**Indian Journal of Pharmacy Practice., 2024; 17(2):191-193.**
https://www.ijopp.org

Case Report

# Gilbert Syndrome Unveiled: A Rare Presentation Pattern of Gilbert Syndrome Phenotype

**Neethu Jose*, Betsy Mathew**

Department of Medicine, Dr. Chandramma Dayananda Sagar Institute of Medical Education and Research, Harohalli, Karnataka, INDIA.

**ABSTRACT**

Gilbert syndrome is a relatively common, benign liver condition characterized by elevated levels of unconjugated bilirubin in the blood. In this instance, we present the case of an 18-year-old woman who developed jaundice subsequent to receiving a blood transfusion for iron deficiency anemia. Initially, the manifestation was suspected to be a haemolytic transfusion reaction, but further examination revealed that unconjugated hyperbilirubinemia was not linked to haemolysis. The patient reported a history of mild, self-limiting, recurrent jaundice episodes. A clinical diagnosis of Gilbert syndrome was established, and remarkably, bilirubin levels gradually normalized without any interventions. This case highlights an atypical presentation of Gilbert Syndrome.

**Keywords:** Gilbert syndrome, Hyperbilirubinemia, Jaundice, Transaminases.

**Correspondence:**
**Dr. Neethu Jose**
Department of Medicine, Dr. Chandramma Dayananda Sagar Institute of Medical Education and Research, Harohalli-562112, Karnataka, INDIA.
Email: neethujose09@outlook.com

**Received:** 14-01-2024;
**Revised:** 08-02-2024
**Accepted:** 22-02-2024.

## INTRODUCTION

Gilbert's Syndrome (GS) is a benign autosomal recessive hereditary condition caused by a mutation in the UGT1A1 gene, leading to impaired bilirubin glucuronidation. It stands as the most prevalent hereditary Unconjugated Hyperbilirubinemia (UCB), impacting approximately 5-10% of the adult population.[1,2] This genetic anomaly results in mild unconjugated hyperbilirubinemia, accompanied by normal liver enzyme levels and histology, while tests for hemolysis yield negative results. Jaundice episodes can be triggered by intercurrent illnesses, prolonged fasting, and stress, with the syndrome typically manifesting post-adolescence.[3,4] The diagnosis primarily relies on clinical evaluation, and specific diagnostic tests, such as an increase in serum bilirubin during fasting or intravenous nicotinic acid, and a decrease upon administration of phenobarbitone inducing hepatic conjugating enzymes, are seldom necessary. Importantly, individuals with GS generally have a normal life expectancy. In this context, we present a case with a distinctive and uncommon presentation of Gilbert's Syndrome, contributing to the evolving understanding of this genetic condition.

## CASE REPORT

An 18-years-old women presented at the outpatient department of Dr. Chandramma Dayananda Sagar Institute of Medical Education and Research, reporting fatigue and poor appetite persisting for two months. A diagnosis of severe iron deficiency anemia was established, prompting the administration of one unit of packed red blood cells through transfusion. Unexpectedly, she developed jaundice the day following the blood transfusion. Concerns arose regarding a potential haemolytic transfusion reaction, given the observed increase in unconjugated bilirubin post-transfusion. However, a comprehensive evaluation revealed an absence of typical haemolytic indicators, such as a decline in haemoglobin levels, an increase in reticulocyte count, haemoglobinuria, or elevated LDH. Peripheral smear analysis indicated no evidence of haemolysis, and the Coomb's test yielded negative results. Further investigations, including viral hepatitis markers, liver transaminase levels, and ultrasound examination of the liver, all returned normal findings.

Upon further inquiry, the patient disclosed a history of recurring self-limiting episodes of jaundice over the past three years. Consequently, the clinical diagnosis pointed towards Gilbert syndrome, with stress and fasting identified as precipitating factors. The episode of unconjugated hyperbilirubinemia spontaneously resolved within a brief span of five days. This case also underscores the significance of thorough patient history in uncovering latent conditions and contributes to the understanding of the variable presentation of Gilbert syndrome, particularly its response to stress and fasting as triggering

