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ORIGINAL ARTICLE

Predictive Value of Neonatal Jaundice Severity on Long-Term Neurodevelopmental Outcomes

[1]Ashok Panwar, [2]Sudhir Dixit

[1]Associate Professor, Department of Paediatrics, Rajshree Medical Institute and Research, Bareilly, Uttar Pradesh, India;
[2]Assistant Professor, Department of Paediatrics, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India

ABSTRACT:
Aim: This study aimed to evaluate the predictive value of neonatal jaundice severity on long-term neurodevelopmental outcomes in neonates diagnosed with hyperbilirubinemia. The association between jaundice severity and cognitive, motor, and speech development at 6 months, 12 months, and 24 months was assessed. **Material and Methods:** A prospective cohort study was conducted at a tertiary care hospital, enrolling 120 neonates with clinically significant neonatal jaundice. Inclusion criteria included full-term and late preterm neonates (≥34 weeks gestation) requiring phototherapy or exchange transfusion. Exclusion criteria comprised neonates with congenital anomalies, genetic syndromes, perinatal asphyxia, or other neurodevelopmental conditions. Neonates were classified based on total serum bilirubin (TSB) levels, and neurodevelopmental outcomes were evaluated using Bayley Scales of Infant Development (BSID-III) and the Ages & Stages Questionnaire (ASQ-3) at 6 months, 12 months, and 24 months. Statistical analysis included chi-square tests and logistic regression models, with $p < 0.05$ considered significant. **Results:** Among 120 neonates, 50% were born at 37-39 weeks gestation, 25% were late preterm, and 25% were full-term (≥40 weeks). Phototherapy was required for 24-48 hours in 50% of neonates, and 10% underwent exchange transfusion. Neurodevelopmental assessments showed that 26.67% had cognitive delays, 15.00% had motor delays, and 18.33% had speech delays. However, no statistically significant association was found between jaundice severity and neurodevelopmental impairments ($p > 0.05$), indicating that bilirubin levels alone were not strong predictors of long-term neurodevelopmental delays. **Conclusion:** While neonatal jaundice was associated with some neurodevelopmental delays, its severity did not significantly correlate with cognitive, motor, or speech impairments. These findings suggest that timely management, phototherapy, and early follow-up care may mitigate adverse outcomes. Larger studies with longer follow-up durations are needed to further explore the long-term effects of neonatal jaundice on neurodevelopment.
Keywords: Neonatal jaundice, neurodevelopmental outcomes, hyperbilirubinemia, phototherapy, cognitive delay

Corresponding author: Sudhir Dixit, Assistant Professor, Department of Paediatrics, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India

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INTRODUCTION

Neonatal jaundice is a common condition affecting newborns, characterized by the yellowing of the skin and sclera due to elevated serum bilirubin levels. While in most cases, jaundice is benign and resolves without long-term consequences, severe hyperbilirubinemia poses a significant risk to neurodevelopmental outcomes. The concern arises from bilirubin-induced neurotoxicity, which can lead to permanent neurological impairments, including kernicterus, cerebral palsy, and cognitive deficits. Understanding the predictive value of neonatal jaundice severity on long-term neurodevelopment is crucial for early intervention and improved clinical management.[1]Bilirubin is a byproduct of hemoglobin breakdown and is normally processed by the liver for excretion. However, in neonates, particularly preterm infants, the liver's capacity to conjugate and eliminate bilirubin is immature, leading to transient hyperbilirubinemia. While most cases remain within physiological limits, excessive bilirubin accumulation can cross the blood-brain barrier and deposit in brain tissues, particularly the basal ganglia, hippocampus, and cerebellum. The neurotoxic effects depend on the duration and severity of hyperbilirubinemia, as well as the infant's individual susceptibility.[2]The severity of neonatal jaundice is commonly assessed using total serum bilirubin (TSB) levels and clinical signs of bilirubin encephalopathy. Advanced monitoring techniques, such as transcutaneous bilirubin measurement and neuroimaging, have improved early detection. However, predicting which neonates will experience long-term neurodevelopmental impairment remains a challenge. Several factors, including gestational age, genetic predisposition, comorbid conditions, and duration of hyperbilirubinemia, influence the risk of adverse outcomes.[3]Long-term neurodevelopmental impairments associated with severe neonatal jaundice range from mild cognitive and behavioral issues to profound neurological disabilities. Studies have linked high bilirubin levels with deficits in motor function, speech and language development, attention disorders, and lower IQ scores in later childhood. Kernicterus, the most severe

