

Hepatic Steatosis, its Complication and Correlation with Risk Factor and Management

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ABSTRACT

Liver detoxifies the various metabolic products inside the body and converts toxic substance to less toxic by different phases of detoxification reaction. It play broad-spectrum role (synthetic, storage, metabolic, protective secretory and Excretory). Sedentary life style, Unhygienic food, adulterated food, high dose of alcohol, fatty diet adversely affect the normal functioning of liver. Fatty Liver Disease refers to a reversible condition in which there is accumulation of triglyceride fat into intra-cytoplasmic Vacuole. If fatty liver is not treatable at time then it goes to various stages (NAFLD, NASH, Fibrosis, Cirrhosis and Hepatocellular Carcinoma). Diet and aerobic exercise plays an important role in management of Liver disease. The present article focused on fatty liver disease is manageable at earlier stage by spreading awareness program among the individual.

Keyword: Fatty Liver, Obesity, Insulin Resistance, Non Alcoholic Fatty Liver Disease (NAFLD), Nonalcoholic Steatohepatitis (NASH), Cirrhosis

INTRODUCTION

Liver is a vital organ, contribute their role in metabolism and excretion of xenobiotics from the body.¹ Fatty Liver Disease (FLD) also known as hepatic steatosis refer to a reversible condition in which there are accumulation of Triglycerides (TG) fat into intra- cytoplasmic vacuole. The prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) ranges from 9% to 36.9% of the population in different parts of the world.² Most patients with a fatty liver disease have excess body weight; obesity is a common and well-documented risk factor for NAFLD (Non Alcoholic Fatty Liver Disease) and a predictor of advanced disease. Both BMI and visceral obesity are risk factors for Non Alcoholic Fatty Liver Disease.

Liver diseases, containing a wide range of hepatic pathologies from steatosis, hepatitis, and cirrhosis to hepatocellular carcinoma (HCC), are leading causes of morbidity and mortality worldwide and have caused huge socioeconomic burdens (S. Li, H. Y. Tan 2015).³

The underlying mechanisms linking Non Alcoholic Fatty Liver Disease and insulin resistance are a major focus of current research. The present review article mainly concerned with various aspect of biochemical alteration takes place in pathogenesis of fatty liver disease and its correlation with other factor in progression of different stages. The aim of present study is to suggest what would be the possible way to treat the patients of fatty liver disease and associated Problems which is a big challenge globally.

REVIEW OF LITERATURE

Liver normally contains about 5% of Lipids out of which 20% Triglyceride, increases level of Triglyceride upto 30% in case of fatty liver disease. Fatty Liver or Hepatic steatosis a disease which adversely affect normal functioning of Liver resulting various complication if not diagnosed and treated at time.

Epidemiology of Fatty Liver Disease: The prevalence of NAFLD is high in conditions associated with insulin resistance such as obesity, type 2 diabetes mellitus, dyslipidemia, and the metabolic syndrome. In the general population the prevalence of Non Alcoholic Fatty Liver Disease and Nonalcoholic steatohepatitis is approximately 20 and 3%, respectively, In obese populations NAFLD may affect up to 75% of subjects. NAFLD is a Liver disease that is rapidly increasing in incidence and is currently the most common cause of liver disease worldwide.

Stages of Fatty Liver Disease and their Progression:

The four stages of Liver disease are inflammation, fibrosis, cirrhosis and Liver failure.⁴ Inflammation is a warning sign that the body is trying to fight an infection or heal an injury. The prognosis is good at this stage, but if left untreated, the inflamed liver starts to scar, and excess scar tissue replaces healthy Liver tissue. This process, called fibrosis, forces the liver to work harder since blood flow may be restricted.

Non Alcoholic Fatty Liver Disease (NAFLD) vs NASH

(Non Alcoholic Steatohepatitis): NAFLD is a benign condition, whereas NASH can progress to cirrhosis and ultimately to hepatocellular carcinoma (HCC). The precise mechanism of NASH is poorly understood, although insulin resistance, oxidative stress and multiple parallel hits theory have been reported.

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How to cite this article: Subodh Kumar, Uday Narayan Singh. Hepatic steatosis, its complication and correlation with risk factor and management. International Journal of Contemporary Medical Research 2019;6(7):G4-G7.

