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Short communication

Understanding Non Alcoholic Fatty Liver Disease: Causes, Symptoms and Treatment

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ABSTRACT:

The frequency of non alcoholic fatty liver disease (NAFLD), which affects both adults and children globally, is rising. It frequently co-occurs with symptoms of the metabolic syndrome and is linked to insulin resistance. With a 30% global prevalence, non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent liver illnesses. NAFLD, also known as non-alcoholic fatty liver disease, is characterized by an increase in liver fat without a known underlying cause, such as excessive alcohol consumption. The fatty deposits may harm the liver. It is anticipated that the prevalence of NAFLD will continue to rise as a result of the increased incidence of obesity in both the adult and paediatric populations. Around the world, it is a significant contributor to chronic liver disease, including cirrhosis and hepatocellular carcinoma (HCC). Due to the intricacy of its pathophysiology and the clinical circumstances surrounding its emergence, NAFLD has a wide range of clinical phenotypes and heterogeneity, which leads to a wide range of clinical prognoses. Although extra hepatic malignancies and cardiovascular disease are the main killers of NAFLD patients, severe liver fibrosis is a crucial prognostic indicator for liver-related outcomes and total mortality and can be detected using a combination of non-invasive testing. Oesophageal varices and hepatocellular cancer should both be screened in cirrhotic patients. NAFLD does not yet have an approved treatment, but several medications are in advanced stages of development. Weight loss and lifestyle changes continue to be essential components of NAFLD management. In this article, we defined NAFLD in general terms and categorized its subtypes in light of the state of this field's knowledge.

Keywords: NAFLD, liver, prevalence, disease

1. Introduction:

Schaffner used the phrase non-alcoholic fatty liver disease (NAFLD) for the first time in 1986[1]. NAFLD is presently the most quickly rising cause of liver-related death worldwide[2] because to its high prevalence, and it is also becoming more and more of a factor in end-stage liver disease[3], primary liver cancer[4], and liver transplantation, all of which have significant health economic costs. NAFLD is undervalued as a significant chronic disease[5], and there aren't many national initiatives or policies for it[6]. The most prevalent chronic liver disease in our clinical practice today is non-alcoholic fatty liver disease (NAFLD), which is a serious public health issue on a global scale[7-10]. Radiological or histological evidence that show fatty alterations in the liver are used to make the diagnosis of NAFLD. The gold standard for confirming fatty alterations is a biopsy, although it has drawbacks such as sample inaccuracy, interobserver variability, and invasiveness. To identify fatty alterations in the liver, non-invasive techniques including computed tomography (CT), ultrasonography (US), and MRI are utilized. Because of this, reports on the incidence and prevalence of NAFLD vary depending on the diagnostic method.

The annual incidence (diagnosis made using abdominal US) in the general population was approximately 48.2 cases/1,000 persons (range, 13.4–77.7)[11-13]. According to a meta-analysis, Korea had a yearly incidence rate of 45.1 cases per 1,000 people[14,15]. NAFLD prevalence ranged from 21 to 44%[16–18]. The prevalence rate of NAFLD was found as 12.6–51.0% in a meta-analysis done in Korea[19,20]. The most common cause of death in NAFLD is cardiovascular disease, which usually coexists with NAFLD and metabolic syndrome. Cardiovascular disease affects both the liver and the extra-liver[10]. The National Cholesterol Education Program (NCEP) Adult Treatment Panel (AT) defines metabolic syndrome as the presence

of three or more of the following five conditions: a waist circumference greater than 102 cm (40 inches) for men and 89 cm (35 inches) for women, a blood pressure greater than 130/85 mmHg, a fasting triglyceride (TG) level greater than 150 mg/dl, a fasting high-density lipoprotein (HDL)[21,22].

2. Pathogenesis:

Overeating, which results in adipose depot enlargement and ectopic fat deposition, is the main cause of NAFLD. In this situation, the visceral adipose tissue compartment is invaded by macrophages, which results in an inflammatory state that encourages insulin resistance. Inappropriate lipolysis in conditions of insulin resistance causes the liver's metabolic capacity to be exceeded by increased de-novo lipogenesis and unchecked transport of fatty acids. Lipotoxic lipids are produced as a result of the imbalance in lipid metabolism, which causes cellular stress (such as oxidative stress and endoplasmic reticulum stress), inflammasome activation, and apoptotic cell death. These events then stimulate inflammation, tissue regeneration, and fibrogenesis[23,24]. The evolution of liver fibrosis is thought to be aided by inflammatory and profibrogenic macrophages, which may also be involved in other tissues' chronic inflammatory processes[25]. NAFLD has a heritable component, and genetic variations among people can affect disease risk estimations by 20–70%[26]. The PNPLA3 gene single-nucleotide polymorphism is the genetic variation most closely linked to NAFLD susceptibility[27]. Many genetic risk variations have a synergistic interaction with obesity, and these genes or genetic risk variants may influence many features, often with different consequences on NAFLD and concomitant illnesses like coronary artery disease[28,29]. There is a possibility that the liver and other organs, particularly the stomach and adipose tissue, interact and communicate with one another in ways that cause metabolic dysregulation and inflammation in NAFLD[30-32].

