Original Article

Frequency of Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Neonates with Jaundice

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Abstract

Objective: To determine the frequency of glucose-6-phosphate dehydrogenase deficiency among neonates presenting with jaundice.

Methods: It was a Descriptive cross-sectional study using non-probability consecutive sampling conducted in the Department of Pediatrics, Saidu Group of Teaching Hospitals, Saidu Medical College, Swat, Pakistan, from 22nd July 2023 to 22nd January 2024. A total of 130 neonates aged 1–28 days with clinical jaundice were enrolled. Baseline demographic and clinical data were collected. Laboratory evaluation included serum bilirubin, hemoglobin, reticulocyte count, and glucose-6-phosphate dehydrogenase activity by decolorization test. A decolorization time exceeding 60 minutes was considered diagnostic for enzyme deficiency.

Results: Of the 130 neonates, 70% were aged 1–14 days, and 30% were 15–28 days. Term neonates constituted 68%, while 32% were preterm. Male-to-female ratio was 1.3:1 (58% vs. 42%). Glucose-6-phosphate dehydrogenase deficiency was detected in 10% of neonates with significantly higher frequency in males (16%) compared to females (2%) (p=0.0077).

Conclusion: Glucose-6-phosphate dehydrogenase deficiency was observed in 10% of neonates with jaundice, with a marked male predominance. Early screening is essential to prevent complications such as severe hyperbilirubinemia and kernicterus in high-risk populations.

Keywords: Anemia, Hemolytic; Glucose-6-Phosphate Dehydrogenase Deficiency; Hyperbilirubinemia, Neonatal; Infant, Newborn; Jaundice.

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common inherited enzymatic disorder of red blood cells, first described in the mid-20th century following observations of hemolytic anemia in individuals exposed to antimalarial drugs.[1] The deficiency results from mutations in the G6PD gene located on the X chromosome, leading to impaired production of reduced nicotinamide adenine dinucleotide phosphate (NADPH), which is vital for protecting red cells against oxidative stress.[2] Globally, more than 400 million people are affected, with the highest prevalence reported in Africa, the Middle East, Asia, and the Mediterranean.[3]

Neonatal jaundice is a frequent clinical problem worldwide, occurring in up to 60% of term and 80% of preterm neonates.[4] While in most infants it is benign and self-limited, in some cases it progresses to severe hyperbilirubinemia with a risk of acute bilirubin encephalopathy and kernicterus.[5] Among the many etiologies of neonatal jaundice, G6PD deficiency is particularly significant because it predisposes neonates to hemolysis and rapid bilirubin rise, often without other identifiable causes.[6]

Several studies from endemic regions have reported variable prevalence of G6PD deficiency in jaundiced neonates, ranging from 3% to 30%, depending on population genetics and screening methods used.[7,8] It is well established that the disorder is more common in males due to its X-linked inheritance, while heterozygous females may show intermediate enzyme activity.[9] Early diagnosis of affected neonates is clinically important, as prompt initiation of phototherapy or exchange transfusion can prevent irreversible neurological damage.[10]

Despite the recognized importance of this condition, significant gaps remain. First, the frequency of G6PD deficiency among neonates with jaundice in many regions of Pakistan remains underexplored, with available data limited to small-scale or single-center reports. [10] Second, most studies have not stratified results by gestational age or sex, leaving uncertainty about which subgroups are most vulnerable. Third, in clinical practice, G6PD screening is not routinely performed in jaundiced neonates, contributing to missed diagnoses and late presentations.[11] These gaps highlight the need for locally relevant data to guide neonatal care and health policy.

The rationale for the present study was to address this deficiency in knowledge by estimating the frequency of G6PD deficiency among neonates presenting with jaundice in a tertiary care setting. By documenting its burden and distribution by sex and gestational age, the study aimed to provide evidence for targeted screening strategies. Such evidence is critical for resource-limited settings, where universal newborn screening is not feasible and where the consequences of delayed recognition of hemolytic jaundice remain devastating. The objective of this study was to determine the frequency of glucose-6-phosphate dehydrogenase deficiency among neonates with jaundice.

Contributions:
N, STM, MM - Conception, Design
N, RA, STM, FH, MM- Acquisition, Analysis, Interpretation
N, STM, IL - Drafting
MA, NS, RA, IL, MM - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

Conflicts of Interest: None
Financial Support: None to report
Potential Competing Interests: None to report

Institutional Review Board Approval
103/PD/23
22-07-2023
Saidu Teaching Hospital

Review began 25/07/2025
Review ended 08/09/2025
Published 30/12/2025

How to cite this article: Hadi NU, Tul Muntaha S, Hafeez M, Ahmad R, Hassan F, Afzal MM. Frequency of Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Neonates with Jaundice. JRMC. 2025 Dec. 31;29(4).

