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Prevalence of Glucose-6-Phosphate Dehydrogenase Deficiency in Cord Blood and Its Relation to Neonatal Indirect Hyperbilirubinemia in Fayoum Governorate

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Abstract

Introduction: A lack of Glucose-6-phosphate dehydrogenase (G6PD) impairs the production of decreased glutathione and contributes to red cells being damaged by oxidative metabolites, resulting in hemolysis. Clinical manifestations of deficits in neonates may include hyperbilirubinemia or even kernicterus.

Aim of the Work: The purpose of this research is to discover the incidence of G6PD deficiency in newborns in cord blood and its relation to neonatal indirect hyperbilirubinemia in Fayoum Governorate.

Subjects and methods: This was descriptive-analytic prospective research that was performed in Fayoum Governorate and carried out on 150 neonates. Their gestational age ranged from 38 to 41 weeks, and both genders were included. There was no significant illness. A cord blood sample was taken for the G6PD enzyme assay quantitatively, CBC, and reticulocyte count, and another Venus sample was taken after five days for direct and indirect bilirubin and Reticulocyte count.

Results: There is a substantially higher mean G6PD enzyme level with a p-value of 0.05 amongst children with a negative family history of G6DP deficiency. There is no substantial association with a *P-value >0.05* between G6PD enzyme levels and the presence of anemia or abnormal tics.

Conclusion: Many different clinical complications are linked to hyperbilirubinemia in newborns. One major cause of newborn jaundice is a lack of the enzyme G6PD.

Keywords: Glucose-6-phosphate dehydrogenase; cord blood; hemolysis; hyperbilirubinemia.

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1. Introduction

G6PD affects about 400 million people all over the world and is thus the most common

kind of enzyme deficiency in humans, most frequently in males due to X-linked heritability [1].

G6PD deficiency is an X-linked recessive disorder with a variety of clinical manifestations, such as neonatal jaundice, hemolysis, and acute jaundice after the consumption of fava beans (favism) or exposure to chemicals and medications [2].

Neonatal bilirubin is the earliest indication of G6PD lack and the most crucial indicator for early detection of this genetic condition [3].

In numerous investigations, the incidence of a G6PD lack in icteric neonates has been determined to range from 3.5-40% [4].

In contrast to fetal erythroblastosis, approximately 5% of neonates with G6PD deficiency develop jaundice within the first 24 hours of life, and their serum indirect bilirubin approaches a climax between days 3 and 5, frequently exceeding 20mg/dL. If jaundice manifests at the end of the first week, its climax may not occur until the second week. Undiagnosed G6PD deficiency can result in severe hemolysis and anemia in newborns [5]. Therefore, early detection of this disorder is crucial.

The World Health Organization (WHO) reports an international infant mortality rate of 0.70 to 1.60 per 1,000 births as a result of G6PD-associated neonatal bilirubin. Babies that make it through acute hyperbilirubinemia are at risk for chronic bilirubin encephalopathy, which can manifest as severe athetoid cerebral palsy, auditory dysfunction, intellectual deficiencies, and other disabilities [6].

The current study aimed to The purpose of this research is to discover the incidence of G6PD deficiency in newborns in cord blood and its relation to neonatal indirect hyperbilirubinemia in Fayoum Governorate.

2. Subjects and methods

The research was conducted in Fayoum Governorate. During a period of four months, from April to July 2017, a total of 150 newborns were delivered in Fayoum.

We included patients with Gestational ages ranging from 38 to 41 weeks, both genders and any mode of delivery (vaginal or Caesarian section).

We excluded patients small and large for gestational age, Neonates with significant illness or major congenital malformations, surgical conditions, and Mothers with negative Rh.

All neonates underwent detailed history evaluation with stress on history of jaundice in the family, history of G6PD lack in the family, blood group, Rh of the mother and frequency, quantity and type of feeding given to the baby.

Clinical examination included vital signs, anthropometric measures, the presence of cephalohematoma, and cardiac, abdominal, chest, and neurological examination.

Laboratory investigations included a Cord blood sample for G6PD enzyme assay quantitively, a complete blood count with reticulocyte count, and blood group and Rh for the mother and the baby at day 5. Direct and indirect bilirubin and Reticulocyte counts were also done.

2.1. Statistical analysis:

The collected data were statistically analyzed by the Statistical Program for Social Science (SPSS) version 22.

3. Results

The demographic characteristics of neonates showed that a total of 150 neonates participated in the investigation. 130 (86.7%) of them were males 20 (13.3%) were females, and 87 (58%) of them lived in urban areas versus 63 (42%) in rural areas.

Table 1 illustrates that among the study group, 18.7% of them had positive consanguinity, 10.7% had a positive history of jaundice, and 2.7% had a positive history of G6PD deficiency.

Table 1: Description of demographic characters among study group.

Variables		**Number (n=150)**
Consanguinity	Negative	122 (81.3%)
	Positive	28 (18.7%)
Family history of jaundice	Negative	134 (89.3%)
	Positive	16 (10.7%)
Family history of G**6PD deficiency**	Negative	146 (97.3%)
	Positive	4 (2.7%)

Table 2 illustrates that at cord blood, 34.7% of the study group had anemia, 64% had a low level of ethics, and 6.7% showed a high level of ethics. On day 5, 75.3% showed a high level of total bilirubin, and 2% had a high direct bilirubin level.

