RESEARCH PAPER

Association Between Delivery Modality and Neurodevelopmental Delay in Term Infants with Neonatal Jaundice: Impact of Early Intervention

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ABSTRACT

Background: Neonatal jaundice is a common condition in the early postnatal period, with potential neurodevelopmental consequences if not managed appropriately. Emerging evidence suggests that mode of delivery, particularly Caesarean section (CS), may influence neurodevelopment through alterations in early microbial colonization.

Objective: To evaluate the association between mode of delivery and neurodevelopmental delay in term infants with neonatal jaundice and to assess the impact of early interventional therapy on developmental outcomes.

Methods: This study included 103 full-term neonates with serum bilirubin levels >15 mg/dL. Neurodevelopmental assessment was performed at 90 days, and early intervention was initiated immediately after diagnosis. Neurodevelopment was assessed using the DDST scale at scheduled intervals.

Results: Neurodevelopmental delay was more frequently observed among infants delivered via CS compared to normal vaginal delivery. A total of 103 neonates were observed in the study; among them, 23.3% were positive at 90 days. Following intervention, improvement was observed at the 6th month (8.33%), 9th month (16.67%), and 12th month (12.5%), while mild or no improvement (62.5%) was observed in individuals. Additionally, incomplete or mild improvement was more common in CS-delivered infants.

Conclusion: The study demonstrates a significant association between neonatal jaundice, neurodevelopmental delay, and mode of delivery, with higher risk observed in CS-delivered infants. Early initiation of interventional therapy significantly improves neurodevelopmental outcomes, highlighting the importance of timely management in affected neonates.

Keywords: Early interventional therapy, Mode of delivery, Neonatal jaundice, Neurodevelopmental delay

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Introduction:

Neonatal hyperbilirubinemia and jaundice occur in the majority of newborns during the early postnatal period. Although physiological jaundice typically resolves spontaneously without clinical intervention, failure to recognize, monitor, and manage excessive bilirubin levels in a timely manner may result in progression to severe hyperbilirubinemia and its associated complications. In vulnerable neonates—particularly those born preterm or those experiencing suboptimal breastfeeding, dehydration, or other perinatal stressors—the risk of bilirubin neurotoxicity is significantly increased (1-10). When serum bilirubin levels exceed the binding capacity of albumin, unconjugated bilirubin may cross the blood–brain barrier, potentially leading to acute bilirubin encephalopathy and long-term neurodevelopmental impairment. Earlier studies have demonstrated the classical association between significant neonatal jaundice and adverse neurodevelopmental outcomes .

In parallel, the mode of delivery has emerged as a critical determinant of both early neonatal health and long-term child development. Vaginal delivery represents a physiological process characterized by exposure to maternal vaginal and intestinal microbiota, whereas Caesarean delivery (CD) bypasses this natural microbial transfer and involves surgical intervention. The rising global rates of Caesarean delivery have generated concern due to associations with altered neonatal immune maturation, respiratory morbidity, and metabolic outcomes.

The Developmental Origins of Health and Disease (DOHaD) paradigm underscores the profound influence of the prenatal and early postnatal environment on lifelong health trajectories. The perinatal period—spanning from the 22nd week of gestation to the seventh day after birth—constitutes a critical window during which foundational biological systems are established. During this time, the neonatal microbiome begins to form, laying the groundwork for immune, metabolic, and neurodevelopmental pathways (11-13). Among maternal microbial sources, the vaginal microbiome serves as a primary inoculum during vaginal birth, facilitating colonization with beneficial microbes that shape the infant's gut microbiota and early immune programming (11,12). Emerging evidence further suggests that maternal microbial communities may influence offspring neurodevelopment through microbial metabolites, immune signalling pathways, and gut–brain axis communication (14).

In contrast, infants born via Caesarean delivery are deprived of direct exposure to maternal vaginal and intestinal flora at birth. Instead, their initial colonization is largely influenced by environmental and hospital-associated microbes. Growing evidence indicates that early-life alterations in gut microbial composition may affect immune maturation and neurodevelopmental processes (15). These findings collectively suggest that mode of delivery may have implications for early brain development and subsequent neurodevelopmental outcomes.

While previous studies have independently examined the relationship between neonatal hyperbilirubinemia and neurodevelopmental delay, as well as the association between mode of delivery and neurodevelopment, no study to date has specifically evaluated the interaction between mode of delivery and neurodevelopmental outcomes among children with a history of neonatal jaundice. Understanding this relationship is crucial, particularly given the increasing rates of Caesarean delivery worldwide and the high prevalence of neonatal hyperbilirubinemia.

