EDITORIAL

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Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH): Diagnosis and Management

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Nonalcoholic fatty liver disease (NAFLD) is a condition characterized by excessive accumulation of lipid (defined as the presence of lipid in >5% of hepatocytes or a lipid content >5% liver weight) in the liver in individuals, who consume little (<20 g of alcohol/d) or no alcohol. When NAFLD is accom-panied with liver cell injury and inflammation it is called nonalcoholic steatohepatitis (NASH). About 30% NAFLD progress to NASH, if untreated, it can lead to fibrosis, cirrhosis or even hepatocellular carcinoma (HCC).

NAFLD is becoming now the most common cause of chronic liver disease worldwide, closely mirroring the epidemiology of type 2 diabetes, obesity and physical inactivity. In the years to come the prevalence of NASH will increase by/to 15%-56%; by 2030 the incidence of decompensated cirrhosis due to NASH will increase by 168%, the incidence of HCC will increase by 137% and the incidence of liver related death by 178%.[1]

At present, NAFLD is the most common cause of hepatic dysfunction in developed countries and predicted to be the same for the developing countries by next few decades.[2,3] Estimates obtained from various clinical records and medical studies suggested that the prevalence of NAFLD is 20% to 30% in western countries.[2,4] The prevalence in the Middle East, Japan and China is almost same as the western world with a prevalence rate of 15-30%. In the Asian countries, the prevalence of NAFLD varies in different regions. However, in Indian subcontinent prevalence of NAFLD is recorded as 16-32% in urban population and approximately 9% in rural areas.[2,5]

Bangladesh is also experiencing an increasing trend of liver disease deaths due to changing in the dietary patterns and sedentary lifestyles.[6,8] World Health Organization (WHO) has been documented in May 2014 that 2.82% of total deaths in Bangladesh are due to liver diseases. It is the 8th most common cause of death in Bangladesh and the age-adjusted death rate is 19.26 per 100,000 population.[6,9] Chronic liver diseases (CLDs) are responsible for 37-69% of liver diseases in Bangladesh and NAFLD is a significant contributor to the burden of CLDs.[9]

The disease is silent in early stages and the clinical picture is very heterogeneous at presentation steatosis at ultrasound and altered LFTs or metabolic risk factors, isolated hyperferritinemia and sometimes cirrhosis of unknown origin.

Screening for NAFLD in general population is not recommended. Simple blood test of first generation (FIB4, NFS fibrosis score) should be applied in primary care settings[10] with a good

negative predictive value. However, confounding factors (age, type 2 diabetes) should be taken into account when interpreting the results. Second generation blood tests alone, or combined with Fibroscan are recommended in secondary care and significantly decreases the number of indeterminate cases. However, liver biopsy is still the gold standard for the diagnosis of NASH.[11]

Because of the evolving landscape in the field with a lot of therapeutic agents being now in the development, it is an unmet need to develop reliable biomarkers for NAFLD. Firstly, an ideal biomarker should be able to distinguish between steatosis and NASH and to assess the severity of fibrosis. This is particularly important since the long-term outcomes and prognosis is strongly correlated with the severity of histological lesions. Secondly, because the bidirectional evolution of histological lesions in NAFLD, an ideal biomarker should also be able to monitor the disease progression or regression and to identify patient's eligibility for therapy. Finally, an ideal biomarker should have prognostic value.

The management of patients with NAFLD should not be limited to the liver, but must pay special attention to associated co-morbidities. Patients with NAFLD should be screened for cardiometabolic complications, particularly cardiovascular disease,[12,13] type 2 diabetes[14,15] and renal function impairmen.[16] Regular screening for HCC is recommended in cirrhotic patients; despite half of NAFLD-related HCC cases developed in the absence of cirrhosis[17] and no screening recommendation can be made in these patients.

As there are no specific therapeutic agents for NASH approved at the date, lifestyle management is crucial. A weight loss of 7–10% with diet can reverse NASH and fibrosis but it is difficult to obtain and maintain. Bariatric surgery can be an option in selected patients[18] but the effect of bariatric surgery in patients with advanced (F3) fibrosis or cirrhosis has to be further determined.

Physical activity is now routinely prescribed in patients with NAFLD but the optimal dose and type of physical activity has to be determined. Although evidence of efficacy is limited, Vitamin E is the most commonly used medication in clinical practice.[19] Some drugs with proven histological efficacy in NAFLD are only available off label.[20] New emerging therapies are now in development. Some of them completed phase IIb trials with promising results and are entering now phase III clinical trials.[21]

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