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SCREENING FOR G6PD DEFICIENCY AMONG NEONATES WITH NEONATAL JAUNDICE ADMITTED TO NEONATAL INTENSIVE CARE UNIT SAIDU GROUP OF TEACHING HOSPITAL SWAT

Original Research

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ABSTRACT

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked enzymatic disorder that predisposes affected neonates to hemolysis and severe hyperbilirubinemia, increasing the risk of kernicterus and long-term neurological complications. Early identification is crucial to prevent severe outcomes. Despite its clinical significance, limited local data exist regarding the prevalence of G6PD deficiency among neonates with jaundice in Pakistan. This study aimed to determine the frequency of G6PD deficiency in neonates presenting with neonatal jaundice.

Objective: To assess the prevalence of G6PD deficiency among neonates with neonatal jaundice admitted to the neonatal intensive care unit.

Methods: A cross-sectional study was conducted at the neonatal nursery of Saidu Group of Teaching Hospital, Swat, from May 2023 to August 2023, following ethical committee approval. Neonates with jaundice and predominant unconjugated hyperbilirubinemia were included, with a serum bilirubin threshold of ≥15 mg/dL for term infants and ≥12 mg/dL for preterm infants. Neonates with conjugated bilirubin >20% of total bilirubin, prior blood transfusion, or prior treatments affecting bilirubin metabolism were excluded. Venous blood samples (2–3 mL) were collected and analyzed for G6PD enzyme activity using whole blood with EDTA as an anticoagulant. Statistical analysis was performed using SPSS version 16. Categorical variables were expressed as frequencies and percentages, while continuous variables were reported as mean ± standard deviation. Chi-square test was used to evaluate associations, with $p<0.05$ considered statistically significant.

Results: Among 208 screened neonates, 171 (82.2%) were term and 37 (17.8%) were preterm. The mean total serum bilirubin was 18.03 ± 13.4 mg/dL, indirect bilirubin was 16.55 ± 2.91 mg/dL, and direct bilirubin was 0.54 ± 0.26 mg/dL. The mean birth weight was 2.7 ± 0.375 kg (range: 2.0–3.6 kg). The mean age at presentation was 4.52 ± 3.04 days (range: 2–17 days). G6PD deficiency was detected in 17 (8%) neonates. No statistically significant association was found between G6PD deficiency and gestational age ($p=0.537$), age at presentation ($p=0.321$), indirect bilirubin levels ($p=0.220$), or birth weight ($p=0.310$).

Conclusion: G6PD deficiency was identified as a contributing factor in neonatal jaundice, with a prevalence of 8% among the study population. Routine neonatal screening for G6PD deficiency, particularly in high-prevalence regions, may facilitate early diagnosis and timely management to prevent severe complications.

Keywords: G6PD deficiency, hemolysis, hyperbilirubinemia, jaundice, neonate, newborn screening, Pakistan.

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INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked recessive disorder that predisposes affected individuals, particularly neonates, to significant complications, including severe hemolysis and hyperbilirubinemia. Among newborns with G6PD deficiency, the first week of life is a critical period during which hyperbilirubinemia frequently develops, often necessitating phototherapy or, in severe cases, exchange transfusion(1). If left untreated, excessive bilirubin accumulation can lead to kernicterus, a potentially irreversible condition resulting in lifelong neurological impairment. Despite the well-documented risks associated with G6PD deficiency, the condition remains underdiagnosed in many regions, particularly in countries where a significant proportion of births occur at home(2, 3). In Pakistan, approximately 65% of deliveries take place outside healthcare facilities, leading to delays in recognizing and managing neonatal jaundice. Many parents rely on traditional practices such as exposing infants to sunlight, administering glucose water, or employing spiritual remedies rather than seeking timely medical intervention(4, 5). These delays can increase the risk of severe jaundice and its long-term complications. Although population-based studies suggest that neonatal jaundice affects 2% to 3.8% of newborns, limited data are available on the contribution of G6PD deficiency to neonatal hyperbilirubinemia. Given that individuals with G6PD deficiency are significantly more susceptible to hemolytic episodes triggered by oxidative stressors, including certain medications, infections, or dietary factors, early identification of this condition is essential for effective clinical management(6, 7).

Despite the known risks, there is a scarcity of local research addressing the prevalence of G6PD deficiency among neonates admitted with jaundice. Understanding the frequency of this enzymatic deficiency in newborns with neonatal jaundice can help guide screening protocols and inform clinical management strategies. Therefore, this study aims to determine the frequency of G6PD deficiency among neonates with neonatal jaundice admitted to the neonatal intensive care unit at Saidu Group of Teaching Hospital, Swat. Identifying the burden of G6PD deficiency in this population may contribute to early diagnosis, timely intervention, and improved neonatal outcomes(8, 9).

