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# Glucose-6-Phosphate Dehydrogenase Deficiency In A Nigerian Neonate with Acute bilirubin Encephalopathy triggered by Ciprofloxacin

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## Abstract

We report a case of G6PD deficiency in a male Nigerian neonate who presented with features of acute bilirubin encephalopathy and severe anemia within the first week of life in the absence of ABO and Rhesus incompatibilities requiring multiple exchange blood transfusions (EBTs) and intensive phototherapy. The hyperbilirubinemia worsened following the commencement of IV Ciprofloxacin and improved significantly once it was discontinued. He was lost to follow-up, having been discharged in a satisfactory neurological state.

**Keywords:** Glucose-6-phosphate dehydrogenase (G6PD) deficiency, Neonate, Jaundice, Acute bilirubin encephalopathy, Ciprofloxacin, Exchange blood transfusion

## Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest hereditary enzymopathy, affecting over 500 million people globally. **[1]** It is unique in that affected individuals can remain asymptomatic throughout life except when exposed to specific haemolytic triggers. **[2,3]** These include infections, drugs like quinine, sulphonamides, quinolones, menthol, foods like fava beans, and everyday household items like naphthalene balls. **[4]**

## Case Report

Our patient was a male neonate referred from a peripheral hospital on the 5th day of life. He presented to the children's emergency room of the University of Benin Teaching Hospital (UBTH) with a 3-day history of yellowness of the eyes and body, poor suck, and fever, both of 1-day duration. His umbilical cord was poorly cared for using toothpaste and local herbs. There was no history of the use of mentholated balm or naphthalene balls. Maternal blood group was unknown, his 2 older siblings and parents did not have neonatal jaundice, nor did maternal uncles suffer acute hemolytic episodes in the past. His parents are non-consanguineous, and the antenatal period was not adversely eventful. He was delivered per vagina following the spontaneous onset of labor at term and cried well following birth. He was exclusively breastfed until presentation.

At presentation, he was irritable, pale, and deeply icteric from his face to his feet. He had cycling movements and fisting as well as weak suck and grasp. The umbilical stump was foul-smelling with brownish debris. He weighed 3300g, was 48cm long, and had a head circumference of 34cm.

Exposure of an affected neonate to these triggers may precipitate severe hyperbilirubinemia, usually necessitating exchange blood transfusion (EBT) with a high risk of bilirubin-induced neurologic deficit where diagnosis and intervention are delayed or unavailable. **[3,5]** This is especially true in Sub-Saharan Africa, where newborn screening for G6PDD is considered too expensive and performed only when there is clinical suspicion rather than as a proactive, preventive measure, as is the practice in more developed countries.

The total serum bilirubin concentration was 25mg/dl with a conjugated fraction of 1.2mg/dl, and his packed cell volume (PCV) was 19 %. His blood group was O-Rhesus+, while the maternal blood group was B-Rhesus+. Micro-ESR was elevated at 15mm in the first hour (corrected for anemia was 6mmHr), which was significant for sepsis. The blood film revealed normocytic, normochromic red blood cells. The direct Coomb's test was negative. Liver function tests, serum proteins, and abdominal ultrasound scans were normal. Blood culture yielded no growth after 10 days of incubation.

Before reviewing the investigation results, an initial assessment of acute bilirubin encephalopathy secondary to ABO incompatibility was made. He had a transfusion with packed red cells at 10mls/kg, and a double exchange transfusion (EBT) was done two hours later. Intensive phototherapy was continued using a Bilitron bed,' and feeds were recommenced six hours after the EBT via a nasogastric tube. Six hours after the EBT, his PCV was noted to have risen to 45 %, and serum bilirubin concentration was 8.0 mg/dl. He was commenced on IV Ampicillin-Sulbactam and Gentamycin as

empirical treatment of presumed neonatal sepsis. His serum bilirubin was monitored for 12 hours while continuing intensive phototherapy. There was neurological improvement with his suck and graspreflexes becoming strong, and the cycling movement had abated. However, the fever persisted, and his blood film remained negative for malaria parasite. Hence, IV Ciprofloxacin was introduced after72 hours of admission. On the 4th day post-EBT, he was noticed to be deeply icteric again, and an urgent serum bilirubin estimation was25.2mg/dl with a conjugated fraction of 14.2mg/dl; his PCV had dropped to 17 %. After that, a repeat double-volume exchange bloodtransfusion was performed with a top-up red cell transfusion at 10mls/kg. With suspicion of G6PD deficiency at this point, IV Ciprofloxacin was discontinued being a possible trigger of acute hemolysis. Blood glucose-6-phosphatase dehydrogenase enzyme activity was assayed, and a value of 235.55MU/10^9 (245 – 299MU/10^9) was obtained. He remained stable after that, and PCV remained above 40 %. Serum bilirubin dropped to 5mg/dl, fever resolved, and primitive reflexes were restored. He was discharged home after his parents had been educated on his diagnosis, triggers to avoid, symptoms and signs of acute hemolysis, and the need for early hospital presentation whenever he was ill. He had two follow-up clinic visits with total serum bilirubin between 3mg/dl and 5.2mg/dl and conjugated fraction 0.7mg/dl - 1mg/dl. He was referred to Paediatric Neurology and hematology clinics.

