

Comparison of Growth and Development of Full Term Neonates with Severe and Moderate Hyperbilirubinemia at their 6 Months: A Tertiary Hospital Based Study in Eastern Region of India

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Received: 01-10-2025 / Revised: 15-11-2025 / Accepted: 21-12-2025

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Conflict of interest: Nil

Abstract

Introduction: Hyperbilirubinemia is a common neonatal condition, affecting a significant proportion of term and preterm infants during the first week of life. Elevated unconjugated bilirubin can lead to neurological impairment, even in full-term neonates. Early identification and assessment are crucial to prevent long-term developmental complications.

Aims: To compare the motor and mental development of full-term neonates with severe versus moderate hyperbilirubinemia at six months of age.

Materials and Methods: This is a tertiary hospital based Prospective observational study. 363 full term neonates in each group with severe and moderate hyperbilirubinemia were selected by convenience sampling to compare the Mental development of neonates with severe and moderate hyperbilirubinemia. Study was conducted in the Sick Neonatal Care Unit of Dr. B.C. Roy P.G.I.P.S at Kolkata in Eastern India between December 2000- March 2022 after approval from institutional ethics committee in a pretested Proforma.

Result: The three groups were comparable with respect to age distribution, sex, birth weight, and gestational age ($p > 0.05$). Motor development scores (MO DASII) at six months were significantly lower in neonates with severe hyperbilirubinemia compared to those with moderate and no hyperbilirubinemia ($p = 0.009$). Similarly, mental development scores (ME DASII) were significantly reduced in the severe hyperbilirubinemia group ($p = 0.001$). A strong positive correlation was observed between motor and mental development scores at six months ($r = 0.824$, $p < 0.001$).

Conclusion: Severe neonatal hyperbilirubinemia is associated with significant impairment in both motor and mental development at six months of age in full-term neonates. These findings emphasize the need for early identification, timely intervention, and structured neurodevelopmental follow-up in neonates with moderate to severe hyperbilirubinemia, particularly in resource-limited settings

Keywords: Neonatal Hyperbilirubinemia; Neurodevelopment; DASII; Motor Development; Mental Development; Full-Term Neonates.

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Introduction

Neonatal hyperbilirubinemia is one of the most common physiological conditions in the early neonatal period, characterized by elevated serum bilirubin due to increased bilirubin production and immature hepatic conjugation mechanisms in newborns. While mild jaundice is often considered benign, elevated unconjugated bilirubin levels are neurotoxic and may cross the blood-brain barrier, posing a risk to the developing central nervous system. This neurotoxicity can lead to a broad spectrum of neurological sequelae, from subtle

neurobehavioral changes to severe motor and cognitive impairment, especially when total serum bilirubin levels are markedly elevated [1]. Several cohort and observational studies indicate that full-term infants with higher bilirubin concentrations are at increased risk of motor and neurodevelopmental delays within the first year of life, even in the absence of classical acute bilirubin encephalopathy [2]. It has been reported that severe hyperbilirubinemia is associated with persistent neurodevelopmental impairment at six months of

age, including delays in motor milestones and cognitive domains [3]. Furthermore, stratification of bilirubin levels suggests that moderate elevations may also adversely affect developmental outcomes, underscoring the need to clarify the differential impact of bilirubin severity on early motor and mental development [4].

In the context of tertiary care settings in India, where neonatal jaundice remains a frequent clinical challenge, understanding how varying degrees of hyperbilirubinemia influence early neurodevelopment is critical. This study, therefore, aims to compare motor and mental developmental outcomes at six months in full-term neonates with severe versus moderate hyperbilirubinemia, thereby contributing evidence to optimize early identification and intervention strategies in resource-limited settings. Aims of the study to compare the motor and mental development of full-term neonates with severe versus moderate hyperbilirubinemia at six months of age.

Materials and Methods

Study design: Prospective observational study.

Place of study: This is a tertiary hospital based Prospective observational study. 363 full term neonates in each group with severe and moderate hyperbilirubinemia were selected by convenience sampling to compare the mental development of neonates with severe and moderate hyperbilirubinemia. Study was conducted in the Sick Neonatal Care Unit of Dr. B.C. Roy P.G.I.P.S at Kolkata in Eastern India between December 2000- March2022 after approval from institutional ethics committee in a pretested Proforma.

Period of study: 2.5 year.

Study Population: A total of 363 neonates were included in the study.

Inclusion Criteria

- Full-term neonates with clinical and laboratory evidence of hyperbilirubinemia.
- Neonates whose parents/guardians provided informed consent.

