Prediction of Glucose-6-Phosphate Dehydrogenase Deficiency in Newborns

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Objective: To evaluate the positive and negative predictive value of the positive family history of G6PD in predicting the actual G6PD of newborns compared to the mean total serum bilirubin (TSB) level for one-week.

Design: A Prospective Study.

Setting: Salmaniya Medical Complex and Jidhafs Maternity Hospital, Bahrain.

Method: The mothers filled a survey, and the newborns underwent serum bilirubin check during the first week of life (day one, day two to four and day five to seven). The G6PD activity status was tested as part of the newborn screen for all the newborns in Bahrain.

Result: Four hundred twenty-seven newborns were included in the study; males were 219 (51.3%). Two hundred eighty-eight (67.4%) of the newborns had G6PD normal activity and 139 (32.6%) were G6PD deficient. Two hundred fifty-one (58.8%) had a positive family history of G6PD deficiency while 176 (41.2%) did not have a family history of G6PD deficiency. The positive predictive value (PPV) for family history of G6PD deficiency is 47.4%, while the negative predictive value (NPV) is 89.1%. The mean serum bilirubin level for newborns with G6PD reduced activity was 139±52µmol/L. The serum bilirubin level was higher if the previous sibling required phototherapy, 157 µmol/L ± 50 µmol/L (P-value<0.001).

Conclusion: Family history could be helpful for clinicians but it should be considered with caution. The negative predictive value is 89.1%, which means that 20 (4.7%) of the newborns had no family history of G6PD deficiency and still have G6PD deficiency.

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The positive predictive value is calculated by dividing the true positive by the sum of the true positive and false positive, while the negative predictive value is calculated as the true negative divided by the sum of the true negative and false negative[1,2].

Glucose-6-phosphate dehydrogenase (G6PD) reduced activity is a global health problem[3]. It affects more than 400 million people around the world[3]. People who have G6PD deficiency are mostly asymptomatic but may experience severe hemolysis and develop jaundice if exposed to certain drugs, infections or ingest fava beans[3-7]. G6PD is very common in the Kingdom of Bahrain[4]. In one study, G6PD deficiency was found in 18% of males and 10% of females based on the newborn screening test[4].

G6PD in a newborn may lead to significant hyperbilirubinemia and it is a risk factor for subsequent bilirubin-induced neurologic dysfunction (BIND)[8-13]. Newborns with G6PD and jaundice are at higher risk compared to a jaundiced newborn without G6PD[8-10]. Clinicians dealing with jaundice in newborns in G6PD endemic areas are often faced with difficulties especially when the newborn G6PD status is still not known.

In this study, we tested the positive and negative predictive values for a positive family history of G6PD in predicting the actual G6PD status of the newborn. The positive and negative family history of G6PD reduced activity in the family helps the clinicians in utilizing the information for managing a newborn with hyperbilirubinemia.

The aim of this study is to evaluate the positive and negative predictive value of positive family history of G6PD in predicting the actual G6PD status of the newborn compared to the mean total serum bilirubin (TSB) level for one-week.

METHOD

A prospective study was performed in Bahrain from May to September 2015. A survey was conducted in the two maternity

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hospitals. Informed consent was obtained from the mothers. The G6PD activity status was tested for all of the newborns. The newborns were followed for one week with three total serum bilirubin readings; the first reading was taken on day one, the second reading was taken between day two and day four and the third reading was taken between day five and seven.

The data was entered and analyzed using Statistical Package SPSS version 20.

RESULT

Four hundred twenty-seven patients were included in the study; 219 (51.2%) were males and 345 (80.8%) were Bahrainis. The consanguinity rate between the newborn parents was 54 (12.7%), and most of the relations were first degree, 46 (10.8%). Two hundred fifty-one (58.7%) had a positive family history of G6PD deficiency. Two hundred seventeen (50.8%) who had a family history of G6PD reduced activity were first-degree relatives. Two hundred eighty-eight (67.4%) had G6PD normal activity, and 139 (32.6%) were G6PD deficient. Sixty-four (15%) of the 427 newborns had a sibling who required phototherapy for hyperbilirubinemia, see table 1.

Table 1: Newborns' Characteristics

Characteristic		n	%
Baby Gender	Male	219	51.4
	Female	208	48.6
Baby Nationality	Bahraini	345	80.9
	Non-Bahraini	82	19.1
Mother and Father Consanguinity	No	373	87.3
	Yes	54	12.7
Previous Sibling/s Required Phototherapy	No	363	84.9
	Yes	64	15
Family History of G6PD Reduced Activity	No	176	41.3
	Yes	251	58.7
Newborn G6PD Activity Status	Normal	288	67.4
	Reduced	139	32.6

One hundred nineteen (27.9%) of the newborns had G6PD deficiency among the 251 newborns with a family history of G6PD reduced activity and 109 (25.5%) had G6PD deficiency among the 217 (50.8%) newborns with a family history of a first-degree relative with G6PD deficiency, see tables 2 and 3. Only twenty-two (15.8%) of the 139 newborns with G6PD reduced activity had at least one sibling who required phototherapy, see table 4.

