**Original Article:**

**Neurobehavioral Profile of Moderate to Late Preterm Infants Admitted in a Tertiary Care Centre in South India**

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**Abstract:** Background and objectives: Neonatal neurobehavioral organization is a multidimensional holistic phenomenon which involves synchronous working of autonomic, sensory and motor systems to influence the developmental maturation of neonates. Homeostasis of all these systems is well developed in term infants but preterm infants, due to their physiological instability and incomplete cortical development, are at higher risk of impaired neurobehavioral organisation. Neurobehavioral maturity of term infants has been documented in many studies but there is dearth of literature in preterm infants, especially moderate to late preterm (MLP) category (32 weeks – 36 weeks of gestation). Thus the present study was aimed to assess the neurobehavioral profile of MLP infants and to compare it with standard reference scores provided in the NAPI manual. Methods: A cross sectional study was planned in which sixty moderate to late preterm infants were included during their stay in neonatal intensive care unit (NICU). Neurobehavioral assessment of preterm infants (NAPI) scale was used to document the neurobehavioral profile of preterm infants. Descriptive statistics was used to describe the baseline maternal and infant’s characteristics. One sample t test was used for comparing the study sample and standard values provided in NAPI Manual for parametric analysis. Wilcoxon signed rank test was used for comparing variable values between two groups which were not following normal distribution. Results: Scarf sign at 34 and 36 weeks of gestation, motor development and vigor and alertness and orientation components of NAPI showed statistically significant difference between our study sample and standard reference values taken from NAPI manual. However statistically insignificant difference was found in popliteal angle, irritability, cry quality and percent sleep ratings domains of NAPI. Conclusion: In the present study on the neurobehavioral profile of our population, we found significant variability in scores for motor development and vigor, alertness and orientation and scarf sign domains for our study sample as compared to western standards provided in the NAPI manual.

**Key Words:** Preterm, Caregiver, Development, Neurobehavior, Alertness, Developmental assessment

**Introduction:**

Neonatal neurobehavioral organization is a multidimensional holistic phenomenon which involves synchronous working of autonomic, sensory and motor systems to influence the developmental maturation of neonates. It represents the inherent ability of the child to interact with the external environment and learn from the environment.
interplay of these subsystems supports the differentiation and modulation of CNS maturation. Any disorganization in one system is reflected in other system leading to immature neurobehavioral organisation of the infant.(2)

Gestational age (GA) is one of the major indicators of neonatal maturity and is inversely proportional to the extent of impairments suffered by preterm infants.(3) Full term infants i.e. born after 37 weeks of gestation, are functionally more mature and show better cortical organization as compared to infants born at earlier gestations. Preterm infants are at risk of developing developmental delays because of immature organs, especially CNS and their inadequacy to deal with the stressful environment of the NICU.(4) Studies have also postulated that last trimester is very crucial for the “wiring” of the brain. This organizational phenomenon is responsible for the development of autonomic stability, motor maturity, state organization, attention, interaction and self-regulation.(5)

Numerous studies are available for neurobehavioral assessment at term gestational ages, but literature is extremely insufficient on assessment of preterm infants born before 36 weeks of gestation are completed. Infants born between 32 weeks 0 days of gestation to 36 week 6/7 days of gestation are classified as moderate to late preterm infants. They were historically considered mature and equivalent to full term peers until recent studies which have proved even this category of infants are at risk of short term and long term complications.(6) A standardised neurobehavioral assessment which can identify the chances of delays in this low-risk category would be a great benefit to the clinicians as well as researchers in the field. Variety of assessment tools are available to assess neurobehavior of new born infants such as- NICU Network Neurobehavioral Scale (NNNS), Hammersmith, Assessment of Preterm Infant Behavior (APIB) and Neurobehavioral assessment of preterm infants (NAPI) etc.(7)

NAPI can be a potential instrument to identify the developmental delays in this category. It has been designed to use in preterm infants as early as from 32 weeks of gestation to term. The best feature of the test is, it has been designed in such a way that large part of it can be just completed by merely observing the infant without handling and does not require professional training. NAPI has been used in number of studies and has been found to be a valid and reliable tool to identify developmental delays. Moreover, it has been found to yield 80% of sensitivity when combined with MRI to predict the cerebral palsy in preterm infants.(8)

Thus the present study was aimed to assess the neurobehavioral profile of moderate to late preterm infants. Considering a lot of differences between the western and Asian population in terms of racial and ethnic composition, legal and health care systems, and financial entitlements that could impact current and future development, we expected to find out difference in neurobehavioral maturation of the neonates. So, the secondary objective of the study was to compare the neurobehavioral profile of western and Indian population by comparing the normative scores given in the NAPI Manual with scores attained by our population.

