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ORIGINAL ARTICLE

Frequency of glucose-6-phosphate dehydrogenase enzyme deficiency in newborns with prolonged jaundice

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ABSTRACT

Objective: The aim of the study was to determine the frequency of glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency in preterm and term newborns with prolonged jaundice.

Material and Methods: A total of 670 preterm and term newborns who applied to Zeynep Kamil Training and Research Hospital Pediatric Health Polyclinic with neonatal jaundice between January 1, 2014, and April 1, 2018, were retrospectively screened and included in the study. Birth weight, sex, gestational week, postnatal age, gender, phototherapy, and need for exchange transfusion were recorded. Laboratory evaluations included blood group typing of mother and newborn, serum total and direct bilirubin levels, reticulocyte count, and erythrocyte G6PD level. SPSS 22.0 was used as an evaluation program.

Results: G6PD enzyme level was detected in 374 (55.8%) of the cases. Enzyme deficiency was detected in 12 (3.2%) cases. There was no statistically significant difference between the G6PD-deficient group and the G6PD-normal group in terms of all parameters except the total biluribin level. There was no case in whom exchange transfusion was performed with high bilirubin values. However, phototherapy was applied in 231 cases due to high bilirubin levels. It was determined that there was no need for phototherapy in all cases with G6PD levels.

Conclusion: G6PD enzyme deficiency should be investigated in patients with prolonged jaundice.

Keywords: Glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency, hyperbilirubinemia, prolonged jaundice.

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INTRODUCTION

Neonatal jaundice is observed in 50%–70% of healthy term babies and 80% of preterm babies.[1–3] Blood group incompatibility and erythrocyte enzyme defects are the most common causes of neonatal jaundice. Although more than fifteen enzyme defects have been identified in erythrocytes, glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency has an important place in that it is the most common and also causes hemolytic anemia.[4–6] Severe neonatal jaundice, favism, acute hemolytic anemia, and hereditary nonspherocytic hemolytic anemia may develop in the neonatal period in G6PD deficiency.[7–9]

Glucose-6-phosphate dehydrogenase is the first and control enzyme of the pentose phosphate metabolic pathway, which protects hemoglobin (Hb) in the erythrocyte and proteins in the cell from oxidant effects. It is inherited as an X-linked recessive manner.[6,10] Jaundice lasting longer than 2 weeks in term infants and longer than 3 weeks in preterm infants is considered prolonged jaundice, and it is recommended to check the G6PD level.[11] Early detection of G6PD deficiency is important in preventing hemolysis triggered by drugs, beans, and infection-like oxidant stress, and in increasing the patient's quality of life.[6]

This study aimed to determine the frequency of G6PD deficiency in the etiology of prolonged jaundice in preterm and term newborns and to compare clinical and laboratory findings according to the enzyme level.

MATERIAL AND METHODS

Preterm and term newborns who were referred to Zeynep Kamil Maternity and Children's Training and Research Hospital Pediatrics Polyclinic between January 1, 2014, and April 1, 2018, were screened retrospectively with ICD-10 code "P59.9: Neonatal jaundice." Patients with a total bilirubin (Tbil) value of ≥10 mg/dL for 3 weeks in preterm newborns and ≥10 mg/dL for more than 2 weeks in term newborns were selected as the sample group. Newborns with direct hyperbilirubinemia were excluded from the study.

Clinical findings (gestational week, postnatal age, gender, birth weight, infant and mother's blood types, whether phototherapy was applied, and whether exchange transfusion was performed) were recorded from the patient records. Laboratory analyses (Tbil, direct bilirubin, G6PD, hemoglobin, and reticulocyte levels were screened.

Glucose-6-phosphate dehydrogenase levels were grouped according to the kit reference range. Cases were grouped as follows: cases with enzyme levels below the lower reference value of the kit (<7.50 U/g Hb) as "low G6PD level" and cases with enzyme levels equal to or above the lower reference of the kit (≥7.50 U/g Hb) as "G6PD level normal group."

This study was approved by the institutional ethical committee on January 9, 2019, with decree 11. SPSS 22.0 program was used to evaluate the findings. In the statistical analysis of quantitative data, the conformity of the data to the normal distribution was investigated by Kolmogorov–Smirnov and Shapiro–Wilk tests. For comparisons between groups (sex, week of birth, and G6PD enzyme level), Student's t-test was preferred for normally distributed variables and Mann–Whitney U test was preferred for non-normally distributed parameters. Pearson's Chi-squared test was used to compare qualitative data. The results were evaluated within the 95% confidence interval, and statistical significance was accepted at p<0.05.

