Non-alcoholic Fatty Liver Disease (NAFLD)

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Nonalcoholic fatty liver disease (NAFLD) refers to the presence of hepatic steatosis when no other causes for secondary hepatic fat accumulation (eg, heavy alcohol consumption) are present. It has a wide histopathological spectrum ranging from simple, bland steatosis (NAFL), which is usually associated with a benign prognosis, to non alcoholic steatohepatitis (NASH), which is believed to possess the potential for progress to cirrhosis, and its inherent complications of liver failure and liver cancer.

Nonalcoholic fatty liver disease (NAFLD) is seen worldwide and is the most common liver disorder in Western industrialized countries .The prevalence of NAFLD in India is around 10–32% based on the data on people undergoing master health check-up and ultrasonography for non-liver related causes. Presuming an overall NAFLD prevalence rate of 20% translates to a staggering 244 million with fatty liver in India.

NAFLD is expected to be the leading indication for liver transplantation in a couple of decades. Fatty liver is characterized by steatosis in > 5 % of hepatocytes. NASH is characterized by steatosis complicated by liver cell injury with substantial lobular inflammation and fibrosis at times.

Association with other disorders : Patients with NAFLD (particularly those with NASH) often have one or more components of the metabolic syndrome like Obesity ,Systemic hypertension ,Dyslipidemia ,Insulin resistance or overt diabetes

Pathogenesis : The pathogenesis of nonalcoholic fatty liver disease has not been fully elucidated. The most widely supported theory implicates insulin resistance as the key mechanism leading to hepatic steatosis, and perhaps also to steatohepatitis. There is a transition from Two hit theory proposed earlier to Multiple Hit hypothesis. The first hit is hepatic triglyceride accumulation leading to steatosis. Subsequent hits include inflammatory cytokines/adipokines, mitochondrial dysfunction and oxidative stress, which in turn lead to steatohepatitis and/or fibrosis. Hepatic iron, leptin, antioxidant deficiencies, and intestinal bacteria have all been suggested as potential oxidative stressors.

Natural History :.Persons with simple steatosis usually have a benign non-progressive course while 10% to 15% with nonalcoholic steatohepatitis (NASH) can develop progressive hepatic

fibrosis and cirrhosis. Among patients with cryptogenic cirrhosis, up to 70 percent have risk factors for NAFLD.

Risk factors for progression — A number of risk factors for liver disease progression have been identified in patients with NAFLD. One of the most important risk factors is histologic evidence of hepatic inflammation. Other factors include Older age, Diabetes mellitus, Elevated serum aminotransferases, Presence of ballooning degeneration plus Mallory hyaline or fibrosis on biopsy ,BMI $\geq$28 kg/m^2 Higher visceral adiposity index.

Coffee consumption which has been associated with a lower risk of progression

Clinical Features : Most patients with NAFLD either are asymptomatic or have nonspecific symptoms, like fatigue and right upper-quadrant abdominal discomfort. On the contrary, at times, cirrhosis or its complications may be the initial presentation. Majority of the patients have normal physical examination.

Lab findings : Patients with NAFLD may have mild or moderate elevations in the aspartate aminotransferase (AST) and alanine aminotransferase (ALT) , although normal aminotransferase levels do not exclude NAFLD

Diagnosis : The diagnosis of NAFLD requires all of the following :demonstration of hepatic steatosis by imaging or biopsy, exclusion of significant alcohol consumption and exclusion of other causes of hepatic steatosis. Liver biopsy remains the gold standard for diagnosis.

Noninvasive investigations to detect **steatosis** include ultrasonography of abdomen which often reveals a hyperechoic texture or a bright liver because of diffuse fatty infiltration .MRI of abdomen with spectroscopy is helpful in quantification of fatty liver . Noninvasive tests to detect **liver fibrosis** include NAFLD fibrosis score based on six variables :age, BMI, hyperglycemia, platelet count, albumin, aminotransferases levels) and liver stiffness assessment with Transient Elastography,

Treatment : Life style modification plays a key role in NAFLD management. Pharmacological agents include insulin sensitising agents, antioxidants (Vitamin E). Vitamin E at daily dose of 800 IU/day orally has been found to improve liver histology in non-diabetic adults with biopsy-proven NASH. Obeticholic acid, a Farnesoid X Receptor agonist has shown promising results in non-alcoholic steatohepatitis patients.