Exclusion Criteria

- Preterm neonates (<37 weeks gestational age).
- Neonates with congenital malformations, perinatal asphyxia, sepsis, or hemolytic disease.
- Neonates whose parents/guardians did not consent to participate.

Study Variable

- Independent variable: Severity of hyperbilirubinemia (moderate vs. severe).
- Dependent variables: Motor and mental development at six months, assessed using standardized developmental assessment scales (e.g., DASII).
- Other variables: Demographic characteristics (age, sex), birth weight, gestational age, total serum bilirubin levels, and duration of phototherapy.

Statistical Analysis: Data were initially entered into Microsoft Excel and subsequently analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized as means and standard deviations, while categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the Kruskal–Wallis test. Chi-square tests, including Fisher’s exact test where appropriate, were applied for categorical data. A p-value ≤ 0.05 was considered statistically significant.

Result

Table 1: Association between demographic parameter with Group

Variable	Category	No Hyperbilirubinemia (n=121)	Moderate Hyperbilirubinemia (n=122)	Severe Hyperbilirubinemia (n=120)	Total (n=363)	p-value
Age Group	1–4.9	57 (47.1%)	58 (47.5%)	67 (55.8%)	182 (50.1%)	0.119
	5–10	55 (45.5%)	51 (41.8%)	50 (41.7%)	156 (43.0%)	
	>10	9 (7.4%)	13 (10.7%)	3 (2.5%)	25 (6.9%)	
Sex	Female	47 (38.8%)	48 (39.3%)	52 (43.3%)	147 (40.5%)	0.739
	Male	74 (61.2%)	74 (60.7%)	68 (56.7%)	216 (59.5%)	
Birth Weight (g)	<2500	42 (34.7%)	37 (30.3%)	36 (30.0%)	115 (31.7%)	0.679
	≥ 2500	79 (65.3%)	85 (69.7%)	84 (70.0%)	248 (68.3%)	

Table 2: Association between Gestational Age (weeks)with Group

Variable	Cate gory	No Hyperbilirubine mia (n=121)	Moderate Hyperbilirubinemia (n=122)	Severe Hyperbilirubin emia (n=120)	Total (n=363)	p- value
Gestational Age (weeks)	37– 38.6	70 (57.9%)	67 (54.9%)	77 (64.2%)	214 (59.0%)	0.328
	39– 42	51 (42.1%)	55 (45.1%)	43 (35.8%)	149 (41.0%)	

Table 3: Kruskal-Wallis Test MO DASII 6Month and ME DASII 6Month

Kruskal-Wallis Test				p-value
	Group	N	Mean Rank	
MO DASII 6Month	No Hyperbilirubinemia	121	195.95	0.009
	Moderate Hyperbilirubinemia	122	191.65	
	Severe Hyperbilirubinemia	120	158.13	
	Total	363		
ME DASII 6Month	No Hyperbilirubinemia	121	201.08	0.001
	Moderate Hyperbilirubinemia	122	191.76	
	Severe Hyperbilirubinemia	120	152.83	
	Total	363		

Table 4: Correlation between MO DASII 6Month VS. ME DASII 6Month

MO DASII 6Month		ME DASII 6Month
	Pearson Correlation	0.824
	P value	0
	Number	363

