

One-Year Follow-up Study of High-Risk Neonates With Tone Abnormalities

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Abstract

Background: As a result of the vast progress in perinatal and neonatal care, an increased survival rate of high-risk neonates (HRNs) has been observed. At the same time, the number of HRNs with chronic morbidities has increased. Hence, HRNs require regular follow-ups for early recognition of tone abnormalities, so as to provide early interventions.

Aim: To know the final outcome of HRNs (at 1 year of age) who were discharged from the neonatal intensive care unit (NICU) of Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital (Dharwad, Karnataka, India)

Materials and Methods: The neonates who met the inclusion criteria were considered HRNs and were assessed for tone abnormalities at 3, 6, 9, and 12 months of corrected age. Active tone was assessed based on spontaneous movements and the 180° flip test. Passive tone was assessed by the Amiel-Tison method. Based on these examinations, the neonates were categorized into 3 groups, as having hypertonia, hypotonia, and minor tone abnormalities. All neonates found to have tone abnormalities were given occupational therapy at the earliest.

Results: Of the 107 HRNs discharged from our NICU, 89 (83.17%) were followed up for 1 year, 13 (12.15%) did not come for follow-ups, and 5 (4.67%) died. Of the 89 neonates, 59 (66.29%)

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were preterm and 30 (33.71%) were term neonates. At 1 year of age, upon examination, 59 (66.29%) neonates were considered normal, 25 (28.09%) had transient tone abnormalities (TTAs), and 5 had cerebral palsy (CP; 5.62%). Normalization of abnormal tone was seen in 83.3% of cases. The survival rate of HRNs was 95.32%.

Interpretation and Conclusion: Our study showed a prevalence of 35.2% for TTAs. Many of the tone abnormalities detected within 6 months of age resolve by 12 months; hence, hasty diagnosis of CP should not be made, till the latter part of the first year. Therefore, HRNs should have a proper follow-up protocol so as to detect tone abnormalities at the earliest and provide early intervention.

Key Words: High-risk neonates, tone abnormalities, hypertonia, hypotonia, minor tone abnormalities, transient tone abnormalities, cerebral palsy

Introduction

With improved perinatal and neonatal care in India, there has been an increase in the survival of neonates who are at risk of long-term morbidities such as developmental delay and visual/hearing problems.

In the past 2 decades, we have witnessed a steady improvement in the quality of perinatal care in India, which has been mainly because of a better understanding of the pathophysiology and management of neonatal problems and also technological advances in neonatal care. Although there are many factors that have been contributing to this increased survival of high-risk neonates (HRNs), unfortunately, there has also been an increase in the incidence of long-term morbidity in them.^{1,2}

The decline in the global neonatal mortality rate by 28% deaths per 1000 live birth (from 33.2 deaths to 23.9) between 1990 and 2009 suggests that an increasing number of neonates with perinatal risk factors are now beginning to survive. This is likely to lead to increased postdischarge mortality rate, morbidities requiring hospitalization, long-term illnesses and disability requiring hospitalization, and long-term illnesses and disability requiring frequent health services. This

will not only affect the quality of life of the neonates who survive but also add significantly to the family's socioeconomic burden.³

Aim

To know the final outcome of HRNs (at 1 year of age) who were discharged from the neonatal intensive care unit (NICU) of Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital (SDM College and Hospital; Dharwad, Karnataka, India)

Materials and Methods

Study design

This prospective cohort study of HRNs was a longitudinal, hospital-based, follow-up study of HRNs whose final outcome was analyzed, with special emphasis on tone abnormalities. HRNs discharged from our NICU were followed up for 1 year (from November 1, 2015, to November 1, 2016).

Inclusion criteria

- Neonates weighing < 1800 g at birth and/or born at gestational age < 35 weeks.

- Neonates with perinatal asphyxia (Apgar score ≤ 3 at 5 min) and/or hypoxic–ischemic encephalopathy; metabolic problems such as symptomatic hypoglycemia and hypocalcemia; infections such as meningitis and/or culture-positive sepsis; shock requiring inotropic/vasopressor support; and/or major morbidities such as intraventricular hemorrhage (IVH) and periventricular leukomalacia.
- Neonates who required mechanical ventilation for > 24 hours.