Methods

Design: A cross sectional study was conducted in which 60 moderate to late preterm infants were assessed for neurobehavior during their stay at the neonatal intensive care unit. The study was approved by institutional research committee and Institutional Ethics Committee (IEC 190/2014). Written informed consent was taken from the parents before participating in the study.

Subjects: All infants born between 32 week 07 days to 36 week 6/7 days were screened from neonatal intensive care unit of our hospital. They were examined between 24-48 hours of delivery to ensure physiological stability and to rule out the labor related influences. Infants were recruited in five gestational categories i.e 32, 33, 34, 35 and 36 weeks. Gestational age (GA) of the infant was determined by reported onset of last menstrual period and first trimester ultrasonography. Later on modified Ballard’s score was used to arrive at the best clinical estimate of GA. Infants with congenital anomalies, severe respiratory distress, genetic or chromosomal disorders were excluded from the study.

Entire procedure was explained to the parents in detail. Demographic details regarding maternal age, maternal complications, birth weight, gender, gestational maturity, Appgar scores were collected from the hospital file.

Neurobehavioral Assessment of Preterm Infants (NAPI) form was used to evaluate the neurobehavior of preterm infants. NAPI assess neurobehavior of infant in seven clusters – scarf sign, popliteal angle, motor development and vigor, alertness and orientation, irritability, cry quality and percent asleep ratings. It is applicable from 32 - 40 weeks of gestation.

Procedure: After confirming the physiological stability and feeding status (90 minute prior to the assessment), preterm infant was assessed for all items according to the sequence given in the NAPI unmanual. Items were performed by a physiotherapist trained for NAPI administration and with good handling skills. A total of 41 items (7 clusters) with 14 behavioral states were recorded by the examiner. Some items- scarf sign, popliteal angle etc., were performed in the open crib with radiant warmer and others- alertness and orientation involved holding the infants on the lap. After completing the examination infant was placed back under the radiant warmer and behavioural state was recorded. Raw scores were changed into converted scores for each cluster using conversion table provided in the manual. Final scores were entered into Statistical Package for Social Sciences (SPSS) for data analysis.

Data was analysed using SPSS version 16. Descriptive statistics was used to report maternal and neonatal demographic details. One sample t test was used for normally distributed data to report the difference between Indian population and western norms as provided in NAPI Manual. For skewed data non parametric test (one sample Wilcoxon signed rank test) was used.

Results

The results are shown in the Tables below.

| Table 1: Baseline characteristics of the study sample (N=60) |
|-----------------|-----------------|-----------------|-----------------|
| Maternal age (years) | 28.4±4.95 |
| Gender (%) | M: 56.7 | F: 43.3 |
| Birth weight (grams) | 1583.2 ± 304 |
| Gestational maturity (%) | AGA: 59.3 | SGA: 41 |


The present study analysed the neurobehavioral status of moderate and late preterm infants in their initial period of development. Behavioural differences were more pronounced in preterm infants belonging to lower gestations as compared to infants in higher gestational age ranges.

Authors propose that brain maturation is a complex process which involves morphological, functional and organisational changes. Although it is a complex phenomenon yet its sequence is always organised and predictable. The behavioural differences observed in the lower to higher gestational ages can be attributed to the differences in the extent of cortical organisation. Cortical growth is predominantly achieved by axonal, dendritic proliferation and cortical folding which leads to enormous increase in brain surface area in the third trimester. Studies have reported preterm infants show lesser cortical folding as compared to term infants. Thus these differences in cortical folding are responsible for neurobehavioral and neurocognitive disorders in preterm infants.

Myelination is the major component in white matter maturation and enables more effective transmission of neural impulses. It starts in third trimester and continues postnatally. Studies have reported that myelination follow certain rules and it has been proposed that proximal pathways myelinate prior to distal, sensory pathways prior to motor and projection fibre tracts get myelinated before association pathways. A study done by Weinstein M et al reported that early maturing tracts are responsible for sensory performance and late maturing tracts are responsible for motor activities. They also concluded that discrepancies in neurodevelopmental changes and neuronal activity in preterm infants can lead to poor neurobehavioral development. Thus the variance in neurobehavioral scores of NAPI demonstrated in our study can also be corresponded to the deficient white mater maturation in 32 weeks as compared to 36 weeks.

