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Original Research Article

Prevalence of Hyperbilirubinemia in Preterm Neonates Admitted to the Nursery of Mufti Mehmood Hospital, Gomal Medical College, D.I. Khan

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Abstract: *Pre-term neonates are known to be more susceptible to various forms of metabolic complications due to immature hepatic function. Hyperbilirubinemia is a common occurrence among pre-term infants and can lead to severe complications if not addressed.* ***Objective:*** *To determine the prevalence of hyperbilirubinemia in preterm neonates admitted to the nursery of Mufti Mehmood Hospital, Gomal Medical College, D.I Khan.* ***Methods:*** *This descriptive cross-sectional study was conducted from 10 October 2024 to 10 March 2025 in the Department of Pediatric Medicine, Mufti Mehmood Hospital, Gomal Medical College, D.I Khan. A total of 96 preterm neonates admitted within 7 days of birth were included. Serum bilirubin level more than 5 mg/dL with visible jaundice was taken as hyperbilirubinemia. Data were analysed using the Statistical Package for the Social Sciences version 26. Stratification was performed, and the chi-square test and Fisher's exact test were applied. P-value ≤0.05 was considered significant.* ***Results:*** *Mean age was 4.14 ± 1.54 days, and mean gestational age was 32.17 ± 2.74 weeks. Hyperbilirubinemia was present in 48 (50%). Significant associations were found with age ≤4 days (69.6%, p<0.001), male gender (63.3%, p=0.008), gestational age ≤32 weeks (100%, p<0.001), and birth weight ≤2000 grams (100%, p<0.001).* ***Conclusion:*** *Hyperbilirubinemia is very common in preterm neonates. Lower gestational age and low birth weight are strongly related to this condition.*

Keywords: Hyperbilirubinemia; Infant, Premature; Jaundice, Neonatal; Phototherapy; Prevalence

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Introduction

Preterm neonates are defined as those born prior to 37 completed weeks of gestation. (1) They are a vulnerable population at increased risk for morbidity and mortality. The severity of prematurity can be described as late preterm, very preterm, and extremely preterm, depending on gestational age, with increasing complications as gestational age decreases. (2) They often display immature organ systems, including the lungs, liver, central nervous system, and gastrointestinal system. (3) This makes them more vulnerable to respiratory distress, feeding difficulties, infections, and metabolic problems. (3) Many physiological processes remain suboptimally developed in these neonates due to liver immaturity and reduced enzymatic activity. (4)

Hyperbilirubinemia is a common clinical problem among preterm neonates and is characterised by a higher incidence compared to term neonates. (5) Increased levels of bilirubin production occur due to increased turnover of red blood cells and decreased clearance of bilirubin due to an immature bilirubin-conjugating system in the liver. (6) In preterm neonates, the decreased activity of uridine diphosphate glucuronosyltransferase (UGT1A1) in the liver contributes to increased levels of unconjugated bilirubin in the blood. (7) Other contributing factors to hyperbilirubinemia include sepsis, birth trauma, bruising, hypoxia and poor feeding, all of which increase bilirubin levels in neonates. (8) In addition, preterm neonates have an immature blood-brain barrier, which makes them susceptible to bilirubin transgression into brain tissues, thereby increasing the risk of kernicterus at relatively lower levels of bilirubin. (9) The incidence of hyperbilirubinemia among preterm neonates is quite high in neonatal intensive care units, and a large number of neonates need to be treated for the condition. (10)

The management of hyperbilirubinemia in preterm neonates depends on gestational age, birth weight, and bilirubin level. (11) Early detection and monitoring of bilirubin levels are very important in preterm neonates. Phototherapy is the primary treatment for hyperbilirubinemia in preterm neonates, and its initiation level in preterm neonates is lower compared to that in term neonates due to the high risk of bilirubin neurotoxicity in preterm neonates. (12) Intensive phototherapy helps convert unconjugated bilirubin to water-soluble bilirubin that can be easily excreted without conjugation. (13) Exchange transfusion may be required in severe cases of hyperbilirubinemia if the bilirubin level is very high or if there is no response to intensive phototherapy. (14)

Local literature is scarce on the prevalence of hyperbilirubinemia in preterm neonates in D I Khan. Considering the high incidence of preterm births, inadequate antenatal care practices, and late arrival at healthcare facilities, it is likely that hyperbilirubinemia is a major issue in this region. The present study is important for determining the local prevalence rate to enhance early detection and management practices and prevent complications from hyperbilirubinemia, including kernicterus.

