

## Neurodevelopmental Outcome of Late Preterm Infants at 12 Months of Age

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Received date: October 12, 2015; Accepted date: November 3, 2015; Published date: November 11, 2015

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### Abstract

**Background:** Late-preterm infants (34-36<sup>+</sup><sub>6</sub> weeks' gestation) are often believed to have no higher risks for morbidity and mortality than term infants. This study aims to evaluate the neurodevelopmental outcome of late preterm infants at 12 months of age, compared to term infants.

**Methods:** Neurodevelopmental assessment was administered using the Bayley Scale of Infant Development. Eighty participants, including 40 late preterm and 40 term infants were included.

**Results:** At 12 months of age, the neurodevelopmental assessments of late preterm infants adjusted for prematurity showed no difference from those of term infants. However, without adjusting for prematurity, late preterm infants had a significantly lower Mental Developmental Index and Psychomotor Developmental Index scores than term infants.

**Conclusion:** The findings in this study reveal that late preterm infants had not completed their developmental maturation at 12 months of age. Monitoring these children may help in the early identification of developmental problems and provide appropriate intervention.

**Keywords:** Infants; Late preterm; Neurodevelopment

### Introduction

Late preterm infants (infants born at 34-36<sup>+</sup><sub>6</sub> weeks of gestation) have recently received increasing attention. Previously, these infants were known as near term infants, so some of them were managed in a similar way to term infants [1,2]. However, present data have revealed that risks of morbidity and mortality in late preterm infants are greater than previously thought [3-7], although there is a lower risk of severe medical morbidity when compared to that of infants born at ≤ 33 weeks gestation. Late preterm infants represent a sizable population of preterm infants. Approximately 70-75% of preterm infants are born between 34-36<sup>+</sup><sub>6</sub> weeks of gestation, which accounts for 8% of all births [8-10].

The growth and neurodevelopment of infants born prematurely are not the same as those of term infants at the same chronological age [11]. Preterm infants without major neurological deficits can have their growth and development "catch-up" around 1-2 years old [12]. Those who do not catch up may be found to have cerebral palsy, cognitive impairment or other developmental disabilities. Since late preterm infants may have some immaturity of the neurological and respiratory systems [6], recent studies have shown that late preterm infants were also more likely than full term infants to have developmental disabilities [10,13,14].

Studies of neurodevelopmental outcomes of late preterm infants are fewer than those of lower gestational age preterm infants. Findings have not been fully conclusive [8] because of different settings,

variations in studied populations, late preterm definitions, and outcome measurements; or the study was carried without a comparison group [5,15-20]. Those outcome measurements were presence or absence of cerebral palsy, intellectual disabilities, and neurological deficits. Few studies have used structured measurements to describe neurodevelopmental/ neurocognitive profiles of these children [20-23]. Previous studies revealed greater cognitive impairment and behavioral problems in late preterm infants than in term infants at 6 years of age [17,21]. However, Baron et al have suggested that uncomplicated late preterm birth does not, in itself, increase the risk of later cognitive impairment [17]. There were reports of similar neurodevelopmental outcomes in late preterm infants with corrected age and term infants at 12 and 18 months, but the outcomes for those late preterm infants were worse when assessed according to their chronological age [20]. The IQ scores of late preterm infants at preschool age were reported to be within the normal range [22].

Because late preterm infants may be at increased risk of developmental problems, early recognition of a delay in neurodevelopment implies that early intervention would have beneficial effects on their development. Those infants who have not caught up their development after 1 year of age need to be closely monitored. Therefore, this study aimed to assess the neurodevelopmental outcomes of late preterm infants at the age of 12 months, using neurodevelopmental assessment scales, and to compare these findings with those of term infants at 12 months of age.

## Material and Methods

All participants were born at Chiang Mai University Hospital and were followed up at the High-Risk Clinic or Child Health Clinic. Late preterm infants with a gestational age between 34 and 36<sup>+6</sup> weeks were enrolled into the study. Infants with congenital malformations, presence of small for gestational age, severe postnatal infectious diseases or metabolic complications were excluded. Those infants with delay in development which were detected by developmental surveillance during health supervision visits received further assessment and appropriate intervention and were not included in the study. Term infants with a gestational age between 37-41 weeks, and a birth weight of 2500 grams or more, without perinatal medical complications, were also enrolled with age and gender-matched, as a comparison group. Neurodevelopmental assessments were administered at the age of 12 ( $\pm$  1) months using the Bayley Scale of Infant Development, 2<sup>nd</sup> edition (BSID-II) [24]. Growth parameters including weight, length, and head circumference were measured as part of health supervision visits.

The BSID-II is an instrument for assessing the developmental functioning of infants and children to detect developmental delay and plan intervention strategies. It consists of 3 scales: the mental scale, motor scale, and behavior rating scale. The mental and motor scales assess the child's current level of cognitive, language, personal-social, and fine and gross motor development. The behavior rating scale assesses the child's behavior during testing. The mental and motor scales are interpreted as the Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI). At the time of this study, there were some concerns regarding the new edition of Bayley-III which was generating considerable controversy, although separate assessment of language development was added [25-27]. The findings that the Bayley-III might give higher-than-expected scores for preterm infants [28] has resulted in the use of Bayley-II in this study. The mean MDI and PDI scores were 100 with a standard deviation of 15. For late preterm infants, both MDI and PDI scores were administered using both their chronological age and the corrected age adjusting for prematurity. Medical records were reviewed and demographic characteristics of the family were obtained from parents. The study protocol was reviewed by the Ethics Research Committee of the Faculty of Medicine, Chiang Mai University. Informed consent was obtained from all parents.

