

## A case report of Gilbert Syndrome

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### Abstract

Gilbert syndrome is benign, often familial condition characterized by recurrent but asymptomatic mild unconjugated hyperbilirubinemia in the absence of haemolysis or underlying liver disease. If, it becomes apparent, it is not until adolescence and then usually in association with stress such as intercurrent illness, fasting or strenuous exercise. Virtually all patients have decreased level of UDP- Glucuronosyltransferase, but there also is evidence for a defect in hepatic uptake of bilirubin as well. This case is reported due to its rarity. The prevalence of Gilbert syndrome in U.S is 3-7% of the population.

**Keywords:** Gilbert Syndrome, familial non-haemolytic jaundice, hereditary non-haemolytic bilirubinaemia, low-grade chronic hyperbilirubinemia

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Augustine Gilbert and Pierre Lereboullet first described Gilbert syndrome, the most common inherited cause of unconjugated hyperbilirubinemia, in 1901. Both autosomal recessive and autosomal dominant patterns have been described. The syndrome is characterized by intermittent jaundice in the absence of haemolysis or underlying liver disease. The hyperbilirubinemia is mild and by definition < 6 mg/dl. However, most patients exhibit levels of 3 mg/dl. Considerable daily and seasonal variations are observed and bilirubin level occasionally may be normal in as many as one-third of patients.

Gilbert syndrome may be precipitated by dehydration, fasting menstrual periods or stress, such as an intercurrent illness or vigorous exercise. Patients may complain of vague abdominal discomfort and general fatigue for which no cause is found. These episodes resolve spontaneously and no treatment is required except for supportive care.

### Case report

A 14 year old boy hailing from Bishal Nagar, Kathmandu admitted in Paediatric ward KMCTH with history of yellowish discolouration of sclera for 10 days. There were no other complaints. Urine colour was normal. Child had history of similar illness one year back and also 3 months back, which subsided on its own. For present complaint, child was shown to Ayurvedic doctor who advised restriction of diet including fatty meals. However, mother noticed the deepening of jaundice in sclera without any abnormality in urine colour. On physical

examination, mild jaundice present, but no other abnormal physical findings were evident.

Investigations done revealed normal haemoglobin, total and differential count ESR and adequate platelets. Reticulocyte was within normal limit (0.5%). Peripheral blood picture showed no abnormality including any features of haemolysis. Osmotic fragility done was within normal limit. Liver function tests were all within normal limit including HBsAg and AntiHCV with the exception of unconjugated hyperbilirubinemia on several occasions.

The maximum total and indirect serum bilirubin reached were 5.3mg/dl and 4.9mg/dl respectively. Thus, keeping possibility of Gilbert syndrome, child was subjected to further test, that is, fasting or provocation test (child kept on 400Kcal/day for 48 hours). Results found as follows;

Before fasting:	
Serum bilirubin	Total-1.5 mg/dl Indirect-0.75 mg/dl
After 48 hours of fasting:	
Serum bilirubin:	Total-3.61mg/dl Indirect-2.16 mg/dl

Urine, stool and chest radiograph examinations done all were within normal limits.

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USG Abdomen was also normal.

### Discussion

Unconjugated hyperbilirubinemia in Gilbert syndrome has long been recognized as due to under activity of the conjugating enzyme system Uridine diphosphate glucuronosyltransferase (UDPGT). Bilirubin UDPGT is responsible for conjugating bilirubin into bilirubin monoglucuronides and diglucuronides and is located primarily in the endoplasmic reticulum of hepatocytes. The UGT1 gene locus for Gilbert syndrome is located on chromosome 2 and is responsible for virtually all bilirubin conjugation and UGT2 playing little, if any role.

Gilbert syndrome is a benign condition with no associated morbidity or mortality affecting all races occurring predominantly in men with a male to female ratio ranging from 2:1-7:1. It usually is diagnosed around puberty, possibly due to inhibition of bilirubin glucuronidation by endogenous steroid hormones. In older subjects, the diagnosis is usually made when unconjugated hyperbilirubinemia is noted on routine blood tests or unmasked by an intercurrent illness or stress.

Diagnosis of Gilbert syndrome can be made in the presence of (1) unconjugated hyperbilirubinemia noted on several occasions;(2) normal results on CBC, reticulocyte count, and blood smear;(3) normal liver function test results; and absence of other disease processes. Additional tests are rarely required for a diagnosis as it is straightforward. However, following investigations are performed occasionally to confirm a diagnosis of Gilbert syndrome.

- **Fasting:** This usually results in a 2- to 3- fold rise in plasma unconjugated bilirubin within 48 hours of a fast that returns to normal levels within 24 hours of resuming a normal diet. Although unconjugated bilirubin levels also rise with fasting in patients with haemolysis or liver disease, the magnitude of the rise is less than that observed with Gilbert syndrome. A similar rise in plasma bilirubin also is observed with normocaloric diets deficient in lipids and reverse promptly with lipid replacement.
- **Nicotinic acid:** Intravenous administration of 50 mg of nicotinic acid results in a 2-to3- fold rise in plasma unconjugated hyperbilirubinemia within 3 hours.
- **Phenobarbital:** Phenobarbital and other enzyme inducers of the bilirubin-UDPGT system will normalize plasma bilirubin in patients with Gilbert syndrome.

- **Rifampicin test:** This test is popular because of non-invasive in nature. It is as reliable as fasting test. Per oral administration of 600-900 mg of rifampicin results in rise in plasma unconjugated hyperbilirubinemia within 2-4 hours.
- **Thin-layer chromatography:** This test is diagnostic for Gilbert syndrome when it shows a significantly higher proportion of unconjugated bilirubin when compared to individuals with chronic haemolysis, liver disease or those who are healthy. If confirmation of the diagnosis is truly essential, chromatographic determination is of potential use. This will show an increased ratio of bilirubin monoglucuronide to diglucuronide, reflecting reduced bilirubin-UDPGT activity.
- **Polymerase chain reaction:** The polymerase chain reaction (PCR) is a novel and rapid method of identifying genetic polymorphisms in the TATA box of the UDPGT1 gene using fluorescence resonance energy transfer.
- **Liver biopsy:** It is not performed routinely and is rarely necessary for a diagnosis. Liver is normal histologically.

### Conclusion

In the light of above case, if a child comes with isolated unconjugated hyperbilirubinemia (< 6 mg/dl) on several occasions in the absence of haemolysis or underlying liver disease; Gilbert syndrome should be entertained in the differential diagnosis of unconjugated hyperbilirubinemia, being the most common inherited cause. It has no deleterious associations and an excellent prognosis, and those who have it can lead a normal lifestyle.

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