Global Journal of Medicine & Public Health

# Prevalence of Glucose-6-Phosphate Dehydrogenase Deficiency among Neonates with Severe Neonatal Hyperbilirubinemia: A Cross-Sectional Study from Assam

*Atiqur Rahman[1#], Indira Das[2], Nazrul Islam Barbhuiyar[3]*

**ABSTRACT**

**Background**

Hyperbilirubinemia is a common issue in neonates, with jaundice affecting a significant proportion of both term and preterm infants. While most cases of neonatal jaundice are benign, a subset requires intervention. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a notable cause of pathological jaundice that can lead to severe hyperbilirubinemia and neurological complications. So, this study aimed to determine the prevalence of G6PD deficiency among neonates with severe hyperbilirubinemia.

**Methods**

A cross-sectional study was conducted at Fakhruddin Ali Ahmed Medical College and Hospital (FAAMCH), Barpeta, Assam, India, between September 2020 and August 2021. Neonates with severe hyperbilirubinemia admitted to the special newborn care unit (SNCU) were included. G6PD deficiency prevalence was determined using qualitative methods. Data were analyzed using SPSS, and statistical significance was set at p-value < 0.05.

**Results**

Among 210 neonates, 23.8% were found to have G6PD deficiency. Male neonates constituted the majority of G6PD deficient cases (68.0%). A significant proportion of G6PD deficient neonates required double volume exchange transfusion (50%) compared to non-G6PD deficient neonates (10%). The mean peak total serum bilirubin levels were significantly higher in G6PD deficient neonates (27.40±8.35 mg/dl) compared to non-G6PD deficient neonates (19.61±5.53 mg/dl).

**Conclusion**

This study provides insights into the prevalence of G6PD deficiency among neonates with severe hyperbilirubinemia. The findings emphasize the importance of considering G6PD deficiency in managing neonatal jaundice and the need for further research to understand the underlying factors contributing to variations in prevalence across different populations.

**Keywords:** G6PD deficiency, Hyperbilirubinemia, Neonatal jaundice, Severe hyperbilirubinemia, Prevalence

**GJMEDPH 2023; Vol. 12, issue 6 | OPEN ACCESS**

**1*Corresponding author** Atiqur Rahman, MD, Medical & Health Officer[1#] , State Health Service, Government of Assam, Assam, India, Former Postgraduate resident, Department of Paediatrics, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam, India; 2.Indira Das, MD, Associate Professor[2] , Department of Paediatrics, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam, India; 3.Nazrul Islam Barbhuiya, MD, Assistant Professor, Department of Paediatrics, Silchar Medical College, Silchar, Assam, India

**Conflict of Interest—none | Funding—none**

**Ethical policy and Institutional Review board statement:** This study was approved by the Institutional Ethics Committee, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam, India (approval no.: FAAMCH/ IEC_PG/498/2020/10574).

## INTRODUCTION

Hyperbilirubinemia is one of the most prevalent problems in neonates. Jaundice is observed during the first week of life in approximately 60% of term neonates and 80% of preterm neonates.[1] Neonatal jaundice is also a common cause of readmission of babies after early discharge. Hyperbilirubinemia is a common and, in most cases, benign problem in neonates. Therapeutic intervention is not required in most cases, but 5-10 % of them have significant hyperbilirubinemia and need phototherapy and other modalities of treatment.[1] Pathological jaundice is referred to as an elevation of TSB levels to the extent where treatment of jaundice is more likely to result in benefit than harm. There is a long list of causes of jaundice in the newborn. Glucose-6-phosphate dehydrogenase deficiency is one of the important causes of pathological jaundice in newborns, where hemolysis occurs and leads to hyperbilirubinemia. Severe hyperbilirubinemia secondary to reduced glucose 6-phosphate dehydrogenase (G6PD) activity is complicated by kernicterus, and it is a serious neurological disease.[2] Glucose-6-phosphate dehydrogenase deficiency is an X-linked deficiency condition and affects more than 400 million people worldwide, representing an overall worldwide prevalence of 4.9%.[3] The G6PD deficiency is an X-linked recessive disease affecting males more than females.[4]Glucose-6-phosphate dehydrogenase (G6PD) is a cytoplasmic enzyme present in all the cells of the body. It converts the co-enzyme NADP to its reduced form NADPH. NADPH is a key component in the cellular antioxidant system. It (NADPH) is required for the reduction of oxidized glutathione (GSSG) by glutathione reductase to its reduced form (GSH) that helps protect the red blood cells by reduction of peroxide and other reactive oxygen species. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most frequent disease involving enzymes of the hexose monophosphate pathway. The most common manifestations are neonatal jaundice and episodic acute haemolytic anaemia, which is induced by infections, certain drugs, and rarely,fava beans.[2]There is a lack of data regarding the prevalence of G6PD deficiency among neonates with severe hyperbilirubinemia from the northeastern part of India. So, considering these issues, this present study aimed to determine the prevalence of G6PD deficiency among newborns with severe hyperbilirubinemia from a tertiary care centre of Assam, India.

