Editorial

Non Alcoholic Fatty Liver Disease (NAFLD)

An Emerging Public Health Challenge

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Non-Alcoholic Fatty Liver Disease (NAFLD) is emerging as a group of clinical conditions which begins with an asymptomatic mild fatty infiltration of the liver as Non Alcoholic Fatty Liver (NAFL) and later to Non-Alcoholic Steatohepatitis (NASH). This further degenerates to fibrosis (cirrhosis) and may culminate into hepatocellular carcinoma.[1] NAFLD is often diagnosed by exclusion of causes like excessive alcohol consumption (30 grams per day for men and more than 20 grams per day for women), viral hepatitis, hepatotoxic agents autoimmune hepatitis etc.[2] Alcoholic fatty liver disease has been reviewed in a previous issue of the Indian Practitioner (2013; March 66:163-167). It is important to realise that NAFL is relatively a benign condition whereas NASH can be progressive and have dire consequences.

There has been a steady increase in the prevalence of NAFLD globally as well as in India. In US, it is as high as 31%.[3] The association of NAFLD with obesity, diabetes and metabolic syndrome is well cognised. NAFLD, being considered as a high risk factor for cardio vascular diseases, needs early identification and management.[2] Prevalence of NAFLD is rising in adults and children throughout our country. This was evident in a focussed update where experts from all the zones of India participated.[4] In an epidemiological study from the South India, the prevalence of NAFLD was higher among patients with diabetes (54.5%) as compared to those who had only impaired glucose tolerance (32.4%), impaired fasting glucose (27.3%) or normal glucose tolerance (22.5%).[5] On the other hand, in a population-based study conducted in the Western India, it was observed that the prevalence of NAFLD was more in men than in women (24.6 % vs 13.6%, $p < 0.001$).[6] In the North India, the prevalence of NAFLD in children was found to be 7.4%.[7]

The aetiopathogenesis of NAFLD has often been linked to over-nutrition, obesity/adiposity and insulin resistance (IR). IR has also a causal relationship with NAFLD despite absence of obesity/ type2 diabetes where the resistance is primarily due to central/ visceral adiposity. Proinflammatory cytokines and oxidative stress constitute the underlying pathophysiological mechanisms for IR and the related conditions of metabolic syndrome, polycystic ovarian disease (PCOD) including NAFLD.[8-9] Gut-derived endotoxin and microbial DNA are implicated as hepatotoxic agents in animal models. In a recent article, the extrapolation of the animal data to humans has been proposed as to gut-liver axis in Journal of Parenteral and Enteral Nutrition 2013 March.

It needs to be emphasised that, imbalanced eucaloric diets or diets deficient in specific macro or micronutrients have not been adequately considered. Increased intake of fructose in diet, irrespective of the caloric intake, has been implicated in causing de-novo hepatic lipogenesis.[10] Soft drinks and packed fruit juices, loaded with fructose, are hugely responsible for today's ill of obesity-driven diseases including NAFLD.[10] Large intake of fatty acids (trans/saturated) and diets with a high ratio of omega-6 to omega-3 fatty acid, are also less emphasised as risk factors for NAFLD.[9] Omega-3 fatty acid has a beneficial role in modulating the processing of lipids by acting as ligands of peroxisome proliferator-activator receptor α (PPARα) and reducing hepatic inflammation.[11] Deficiency of micronutrients such as betaine, choline and protein-energy malnutrition are identified as specific risk factors for NAFLD.[12] The mechanistic understanding for the aetiopathogenesis of NAFLD and its reversal have been understood through several animal models such as those of over-nutrition (high

fructose/ fat diet, hyperphagic diet), under nutrition or specific model of nutritional depletion (methionine-choline deficiency model).[13,14]

It should be recognised that India is facing a double whammy of over nutrition and under nutrition. The latter in some of the situations can extend close to starvation. Starvation-induced autophagy in human liver was identified as a cause for liver cell death.[15] It is thus important to thoroughly evaluate patients with NAFLD for these nutritional factors and appropriately correct those besides providing interventional life-style modification meant for weight loss or prescribe insulin sensitisers like metformin or any of the hepato-protective medicinal plant-based formulations.[14,16,17]

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