Secondary objective of the study was to compare NAPI scores of our babies with standardized scores presented in the manual. The results of our study revealed significant differences in performance of our infants as compared to western population. Compared to the standard scores provided in the NAPI Manual our sample displayed weaker motor development and tone at shoulder girdle and comparable with standard scores. The results of our study is in consensus with other study who also reported lower performance of study samples as compared to standard norms provided in the manual.

Study samples reported lower values of scarf angles as compared to standard samples which is in consensus with other studies. The possible explanation for lower values can be; scarf sign is the measure of passive resistance when the arm is moved towards shoulder. With increasing gestational age this resistance increases in consequence of better motor development and tone at shoulder girdle. This increase in tone is the shifting paradigm from hypotonia to normal physiological flexion at term age. However, preterm infants continue to exhibit lower tones as compared to full term born infants. Thus in addition to early birth, environmental factors would also have a role to play in tone development patterns.

Motor quality assessment is the better indicator of motor dysfunction and is clinically more useful than assessing milestone attainment. Lower motor scores observed in our study are well correlated with the findings of other studies. Motor development is a dynamic process,
multiple factors such as insufficient postnatal weight, height, head circumference may influence the motor development of child. Moreover preterm infants lack proper muscle coordination, strength, inadequate postural control, poor quality of movements, lack of antigravity control which would have contributed to lower scores across all gestations.(22)

Alertness and orientation skills which involve tracking, head turning for animate and inanimate objects is the reflection of brain development. Our study samples exhibited lower scores than standard NAPI samples. These results are contradictory to the findings obtained by Gabriel P et al who reported higher alertness and orientation scores but supported by a recent study conducted by Gorzilio DM et al.(14-23) They reported when compared between moderate to late preterm category prematurity and stress tolerated by infants is the major predictor of lower scores and it improves with increase in gestational age. Infants in NICU are more exposed to adverse stimuli. Acute stress events and minimal protection from negative stimuli are major factors responsible for lower alertness and orientation scores and leading to higher chances of attentional and perceptual problems diagnosed at later age.

Decrease in percentage sleep signifies the better arousal and active state of infant. This is in consensus with other studies who have reported increase arousal levels and decrease lethargy in premature infants as they approach term age.(24-25) Authors propose that neurological maturation, growth and decrease in environmental stressors would have contributed to better arousal.(24-26) Decrease in sleep timings are also well correlated with the emergence of feeding behaviours from 34 weeks onwards and rapid progression to enable full feeds and discharge from the hospital.(27)

In irritability, crying and popliteal angle our study infants were comparable to NAPI study samples. Results of our study exhibited moderate quality of cry in all gestations, authors propose that we should be cautious in interpreting the quality of cry using NAPI because it does not keep into consideration intensity frequency and pitch of crying which are important parameters to grade quality of crying.(28-29)

An explanation for the relatively poor scores across all domains of NAPI when compared with standard reference norms may be that the population in our study usually belongs to low socioeconomic backgrounds and diverse ethnicities factors which are associated with poor developmental outcomes and could have resulted in lower developmental profile of our children.(30)

Results of our study showed explicitly lower scores in scarf sign, motor development and vigor and alertness and orientation component especially at 34 week of gestation as compared to infants born at 32-34 week. On carefully going back to our data we found that mean maternal age in 34 week born infants was 30.38 (range of 21 to 40 years). Since maternal age is also one of the important determinant of neurodevelopment of infant. Higher maternal age would have resulted in lower scores in 34 week category.(31)

The results of the present study highlight the need to incorporate neurobehavioral assessment as a routine standard practice in all NICU’S. Firstly it will enable the clinician to find the high risk infants and provide them early intervention services. Secondly, when parents are able to read and understand the behavioral cues communicated by their infants, it will enable them to modify the activities and support neurobehavioral organisation in better way. This in turn will increase the competency of caregivers and will promote better development of their child.

Limitations of the study
Regarding the limitations of our study authors reveal that the differences in neurobehavioural organisation observed in our study can be attributed to the small sample size used in our study as compared to large sample used for normative scores of NAPI. There was unequal distribution of infants in different gestational categories which make the comparison less reliable. We also emphasize that sample of our study was preterm infants, with maximum number of infants belonging to LBW category which itself would have resulted in lower scores.

Conclusion:
The present study reported the neurobehavioral profile of our population. We found significant variability in scores for motor development and vigor, alertness and orientation and scarf sign domains for our study sample as compared to western standards provided in the NAPI manual. Although we found lower scores in our study sample throughout all gestations and results are supported by various studies, still authors warrant about the generalizability of standard NAPI scores for our population. Future studies need to be conducted to establish normative values of NAPI for Indian babies for reliable comparison.

References