The mean total serum bilirubin for one week for 251 (58.8%) newborns with a positive family history of G6PD reduced activity was 129 µmol/L ± 52 µmol/L and the mean total serum bilirubin for the 176 (41.2%) newborns without family history of G6PD reduced activity was 127 µmol/L ± 53 µmol/L, (P-value=0.698).

Table 2: Family History and the G6PD Status

Family History of G6PD	Baby G6PD Status		Total
	Reduced	Normal	
Positive for Reduced G6PD	119	132	251
Negative for Reduced G6PD	20	156	176
Total	139	288	427

Table 3: Consanguinity and G6PD Reduced Activity

Relative with G6PD Reduced Activity	Baby G6PD Status		Total
	Reduced	Normal	
First Degree Relative	109	108	217
Second Degree Relative	10	24	34
Total	119	132	251

Table 4: Sibling Phototherapy and the G6PD Status

Number of Sibling/s Required Phototherapy	Baby G6PD Status		Total
	Reduced	Normal	
One or More	22	42	64
None	117	246	363
Total	139	288	427

The one week mean serum bilirubin level was 139 µmol/L ± 52 µmol/L for newborns with G6PD reduced activity, while it was 124 µmol/L ± 52 µmol/L for those with normal G6PD activity (P-value=0.005).

Newborns with a sibling who previously required phototherapy had a mean total serum bilirubin level of 157 µmol/L ± 50 µmol/L. Newborns without a sibling who previously required phototherapy for hyperbilirubinemia had a mean total serum bilirubin level of 124 µmol/L ± 51 µmol/L (P-value<0.001), see table 5.

Table 5: Mean Total Serum Bilirubin TSB for One Week

		N	%	Mean TSB ± SD µmol/L	P-value
Family History of Reduced G6PD Activity	Positive	251	58.8	129±52	0.698
	Negative	176	41.2	127±53	
Newborn G6PD Activity Status	Normal	288	67.4	124±52	0.005
	Reduce	139	32.6	139±52	
The Presence of a Sibling Who Required Phototherapy	One or more	64	15.0	157±50	< 0.001
	None	363	85.0	124±51	

The positive predictive value (PPV) for family history of G6PD deficiency is 47.4%, while the negative predictive value (NPV) is 89.1%, see table 2.

DISCUSSION

G6PD deficiency is an enzyme disorder of the red blood cells[14-20]. It shortens the lifespan of the red cells in response to stresses and oxidant exposure[3-9]. It is known as favism, where acute hemolysis occurs after fava beans ingestion or even smell inhalation in certain situations[1,2,14,15].

The majority of the newborns in the study group were Bahrainis. The incidence of G6PD reduced activity in our study was 32%; this is close to the 28% overall incidence in

Bahrain which was detected in a previous newborn screening test[4]. The rate of consanguinity in our study was high (12.7%) and the majority were first degree. Intermarriage is one of the major causes of recessive disorders expression. This problem has to be seriously addressed in our community and preventive measures should be sought.

The mean serum bilirubin level was significantly higher among newborns with G6PD reduced activity if compared to newborns with normal G6PD activity. Nevertheless, newborns that had a sibling who required phototherapy during the neonatal period had a higher mean total serum bilirubin level compared to newborns without a previous sibling who required phototherapy. The presence or absence of a positive family history of G6PD did not reflect any difference in the mean total serum bilirubin level.

In our study, we found that the negative predictive value of the presence of family history of G6PD deficiency is 89.1%, which means that the false negative rate is 4.7% among those newborns who have no family history of G6PD reduced activity. The positive predictive value is low at 47.4%, which means that 52.6% of the newborns who had positive family history of G6PD deficiency, had a normal G6PD status themselves. The high rate of false positive could lead to over-treatment of 52.6% of the newborns with hyperbilirubinemia and positive family history of G6PD reduced activity, while they have a normal G6PD activity.

G6PD reduced activity has a recessive X-linked mode of inheritance; therefore, males who carry the X-chromosome, inherited from their mothers are affected while the females who carry two affected alleles or one affected active allele are diseased[1,2]. Women could be carriers, which could contribute to having unrecognized carriers in the family who could transfer the affected gene to their offspring.

One limitation of the study that should be addressed is the dependence on the mother's knowledge of the presence or absence of a family member who has G6PD reduced activity and the absence of a confirmatory medical test of such history.

CONCLUSION

Family history could be helpful for clinicians, but they must be cautious. The negative predictive value was 89.1%, which means that 20 (4.7%) of the newborns had no family history of G6PD deficiency and still have G6PD deficiency. The previous sibling who required phototherapy could be a predictor for a high serum bilirubin in the newborn. We suggest further multicentric study.

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