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ORIGINAL ARTICLE

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Neonates Presenting with Indirect Hyperbilirubinemia

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ABSTRACT

Objective: To determine the frequency of glucose-6-phosphate dehydrogenase (G6PD) deficiency in neonates presenting with indirect hyperbilirubinemia.

Methods: A prospective cross-sectional study was conducted at Neonatal intensive care unit (NICU) of National Institute of Child Health, Karachi from August 2020 to July 2021. All neonates with either gender born with indirect hyperbilirubinemia >5mg/dl admitted in NICU were consecutively enrolled. G6PD deficiency along with baseline and laboratory characteristics were observed. The presence of G6PD level of <1.3 U/g Hb was labeled as G6PD deficiency.

Results: Of 228 neonates, the mean age was 8.58 ±3.68 days. There were 153 (67.1%) males and 75 (32.9%) females. The frequency of G6PD deficiency was found to be 72 (31.6%). The mean weight was significantly higher among neonates with G6PD deficiency as compared to the patients with no G6PD deficiency, i.e., 2.53 ±0.48 vs. 2.37 ±0.56 (p-value 0.035). A significant difference of hemoglobin level (p-value <0.001), serum total bilirubin level (p-value <0.001), and serum indirect bilirubin level (p-value0.001) was observed in between G6PD deficient and non-deficient neonates. Increased reticulocyte count was also found significantly higher in neonates with G6PD deficiency as compared to the neonates without G6PD deficiency, i.e., 69 (95.8%) and 34 (21.8%) respectively (p-value <0.001).

Conclusion: G6PD deficiency was considerably prevalent in neonates with indirect hyperbilirubinemia. Moreover, hemoglobin level, serum total bilirubin level, serum indirect bilirubin level, and increased reticulocyte count was also observed significant contributing factors for G6PD deficiency.

Keywords: Glucose-6-Phosphate Dehydrogenase Deficiency, Neonates, Indirect Hyperbilirubinemia.

INTRODUCTION

In the first three days of life, 60 percent of full-term newborns and 80 percent of preterm newborns suffer from neonatal indirect hyperbilirubinemia.[1] Reported prevalence for glucose-6-phosphate dehydrogenase (G6PD) deficiency in neonates presenting with jaundice is 6.7-55.1%.[2,3]

Indirect hyperbilirubinemia in newborns is associated with a high risk of serious consequences, including long-term neurologic deficits and mortality.[4] Despite the fact that significant complications of neonatal indirect hyperbilirubinemia have become rare in recent years as a result of therapeutic interventions, severe neonatal indirect hyperbilirubinemia caused by reduced G6PD activity is still complicated by kernicterus, a serious neurological disease.[5]

While most countries' present investigation on G6PD insufficiency is focused on determining the type of mutations and their link to other diseases, or testing new treatment compounds in these individuals, in Pakistan due to limited resources and lack of databases, burden of the disease and risk factors of these at-risk patients are rarely reported. Thus, to effectively manage the disease and to reduce morbidity and mortality, the assessment of disease burden and its associated factors are utmost important.

METHODS

This prospective cross-sectional study was conducted at Neonatal intensive care unit (NICU) of National Institute of Child Health (NICH) Karachi, Pakistan from August 2020 to July 2021. Ethical approval was obtained from Ethical review Committee of NICH prior conducting of the study. Furthermore, informed consent from parents/guardians of all eligible neonate prior enrolment in the study.

All neonates with either gender born with indirect hyperbilirubinemia >5mg/dl admitted in NICU were consecutively enrolled. All Children with direct hyperbilirubinemia, very sick babies, severe birth asphyxia, gross congenital anomaly, and Rh-ABO incompatibility were excluded.

WHO sample size calculator was used for the estimation of sample size. Taking the prevalence for G6PD deficiency in neonates with jaundice as 18.1%[6], confidence level 95%, and margin of error 5%. The estimated sample size came out to be 228.

Neonates were defined as newborn up to 28 days of life. G6PD level of <1.3 U/g Hb was labeled as deficient.[6] This information along with baseline characteristics like age, gender, weight, duration of disease, residence, and family history of consanguinity were observed. In addition, laboratory parameters like hemoglobin level, serum total bilirubin level, serum indirect bilirubin level, and reticulocyte count were noted. The normal value of reticulocyte count in newborns was 2.5% to 6.5% and this value drops within 2 weeks to 0.5% to 2.0%.[7] Increased in the reticulocyte count from normal range was also noted.

Statistical package for Social Sciences (SPSS) version 24 was used for the purpose of statistical analysis. All quantitative variables like age, weight, duration of disease, hemoglobin level, serum total bilirubin level, and serum indirect bilirubin level were expressed in mean ±SD while all qualitative variables like gender, family history of consanguinity, residence, increased reticulocyte count, and G6PD deficiency were expressed in frequencies and percentages. Inferential statistics were explored using independent t-test and chi-square test. The p-value of <0.05 was considered as significant.