Therefore, the present study aims to investigate the association between mode of delivery and neurodevelopmental delay in children with neonatal jaundice. Additionally, this study explores the impact of early interventional therapy on neurodevelopmental outcomes in affected children. Elucidating these relationships may contribute to improved perinatal risk stratification and inform early preventive and therapeutic strategies.

Materials and Methods

This study included 103 full – term neonates with serum bilirubin levels >15 mg/dL who were admitted and treated for mild to moderate neonatal jaundice. 103 participants were participated in this study, all enrolled neonates were full – term and delivered in institutional settings. Maternal and neonates variables, including mode of delivery, maternal age, gravida status, and serum bilirubin levels at admission, were recorded systematically.

Neonatal jaundice in all cases was managed according to the guidelines of the American Academy of Pediatrics(AAP) Subcommittee on Hyperbilirubinemia(16) . Clinical evaluation, laboratory investigations and treatment interventions were carried out in accordance with these established recommendations.

Neonates with preterm birth, birth asphyxia, congenital anomalies, known genetic disorders, malnutrition, metabolic deficiencies, hypoglycemia, or seizures were excluded from the study to eliminate confounding factors that could independently influence neurodevelopmental outcomes. These exclusion criteria ensured that the study specifically evaluated the impact of hyperbilirubinemia in otherwise healthy full-term neonates.

Neurodevelopmental assessment was performed using the Standard Developmental Screening Test (DDST) scale developed by Bharath Raj in 1983 (17), designed to assess developmental status from birth up to 15 years of age. The tool evaluates key domains including motor, social–personal, and speech–language development. Assessments were conducted according to standardized procedures to identify neurodevelopmental delay.

In the sample, 103 children were evaluated for neurodevelopmental delay at 90 days of age. Children identified with developmental delay were enrolled in an early intervention therapy program that continued until 12 months of age. Follow-up assessments were conducted at 6, 9, and 12 months, and outcomes were recorded.

Early intervention therapy was delivered through a structured combination of center-based and home-based management approaches. At the Early Intervention Centre, therapy sessions were conducted once weekly and focused on improving foundational developmental domains including motor, sensory, visual, and auditory skills. Individualized intervention plans were designed based on developmental assessment findings, with emphasis on enhancing muscle tone, postural control, sensory integration, visual tracking, auditory responsiveness, and early communication skills.

Parents were trained to continue therapeutic activities at home on a daily basis to ensure continuity of care. To facilitate vestibular stimulation and postural development, supervised use of a cradle (Jula) in both supine and prone positions was advised. Supervised prone positioning ("tummy time") was encouraged to strengthen neck and trunk musculature. Parents were also instructed to provide consistent verbal interaction, sensory stimulation, and appropriate carrying techniques to support motor and socio-communication development (18).

Children enrolled in the intervention program were formally evaluated at 90-day intervals. Those who achieved age-appropriate developmental milestones during follow-up assessments were discontinued from therapy. Overall, all neonates received early intervention therapy for a total duration of nine months till 12 months of age.

Results:

Total of 103 participants were included in the study, consisting of 56 males (54.4%) and 47 females (45.6%). Regarding the mode of delivery, 55 participants were delivered through normal vaginal delivery, whereas 48 were delivered by caesarean section (CS). Among males, 30 were delivered normally and 26 through caesarean section, while among females 25 were delivered normally and 22 by caesarean section (Table: 1).

Out of the total participants, 24 cases were found to be positive constituting 23.3% of total cases, including 13 males (54.2%) and 11 females (45.8%). Among these positive cases, 10 were associated with vaginal delivery and 14 with caesarean section (Table 2).

With respect to improvement status, 2 cases showed improvement at the 6th month follow-up, both among females delivered through normal vaginal delivery. At the 9th month follow-up, improvement was observed in 4 cases, including three cases from normal delivery and one case from caesarean section. At the 12th month follow-up, 3 additional cases improved, consisting of one male from normal delivery and two females from caesarean section.

However, 15 cases did not show complete improvement, with the majority belonging to the caesarean section group (11 cases) constituting 73.33%, while 4 (26.67%) belonged to normal delivery (Table 3).