Exclusion criteria

- Neonates weighing > 1800 g at birth and/or born at gestational age > 35 weeks.
- Neonates appropriate-for-gestational age (AGA; between 3rd and 97th percentile).
- Neonates with Apgar score > 3 at 5 minutes and those with inborn errors of metabolism or other genetic disorders.
- Neonates born to HIV-positive mothers.
- Neonates whose mothers were not willing to participate in the study.

Sample size

The minimum sample size planned was 100 neonates, based on the admission and discharge rates in our NICU. Sample size was calculated using the formula

$$\text{Sample size} = 4pq/l^2$$

Where,

p = Prevalence

q = $100 - p$

l = Absolute precision

The prevalence of HRNs as per literature is 20%. Hence,

p = 20%

q = $100 - 20 = 80$

l = 8

Sample size = $4 \times 20 \times 80 / 8^2$

Sample size = 100

The sample size estimated in our study was 100 neonates, and 107 neonates were enrolled.

Of the 107 HRNs who were discharged from our NICU, 89 (83.17%) were followed up for 1 year, 13 (12.15%) did not come for follow-ups, and 5 (4.67%) died (Table 1).

Of the 89 neonates who were followed up, 59 (66.29%) were preterm and 30 (33.71%) were term neonates. At 1 year of age, upon examination, 59 (66.29%) neonates were considered normal, 25 (28.09%) had transient tone abnormalities (TTAs), and 5 had cerebral palsy (CP, 5.62%) (Figure 1).

Of the 59 preterm HRNs, 12 (13.48%) were born at < 30 weeks of gestation, 17 (19.10%) were born between 30 and 32 weeks, and 30 (33.71%) were born at > 32 (Figure 2).

Table 1. Percentage Distribution of the Study HRNs

	No. of HRNs, n (%), $N = 107$
Followed up	89 (83.17)
Died	5 (4.67)
Not followed up	13 (12.15)

HRNs, high-risk neonates.

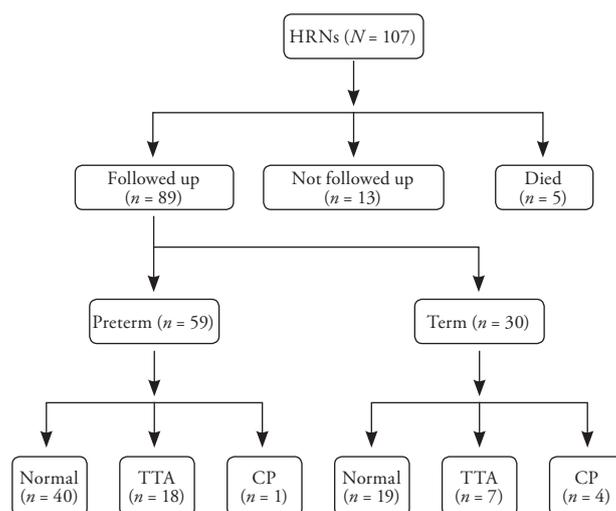


Figure 1. Schematic Representation of the Study Neonates

CP, cerebral palsy; HRN, high-risk neonates; TTA, transient tone abnormality.

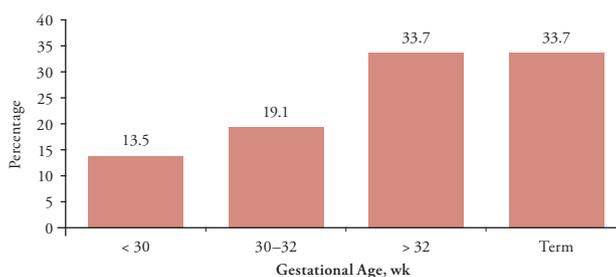


Figure 2. Percentage Distribution of Study HRNs According to Gestational Age

HRNs, high-risk neonates.

