

Case report:

A case of Gilbert's syndrome diagnosis during pregnancy

Soo Huat Teoh^{1}, Yoke Lan Ng², Norlina Anuar³, Rahmah Kamaludin⁴*

Abstract

Gilbert's syndrome (GS) is a benign condition that presents with recurrent jaundice due to isolated hyperbilirubinemia which predominates by its unconjugated component. It is a diagnosis of exclusion and often missed by attending physician. The uncertainty of diagnosis may cause anxiety among patients especially in pregnant women fearing the condition impacting the outcome of their pregnancies. We present a case of a primigravida woman with recurrent jaundice for the last ten years who had not been given a definitive diagnosis of her illness despite on regular follow up in tertiary centre. She was anxious about her undiagnosed condition and the possibility of it affecting her pregnancy. Gilbert's syndrome was diagnosed after evaluating information from the tertiary centre and she was assured regarding the prognosis of her pregnancy. She went into labour at term without complication and her postpartum period was uneventful.

Keywords: Gilbert's syndrome; hyperbilirubinemia; pregnancy

*Bangladesh Journal of Medical Science Vol. 19 No. 02 April'20. Page : 333-335
DOI: <https://doi.org/10.3329/bjms.v19i2.45018>*

Introduction

Jaundice is one of the common presenting complaints in clinical setting and it is confirmed by a liver function test (LFT) showing hyperbilirubinemia. Hyperbilirubinemia can generally be divided into conjugated, unconjugated and mixed type. The differential diagnoses will depend on the type of hyperbilirubinemia. Gilbert's syndrome (GS) is one of the cause of unconjugated hyperbilirubinemia and sometimes presented as mixed type.¹⁻² It has an autosomal recessive inheritance pattern which results in deficiency of the enzyme uridine

diphosphoglucuronate-glucuronosyl transferase 1A1 (UGT1A1).² The conjugation process of bilirubin to water soluble glucuronic acid is disrupted thus affecting its excretion into bile.²⁻³

GS is commonly asymptomatic unless patients having concurrent triggering factors such as dehydration, fasting state and acute illnesses.³ The prevalence of GS has been reported to be between 2% to 20% for different populations with South Asian and Middle Eastern more prevalent than Europeans.^{1,5} In addition, GS is more common in men than women in a ratio of 2 to 7:1.⁴

1. Soo Huat Teoh, Medical Lecturer & Family Physician, Lifestyle Science Cluster, Advanced Medical & Dental Institute, Universiti Sains Malaysia, 13200 Kepala Batas, Penang, MALAYSIA. email: soohuat@usm.my
2. Yoke Lan Ng, Family Medicine Specialist, Klinik Kesihatan Inanam, 89350 Kota Kinabalu, Sabah, Ministry of Health MALAYSIA. email: lanyoke1976@gmail.com
3. Norlina Anuar, Family Medicine Specialist, Klinik Kesihatan Greentown, 30450 Perak, MALAYSIA. email: norlinaanuar@yahoo.com
4. Rahmah Kamaludin, Family Medicine Specialist, Klinik Primer PPUKM Cheras, Hospital Canselor Tuanku Mukhriz, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Ministry of Health MALAYSIA. email: rahmahkamaludin82@gmail.com

Correspondence to: Soo Huat Teoh, Medical Lecturer & Family Physician, Lifestyle Science Cluster, Advanced Medical & Dental Institute, Universiti Sains Malaysia, 13200 Kepala Batas, Penang, MALAYSIA. email: soohuat@usm.my

Case report

Madam SABM, a 25 years old Malay lady, primigravida at 34 weeks of gestation came to primary care health clinic for routine antenatal follow up. She did not have any active complaint; vital signs were normal, abdominal scan revealed normal featured fetus, and routine urine albumin and sugar test were normal. However, she was noted to be jaundiced.

On further questioning, she complained of recurrent jaundice for the last ten years ago. She denied history suggestive of obstructive jaundice (right upper quadrant pain, pale coloured stool or tea coloured urine) and the symptom commonly happens during Muslim's fasting month. Coincidentally, her elder sister also reported similar problem since teenage years but did not consult a doctor.

Madam SABM had been followed up every six months in tertiary centre with increased frequency to monthly for current pregnancy, but there was no definitive diagnosis given to her. She was anxious and concerned about her condition affecting her pregnancy outcome. At the same time, she felt financially and physically burdened of travelling frequently to hospital and clinics for blood test and review.

The medical report from the tertiary centre revealed that she had been under follow up with impression of 'isolated hyperbilirubinemia under investigations' for the past six years. Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP) in LFT were normal throughout the follow up. In addition, infective screening such as Hepatitis B, Hepatitis C, and Human Immunodeficiency Virus were non-reactive. Hepatobiliary system ultrasonography was also reported to be normal. The only salient feature was raised total bilirubin level ranging from 100 to 140 $\mu\text{mol/L}$ which predominated by indirect bilirubin level ranging from 70 to 90 $\mu\text{mol/L}$.

She was diagnosed to have GS after evaluating clinical and laboratory information above. Madam SABM was then informed about the diagnosis and reassured the pregnancy outcome in GS patients. Subsequently, she delivered a term baby boy with birth weight of 3.5kg via normal spontaneous vaginal delivery. There were no postpartum or neonatal complications experienced. She continued her follow up in primary care health clinic with two monthly follow up (lasted six months) and total bilirubin

was fluctuating but was never above 140 $\mu\text{mol/L}$ depending on stressors she experienced. She reported to be less anxious about her clinical condition.