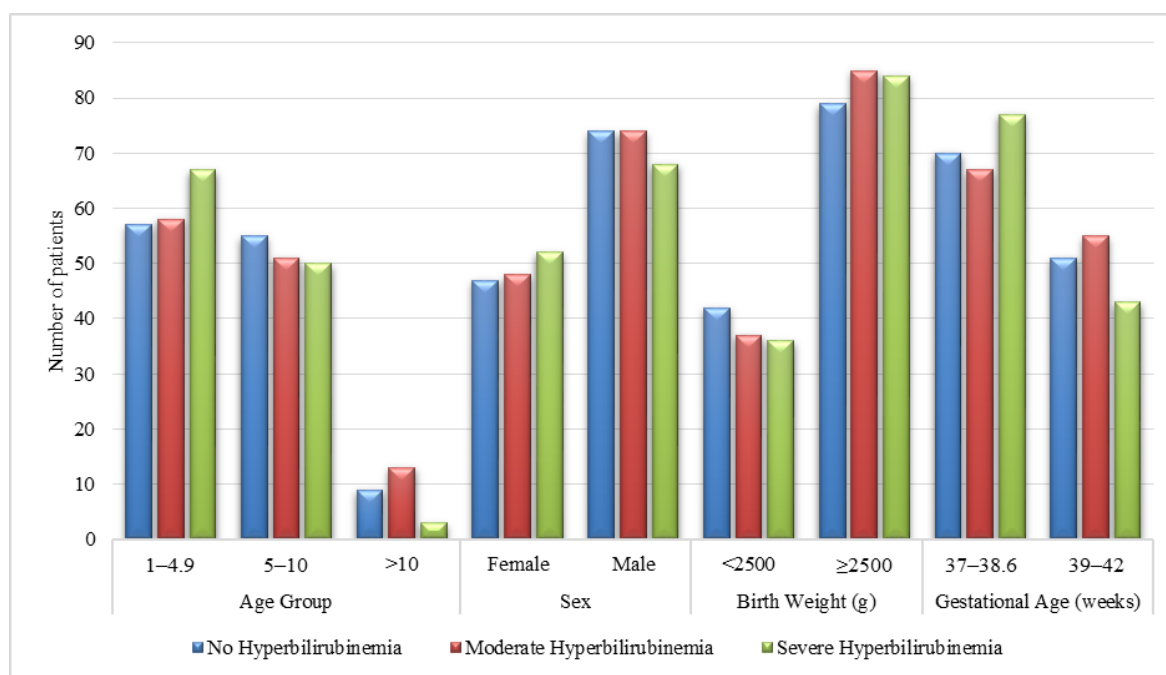


Figure 1: Association of Demographic Factors with Severity of Hyperbilirubinemia

A total of 363 neonates were included in the study, divided into three groups: no hyperbilirubinemia (n = 121), moderate hyperbilirubinemia (n = 122), and severe hyperbilirubinemia (n = 120).

Age distribution: In the no hyperbilirubinemia group, 57 neonates (47.1%) were aged 1–4.9 months, 55 (45.5%) were 5–10 months, and 9 (7.4%) were >10 months. In the moderate hyperbilirubinemia group, 58 neonates (47.5%) were 1–4.9 months, 51 (41.8%) were 5–10 months, and 13 (10.7%) were >10 months. In the severe

hyperbilirubinemia group, 67 neonates (55.8%) were 1–4.9 months, 50 (41.7%) were 5–10 months, and 3 (2.5%) were >10 months. The difference in age distribution among the three groups was not statistically significant ($p = 0.119$).

Sex distribution: In the no hyperbilirubinemia group, 47 neonates (38.8%) were female and 74 (61.2%) were male. In the moderate hyperbilirubinemia group, 48 neonates (39.3%) were female and 74 (60.7%) were male. In the severe hyperbilirubinemia group, 52 neonates (43.3%) were female and 68 (56.7%) were male. There was no significant association between sex and hyperbilirubinemia severity ($p = 0.739$).

Birth weight: Among neonates with no hyperbilirubinemia, 42 (34.7%) had a birth weight <2500 g and 79 (65.3%) had a birth weight \geq 2500 g. In the moderate hyperbilirubinemia group, 37 neonates (30.3%) were <2500 g and 85 (69.7%) were \geq 2500 g. In the severe hyperbilirubinemia group, 36 neonates (30.0%) were <2500 g and 84 (70.0%) were \geq 2500 g. Birth weight distribution did not differ significantly among the groups ($p = 0.679$).

A total of 363 neonates were analyzed for gestational age distribution. In the no hyperbilirubinemia group, 70 neonates (57.9%) were born at 37–38.6 weeks and 51 neonates (42.1%) were born at 39–42 weeks. In the moderate hyperbilirubinemia group, 67 neonates (54.9%) were 37–38.6 weeks and 55 neonates (45.1%) were 39–42 weeks. In the severe hyperbilirubinemia group, 77 neonates (64.2%) were 37–38.6 weeks and 43 neonates (35.8%) were 39–42 weeks. The difference in gestational age distribution among the three groups was not statistically significant ($p = 0.328$).

The Kruskal-Wallis test was used to compare motor (MO) and mental (ME) development scores at 6 months among neonates with no, moderate, and severe hyperbilirubinemia. Motor Development (MO DASII 6Month): The mean rank of MO DASII scores was highest in the no hyperbilirubinemia group (195.95), slightly lower in the moderate hyperbilirubinemia group (191.65), and lowest in the severe hyperbilirubinemia group (158.13). This difference was statistically significant ($p = 0.009$), indicating that neonates with severe hyperbilirubinemia had lower motor development scores at 6 months. Mental Development (ME DASII 6Month): Similarly, the mean rank of ME DASII scores was highest in the no hyperbilirubinemia group (201.08), slightly lower in the moderate hyperbilirubinemia group (191.76), and lowest in the severe hyperbilirubinemia group (152.83). This difference was also statistically significant ($p = 0.001$), suggesting that severe

hyperbilirubinemia adversely affected mental development at 6 months.

