Investigation of Gilberts Syndrome

INTRODUCTION

Gilbert's syndrome is a common (occurring in 5-8% of population) and benign condition characterized by recurrent episodes of mild jaundice, the total bilirubin concentration typically not exceeding 65-85 µmol/L. In Gilbert's syndrome other tests of liver function and liver histology are normal. It is important to recognise this syndrome because the hyperbilirubinaemia may be mistaken as a sign of liver disease. Individuals with Gilbert's should be reassured as this syndrome is not associated with liver disease.

Jaundice in Gilbert's syndrome is often triggered by periods of inter-current illness, caloric deprivation, or other physiological stress such as heavy physical exertion, lack of sleep or dehydration. The mechanism of jaundice is due to reduced activity of the enzyme UDP-glucuronyl transferase which leads to impaired conjugation and excretion of bilirubin.

If a patient has suspected Gilbert's syndrome they should be assessed for symptoms suggestive of underlying liver disease (abdominal pain, itch, pale stool, dark urine) as well as checking for signs of inter-current illness or other possible trigger.

LABORATORY INVESTIGATION

Patients suspected Gilbert's syndrome should have the following laboratory investigations:

- Liver function tests (LFTs) with conjugated bilirubin
- Full blood count (with haptoglobin and LDH if patient is known to be anaemic)
- Reticulocyte count

A diagnosis of Gilbert's can be made in patients with:

- Confirmed unconjugated hyperbilirubinaemia (conjugated bilirubin within the normal range and/or <20% total bilirubin)
- Otherwise normal LFTs
- No evidence of haemolysis (e.g. low haemoglobin and haptoglobin, increased reticulocyte count, increased LDH)
- No other evidence of liver disease

All LFTs ordered by GP's and outpatients departments are examined for isolated hyperbilirubinaemia and if not already requested, conjugated bilirubin is automatically added by the laboratory when the total bilirubin is >50 μmol/l and other LFTs are unremarkable.

A comment is added to any LFT where:

- Patient is >3 months old
- Total bilirubin is between 25-100 μmol/l
- The conjugated bilirubin fraction accounts for <25% of the total bilirubin level i.e. increased total bilirubin in Gilbert's syndrome should be due largely (>75%) to unconjugated bilirubin.

The comment states: ***"In the absence of intravascular haemolysis or other liver pathology, an increased unconjugated bilirubin (i.e.>75% of an elevated total) is consistent with GILBERTS SYNDROME"***

Clinicians may consider sending fasted samples for repeat liver function tests including conjugated bilirubin and a full blood count.

In Gilbert's Syndrome fasting should increase unconjugated bilirubin up to 3-fold, however this test has low specificity and therefore is not recommended in primary care. Usually a diagnosis can be made without the need for fasted investigations.

If the isolated unconjugated hyperbilirubinaemia is more pronounced (i.e. >40 μM) then rarer causes such as Crigler-Najjar syndrome should be considered and genetic testing undertaken.

REFERENCES

British Society of Gastroenterology: Guidelines on the management of abnormal liver blood tests, 2017.

NICE CKS for Gilbert's Syndrome. Last revised October 2015.