Section: Paediatrics

Original Research Article

CONGENITAL SCREENING FOR G6PD DEFICIENCY AND HYPOTHYROIDISM AND ITS CLINICAL PRESENTATION IN NEONATAL PERIOD

Veeranna Kotrashetti[1], Kapil Bainade[2], Sheenu Gupta[3]

[1]*Professor & Head, Department of Paediatrics, Dr. D Y Patil Medical College and Hospital, Nerul, Navi Mumbai, India.*
[2]*Associate Professor, Department of Paediatrics, Dr. D Y Patil Medical College and Hospital, Nerul, Navi Mumbai, India.*
[3]*Professor, Department of Paediatrics, BSP Medical College, Nerul, Ch. Sambhajinagar, India.*

Received *: 16/06/2025*
Received in revised form *: 02/08/2025*
Accepted *: 24/08/2025*

Corresponding Author:
Dr. Harsha Vardhan Badiginchala,
Junior Resident, Department of Paediatrics, Dr. D Y Patil Medical College and Hospital, Nerul, Navi Mumbai, India..
Email: harshavardhan015b@gmail.com

DOI: 10.70034/ijmedph.2025.3.470

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 2562-2567

ABSTRACT

Background: Newborn screening has become an essential component of neonatal care, aiming to detect congenital disorders early in life, when interventions are most effective. Among these disorders, glucose-6-phosphate dehydrogenase deficiency and congenital hypothyroidism are of particular concern due to their potential to cause serious health consequences if undiagnosed. This study was conducted to determine the prevalence of G6PD and CH among neonates and assess their early clinical manifestations.

Materials and Methods: A hospital-based prospective study was conducted over two years at a tertiary care hospital in Navi Mumbai. A total of 678 term neonates were screened. Cord blood samples were analyzed for TSH using chemiluminescent immunoassay and for G6PD activity using the fluorescent spot test. Repeat venous TSH testing was performed between days 2 and 5 in neonates with elevated initial TSH levels. Demographic and clinical data were recorded and analyzed.

Results: Of the 678 neonates screened in the current study, the prevalence of G6PD deficiency was 0% and the prevalence of Congenital Hypothyroidism was 0.3%. A statistically significant association was observed between elevated TSH levels and NICU admission ($p = 0.009$), but no other maternal or neonatal factors were significantly associated.

Conclusion: Routine screening for CH is both feasible and effective in identifying neonates at risk for lifelong developmental impairments. Though no G6PD cases were found, its continued inclusion in NBS programs remains essential, especially in high-risk populations. The findings emphasize the need for broader implementation of NBS protocols and long-term follow-up for at-risk infants.

Keywords: Newborn screening, Congenital hypothyroidism, G6PD deficiency, Neonatal screening, Thyroid-stimulating hormone, Neonatal hyperbilirubinemia.

INTRODUCTION

Newborn screening (NBS) represents one of the most effective public health strategies aimed at the early detection of congenital disorders that may lead to significant morbidity or mortality if not treated promptly. The concept of NBS began in the 1960s with Robert Guthrie's pioneering work on phenylketonuria screening using dried blood spot samples from the heel of newborns.[1] Since then, the scope of screening has expanded dramatically and now includes a wide range of genetic, endocrine, hematologic, and metabolic disorders that are otherwise asymptomatic at birth but have severe consequences if untreated.[2]

Among the most significant disorders routinely included in NBS programs are congenital hypothyroidism (CH) and glucose-6-phosphate dehydrogenase (G6PD) deficiency. Both conditions are particularly relevant in the neonatal period due to their silent nature at birth and the risk of long-term sequelae if diagnosis and treatment are delayed.

Congenital hypothyroidism, characterized by deficient thyroid hormone production, can lead to irreversible intellectual disability, motor delay, and growth failure if not treated in the first few weeks of life.[3,4] On the other hand, G6PD deficiency is an X-linked enzymatic disorder that predisposes affected neonates to hemolytic anemia and severe neonatal hyperbilirubinemia, especially when exposed to oxidative stressors such as certain foods, drugs, or infections.[5,6]