Pearson correlation analysis was performed to assess the relationship between motor (MO DASII) and mental (ME DASII) development scores at 6 months in the study population. A strong positive correlation was observed between MO and ME DASII scores ($r = 0.824$, $p < 0.001$), indicating that neonates with higher motor development scores also tended to have higher mental development scores.

Discussion

Neonatal hyperbilirubinemia remains a common clinical problem in the neonatal period, with increasing evidence suggesting its potential impact on early neurodevelopment. In the present study, we evaluated the association between the severity of hyperbilirubinemia and motor as well as mental developmental outcomes at 6 months of age in full-term neonates.

In our study, demographic characteristics such as age distribution, sex, birth weight, and gestational age were comparable among neonates with no, moderate, and severe hyperbilirubinemia, with no statistically significant differences observed ($p > 0.05$). This demographic comparability suggests that the observed differences in neurodevelopmental outcomes were primarily attributable to the severity of hyperbilirubinemia rather than confounding baseline factors.

A key finding of our study was the significant decline in motor development scores with increasing severity of hyperbilirubinemia. The mean rank of MO DASII scores was highest in the no hyperbilirubinemia group (195.95), followed by the moderate hyperbilirubinemia group (191.65), and lowest in the severe hyperbilirubinemia group (158.13), with this difference being statistically significant ($p = 0.009$). This finding indicates that severe hyperbilirubinemia is associated with impaired motor development by 6 months of age. These findings are consistent with the study by Akkaya et al. [5], who reported delayed motor development and altered sensory processing skills in infants with a history of neonatal hyperbilirubinemia. Similarly, Kahraman et al. [6] demonstrated abnormalities in motor repertoire among infants aged 3–5 months exposed to elevated bilirubin levels, suggesting early disruption of motor maturation even in the absence of overt bilirubin encephalopathy.

Mental development was also significantly affected in our cohort. The mean rank of ME DASII scores was highest in neonates without hyperbilirubinemia (201.08), followed by those with moderate hyperbilirubinemia (191.76), and lowest in those with severe hyperbilirubinemia (152.83). This difference was highly significant ($p = 0.001$),

indicating a strong association between severe hyperbilirubinemia and delayed cognitive development at 6 months.

Our findings are in agreement with Vallamkonda et al. [7], who reported adverse neurodevelopmental outcomes at 12–15 months among term neonates with hyperbilirubinemia using General Movement Assessment. Furthermore, a recent systematic review by Merino-Andrés et al. [8] concluded that neonatal hyperbilirubinemia is associated with a broad spectrum of neurodevelopmental impairments, including both motor and cognitive deficits, reinforcing the biological plausibility of our observations.

Importantly, earlier work by Soorani-Lunsing et al. [9] challenged the assumption that moderate hyperbilirubinemia is entirely benign, reporting subtle but measurable effects on brain development in otherwise healthy term neonates. This observation aligns with the trend noted in our study, where even moderate hyperbilirubinemia showed lower DASII scores compared to neonates without hyperbilirubinemia, although the decline was more pronounced in the severe group.

Long-term consequences of neonatal hyperbilirubinemia have also been highlighted by Seidman et al. [10], who demonstrated poorer physical and cognitive performance at 17 years of age among individuals with a history of neonatal jaundice. In the Indian context, Özgürhan and Cömert [11] reported significant neurodevelopmental delays in term newborns with clinically significant hyperbilirubinemia, emphasizing the relevance of early detection and follow-up in resource-limited settings. Another important observation in our study was the strong positive correlation between motor and mental development at 6 months ($r = 0.824$, $p < 0.001$). This finding suggests that impairment in motor development is closely associated with cognitive delay, supporting the concept of global neurodevelopmental vulnerability due to bilirubin neurotoxicity. Similar associations between motor and cognitive domains have been reported by Akkaya et al. [5] and summarized in the systematic review by Merino-Andrés et al. [8].

Conclusion

This tertiary hospital-based study from eastern India demonstrates that while demographic variables such as age, sex, birth weight, and gestational age were comparable among full-term neonates with no, moderate, and severe hyperbilirubinemia, the severity of hyperbilirubinemia had a significant adverse impact on neurodevelopmental outcomes at 6 months of age. Neonates with severe hyperbilirubinemia showed significantly lower motor and mental development scores compared to those with moderate or no hyperbilirubinemia, as

evidenced by significantly reduced MO DASII and ME DASII mean ranks. Furthermore, the strong positive correlation between motor and mental development scores highlights the interrelated nature of neurodevelopmental domains and suggests a global effect of bilirubin neurotoxicity. These findings underscore the importance of early identification, prompt management, and structured neurodevelopmental follow-up of neonates with moderate to severe hyperbilirubinemia to mitigate potential long-term developmental impairments.

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