## Discussion

Glucose-6 phosphate dehydrogenase deficiency is the most common human enzymopathy known.1 The prevalence of G6PD deficiency in Nigerian children is estimated at 15.3 % with a male preponderance (24.1 % of males and 6.6 % of females affected). **[6,7]** This is not unexpected as it is an X-linked recessive disorder such that heterozygous female carriers are asymptomatic. **[3,8]** Most males who are G6PD deficient remain asymptomatic until much later in life. The index patient was a male Nigerian neonate with severe hyperbilirubinemia at the presentation time. He was investigated along that line, and the more common possible aetiologies, including ABO incompatibility, Rhesus incompatibility, and sepsis, were excluded as possible causes.

In most cases, the neonate would present with jaundice, but the blood film would typically not suggest acute hemolysis. **[8]** This was the case in the index patient as the blood film showed only normocytic, normochromic anemia.

Defective hepatic bilirubin conjugation, clearance, and physiologic neonatal hemolysis are expected synergistic factors responsible for the causation of jaundice in the early newborn period. Patients with WHO class 1 G6PD deficiency have less than 1 % enzyme activity which predisposes them to oxidant stress-induced hemolysis and severe hyperbilirubinemia with an increased risk of kernicterus. **[9]** The index patient presented with severe hyperbilirubinemia and features of acute bilirubin encephalopathy, making it very likely that he had the class 1 variant of G6PD deficiency. The borderline low serum level of G6PD enzyme in the index patient, even during ongoing hemolysis, suggests that the enzyme activity would be much lower in his stable state.

Acute hemolysis in G6PD deficient individuals usually follows exposure to an inciting agent. Treatment hinges on identifying and removing the offending agent while rapidly lowering serum bilirubin with EBT and phototherapy. **[3,9]** Severe acute hemolysis, evidenced by a precipitous drop in PCV and simultaneous rise in serum bilirubin concentration, was detected four days into the admission of this patient following the commencement of IV Ciprofloxacin, despite exchange blood transfusion and intensive phototherapy. These changes were resolved following an EBT and discontinuation of IV Ciprofloxacin. Our patient remained stable until discharge and during follow-up with no repeat episode of acute hemolysis.

G6PD assay is not routinely done in newborns in our locale, even when they present with jaundice. This is because it is mainly unavailable and relatively expensive in the few diagnostic facilities offering this service. Hence the diagnosis is often noticed. In our index patient's case, his parents could afford the cost of the assay, and although the results were retrieved days after samplecollection, the clinical suspicion and timely withdrawal of ciprofloxacin aided recovery.

G6PD assay is best performed several weeks after the acute hemolysis to get a reliable picture. The release of reticulocytes and immature red blood cells at the time of hemolysis would give a falsely high serum concentration of the enzyme. As such, low-normal values in the face of ongoing hemolysis should further heighten the clinician's suspicion of G-6-PD deficiency. **[9,10]** Our patient's enzyme assay was lower than the reference range despite ongoing hemolysis suggesting a severe variant, likely the WHO class 1 variant. Other classes are II – V and have higher enzyme activities between 1 and 110 %. They are primarily asymptomatic throughout life.**[9]**

## Conclusion

This case highlights the clinical importance of G6PD deficiency as a plausible cause of neonatal hemolysis and jaundice. We recommend that all children presenting with neonatal jaundice should be screened regardless of medical histories.

## Limitation

1. Being that our patient was lost to follow-up, we are unable to comment about his eventual neurologic outcome.
2. We were also not able to repeat the G6PD assay in his stable state to appropriately classify disease severity.

## Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

1. Luzzatto L, Ally M, Notaro R (2020) Glucose-6-phosphate dehydrogenase deficiency. Blood. 136(11): 1225–40.
2. Mehta AB (1994) Glucose-6-phosphate dehydrogenase deficiency. Postgrad Med J. 70(830): 871–7.
3. Dhillon AS, Darbyshire PJ, Williams MD, Bissenden JG (2003) Massive acute haemolysis in neonates with glucose-6-phosphate dehydrogenase deficiency. Arch Dis Child Fetal Neonatal Ed. 88(6): F534-F536.
4. Village EG. http://pediatrics.aappublications.org/content/115/2/496.full.html. 2014;
5. Cappellini M, Fiorelli G (2008) Glucose-6-phosphate dehydrogenase deficiency. Lancet. 371(9606): 64–74.
6. Williams O, Gbadero D, Edowhorhu G, Brearley A, Slusher T, et al. (2013) Glucose-6-Phosphate Dehydrogenase Deficiency in Nigerian Children. 8(7): 4–11.
7. Howes RE, Piel FB, Patil AP, Nyangiri OA, Gething PW, et al. (2012) G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria Endemic Countries: A Geostatistical Model-Based Map. PLoS Med. 9(11): e1001339.
8. Elella SA, Tawfik M, Barseem N, Moustafa W (2017) Prevalence of glucose-6-phosphate dehydrogenase deficiency in neonates in Egypt. Ann Saudi Med. 37(5): 362–365.
9. Gautam K (2016) Glusoce-6-phosphate dehydrogenase-History and diagnosis. Journal of Pathology of Nepal. 6(12): 1034-1039.
10. Programme HD, Niwa S. UpdatelLe point. 1989;