Methodology

This descriptive cross-sectional study was conducted in the Department of Pediatric Medicine at Mufti Mehmood Hospital, Gomal Medical College, D.I Khan, from 10th October 2024 to 10th March 2025. Ethical approval was obtained from the hospital's Institutional Ethical Review Committee and the CPSP before data collection began. The approval was granted on 29-08-2024 with certificate No. 127/GJMS/JC. A sample size of 96 was calculated using the WHO calculator for a single proportion, with a 95% confidence level, a 10% margin of error, and an expected frequency of hyperbilirubinemia in preterm neonates of 46.2%. (15) All preterm neonates admitted to the nursery within 7 days of birth and of either gender were included. Preterm neonates were defined as babies born at gestational age <37 weeks, assessed on LMP. Neonates having hepatitis confirmed on positive ELISA, congenital anomalies, sepsis, history of exchange transfusion, respiratory distress, biliary atresia (direct hyperbilirubinemia) and ABO incompatibility were excluded from the study. Written informed consent was taken from parents or guardians

before inclusion in the study. After consent, demographic variables, including age, gestational age, gender, mode of delivery (SVD/Cesarean), birth weight, and residence (rural/urban), were recorded.

History was obtained from the parents, and the investigator performed a detailed clinical examination. Gestational age was calculated based on the date of the last menstrual period. Newborns were checked for yellow discolouration of the skin and sclera. A blood test was performed to measure bilirubin levels. All newborns were treated according to the nursery management protocol. Hyperbilirubinemia in newborns was defined as jaundice of the skin with a bilirubin level of more than 5 mg/dL.

Data were entered and analysed using SPSS version 26. Age, gestational age, birth weight and bilirubin levels were presented as mean ± SD or median (IQR) as appropriate. Gender, place of residence, mode of delivery, and hyperbilirubinemia were expressed as frequencies and percentages. Effect modifiers, including age, gestational age, gender, birth weight, place of living and mode of delivery, were controlled through stratification. Post-stratification chi-square test was applied, and a p-value ≤0.05 was considered statistically significant.

Results

The study examined 96 preterm neonates, with a mean age of 4.14 ± 1.54 days and a mean gestational age of 32.17 ± 2.74 weeks. The mean bilirubin level was recorded as 7.97 ± 4.79 mg/dl, and the mean birth weight of the neonates was 1995.92 ± 489.95 grams. Among the study participants, 49 (51.0%) were male, and 47 (49.0%) were female. With regard to place of residence, the majority of the neonates belonged to rural areas (66, 68.8%), while 30 (31.3%) were from urban settings. In terms of mode of delivery, 68 (70.8%) were delivered via C-section and 28 (29.2%) through spontaneous vaginal delivery (Table 1).

Table I: Patient Demographics

Demographics	Mean ± SD
Age (days)	4.14 ± 1.54
Gestational Age (weeks)	32.17 ± 2.74
Bilirubin (mg/dl)	7.97 ± 4.79
Birth Weight (grams)	1995.92 ± 489.95
Gender	
Male n (%)	49 (51.0%)
Female n (%)	47 (49.0%)
Place of Living	
Rural n (%)	66 (68.8%)
Urban n (%)	30 (31.3%)
Mode of Delivery	
SVD n (%)	28 (29.2%)
C-Section n (%)	68 (70.8%)

The frequency of hyperbilirubinemia among preterm neonates was 48 (50%), and the remaining 48 (50%) did not have hyperbilirubinemia, yielding a total sample size of 96 (100%) (Table 2).