Table 2: Frequency of laboratory investigations among study group

Variables		**Laboratory investigations**
Hemoglobin (cord blood)	Anemia <14 mg/dl	52 (34.7%)
	Not anemia >14 mg/dl	98 (65.3%)
Retics at birth	0-3%	69 (64%)
	3-7%	44 (29.3%)
	>7%	10 (6.7%)
Total bilirubin at day 5	Normal <5 mg/dl	37 (24.7%)
	High >5 mg/dl	113 (75.3%)
Direct bilirubin at day 5	Normal <1 mg/dl	147 (98%)

	High >1 mg/dl	3 (2%)

The mean G6PD enzyme level in cord blood was (12.7±4.9) u/g Hb, with 15 (10%) showing a low level of enzyme and 135 (90%) having a normal level of enzyme. There is a substantially higher mean G6PD enzyme level with a *P-value <0.05* amongst children with a negative family history of G6PD deficiency. To the contrary, there is no substantial variance with a *P-value >0.05* in G6PD enzyme level between different consanguinities or family histories of jaundice, which indicates no effect of these variables as regards G6PD enzyme level (**Table 3**).

Table 1: Comparisons of G6PD enzyme level in different medical history among study group

Variables		**G6PD enzyme level**	*P-value*
Consanguinity	Negative	12.4±4.9	0.09
	Positive	14.1±4.7	
Family history of jaundice	Negative	12.7±5.2	0.8
	Positive	12.4±2.7	
Family history of G**6PD deficiency**	Negative	12.9±4.7	**0.001***
	Positive	4.6±6	

* Significant.

Table 4 provides evidence that there is no substantial association with a *P-value >0.05* amongst G6PD enzyme levels and sex, the presence of anemia, or abnormal relics, which indicates no effect of G6PD enzyme level on these variables.

Table 4: Comparisons of hemoglobin and retics in different G6PD enzyme levels.

Variables		**G6PD enzyme level**		*P-value*
		Deficient	**Normal**	
Sex	Males	12 (9.3%)	118 (70.7%)	0.4
	Females	3 (15%)	17 (85%)	
Hemoglobin	Anemia <14 mg/dl	4 (26.7%)	48 (35.6%)	0.4
	Normal >14 mg/dl	11 (73.3%)	87 (64.4%)	
Retics	0-3%	10 (66.7%)	86 (63.7%)	0.6
	3-7%	5 (33.3%)	39 (28.9%)	
	>7%	0 (0%)	10 (7.4%)	

Table 5 evidences that there is no substantial association with a *P-value >0.05* amongst G6PD enzyme levels and the presence of hyperbilirubinemia, which indicates no effect of G6PD enzyme level on bilirubin level.

Table 5: Comparisons of bilirubin levels in different G6PD enzyme levels

Variables		G6PD enzyme level		*P-value*
		Deficient	**Normal**	
Total bilirubin	Normal <5	3 (20%)	34 (25.2%)	0.7
	High (>5)	12 (80%)	101 (74.8%)	
Direct bilirubin	Normal (<1)	14 (100%)	131 (97.1%)	0.5
	High (>1)	0 (0%)	4 (2.9%)	

4. Discussion

Neonatal jaundice is a prevalent health problem on a global scale. Approximately 1,1 million infants worldwide suffer severe hyperbilirubinemia with or without bilirubin encephalopathy each year; the majority of these infants reside in sub-Saharan Africa and South Asia. Severe neonatal jaundice results in acute bilirubin encephalopathy or kernicterus, with an increased probability of neonatal mortality and long-term neurologic injury, such as cerebral palsy, sensory neural hearing loss, intellectual difficulties, or gross growth retardation [7]

Neonatal jaundice is a common consequence of G6PD deficiency, a genetic disease noted more frequently in male cases due to the X-linked nature of this enzymatic deficiency. Nevertheless, in female patients, a deficiency in activity may be severe enough to cause hemolysis, especially if they are heterozygous. This disorder mostly impacts people of African, Asian, Mediterranean, and Middle Eastern descent [4]

G6PD deficiency affects 8.9% of Egyptian infants. Because G6PD deficiency makes red blood cells more vulnerable to agents like oxidants present in fresh beans, certain medications, and oxidative stress resulting from infections, it is commonly referred to as fava bean anemia or favism (after consumption of fava beans) in Egypt. There have only been a few studies done on the prevalence of G6PD deficiency in jaundiced Egyptian infants [8].

Thus, we conducted the current research to find out the prevalence of G6PD deficiency in newborns using the cord blood screening method in Fayoum Governorate and its relation to neonatal indirect hyperbilirubinemia for better management and prevention of serious sequelae.

The present study was designed to be a descriptive-analytic prospective study that was performed in Fayoum City. During a period of four months, from April to July 2017, a total of 150 newborns delivered at Fayoum University Hospital, Fayoum General Hospital, and Abshway Central Hospital were enrolled in the study.