DOI: <http://dx.doi.org/10.21276/ijcmr.2019.6.7.32>

Insulin resistance vs fatty Liver Disease: Insulin resistance contributes to Non Alcoholic Fatty Liver Disease directly by increasing *de novo* lipogenesis and indirectly by increasing FFA flux to the liver via decreased inhibition of lipolysis. Zinc is an important micronutrient in that it plays a key role in the metabolism of macronutrients⁵, as well as the synthesis, storage, release, and actions of insulin.⁶ Diets high in saturated fat have been shown to induce insulin resistance.^{7,8} Significant improvement in insulin sensitivity and weight loss with high volume aerobic exercise.⁹

Role of Micronutrients in Fatty Liver Disease: Micronutrients are defined as nutrients that are needed in only microgram or milligram quantities for physiologic functions¹⁰ as defined by the World Health Organization.¹¹

Role of PreBiotics and Probiotics in fatty Liver: Probiotics are live microorganisms which when consumed may confer a health benefit to the host¹² Certain species of Lactic Acid Bacteria (LAB) and Bifidobacteria spp. are commonly used in the manufacture of probiotic products because of their well-known beneficial effect to host health and they are Generally Recognized as Safe.¹³ There is a definite role of normal gut microbiota in development of intestinal immunity¹⁴ "low bacterial richness" may play a role in obesity, metabolic syndrome, and fatty liver. Under conditions involving a damaged intestinal barrier ("leaky gut"), the gut-liver axis may enhance the natural interactions between intestinal bacteria/bacterial products and hepatic receptors (e.g., toll-like receptors), thus promoting the following cascade of events: oxidative stress, insulin-resistance, hepatic inflammation, and fibrosis.

Role of Vitamin in Steatosis: In experimental models, vitamin E has antisteatotic, anti-inflammatory, and antifibrotic effects. Effects on steatosis may in part be owing to vitamin E's inhibitory effect on hepatocyte fatty acid uptake. Namely, in guinea pigs fed an obesogenic diet, vitamin E prevents the up-regulation of the hepatic fatty acid receptor CD36.¹⁵

Role of Ginger in Fatty liver management: Anti-inflammatory^{16,17}, antioxidant¹⁷ and hypolipidemic action¹⁸ of ginger has been established earlier. Its essential oil exerts a protective effect against the non-alcoholic fatty liver disease occurring because of obesity.¹⁹ Ginger can aid in accelerating weight loss and managing obesity by helping boost your metabolism.²⁰ It increases exercise endurance capacity so that you work out well and get back into shape to fit in that outfit you were so excited to wear. to improve your insulin resistance and control diabetes, consider adding this root to your diet.²¹

PATHOGENESIS OF FATTY LIVER DISEASE

It is difficult to distinguish alcoholic Fatty Liver Disease (AFLD) from Non Alcoholic Fatty Liver Disease (NAFLD) both show micro-vesicular & macro-vesicular fatty changes (most common) at different stages. Pathogenesis of Non Alcoholic Fatty Liver Disease (NAFLD) is not clear yet,

the most important factor of the development of NAFLD is insulin resistance. Insulin resistance increase fat breakdown from adipose tissue, which in turn, increases circulating free fatty acids having as a final result the retention of lipids within the liver, called steatosis (Fatty Liver).²² The major proposed pathways of disease from dysbiosis (derangement of the gut microbiome) are through the gut-liver axis resulting in increased inflammation, steatosis, and fibrosis.²³ In addition, several mechanisms may play a role in the pathogenesis of NAFLD, including insulin resistance, oxidative stress, and cytokine toxicity.²⁴

Correlation of various Factor: There is positive correlation between alcohol intake and fatty liver progression. It has direct hepatotoxic effect and causes a decreased oxidation of fat in the liver. Age >45, Obesity (BMI \geq 30) Ratio of AST/ALT > 1 & DM are associated with increased risk for development of significant fibrosis. Inflammatory activity when present may reflect the combined effect of oxidative stress, subsequent lipid peroxidation and abnormal cytokine expression, especially increased TNF. Previous study demonstrate that there is positive co-relationship found between increase Body Mass Index (BMI) and Nonalcoholic fatty liver disease (NAFLD).^{25,26}

Scoring System: Currently the two most commonly use scoring systems are the METAVIR and the Batts-Ludwigs. The METAVIR scoring system is a system for assessing the degree of liver fibrosis (F0 to F4).⁴ Increasing fibrosis eventually leading to cirrhosis.