**DOI:** 10.5530/ijopp.17.2.31

**Table 1: Clinical Investigations of the Presented Patient.**

| Labs | Day 1 | Day 2 | Day 3 | Day 6 |
|---|---|---|---|---|
| Haemoglobin g/dL) | 3.66 | 6.13 | | 5.89 |
| Reticulocyte Count (%) | 1.3 | | 2 | |
| Total Bilirubin (mg/dL) | 1.3 | 5.04 | | 1.36 |
| Direct Bilirubin (mg/dL) | 0.3 | 0.86 | | 0.33 |
| AST/ALT (IU/L) | 12/4 | 15/4 | | |
| ALP/GGT (IU/L) | 85/12 | 80/13 | | |
| Peripheral Smear | | No haemolysis features | | |
| LDH (U/L) | | 120 | | |
| Urine Analysis | | No haemoglobinuria | | |

elements. The clinical evidences of patient have been summarised in Table 1.

## DISCUSSION

Gilbert syndrome is a relatively common, benign liver condition characterized by elevated levels of unconjugated bilirubin in the blood. The syndrome results from a genetic mutation affecting the UGT1A1 gene responsible for bilirubin processing.[1] Unlike more serious liver disorders, individuals with Gilbert syndrome typically lead normal lives without significant health implications. The condition is often asymptomatic or presents with mild and intermittent jaundice and sometimes it goes unnoticed. Understanding Gilbert syndrome is crucial for proper diagnosis and management, ensuring individuals with this genetic variation receive appropriate medical care and support. Here we present this case to demonstrate how GS could be misdiagnosed and the pitfalls encountered.

Our patient initially presented with normal Liver Function Tests (LFT), and subsequently developed evident jaundice following a blood transfusion for severe anemia. Initially suspected as a transfusion reaction, a meticulous assessment ruled out any form of haemolysis. The manifestation of unconjugated hyperbilirubinemia alongside normal transaminase levels led to the realization that the patient had been misdiagnosed, revealing a pre-existing case of Gilbert Syndrome (GS). It is noteworthy that stress, fasting, intense physical activity, sleep deprivation, dehydration, alcohol consumption, surgery, concurrent illnesses, infections, and menstruation are recognized triggers for an increase in unconjugated bilirubin levels in individuals with GS. This case emphasizes the importance of a systematic diagnostic approach, particularly when unexpected clinical presentations arise, and underscores the relevance of recognizing underlying genetic conditions in patient care.[1]

GS is a diagnosis of exclusion with normal liver enzymes, clotting, albumin and negative haemolysis screen.[1] "Over investigation" is the major problem with GS which is a benign condition.[5,6] Particularly in India once jaundice is observed, patients opt for native medications and a rigorous diet. Some of these medications are even hepatotoxic. Counselling the patient and family about the benign nature of the illness is of paramount importance.[5] Serum bilirubin has anti-inflammatory, antioxidant, anti-mutagenic properties[2] and may even have a survival benefit in patients with GS.[4] Mildly elevated total bilirubin concentration is associated with protection from Cardiovascular Diseases (CVD), type 2 diabetes mellitus, certain cancers, and all-cause mortality rates.[4] Total bilirubin concentration is usually in the range of 1-5 mg/dL in GS. Higher values of total bilirubin may require genotyping for other diseases like Criggler Najjar Type 2.[4] The bilirubin level of a GS patient can rise abnormally high in various conditions and this can mislead the physicians and surgeons towards false diagnosis.[6,7] Generally, the treatment of GS includes reassurance, avoiding fasting and stressful conditions.

The misdiagnosis of Gilbert syndrome remains a noteworthy concern in the medical field due to its subtle and often asymptomatic nature. The mild and intermittent jaundice associated with elevated unconjugated bilirubin levels can be easily overlooked or attributed to other common conditions, leading to misinterpretations. Since the syndrome is typically benign and does not pose a significant threat to health, it might be overshadowed by more urgent clinical concerns. Additionally, the lack of distinct symptoms can contribute to its underdiagnosis or confusion with other liver disorders or in our case a transfusion-related reactions. Raising awareness among healthcare professionals about the distinct features of Gilbert syndrome and incorporating genetic testing into diagnostic protocols are crucial steps to minimize the risk of misdiagnosis, ensuring individuals receive accurate information and appropriate medical guidance.