Table 2: Frequency of Hyperbilirubinemia Among Preterm Neonates

Hyperbilirubinemia	Frequency	% age
Yes	48	50%
No	48	50%
Total	96	100%

Regarding the association of hyperbilirubinemia with demographic factors, among neonates aged ≤4 days, 39 (69.6%) had hyperbilirubinemia, whereas among neonates aged>4 days, only 9 (22.5%) had hyperbilirubinemia; this association was statistically significant (p<0.001). In terms of gender, hyperbilirubinemia was present in 31 (63.3%) male neonates compared to 17 (36.2%) female neonates, and the difference was statistically significant (p=0.008). When gestational age was considered, all neonates with gestational age ≤32 weeks (48, 100.0%) showed hyperbilirubinemia, while none of the neonates with gestational age >32 weeks were affected; this finding was highly significant (p < 0.001). Regarding place of living, hyperbilirubinemia was present in 34 (51.5%) rural and 14 (46.7%) urban neonates, and no significant association were found (p=0.660). For mode of delivery, 16 (57.1%) neonates delivered by SVD and 32 (47.1%) delivered by C-section had hyperbilirubinemia, and this association was also not statistically significant (p=0.369). Among neonates with birth weight ≤2000 grams, all 48 (100.0%) had hyperbilirubinemia, whereas none of the neonates with birth weight >2000 grams was affected, and this result was statistically highly significant (p<0.001) (Table III).

Table 3: Association of Hyperbilirubinemia with Demographic Factors

Demographic Factors	Subgroups	Hyperbilirubinemia		p-value
		Yes n(%)	No n(%)	
Age (days)	≤4	39 (69.6%)	17 (30.4%)	<0.001**
	>4	9 (22.5%)	31 (77.5%)	
Gender	Male	31 (63.3%)	18 (36.7%)	0.008**
	Female	17 (36.2%)	30 (63.8%)	
Gestational Age (weeks)	≤32	48 (100.0%)	0 (0.0%)	<0.001*
	>32	0 (0.0%)	48 (100.0%)	
Place of Living	Rural	34 (51.5%)	32 (48.5%)	0.660**

	Urban	14 (46.7%)	16 (53.3%)	
Mode of Delivery	SVD	16 (57.1%)	12 (42.9%)	0.369**
	C-Section	32 (47.1%)	36 (52.9%)	
Birth Weight (grams)	≤2000	48 (100.0%)	0 (0.0%)	<0.001*
	>2000	0 (0.0%)	48 (100.0%)	

***Fischer Exact Test **Chi-square Test**

Discussion

A total of 96 preterm neonates were included in the current study, and hyperbilirubinemia was present in 48 (50%), indicating that it is a relatively common condition among preterm neonates in that region. The mean gestational age of the neonates included in the study was 32.17 ± 2.74 weeks. Hyperbilirubinemia was found to be universally present among neonates with gestational age ≤ 32 weeks (48/48, 100.0%), whereas it was completely absent among neonates with gestational age > 32 weeks (0/48, 0.0%) ($p < 0.001$). This could be explained scientifically by the fact that neonates are premature and that liver function is immature, with reduced bilirubin-conjugating capacity due to reduced glucuronyl transferase activity, leading to an accumulation of unconjugated bilirubin, which is responsible for jaundice. Another factor associated with hyperbilirubinemia is neonatal age. It was found that 39 (69.6%) of 56 neonates with neonatal age ≤ 4 days had developed hyperbilirubinemia, whereas only 9 (22.5%) of 40 neonates with neonatal age > 4 days had developed hyperbilirubinemia ($p < 0.001$), which could be explained by the natural peak of bilirubin that is seen during early neonatal age because of increased breakdown of fetal hemoglobin. Another factor associated with neonatal hyperbilirubinemia is birth weight, with 100% (48/48) of neonates with birth weight ≤ 2000 g developing hyperbilirubinemia. In contrast, none of those with birth weight > 2000 g developed it (0/48) ($p < 0.001$), which could be explained by low birth weight being associated with low albumin levels, which are responsible for bilirubin binding, and with low liver enzyme activity. It was found that gender is another factor that is associated with neonatal hyperbilirubinemia, with male neonates being more commonly affected by it (31/49, 63.3%) than female neonates (17/47, 36.2%) ($p = 0.008$), which could be explained by male neonates having more hemolysis of red blood cells and by lower bilirubin-conjugating enzyme activity in males. However, the exact mechanism by which gender influences bilirubin metabolism is still unclear.