3. Prevalence:

The prevalence of NAFLD was estimated between 17%-46% (on average about 25%) in western adults[33]. The prevalence in China, Japan, Korea, and the Middle East is essentially comparable to that in western nations[34]. NAFLD is prevalent in adults at 38.6% and children at 35.4%, according to a recent meta-analysis of research conducted in India[35]. According to a study from India, the prevalence of NAFLD is higher (16–32%) in urban populations than it is in rural communities (9%). 18.5% of the population in Bangladesh had NAFLD, according to an ultrasound-based study. In them, it was found in 36.93% of obese people and 7.1% of non-obese people[36]. Another study conducted in Bangladesh found that 33.86% of the population, or one third of the population, had NAFLD, with the prevalence being highest among people between the ages of 31 and 60 [37,38].

4. Risk factor for progressive disease:

A greater than two-fold increased risk of advanced fibrosis, cirrhosis-related comorbidities, and liver disease mortality is linked to type 2 diabetes. Although the impact sizes are smaller than for type 2 diabetes, obesity (defined as a body mass index >30 kg/m2), lipid abnormalities (defined as low concentrations of HDL cholesterol and high concentrations of triglycerides), and hypertension are similarly linked to an increased chance of developing serious liver disease[39]. Advanced fibrosis is more common in NAFLD patients older than 60 years old than in younger patients, reflecting a longer duration of metabolic dysfunction and liver disease[40]. Hepatocellular carcinoma development, liver-related mortality, and all-cause mortality are all linked to a variation of the PNPLA3 gene[41,42]. Other risk factors include Hypothyroidism, Hypopituitarism

Dyslipidemia, Hypogonadism, Metabolic syndrome (MetS), Obstructive sleep apnea (OSA), Polycystic ovarian syndrome (PCOS), Pancreatoduodenal resection, Psoriasietc[43].

5. Causes of fatty liver that are common:

Excessive alcohol intake, HCV infection, Macrovascularsteatosis, Starvation, Wilson’s disease, Intestinal bypass surgery, Microvascularsteatosis, Acute fatty liver of pregnancy, HELLP syndrome, Reye’s syndrome, Inborn errors of metabolism, Medication: Anti-retroviral drugs, Corticosteroids, Amiodarone, Methotrexate, Tamoxifen, Tetracycline, Vinyl chloride, Valproic acid etc[43,44].

6. Clinical properties:

The majority of NAFLD patients are asymptomatic, although some may experience minor right upper abdomen discomfort, weakness, hepatomegaly, acanthosis nigricans, or lipomatosis. Finding a bright liver on an ultrasound scan and receiving abnormal LFTs, such as elevated ALT and AST, are two common ways to diagnose NAFLD or NASH. Many patients have chronic liver conditions such cirrhosis and its consequences[44].

7. Prevention & management:

Primary care professionals have a critical role in the prevention, diagnosis, risk assessment, and management of NAFLD because primary care is the first point of contact for the majority of persons with health concerns (including metabolic risk factors). Even among those with high genetic risk, evidence show that improved diet quality and continued or increased physical activity reduce the chance of developing NAFLD. However, primary prevention of NAFLD has received little research[45-48]. The question of whether screening for NAFLD is worthwhile is pertinent given that there are

now a variety of non-invasive tests available to diagnosis fatty liver and liver fibrosis, especially when patients take part in secondary prevention programs for diabetes or metabolic syndrome. Hepatology associations' recommendations for screening patients for NAFLD vary; some encourage screening in high-risk groups (such as those with obesity, type 2 diabetes, or metabolic syndrome), while others do not. This discrepancy may be due in part to the lack of effective therapeutic interventions[49,50]. To determine whether screening might improve clinical results and whether it is cost-effective, more research is required. However, if NAFLD has been identified, we advise risk stratification by checking for advanced fibrosis or cirrhosis, measuring cardiovascular risk, and examining coexisting conditions. For patients with NAFLD, certain regional specialized networks and local health districts are looking into integrated management strategies and referral channels[51-54]. Weight loss improves NAFLD and all of its cardiometabolic comorbidities, which then favourably influences risk factors for cardiovascular disease and cancer. Although NASH makes a separate contribution to the risk of cancer and cardiovascular disease, we do not yet know whether liver-specific therapeutic strategies will lower these risks. Regardless of weight loss, exercise has a significant positive impact on NAFLD, NASH, and the cardiovascular system. Regular moderate-intensity aerobic activity, such as brisk walking, jogging, running, swimming, or cycling, can reduce insulin resistance and NAFLD (approximately 150–200 minutes per week).

8. Medicinal treatment:

There are currently no approved pharmaceuticals for the treatment of NAFLD and its various variants. However, other medications, including a few lipid-lowering medications, antihypertensive medicines, and other compounds like obeticholic acid, have been studied over the past few decades. Some important drugs with their dosage amount[8,9]

i. Pioglitazone (30-45 mg/d)

ii. Semaglutide (0.4mg subcutaneous/d)

iii. Liraglutide (1.8 mg subcutaneous /d)

iv. Vitamin E (800 IU/d)

v. Thiazolidinediones

vi. Saroglitazar (4 mg/d)

vii. Vitamin E (800 IU/d)

9. Summary:

There are several different types of patients that have NAFLD. Although metabolic syndrome is frequently the main contributing factor, a complex and dynamic heterogeneous interaction of several variables is also present. NAFLD is a liver condition that calls for interdisciplinary treatment. On first assessment, potential causes and risk factors for liver disease should be checked. Currently, weight loss along with lifestyle changes is the only effective therapy for NAFLD. Despite several improvements in medical research, there is no medication that has been authorised to treat the condition.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest regarding this paper.

Availability of data and materials

The data and materials used to support the findings of this study are publicly available.

Author contribution

All author contributed significantly to design and development of this work.

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