Diagnosis: Liver biopsy is the gold standard in diagnosing Non Alcoholic Fatty Liver Disease and the most accurate tool for grading fibrosis however is invasive and carries the risk of complications.²⁷ Computed Tomography (CT) and ultrasonography are performed to detect Non Alcoholic Fatty Liver Disease, but these are not sufficient to distinguish between Non Alcoholic Fatty Liver Disease (NAFLD) and Non Alcoholic Steatohepatitis (NASH). The distinct diagnosis of NAFL and NASH is currently made by liver biopsy, requiring hospitalization.

Histological Finding: The histological findings are fairly well defined. In general they are divided into two main subtypes – those that show pure steatosis without inflammation (NAFL), and those that show steatosis with inflammation (NASH). The presence of hepatic fibrosis is the most important factor that will determine the outcome of patients with NAFLD.

Is Fatty Liver Reversible? Of course, the treatment of fatty liver depends on its cause, and, in general, treating the underlying cause will reverse the process of steatosis if implemented at an early stage. The ability of probiotics to reverse gut dysbiosis has generated increasing interest in efforts to study probiotics as an alternative therapeutic option in patients with Fatty Liver Disease. Bariatric Surgery while not recommended in 2017 as a treatment for Fatty Liver Disease (FLD) alone, has been shown to revert Fatty Liver

Disease, Non Alcoholic Fatty Liver Disease, Non Alcoholic Steatohepatitis and advanced steatohepatitis in over 90% of people who have undergone this surgery for the treatment of obesity.

Management Of Fatty Liver Disease (Hepatic Steatosis):

There is no effective treatment for Fatty Liver till date, weight loss and low fat diet is the best option. Earlier study suggested that metformin when used in combination with probiotics was significantly better than metformin alone in reducing liver inflammation.²⁸ At least six clinical studies that assessed serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) to evaluate liver function demonstrated significant improvement with probiotic and symbiotic treatment.²⁹

MANAGEMENT OF FATTY LIVER DISEASE

1. Management of weight primary Treatment (by Aerobic exercise & Meditation)
2. Use of Prebiotics and Probiotics to maintain gut microbiota.
3. Abstention from alcohol (because it causes weight gain and insulin resistant)
4. By use of insulin-sensitizing agents (Thiazolidinediones): improve both hepatic as well as whole body insulin sensitivity.
5. In addition to insulin –sensitizing agents, lipid lowering medications and antioxidant and cytoprotective therapies (Ursodeoxycholic acid) have been tried in NAFLD & NASH
6. Use of Omega 3 essential fatty acids: Downregulate sterol regulatory element binding protein 1c and upregulate peroxisome proliferator activated receptor α , which would favor fatty acid oxidation and reduce steatosis
7. Treatment of NASH comprises change in life style, including eating habits and exercise that will lead to weight loss, and drug intake including vitamin-E
8. Use of Pioglitazone in Type-2DM patients with Fatty Liver showed increased in adiponectin levels, and that has been associated with decreases in hepatic fat.
9. Stop Alcohol intake because it causes weight gain and insulin resistance
10. Use of 250mg. of ginger extract (equivalent to 1.5 gm of pure ginger powder) for 30 days orally twice daily after meal documented to ameliorate inflammation, oxidative stress and hyperlipidemia.^{16,17,30}
11. Bariatric surgery in case of Obese people also effective but require more research to recommended

CONCLUSION

We can prevent Fatty Liver Disease progression in earlier stage by identifying the risk factor, diet management and proper medication. Weight management is primary treatment for Fatty Liver Disease who are obese or overweight, so aerobic exercise must be included in our daily activities. Gut Microbiota play major role in Immunity. Low bacterial richness in gut" may play a role in obesity, metabolic

syndrome, and fatty liver. The ability of probiotics to reverse gut dysbiosis has generated increasing interest in efforts to study probiotics as an alternative therapeutic option in patients with Fatty Liver Disease. The underlying mechanisms linking Non Alcoholic Fatty Liver Disease and insulin resistance are a major focus of current research. In clinical practice, nonalcoholic fatty liver disease (NAFLD) typically comes to the attention of the healthcare practitioner because laboratory testing reveals elevated level of liver aminotransferases.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 18-06-2019; **Accepted:** 28-06-2019; **Published:** 25-07-2019