

Neurological Examination and Hearing Assessment of Premature Infants with Gestational Age of Less Than 32 Weeks at Follow-up

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ABSTRACT

Background: The survival of premature infants has improved in the recent era due to advances in perinatal and neonatal healthcare practices. These infants are at risk of neuro-sensorimotor impairment, as well as learning and behavioral disorders.

Methods: A longitudinal follow-up study was planned over 6 months at a High-Risk Clinic, Civil Hospital, Ahmedabad, India, to conduct the neurological examination and hearing assessment of premature infants born with gestational age less than 32 weeks. Infants who were born preterm at <32 weeks of gestational age and those attending the high-risk clinic at 3, 6, 9, and 12 months of corrected gestational age were enrolled in the study. These infants were assessed for tone via the Amiel-Tison method and hearing impairment via BERA.

Results: During the study period, 69 infants were included with a mean gestational age of 30.4±1.2 weeks. On the assessment of tone, at 3 months of corrected age, 3 and 1 infants had hypertonia and hypotonia, respectively. At 6 months of corrected age, 4 and 3 infants had hypertonia and hypotonia, respectively. Moreover, 1 and 2 infants had hypertonia and hypotonia at 9 months of corrected age, respectively, and 1 infant had hypertonia at 12 months of corrected age. Out of 69 enrolled infants, 5 (7%) infants had hearing loss at 3 months of corrected gestational age, whereas 64 (93%) infants had normal hearing assessment via BERA at the corrected gestational age of 3 months.

Conclusion: Preterm infants are at very high risk of neurodevelopmental impairment and need frequent follow-up visits and early intervention.

Keywords: Hearing assessment, Neurological examination, Premature infants

Introduction

Preterm birth is a major global problem and accounts for 5%-18% of live birth globally, and the incidence of preterm birth is 12.8% in India (1). Preterm birth is a leading cause of death worldwide (2). Extremely premature infants are more vulnerable than more mature infants. With advances in perinatal and neonatal healthcare practices, the survival of premature infants has improved (3). These infants are at high risk of developing morbidities, such as Necrotizing enterocolitis, Bronchopulmonary dysplasia (BPD), Intraventricular hemorrhage (IVH), and Retinopathy of prematurity (ROP) (4). These

infants are also at risk of neuro-sensorimotor impairment, as well as learning and behavioral disorders (5). These infants are highly vulnerable and need frequent follow-ups after discharge to be assessed for the neurodevelopmental outcome and early intervention. There is sufficient Western literature on the given problem; however, data is still not sufficient for the Indian population, especially for the low socio-economic group. Hence, this study aimed to observe the abnormal neurological examination in infants born prematurely with a gestational age of less than 32 weeks.

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Methods

This longitudinal follow-up study was planned from 1 July 2022 to 31 December 2022 at a High-Risk Clinic of the Civil Hospital, Ahmedabad, India, to conduct the neurological examination and hearing assessment of premature infants with less than 32 weeks of gestational age discharged from a tertiary care hospital. Infants who were born preterm at ≤ 32 weeks of gestational age, as well as those attending the high-risk clinic at 3, 6, 9, and 12 months of corrected gestational age were enrolled in the study after the obtainment of the written informed consent. On the other hand, the infants who were born preterm at ≤ 32 weeks of gestational age but had a congenital malformation, and those who had lost follow-ups and had not provided consent were excluded from the study. Infants who were born prematurely (≤ 32 weeks of gestation) were followed up at 3, 6, 9, and 12 months of corrected gestational age at a High-Risk Clinic of Civil Hospital. Caretakers who gave consent for enrolling the infant in the study were recruited. Baseline characteristics, such as gestational age, birth weight, gender, and comorbidities (septicemia, hyperbilirubinemia, respiratory distress syndrome [RDS], convulsion BPD, and IVH) during the NICU stay were documented. Stages of ROP and intervention administered were documented as well. Infants were assessed for tone and hearing impairment.