Table 1: Distribution of Study Participants by Gender and Type of Delivery (N = 103)

Gender	Normal Delivery	Caesarean Section	Total
Male	30 (29.13%)	26 (25.24%)	56 (54.37%)
Female	25 (24.27%)	22 (21.36%)	47 (45.63%)
Total	55 (53.4%)	48 (46.6%)	103 (100%)

Table 2: Distribution of Positive Cases by Gender and Type of Delivery (N = 24)

Gender	Normal Delivery	Caesarean Section	Total
Male	6 (25%)	7 (29.17%)	13 (54.17%)
Female	4 (16.67%)	7 (29.16%)	11 (45.83%)
Total	10 (41.67%)	14 (58.33%)	24 (100%)

Table 3: Improvement Status of Positive Cases According to Delivery Type and Gender (N = 24)

Follow-up Outcome	Normal Delivery Male	Normal Delivery Female	CS Delivery Male	CS Delivery Female	Total
6th Month Follow-up Improvement	0	2 (8.33%)	0	0	2 (8.33%)
9th Month Follow-up Improvement	1 (4.17%)	2 (8.33%)	1 (4.17%)	0	4 (16.67%)

12th Month Follow-up Improvement	1 (4.17 %)	0	0	2 (8.33 %)	3 (12.5 %)
Mild Improvement	4 (16.67%)	0	6 (25.0 %)	5 (20.83%)	15 (62.5 %)
Total	6 (25.0 %)	4 (16.67%)	7 (29.17%)	7 (29.17%)	24 (100 %)

The improvement status of positive cases at (N=24) different follow -up intervals indicate that at the 6th month follow-up showed a improvement rate of 8.33%,at the 9th Month follow-up the improvement rate is 16.67%. at the 12th Month follow-up the 12.5% of individuals showing improvement.

In terms of patients who experienced mild or partial improvement (or no complete improvement), had 62.5%.

Discussion:

The findings of the present study demonstrate that, the proportion of positive cases following neurodevelopmental evaluation was higher among children delivered via Caesarean section (CS) compared to those born through normal vaginal delivery. These observations are consistent with earlier reports indicating an association between CS delivery and adverse neurodevelopmental outcomes (19–20).

The increased prevalence of positive neurodevelopmental cases among CS-born children may be attributed to the absence of early exposure to maternal microbiota, which plays a crucial role in establishing neonatal microbial colonization. This early colonization provides the foundation for immune, metabolic and neurodevelopmental pathways. Among maternal microbial sources, the vaginal microbiome serves as the primary inoculum during vaginal birth, facilitating colonization with beneficial microbes that shape the infant gut microbiota and contribute to early immune programming (11–13).

Emerging evidence further suggests that maternal microbial communities influence offspring neurodevelopment through microbial metabolites, immune signaling pathways, and gut–brain axis communication (14). In contrast, CS delivery bypasses this critical exposure, resulting in an altered gut microbiome characterized by reduced diversity, decreased levels of beneficial taxa, and delayed microbiota maturation (12, 21–22). Such early-life dysbiosis has been widely implicated in adverse neurodevelopmental outcomes. A meta-analysis has reported that CS delivery is associated with a significantly increased risk of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD).

The underlying mechanisms linking dysbiosis to impaired neurodevelopment may involve disruption of the gut–brain axis (GBA). Early microbial imbalance can alter the synthesis of neuroactive compounds and short-chain fatty acids (SCFAs), which are essential modulators of neural signaling, as described by Ahmed et al. (11). These findings support the observations of the present study.

Furthermore, the results highlight the importance of early interventional therapy in mitigating the adverse effects of CS delivery on neurodevelopment. Improvement was observed in positive cases following by early intervention.

An important observation of the present study is that, cases showing incomplete or only mild improvement were more frequently associated with CS delivery than with normal vaginal delivery. This finding further suggests that CS delivery plays a significant role not only in neurodevelopmental delays but also in the trajectory of recovery. This may again be explained by microbiome dysbiosis and its impact on the microbiota–gut–brain axis.

Previous studies have demonstrated that gut microbiota and their metabolites interact with both the immune system and the central nervous system during critical developmental windows. The perinatal period, particularly the first 1,000 days of life, represents a highly sensitive phase during which environmental insults can exert long-lasting effects on the microbiota–gut–brain axis (23). Another study suggests that while CS delivery may influence infant brain development, these effects could be transient (24).

Taken together, the findings of the present study indicate that early interventional therapy, particularly when initiated promptly upon detection of neonatal jaundice with bilirubin levels exceeding 15 mg/dl, is associated with a reduced number of positive neurodevelopmental cases and improved therapeutic outcomes.

Conclusion:

The findings of the present study indicate a significant association between neonatal jaundice, neurodevelopmental delay and mode of delivery. This association is more pronounced among children delivered by Caesarean section (CS) compared to those born through normal vaginal delivery. Furthermore, early interventional therapy plays a crucial role in mitigating adverse neurodevelopmental outcomes. The therapeutic benefits are more evident among children born through normal delivery; however, the effectiveness of intervention is strongly influenced by the timing of initiation. Early commencement of interventional therapy, particularly during the initial stages following the detection of neonatal jaundice, results in better neurodevelopmental outcomes and a greater degree of recovery.

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