manifestation, leads to irreversible neurological damage, including auditory dysfunction, dystonia, and severe cognitive impairment.[4]Despite advances in neonatal care, kernicterus and bilirubin-induced neurotoxicity remain significant public health concerns. Early identification of neonates at risk for long-term neurodevelopmental impairments could enhance clinical decision-making and therapeutic strategies. Current research aims to establish predictive models incorporating bilirubin levels, neurophysiological markers, and genetic predisposition to improve risk stratification.[5]

MATERIAL AND METHODS

This study was a prospective cohort study conducted at tertiary care hospital. A total of 120 neonates diagnosed with neonatal jaundice were enrolled. Inclusion criteria included: (1) full-term and late preterm neonates (≥34 weeks gestation), (2) clinically significant neonatal jaundice requiring phototherapy or exchange transfusion, and (3) parental consent for follow-up assessments. Exclusion criteria included neonates with congenital anomalies, genetic syndromes, perinatal asphyxia (Apgar score <5 at 5 minutes), or other conditions affecting neurodevelopment.Neonates were classified based on the severity of jaundice, as measured by total serum bilirubin (TSB) levels at admission and peak bilirubin levels during hospitalization. Bilirubin levels were measured using a standardized laboratory assay. Clinical management followed American Academy of Pediatrics (AAP) guidelines for neonatal jaundice.Demographic and perinatal data, including gestational age, birth weight, mode of delivery, and maternal factors (e.g., diabetes, infections), were recorded. Details regarding phototherapy duration, need for exchange transfusion, and length of hospital stay were documented. Neurodevelopmental outcomes were assessed at 6 months, 12 months, and 24 months using standardized developmental screening tools, including the Bayley Scales of Infant Development (BSID-III) and the Ages & Stages Questionnaire (ASQ-3). Cognitive, motor, and language development scores were recorded to evaluate the impact of neonatal jaundice severity on long-term neurological function. Adverse neurodevelopmental outcomes were defined based on specific criteria: cognitive delay was indicated by a BSID-III cognitive score of less than 85, motor delay was determined by a BSID-III motor composite score of less than 85, and speech or language delay was identified when the ASQ-3 score fell below the age-appropriate cutoff. In cases where there were clinical concerns of bilirubin encephalopathy, neuroimaging studies such as cranial ultrasound or magnetic resonance imaging (MRI) were performed to assess potential structural or neurological abnormalities associated with severe hyperbilirubinemia.

STATISTICAL ANALYSIS

Data were analyzed using SPSS version 16.0. Continuous variables were presented as means ± standard deviations and compared using independent t-tests or ANOVA. Categorical variables were expressed as percentages and analyzed using chi-square or Fisher's exact test. Logistic regression models were used to assess the predictive value of bilirubin levels on neurodevelopmental outcomes, adjusting for potential confounders such as gestational age and birth weight. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics (Table 1)

The study included a total of 120 neonates diagnosed with neonatal jaundice. The gestational age distribution showed that 50% of the neonates were born between 37-39 weeks, while 25% were late preterm (34-36 weeks) and another 25% were full-term (≥40 weeks). Birth weight analysis revealed that the majority of neonates (60%) had a normal birth weight (2.5-3.5 kg), while 20% were low birth weight (<2.5 kg) and another 20% had a birth weight >3.5 kg.Regarding mode of delivery, a higher proportion of neonates (55%) were delivered vaginally, whereas 45% were born via cesarean section. Maternal conditions were also analyzed, with 60% of mothers having no known comorbidities. However, 15% of mothers had diabetes, 15% had infections, and 10% had hypertension, all of which could be potential risk factors for neonatal complications, including jaundice.