Tone assessment

Atypical muscle tone is a common clinical feature observed in children with neurodevelopmental disorders. It can occur in many conditions, such as early brain injury or cerebral palsy (CP). Persistent hypertonia is problematic because it can restrict movement and lead to secondary impairments, such as contracture, pain, and limited motor development. Persistent hypotonia produces other issues, such as poor joint stability, poor postural alignment, decreased activity tolerance, and delayed motor skill acquisition. Tone can be easily assessed in a crowded clinic practice. The Amiel-Tison method is a validated tool for tone assessment in infants (6), and hence, it was decided to evaluate the babies for tone using the Amiel-Tison method in this study. The tone was documented as normal, with hypotonia, and hypertonia. Infants who were having abnormal tone were referred to a physiotherapist for early intervention.

Retinopathy of Prematurity

Infants born prematurely are at high risk of

developing ROP. Details about the ROP screening (zone and stage) and treatment administered were documented on the follow-up visits. Those who developed ROP and those who required treatment were counseled for regular follow-up with an ophthalmologist till 5 years of age.

Hearing assessment

Infants born prematurely are at high risk of sensorineural hearing loss. Infants were assessed for hearing impairment using BERA at 3 months of corrected gestational age. Infants who had abnormal results of BERA were referred to a speech therapist, and guidance was provided in cases when a cochlear implant was needed.

Results

This study was conducted on 69 infants who were fulfilling the inclusion criteria. Out of whom, 62 (80.9%) infants were born between 28 and 32 weeks of gestation, and 7 (10.1%) infants were born with gestational age less than 28 weeks. The mean gestational age in the study group was 30.4 ± 1.2 weeks, and the majority of infants ($n=39$; 56.5%) were male. In addition, 10 (14.5%), 50 (72.5%), and 9 (13%) infants had birth weight less than 1000, 1000-1500, and 1500-1800 grams, respectively. Moreover, 34 (49.2%) infants had a history of septicemia, 33 (47.8%) neonates had a history of ROP which require treatment, 32 (46.3%) cases had a history of seizures, 20 (28.9%) infants had a history of respiratory distress, 9 (13%) neonates had a history of hyperbilirubinemia, 10 (14.4%) cases had a history of IVH, and 2 (2.9%) infants had a history of BPD. In the present study, 32 infants had a history of seizures during their neonatal period due to IVH ($n=10$), hypocalcemia ($n=8$), meningitis ($n=6$), hypoglycaemia ($n=5$), and hypoxia ($n=3$) (Table 1).

On the assessment of tone at the corrected age of 3 months, out of 69 infants, 3 neonates had hypertonia, and 1 infant had hypotonia. The remaining 65 infants had normal tones. Following that, on the assessment of tone at the corrected age of 6 months, out of 69 infants, 4 cases had hypertonia, 3 neonates had hypotonia, and the remaining 62 infants had normal tone. The 3 infants who had hypertonia at the corrected age of 3 months continue to have hypertonia at 6 months of corrected age and 1 infant had developed hypertonia at the corrected age of 6 months. Furthermore, 1 infant who had hypotonia at the corrected age of 3 months continue to have hypotonia at 6 months of age