## CONCLUSION

In conclusion, Gilbert syndrome sheds light on the fascinating intricacies of genetic variations influencing bilirubin metabolism. The key lies in distinguishing Gilbert syndrome from other liver disorders, as its mild and intermittent jaundice often goes unnoticed. As medical knowledge advances, understanding the

genetic underpinnings becomes increasingly crucial for accurate diagnosis and tailored management.

## ABBREVIATIONS

**GS:** Gilbert syndrome; **UCB:** unconjugated hyperbilirubinemia; **LDH:** Lactate dehydrogenase.

## ETHICS APPROVAL, CONSENT TO PARTICIPATE AND PATIENT CONSENT

The Institutional Ethics Committee was obtained before drafting the manuscript and prior to the publication. The patient was informed regarding the publication, where the patient as well the patient's party agreed to publish without revealing any identity of theirs.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## SUMMARY

Gilbert's Syndrome (GS) is a benign autosomal recessive hereditary condition caused by a mutation in the UGT1A1 gene, leading to impaired bilirubin glucuronidation. In this context, we present a case with a distinctive and uncommon presentation of Gilbert's Syndrome, contributing to the evolving understanding of this genetic condition. An eighteen-years-old women presented at the outpatient department reporting fatigue and poor appetite persisting for two months. A diagnosis of severe iron deficiency anemia was established, prompting the administration of one unit of packed red blood cells through transfusion. Unexpectedly, she developed jaundice the day following the blood transfusion. However, a comprehensive evaluation revealed an absence of typical haemolytic indicators, such as a decline in haemoglobin levels, an increase in reticulocyte count, haemoglobinuria, or elevated LDH. Peripheral smear analysis indicated no evidence of haemolysis. Upon further inquiry, the patient disclosed a history of recurring self-limiting episodes of jaundice over the past three years. Consequently, the clinical diagnosis pointed towards Gilbert syndrome, with stress and fasting identified as precipitating factors. The misdiagnosis of Gilbert syndrome remains a noteworthy concern in the medical field due to its subtle and often asymptomatic nature. The mild and intermittent jaundice associated with elevated unconjugated bilirubin levels can be easily overlooked or attributed to other common conditions, leading to misinterpretations.

## REFERENCES


1. King D, Armstrong MJ. Overview of Gilbert's syndrome. Drug Ther Bull. 2019;57(2):27-31. doi: 10.1136/dtb.2018.000028, PMID 30709860.
2. Zöhrer PA, Hana CA, Seyed Khoei N, Mölzer C, Hörmann-Wallner M, Tosevska A, *et al.* Gilbert's syndrome and the gut microbiota–insights from the case-control BILIHEALTH study. Front Cell Infect Microbiol. 2021;11:701109. doi: 10.3389/fcimb.2021.701109, PMID 34604105.
3. Pavlovic Markovic A, Stojkovic Lalosevic M, Mijac DD, Milovanovic T, Dragasevic S, Sokic Milutinovic A, *et al.* Jaundice as a diagnostic and therapeutic problem: A general practitioner's approach. Dig Dis. 2022;40(3):362-9. doi: 10.1159/000517301, PMID 34015787.
4. Wagner KH, Shiels RG, Lang CA, Seyed Khoei N, Bulmer AC. Diagnostic criteria and contributors to Gilbert's syndrome. Crit Rev Clin Lab Sci. 2018;55(2):129-39. doi: 10.1080/10408363.2018.1428526, PMID 29390925.
5. Kulkarni RG, Lakshmidevi KB, Ronghe V, Dinesh US. Gilbert's syndrome in healthy blood donors what next?? Asian J Transfus Sci. 2016;10(1):63-6. doi: 10.4103/0973-6247.165835.
6. Rasool A, Sabir S, Ashfaq M, Farooq U, Khan MZ, Khan FY. Gilbert's syndrome-a concealed adversity for physicians and surgeons. J Ayub Med Coll. 2015;27:707-10.
7. Sood V, Lal BB, Sharma S, Khanna R, Siloliya MK, Alam S. Gilbert's syndrome in children with unconjugated hyperbilirubinemia–an analysis of 170 cases. Indian J Pediatr. 2021;88(2):154-7. doi: 10.1007/s12098-020-03271-6, PMID 32221786.


**Cite this article:** Jose N, Mathew B. Gilbert Syndrome Unveiled: A Rare Presentation Pattern of Gilbert Syndrome Phenotype. Indian J Pharmacy Practice. 2024;17(2):191-3.