## Material & methodology

### Study design, duration and settings

This was a hospital-based cross-sectional study carried out in the Department of Pediatrics in collaboration with the Department of Biochemistry of Fakhruddin Ali Ahmed Medical College and Hospital (FAAMCH), Barpeta, Assam, India between September 2020 and August 2021.

### Study population

The study population consisted of neonates admitted to the special newborn care unit (SNCU) of FAAMCH with severe neonatal hyperbilirubinemia during the study period.

### Sample size and sampling

The sample size was estimated by using the following formula $n=Z^2pq/d^2$. Where Z= 1.96 (at 95% confidence), p= 15.1% (prevalence of G6PD deficiency among North-Eastern India)[4] and d=5% (absolute precision). This gives a value of 203 which was rounded off to 210 and taken as sample size.

### Inclusion and exclusion

**Inclusion criteria:** Newborns with severe hyperbilirubinemia were admitted in SNCU, FAAMCH. For this study, severe hyperbilirubinemia was defined as total bilirubin (TB) >95th percentile on the hour-specific Bhutani normogram, who required a minimum treatment with phototherapy.

**Exclusion criteria:** Neonates with conjugated hyperbilirubinemia. Eligible neonates whose guardians did not give consent for the study.

### Data collection

Data were collected in a predesigned proforma. Data regarding family history of jaundice, anaemia, liver disease; pregnancy history illness during pregnancy, infant of a diabetic mother, maternal drug use during pregnancy; labour and delivery history: birth trauma, oxytocin use, infants with hypoxic-ischemic insult, delayed cord clamping; Infant history delayed or infrequent stool, poor caloric intake, vomiting was taken. Clinical and biochemical examinations were done and recorded.Serum bilirubin was estimated by the calorimetric method in Vitros 5600 analyser. G6PD status estimation was done by a qualitative method using AutoZyme NEW G6PDH

**Data analysis**

Data were analyzed and interpreted to pursue defined objectives by using tables and graphs using Microsoft Excel and IBM SPSS, version 26.0 (Armonk, NY: IBM Corp.). Qualitative variables were summarized using percentages, and quantitative variables were summarized using mean (SD). T-test was done to compare the means, and a p-value of <0.05 was considered statistically significant.

**Ethical consideration**

This study was approved by the Institutional Ethics Committee, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam, India (approval no.: FAAMCH/ IEC_PG/498/2020/10574). Informed written consent was taken from the parents of the neonates before enrolment and neonates were treated in SNCU as per AAP guidelines for phototherapy and exchange transfusion.

