Preamble: 4. the experience of the authors

Preamble: This guidance describes a wide spectrum of approaches toidentify the adults, young people and children with non-alcoholic fatty liverdisease (NAFLD) who have advanced liver fibrosis and are most at risk offurther complications.

It outlines the lifestyle changes and pharmacologicaltreatments that can manage NAFLD and advanced liver fibrosis. This guidance isdeveloped by a panel of expert hepatologist with data supported system. Guidance document is little different from guideline as guidelines are developedby a multidisciplinary panel of experts and rate the quality of the evidenceand the strength of each recommendation using the grading of recommendations, assessment development, and evaluation system.

Guidancestatements are not recommendations, but help clinicians to understand andimplement the most recent evidence. This is the first practice guidance on Nonalcoholic fatty liverdisease commissioned by Fatty liver study group of Hepatology society, Bangladesh based on the following:
1. Review and analysis of therecently published world literature on the topic2. Research data on the topicof south Asian region. 3. Guideline policies ofAASLD4. The experience of theauthors and independent reviewers with regard to NAFLD.

This practice guidance is developed for use by physicians andother health professionals. The data have been retrieved by an extensive PubMedsearch up to December 2017. Specific guidance statements are evidence basedwhenever possible, and, when such evidence is not available or is inconsistent, guidance statements are made based on the consensus opinion

of the authors. Definitions: Non-alcoholicfatty liver disease has been defined as the accumulation of fat in the liver inthe absence of recent or ongoing intake of significant amount of alcohol.

Two criteria must be fulfilled for defining NAFLD(1) evidence of hepatic steatosis (HS), either by imaging orhistology, and (2)lack of secondary causes of hepatic fat accumulation such as significantalcohol consumption, NAFLD can be categorized histologically into nonalcoholic fattyliver (NAFL) or nonalcoholic Steatohepatitis. NAFL is defined as the presence of ? 5% HSwithout evidence of hepatocellular injury in the form of hepatocyte ballooning. NASH is defined as the presence of ? 5%HS and inflammation with hepatocyte injury (e. g., ballooning), withor without any fibrosis. Encompasses the entirespectrum of FLD in individuals without significant alcohol consumption, rangingfrom fatty liver to SH to cirrhosis.

Presence of ? 5% HS withoutevidence of hepatocellular injury in the form of ballooning of the hepatocytesor evidence of fibrosis. The risk of progression to cirrhosis and liver failureis considered minimal. Presence of ? 5% HS withinflammation and hepatocyte injury (ballooning) with or without fibrosis. Thiscan progress to cirrhosis, liver failure, and rarely liver cancer. Presence of cirrhosis withcurrent or previous histological evidence of steatosis or SH.

Till date, liver biopsyremains the gold standard for diagnosing NASH. Though, liver biopsy is notfeasible in studies of the general population, there is no direct assessment ofthe incidence or prevalence of NASH. But, there have been some attempts toestimate the prevalence of NASH by indirect means. There is a bidirectional association between NAFLD andcomponents

of Mets. Features of metabolic syndrome (MetS) are highly prevalentin patients with NAFLD, and also increase the risk of developing NAFLD. Table 3showing some established and emerging conditions that are associated withNAFLD. Worldwide, obesity remains the most important and well-described risk factor for NAFLD.

The results of several cross-sectional studies and case-control studies haveshown that people with NAFLD have higher waist circumference (WC) or BMI thanthose without NAFLD, and have reported significant associations betweenabdominal obesity (OR = 1. 10-1. 13; 95% CI, 1. 02-1. 22 per 1-cm increase in WC)and NAFLD.

(108) In the Dionysos study, NAFLD was present in 94%, 67%, and 24. 5%of the obese, overweight, and normal weight populations, respectively. 109 Although the mechanisms responsible forthe increased risk of NAFLD with abdominal obesity have not been fullyelucidated, current findings suggest that obesity leads to insulin resistance, which, in turns, leads to NAFLD. 110At the other end of the distribution, data on the prevalence of NAFLDamong high-risk individuals with severe obesity have become widely published. On average, these studies reported that 76% (range 33 to 99%) of the patientsundergoing bariatric surgery have steatosis, 37% (range 9.

