

NASPGHAN CLINICAL GUIDELINES

1. Selected children should be screened for NAFLD

a. Screening should be considered beginning between ages 9 and 11 years for all obese children (BMI = 95th percentile) and for overweight children (BMI 85th and <94th percentile) with additional risk factors (central adiposity, insulin resistance, prediabetes or diabetes, dyslipidemia, sleep apnea or family history of NAFLD/NASH).

b. Earlier screening can be considered in younger patients with risk factors such as severe obesity, family history of NAFLD/NASH, or hypopituitarism.

c. Consider screening of siblings and parents of children with NAFLD if they have known risk factors for NAFLD (obesity, Hispanic ethnicity, insulin resistance, prediabetes, diabetes, dyslipidemia).

2. Currently, the best screening test for NAFLD in children is ALT; however, it has substantial limitations.

a. Interpretation of ALT should be based upon sex-specific upper limits of normal in children (22 U/L for girls and 26 U/L for boys) and not individual laboratory upper limits of normal.

b. Persistently (>3 months) elevated ALT more than twice the upper limit of normal should be evaluated for NAFLD or other causes of chronic hepatitis.

c. ALT of >80 U/L warrants increased clinical concern and timely evaluation, as the likelihood of significant liver disease is higher.

d. Clinically available routine ultrasound is not recommended as a screening test for NAFLD in children due to inadequate sensitivity and specificity.

3. Follow-up screening for NAFLD is recommended.

a. When the initial screening test is normal, consider repeating ALT every 2 to 3 years if risk factors remain unchanged.

b. Consider repeating screening sooner if clinical risk factors of NAFLD increase in number or severity. Examples include excessive weight gain or development of other medical problems that increase risk of NAFLD, such as type 2 diabetes or obstructive sleep apnea.

4. When evaluating a child suspected to have NAFLD, it is recommended to exclude alternative etiologies for elevated ALT and/or hepatic steatosis and investigate the presence of coexisting chronic liver diseases.

5. Liver biopsy should be considered for the assessment of NAFLD in children who have increased risk of NASH and/or advanced fibrosis. Potential clinical signs of increased risk of fibrosis in children with NASH may include higher ALT (>80 U/L), splenomegaly, and AST/ALT >1. Known clinical risk factors for NASH and advanced fibrosis include panhypopituitarism and type 2 diabetes.

6. The use of ultrasound is not recommended for the determination or quantification of steatosis due to poor sensitivity and specificity. Ultrasound may be useful for assessing other causes of liver disease such as masses, gallbladder disease, changes associated with portal hypertension, and so on.

7. The use of CT is not recommended for determination or quantification of steatosis due to radiation risk.

8. Pending the development of more accurate biomarkers to noninvasively assess improvement in NAFLD, sustained decrease in ALT from baseline may be used as a surrogate marker of response to treatment, particularly for durations of 1 year.
9. Assessment of change in fibrosis over time is reasonable as a treatment outcome in children over longer time periods (2 years) and currently requires a liver biopsy for assessment.
10. Lifestyle modifications to improve diet and increase physical activity are recommended as the first-line treatment for all children with NAFLD.
11. Avoidance of sugar-sweetened beverages is recommended as a strategy to decrease adiposity.
12. Increasing moderate- to high-intensity physical activity and limiting screen time activities to <2 hours per day is recommended for all children including those with NAFLD.
13. No currently available medications or supplements are recommended to treat NAFLD because none have been proven to benefit the majority of patients with NAFLD.
14. Bariatric surgery is not recommended as a specific therapy for NAFLD given lack of outcome data in adolescents. Bariatric surgery may be considered for selected adolescents with BMI ≥ 35 kg/m², who have noncirrhotic NAFLD and other serious comorbidities (eg, T2DM, severe sleep apnea, idiopathic intracranial hypertension) that are likely to improve with WLS.
15. Children with NAFLD should be screened for dyslipidemia at diagnosis and periodically as indicated by current lipid guidelines for children.
16. It is recommended to monitor blood pressure in children with NAFLD.
17. It is recommended to screen children with NAFLD for diabetes at diagnosis and annually (or sooner if clinical suspicion arises) using either a fasting serum glucose level or an HbA1c level. A glucose tolerance test may be useful if the fasting glucose or HbA1c are in the prediabetic range (Table 3).
18. It is recommended to follow children with NAFLD on a yearly basis at a minimum to monitor for progression of disease and provide treatment.
19. When providing lifestyle counseling, more frequent visits (more contact hours with program staff) are associated with better weight management outcomes in overweight and obese children and therefore may also benefit overweight children with NAFLD/NASH.
20. A repeat liver biopsy to assess progression of disease (particularly fibrosis) and to guide treatment is reasonable to consider 2 to 3 years after the first liver biopsy, especially in patients with new or ongoing risk factors, such as type 2 diabetes mellitus, NASH, or fibrosis at diagnosis.

21. In addition to standard counseling of adolescents, healthcare providers should counsel adolescents regarding the potential effects of increased fibrosis progression with binge drinking.
22. Families of children with NAFLD should be counseled about risks of secondhand smoke exposure and adolescents with NAFLD should be counseled against smoking and use of electronic nicotine delivery devices.
23. Children with NAFLD should be vaccinated routinely against hepatitis A.
24. Children with NAFLD should have prior receipt of hepatitis B vaccine verified and be immunized if no prior vaccination was received.
25. Baseline liver enzyme levels should be obtained in children with NAFLD before starting any medication known to be hepatotoxic. There is insufficient evidence to guide frequency of monitoring for enzyme elevation after initiation of potentially hepatotoxic medications and monitoring should be guided by the baseline severity of the liver disease and the relative potential for hepatotoxicity of the medication.
26. If potentially hepatotoxic drugs are being considered in patients with NAFLD, a baseline liver biopsy may be reasonable to consider for assessing the severity of liver disease before beginning the medication.
27. Providers should remain alert to psychosocial issues and screen children with NAFLD for these when indicated.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; CT = computed tomography; HbA1c = glycosylated hemoglobin; NAFLD= nonalcoholic fatty liver disease; NASH=nonalcoholic steatohepatitis; T2DM = type 2 diabetes mellitus;WLS = weight loss surgery.

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