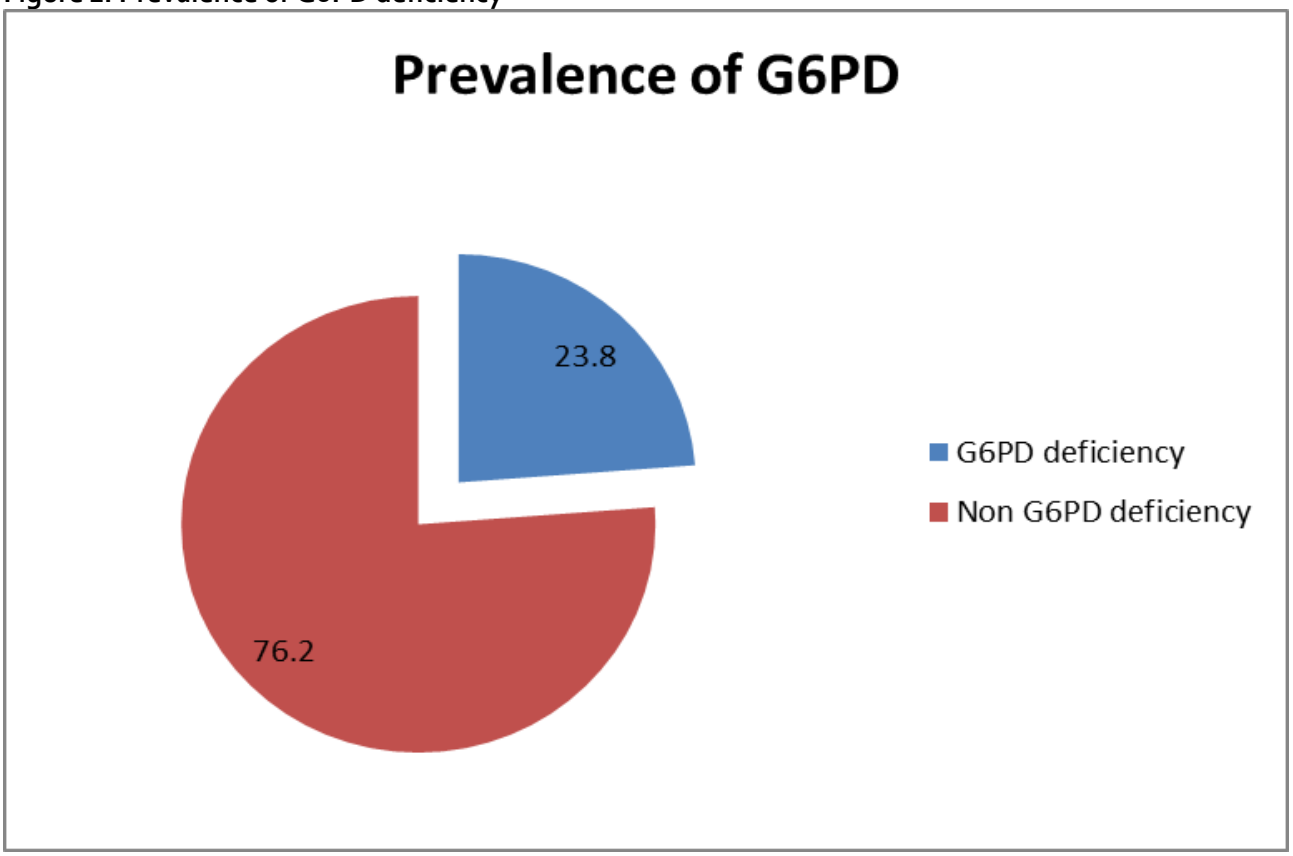
**Results**

Among the 210 neonates, the majority were male children (62.4%), inborn (53.8%), and born by normal vaginal delivery (58.6%). The prevalence of G6PD deficiency among our study sample was 23.8% (Figure 1).

**Table 1: Characteristics of the sample (N=210):**

| Variables | Frequency | Percentage |
|---|---|---|
| Gender | | |
| Male | 131 | 62.4 |
| Female | 79 | 37.6 |
| Admission types | | |
| Inborn | 113 | 53.8 |
| Outborn | 97 | 46.2 |
| Mode of delivery | | |
| Normal vaginal delivery | 123 | 58.6 |
| Assisted vaginal delivery | 5 | 2.4 |
| LSCS | 82 | 39 |
| Gestational age (in weeks) | | |
| <37 weeks | 63 | 30 |
| ≥37 weeks | 147 | 70 |
| Birth weight | | |
| <1.5 kg | 17 | 8.1 |
| 1.5-2.5 kg | 65 | 31 |
| >2.5 kg | 128 | 61 |
| Age at admission | | |
| <1 day | 1 | 0.5 |
| 1-3 days | 38 | 18.1 |
| 3-7 days | 144 | 68.6 |
| 7-14 days | 26 | 12.4 |
| >14 days | 1 | 0.5 |

**Figure 1: Prevalence of G6PD deficiency**




Most of the neonates who had G6PD deficiency were male (68.0%,34/50), with male to female ratio of 2.1:1; however, the gender difference was not statistically significant (p-value=0.347). Among the participants who had G6PD deficiency, 50% (25/50) required double volume exchange transfusion (DVET), as compared to non-G6PD deficient neonates, where only 10% (16/160) of cases required double volume exchange transfusion, while the rest were treated with phototherapy. Total serum bilirubin levels among the G6PD deficient and non-G6PD deficient neonates were statistically significant (Table 2).

