G6PD Enzyme Deficiency in Neonatal Hyperbilirubinemia

Thesis

Submitted for Partial Fulfillment of Master Degree
In Pediatrics

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2018

سورة البقرة الآية: ٣٢

Acknowledgments

First and forever, thanks to **Allah**, *Almighty for giving me the strength and faith to complete my thesis and for everything else.*

I would like to express my deepest gratitude and appreciation to **Prof. Dr. Mohamed Sami El Shimi,** *Professor of Pediatrics, Faculty of Medicine – Ain Shams University, who initiated and designed the subject of this thesis, for his kindness, over available, untiring supervision, helpful criticism and support during the whole work. I really have the honor to complete this work under his supervision.*

My extreme thanks and gratefulness **Prof. Dr. Mona Hussein El Samahy,** *Professor of Pediatrics, Faculty of Medicine – Ain Shams University, I'm much grateful for her patience and strict supervision. Her valuable advice helped me a lot to pass many difficulties.*

I would like also to thank with all appreciation **Dr. Nancy Mohamed Abou Shady,** *Assistant Professor of Pediatrics, Faculty of Medicine – Ain Shams University, for the efforts and time she has devoted to accomplish this work.*

Last but not least, I would like to thank my father, my mother, my brother and my sister for their kind care and support.

Hazem Khaled Ahmed Abu Setta

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List of Abbreviations

Abbrev.	Full-term
ABE	: Acute bilirubin encephalopathy
Bf	: Free bilirubin
BIND	: Bilrubin induced neurological dysfunction
CN-I	: CN-Crigler-Najjar syndrome type I
COHb	: Carboxyhemoglobin
CRP	: C-Reactive Protein
Direct Bil	: Direct Bilirubin.
ETCO	: End tidal CO
G6PD	: Glucose-6-phosphate dehydrogenase
Hb	: Hemoglobin. RBCS: Red blood cells.
RBCs	: Red blood cells
Retics	: Reticulocytic count.
SD	: Standard deviation
SPSS	: Statistical package for social science
TLC	: Total Leucocytic count.
Total Bil	: Total Bilirubin.
TSB	: Total serum bilirubin
UCB	: Unconjugated bilirubin
UGT	: Uridine glucuronyl transferase
UGT1A1	: Uridine-diphosphate-glucurono-syltransferease 1
6PGD	: 6-phosphogluconate dehydrogenate

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Abstract

Background: Jaundice is the most common condition requiring medical attention in newborns. The yellow colouration of the skin and sclera in newborns with jaundice is the result of accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal transitional phenomenon. **Aim of the Work:** to determine the frequency of G6PD deficiency in Egyptian neonates presented with neonatal jaundice in order to know the magnitude of the problem and try to provide the proper care for these cases. **Patients and Methods:** The present Study was conducted in the NICU of Ain Shams University. A total of 200 icteric neonates were enrolled in the study. **Results:** The study showed a significant increase in weight & artificial feeding dependent [(pathological jaundiced) neonates (Group B)] more than physiological jaundiced neonates (Group A). Significant male predominance, increase in Apgar score at 5 minutes & significant breastfeeding dependent neonates in group A more than group B. Also, significant negative correlation between G6PD enzyme and Neutrophils. Significant positive correlation between G6PD enzyme and Lymphocytes. Incidence of G6PD deficiency among neonates with neonatal jaundice is 4%. **Conclusion:** Neonatal hyperbilirubineamia is one of the most common problems and requires hospital admission for investigation and treatment. Despite a low prevalence of G6PD deficiency tests be performed in all Iranian and Mediterranean icteric newborns, unless other investigators ascertain and document that G6PD deficiency tests are not necessary to be done routinely. In additions, we recommend that measurement of the enzyme UGT to be made available for the clinical use in the evaluation of neonatal hyperbilirubinaemia. **Recommendations:** Given the potential of the hemolytic danger, health care professionals should always bear in mind of the adverse consequences when administering drugs to patients with glucose-6-phosphhate dehydrogenase deficiency. In addition, Measurement of the enzyme UGT be made available for the clinical use in the evaluation of neonatal hyperbilirubinaemia.

Key words: G6Pd enzyme, neonatal hyperbilirubinemia, care

Introduction

The enzyme glucose-6-phosphate dehydrogenase (G6PD) is one of the most important enzymes in the human body, present in various amounts in many cells, including red blood cells ***(Farhoud and Yazdanpanah, 2008).***

Deficiency of G6PD is a frequent enzyme deficiency of the human being, with estimated 400 million affected people in the world ***(Nouri et al., 2006).***

It is an inherited X-linked recessive disorder with varied clinical presentations including neonatal jaundice, hemolysis, acute icterus after exposure to chemicals and drugs, anemia, acute jaundice following consumption of fava beans (favism), and also congenital chronic non-spherocytic hemolytic anemia ***(Gari et al., 2010).***

Of these manifestations, neonatal jaundice is the earliest one, and the most critical sign for early diagnosis of this genetic disorder ***(Behrman et al., 2012).***

Early diagnosis of deficiency of G6PD is quite important, because this disorder may cause severe hemolysis and anemia in the newborn, if undiagnosed. On the other hand, its detection is simple, rapid and cost-effective by the current laboratory methods ***(Moiz et al., 2012).***

Aim of the Work

The aim of this study is to determine the frequency of G6PD deficiency in Egyptian neonates presented with neonatal jaundice in order to know the magnitude of the problem and try to provide the proper care for these cases.