Globally, CH has an incidence ranging from 1 in 2000 to 1 in 4000 live births, with reports of increasing detection rates in recent years due to better awareness and reduced TSH thresholds in screening programs.[7,8] Similarly, G6PD deficiency affects over 400 million people worldwide, with a higher prevalence in populations from tropical and subtropical regions, including parts of Asia, Africa, and the Mediterranean basin. [9,10] In India, where approximately 30,000 children are born daily, the burden of these congenital conditions is especially significant. Reports suggest a variable prevalence for G6PD deficiency ranging from 0.5% to 4%, and for CH from 1 in 1,000 to 1 in 1,500 live births.[11,12,13,14] Despite these prevalence rates, universal newborn screening is not uniformly practiced across India. The implementation of NBS in many healthcare settings is limited by infrastructural constraints, lack of awareness among healthcare providers and families, and variability in institutional protocols. Consequently, many affected neonates remain undiagnosed during the critical early window of therapeutic opportunity, leading to long-term disability and increased healthcare costs.[15] This underscores the urgent need for structured and standardized screening programs that are both feasible and cost-effective, particularly in high-volume tertiary care hospitals that serve diverse populations.

In this context, the present study was conducted to determine the prevalence of G6PD deficiency and congenital hypothyroidism among term neonates delivered at a tertiary care hospital in Navi Mumbai. Additionally, the study aimed to assess the clinical profiles of neonates with suspected or confirmed CH and G6PD deficiency, and to evaluate the associations between maternal, perinatal, and neonatal variables and these conditions.

MATERIALS AND METHODS

This was a hospital-based, prospective observational study conducted among 678 neonates over a period of two years in the Department of Paediatrics at a tertiary care hospital in Navi Mumbai, focusing specifically on neonates delivered in the institution during the study period. The inclusion criteria consisted of all full-term newborns delivered at the hospital over the study duration and whose parents agreed to participate in the screening process. Exclusion criteria included preterm neonates, low birth weight babies, babies born outside the hospital, and those whose parents refused consent. A purposive sampling technique was used to select eligible participants. Before initiating the study, ethical clearance was obtained from the Institutional Ethics Committee. Informed written consent was collected from the parents or guardians of all neonates enrolled in the study.

For each participant, relevant demographic and clinical details were recorded using a structured and validated questionnaire. This included maternal data (age, comorbidities, blood group), details of delivery (mode of delivery, gestational age), and newborn characteristics (birth weight, gender, APGAR score, neonatal complications). Cord blood samples were collected immediately after birth from the umbilical cord vein and artery. Approximately 3 mL of cord blood was collected in ethylenediaminetetraacetic acid (EDTA) containers and promptly transported to the laboratory. The screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency was performed using the fluorescent spot test. For the evaluation of congenital hypothyroidism, thyroid-stimulating hormone (TSH) levels were measured using the chemiluminescent immunoassay (CLIA) technique, using the Abbott Architect i2000 system. If the initial cord blood TSH level was elevated (i.e., >20 mIU/L), a repeat venous blood sample or heel prick was collected between the second and fifth day of life for confirmation. The repeat blood samples were collected by a medical professional and transported under standardized conditions for analysis. All enrolled neonates were clinically monitored during their hospital stay. Clinical outcomes such as the presence of jaundice, need for phototherapy, NICU admission, and other relevant symptoms were documented.

The data obtained was recorded and organized using Microsoft Excel 2019. Statistical analysis was performed using IBM SPSS Statistics Version 26. Descriptive statistics, including means, standard deviations, and percentages, were used to summarize the demographic characteristics and prevalence rates. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The present study was conducted among 678 newborns delivered at a tertiary care hospital in Navi Mumbai during the study period.

The most common maternal age group was 26–30 years, comprising 40.4% of the study population, followed by the 31–35 years group (23.5%) and the 21–25 years group (22.7%). A smaller proportion of mothers were aged above 35 years (10.3%) or below 20 years (3.1%). The most frequently observed maternal blood groups were B positive (29.4%), O positive (29.1%), and A positive (27.4%). AB

positive constituted 9.3% of the sample, while Rh-negative blood types, such as A-, B-, and O-, were less common, together comprising only a small percentage of the study population. In terms of maternal comorbidities, hypertension (13.6%) and diabetes (10.8%) were the most commonly reported conditions. Hypothyroidism was present in 9.6% of mothers, whereas hyperthyroidism was much less frequent (0.4%). Other conditions such as beta-thalassemia, tuberculosis, hepatitis B, sickle cell anemia, and HIV were reported in less than 1% of cases.