**Table 2: Total serum bilirubin level in relation to G6PD status**

| G6PD deficiency status | Mean level of TSB in mg/dl | p-value |
|---|---|---|
| G6PD deficient | 27.40 (±8.35) | <0.001* |
| Non-G6PD deficient | 19.61 (±5.53) | |

*TSB- Total serum bilirubin, *Statistically significant*


ISSN# 2277-9604

## DISCUSSION

This study was done to evaluate the prevalence of G6PD deficiency among newborns with severe hyperbilirubinemia from a tertiary care centre in Assam, India and the study revealed that the prevalence of G6PD deficiency among the study population was 23.8%. Notably, the prevalence of G6PD deficiency in neonates with hyperbilirubinemia exhibited considerable variation across the existing literature. For instance, in a study conducted by Dabboubi et al. In Tunisia, Africa, involving 154 icteric newborns, the prevalence of G6PD deficiency was reported to be 18.83%.[5] Conversely, a study carried out in North-east India demonstrated a lower prevalence of G6PD deficiency (5.07%) among babies.[6] Similarly, Pahlavnzadah et al. observed a prevalence of 18.1% among 105 icteric neonates in their study.[7] In the study by Isa H M et al., focusing on neonatal hyperbilirubinemia and G6PD deficiency and encompassing 1046 neonates, 442 individuals (42%) were found to be G6PD deficient.[8] Furthermore, Deori et al. reported a relatively higher prevalence of 44% among G6PD deficient neonates in their study involving 300 neonates.[9] The variability in the prevalence rates of G6PD deficiency reported in different studies across various regions highlights the heterogeneity of G6PD deficiency occurrence in neonates with hyperbilirubinemia. The observed variations may be attributed to genetic factors and the distinct genetic backgrounds of the studied populations. However, it is crucial to emphasize that regional variations can have significant implications for clinical management and preventive measures for neonatal hyperbilirubinemia and G6PD deficiency.

In the current study, the gender distribution among G6PD deficient neonates was examined, revealing that 34 neonates (68%) were males and 16 neonates (32%) were females, resulting in a male-to-female ratio of 2.1:1. Khanim et al. conducted a study on G6PD deficiency in jaundiced neonates at a tertiary care centre in North East India and found a male-to-female ratio of 2:1, with 53 males and 24 females in their cohort, which is consistent with our findings.[6] Similar to our finding, in a study conducted by Dabboubi et al. focusing on G6PD deficiency in Tunisian jaundiced neonates, a higher incidence of G6PD deficiency (11.03%) was observed in male neonates compared to females (7.79%).[5] Similarly, in another study by Deori et al. involving 300 neonates, it was reported that 44% of the neonates had G6PD deficiency with a male-to-female ratio of 16:1.[9] This association was found to be statistically significant ($p < 0.05$). However, it is worth noting that Paneliya et al. reported contrasting results in their study. Among 350 cases, they observed 181 female neonates (51.71%) and 169 male neonates (48.29%), resulting in a female-to-male ratio of 1.07:1.[10] The gender distribution of G6PD deficient neonates varied among the studies, with our investigation demonstrating a higher proportion of male cases. The discrepancies observed in these different studies warrant further exploration to better understand the underlying factors contributing to G6PD deficiency in neonates of different genders. Among the G6PD deficient cases, 50% required double volume exchange transfusion (DVET) along with phototherapy, while the remaining 50% were treated solely with phototherapy. In contrast, among the non-G6PD deficient cases, only 10% (16/160) required DVET, while 90% (144/160) cases received phototherapy alone. These findings are consistent with previous research. Khanim et al. observed that 45% of G6PD deficient neonates developed significant hyperbilirubinemia necessitating DVET, highlighting a marked difference in DVET requirement between G6PD deficient and G6PD normal neonates ($p<0.001$).[6] Similarly, Pahlavnzadah et al. reported that 31.5% of G6PD deficient neonates required exchange transfusion, a significantly higher rate compared to G6PD sufficient neonates (4.6%) ($p<0.05$).[7] Moreover, Celik et al. found that the proportion of G6PD deficient infants requiring exchange transfusion was 16.4%, whereas it was only 3.3% in G6PD normal infants ($p<0.05$).[11] These findings collectively underscore the importance of considering G6PD deficiency status in managing neonatal hyperbilirubinemia and highlight the potential benefits of DVET in cases of G6PD deficiency. This knowledge could aid in improving clinical decision-making and optimizing treatment strategies for affected neonates.