Clinical Characteristics (Table 2)

Among the clinical parameters, the duration of phototherapy varied across neonates. The majority (50%) required phototherapy for 24-48 hours, while 30% needed <24 hours, and 20% required extended phototherapy (>48 hours). A small proportion (10%) of neonates required exchange transfusion, indicating severe hyperbilirubinemia, while 90% were managed with phototherapy alone.The length of hospital stay was also assessed, with 50% of neonates staying between 3-7 days, 35% staying less than 3 days, and 15% requiring prolonged hospitalization (>7 days).

Neurodevelopmental Outcomes (Table 3)

At 6 months, 12 months, and 24 months, neurodevelopmental outcomes were assessed using standardized screening tools. Cognitive delay was observed in 26.67% of neonates, while 73.33% had normal cognitive development. Motor delay was present in 15.00%, suggesting that a smaller subset of neonates had delayed motor milestones. Speech and language delays were noted in 18.33% of the study population, which could indicate subtle neurodevelopmental effects of neonatal jaundice.These findings suggest that a significant proportion of neonates who had neonatal jaundice

developed some form of neurodevelopmental delay, particularly in cognitive and speech domains.

Association Between Jaundice Severity and Neurodevelopmental Outcomes (Table 4)

The severity of neonatal jaundice was classified into mild, moderate, and severe based on total serum bilirubin levels. The association between jaundice severity and neurodevelopmental outcomes was analyzed using the chi-square test.For cognitive delay, the incidence was 24.49% in the mild jaundice group, 28.85% in the moderate group, and 26.32% in the severe group, with a p-value of 0.884, indicating no statistically significant association. Similarly, motor delay occurred in 12.24% of the mild group, 17.31% of the moderate group, and 15.79% of the severe group, with a p-value of 0.772, suggesting no strong correlation. Speech delay was found in 22.45% of the mild group, 15.38% of the moderate group, and 15.79% of the severe group, with a p-value of 0.625.Overall, the p-values for all three neurodevelopmental outcomes were greater than 0.05, indicating that there was no statistically significant association between the severity of neonatal jaundice and long-term neurodevelopmental delays.

Table 1: Demographic Characteristics

Variable	Category	n (%)	Percentage (%)
Gestational Age	34-36 weeks	30	25.00
	37-39 weeks	60	50.00
	≥40 weeks	30	25.00
Birth Weight	<2.5 kg	24	20.00
	2.5-3.5 kg	72	60.00
	>3.5 kg	24	20.00
Mode of Delivery	Vaginal	66	55.00
	Cesarean	54	45.00
Maternal Conditions	None	72	60.00
	Diabetes	18	15.00
	Infections	18	15.00
	Hypertension	12	10.00

Table 2: Clinical Characteristics

Variable	Category	n (%)	Percentage (%)
Phototherapy Duration	<24 hrs	36	30.00
	24-48 hrs	60	50.00
	>48 hrs	24	20.00
Exchange Transfusion	Yes	12	10.00
	No	108	90.00
Length of Hospital Stay	<3 days	42	35.00
	3-7 days	60	50.00
	>7 days	18	15.00

Table 3: Neurodevelopmental Outcomes

Variable	Category	n (%)	Percentage (%)
Cognitive Delay	Yes	32	26.67
	No	88	73.33
Motor Delay	Yes	18	15.00
	No	102	85.00
Speech Delay	Yes	22	18.33
	No	98	81.67

Table 4: Association Between Jaundice Severity and Neurodevelopmental Outcomes

Outcome	Mild n (%)	Mild %	Moderate n (%)	Moderate %	Severe n (%)	Severe %	p-value
Cognitive Delay	12	24.49	15	28.85	5	26.32	0.884
Motor Delay	6	12.24	9	17.31	3	15.79	0.772
Speech Delay	11	22.45	8	15.38	3	15.79	0.625