https://doi.org/10.37939/jrmc.v29i4.2528

Original Article

Materials And Methods

This descriptive cross-sectional study employing non-probability consecutive sampling was conducted in the Neonatal Unit of the Department of Pediatrics, Saidu Group of Teaching Hospitals, Saidu Medical College, Swat, Pakistan, over six months from 22nd July 2023 to 22nd January 2024. A sample size of 130 neonates was calculated using the World Health Organization sample size calculator, with an expected frequency of glucose-6-phosphate dehydrogenase (G6PD) deficiency of 9%, a margin of error of 5%, and a confidence level of 95%. Approval for the study was obtained from the Institutional Ethical Review Committee of Saidu Medical College (Letter No. SMC/ERC/2023/0722, dated 15th July 2023). Written informed consent was secured from the parents or legal guardians of all enrolled neonates. Confidentiality of patient data was maintained. All neonates aged 1–28 days of either sex who presented with clinical jaundice were eligible for inclusion. Very preterm neonates (gestational age <32 weeks), critically ill, with major congenital anomalies or with direct hyperbilirubinemia defined as direct bilirubin >2 mg/dL or >20% of total serum bilirubin were excluded. Data collection was performed by a team of trained pediatric residents under consultant supervision. Demographic details, including age, sex, and gestational age, as well as clinical history, were recorded on a structured proforma. All neonates underwent physical examination and laboratory investigations, including complete blood count with reticulocyte count, blood group of both neonate and mother, direct and indirect Coombs test, total and direct serum bilirubin, and G6PD decolorization test. G6PD activity was measured in EDTA blood hemolysate incubated at 37 °C with buffer under mineral oil. Decolorization within 20–60 minutes was normal; times exceeding 60 minutes indicated a deficiency. All data were entered and analyzed using SPSS version 24. Descriptive statistics were applied: means and standard deviations were reported for quantitative variables such as age, hemoglobin, reticulocyte count, and bilirubin levels, whereas frequencies and percentages were calculated for categorical variables such as sex, gestational age, and G6PD deficiency. Post-stratification chi-square tests were applied to determine associations with potential effect modifiers. Exact p-values were reported, and a p-value ≤0.05 was considered statistically significant. Ninety-five percent confidence intervals (CI) were calculated where applicable.

Results

A total of 130 neonates were included in the study. Mean bilirubin level was 11±5.55 mg/dL. Mean reticulocyte count was 6.4±2.4%. Mean hemoglobin level was 10±2.19 g/dL. Demographics like age and gestational age are shown in Table 1.

Table 1: Age, Gestational Age: (N=130)

		Frequency	Percentage	Mean± SD
AGE	1-14 Days	91	70%	10 ±7.62
	15-28 Days	39	30%	
Gestational Age (weeks)	Pre Term	42	32%	37±4.39
	Term	88	68%	

Stratification of G6PD deficiency with respect to age, gender, and gestational age is shown in Table 2.

Table 2: Stratification of G6PD Deficiency by Age, Gender, and Gestational Age (N = 130)

Variable	Category	G6PD Deficient n (%)	Non-Deficient n (%)	Total	p-value
Age (days)	1–14	9 (9.9)	82 (90.1)	91	0.949
	15–28	4 (10.3)	35 (89.7)	39	
Gender	Male	12 (16.0)	63 (84.0)	75	**0.0077***
	Female	1 (1.8)	54 (98.2)	55	
Gestational Age	Preterm	4 (9.5)	38 (90.5)	42	0.900
	Full term	9 (10.2)	79 (89.8)	88	

**Significant at p < 0.05*

Demographics like gender distribution, shown in Figure 1. G6PD enzyme deficiency among neonates was analyzed and is shown in Figure 2.

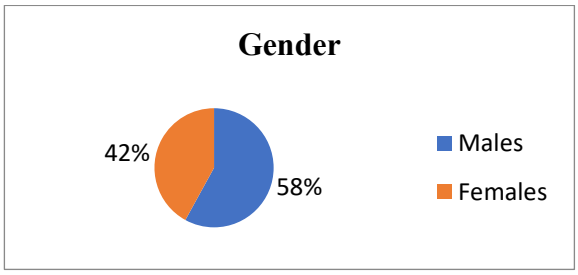

Figure 1: Gender Distribution. (N=130)

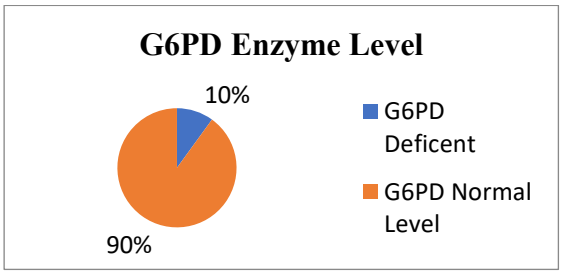

Figure 2: G6PD Enzyme Deficiency. (N=130)

Overall, 13 (10%) neonates were diagnosed with G6PD deficiency. The disorder was significantly more frequent among male infants (p = 0.0077), while differences by age group and gestational age were not statistically significant (p = 0.949 and p = 0.900, respectively).

