PAEDIATRIC NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) MANAGEMENT

BACKGROUND:

Nonalcoholic fatty liver disease (NAFLD) is rapidly becoming the most common cause of chronic liver disease in children living in developed nations.
It is defined as macrovesicular steatosis in more than 5% of hepatocytes in the absence of other etiologies or disorders that may lead to fat deposition in the liver. NAFLD exists within a spectrum of liver pathology that ranges from isolated steatosis to steatosis with inflammation and cellular injury (nonalcoholic steatohepatitis, NASH) and cirrhosis.

NAFLD has become a major public health concern due to its striking increase in prevalence in childhood which is closely related to increase in obesity rates in the paediatric population, and its association with future development of liver dysfunction, diabetes, cardiovascular disease and cancer.

Paediatric NAFLD is suspected mainly by analysis of anthropometrical and biochemical parameters and/or ultrasound liver brightness.

PATIENTS TO BE INVESTIGATED:

One should suspect NAFLD in any child with elevated aminotransferases +/- presence fatty changes on ultrasound:

1. with obesity, and/or
2. with a history of interventions e.g. chemotherapy, cranial surgery and bone marrow transplantation, or
3. with an other underlying metabolic disease, e.g. Diabetes, Turner, Alstrom, Bardet-Biedl or polycystic ovary syndrome

Be aware that:

- you cannot rely on standard liver function tests alone to rule out NAFLD (i.e. normal LFTs does not rule out NAFLD),
- a normal USS does not rule out NAFLD as fatty changes can only be seen once there is fat accumulation in >30% of hepatocytes,
- in the presence of abnormal LFTs other liver diseases/diagnoses must be ruled out,
- Steatosis in a child $\leq$ 3yrs is unlikely to be due to NAFLD alone and an underlying metabolic/endocrine cause should be suspected and ruled out,
- NAFLD is a risk factor for presence or potential development of Type II Diabetes, hypertension and Chronic kidney disease and metabolic syndrome.

CLINICAL ASSESSMENT AT EACH VISIT:

❑ HEIGHT (cm)	clinic nurse
❑ WEIGHT (kg)	clinic nurse
❑ Calculate Body Mass Index (BMI, kg/m^2)	doctor/nurse
❑ Blood Pressure (using appropriate cuff size)	clinic nurse
❑ Waist circumference (cm)	doctor/nurse
❑ Clinical examination, incl:	doctor
○ Acanthosis nigricans	
○ Striae	
○ Palmar erythema/spider naevi	
❑ Liver fibrosis/stiffness by Fibroscan	doctor

ROUTINE BLOOD & URINE INVESTIGATIONS AT EACH VISIT:

- frequency at discretion of clinician

❑ FBC & Coagulation screen
❑ Full biochemical profile
❑ Uric Acid level
❑ Fasting bloods:
  ○ Glucose[1] and HbA1c[2]
  ○ Cholesterol, Triglycerides
❑ Non-invasive markers of Hepatic Fibrosis (ELF test)

❑ Urine tests:
  ○ Routine urine dipstick analysis (look out for proteinuria)

[1]Fasting Glucose >5.6mmol/L	*= suggestive of impaired fasting glycaemia* *= consider Oral Glucose Tolerance Test (OGTT)*
[2]HbA1c >6.5% (standardized to the DCCT assay)	*= suggestive of diabetes* *= a value <6.5% does not exclude diabetes, just Makes it less likely*

See also Appendix B: screening for impaired fasting glycaemia and impaired glucose tolerance

DIAGNOSTIC BLOOD & URINE INVESTIGATIONS AT FIRST* VISIT ONLY:

* tests for exclusion of other main causes of hepatic steatosis

- ❑ Auto antibody , immunoglobulin and complement screens (including anti tissue transglutaminase IgA, i.e. anti-TTG)
- ❑ Copper, caeruloplasmin
- ❑ Alpha-1-Antitrypsin level (Phenotype if low A1AT level)
- ❑ Thyroid Function test
- ❑ Creatinine Kinase (CK)
- ❑ amino and organic acids
- ❑ Ferritin
- ❑ Lysosomal Acid Lipase (to look for LAL-D = Lysosomal Lipase Deficiency)
- ❑ Fasting bloods:
    - Full lipid profile (incl cholesterol, triglycerides, HDL and LDL)
    - Plasma free fatty acids
    - 3-hydroxybutyrate
    - acyl carnitine profile
- ❑ Viral Hepatitis Screen (incl HCV)

- ❑ Urine tests:
    - amino and organic acid screen

OTHER INVESTIGATIONS:

- ❑ Ultrasound scan of abdomen (and ovaries if female)
    - At first visit (unless stated otherwise by consultant)
    - Every 2 years thereafter or sooner if clinically indicated

- ❑ Second line investigations (**clinical indication only**)
    - Cortisol (e.g. if clinically has Cushingoid features)
    - steroid metabolites (as per ESPGHAN consensus statement 2012) – if clinical concern d/w endocrine team first
    - Lactate (fasting lactate to be checked in children ≤ 3yrs where NAFLD is a less likely cause of steatosis)