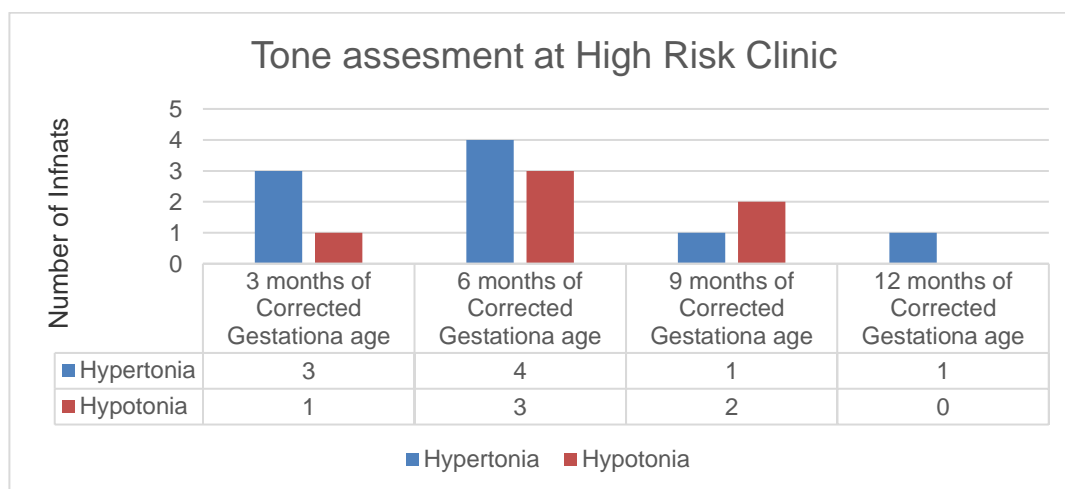
Table 1. Baseline characteristics of the study infants

Baseline Characteristics	Number of Infants (n=69)
Mean gestational age	30.4±1.2weeks
<28 weeks	7 (10.1%)
28-32 weeks	62 (89.9%)
Birth weight (grams)	
< 1000 grams	10 (14.5%)
1000-1500 grams	50 (72.5%)
1500-1800 grams	9 (13%)
Gender	
Male	39 (56.5%)
Female	30 (43.5%)
Risk factors	
Septicemia	34 (49.2%)
Seizures	32 (46.3%)
Respiratory distress syndrome	20 (28.9%)
Intraventricular hemorrhage	10 (14.4%)
Hyperbilirubinemia	9 (13%)
Bronchopulmonary dysplasia	2 (2.89%)
Retinopathy of prematurity (any stage)	39 (56.5%)
Retinopathy requiring treatment	33 (47.8%)

and 2 infants had developed hypotonia at the corrected age of 6 months. There was more number of infants who had tone abnormalities at the 6 months of corrected age, compared to 3 months of corrected age. The new infants who had developed tone abnormality at 6 months of corrected age were mild in nature.

Considering the assessment of tone at the corrected age of 9 months, out of 69 infants, 1 neonate had hypertonia, 2 cases had hypotonia, and the remaining 66 infants had normal tone. Moreover, 4 infants had hypertonia at the corrected age of 6 months, out of whom, 1 infant had hypertonia at the corrected age of 9 months, and the remaining 3 infants had normal tone at the corrected age of 9 months. Additionally, out of 3 infants who had hypertonia at the corrected age of

6 months, 1 infant had hypotonia at the corrected age of 9 months, and the remaining 2 infants had normal tone at the corrected age of 9 months. On the assessment of tone at the corrected age of 12 months, out of 69 infants, 1 neonate had hypertonia and the remaining 68 infants had normal tone. At the corrected age of 12 months, only 1 infant had hypertonia, and the remaining 2 infants who had hypotonia had normalization of tone. The gradual normalization of tone in the present study may be due to the early identification of tone abnormality and starting of early intervention in the form of physiotherapy. Out of 69 enrolled infants, 5 (7%) neonates had hearing loss at 3 months of corrected gestational age, whereas 64 (93%) infants had normal hearing assessment via BERA at the corrected age of 3 months (Figure 1 & 2).

