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Screening of G6PD Deficiency in Cord Blood for Newborns Delivered in the Maternity Hospital in Hawler Governorate

Dr. Avan A Ramadan[1], Dr. Tara H Khorsheed*[2], Dr. Dler A Saber [3]

1. MSC of pediatrics, department of pediatrics at Azadi Teaching Hospital
2. MSC of Embryology, department of infertility at Azadi Teaching Hospital
3. High Diploma of oncology, department of oncology and hematology at Kirkuk Oncology Center

***Corresponding Author: contact email** tarahzangana33@gmail.com*

Original Article

ABSTRACT

***Background**: Glucose -6- phosphate dehydrogenase (G6PD) is a commonly occurring genetic enzyme disorder, causing the most devastating potential complication in the newborn which may result in kernicterus . **Objectives**: To determine the prevalence of G6PD deficiency in newborns, and to assess the relationship of G6PD deficiency with history of consanguinity and family history and neonatal outcomes*

***Patients and Methods**: This study was prospective and undertaken from the 1st of February to the 21st of the same month, 2013. A total 500 newborn delivered in the Maternity Hospital at Erbil city were screened for the qualitative measurement of G6PD activity by a commercial kit (KIMI, Pajouhan). The sample of cord blood in heparinized tube were transferred to the lab within 2 hours of delivery. The results were interrupted as sufficient or deficient. **Result**: Of the 500 newborn screened, 36 neonates were found to have G6PD deficiency (21 males, 15 females).the overall frequency of G6PD deficiency was 7.2%. frequency in male population was 4.2% (21 out of 251 male neonates) and in female population was 3.0% (15 out of 249 female neonates). The male to female ratio was 1.4:1. The enzyme activity was interpreted as sufficient or deficient, with normal blood film of all deficient neonates. Family history has a positive effect on prevalence of G6PD (p=0.0005) , while consanguinity has no effect on prevalence of G6PD deficiency (p=0.11).*

***Conclusion**: routine neonatal screening in Erbil, with this relatively high prevalence of G6PD deficiency 7.2% (4% male, 3.2% female) is justified and meets the World Health Organization recommendation.*

Keywords: G6PD, Epidemiology, Pathophysiology, Cord blood

1.INTRODUCTION

Glucose 6 phosphate dehydrogenase deficiency was discovered in 1950s as an outgrowth of an investigation of hemolytic anemia occurring in some individuals treated for malaria with 6-methoxy-8-aminoquinoline drugs. cords reported the occurrence of acute hemolysis in these patients in 1926 [1].G6PD deficiency is a wide spread genetic defect and hereditary deficiency of G6PD turned out to be among most common genetic disorders affecting more than 400 million people worldwide [2]. It occurs with increased frequency throughout Africa, Asia, the Mediterranean, and the Middle east. In the United State, black males are most commonly affected, with a prevalence of approximately 10% [3]. Meanwhile frequency of g6pd deficiency among predominantly Kurdish population in Northern Iraq is 10.9% which is higher than that reported from neighboring Iranian Kurdish population [4.]

Pathophysiology

The G6PD/NADPH pathway is the only source of reduced glutathione in red blood cells. The role of red cells as oxygen carriers put them at substantial risk of damage from oxidizing free radicals except for the protective effect of G6PD/NADOH/glutathione [5].

When all remaining reduced glutathione is consumed, enzymes and other proteins (including hemoglobin) are subsequently damaged by the oxidants, leading to electrolyte imbalance, cross-bonding and protein deposition in the red cell membranes. Damaged red cells are phagocytized and sequestered (taken out of circulation) in the spleen [6]. The hemoglobin is metabolized to bilirubin (causing jaundice at high concentration). The red cells rarely excreted directly by the kidney, but this can occur in severe cases, causing acute renal failure [7].

classification of G6PD deficiency:

the world health organization classifies G6PD genetics variants into 5 classes [7]:

1. severe deficiency (<10% activity) with chronic (non spherocytic)hemolytic anemia.
2.severe deficiency (10%activity)with intermediate hemolysis.
3. mild deficiency(10-60%activity) hemolysis with stressors only.
4. non-deficient variants, no clinical squeal.
5. increased enzyme activity, no clinical symptoms.

