EVALUATION OF SERUM FERRITIN IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) (Thesis)

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ABSTRACT:

Non-alcoholic Fatty Liver Disease (NAFLD) is a form of liver disease resembling alcoholic liver disease in a patient who did not consume significant amount of alcohol. Our study is concerned with the relation between serum ferritin and patients suspected to have fatty liver.

This study included 50 Patients with non-alcoholic steatohepatitis. And 25 controls same age and sex. All the patients were subjected to detailed medical history and clinical examination.

Full physical examination was performed including measurement of weight, height and body mass index (BMI), systolic and diastolic blood pressures (SBP and DBP, respectively), abdominal examination with stress on hepatosplenomegaly and ascites in addition to examination of the other systems of body. Abdominal ultrasonography was carried on to detect fatty liver and exclusion of other hepatic or abdominal problems.

Routine laboratory tests including liver function tests (liver enzymes -ALT and AST-, serum total bilirubin, albumin, prothrombin time and INR), complete blood count (CBC), fasting plasma glucose (FPG), (HbAiC) and fasting lipid profile including serum total cholesterol, triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were performed. Serum ferritin and iron were determined.

Our results showed elevated serum ferritin in NAFLD patients and showed statistically significant difference in comparative study between patients and control group as regards(BMI, fasting plasma glucose,

HBA1C, cholesterol, TG, LDL, serum Iron, TIBC, Serum Uric Acid) and showed high statistically positive correlation between serum ferritin and other studied parameters (BMI, FPG, HBA1C, LDL, serum Iron, TIBC, cholesterol).

Key words:

Serum - Ferritin – Non-Alcoholic – Fatty - Liver

Table of Content

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LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CYT E: Cytochrome Enzyme

ETC: Electron Transport Chain

FBG: Fasting blood Glucose

HBA1C: Glycosylated hemoglobin

HCC: Hepatocelleular carcinoma

NAFLD: Non-Alcoholic Fatty Liver Disease

NASH: Non Alcoholic Steatohepatitis

TIBC: Total Iron Binding Capacity

TG: Triglycerides

US-FLI Ultrasound Fatty Liver Indicator

VLDL: Very Low Density Lipoprotein

AIM OF THE STUDY

To Evaluate serum ferritin in nonalcoholic fatty liver disease (NAFLD).

REVIEW OF LITERATURE

NON-ALCOHOLIC FATTY LIVER

Fatty liver is defines as an excessive deposition of fat and triglyceride in liver. It is caused by failure of normal hepatic fat metabolism either due to a defect in the hepatocyte or to delivery of excess fat, fatty acids for carbohydrate beyond the secretory capacity of the liver cells for lipids.associations between obesity, T2DM, and steatosis Have long been recognized, as has the high prevalence of cirrhosis in diabetes. Cases of fatty liver disease with inflammation that resembled alcoholic steatohepatitis but occurring in nondrinkers were described 30 years ago, first in the Japanese literature and then in the United States**.(Adler and schaffner, 1979)).**

Ludwig coined the term nonalcoholic steatohepatitis (NASH) in 1980 **(Ludwig et al 1980).** The more embracing term nonalcoholic fatty liver disease (NAFLD) has been adopted to cover the full spectrum of metabolic fatty liver disorders, **(Angulo , 2002)**particularly when histology is undefined.

Other causes of steatohepatitis are sometimes referred to as “secondary NASH” but are better linked semantically to their known cause, for example, “alcoholic steatohepatitis” or “drug-induced steatohepatitis” **(Farrell ,et al 2005)**. Until 10 years ago, no clues existed to the natural history or etiopathogenesis of NAFLD, and particularly how it could result in steatohepatitis or cirrhosis, but in the last decade there has been an explosion of interest in this disorder**(Farrell ,et al 2005)**..

Earlier classifications attempted to differentiate benign steatosis (with or without minor inflammation) from lesions that predicate adverse outcomes; the latter include ballooning degeneration of hepatocytes, Mallory bodies, and fibrosis.**(Matteoni et al 1999)**

In 1999 to reach a pathological classification, the Pathology Committee of the NIH NASH Clinical Research Network have proposed a scoring system comprising 14 histological features.11 Although substantial sampling error can occur with needle biopsy of NAFLD,12 interrater variability between expert pathologists was high for fibrosis (kappa score, 0.84) and steatosis (0.79), lower for injury (0.56) and lobular inflammation (0.45).The unweighted sum of scores for steatosis, lobular inflammation, and hepatocellular ballooning was used to construct a new NAFLD activity score. This activity score can be used to classify cases into “NASH,” “borderline,” and “not NASH,” but agreement on diagnostic category is only moderate (0.61) **(Matteoni et al 1999)**.