**Figure 1.** Tone assessment of enrolled Infants at High Risk Clinic

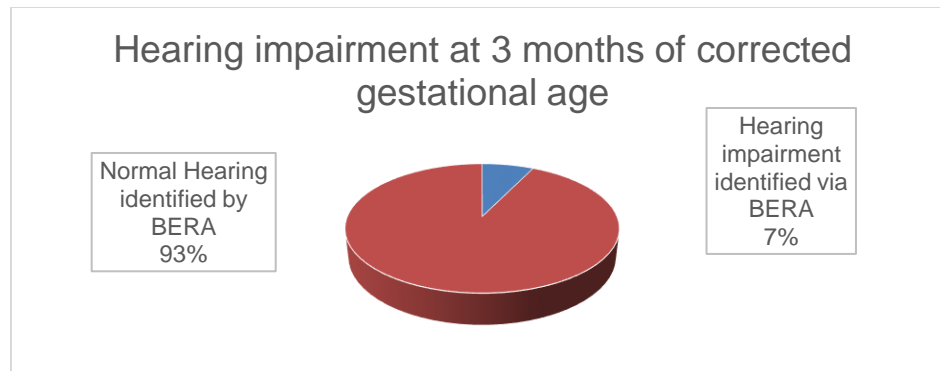


Figure 2. Hearing impairment at 3 months of corrected gestational age

Discussion

The present study evaluated infants with gestational age of less than 32 weeks. Gestational age, birth weight, and gender all had an impact on the short- and long-term outcomes of the infants (7). In the present study, 10.1% of the study population was belonging to an extreme preterm group, whereas 89.9% were more mature infants (28-32 weeks of gestational age). In the study population, 14.5% were extremely low-birth-weight infants, 72.5% were between 1000 and 1500 grams, while 13% were between 1500 and 1800 grams. This also suggests that the majority (88.5%) of the infants were appropriate for gestational age, and only 11.5% of the infants were small for gestational age. Males accounted for 56.5% of the study population.

Among the risk factors for neurodevelopment, RDS, hyperbilirubinemia, septicemia, seizures, ROP, BPD, and IVH were evaluated. In the present study, 20 (28.9%) infants developed RDS, out of which, 15 neonates required surfactant therapy, and 9 neonates needed mechanical ventilation during their NICU stay. Moreover, in the study population, 23.5% suffered from hyperbilirubinemia and 6.2% had septicemia. Following that, 56.5% of the infants had any stage ROP, and 48% of the infants required laser photocoagulation therapy. Out of enrolled infants, 14.4% of the study group developed IVH, and 2.9% of the study group developed BPD during their NICU stay.

Severe RDS can increase the number of days on a mechanical ventilator, which in turn can maximize the rates of BPD, which is an important cause of adverse neurodevelopmental outcomes. Thus, RDS indirectly can lead to adverse neurodevelopmental outcomes. The incidence of RDS as documented by Sun H et al. is 22% in very low birth weight (VLBW) infants (8). A similar incidence of RDS in VLBW infants was

documented by Oommen et al. (9). In our study, 13.8% of the study population had developed RDS since the study population consisted of more mature infants. Furthermore, the incidence of sepsis was lower in the study population. Chorioamnionitis is an important risk factor for both RDS and adverse neurodevelopmental outcomes. The lower incidence of sepsis indirectly could have contributed to a lower incidence of RDS. The lower incidence of RDS in the present study may be due to the administration of antenatal steroids to high-risk mothers.

Neonatal sepsis is an independent risk factor for adverse neurodevelopmental outcomes (10). According to the data from the National Institute of Child Health & Human Development Neonatal Research Network, the incidence of late-onset sepsis in VLBW infants is 22% (11). In the Indian population, the rate of sepsis is 13.6% in VLBW infants (9). In the present study, the incidence of septicemia was 6.2%. These rates of sepsis were lower in the study population because the population consisted of more mature infants with the majority of them having appropriate weight for the gestational age.

Hyperbilirubinemia is an important risk factor for adverse neurodevelopmental outcomes, especially sensory neural hearing loss. Regarding the findings of the study by Aynalem et al., the incidence of hyperbilirubinemia in VLBW infants is 46%. In a similar study from India by Devi et al., the incidence of hyperbilirubinemia in preterm infants was 42% (12). In the present study, 23.2% of the study population developed hyperbilirubinemia and 6% developed hearing impairment. In addition, 4 preterm neonates in the present study had bilirubin of more than 15 mg/dl, and 7 preterm neonates had received aminoglycoside antibiotics during their NICU stay. Hearing impairment in the present study is considerably higher than that in

other studies conducted on similar population groups (9).