Pathological jaundice typically develops over the course of 24 hours when serum bilirubin levels exceed 5 mg/dl/day. Moreover, males seem to be more susceptible to jaundice [9].

The preponderance of patients in the current research were male (86.7%). In agreement with our results, Najib et al, (2013), conducted cross-sectional research to determine the characteristics of all neonates younger than 28 days who were recommended for severe indirect hyperbilirubinemia. 58% of the cases that received an investigation were male [10].

El-Menshay et al. (2009) also investigated the frequency of G6PD deficiency in connection with neonatal hyperbilirubinemia in Egyptian neonates. The investigation involved 53 neonates with neonatal jaundice, consisting of 40 males (75.5%) and 13 females (24.5%) in a ratio of 3:1 [11].

Regarding the primary result of this current investigation, we discovered that 10% of the neonates examined were deficient in G6PD. Abo El Fotoh and Rizk (2016) observed an incidence of 8.9% for G6PD in neonatal hyperbilirubinemia in Egypt [12]. Similarly, Kasemy et al. (2020) determined the incidence of G6PD deficiency in jaundiced neonates [4]. From June 2018 to July 2019, a cross-sectional investigation was conducted on 487 Egyptian newborns with indirect hyperbilirubinemia. There was a prevalence of 10.10% for G6PD deficiency. Similar results have been seen in other nations in the region. For instance, Dawodu et al. (1998) stated that 9.5% of the 85 neonates with hyperbilirubinemia at the Al Ain Hospital in the UAE had G6PD deficiency. A meta-analysis of five retrospective studies was conducted [13]. Al-Touma and Frankool (2009) examined the molecular basis of G6PD deficiency in hyperbilirubinemia neonates in the Iraqi region of the Middle Euphrates [14]. The investigation included a total of 917 male newborns born at full term. The frequency of severe G6PD deficiency was 10.65% in the Iraqi province of Middle Euphrates. Liu et al. (2015) discovered that 11.7% of neonates with hyperbilirubinemia had a G6PD deficiency [15].

Particularly, other reports from Egypt and other Eastern Mediterranean nations revealed a higher or lower incidence of G6PD deficiency compared to ours. Abo Elella et al. (2017) wanted to figure out the local incidence of neonatal G6PD deficiency. The 2015 birth cohort was prospectively evaluated for G6PD deficiency [5]. In partnership with the Ministry of Health's central labs, dried blood spot samples were gathered on filter paper. The overall incidence of G6PD deficiency was 4.3%, with G6PD deficiency affecting 119 neonates (91 males and 28 females). El-Menshay et al. (2009) found that 16 of 53 cases (30.2%) were G6PD-deficient [11]. Past findings from Bahrain and Iran indicated that 42% and 18.1% of neonates with indirect hyperbilirubinemia, respectively, had G6PD deficiency [16, 17].

The precise causes of such heterogeneity remain unknown. It can nevertheless be related to methodological and clinical distinctions, such as the tiny sample size chosen for the research. The wide spectrum of G6PD deficiency frequency in Egypt could be revealed by the country's unique geographical location among three continents with diverse ethnic populations. In patients with G6PD deficiency, a variety of likelihood factors, including male gender, African ancestry, consanguinity, and positive family history, were identified as hazards [18].

In the current research, we discovered that neonates with G6PD deficiency were more likely to have a positive relative history of G6PD deficiency, whereas gender did not affect the frequency of G6PD deficiency. Consistent with these results, two Yemeni investigations found that G6PD deficiency was more frequent in children with relatives who have a history of the disorder [17, 19]. In the study by Isa, neonates with G6PD deficiency were more likely to be from families with a history of G6PD [16].

The absence of a substantial correlation between neonate gender and G6PD deficiency in this current research corresponds with results from Brazil and Niger [18, 20]. As opposed, G6PD deficiency was considerably more prevalent among male neonates than female neonates in Egypt (6.2% vs. 2.1%, respectively), with a male-to-female ratio of 3.2:1 [5]. The substantial relationship between sex and G6PD deficiency has also been reported in Turkey [21] and Shirvan, Iran [22]. Due to the hereditary nature of G6PD deficiency, the kind of marriage among the parents may influence the inheritance of this disorder. In light of these findings, we found no correlation between G6PD deficiency and consanguinity in the current research. Yemeni [19], Egyptian [12], and Qatari studies indicate the exact inverse. Notably, consanguineous marriages might be responsible for more than half of all marriages in the Eastern Mediterranean region, influencing the community control of inherited disorders [23].

Conclusion

G6PD insufficiency is a prevalent enzyme abnormality in our newborn population (particularly in males), resulting in severe indirect hyperbilirubinemia that requires therapy. 10% of those with indirect hyperbilirubinemia were found to have a G6PD deficiency, according to the study's findings. The G6PD defective group had a substantially greater number of affected family members than the non-deficient group. This discovery emphasizes the value of G6PD testing in all babies undergoing phototherapy, but notably in those with a poor response or unexplained cause.

Ethical approval: The Ethics Committee of Research at Fayoum University's School of Medicine approved the current study.

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Conflicts of Interest: None declared.

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