RESULTS

Of 228 neonates, the mean age of the neonates was 8.58 ±3.68 days. There were 153 (67.1%) males and 75 (32.9%) females. The mean weight of the neonates was 2.42 ±0.54 kg. The mean duration of disease was 6.45 ±3.04 days. Gestational age status showed that 177 (77.6%) neonates had appropriate gestational age and 51 (22.4%) had small gestational age. Most of the neonates belonged to urban residence, i.e., 195 (85.5%). Family history showed that consanguinity was observed in 203 (89%) neonates.

The frequency of G6PD deficiency was found to be 72 (31.6%). The mean weight was significantly higher among neonates with G6PD deficiency as compared to the patients with no G6PD deficiency, i.e., 2.53 ±0.48 vs. 2.37 ±0.56 (p-value 0.035). An insignificant association of G6PD deficiency was found with age (p-value 0.079), gender (p-value 0.610), duration of disease (p-value 0.915), gestational age (p-value 0.472), residence, ethnicity (p-value 0.329), and family history (p-value 0.683) (Table 1).

The mean hemoglobin level was found significantly higher among neonates with G6PD deficiency as compared to the neonates with no G6PD deficiency, i.e., 13.43 ± 2.49 g/dL vs. 15.67 ± 2.86 g/dL (p-value <0.001) respectively. Serum total bilirubin level was also found significantly higher among neonates with G6PD deficiency as compared to the neonates with no G6PD deficiency, i.e., 33.01 ± 6.55 mg/dL vs. 19.67 ± 6.24 mg/dL (p-value <0.001). Similarly, serum indirect bilirubin level was found significantly higher among neonates with G6PD deficiency as compared to the neonates with no G6PD deficiency, i.e., 29.70 ± 6.37 g/dL vs. 17.06 ± 5.81 g/dL (p-value <0.001) respectively (Table 2).

Increased reticulocyte count was also found significantly higher in neonates with G6PD deficiency as compared to the neonates without G6PD deficiency, i.e., 69 (95.8%) and 34 (21.8%) respectively (p-value <0.001) (Figure 1).

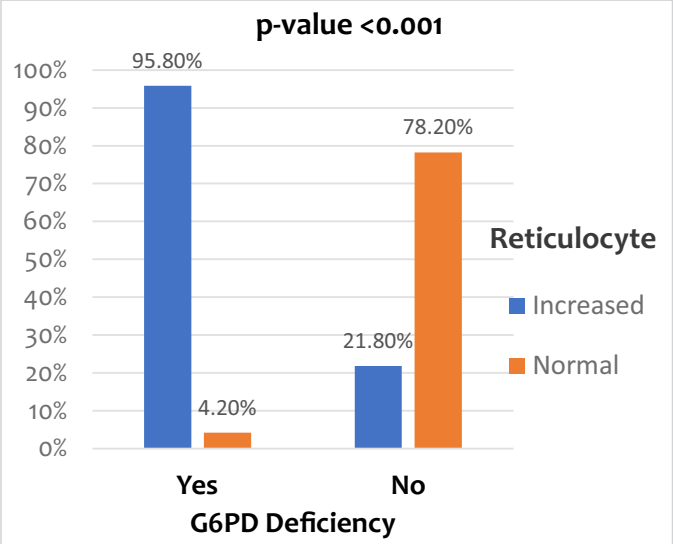

Figure 1: G6PD deficiency in patients with and without increased reticulocytes (n=228)

DISCUSSION

G6PD is an important enzyme presents in red blood cells that needs prompt diagnosis as the deficiency of G6PD may leads to severe hemolysis and anemia in the newborn.[8-10] It has been observed that there is a link between reduced enzyme activity and hyperbilirubinemia, and that early detection and treatment are necessary to avoid consequences.[11]

Table 1: Comparison of G6PD deficiency with baseline characteristics (n=228)

		G6PD Deficiency		
	Total (n=228)	Yes (n=72)	No (n=156)	p-value
Age, days	8.58 ±3.68	8.56 ±4.49	8.59 ±3.26	0.969†
≤9	136	49 (36.0)	87 (64.0)	0.079‡
>9	92	23 (25.0)	69 (75.0)	
Gender				
Male	153	50 (32.7)	103 (67.3)	0.610‡
Female	75	22 (29.3)	53 (70.7)	
Weight, kg	2.42 ±0.54	2.53 ±0.48	2.37 ±0.56	0.035†*
≤2.5	136	44 (32.4)	92 (67.6)	0.760‡
>2.5	92	28 (30.4)	64 (69.6)	
Duration of Disease, days	6.45 ±3.04	6.85 ±4.20	6.27 ±2.31	0.188†
≤6	131	41 (31.3)	90 (68.7)	0.915‡
>6	97	31 (32.0)	66 (68.0)	
Gestational age, weeks				
AGA	177	58 (32.8)	119 (67.2)	0.472‡
SGA	51	14 (27.5)	37 (72.5)	
Residence				
Rural	33	14 (42.4)	19 (57.6)	0.147‡
Urban	195	58 (29.7)	137 (70.3)	
Ethnicity				
Urdu Speaking	68	18 (26.5)	50 (73.5)	0.329‡
Sindhi	50	19 (38.0)	31 (62.0)	
Punjabi	53	20 (37.7)	33 (62.3)	
Others	57	15 (26.3)	42 (73.7)	
Family History				
Consanguinity	203	65 (32.0)	138 (68.0)	0.683‡
Non-Consanguineous	25	7 (28.0)	18 (72.0)	