The prevalence of hyperbilirubinemia in the present study was 48 (50%) among preterm neonates, higher than the findings reported by Asaye et al. (17), who found 42.3%, and Kabyemera et al. (18), who reported 39.3%. This difference may be due to the present study including only preterm neonates. In contrast, the above-mentioned studies included both term and preterm neonates, and preterm neonates are more susceptible to hyperbilirubinemia due to immature hepatic enzyme activity and poor bilirubin conjugation capacity. Gestational age was significantly associated with hyperbilirubinemia ($p < 0.001$), as all neonates with gestational age ≤32 weeks had hyperbilirubinemia (48, 100.0%). This finding is in agreement with Asaye et al. (17), who also reported prematurity as a significant risk factor with AOR 3.504 (p=0.006), and Kukkadapu et al. (19), who found that prematurity was significantly associated with hyperbilirubinemia in 73.3% of low birth weight neonates (p<0.001). Similarly, Salman et al. (20) found that jaundice was significantly more common in late preterm neonates (24, 22.4%) than in term neonates (7, 6.5%) ($p < 0.01$). The scientific reason for this similarity is that preterm neonates have deficient glucuronyl transferase enzyme activity, which reduces bilirubin conjugation and leads to its accumulation in the blood. Birth weight ≤2000 grams was associated with hyperbilirubinemia in 48 (100.0%) neonates (p<0.001) in present study, which is consistent with Kukkadapu et al. (19) who also reported significantly higher prevalence of hyperbilirubinemia in low birth weight infants 60% as compare to normal birth weight 42% (p=0.04), and also found earlier onset and higher peak bilirubin levels in low birth weight neonates. Sindhu et al. (21) also reported that rebound hyperbilirubinemia was significantly associated with low birth weight (p=0.005), where 26 (92.2%) of rebound cases had low birth weight. This consistent finding across studies suggests that low birth weight neonates have reduced albumin levels and poor hepatic clearance, which makes them more vulnerable to hyperbilirubinemia. Regarding neonatal age, neonates aged ≤4 days were more affected, 39 (69.6%), compared to older neonates, 9 (22.5%) (p<0.001). This is in agreement with Kabyemera et al. (18), who found that neonates aged 2-7 days had significantly higher odds of hyperbilirubinemia (AOR 2.0, p=0.031) compared to those less than one day of age. Similarly, Asaye et al. (17) also reported a significant association with age 1-7 days (AOR 8.171, p=0.009). The reason for this is that bilirubin naturally peaks in the first few days of life due to the breakdown of fetal haemoglobin and limited hepatic clearance in the early neonatal period.

Male gender was more affected in the present study, 31 (63.3%), compared to female, 17 (36.2%) (p=0.008), which is consistent with Asaye et al. (17), who also found male sex as a significant risk factor (AOR 2.234, p=0.035). Gasmelseed et al. (22) and Rauf et al. (23) also reported a male predominance, with 54.4% and 60% male neonates, respectively. However, they did not report gender as a statistically significant factor separately. The possible reason is that male neonates have a relatively higher rate of hemolysis and lower activity of certain bilirubin-metabolising enzymes. Place of living and mode of delivery were not significantly associated with hyperbilirubinemia in the present study (p=0.660 and p=0.369, respectively), which is comparable to findings of Sindhu et al. (21) and Salman et al. (20), who also found no significant association of mode of delivery with jaundice (p=0.885 and p=0.316, respectively). This suggests that these factors do not have a direct pathophysiological role in the development of hyperbilirubinemia, and the condition is more strongly determined by neonatal maturity and hepatic functional capacity.