8 to 72. 5%) haveNASH, 23% (range 7. 3 to 49%) fibrosis, and 5.

8% (range 1. 6 to 10%) cirrhosis. Severalstudies have described a higher prevalence of NAFLD among people with type 2diabetes compared with nondiabetics, with prevalence estimates ranging from 40%to 69. 5%. 61, 86, 87 Moreover, a recentcase-control study using proton-MRS demonstrated

that people with type 2diabetes have on average 80% more liver fat than age-, weight-, and sex-matchedcontrols. This difference was not explained by the type of medications used. Furthermore, aspartate aminotransferase (AST) and alanine aminotransferase(ALT)underestimated liver fat content among people with diabetes; for any given ALTor AST level, adults with type 2 diabetes had 40 to 200% more liver fat thannondiabetic adults.

88Patients with type 2 diabetes not only have a higher prevalence of NAFLD, butalso appear to have more severe forms of the disease, including NASH andfibrosis. Dyslipidemia: Dyslipidemia that is characterized by hightriglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) levels predisposespatients to arthrosclerosis. 16Approximately 20–80% of NAFLD patients also have dyslipidemia. 17 The prevalence ofNAFLD in individuals with dyslipidemia attending lipid clinics has beenestimated to be 50%.(29, 30) A very common change in the metabolic profileamong patients with T2DM, MS, and obesity is an alteration of serum lipidlevels (dyslipidemia), suggesting a close relationship between T2DM, MS, andobesity and NAFLD.

It has been shown that NASH significantly boosts the levelof oxidized low-density lipoprotein cholesterol (LDL-C). High LDL-C is awell-established risk factor for arthrosclerosis. 18 Themost common form of dyslipidemia in NAFLD patients is atherogenic dyslipidemia, which is characterized by hypertriglyceridemia, low HDL-C levels, and high LDL-Clevels. Age, sex, and ethnicity: NAFLD is seen in allage groups, prevalence peaks in the fourth decade in men and sixth decade inwomen (Ruhl & Everhart 2003). The

prevalence of NAFLD in India above 20years age was 18. 9% (Amarapurkar et al. 2007).

The prevalence of NAFLD increasedwith increasing age. More recent studies are showing that the prevalence ofNAFLD in men is equal to or greater than the prevalence in women (Amarapurkaret al. 2007).

But these findings are not consistent with our population. Recently in a large cohort, it revealed that NAFLD is more prevalent in femaleamong Bangladeshi population and prevalence of NASH was 42. 4% in NAFLD which ismuch higher. (Alam et al. 2013). In fact, both theprevalence of NAFLD and stage of liver disease appear to increase with age.

· Despite using different diagnostictools, US population-based studies all found that Hispanics have the highestand non-Hispanic blacks have the lowest prevalence of NAFLD. Echoing theracial/ethnic differences in the NAFLD prevalence, Younossi et al17recently reported that NASH was independently associated with being Hispanicodds ratio (OR), 1. 72; 95%CI: 1.

28-2. 33 and inversely associated with beingAfrican-American (OR, 0. 52; 95%CI: 0. 34-0. 78). Furthermore, in a study usingproton-MRS Peterson et al found that even after adjusting for BMI and age, Asian Indian men have significantly higher HT compared with their Caucasiancounterparts (1.

54 vs. 0. 77%). 103It is intriguing that most of the recent data suggest that theethnic differences reported for NAFLD may be explained by the genetic variationrelated to the patatin-like phospholipase domain-containing protein

3 (PNPLA-3)gene.(40) In summary, the incidence of NAFLD varies across the world, rangingfrom 28. 01 per 1, 000 person-years (95% CI, 19. 34-40. 57) to 52. 34 per 1, 000person years (95% CI, 28. 31-96. 77).