Discussion

In this study, glucose-6-phosphate dehydrogenase (G6PD) deficiency was observed in 10% of neonates with jaundice, with a clear male predominance. Term infants were more frequently affected than preterm infants, although this difference was not statistically significant. These findings underscore the importance of considering G6PD deficiency as a major contributor to neonatal hyperbilirubinemia in our setting, particularly among male neonates.

Male to female distribution in our study showed that 58% of affected neonates were male and 42% female, with G6PD deficiency detected in 16% of males compared with only 2% of females. This finding is consistent with the X-linked inheritance pattern of the disorder. Kasemy et al. reported a similar male predominance, with 69.9% of affected neonates being male and 30.4% female, and enzyme deficiency documented in 10% of cases (p=0.001).[12] Yi-Kang et al. also demonstrated a higher frequency in males, reporting G6PD deficiency in 19.5% of jaundiced neonates, significantly higher than in non-jaundiced infants (10%, p<0.001).[13] The difference in frequency between our study and that of Yi-Kang et al. may be due to genetic diversity and a larger sample size in the latter study.

Age distribution in our cohort revealed that 70% of cases were between 1–14 days, while 30% were between 15–28 days. Stratification showed no significant association of deficiency with age. Akhter et al. reported a slightly higher mean age of 16 days with 13% prevalence of enzyme deficiency.[14] The difference in mean age compared to our study may reflect referral bias, as our neonatal unit receives early admissions. Similarly, Xu et al. noted a frequency of 8.3% among neonates with jaundice, also concentrated in the first two weeks of life, suggesting early presentation is typical of enzyme deficiency.[15]

The prevalence of G6PD deficiency in our study (10%) aligns with studies from the Middle East and South Asia. Saleh et al. Reported a prevalence of 10% among 658 neonates in the UAE, with affected neonates showing poor response to phototherapy.[16] Hamali et al. Observed an incidence of 8.4% in Saudi Arabia, with a stronger correlation in males.[17] Zhou et al. Reported a prevalence of 7% in Chinese neonates,[18,] while Shahzeen et al. Documented 8.3% in Pakistani neonates. [11] Tang et al. Also evaluated a large-scale newborn screening program in China, reporting a prevalence of 6.2% with higher rates in males, supporting the role of universal enzymatic screening in identifying at-risk neonates.[19] The minor variations in prevalence across studies may be attributed to differences in cut-off values for enzyme activity, methodology of screening, and underlying genetic heterogeneity.

When compared with African data, our prevalence appears lower. Kassahun et al. in a meta-analysis reported a pooled prevalence of 24% among African neonates with jaundice, with wide variation between Nigerian neonates (24%) and South African neonates (3%).[20] Vidavalur et al. in Nigeria also reported high prevalence (26.4%) with severe hyperbilirubinemia and higher mortality.[21] This contrast can be explained by the presence of different G6PD variants in African populations, many of which are associated with more severe enzyme deficiency and hemolytic risk.

Biochemical parameters in our study showed a mean hemoglobin of 10 g/dL, reticulocyte count of 6.4%, and bilirubin of 11 mg/dL. Kasemy et al. Reported higher mean hemoglobin (12.8 g/dL) and bilirubin (15 mg/dL),[12] while Yi-Kang et al. Documented mean hemoglobin of 14 g/dL and bilirubin values significantly elevated in enzyme-deficient neonates (p<0.001).[13] Shahzeen et al. Observed higher hemoglobin and bilirubin levels compared to ours.[11] Kaplan et al. Highlighted that G6PD deficiency predisposes to hemolysis-driven hyperbilirubinemia, where the degree of hemolysis strongly influences bilirubin accumulation.[22] These variations may therefore reflect differences in baseline nutritional status, consanguinity patterns, genetic variants, and thresholds for hospitalization.

Regional comparisons further strengthen the importance of screening. Eissa et al. In Iraq found a prevalence of 16% among neonates with jaundice, significantly higher than controls (6%), with affected neonates experiencing more severe indirect hyperbilirubinemia and prolonged hospital stays.[23] Their findings are consistent with our observations and reinforce the clinical importance of early detection.

The overall interpretation of our findings is that G6PD deficiency remains an important cause of neonatal hyperbilirubinemia in our local population, comparable to reports from other Asian and Middle Eastern settings. The lack of routine neonatal screening in Pakistan likely contributes to delayed recognition, with many neonates presenting at or near exchange transfusion thresholds. This underscores the need for heightened clinical suspicion, particularly in male neonates with unexplained jaundice.

Our study had some limitations. It was conducted in a single tertiary care hospital with a relatively small sample size, which may not fully represent the wider population. In addition, molecular analysis of G6PD variants was not performed, limiting genetic characterization of deficiency in our cohort.

Future research should focus on multicenter studies with larger sample sizes and the incorporation of molecular testing to identify prevalent variants in Pakistan. Such data will strengthen the case for newborn screening programs and preventive strategies to reduce the risk of kernicterus and mortality.

Conclusions

Glucose-6-phosphate dehydrogenase deficiency was observed in 10% of neonates with jaundice, with a marked male predominance. Early screening is essential to prevent complications such as severe hyperbilirubinemia and kernicterus in high-risk populations.

Author Information

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