Table 1: Clinical and laboratory findings of G6PD enzyme level groups

	n	Mean	SD	Total (%)
"Low" group				
Gestational week	12	38.12	1.45	3.2
Birth weight (g)	11	3326.82	315.61	3.4
Postnatal age (days)	12	21.25	7.86	3.2
Tbil (mg/dL)	12	11.35	0.82	3.2
Dbil (mg/dL)	12	0.50	0.14	3.2
G6PD (U/g Hb)	12	5.92	2.04	3.2
Hb (g/dL)	11	13.36	2.59	3.1
Reticulocyte (%)	6	1.11	0.32	4.4
"Normal" group				
Gestational week	362	37.79	1.82	96.8
Birth weight (g)	316	3116.77	540.61	96.6
Postnatal age (days)	361	23.15	8.20	96.8
Tbil (mg/dL)	362	13.33	2.23	96.8
Dbil (mg/dL)	360	0.55	0.14	96.8
G6PD (U/g Hb)	362	20.76	6.77	96.8
Hb (g/dL)	348	13.63	2.42	96.9
Reticulocyte (%)	130	1.33	1.87	95.6

G6PD: Glucose-6-phosphate dehydrogenase; Tbil: Total bilirubin; Dbil: Direct hyperbilirubinemia; Hb; Hemoglobin; SD: Standard deviation.

RESULTS

A total of 670 patients were included in the study. There were 374 cases whose G6PD enzyme levels were checked. G6PD enzyme deficiency was detected in 12 (3.2%) cases. The clinical and laboratory data of all cases are summarized in Table 1. A significant difference was found between the groups with low and normal G6PD enzyme levels only in terms of Tbil levels (p<0.05). No difference was observed in terms of other parameters (p>0.05) (Table 2).

There was no case in whom exchange transfusion was performed with high bilirubin values. However, phototherapy was applied in 231 cases due to high bilirubin levels. When a total of 670 cases with prolonged jaundice were evaluated in the study, 4.0% (27 cases) needed phototherapy in the preterm newborn group, while this rate was 30.4% (204 cases) in the term newborn group (p<0.05) (Table 3). It was determined that there was no need for phototherapy in all cases with G6PD levels.

DISCUSSION

This study, which aimed to determine the frequency of G6PD enzyme deficiency in the etiology of prolonged jaundice in preterm and term newborns, was carried out in a study group consisting of 670 newborns with prolonged jaundice. G6PD enzyme level was detected in 374 (55.8%) of the cases. Enzyme deficiency was detected in 12 (3.2%) cases of which 8 (2.1%) were male and 4 (1.1%) were female.

Table 2: Statistical calculations between groups depending on G6PD level

Parameters	"Low" group			"Normal" group			p
	n	Min–max	Median	n	Min–max	Median	
Gestational week	12	36.00–40.71	37.86	362	32.00–41.29	38.00	0.913
Birth weight (g)	11	2830.0–3800.0	3330.00	316	1800.0–4550.0	3170.00	0.182
Postnatal age (days)	12	14.00–32.00	18.00	361	14.00–54.00	21.00	0.278
Tbil (mg/dL)	12	10.02–12.55	11.62	362	10.00–22.12	12.87	0.001
Dbil (mg/dL)	12	0.24–0.72	0.48	360	0.26–1.44	0.53	0.283
Hb (g/dL)	11	8.80–16.60	13.45	348	7.40–20.20	13.30	0.988
Reticulocyte (%)	6	0.84–1.63	1.00	130	0.16–18.60	1.00	0.719

*: Significant values were obtained by Mann–Whitney U test; G6PD: Glucose-6-phosphate dehydrogenase; Tbil: Total bilirubin; Dbil: Direct hyperbilirubinemia; Hb: Hemoglobin; Min: Minimum; Max: Maximum.

Glucose-6-phosphate dehydrogenase enzyme deficiency, which affects approximately 400 million people worldwide, is one of the most heterogeneous genetic diseases. It is also one of the most common of all clinically significant enzyme disorders. G6PD enzyme deficiency has been reported between 2% and 27% according to ethnic differences.[12,13] In cases with hyperbilirubinemia, its frequency has been reported to be 10.5%–22.1%.[12,14] While a low prevalence rate of 1.5%[15] was found in Spain, 2.1%[16] in France, and 1.6%[17] in Singapore, Saudis,[18] Nigerians,[19] Bahraini,[20] and African Americans[21] reported very high rates of 18.4%, 40%, 42%, and 14%, respectively.

