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Evolution of glucose 6 phosphate dehydrogenate levels among newborns delivered with neonatal jaundice in Omdurman maternity hospital - Sudan

ISAM AHMED SADIK[1]
Phd, Clin. Biochemist
Associate Professor of Clinical Biochemistry
Omdurman Islamic University
MASHAER ABIDLQADER
MD, Pediatrician
Consultant Pediatrician, Neelain University
NAZRA SAYED OSMAN
MD, Pediatrician
Consultant Pediatrician, Turkey Hospital, Khartoum
NAGAH ABD ELWAHAB MOHAMMED
Phd, Clin. biochemist
Associate Professor of Clinical Biochemistry
Sudan University of Science and Technology
MOHMED ABID ALHMEED
MD, Pathologist
Associate Professor of Pathology, Omdurman Islamic University
ABDEL RAHAEM H.A. EL-BASSIR
Biologist
Assistant Professor, Omdurman Islamic University

Abstract:

Introduction: *Glucose-6-phosphate dehydrogenate deficiency, an X-linked recessive disorder, is the most common enzymopathy producing disease in humans. It is known to cause severe neonatal hyperbilirubinaemia.*

Aims and Objectives*: To determine G6PD levels in neonates delivered at Omdurman maternity Hospital with a view to determine the prevalence of G6PDdeficiency.*

[1] Corresponding author: isnaalah@outlook.com

Methodology*: Samples of blood were collected at delivery, from150 babies who met set criteria and 50 babies set as control Blood was assayed for G6PD levels using a quantitative in vitro test (RANDOX©).*

Results*: five subjects from 150 neonates have G6PD deficiency 3.3% one male with and 4 females. Male20% with expressed intermediate activity of G6PD and all 4 females (80%)with full enzyme deficiency.*

Conclusion*: There is a low prevalence of G6PD deficiency babies delivered at Omdurman maternity Hospital. enzyme deficiency appears to occur in females more than males.*

Key words: neonate, hyperbilirubinaemia, Glucose-6-phosphate dehydrogenate deficiency, maternity, hospital

INTRODUCTION:

Glucose-6-phosphate dehydrogenate deficiency, is the commonest inherited red cell enzymopathy worldwide. It affects around 400 million people globally with the highest prevalence in the tropics and subtropics [(1).]The highest prevalence rates occur in persons of African, Asian, Mediterranean or Semitic descent [(2).] Glucose-6-phosphate dehydrogenase deficiency causes a clinical spectrum of illness which includes a purely asymptomatic state, acute haemolytic episodes (from drugs, infections, ingestion of fava beans, diabetes mellitus), chronic haemolysis (hereditary non-spherocytic haemolytic anemia), and neonatal jaundice[(3).] Neonatal jaundice with pathological hyperbilirubinaemia develops more frequently in cases of G6PD[(4,5)]

The inheritance pattern in G6PD deficiency is X linked. Therefore, hemizygous males suffer from the effects of deficiency. Girls who are either homozygous or who are phenotypically deficient heterozygous (due to Lyonization) can demonstrate the manifestations of the disease. Genotypically

heterozygous females are generally asymptomatic. However, homozygous females showing clinical manifestations are also encountered(6).

Severe variant of G6PD deficiency may develop hyperbilirubinaemia sufficiently severe to cause kernicterus and death(7). Though rare, significant hyperbilirubinemia poses a potential threat for permanent neurological deficit or kernicterus(8). Studies indicate that insufficient hepatic metabolism of unconjugated bilirubin rather than increased hemolysis is the major contributor to neonatal hyperbilirubinemia. In addition, the UGT1A1gene mutation of promoter or coding region in G6PD(9) contributes to a Gilbert like condition in G6PD deficient infants. To date 400 biochemical G6PD variants[10,11]have been identified corresponding to 186 G6PD mutations [12,13]

Early detection of the at-risk populations helps in prevention of morbidity associated with the enzyme deficiency. One way of detecting the at-risk is by screening newborns. Newborn screening for G6PD deficiency has been implemented and incorporated into the screening program in several countries, such as in the Middle East, Eastern Europe and Southeast(7). This is however not the situation in Sudan. Although, not a major cause of neonatal mortality, its morbidity during neonatal period makes its early recognition and management important. Amongst the various etiological factors. The objective of our study was to determine the incidence of G6PD deficiency in hyperbilirubinemic neonates in Omdurman- Khartoum hospitals.

MATERIALS AND METHODS

This observation descriptive cross-sectional study was conducted at Maternity hospital in Omdurman which is located in Sudan The hospital is considered as referral centre for the

area of Omdurman. One hundred and fifty (150) neonates borne with jaundice, with no evidence of other disease admitted at hospitals and 50 neonates without jaundice and other disease in the same age, as control. The period of this study was from March to June 2014

Exclusion criteria included babies whose gestational age was greater than 42 weeks, babies with severe birthasphyxia, and those with congenital abnormalities. The samples collected in ethylenediamine tetraaceticacid (EDTA) anticoagulated tubes were screened for G6PD deficiency levels were assayed using diagnostic kit manufactured by RANDOXLaboratories Limited (Ardmore Diamond Road, Crumlin, Co.Antrim, United Kingdom, BT294QY.