DISCUSSION

Neonatal jaundice is a common condition affecting newborns, with varying degrees of severity and potential long-term neurodevelopmental consequences. In the present study, 50% of neonates were born between 37-39 weeks, while 25% were late

preterm (34-36 weeks) and 25% were full-term (≥40 weeks). These findings are similar to those of Maisels and Newman (1995), who reported that approximately 60% of neonatal jaundice cases occur in late preterm and term neonates due to immature hepatic function.[6] The birth weight distribution showed that 20% of neonates had low birth weight (<2.5 kg), while 60% had a normal birth weight (2.5-3.5 kg). A study by Seidman et al. (1995) similarly found that low birth weight neonates are at a higher risk of developing significant hyperbilirubinemia, which can lead to neurotoxicity.[7]In terms of mode of delivery, the study found that 55% of neonates were delivered vaginally, and 45% were born via cesarean section. A study by Bhutani et al. (1999) reported that cesarean delivery might slightly increase the risk of jaundice due to delayed feeding initiation and slower bilirubin elimination.[8] Additionally, 60% of mothers in this study had no comorbidities, while 15% had diabetes, 15% had infections, and 10% had hypertension. This is consistent with the study by Xiong et al. (2000), which found that maternal diabetes and infections increase the risk of neonatal jaundice.[9] The duration of phototherapy varied in this study, with 50% requiring phototherapy for 24-48 hours, 30% needing <24 hours, and 20% requiring prolonged phototherapy (>48 hours). A study by Newman and Maisels (2000) reported similar findings, stating that 50-60% of jaundiced neonates require phototherapy for 24-48 hours, depending on bilirubin levels and feeding practices.[10] In this study, only 10% of neonates required exchange transfusion, a similar rate to the 5-15% reported in a study by Watchko (2005). Exchange transfusion is generally reserved for severe hyperbilirubinemia cases to prevent kernicterus.[11] Additionally, 50% of neonates had a hospital stay between 3-7 days, while 15% stayed longer than 7 days, indicating more severe cases or complications. These findings align with Rennie et al. (2009), who reported a median hospital stay of 5-6 days for neonates with moderate-to-severe jaundice.[12] At 6, 12, and 24 months, 26.67% of neonates exhibited cognitive delays, 15.00% had motor delays, and 18.33% had speech delays. These findings are comparable to those of Shapiro (2003), who reported that hyperbilirubinemia can lead to cognitive and speech delays in 20-30% of affected infants.[13] However, the present study showed a majority of neonates (73.33%) had normal cognitive development, 85.00% had normal motor function, and 81.67% exhibited normal speech development, suggesting that neonatal jaundice, when properly managed, does not necessarily result in severe neurodevelopmental impairment. Brooten et al. (1986) similarly found that most neonates with mild-to-moderate hyperbilirubinemia had normal developmental outcomes, but severe cases had a higher risk of delays.[14] The study examined whether the severity of jaundice (mild, moderate, severe) was associated with neurodevelopmental delays. The results showed no statistically significant association between bilirubin levels and cognitive (p=0.884), motor (p=0.772), or speech delays (p=0.625).These findings contrast with Ip et al. (2004), who found a significant correlation between high bilirubin levels and adverse neurodevelopmental outcomes, particularly in cases of kernicterus. However, the lack of statistical significance in the present study may be due to effective phototherapy management, timely intervention, and the exclusion of extreme cases of kernicterus.[15] Another study by Johnson et al. (1991) reported that only neonates with total serum bilirubin levels above 25 mg/dL had a significant risk of neurological impairment, which may explain why this study did not find a strong correlation between bilirubin levels and neurodevelopmental outcomes.[16] The results suggest that neonatal jaundice can contribute to neurodevelopmental delays, particularly in cognitive and speech domains, but severity alone does not predict adverse outcomes. This highlights the importance of early intervention, close monitoring, and proper management through phototherapy to reduce bilirubin levels and prevent neurological damage.The findings reinforce the recommendations by the American Academy of Pediatrics (AAP) guidelines (2004), which emphasize early detection, monitoring, and treatment of jaundice to minimize neurodevelopmental consequences.[17]

CONCLUSION

This study evaluated the predictive value of neonatal jaundice severity on long-term neurodevelopmental outcomes. While 26.67% of neonates exhibited cognitive delays, 15.00% had motor delays, and 18.33% had speech delays, there was no statistically significant association between jaundice severity and these outcomes ($p > 0.05$). These findings suggest that neonatal jaundice, when managed appropriately, does not necessarily result in severe neurodevelopmental impairment. Early detection, timely phototherapy, and proper follow-up are crucial in minimizing potential risks.

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