Nonalcoholic fatty liver disease (NAFLD)

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- A two- to three-fold rise in the rates of obesity and overweight in children over the last 2 decades is probably responsible for the epidemic of NAFLD.
- Emerging data suggest that children with NASH progress to cirrhosis which may ultimately increase liver-related mortality.
- NAFLD is more common in boys than girls . These sex differences implicate estrogens as potentially protective, or indicate that androgens may aggravate NASH
- Fetuin, a protein secreted by liver, is increasingly thought to be an important mediator of hepatic insulin resistance.
- fetuin-A could be a potential biomarker for diagnosis and treatment response in NAFLD.
- Increasing concentration of serum AST, GGT and higher titers of anti-smooth muscle antibody (ASMA) were independent predictors of severity of NASH, and increasing concentration of serum AST, higher white blood cell count and lower hemoglobin concentrations were independent predictors of advanced fibrosis.
- Hepatic steatosis may have more of an adverse health impact on cardiovascular outcomes than on liver disease itself
- Two types of NASH have been described, 1 associated with adults and the other with pediatrics.[4]
- Type 1 (adult) NASH is characterized by steatosis, hepatocyte ballooning, Mallory hyaline, and pericellular/sinusoidal fibrosis, most with distinct centrilobular distribution.
- Type 2 (pediatric) NASH is characterized by portal-based fibrosis sometimes associated with portal inflammation and without centrilobular distribution, and more strongly linked to Hispanic and Asian backgrounds and male sex
- Studies have shown that 32% to 83% of children have features of both types.
- The presence of steatosis in more than 5% of hepatocytes is the minimum criterion for the diagnosis of NAFLD. Tissue distribution of steatosis in paediatric NAFLD is distinctive, because it initially involves a periportal zone (acinar zone 1) or displays an azonal distribution
- Diet and exercise: Studies in adults with NAFLD suggest that weight loss leads to significant improvement in serum ALT and liver histology.
- a mean weight loss of approximately 5 kg resulted in improvement in serum ALT and AST in most children with NAFLD.

- No information exists on recommending any type of diet. A low-carbohydrate diet has been shown to lead to reduction in serum ALT and hepatic steatosis.
- Unhealthy diet and sedentary lifestyle, such as excessive television watching coupled with extremely reduced physical activity, are the major causes of energy imbalance between intake and consumption of calories that lead to obesity and related diseases, such as metabolic syndrome and NAFLD.
- Particularly, low-cost diets including those enriched in fat, sugar and salt, and energy-dense and micronutrient-poor foods increase the risk of obesity, metabolic syndrome and NAFLD in children and adolescents of industrialized countries
- In summary, diet enriched in fat and fructose may act by favouring the occurrence of metabolic and cellular/molecular alterations that account for NAFLD pathogenesis.
- On the basis of the main factors involved in NAFLD pathogenesis, to date, three types of targeting pharmacological interventions have been tested in paediatric individuals:
- insulin sensitizers(metformin),
- antioxidant agents(vitamin E)
- cytoprotective agents(URSOBIL).
- Vitamin E is an anti-oxidant potentially effective in reducing oxidative stress. As oxidative stress is considered a key component in NASH pathogenesis, vitamin E is under investigation as a treatment for pediatric NASH.
- An open label study of vitamin E (400 to 1200 units per day orally) given for 2-4 months led to improvement in serum ALT in obese children.
- Metformin is the only insulin-sensitizing agent evaluated for the treatment of NAFLD in children.
- Studies in adults with NASH suggest that metformin improves NASH by inducing weight loss.
- A pilot study of metformin in pediatric NASH demonstrated that metformin (500 mg twice daily) treatment over six months resulted in improvement in serum ALT and reduction in hepatic steatosis
- Well-designed studies in pediatric NASH are necessary before considering pioglitazone in clinical practice.
- Ursobil : It may have a cytoprotective effect by possibly reducing bile-salt mediated mitochondrial injury within hepatocytes. However, it failed to show any benefit in RCT in adults with NASH and children with NAFLD.