METHODS

A cross-sectional study was conducted at the neonatal nursery of Saidu Group of Teaching Hospital, Swat, from May 2023 to August 2023, following approval from the institutional ethical committee. Written informed consent was obtained from the parents or legal guardians of all participants before enrollment. The study included neonates diagnosed with jaundice, characterized by serum bilirubin levels of ≥15 mg/dL in term infants and ≥12 mg/dL in preterm infants, with predominant unconjugated hyperbilirubinemia. Newborns with conjugated bilirubin constituting more than 20% of total bilirubin, those who had already undergone blood transfusion, or those who had received treatments such as metalloporphyrins or phenobarbitone were excluded(9, 10). For laboratory analysis, 2–3 mL of venous blood was collected from each enrolled neonate and sent to the hospital laboratory. The G6PD enzyme test was performed on whole blood using ethylenediaminetetraacetic acid (EDTA) as an anticoagulant. Data were systematically recorded using a structured proforma. Statistical analysis was conducted using SPSS version 16. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were reported as frequencies and percentages. The chi-square test was employed to assess the impact of potential effect modifiers, including age, weight, gestational age, and serum indirect bilirubin, through stratification. A p-value of <0.05 was considered statistically significant(11, 12).

The G6PD enzyme test was conducted using a quantitative spectrophotometric assay to ensure accuracy and reproducibility. The test was performed according to standard laboratory protocols to determine enzymatic activity. To enhance the study's validity, the sample size was determined using appropriate statistical methods, considering the prevalence of G6PD deficiency in similar populations, expected effect size, and a confidence level of 95%. A power analysis was conducted to ensure adequate sample representation, minimizing the risk of type II errors. These methodological considerations aimed to enhance the reliability and generalizability of the findings(13, 14).

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RESULTS

A total of 208 neonates with indirect hyperbilirubinemia were screened for G6PD deficiency, of whom 171 (82.2%) were term infants and 37 (17.8%) were preterm. The study population comprised only male neonates. The mean total serum bilirubin (TSB) was 18.03 ± 13.4 mg/dL, with an average indirect serum bilirubin level of 16.55 ± 2.91 mg/dL and a direct bilirubin level of 0.54 ± 0.26 mg/dL. The mean birth weight of the neonates was 2.7 ± 0.375 kg, ranging from 2.0 to 3.6 kg. The age of presentation varied from 2 to 17 days, with a mean age of 4.52 ± 3.04 days. Among the total neonates screened, G6PD deficiency was detected in 17 (8%) cases. Stratification based on gestational age revealed that 14 (82.3%) of the G6PD-deficient neonates were term, while 3 (17.6%) were preterm (p = 0.537). Analysis of age groups showed that 15 (88.2%) affected neonates were aged 0 to 6 days, while only 2 (11.7%) were between 7 and 28 days old (p = 0.321). Indirect bilirubin levels of ≥17.5 mg/dL were observed in 11 (64.7%) of G6PD-deficient neonates, compared to 93 (48%) in the non-deficient group (p = 0.220). Regarding birth weight, 8 (47%) G6PD-deficient neonates weighed less than 2.5 kg, while 9 (53%) had a birth weight of 2.5 kg or more (p = 0.310). Statistical analysis using Fisher's exact test and the chi-square test showed no significant association between G6PD deficiency and gestational age, age at presentation, indirect bilirubin levels, or birth weight.

Table 1. Analysis of G6PGD deficiencies stratified by several factors

Factors	**G6PD deficiency**		**Value of P**
	No N =191	**Yes N= 17**	
Gestational age			
Preterm	35(18%)	3(17.6%)	**0.537**
Term	156(82%)	14(82.3%)	
Age in days			
0 to 6	156(82%)	15(88.2%)	**0.321**
7 to 28	35(18%)	2(11.7%)	
Indirect bilirubin (mg/dl)			
Below 17.5	98(52%)	6(35.2%)	**0.220**
17.5 or above	93(48%)	11(64.7%)	
Weight in kilograms			**0.310**
Below 2.5	64 (33%)	8(47.0%)	
2.5 or above	124(67%)	9(53%)	
Fisher exact test and chi-square test were used for the determination of P value			

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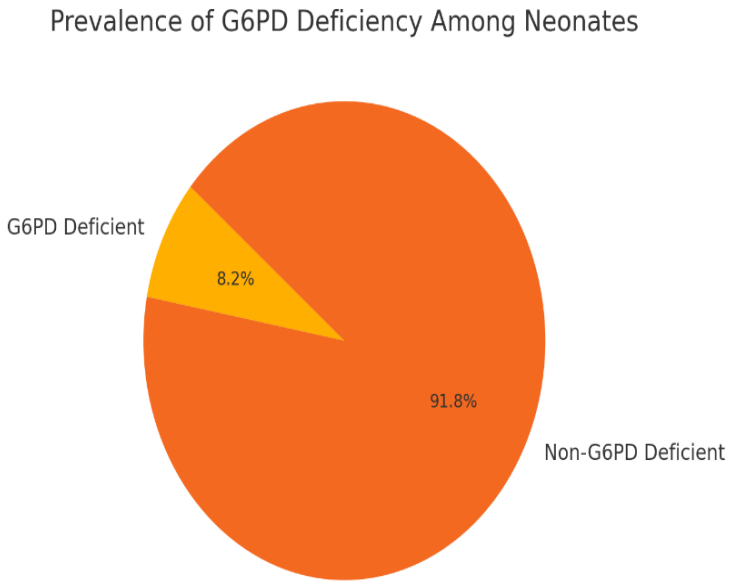

