Assessment of the Co-incidence Between Non alcoholic Fatty Liver Disease And Carotid Atherosclerosis

Thesis

Submitted for partial fulfillment of

Master degree in tropical medicine

By

Ahmed Abd El- Mageed Morsy

M.B.B.CH. Ain Shams University

Supervised by

Professor Doctor/ Soheir Abd El- kader El-Sayed

Professor of Tropical Medicine

Faculty of Medicine

Ain Shams University

Doctor/ Runia Fouad El-Folly

Lecturer of Tropical Medicine

Faculty of Medicine

Ain Shams University

Doctor/ Amr Mahmmoud Ahmed

Lecturer of Radiology Medicine

Faculty of Medicine

Ain Shams University

2011

تقييم مشاركة الإصابةبين مرض الكبد الدهني وتصلب الشرايين السباتيه

رسالة

توطئة للحصول علي درجة الماجيستير
في طب المناطق الحارة

مقدمه من

الطبيب/ أحمد عبد المجيد مرسى

بكالوريوس الطب والجراحة

كلية الطب جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ سهير عبد القادر السيد

أستاذ طب المناطق الحارة

كلية الطب جامعة عين شمس

الدكتور/ رنيا فؤاد الفولى

مدرس طب المناطق الحارة

كلية الطب جامعة عين شمس

الدكتور/ عمرو محمود أحمد

مدرس الأشعه التداخليه

كلية الطب جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠٠٩

Nonalcoholic fatty liver disease (NAFLD) is a highly prevalent condition characterized by fatty infiltration of liver cells resembling that of alcohol-induced liver injury but occurring in patients who do not abuse alcohol.

The spectrum of ***NAFLD*** ranges from fatty liver alone to steatohepatitis, and may progress to end-stage liver disease. ***NAFLD*** is strongly associated with obesity, type 2 diabetes, and dyslipidemia.

Thus, ***NAFLD*** shares many features of the metabolic syndrome (MetS), a highly atherogenic condition, and its presence could signify a substantial cardiovascular risk above and beyond that conferred by individual risk factors.

The possible relationship between hepatic steatosis and carotid lesions might have important practical consequences, considering the frequent incidental finding of bright hepatomegaly in subjects undergoing abdominal ultrasound for any reason or hepatic steatosis by liver biopsy. In these subjects, an ultrasound assessment of carotid arteries might also be advisable.

List of Contents

List of Abbreviations

ALT……..……..Alanine Aminotransferase.

AMP …….Adenosine mono phosphate.

AMPK …… .....Adenosine monophosphate-activated protein kinase.

Apo…….Apolipoprotein .

ASH ……..…… ….Alcoholic steatohepatitis.

AST……Aspartate Aminotransferase.

ATP…… …Adenosine Triphosphate

BMI ……Body Mass Index.

CETP……. ….Cholesteryl ester transfer protein

CIMT…….. …Carotid intima-media thickness

CRP ……..……. …C-reactive protein

CT ……..……. …Computed Tomography

CVD ……..…..……Cardiovascular disease

DM…….. ..Diabetes Mellitus.

HCC ……...Hepatocellular Carcinoma

HDL ……..….High-density lipoprotein

HMG COA..…… .hydroxymethylglutaryl coenzyme A

HU……. Hounsfield units.

ICAM – 1 ……...Intercellular adhesion molecule 1

IL ……...Interleukin

IRS-1 And IRS-2 …..Insulin Receptor Substrates 1 And 2

LDL……..……..Low Density Lipoprotein.

MR ……Magnetic Resonance

MRS ……. Magnetic resonance spectroscopy

MTTP……... microsomal triglyceride transfer protein

NADH……... Nicotinamide-adenine dinucleotide hydrogenase

NAFLD…….Non-Alcoholic Fatty Liver Disease

NCEP …….. .National Cholesterol Education Program

NO ……. Nitric oxide

NASH……..…. Non Alcoholic Steatohepatitis

NHANES..... National Health and Nutrition Examination Survey

PCOS …….polycystic ovary syndrome

PF4 …….platelet factor 4

PI-3 Kinase ……… Phosphatidyl Inositol-3 Kinase

PPAR-g ……..peroxisome proliferator-activated receptor-g

ROS ……....reactive oxygen species

SREBP -1……Sterol regulatory element –binding protein-1

SVR ……sustained virologic response.

TNF……..Tumor Necrosis Factor

TZDs …… thiazolidinediones

U S……..…Ultrasound.

UDCA ……...Ursodeoxycholic Acid

VCAM – 1 ……....vascular cell adhesion molecule 1

VLDL…….Very-Low-Density Lipoprotein.

W/H……Weight/Hight.

LIST OF TABLES

List of Figures

Assessment of the Co-incidence Between Non alcoholic Fatty Liver Disease And Carotid Atherosclerosis

Thesis

Submitted for partial fulfillment of

Master degree in tropical medicine

By

Ahmed Abd El- Mageed Morsy

M.B.B.CH. Ain Shams University

Supervised by

Professor Doctor\ Sohair Abd El- kader El-Sayed

Professor of Tropical Medicine
Faculty of Medicine
Ain Shams University

Doctor\ Runia Fouad El-Folly

Lecturer of Tropical Medicine
Faculty of Medicine
Ain Shams University

Doctor\ Amr Mahmmoud Ahmed

Lecturer of Radiology Medicine
Faculty of Medicine
Ain Shams University

Faculty of Medicine

Ain Shams University

2009

Assessment of the Co-incidence between Non alcoholic Fatty Liver Disease and Carotid Atherosclerosis

INTRODUCTION:

Non alcoholic fatty liver disease (***NAFLD***), as conventionally recognized is a metabolic disorder largely confined to residents of affluent industrialized western countries, however, obesity and insulin resistance; the common substrates of ***NAFLD*** are not restricted to the west as witnessed by their increasingly universal distribution ***(Williams, 2006).***

NAFLD is founded to be closely related to increased new metabolic disorder even in previously non obese, non diabetic adults ***(Kim et al., 2004).***

It includes a wide spectrum of hepatic alteration of metabolic origin. According to current estimates, the prevalence of ***NAFLD*** in general population ranges from 5% to 33%. Up to more than 75% of obese adult subjects can be affected by ***NAFLD (Farrell and Larter, 2006).***

The prevalence of ***NAFLD*** has grown to epidemic proportions; it is currently the most common cause of abnormal liver biochemistry and cryptogenic cirrhosis, and a frequent indication for liver transplantation **(*Clark, 2006).***

It is well recognized that ***NAFLD*** exists as a spectrum consisting of two major phenotypes that have drastically different natural histories.

While the majority of patients have simple steatosis, which has a benign clinical course, approximately 10-20% of individuals have nonalcoholic steatohepatitis (NASH), a potentially serious condition ***(Adams et al., 2005 and Harrison et al., 2003).***

In one study, patients with NASH had significantly reduced survival compared to the general population and a higher risk of liver-related (2.8% vs. 0.2%) and cardiovascular death (15.5% vs 7.5%) ***(Ekstedt et al., 2006)***.

End-stage liver disease occurred in 10% of patients during follow-up, including three cases of hepatocellular carcinoma. In contrast, survival of patients with simple steatosis was similar to that of the control population and none of these patients developed liver failure. Although there are currently no approved therapies for ***NAFLD***, new treatments including insulin-sensitizing agents are under investigation in large-scale clinical trials ***(Belfort et al., 2006).***

NAFLD is strongly associated with obesity, type 2 diabetes, and dyslipidemia, and most patients have evidence of central adiposity and are insulin resistant ***(Marchesini et al., 2001).***

Thus, ***NAFLD*** shares many features of the metabolic syndrome (MetS), a highly atherogenic condition ***(Grundy et al., 2004).***

The potential cardiovascular risk associated with ***NAFLD*** has not been particularly investigated despite the evidence that mortality rates from coronary heart disease (CHD) equaled those attributable to cirrhosis in a large cohort of patients with biopsy-proven ***NAFLD*** followed for up to 18 years ***(Matteoni et al., 1999).***

AIM OF THE WORK:

The aim of the work is to assess the co-incidence and prevalence between ***NAFLD*** as a cardiovascular risk factor and carotid atherosclerosis.

PATIENTS AND METHODS:

✓ **Patient Recruitment :**

- ***Study Design:*** This study was designed to be cross section study.
- ***Study Setting:*** Patients with clinical data of clinical, biochemical and sonographical criteria of ***NAFLD*** will be recruited from those attending Tropical Medicine Department - Ain Shams University, and EL-Sahel Teaching Hospital.
- This study will include number of (72) cases. They will be divided into two groups

Group 1; Formed of 52 patients diagnosed as ***NAFLD*** with diabetes mellitus type 2 or obesity or hyperlipedemia.
Group 2; Diseased Control formed of 20 cases diagnosed as ***NAFLD*** without other predisposing factor.

Inclusion criteria **(for study group):**
1. Clinical, biochemical, and sonographical criteria of ***NAFLD*** [The presence of steatosis in ultrasound scan with or without elevated ALT and\or AST, negative or occasional historic alcohol intake (<140gm\week),

negative diagnosis of liver diseases (HBV, HCV, autoimmune hepatitis and metabolic liver disease) ***(Raquel et al., 2009)***].

2. HCV-Ab -ve and HBsAg –ve (group 1, 2).
3. Elevated lipid profile (group 1).
4. Elevated FBS and 2hr PP (group 1).
5. Elevated BMI whereas BMI >30 (group 1).

Eligibility Criteria:

- Male & female Patients with ***NAFLD***,
- Age in both groups; above age of 20 years old and below age of 50 years.

Exclusion Criteria (**for all groups**):

1. Alcoholic patient.
2. Other causes of chronic liver disease and steatosis.
3. Patients with advanced systemic disease as heart failure or any debilitating disease that will affect life expectancy.

Methods:

The following will be done for all patients:

1. ***Full medical history*** including their age, sex and previous history of liver disease including risk factors of infection with HCV as parentral antibilharzial therapy, blood transfusion, previous operation and others).
2. ***Thorough clinical examination*** with special stress on general clinical manifestations of chronic liver disease (***NAFLD***), assessment of BMI and careful abdominal examination.

3. ***Laboratory investigation:***

- Complete blood picture.
- Liver profile tests including [ALT, AST, total and direct bilirubin, serum albumin, prothrombin time and international randomization ratio (INR)].
- Hepatitis markers (HCV Abs and HBV sAg).
- Lipid profile (serum cholesterol, LDL, HDL, and serum triglyceride).
- Glucose profile (fasting blood sugar, 2 hours postprandial, HbA1c in diabetic patient).

4. ***Imaging:***

- The diagnosis of ***NAFLD*** was based on the exclusion of known etiologic factors of liver disease and on ultrasound examination but was not confirmed by liver biopsy for ethical reasons. However, ultrasound examination is by far the commonest way of diagnosing ***NAFLD*** in clinical practice ***(Caturelli et al., 1992).***
- **Abdominal ultrasound**; Following the American gastroenterological association (AGA) classification of ***NAFLD*** steatosis was defined as the presence of diffuse hyperechoic echo-texture ***(Sanyal et al.,2002).*** Bright liver increased liver echo-texture compared with the kidneys, vascular blurring and deep attenuation of the ultrasonic beam ***(Palmentieri et al., 2006).***