ISSN# 2277-9604

The mean peak total serum bilirubin (TSB) levels were found to be 27.40±8.35 mg/dl and 19.61±5.53 mg/dl in G6PD deficient and non-G6PD deficient neonates, respectively. The observed differences in TSB levels between the two groups were statistically significant, with a p-value <0.05. These findings align with a study conducted by Sinha et al., which reported mean peak TSB levels of 25.17±5.60 mg/dl in G6PD deficient neonates and 17.36±2.80 mg/dl in G6PD non-deficient neonates.[12]

Additionally, another study by Atay et al. revealed mean maximum serum bilirubin levels of 21.2±3.94 mg/dl in G6PD normal neonates and 24.98±5.9 mg/dl in G6PD deficient neonates.[13]These results demonstrate a significant association between G6PD deficiency and elevated peak TSB levels in neonates, underscoring the clinical relevance of G6PD status in managing neonatal jaundice.Though this study sheds light on the G6PD deficiency prevalence among hyperbilirubinemia neonates from the state of Assam, India, it has limitations too. The main limitations of the present study include a single-centre experience, and a cross-sectional study design. This limits the generalizability of the results to the larger population.

## CONCLUSION

The findings of our study add valuable data to the growing body of knowledge on the prevalence of G6PD deficiency in neonates with severe hyperbilirubinemia. The substantial prevalence rate observed underscores the importance of considering G6PD deficiency as a potential risk factor in this population. However, further research and larger-scale studies are warranted to explore the underlying factors contributing to the observed disparities in G6PD deficiency prevalence across different populations. Understanding these factors can aid in tailoring appropriate screening and intervention strategies to improve neonatal care outcomes.

## REFERENCES


1. Ansong-Assoku B, Shah SD, Adnan M, et al. Neonatal Jaundice. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532930/
2. Prchal JT, Gregg XT. Red cell enzymes. Hematology Am Soc Hematol Educ Program. 2005:19-23.
3. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: a systematic review and meta-analysis. Blood Cells Mol Dis. 2009;42:267-78.
4. Shah I, Jarullah J and Jarullah B. Prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in India: A Systematic Review. *Adv Biosci Biotechnol*. 2018; 9:481-96.
5. Dabboubi R, Amri Y, Hamdi S, Jouini H, Sahli C, Fredj SH, et al. Glucose-6-phosphate dehydrogenase deficiency in Tunisian jaundiced neonates. *Annales de Biologie Clinique*. 2020; 78:411-16.
6. Islam AKS, Bora R, Ramasamy S, Boruah M. Study of glucose 6-phosphate dehydrogenase (G6PD) deficiency in jaundiced neonates of a tertiary care centre of north-east India. J Evolution Med Dent Sci. 2016;5:2271-75.
7. Pahlavanzadeh M, Hekmatimoghaddam S, Teremahi Ardestani M, Ghafoorzadeh M, Aminorraaya M. G6PD Enzyme Deficiency in Neonatal Pathologic Hyperbilirubinemia in Yazd. Iran J Ped Hematol Oncol. 2013;3:69-72.
8. Isa HM, Mohamed MS, Mohamed AM, Abdulla A, Abdulla F. Neonatal indirect hyperbilirubinemia and glucose-6-phosphate dehydrogenase deficiency. Korean J Pediatr. 2017; 60:106-11.
9. Deori R, Kalita S, Baruah S. Association of Glucose-6-phosphate dehydrogenase deficiency and hyperbilirubinemia in neonates. IOSR Journal of Dental and Medical Sciences. 2018: 17. 30-5.
10. Paneliya B, Mario R, Deb S, Gogoi PR. Incidence of G6PD deficiency and its association with neonatal jaundice in babies born at a tertiary care hospital in Meghalaya. Int J Sci Res. 2016; 5:70-3.
11. Celik HT, Günbey C, Unal S, Gümrük F, Yurdakök M. Glucose-6-phosphate dehydrogenase deficiency in neonatal hyperbilirubinaemia: Hacettepe experience. J Paediatr Child Health. 2013; 49:399-402.
12. Sinha R, Sachendra B, Syed VS, Nair L, John BM. To study the prevalence of glucose 6 phosphate dehydrogenase(G6PD) deficiency in neonates with neonatal hyperbilirubinemia and to compare the course of the neonatal jaundice in deficient versus nondeficient neonates. J Clin Neonatol. 2017; 6:71-4
13. Atay E, Bozaykut A, Ipek IO. Glucose-6-phosphate dehydrogenase deficiency in neonatal indirect hyperbilirubinemia. J Trop Pediatr. 2006; 52:56-8.