Data collection

Data were collected pro forma for each HRN after valid consent from the parents.

Data analysis

Data obtained from this study were entered into Microsoft Excel and subsequently analyzed with the help of SPSS software version 13.0 (SPSS Inc, Chicago, IL, USA). The X^2 test was used to study the association between study variables in the study groups. Logistic regression was used to compare the association between risk factors and TTAs. Odds ratio with 95% confidence interval (CI) was calculated to measure the different risk factors. The significance level was set at .005 and CIs were at 95%.

Study procedure

Neonates who met the inclusion criteria were considered HRNs. One hundred seven HRNs who were discharged from a level 3 NICU of SDM College and Hospital during a 3-month period, from August 1, 2015, to October 31, 2015, were enrolled in this

prospective follow-up study. These 107 HRNs were later followed up for 1 year, from November 1, 2015, to October 31, 2016. Informed consents were taken from their parents. All necessary data regarding their NICU stay were documented, and regular follow-up was advised. The HRNs were followed up in the high-risk clinic at our outpatient department.

The corrected age was considered in all the preterm neonates. Evaluation of muscle tone was the fundamental part of this study. The neonates were assessed for tone abnormalities at 3, 6, 9, and 12 months of corrected age in case of preterm neonates, whereas for term neonates, the normal chronological age was considered. The evaluation of muscle tone was based on the study of spontaneous posture, passive tone, and active tone. Passive tone was measured by popliteal angle, adductor angle, and dorsiflexion angles in the lower extremity and scarf sign in the upper extremity. Assessment of passive tone was done with the Amiel-Tison method, using a goniometer.⁴ Table 2 shows the normal range of angle to assess passive tone with the Amiel-Tison method.

Active tone comprises spontaneous movements and movements provoked by maneuvers such as pull to sit and pull to stand. Based on these examinations, the neonates were categorized as having hypertonia, hypotonia, and minor tone abnormalities such as mild hypertonia or hypotonia in one extremity, mild adductor or abductor spasm at the hip joint, and mild hypertonia of the neck extensors. Hypertonia was defined as increased tonus in the upper extremities and/or trunk and increased adductor and extensor tonus in lower extremities. Hypotonia was defined as decreased muscle tone and increased joint mobility.⁵ All neonates found

Table 2. Normal Range of Angle To Assess Passive Tone With the Amiel-Tison Method

Corrected Age, ^a mo	Adductor Angle	Popliteal Angle	Dorsiflexion Angle	Scarf Sign
0-3	40°-80°	80°-100°	60°-70°	Elbow does not cross the midline
4-6	70°-110°	90°-120°	60°-70°	Elbow at the midline
7-9	110°-140°	110°-160°	60°-70°	Elbow crosses the midline
10-12	140°-160°	150°-170°	60°-70°	Elbow goes beyond the axillary line

^aCorrected age = chronological age - (40 - gestational age) × 4.

to have tone abnormalities were given occupational therapy.

If there were no tone abnormalities at 6 and 12 months, the group was called the normal high-risk group. If tone abnormalities were present at 6 months but disappeared at 12 months, they were called the TTA group. Those neonates with persistent tone abnormalities at 6 and 12 months were said to have persistent tone abnormalities^{6,7} and were referred to the physiotherapy center for further developmental assessment and rehabilitation.

In all the follow-up visits, anthropometry was done. Also, other neurodevelopmental assessments such as hearing screen tests, primitive reflexes, protective reflexes, and motor and mental milestones were screened, but the priority was tone abnormalities and assessing TTAs in HRNs. Neonates with dreaded complications such as IVH and seizures and those who underwent exchange transfusion were followed up more frequently and were asked to visit just 2 weeks after discharge.

Results

One hundred seven neonates who were discharged from our NICU were enrolled in this study. Among them, families of 13 neonates lived in far-off areas and could not come for regular follow-up and 5 neonates died after going home. The remaining 89 neonates were followed up to 1 year to find the final outcome.