In a study by Grether et al., among the children who had CP, 14% had developed seizures during the neonatal period (13). Etiology behind the neonatal seizure and neonatal seizure per se contributes to the adverse neurodevelopmental outcome. The incidence of neonatal seizures in a tertiary care center in India is quite high. In a study from a tertiary care center in northern India, the reported incidence of neonatal seizure was 39.13% (14). In the present study, 46% of the infants had the occurrence of at least one episode of clinical seizure. These seizures were due to IVH (n=10), hypocalcemia (n=8), meningitis (n=6), hypoglycaemia (n=5), and hypoxia (n=3). This high incidence of neonatal seizure would have contributed to the adverse neurodevelopmental outcome.

ROP is an important complication of preterm birth and is the second most common cause of childhood blindness. A clear association has been found between the zonal involvement of ROP and the severity of neurodevelopmental impairment. Those who have zone 1 involvement have more severe neurodevelopmental impairment (5). The prevalence of ROP in the urban population in India is 16%. Some other studies from India have shown the prevalence of ROP ranging from 38% to 51.9% (15). In our study, 56.5% of the preterm infants developed ROP and 48% required treatment via laser photocoagulation. In the present study, 75.3% of the infants required FiO₂ more than >0.3 during their NICU stay. Enrolled infants had various comorbid conditions, such as RDS (28.9%), septicemia, including pyogenic meningitis (49.2%), IVH (14.4%), and BPD (2.89%) during their NICU stay. Due to these conditions, 75.3% of the infants required FiO₂ more than >0.3 in the present study. The prevalence of ROP in our population was considerably high owing to the increased usage of oxygen in the population and prematurity (gestational age < 32 weeks).

In the present study, the tone was used to predict the development of CP. The incidence of hypertonia at 12 months of corrected gestational age in the study population was 1.4%. These results are almost similar to a study by Oommen et al. where 1.67% had CP at 2 years of corrected gestational age (9). In a study by Mukhopadhyay, the incidence of CP was 3% at one-year corrected gestational age (16). Our study population had a CP rate comparable to other similar populations from India. In the aforementioned study (16), the incidence of hypotonia was 3% at one-year corrected gestational age, whereas in our study, at

one-year corrected gestational age, there was no infant with hypotonia.

In a study, hearing impairment was present in 6% of the population; however, in the study by Oommen et al., only 2% had hearing impairment (9). This could be attributed to the high incidence of hyperbilirubinemia in the study population.

The present study is undertaken on preterm infants with gestational age ≤ 32 weeks. The center in this study was a government hospital in Western India, and the majority of neonates were belonging to lower and lower-middle socioeconomic groups. Very few studies are undertaken on such premature infants in India, especially those belonging to lower socioeconomic status. Major important risk factors were documented that would affect neurodevelopment. Here, the tone was also evaluated using the Amiel-Tison method which is a validated tool for tone assessment. Tone correlates well with the development of CP. BERA, which is a very reliable tool for hearing assessment, was used in the present study which again strengthens the reliability of the findings.

The limitation of the present study is that the sample size is small, and there were no details about antenatal corticosteroid and magnesium sulphate administration which are very important for altering neurodevelopment. It would have been better if the present study used diagnostic developmental assessment tools, such as the Bayley scale of infant development; however, it was not possible in a crowded clinic practice.

Conclusion

Preterm infants are at very high risk of neurodevelopmental impairment and need frequent follow-up visits, as well as early interventions.

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Conflicts of interest

There is no conflict of interest in the present study.

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This observational study utilized no funds.

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