    - 24-hour urinary copper analysis (an acid washed urine collection bottle can be obtained for clinical chemistry reception desk) – should only be considered if Wilson's Disease suspected

INDICATION FOR LIVER BIOPSY:

NB: Is the only single test that can reliably distinguish between simple steatosis (NAFLD) and NASH

- ❑ In any patient with suspected NAFLD/NASH but who has signs/evidence of chronic liver disease, e.g. splenomegaly, abnormal diagnostic investigations (e.g. positive autoantibodies), strong family history, etc

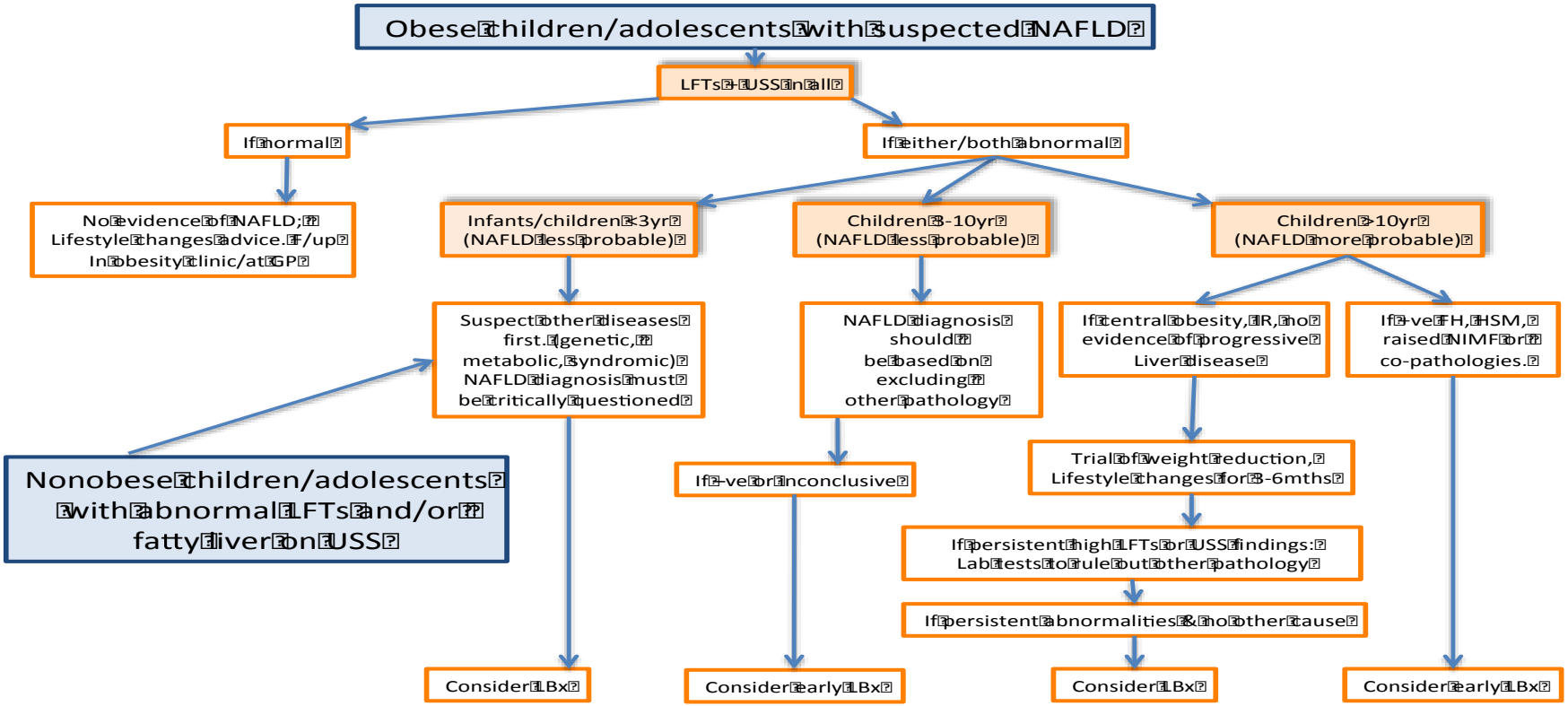
- ❑ To reach a diagnosis in patients with persistently abnormal LFTs (e.g. more than twice the upper limit of normal one 2 occasions at least 6 months apart) in the absence of evidence of chronic liver disease or other risk factors

Guidelines apply to : All Liver Unit patients

Guidelines developed : 2004 (Dr Helen Evans)
Guidelines updated : 2006 (Dr Ulrich Baumann), 2009 & 2011 (Dr Indra van Mourik)
Current Update : 2015 (Dr Indra van Mourik)
Review Year : 2018

APPENDIX A: Overall Management Algorithm for Children with suspected NAFLD/NASH

(extracted from ESPGHAN consensus statement 2012)



APPENDIX B: Algorithm for monitoring for impaired fasting glycaemia and impaired glucose tolerance test (as per Prof T Barrett's advice)