2. PATIENTS and METHODS

***Study design*:** The prospective study was undertaken over 3 weeks period. The target group included 500 newborns (out of 967 delivery during that period) delivered at the Maternity Teaching Hospital in Erbil Government, Iraqi Kurdistan, for the period from 1st Feb.to 21st Feb. 2013. The included sample were newborns in the delivery room, of both vaginal delivery and cesarean section.one ml of the blood sample collected in to a heparinized tube, and were transferred to Areo, the private laboratory clinic in Erbil city within two hours of collection.

***Sample of the study*:** G6PD quantitative enzymatic level estimation were done by fluorescent spot test, using a commercial kit. The kit consisted of 2 parts, a solution and a filter paper.

Blood film were obtained for the 36 G6PD deficient neonate, to determine hemoglobin level, reticulocytes count, and evidence of hemolysis.

These deficient neonate were followed up for the development of jaundice for the three weeks of life, and if received treatment or not.

Data management and statistical analysis:

Data were collected and entered into SPSS version 25 to generate the general characteristics of the study. Each entry was double checked to avoid errors or inconsistency.Variables summarized and presented as frequency and percentages. Cross-tabulation used for analysis of the results, chi square Fisher's exact test used to determine the P value. Level of significance, P. value, set at < 0.05 to be significant.

3. RESULTS

Five hundred subjects enrolled in the study, no case was excluded. They were 251 (50.2%) male and 249 (49.8%) females, and were screened over a period of nearly three weeks, as known in table 1. The table also shows the frequency of G6PD deficiency, 36 neonates were found to be G6PD deficient, of them 21 males, and 15 females.

Gender of G6PD deficient neonates: The overall frequency of G6PD deficiency was 7.2% frequency were 4.2% and 3%, in male and female neonates, respectively, as shown in table 2.

Family history of G6PD deficiency: Out of the 500 newborn that were screened ,30 had positive family history of G6PD (6%), 12 were males and 18 were females. Of the 30 with the +ve family history of G6PD deficiency, 10 had G6PD deficiency(4 males and 6 females), as shown in table 3, which shows the relation between those of positive family history and the frequency of G6PD

deficiency. p value=0.0005 for the positive family history, significant from statistical point of view.

Frequency of consanguinity: The frequency of the consanguinity was 196 (39.2%). As shown in table 4. Of the 196 (39.2%) newborn with +ve family history of consanguinity, 19 of them had G6PD deficiency. The p value of 0.11 considered consanguinity not significant as a factor affecting the prevalence of G6PD deficiency as shown in table 4. In this study, hematological estimation had done for patient's parents. The results showed that the blood film of the parents were normal with no evidence of hemolysis. Furthermore, their mean reticulocytes count were 1.7 and mean hemoglobin was 12.2 mg/dl.

In the present study only 7 neonates developed jaundice after follow up, this number considered insignificant outcome of G6PD deficiency with P value of 0.103 as shown in table 5.

Table 1. level of G6PD and sex of the neonate

Level of G6PD	**Male**		**Female**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Sufficient	230	91.6	234	94.0	464	92.8
Deficient	21	8.4	15	6.0	36	7.2
Total	251	50.2	249	49.8	500	100.0

Table 2. the gender of G6PD deficiency

Gender	**No.**	**%**
Male	21	4.2
Female	15	3
Total	**36**	**7.2**

Table 3. Relationship between level of G6PD deficiency and family history of G6PD in both genders of neonates.

Gender	**Level of G6PD**	**Family history of G6PD**		**Total**
		Negative	**Positive**	
Male	Sufficient	222	8	230
	Deficient	17	4	21
Total		**239**	**12**	**251**
Female	Sufficient	222	12	234
	Deficient	9	6	15
Total		**231**	**18**	**249**

Table 4. Frequency distribution of consanguinity of parents of the studied group

Consanguinity	Frequency	Percent
No	304	60.8
Yes	196	39.2
Total	**500**	**100.0**

Table 5. Relationship between consanguinity of parents and level of G6PD deficiency

Consanguinity	Level of G6PD		Total
	Sufficient	Deficient	
Yes	177	19	196
No	287	17	304
Total	**464**	**36**	**500**

Table 6. Relationship between outcome and gender of the G6PD deficient patient.