Other aspects of NASH pathology, **(Matteoni et al 1999)** such as Mallory bodies and portal versus pericellular fibrosis, are more difficult to quantify or lack reproducibility. Nonetheless, Gramlich and colleagues (2004) emphasize the relationships between ballooning degeneration and Mallory bodies and perisinusoidal and perivenular fibrosis, **(Gramlich, et al 2004)** confirming the concept that hepatocyte injury, an essential feature of NASH,**(Kleiner ,et al (2005)** is the critical component of NAFLD that correlates with fibrogenesis.Authors have differed on the level of alcohol consumption that can reliably distinguish between alcoholic steatohepatitis and NASH, from total abstinence (as in the original descriptions) to 20 to 40 g ethanol/day. **(McCullough ,et al 2006)**

The latter approaches the threshold associated with an increased risk of cirrhosis in women. Small amounts of alcohol intake (1-2 standard drinks or 10-20 g ethanol/ day) do not worsen hepatitis C. National Institutes of Health Consensus Development Conference Statement: Although this finding is also likely to be true for NAFLD, it is harder to prove; lifetime total consumption may be more important. **(Hayashi ,et al 2004)**

Lower levels of regular alcohol intake reduce the risk of cardiac events and improve insulin sensitivity in persons with T2DM, and probably in the metabolic syndrome. Because these are the most important risk factors for severity in NASH, it is possible that low-level alcohol intake has benefits rather than detriments**(Hayashi ,et al 2004).**

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The NIH clinical research network on NAFLD/NASH has therefore agreed that the maximum allowable level of alcohol intake for definition of NAFLD is 2 standard drinks a day (140 g ethanol/week) for men, and one standard drink a day (70 g ethanol/week) for women; similar levels are adopted by the first book on NAFLD/NASH **(Farrel et al 2005).**

Scope and Future Dimensions

Epidemiology. NAFLD/NASH has a very high prevalence in North and South America, much of Asia-Pacific (including Australia and New Zealand), the Middle East, and Europe. It is now the leading cause of referral to hepatology clinics in most regions, but accurate estimates of its incidence, prevalence, and natural history are lacking. Whereas NASH

has been referred to as a disease of the “West,” altered socioeconomic circumstances and related changes in food intake, food composition, and physical activity (together referred to as “lifestyle”) may each play a role**(Farrel et al 2005).**.

Few studies document the relative importance of these factors, but a high intake of saturated fats was noted in one study, and another found a correlation between higher carbohydrate intake and liver inflammation. NAFLD/NASH is now regarded as a manifestation of the metabolic (or insulin resistance) syndrome, and the link between obesity, T2DM, cardiovascular disease and NAFLD is likely to reflect shared pathogenic factors**(Farrel et al 2005).**.

Case definition and case ascertainment bedevil epidemiological studies of NAFLD/NASH and NASH-cirrhosis. 15 Available data are based on tests that lack sensitivity and specificity, particularly unexplained aminotransferase elevations and abnormal (“bright”) hepatic ultrasonography. . Based on the Third National Health and Nutritional Examination Survey (NHANES III), which determined aminotransferase levels and excluded known causes of liver disease, the likely prevalence of NAFLD in North America and similar regions is 3% to 23% **(clark et al 2002).**

Population surveys using hepatic ultrasonography indicate similar prevalence (approximately 22%; 16% in lean, 76% in obese individuals). **(Nomura , et al 1988)** the Third National Health and Nutritional Examination Survey(NHANES III) was conducted a decade ago. A recent study using proton magnetic resonance spectrometry found approximately 30% of the U.S. population (including 45% Hispanics, 33%

whites, 21% blacks; 42% white males, 24% white females) had increased hepatic triglyceride content. Another recent study based on ultrasonography found an apparent prevalence of NAFLD of 29% among healthy Japanese adults **(Jimba et al 2005).**

Extrapolating data from liver biopsy or autopsy studies, 10% to 25% of such individuals, or 2% to 7% of the population, may have NASH and fibrosis or cirrhosis. In 20-year-old autopsy studies, the frequency of steatosis among those who died suddenly was 16% to 24%, and NASH was present in 2.1% to 2.4%.28,29 Likewise, steatosis is found in approximately 20% of liver donors with normal aminotransferase levels.**(**.More than 60% of men and 45% of women in Australia and the United States are overweight, at least one third of whom are obese; values range from 26% to 28% in some states.**(Marcos ,et al 2000)**..

The prevalence of T2DM approximates 8%. It has been estimated that approximately 75% of those with obesity orT2DMhave NAFLD, whereas autopsy and biopsy studies show that approximately 20% of obese subjects have NASH. **(Wanless and lents et al 1990).**Thus, despite uncertainties about the precise prevalence of NAFLD and NASH, clearly obesity is now an important cause of cirrhosis.15 Because the prevalence of obesity and T2DM in North America and around the world has continued to rise since 1985, and because the frequency with which NASH is diagnosed in childhood is also increasingthe prevalence of NAFLD/NASH will likely continue to rise,**(Roberts , 2002)**.

This disorder will therefore contribute substantially to the burden of chronic liver disease in coming decades. Risk Factors. Obesity, hyperglycemia, T2DM, and hypertriglyceridemia are the best known.,