After the first follow-up, of the 89 HRNs, 56 had normal tone, 29 had hypertonia, 3 had mild tone abnormalities, and 1 was hypotonic. On further follow-up, most of the tone abnormalities became normalized,

hence the number of cases in the high-risk group increased (Table 3).

In the normal high-risk group, during the second follow-up, the normal high-risk category increased by 22.47% (ie, number of normal HRNs increased from 56 to 76). At the third follow-up, the normal high-risk category increased by 11.23% (ie, number of normal HRNs increased from 72 to 82). At the fourth follow-up, the normal high-risk category increased by 3.37% (ie, number of normal HRNs increased from 81 to 84).

In mild tone abnormalities group, during the second follow-up, there was a remarkable normalization of the tone, which was considered to be as of the normal high-risk group. In the hypertonia group, during the second follow-up, about 17 neonates (19.1%) showed normalization of the tone. At the third follow-up, about 6 neonates (6.74%) showed normalization of the tone. At the fourth follow-up, about 6 neonates (2.25%) showed normalization of the tone.

Of the 29 neonates in the hypertonia group, only 4 (4.49%) had persistent hypertonia, whereas the rest of the neonates improved by the end of the fourth follow-up (ie, 25 neonates [28.08%] showed improvement).

In the hypotonia group, only 1 neonate had hypotonia during the first follow-up. On further follow-ups, at the third and fourth follow-ups, the neonate had persistent hypotonia and was diagnosed as having hypotonic CP at the end of last follow-up. The neonate was referred to the physiotherapy center.

Table 3. Percentage Distribution of Neonates According to Different Outcomes During the Follow-up Visits

Follow-up	First, n (%)	Second, n (%)	Third, n (%)	Fourth, n (%)
Normal	56 (62.92)	76 (85.39)	82 (92.13)	84 (94.38)
Minor Tone Abnormalities ^a	3 (3.37)	0 (0)	0 (0)	0 (0)
Hypertonia	29 (32.58)	12 (13.48)	6 (6.74)	4 (4.49)
Hypotonia	1 (1.12)	1 (1.12)	1 (1.12)	1 (1.12)
Total	89 (100)	89 (100)	89 (100)	89 (100)

^aMinor tone abnormalities such as mild hypertonia or hypotonia in one extremity, mild adductor or abductor spasm at the hip joint, and mild hypertonia of the neck extensors.

Outcome

At the end of the fourth follow-up, of the 89 HRNs, 25 (28.09%) showed normalization of tone. Among the remaining, 59 (66.29%) HRNs were normal, 1 (1.12%) had persistent hypotonia on all the follow-ups, and about 4 (4.49%) had persistent hypertonia in all limbs. All the 5 neonates were considered as having CP and were referred to the rehabilitation center of SDM College and Hospital, whereas in case of mild tone abnormality group all 4 neonates became normal at the end of the study (Table 4).

Table 4. Percentage Distribution of HRNs According to the Final Outcome

HRNs	No. of Neonates, <i>n</i> (%), <i>N</i> = 107
Normal	59 (55.14)
TTA	25 (23.36)
CP	5 (4.67)
Died	5 (4.67)
Did Not Follow Up	13 (12.15)

CP, cerebral palsy; HRNs, high-risk neonates; TTA, transient tone abnormality.

Discussion

One hundred seven HRNs discharged from our NICU were enrolled in this study. Families of 13 neonates lived in far-off areas and could not come for regular follow-up and 5 neonates died after discharge. The remaining 89 (83.17%) neonates were followed up for 1 year to find the final outcome. At the end of 12 months, 59 neonates had no abnormalities and were considered normal, 25 had TTAs, and only 5 had persistence of tone abnormalities and were considered as having CP.

In a study by Karlsson et al,⁸ of 123 HRNs, 4 had an adverse developmental outcome at 18 months of age. Our study also has a similar incidence of adverse neurodevelopment outcomes, probably due to the increased number of preterm deliveries and lack of advanced neuroprotective strategies.