Table 1: Maternal details among the study participants

Variables		Frequency	Percentages
Age	<20	21	3.1
	21-25	154	22.7
	26-30	274	40.4
	31-35	159	23.5
	>35	70	10.3
Maternal Blood group	A+	186	27.4
	B+	199	29.4
	O+	197	29.1
	A-	13	1.9
	B-	13	1.9
	O-	7	1
	AB+	63	9.3
	AB-	0	0
Symptoms	Diabetes	73	10.8
	Hypertension	92	13.6
	Hypothyroidism	65	9.6
	Hyperthyroidism	3	0.4
	G6PD deficiency	0	0.1
	Beta thalassemia	4	0.6
	TB	4	0.6
	Hepatitis B	2	0.3
	Sickle cell anemia	2	0.3
	HIV	2	0.3

A significant majority (71.2%) of deliveries were performed via lower segment cesarean section (LSCS), while only 28.8% were spontaneous vaginal deliveries. Majority of neonates were born at term (70.6%). Late preterm births accounted for 18.7%, while early preterm births were seen in 8.8% of the neonates. Only 1.3% were classified as extreme preterm, and a very small fraction (0.4%) were post-term.

Table 2: Delivery related details among the study participants

Variables		Frequency	Percentages
Mode of delivery	Spontaneous vaginal delivery	195	28.8
	Lower section caesarean section	483	71.2
Gestational age	Extreme Preterm	9	1.3
	Early Preterm	60	8.8
	Late preterm	127	18.7
	Term	479	70.6
	Post-term	3	0.4

Out of 678 neonates, 54.4% were boys, and 45.6% were girls. 62.1% of neonates had normal birth weight, while 29.9% were classified as low birth weight. Very low birth weight and extremely low birth weight accounted for 5.3% and 2.7% respectively. NICU admission was required for 55.3% of the neonates, indicating a substantial proportion required close monitoring or medical support. Neonatal hyperbilirubinemia was observed in 38.9% of neonates, while the remaining 61.1% did not develop this condition. Despite the large number of neonates, none were diagnosed with G6PD deficiency through the screening process. Neonatal blood group distribution showed that O positive was the most common (31%), followed by B positive (28.6%) and A positive (26.5%). Regarding congenital hypothyroidism, 2.4% of neonates had an initial TSH level >20 mIU/L. Among these, repeat venous TSH testing revealed that only 2 neonates (12.5%) had persistently elevated TSH values, confirming congenital hypothyroidism.

Table 3: Neonatal data among the study participants

Variables		Frequency	Percentages
Gender	Boy	369	54.4
	Girl	309	45.6
Birth weight	Extremely low birth weight	18	2.7
	Very low birth weight	36	5.3

	Low birth weight	203	29.9
	Normal	421	62.1
	Extremely low birth weight	18	2.7
NICU admissions	Yes	375	55.3
	No	203	44.7
Neonatal hyperbilirubinemia	Yes	264	38.9
	No	414	61.1
G6PD deficiency	Yes	0	0
	No	678	100
Congenital Hypothyroidism	TSH >20	16	2.4
	TSH <20	662	97.6
Repeat Venous blood TSH >20	TSH >20	2	12.5
	TSH <20	14	87.5
Blood group	A+	180	26.5
	B+	194	28.6
	O+	210	31
	A-	6	0.9
	B-	12	1.8
	O-	5	0.7
	AB+	67	9.9
	AB-	4	0.6

Maternal comorbidities such as diabetes, hypertension, and hypothyroidism did not show any statistically significant association with elevated TSH levels (p-values >0.05). The mode of delivery approached significance (p = 0.058), with a higher proportion of elevated TSH noted among neonates born via spontaneous vaginal delivery compared to cesarean section, although this did not reach statistical significance.

Importantly, NICU admission showed a statistically significant association with elevated TSH (p = 0.009), indicating that neonates requiring NICU care were more likely to have higher TSH levels. This could reflect underlying illness, or other perinatal complications influencing thyroid function.

Other factors such as crying at birth, presence of neonatal hyperbilirubinemia, and need for phototherapy did not show statistically significant associations with elevated TSH levels.

Table 4: Factors associated with Cord Blood TSH

Variables		Cord Blood TSH		Chi-square value	p-value
		TSH >20 (%)	TSH <20 (%)		
Maternal comorbidity	Diabetes	2 (2.7)	71 (97.3)	0.051	0.821
	Hypertension	1 (1.1)	91 (98.9)	0.749	0.387
	Hypothyroidism	1 (1.5)	64 (98.5)	0.289	0.866
Spontaneous vaginal delivery	Yes	8 (50)	187 (28.2)	3.608	0.058
	No	8 (50)	475 (71.8)		
Lower section caesarean section	Yes	8 (50)	475 (71.8)	3.608	0.058
	No	8 (50)	187 (28.2)		
Cried immediately after birth	Yes	13 (81.3)	596 (90)	1.318	0.251
	No	3 (18.8)	66 (10)		
NICU admission	Yes	14 (87.5)	361 (54.5)	6.870	**0.009***
	No	2 (12.5)	301 (45.5)		
Neonatal hyperbilirubinemia	Yes	9 (56.3)	255 (38.5)	2.066	0.151
	No	7 (43.8)	407 (61.5)		
Phototherapy	Yes	9 (56.3)	255 (38.5)	2.066	0.151
	No	7 (43.8)	407 (61.5)		

"Values are expressed as frequencies and percentages, and the p-value is by the chi-square test. A p-value of less than 0.05 is considered statistically significant."