It is worth noting that this study has limitations that should be considered when interpreting its findings. First, it is worth noting that this study was conducted at a single centre, namely a single hospital. Its findings may not be applicable to all preterm neonates in the country. It is also possible that the small sample size of 96 neonates may impact the findings. It is also worth noting that, due to its cross-sectional study design, causality regarding the demographic factors and hyperbilirubinemia cannot be established. It is also possible that other potential confounding factors, such as feeding, maternal complications, and family history of jaundice, were not considered in the study and may have impacted its findings.

Conclusion

The current study concludes that hyperbilirubinemia is a highly prevalent condition among preterm neonates. A significant incidence of hyperbilirubinemia was noted among this vulnerable population. It was found that gestational age, birth weight, age of the neonate, and gender had a significant association with hyperbilirubinemia. Place of residence and mode of delivery did not show any significant associations.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-No. 127/GJMS/JC)

Consent for publication

Approved

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Conflict of interest

The authors declared no conflict of interest.

Author Contribution

SK (Trainee Medical Officer)
Manuscript drafting, Study Design,
TM (Associate Professor)
Review of Literature, Data entry, Data analysis, and drafting articles.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

References

1. Morniroli D, Tiraferri V, Maiocco G, De Rose DU, Cresi F, Coscia A, *et al.* Beyond survival: the lasting effects of premature birth. *Front Pediatr.* 2023;11:1213243. https://doi.org/10.3389/fped.2023.1213243
2. de Paula ICSF, Dos Santos CS, Werneck RI, de Araujo CM, Rodrigues ÁOLJ, Mendes AL, *et al.* Global prevalence of neonatal mortality in preterm infants: a systematic review and meta-analysis. *BMC Pregnancy Childbirth.* 2025;25(1):1316. https://doi.org/10.1186/s12884-025-08490-3
3. Jang KB, Seo E, Kim Y. Dynamic interactions between the gut microbiome, health, and metabolic disorders in preterm infants. *J Microbiol Biotechnol.* 2025;35:e2508033. https://doi.org/10.4014/jmb.2508.08033
4. Reiss JD, Mataraso SJ, Holzapfel LF, Marić I, Kasowski MM, Martin CR, *et al.* Applications of metabolomics and lipidomics in the neonatal intensive care unit. *Neoreviews.* 2025;26(2):e100-e114. https://doi.org/10.1542/neo.26-2-011
5. Gedefaw GD, Abuhay AG, Daka DT, Wondie WT, Gonete AT, Getaneh FB, *et al.* Time to recovery and its predictors among neonates undergoing phototherapy at the comprehensive specialised hospitals of northwest Ethiopia. *Sci Rep.* 2024;14(1):31665. https://doi.org/10.1038/s41598-024-80964-4
6. Safo-Mensah N, Amfo-Swanzy O, Ashong J, Okai E, Amoako MF, Lomotey P, *et al.* Determinants of jaundice severity in neonates admitted at a teaching hospital in Ghana. *PLoS One.* 2025;20(6):e0325003. https://doi.org/10.1371/journal.pone.0325003
7. Hanafusa H, Abe S, Ohyama S, Kyono Y, Kido T, Nakasone R, *et al.* Influence of UGT1A1 genetic variants on free bilirubin levels in Japanese newborns: a preliminary study. *Int J Environ Res Public Health.* 2022;19(20):13090. DOI: https://doi.org/10.3390/ijerph192013090
8. Thielemans L, Peerawaranun P, Mukaka M, Paw MK, Wiladphaingern J, Landier J, *et al.* High levels of pathological jaundice in the first 24 hours and neonatal hyperbilirubinaemia in an epidemiological cohort study on the Thailand-Myanmar border. *PLoS One.* 2021;16(10):e0258127. https://doi.org/10.1371/journal.pone.0258127