Discussion

GS is a diagnosis of exclusion thus making the diagnostic process difficult and prolonged. Clinical suspicion and knowledge about GS is required to confidently diagnose it. Madam SABM had presented with few important histories which pointed towards the diagnosis of GS. One of it was the frequent appearance of jaundice during the Muslim's fasting month and coincidentally current presentation was also in Ramadhan. A small study conducted by Felsher et al in 1970 found a reciprocal relationship between calorie consumption and bilirubin level among patients with GS.⁶ They observed that an abrupt rise in the unconjugated bilirubin always occurred within 24 hours after the fasting started, while the level reduced significantly in 12 to 48 hours after increasing the calorie intake.

Another important history is the presence of similar problem in her elder sister which suggested possibility of inherited disorder. However, autosomal recessive inheritance could not be inferred from the limited family history obtained. In addition to mildly elevated total bilirubin level with predominant unconjugated hyperbilirubinemia, normal results from other investigational modalities also supported the diagnosis of GS.³

There are limited studies available regarding the outcome of pregnancy in patients with GS. Of note, there is only one case report by Mohan et al which reported a favourable obstetric outcome which was similar with this case.⁷ Despite the positive outcome in this case, Madam SABM experienced anxiousness throughout her six years follow up due to her undiagnosed problem which heightened during current pregnancy. Her experience concurred with the finding from Bronner et al whereby high anxiety score was found during patients' diagnostic phase.⁸ A review of literature by Alder et al found anxiety during pregnancy had been associated with poor obstetric and neonatal outcomes.⁹ Therefore, reassuring her regarding the benign nature of GS is of great importance to reduce her anxiety level. It has been observed in several studies that reassurance from the physician during the diagnostic period reduced anxiety level, decreased help seeking, less

awareness of symptoms, and a change in patients' belief that the symptom could represent a serious disease.¹⁰

Conclusion

Diagnosis of GS is often missed or delayed. High index of suspicion is required to diagnose it and delay in diagnosis causes anxiety among patients especially in pregnant women as the obstetrical outcome is their major concern. Additionally, anxiety has also been found to affect pregnancies outcome thus utilisation of medical reassurance to alleviate anxiety in pregnant GS patient is beneficial.

Ethical Approval about publication from the concerned hospital:

Ethics approval was obtained prior submission.

Disclosure of funding: None

Conflict of interest: None declared

Individual Contribution of the Authors:

Conceptual work: Teoh SH, Ng YL, Anuar N, Kamaludin R

Data collection: Teoh SH, Ng YL, Anuar N, Kamaludin R

Manuscript writing: Teoh SH, Ng YL, Anuar N, Kamaludin R

Editing of final manuscript: Teoh SH, Ng YL, Anuar N, Kamaludin R

References:

1. Wagner K-H, 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. <https://doi.org/10.1080/10408363.2018.1428526>
2. Fretzayas A, Moustaki M, Liapi O, Karpathios T. Gilbert syndrome. *Eur J Pediatr* 2012;**171**(1):11-5. <https://doi.org/10.1007/s00431-011-1641-0>
3. Roy-Chowdhury J, Roy-Chowdhury N, Wang X. Gilbert syndrome and unconjugated hyperbilirubinemia due to bilirubin overproduction. In: Lindor KD, Grover S, editors. UpToDate. [Internet]. Waltham, MA: UpToDate 2018 [cited November 11, 2018]. Available from: <https://www.uptodate.com/contents/gilbert-syndrome-and-unconjugated-hyperbilirubinemia-due-to-bilirubin-overproduction>
4. Beutler E, Gelbart T, Demina A. Racial variability in the UDP-glucuronosyltransferase 1 (UGT1A1) promoter: a balanced polymorphism for regulation of bilirubin metabolism? *Proc Natl Acad Sci U S A* 1998;**95**(14):8170-4. <https://doi.org/10.1073/pnas.95.14.8170>
5. Hemmati F, Saki F, Saki N, Haghighat M. Gilbert syndrome in Iran, Fars Province. *Ann Saudi Med* 2010;**30**(1):84. <https://doi.org/10.5144/0256-4947.59376>
6. Felsher BF, Rickard D, Redeker AG. The reciprocal relation between caloric intake and the degree of hyperbilirubinemia in Gilbert's syndrome. *N Engl J Med* 1970;**283**(4):170-172. <https://doi.org/10.1056/NEJM197007232830403>
7. Mohan M, Lakshmi Sailaja P, Reddy PVN. Pregnancy with Gilbert Syndrome-A Case Report. *J Clin Diagn Res* 2014;**8**(6):OD01-OD2. <https://doi.org/10.7860/JCDR/2014/9327.4426>
8. Bronner MB, Nguyen MH, Smets EMA, Ven AWH, Weert JCM. Anxiety during cancer diagnosis: Examining the influence of monitoring coping style and treatment plan. *Psychooncology* 2018;**27**(2):661-7. <https://doi.org/10.1002/pon.4560>
9. Alder J, Fink N, Bitzer J, Hösli I, Holzgreve W. Depression and anxiety during pregnancy: a risk factor for obstetric, fetal and neonatal outcome? A critical review of the literature. *J Matern Fetal Neonatal Med* 2007;**20**(3):189-209. <https://doi.org/10.1080/14767050701209560>
10. Coia P, Morley S. Medical reassurance and patients' responses. *J Psychosom Res* 1998;**45**(5):377-386.