DISCUSSION

This prospective hospital-based study aimed to evaluate the prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency and congenital hypothyroidism (CH) in neonates, along with associated clinical and demographic factors. Among the 678 neonates screened, the prevalence of CH was 0.3%, whereas no cases of G6PD deficiency were detected. These findings provide insights into the local burden of these conditions and their clinical implications.

The observed CH prevalence of 0.3% (2.4% had elevated cord TSH, but only 2 out of 16 were confirmed) corresponds to a rate of 1 in 339 neonates, which is slightly higher than the national average reported in earlier studies but consistent with more recent findings. Desai et al. reported the prevalence of CH in India as approximately 1 in 1,000 to 1 in 1,500 live births, with regional variation depending on population genetics and screening thresholds.[12] Corbetta et al. demonstrated that lowering the TSH screening cutoff increased detection rates, thereby suggesting a potential underestimation of CH when using higher thresholds.[7] Our use of >20 mIU/L as a

screening threshold could have missed some milder or transient forms of hypothyroidism.

NICU admission showed a statistically significant association with elevated TSH levels ($p = 0.009$), reflecting a similar pattern reported by LaFranchi et al., who indicated that critically ill neonates often exhibit delayed TSH rise due to hypothalamic-pituitary axis immaturity or non-thyroidal illness.[16] Studies from the United States and Europe also recommend repeat screening in neonates admitted to the NICU, especially those born preterm or with low birth weight, due to transient hypothyroxinemia or delayed TSH elevation.[4,17] This supports the need for follow-up testing in high-risk neonates in our setting.

In contrast to CH, no neonate in our study tested positive for G6PD deficiency. This is surprising given the estimated national prevalence ranging from 0.5% to 4% in India, as reported in multiple regional studies.[11,13] For instance, a study in North India by Goyal et al. identified a G6PD deficiency prevalence of 2.3% using the fluorescent spot test.[14] Another study in Karnataka reported a prevalence of 9.4%.[18] The absence of G6PD cases in our study may be due to the relatively homogenous population served by the hospital, the small sample size, or true lower prevalence in this geographical area. Additionally, limitations in sensitivity of the fluorescent spot test used may have contributed to underdetection, especially in female heterozygotes or in cases with borderline enzyme activity.[6]

No statistically significant associations were found between elevated TSH and maternal comorbidities such as diabetes, hypertension, or hypothyroidism. These findings align with prior literature suggesting that while maternal thyroid disease may influence neonatal thyroid function, most neonates maintain euthyroid status due to placental regulation and maternal-fetal compensation.[19] Furthermore, no significant association was observed between mode of delivery and CH, though a trend toward higher TSH in vaginally delivered neonates approached statistical significance ($p = 0.058$). Similar trends have been reported in studies indicating transient TSH surge due to birth stress in neonates delivered vaginally.[20]

Our study had few limitations. This was a single-center study with a limited sample size, potentially affecting the generalizability of findings. The absence of G6PD cases may reflect sampling bias or limitations in test sensitivity. Additionally, the study excluded preterm and low birth weight neonates, who are high-risk groups for thyroid dysfunction.

CONCLUSION

The present study underscores the clinical value of routine newborn screening for congenital hypothyroidism (CH), with a detected prevalence of 0.3%. Although no cases of glucose-6-phosphate dehydrogenase (G6PD) deficiency were found, the importance of screening for this condition remains, especially given its known prevalence in various Indian populations. A significant association between elevated TSH and NICU admission highlights the need for follow-up testing in high-risk neonates to detect delayed thyroid dysfunction. The findings advocate for strengthening universal newborn screening protocols, even in resource-limited settings, to facilitate early diagnosis and intervention, thereby preventing long-term complications such as neurodevelopmental delays. Broader, multicentric studies including diverse and high-risk neonatal populations are needed to better assess the prevalence and clinical patterns of CH and G6PD deficiency in India. Continued efforts to raise awareness among clinicians and caregivers about the benefits of early screening will enhance neonatal health outcomes nationwide.