Figure 2 Prevalence of G PD Deficiency Among Neonates

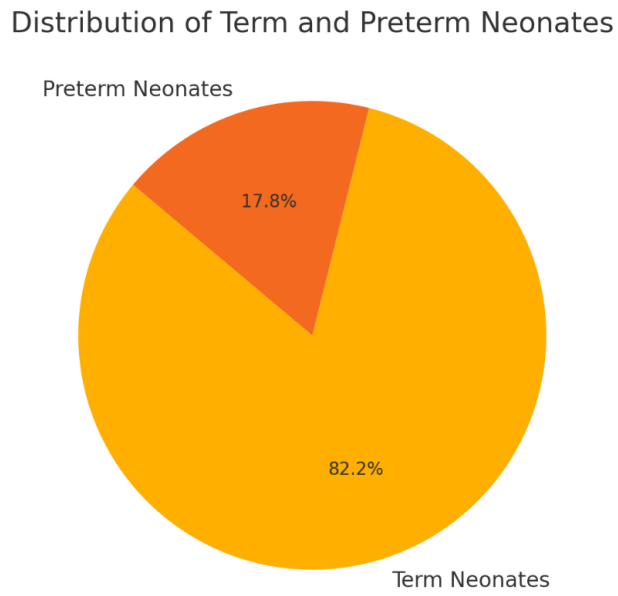

Figure 1 Distribution of Term and Preterm Neonates

DISCUSSION

In the present study, 208 neonates with hyperbilirubinemia were screened for G6PD deficiency, with a prevalence of 8% observed among the participants. This prevalence is higher than reported in studies from Saudi Arabia and Iran, where the incidence was found to be 2% and 3.2%, respectively. However, similar findings have been documented in other studies conducted in Pakistan, where the prevalence ranged between 9% and 16%, suggesting a relatively higher burden in the regional population. These variations may be attributed to genetic predisposition, ethnic diversity, and differences in screening methodologies or sample selection criteria across different geographic regions(15, 16). Findings from this study indicate that G6PD deficiency was more frequently observed in term neonates compared to preterm infants, with a higher prevalence in neonates aged 0 to 6 days at presentation. This aligns with previous literature, which suggests that G6PD-deficient neonates tend to develop jaundice earlier than those with other causes of neonatal hyperbilirubinemia, such as idiopathic jaundice or ABO/Rh incompatibility. Given that neonatal jaundice is a leading cause of hospital admissions and potential long-term complications, early identification of G6PD deficiency is crucial in guiding clinical management. The findings reinforce the significance of routine neonatal screening, particularly in populations where G6PD deficiency is prevalent, to facilitate timely intervention and prevent complications such as kernicterus(17, 18).

Despite its strengths, the study has some limitations. The absence of female neonates in the study population restricts the generalizability of findings, as G6PD deficiency, although more common in males, can also affect heterozygous females due to lyonization. Additionally, the study did not explore the correlation between G6PD deficiency and the severity of jaundice, the need for phototherapy, or exchange transfusion, which could have provided valuable insights into disease burden and management implications. The lack of information regarding genetic subtypes of G6PD deficiency also limits the ability to distinguish between mild and severe enzyme deficiencies, which could influence clinical outcomes(18, 19). Given the strong association between severe neonatal jaundice and G6PD deficiency, there is an urgent need for larger-scale epidemiological studies incorporating a more diverse sample, including female neonates, to assess the true burden of the condition. Future research should also focus on cost-effectiveness analyses of implementing routine neonatal screening programs, especially in high-prevalence regions, to facilitate early diagnosis and management. Strengthening awareness and accessibility to neonatal care services, particularly in resource-limited settings, remains crucial in mitigating the long-term neurological consequences of untreated hyperbilirubinemia. Integrating screening into existing newborn care protocols may serve as an effective strategy in preventing severe complications associated with G6PD deficiency(20).

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CONCLUSION

This study highlights glucose-6-phosphate dehydrogenase (G6PD) deficiency as a significant contributing factor to neonatal jaundice, reinforcing its importance in early screening and diagnosis. The findings emphasize the need for prompt identification of affected neonates to prevent complications associated with severe hyperbilirubinemia. Recognizing G6PD deficiency as a prevalent risk factor underscores the necessity of integrating screening programs into neonatal care, particularly in regions where the condition is more common. Early detection and appropriate management strategies can play a crucial role in reducing the risk of long-term neurological complications, ultimately improving neonatal health outcomes.

AUTHOR CONTRIBUTIONS

Author	Contribution
Inam Ullah	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Sandeef Kumar*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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