Chaudhari et al⁹ found the Amiel–Tison neurologic test to be more sensitive in detecting abnormal motor development at 3, 6, and 9 months compared with the

Bayley Scales of Infant Development (BSID) but lost its advantage over BSID at 12 months.

Gestational age and outcome of high-risk neonates

In our study, of the 107 HRNs, 89 were followed up to 1 year of age. Of the 89 HRNs, 59 (66.29%) were preterm and 30 were term (33.71%) neonates.

Of the 59 preterm neonates, 13.48% were born at < 30 weeks of gestational age, 19.10% were born between 30 and 32 weeks of gestational age, and 33.71% were born at > 32 weeks of gestational age.

We found TTAs to be more prevalent (30.51%) in preterm neonates compared with term neonates (23.33%). Similarly, Brandt et al¹⁰ have stated that TTAs occur more commonly in preterm neonates when compared with full-term neonates.

We also found CP to be more prevalent (13.33%) in term neonates compared with preterm neonates (1.69%). Similarly, Stanley et al¹¹ reported that very preterm birth (gestation < 32 wk) is a strong predictor of later CP. O’Shea et al¹² also reported that approximately 10% of the smallest (< 1000 g) preterm neonates will develop CP, and Winter et al¹³ reported a 32% rate of CP in neonates weighing < 1500 g.

Final outcome of tone abnormalities

In our study, 59 (66.29%) neonates had a normal tone at the second follow-up and fourth follow-up and became a normal high-risk group; 25 (28.09%) neonates normalized at 12 months; and 5 (5.62%) neonates had persistent abnormal tone and were diagnosed with CP and were referred to the rehabilitation center. All those neonates with minor tone abnormalities showed normalization of tone before the second follow-up and were considered the normal high-risk group. We found that in 82.5% of the cases, abnormal tone normalized at 12 months. Another study had similar results, where Chaudhari et al⁷ found that 87% of HRNs started normalizing at 9 months and formed TTAs.

Limitations

- In most studies, neuromotor assessments were done up to 18 months of age.¹² As our study was done as a part of a dissertation for the fulfillment of MD pediatrics degree, duration of the study had to be limited, and hence, it was decided to do a neuromotor assessment up to 1 year of age.
- Developmental scales were not used in the study as the study was done mainly to know the tone abnormalities, survival rate of HRNs, and the transition of abnormal tone to normal.
- Developmental scales were used only by the occupational child physiotherapist after early detection of tone abnormalities.

Conclusions

- Our study cohort consisting of preterm and full-term neonates, with more number of preterm neonates, shows that many of the tone abnormalities detected at 6 months of age are transient and resolve by 12 months of age. Hence, a hasty diagnosis of CP should not be made till the latter part of the first year.
- Many of the tone abnormalities detected within 6 months resolve by 12 months, hence HRNs should be followed up to detect complication/s at the earliest and provide early intervention.
- TTAs were seen more in extremely low-birth-weight (ELBW) neonates (< 1000 g) compared with very-low-birth-weight (VLBW) and low-birth-weight (LBW) neonates, and this was similar in neonates born at < 30 weeks of gestational age. This may be due to the poor muscle strength in ELBW neonates compared with VLBW and LBW neonates.
- The prevalence of TTAs was more in premature neonates compared with that in term neonates. This may be due to the fact that muscle tone, or the resistance of a muscle to stretch, is generally much lower actively and passively in a preterm neonate compared with that in a full-term neonate.
- Our study showed a prevalence rate of 35.2% for TTAs.

- The mortality rate was 4.67%; follow-up assessment of HRNs led to a dramatic increase in the survival rates of HRNs, especially ELBW and VLBW neonates.
- Most mild motor abnormalities detected in the first few months improved and usually completely resolved over time.
- Those neonates without any transient abnormal motor signs have the lowest rate of subsequent abnormality.
- Neonates with severe risk factors and coexistence of multiple risk factors have the worst neuromotor outcome.
- Neonates with multiple risk factors showed poor neuromotor outcome, despite early intervention.
- The tone abnormalities in our high-risk cohort disappeared in 87.5% of cases.

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