9. Mishra S, Wanare H. Hierarchical decision model for in vitro bilirubin content prediction from absorption spectrum of whole blood. *J Biomed Opt.* 2023;28(6):067001. https://doi.org/10.1117/1.JBO.28.6.067001
10. Ghobrial EE, Al Sayed HM, Saher AEM, Mahmoud BER. Neonatal jaundice: magnitude of the problem in Cairo University's neonatal intensive care unit as a referral centre. *Afr Health Sci.* 2023;23(1):656-666. DOI: https://doi.org/10.4314/ahs.v23i1.70
11. van der Geest BAM, de Mol MJS, Barendse ISA, de Graaf JP, Bertens LCM, Poley MJ, *et al.* Assessment, management, and incidence of neonatal jaundice in healthy neonates cared for in primary care: a prospective cohort study. *Sci Rep.* 2022;12(1):14385. https://doi.org/10.1038/s41598-022-17933-2
12. Choi Y, Park S, Lee H. Neonatal jaundice requiring phototherapy risk factors in a newborn nursery: machine learning approach. *Children (Basel).* 2025;12(8):1020. https://doi.org/10.3390/children12081020
13. Uchida Y, Takahashi Y, Kurata C, Morimoto Y, Ohtani E, Tosaki A, *et al.* Urinary lumirubin excretion in jaundiced preterm neonates during phototherapy with blue light-emitting diode vs green fluorescent lamp. *Sci Rep.* 2023;13(1):18359. https://doi.org/10.1038/s41598-023-45147-7
14. Hemmati F, Mahini SM, Bushehri M, Asadi AH, Barzegar H. Exchange transfusion trends and risk factors for extreme neonatal hyperbilirubinemia over 10 years in Shiraz, Iran. *Iran J Med Sci.* 2024;49(6):384-393. https://doi.org/10.30476/ijms.2023.99176.3123
15. Aynalem S, Abayneh M, Metaferia G, Demissie AG, Gidi NW, Demtse AG, *et al.* Hyperbilirubinemia in preterm infants admitted to neonatal intensive care units in Ethiopia. *Glob Pediatr Health.* 2020;7:2333794X20985809.
16. Creeden JF, Gordon DM, Stec DE, Hinds TD Jr. Bilirubin as a metabolic hormone: the physiological relevance of low levels. *Am J Physiol Endocrinol Metab.* 2021;320(2):E191-E207. https://doi.org/10.1152/ajpendo.00405.2020
17. Asaye S, Bekele M, Getachew A, Fufa D, Adugna T, Tadese E. Hyperbilirubinemia and associated factors among neonates admitted to the neonatal care unit in Jimma Medical Centre. *Research Square.* 2022. DOI: https://doi.org/10.21203/rs.3.rs-1808478/v1
18. Kabyemera R, Mumwi M, Rwezaula R, Kidenya B, Hokororo A. Prevalence and factors associated with hyperbilirubinemia and the utility of transcutaneous bilirubin among neonates admitted to Bugando Medical Centre, Mwanza, Tanzania. *Journal of African Neonatal.* 2025;1:1-8.
19. Kukkadapu S, Tumma UK. Prevalence of neonatal hyperbilirubinemia in low birth weight and normal birth weight babies. *International Journal of Current Pharmaceutical Review and Research.* 2025;17(10):822-826. https://doi.org/10.22159/ijcpr.2025v17i10.137
20. Salman M, Rathore H, Ariff S, Ali R, Khan AA, Nasir M. Frequency of immediate neonatal complications (hypoglycemia and neonatal jaundice) in late preterm and term neonates. *Cureus.* 2021;13(1):e12512. https://doi.org/10.7759/cureus.12512
21. Sindhu, Naz F, Kumar M, Raza A, Usman M, Lohana M. Prevalence and factors associated with significant rebound hyperbilirubinemia after phototherapy among neonates: a cross-sectional survey. *Pakistan Journal of Medical and Health Sciences.* 2022;16(11):552-554.
22. Gasmelseed SAA, Magzoub OS, Aledresi MAAA. Prevalent causes and outcomes of unconjugated hyperbilirubinemia in neonates. *World Journal of Advanced Research and Reviews.* 2025;27(02):1465-1473. https://doi.org/10.30574/wjarr
23. Rauf S, Salah-ud-Din B, Abbas G, Nawaz Z. Incidence and risk factors of acute bilirubin encephalopathy in neonates with hyperbilirubinemia presenting at secondary care hospital. *Pakistan Journal of Medical Sciences.* 2023;39(2):583-586. https://doi.org/10.12669/pjms.39.2.5520