REFERENCES

1. Guthrie R, Susi A. A simple phenylalanine method for detecting phenylketonuria in large populations of newborn infants. Pediatrics. 1963 Sep 1;32(3):338-43.
2. Strahan JE, Canfield MA, Drummond-Borg LM, Neill SU. Ethnic and gender patterns for the five congenital disorders in Texas from 1992 through 1998. Tex Med. 2002 Sep;98(9):80-6.
3. Rastogi MV, LaFranchi SH. Congenital hypothyroidism: Orphanet J Rare Dis. Journal of Continuing Education Topics & Issues. 2012 Jan 1;14(1):33-4.
4. Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, Van Vliet G, Polak M, Butler G, ESPE-PES-SLEP-JSPE-APEG-APPES-ISPAE, and the Congenital Hypothyroidism Consensus Conference Group. European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. The Journal of Clinical Endocrinology & Metabolism. 2014 Feb 1;99(2):363-84.
5. Cappellini MD, Fiorelli GE. Glucose-6-phosphate dehydrogenase deficiency. The lancet. 2008 Jan 5;371(9606):64-74.
6. Frank JE. Diagnosis and management of G6PD deficiency. American family physician. 2005 Oct 1;72(7):1277-82.
7. Corbetta C, Weber G, Cortinovis F, Calebiro D, Passoni A, Vigone MC, Beck-Peccoz P, Chiumello G, Persani L. A 7-year experience with low blood TSH cutoff levels for neonatal screening reveals an unsuspected frequency of congenital hypothyroidism (CH). Clinical endocrinology. 2009 Nov;71(5):739-45.
8. Hinton CF, Harris KB, Borgfeld L, Drummond-Borg M, Eaton R, Lorey F, Therrell BL, Wallace J, Pass KA. Trends in incidence rates of congenital hypothyroidism related to select demographic factors: data from the United States, California, Massachusetts, New York, and Texas. Pediatrics. 2010 May;125 Suppl 2:S37-47.
9. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of G6PD deficiency: A systematic review and meta-analysis. Blood Cells Mol Dis. 2009;42(3):267-278.
10. WHO Working Group. Glucose-6-phosphate dehydrogenase deficiency. Bull WHO. 1989;67:601-11.
11. Moinuddin MK, Gagandeep V, Mutalik S. Prevalence of glucose 6 phosphate dehydrogenase (G6PD) deficiency in a community by newborn screening. Int J Contemp Pediatr. 2017 May;4(03):1018-20.
12. Desai MP, Sharma R, Riaz I, Sudhanshu S, Parikh R, Bhatia V. Newborn Screening Guidelines for Congenital Hypothyroidism in India: Recommendations of the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE) – Part I: Screening and Confirmation of Diagnosis. Indian J Pediatr. 2018;85(6):440-7.

13. Verma IC. Burden of genetic disorders in India. The Indian Journal of Pediatrics. 2000 Dec;67:893-8.
14. Goyal M, Garg A, Goyal MB, Kumar S, Ramji S, Kapoor S. Newborn screening for G6PD deficiency: A 2-year data from North India. Indian journal of public health. 2015 Apr 1;59(2):145-8.
15. Bailey DB, Zimmerman SJ. The Future of Newborn Screening: Why and How Partnerships Will Be Needed for Success. N C Med J. 2019 Jan-Feb;80(1):28-31.
16. LaFranchi SH. Approach to the diagnosis and treatment of neonatal hypothyroidism. The Journal of Clinical Endocrinology & Metabolism. 2011 Oct 1;96(10):2959-67.
17. Fisher D. Next generation newborn screening for congenital hypothyroidism?. The Journal of Clinical Endocrinology & Metabolism. 2005 Jun 1;90(6):3797-9.
18. Devendra R, Gupta V, Biradar SS, Bhat P, Hegde S, Hoti SL, Mukherjee MB, Hegde HV. G6PD A-is the major cause of G6PD deficiency among the Siddis of Karnataka, India. Annals of Human Biology. 2020 Jan 2;47(1):55-8.
19. Unüvar T, Demir K, Abacı A, Büyükgebiz A, Böber E. The role of initial clinical and laboratory findings in infants with hyperthyrotropinemia to predict transient or permanent hypothyroidism. Journal of clinical research in pediatric endocrinology. 2013 Sep 1;5(3):170-3.
20. Chan LY, Leung TN, Lau TK. Influences of perinatal factors on cord blood thyroid-stimulating hormone level. Acta obstetricia et gynecologica Scandinavica. 2001 Jan 1;80(11):1014-8.