In a literature search, in a study involving 100 term newborns with prolonged jaundice, the frequency of G6PD enzyme deficiency was reported as 3% (2 cases) out of 66 cases requiring hospitalization due to jaundice.[22] In a similar study performed on 53 term newborns born in Trakya University Hospital with prolonged jaundice, G6PD enzyme deficiency was found in 3 (5.7%) cases.[23] In another study conducted in Ankara on 82 patients with prolonged jaundice, the rate of G6PD enzyme deficiency was reported as 1.2%.[24] An evaluation study was conducted on 237 term newborns, 137 (57.8%) of whom were boys, who were followed up in the newborn unit of Yüzüncü Yıl University Faculty of Medicine with the diagnosis of pathological indirect hyperbilirubinemia and prolonged jaundice. G6PD enzyme deficiency was found to be 0.4% as the cause of prolonged jaundice. The reason for this very low rate in the same study can be explained by the fact that the G6PD level was checked only in cases whose cause of hyperbilirubinemia could not be determined, but not in all cases.[25] In another study in England in which cases with prolonged jaundice were analyzed, G6PD deficiency was found at a rate of 1.9%.[26]

In a study investigating G6PD enzyme deficiency on a total of 100 male newborns hospitalized for hyperbilirubinemia in the Süleymaniye Semiha Şakir Maternity Hospital Pediatrics Clinic, enzyme deficiency was found in 6 (6.0%) cases.[27] G6PD enzyme deficiency was found in 3 (0.5%) of 575 newborns with indirect hyperbilirubinemia who were hospitalized in the neonatal intensive care unit of Ankara Dışkapı Pediatrics Training and Research Hospital.[28] In a study conducted at Hacettepe University in Ankara, G6PD enzyme deficiency was found in only 55 (1.12%) of 4906 cases of term and preterm newborns with indirect hyperbilirubinemia.[29] In another study conducted in Istanbul in 68 newborns with hyperbilirubinemia, the rate of G6PD enzyme deficiency was found to be 2.94%.[30] In another study investigating the clinical and laboratory characteristics and risk factors of 240 babies admitted to the neonatal unit for jaundice, G6PD enzyme deficiency was found in 2 (0.83%) newborns.[31]

Table 3: Distribution of groups according to need for phototherapy treatment

	Phototherapy performed		Phototherapy not performed		p
	n	Total (%)	n	Total (%)	
Gender					
Boy	145	62.8	259	59.0	0.343
Girl	86	37.2	180	41.0	
Birth week					
Preterm	27	11.7	112	25.5	0.000
Term	204	88.3	327	74.5	

*: Significant values were obtained by Pearson's Chi-squared test.

Glucose-6-phosphate dehydrogenase enzyme deficiency was found to be the cause of hyperbilirubinemia in 24 (3.8%) of 624 term newborns, 330 boys and 294 girls, with indirect hyperbilirubinemia followed in Zeynep Kamil Maternity and Children's Training and Research Hospital between March 2001 and September 2004. Eighteen (75%) of the cases with G6PD enzyme deficiency were male and 6 (25%) were female. In this study, which was carried out in our hospital in different years, exchange transfusion was performed in a total of 98 inpatients. G6PD enzyme deficiency was found in 8 of these cases, and G6PD enzyme level was found to be normal in the remaining 90 cases.[32] The rate of G6PD enzyme deficiency detected in this study (3.8%) was found to be in alignment with the rate found in our study (3.2%).

As a result, the frequency of G6PD enzyme deficiency in our study (3.2%) was lower than some studies[3,22,33,34] and higher than some studies[24,29,31] reported in the literature. It was also found to be parallel to several studies.[22,30] In addition, the rate of G6PD enzyme deficiency of 3.2% obtained in this study was found to be higher than the rates (0.5%–2.9%) reported for Turkey by the World Health Organization.[35] We think that this is because our study included only newborns with prolonged jaundice.

In our study, we found that the rate of phototherapy in term babies was higher than in preterm babies. We think that this difference is because premature babies are followed up more in the neonatal control outpatient clinic, and, in fact, premature babies need more phototherapy.

CONCLUSION

We found the frequency of G6PD enzyme deficiency to be 3.2% in infants with prolonged jaundice in our study. Although this rate is not significantly high, it should be noted that pathological jaundice should be examined with detailed research. It should not be forgotten that hemolytic jaundice can develop in any period of the neonatal period without any previous symptoms. G6PD enzyme deficiency should be investigated in patients with prolonged jaundice leading to hemolysis.

Statement

Ethics Committee Approval: The Zeynep Kamil Maternity and Children's Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 09.01.2019, number: 11).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – HT; Design – HT; Supervision – RGSY, AB; Resource – HT; Materials – HT; Data Collection and/or Processing – HT, RGSY; Analysis and/or Interpretation – HT, RGSY; Literature Search – HT; Writing – HT; Critical Reviews – HT, AB.

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