Gender	Having jaundice		No symptoms		Total
	No.	%	No.	%	
Male	2	9.5	19	90.5	21
Female	5	33.3	10	66.7	15
Total	7	19.4	29	80.6	36

DISCUSSION

G6PD deficiency has long been recognized as a common inherited hematological disorder in Iraqis including Kurds [6]. Kurds make up about 20% of the population of Iraq, and they live in Northern and Northeastern Iraq. The area covered by the current by the current study in northern Iraq lies at the center of Kurdish inhabited areas Mediterranean Region [8,13]. Earlier limited studies on G6PD deficiency among Iraqi Kurdish males living in Baghdad have reported frequencies of 7.6-8.8% [8,9], which is higher than the frequency of the males 4% as documented in this study. The later rate is also lower than rates reported from neighboring Kurdish population of Western Iran 10, but is remarkably less than reports from Kurdish Jews, who have one of the highest rates worldwide of up to 58% [11].

Previous studies from other parts of Iraq revealed variable results from Baghdad (6.1-12.4%)[12], and 15.3% from Basra [5], Iraq is situated within a region of high frequency of G6PD deficiency genotype, with a carrier frequency in the population of 6.3% [12]. A ratio of males to females was 1.4:1 in our study in our study, while in the previous studies in Baghdad [14] and Mosul [15] were 1.6:1 and 3.4:1 respectively. Other studies in other countries like Egypt showed a male to female ratio of 3.2:1 [16]. Although it mainly affects males but it should not be excluded in female cases of hemolysis as G6PD deficiency is an X-linked hereditary disease mainly affecting males, but should also be considered in females with an oxidative hemolysis as reported in other studies [18]. The preponderance of females noted in some studies in other countries in eastern Mediterranean Region may be due to high rates of consanguinity [11], leading to increased numbers of homozygous females in addition to a high frequency of inactivation of the normal X chromosome in female heterozygotes [15] . while in our study history of consanguinity was a non- significant factor (p value >0.05).

As our results showed that from the seven neonates 1.4% who developed jaundice later on, neonatal jaundice was found in study in Baghdad (11.5%) [14]. And the previous study in Mosul (14.8%) 17 and 10.9% of neonates were found to have G6PD deficiency in similar study done among Kurdish people in northern of Iraq [4]. Sever neonatal jaundice, particularly when it requires exchange transfusion, should alert pediatricians to the possibility of G6PD deficiency 8. Currently most hospitals routinely test for G6PD when screening neonates before they are discharged from hospital [10], while it is not done routinely in our hospitals in Iraq unless there is positive family history or severe hemolysis or neonatal jaundice. Newborn screening for G6PD deficiency is not performed also routinely in the United States [19].

A positive family history of G6PD deficiency in this study was reported to be 6% which was significant (p value of 0.0005), but reported to be at higher rate in Baghdad [14] and Mosul 13.6% [17]. This may be due to the observation that many patients are asymptomatic and unaware they are G6PD deficient unless they are investigated or exposed to an oxidizing agent [9].

CONCLUSIONS

Consanguinity considered as non-significant factor affecting the frequency of G6PD deficiency. Family history of G6PD deficiency in previous member considered significant factor affecting the frequency of G6PD deficiency. The frequency of neonatal jaundice among G6PD deficient neonates was non-significant outcome , as many were asymptomatic in the neonatal period.

Therefore we recommend the necessity of neonatal screening on cord blood samples of both sexes for G6PD deficiency and the need to watch closely for development of hyperbilirubinemia. Additionally, health education is needed to increase the awareness of health professionals and the public about this problem.

Ethical Clearance

Before collecting blood samples, this study was approved by Scientific Committee at Erbil Council for Medical Specialization. Informed consents were obtained from all mothers accepted to participate in the study.

Conflict of interest: None declared by the authors

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