LABORATORY METHOD:

For G6PD assay, 2ml of blood collected into EDTA containing bottles after delivery. Enzyme level was assayed using a quantitative in vitro test (RANDOX©). Its principle is based on reduction of $NADP^+$ by G6PD present in red blood cells. The NADPH generated fluoresces under UV light at a wave length of 340nm. Enzyme activity is determined by the rate of absorbance change. Red blood cell G6PD value of % 2.9U/gHb was regarded as normal.(14)

The study was approved by the ethical committee of Omdurman Islamic University for medical and health researches and The National Committee for Research Ethics(Ministry of Health) where the study was performed. SPSS for Windows (version 11.5; SPSS, Chicago, IL) was used for data management and statistical analysis. Relations among the different groups and variables were analyzed as percentages.

RESULTS:

The results obtained from the present study have shown that 5 (3.3%) neonates have G6PD deficiency and 145(96.7%) females 75(51%) male 70 (48.4%) subjects with normal glucose 6 dehydrogenase level, among 5 subjects whom suffering G6PD deficiency four of them(80%) all females, and only one (male) 20 % have intermediate activity of G6PD (Table1). Serum bilirubin levels were expressed as in three levels I,II ,III. Measure of the Bilirubin in first level *(10-14mg/dl)* 40(26.6%), second *(15-20mg/dl)* 48(30%), and in third more than 20 *mg/dl* 62(41.3%), respectively (Table 2)

All Neonates with G6PD need phototherapy and no one of them need exchange transfusion. One girl who developed kernicterus was delivered at home and brought to hospital on the 4th day after the development of jaundice. Jaundice is diagnosed and serum bilirubin is 345 μmol (20 mg/dl) and there is no family history of jaundice and treated was only with phototherapy. And there is no one die in all of our neonates in study. We tested also 50 neonatal concern as control and all result of them shown normal bilirubin level and normal activity of G6PD. Glucose-6-Phosphate Dehydrogenase levels that Were ≥2.9U/gHb were regarded as normal, while values ≤2.8U/gHb were regarded as deficient **.**

Table 1. The distribution of Glucose 6 phosphate Dehydrogenase deficiency in new born with neonatal jaundice.

Glucose 6 phosphate deficiency Status	Female	Male
Normal	75 (95%)	70 (98.6%)
Deficient	4 (5%)	1 (1.4%)
Total	79 (100%)	71 (100%)

Table 2: Distribution of serum bilirubin level within all subjects and severity of jaundice among infants with normal and G6PD deficiency

Serum bilirubin Mg/dl`	All subjects	Female	Male	Status of G6FD Normal	Status of G6FD deficiency
Level I (10-14)	40(26.6%)	18(22.8%)	22(31%)	40(27.6%)	0(0%)
Level II(15-20)	48(32%)	25(31.6%)	23(32,4%)	44(30.3%)	4/150(3%)
Level III ≥ 20	62(41.4%)	36(45.6%)	26(36,6%)	61(42.1%)	1/150(.7%)

DISCUSSION:

Our study shows that there is a relationship between neonatal jaundice and G6PD deficiency in neonates who were born in maternity hospital in Omdurman, which is second city in the capital of Sudan (Khartoum), which is the reference hospital. Five newborns jaundiced 3.3%presented with red cell G6PD deficiency all of them treated with phototherapy.

In this current study the majority of cases 4/150 3%(G6PD-dificiency) fall in the second category, which bilirubin level fall in the range 15-20mg/dl.

Neonatal jaundice is the most common clinical manifestation of G6PD deficiency. It has been reported that one-third of children with G6PD deficiency develop neonatal jaundice. [15]

In this current study glucose 6phosphate dehydration deficiency is 3.3% and in other countries worldwide ranges from 0.09% in Italy [16] 3.2% in Iran [17] 12.8%in the African-American population in the US [18], (4%) icteric Egyptian infants [19], an X-linked recessive disorder. from these observation it was evident that the risk of G6PD-deficient infants developing severe jaundice varies widely in different countries and population. It has been suggested that this variation may be due to additional environmental or genetic factor or both [20].

In this current study most of neonate suffering from hyperbilirubinaemia, 41% (61 cases) the levels of bilirubin is over 20mg/dl and this may be danger values.

In the present study, serum total and indirect bilirubin levels were significantly higher among the G6PD deficiency subjects compared to subjects with normal G6PD activity. This observation was consistent with several studies that reported higher maximum total serum bilirubin levels in G6PD deficient jaundiced neonates compared to G6PD normal icteric neonates.[21-23]

Early detection of G6PD deficiency is useful in neonatal jaundice cause to avoid health problems which may result from hemolytic jaundice in the future. It's necessary to study the distribution of this enzyme deficiency among the different ethnic group and identify the high prevalence areas all around Sudan.

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