AGA: Appropriate for Gestational Age, G6PD: Glucose-6-phosphate dehydrogenase, SGA: Small for Gestational Age
All qualitative variable presented data presented as number (%) and quantitative variable as mean ±SD
†Independent t-test applied, ‡Chi-square test applied, *p-value ≤ 0.05

Table 2: Comparison of G6PD deficiency with laboratory characteristics (n=228)

	G6PD Deficiency			
	Total (n=228)	Yes (n=72)	No (n=156)	p-value
Hemoglobin, g/dL	14.97 ±2.94	13.43 ±2.49	15.67 ±2.86	<0.001*
Serum Total Bilirubin, mg/dL	23.89 ±8.87	33.01 ±6.55	19.67 ±6.24	<0.001*
Serum Indirect Bilirubin, mg/dL	21.05 ±8.39	29.70 ±6.37	17.06 ±5.81	<0.001*

All qualitative variable presented data presented as number (%) and quantitative variable as mean ±SD
†Independent t-test applied, ‡Chi-square test applied, *p-value ≤ 0.05

The findings of this reported that the frequency of G6PD deficiency was found to be 31.6%. A considerably higher prevalence was reported from Basra, Iraq in which the deficiency was reported to be 51%.[3] However, the current study prevalence was considerably higher compared to studies reported from Iran, Iraq, India, and Egypt.[3,10,12,13] In a recent study conducted in Dohuk, Iraq, among all neonates with hyperbilirubinemia, G6PD deficiency was observed in 16% of the neonates.[3] A study from Iran has reported G6PD that among neonates with pathologic hyperbilirubinemia, deficiency of G6PD was found to be 18.1%.[10] A West-Indian study has reported G6PD deficiency among icteric neonates as 4.8%.[14] While in Egypt, the deficiency among was reported to be 14.4%.[13] Surprisingly, in a study reported from Peshawar city of Pakistan has reported G6PD deficiency among neonatal jaundice as 9%.[15]

In the current study, increased reticulocyte count was also found significantly higher in neonates with G6PD deficiency as compared to the neonates without G6PD deficiency. Contrary to the current study finding, an insignificant difference of reticulocyte count was reported in a previous study by Eissa et al.[3] The possible reason behind the difference could be that in the current study all neonates with Rh-ABO incompatibility were not enrolled. However, Eissa et al included these neonates as well. In our through literature search, studies reported these factors were scarce.[3]

According to the current study findings, the mean weight was significantly higher among neonates with G6PD deficiency as compared to the patients with no G6PD deficiency. Though, in previous study weight comparison was not reported. However, Goyal et al in their study reported low birth weight in forty percent of the neonates with G6PD deficiency.[16]

As per the current study findings, a significant difference of hemoglobin level, serum total bilirubin level, and serum indirect bilirubin level was observed in between G6PD deficient and non-deficient neonates. Similar findings were reported in studies conducted by Sinha et al[17], Abolghasemi et al[18], Boskabadi et al[19], and Al-Omran et al.[20]

The findings of the current study could be highlighted in the light of limitation that this was a single center which was carried out in a limited number of sample size. Secondly, certain important predictor variables like phototherapy requirement, days of hospitalization, molecular pathology, and therapeutic interventions were not studied. Lastly, in the current study, no follow-up was performed due to which the discharge outcome and other related information were not observed. Despite of these limitations, this study has given an insight about the burden of G6PD deficiency and its related factors in neonates admitted in a large tertiary care hospital of metropolitan city of Pakistan. Further large scale multicenter analytical studies are recommended that assess more confounding factors in at-risk neonates. Furthermore, previously studies conducted in international population have evaluated the genetic and molecular profile of these neonates which is not yet studied in our population. The understanding of these characteristics is important particularly in patients with prolonged jaundice as stated in various studies[21-23] as well to effectively manage the disease and control its prevalence in the future.

CONCLUSION

G6PD deficiency was considerably prevalent in neonates with indirect hyperbilirubinemia. Moreover, hemoglobin level, serum total bilirubin level, serum indirect bilirubin level, and increased reticulocyte count was also observed significant contributing factors for G6PD deficiency.

ETHICAL APPROVAL: The study was approved by the Institutional Ethical Review Board, National Institute of Child Health Karachi (IERB No: 10/2020, dated: 20-07-2020).

AUTHORS' CONTRIBUTIONS:

AR: Data collection, statistical work and drafting of the manuscript.

MK: Conception and design of the study, critical reviewed the manuscript.

Both authors gave final approval to submit the manuscript.

CONFLICT OF INTEREST: The authors declared no conflict of interest.

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