaints, drug history, jaundice, and specific illness 2. h/o alcoholism and quantity 3. general examination including BMI 4. systemic examination 5. routine blood investigation including FBS, lipid profile, viral markers for hepatitis virus b and c. 6. carotid artery doppler for measurement of CIMT and detection of atherosclerotic plaque 7. ophthalmic examination for any associated fundus change

STATISTICAL ANALYSIS: The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer by using SPSS software and Sigma Stat 3.5 version (2012). Using this software, percentage, mean, standard deviation and 'p' value were calculated through one way ANOVA, Pearson correlation and Chi square test and P value of < 0.05 was taken as significant.

III. Results

1. There is strong association between carotid intima media thickness and NAFLD as pvalue is 0.001. 2. There is strong association between HDL and NAFLD as pvalue is 0.001 3. There is strong association between BMI and NAFLD as pvalue is 0.008 4. There is strong association between RETINAL ARTERY CHANGES and NAFLD as pvalue is 0.004 5. There is strong association between SEX and NAFLD as pvalue is 0.001. (as female prevalence is more in NAFLD patients)



IV. Discussion:

As the MPV increases the severity (MRS)^{2,3} of stroke increases.

In this study, CIMT and retinal artery changes in NAFLD patients was compared with control, which showed that mean CIMT and retinal artery changes were significantly much more than the control group

The results of our study are consistent with results of previous studies that are considered CIMT was associated with an increase in NAFLD and suggested it as the marker of early diagnosis of generalized atherosclerosis (Chiang et al., 2010; Guleria et al., 2013; Targher and Arcaro, 2007; Targher et al., 2008). This actually means that type II diabetic patients with NAFLD are at greater risk of premature atherosclerosis and Coronary Vessels Disease (CVD).

As we stated before ultrasound screening method is a cheap and readily available. NAFLD estimates for up to one third of the total population and in the majority of patients with cardiovascular, metabolic and abdominal obesity, type II diabetes risk factors, can be seen. Our findings revealed NAFLD effect on CIMT was significant. In agreement with this finding, De Andrade et al. (2014) measured CIMT in a cross-sectional study on diabetes patients and showed that CIMT and CVD risk may be higher in those with a family history of type II diabetes. Besides, Nahandi et al. (2014) evaluated the effect of NAFLD on CIMT as a risk factor for atherosclerosis in patients with type II diabetes and reported that there is a significant association between the presence of NAFLD and CIMT and its related atherosclerosis. Mohammadi et al. (2011) examined patients with confirmed NAFLD for determination of CIMT and presence of carotid atherosclerotic plaque and reported that NAFLD with type II diabetes can be associated with increased CIMT and increased risk of atherosclerosis. Moreover, Han et al. (2013) studied gender differences in the association between CIMT in healthy individuals and age-related increases in CIMT were correlated with a reduction in cardiac function only in women. Our findings showed a considerable association between NAFLD and increased CIMT, in which this association is not affected by the severity of fatty liver. And also considerable association between retinal artery changes and NAFLD also observed. Considerable association between NAFLD and obesity and HDL levels are also observed. The internal carotid artery provides blood to the eye, therefore the pathology due to

arteriosclerosis of these arteries may have a direct impact on retinal circulation and may coexist with retinal arteriosclerosis. So in our study, it is clear that, increase in carotid intima media thickness cause increased retinal artery changes.

Hence all our NAFLD patients are treated with statins and other cardioprotective drugs, and also they are advised to follow up regularly once in every 6 months. They are advised to take treatment for NAFLD with insulin sensitizers. So, immediate ultrasound screening and treatment for the patients with NAFLD are recommended to prevent CVD complications such as atherosclerosis considering early stages of fatty liver disease.

V. Conclusion

Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most common liver diseases reported all over the world. Carotid Intima Media Thickness (CIMT) is a useful tool for detection of sub-clinical atherosclerosis.

In our study, we found that, there is strong association between, NAFLD and 1. Carotid intima media thickness 2. Retinal artery changes we also found significant association between NAFLD and body mass index and HDL levels.

So all patients with NAFLD should be investigated with carotid Doppler, and they all should be treated with statins and other cardioprotective drugs to prevent cardiovascular complication.

They all should get treatment for obesity and with insulin sensitizers to prevent the progression of NAFLD. This simple and non-invasive practice will help in early diagnosis of cardiovascular disease, especially in overt cases.

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