Neonatal Hyperbilirubinemia

Definition:

Neonatal Jaundice is one of the most common neonatal problems. Although up to 60% of term newborns have clinical jaundice in the first week of life, few have significant underlying disease. However hyperbilirubinemia in the neonatal period can be associated with severe illness such as hemolytic disease, metabolic and endocrine disorders, anatomic abnormalities in the liver, and infections ***(Stoll and Kliegman, 2004).***

Neonatal hyperbilirubinemia is defined as a total serum bilirubin level more than 86 μmol/L (5 mg/dL) ***(Porter and Dennis, 2002).***

It is a common problem that occurs in about 60% of newborns during the first week of life ***(Maisels and McDonagh, 2008).***

Most cases of neonatal hyperbilirubinemia are physiological and total serum bilirubin level less than 205 μmol/L (12 mg/dL) usually has no serious consequences ***(Bhutani and Johnson, 2009).***

However, the newborn with a total serum bilirubin level more than 342 μmol/L (20 mg/dL) is a concern. The severe hyperbilirubinemia can lead to kernicterus and neuro-developmental abnormalities such as hearing loss, athetosis, and, rarely, intellectual deficits ***(Bhutani et al., 2013).***

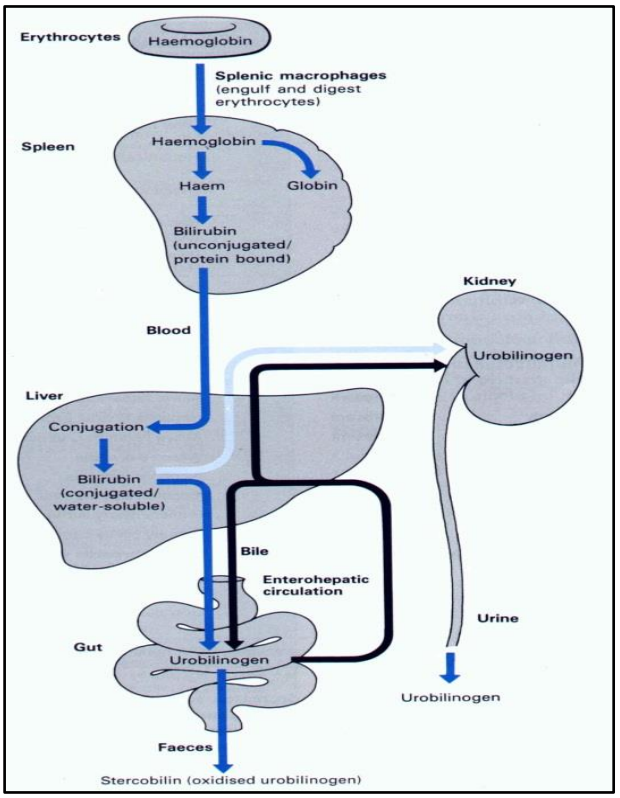

Figure (1): Bilirubin metabolism.

- ***Bilirubin metabolism :***

Bilirubin Production: Bilirubin is a product of heme catabolism, approximately 80 to 90 percent of Bilirubin is produced during the breakdown of haemoglobin from red blood cells (RBCs) or from ineffective erythropoiesis. The remaining, 10 to 20 percent is derived from the breakdown of other heme- containing proteins, such as cytochromes and catalase ***(Wrong add Stevenson, 2007).***

In the first oxidation step, biliverdin is formed from heme through the action of heme oxygenase. The rate

limiting step in the process, releasing iron and carbon monoxide ***(Stevenson et al., 2004)***.

Measurements of CO production, such as: end tidal CO (ETCO) or carboxyhemoglobin (COHb), both corrected for inhaled CO, can be used as indices of in vivo bilirubin production ***(Wrong and Stevenson, 2007)***.

Nontoxic biliverdin is catalyzed by biliverdin reductase to unconjugated bilirubin which is a natural antioxidant at low levels, but neurotoxic at high levels ***(Shapiro, 2003).***

One gram of haemoglobin results in the production of, 34mg of bilirubin. A normal term newborn produces about' 2 to 3 times as compared to adult ***(Agarwal and Deorari, 2002).***

Bilirubin exists in four different forms in serum: (1) unconjugated bilirubin inversely bound to serum albumin, which comprises the major portion of unconjugated bilirubin in serum, (2) a relatively minute fraction of unconjugated bilirubin not bound to serum albumin (free bilirubin) and can cross BBB, (3) conjugated bilirubin mainly, monoglucuronides and, diglucuronides readily execretable through the renal and' biliary system "and, (4) conjugated bilirubin covalently bound to serum albumin (delta bilirubin) with a plasma disappearance rate similar to that of serum albumin. Delta bilirubin, virtually absent in the first two weeks of life and is found in detectable amounts in normal older neonates and in children and in