Data were analyzed using the SPSS. Mean, standard deviation, and percentages were described. The statistical differences between the late-preterm and full-term infants were calculated using the student's t

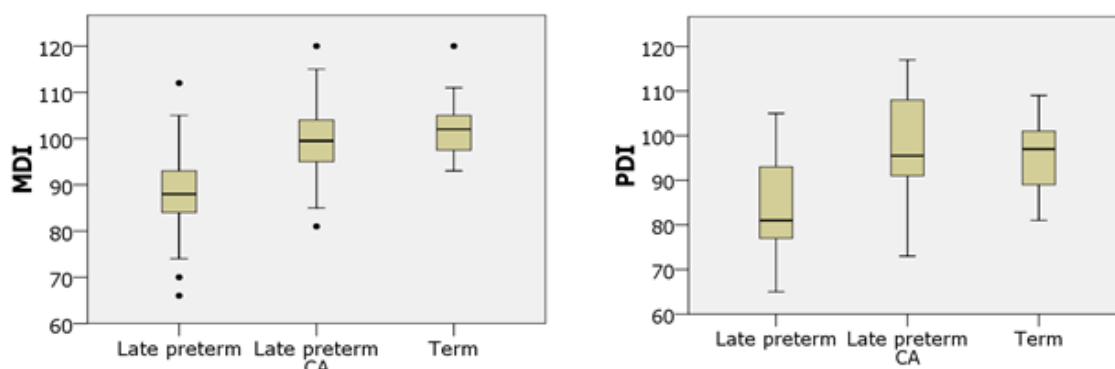
test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. A p value of <0.05 was considered statistically significant.

## Results

There were 80 infants enrolled into the study, including 40 late preterm and 40 term infants. Forty-five percent of the infants in each group were male. The mean chronological age of late preterm and term infants was 12.2 (0.7) and 12.1 (0.4), respectively. The mean gestational age for the late preterm infants was 35.0 (0.8) weeks. The mean birth weight, length, and head circumference of both groups are shown in Table 1. The family characteristics of late preterm and term infants were comparable. The most common pregnancy complication was premature labor which was greater in the late preterm group.

	Late preterm infants (N= 40)	Term infants (N= 40)	P
<b>Infant characteristics</b>			
Gender, male (%)	18 (45%)	18 (45%)	1.00
Gestational age, mean $\pm$ SD	35.0 (0.8)	38.5 (1.2)	<0.001
Birth weight, mean $\pm$ SD	2136.0 (494.8)	3156.5 (289.6)	<0.001
Length, mean $\pm$ SD	44.1 (3.0)	49.5 (5.2)	<0.001
Head circumference, mean $\pm$ SD	31.1 (1.8)	34.1 (3.6)	<0.001
<b>Family characteristics</b>			
Paternal age, mean $\pm$ SD	35.7 (6.8)	35.5 (8.4)	0.92
Maternal age, mean $\pm$ SD	32.4 (5.8)	31.7 (4.9)	0.55
Paternal education: y, mean $\pm$ SD	13.5 (2.6)	11.5 (5.9)	0.08
Maternal education: y, mean $\pm$ SD	13.9 (3.4)	11.9 (5.7)	0.06
Family income, mean $\pm$ SD	26,564 (17,542)	21,434 (13,818)	0.16
SD: Standard Deviation			

**Table 1:** Characteristics of late preterm and term infants with their families.



**Figure 1:** The mean MDI (A) and PDI (B) scores of late preterm infants at 12 months of age, with adjustment for prematurity, compared to those of term infants MDI: Mental Developmental Index; PDI: Psychomotor Developmental Index; CA: Corrected Age

Growth parameters including the mean weight and length of late preterm infants at 12 months of age were significantly lower than those of term infants. However, the mean head circumference of infants from both groups showed no significant difference. Regarding the neurocognitive assessment, the MDI and PDI scores of late preterm infants, administered by adjusting for prematurity, showed no difference when compared to those of term infants (Figure 1).

The mean adjusted MDI and PDI scores of late preterm infants were 99.6 (7.7), range 81-120; and 97.8 (11.4), range 73-117, respectively. When administered using their chronological age, the MDI and PDI scores of late preterm were significantly lower than those of term infants ( $p < 0.001$  and  $0.001$ ), as shown in Table 2. There were 4 late preterm infants but no term infants scoring below 2 SD of the Bayley Scales.

	Late preterm infants (N= 40)	Term infants (N= 40)	t	P
Chronological age, mean $\pm$ SD	12.2 (0.7)	12.1 (0.4)	1.33	0.19
Weight, mean $\pm$ SD	8251.3 (1307.3)	9044.5 (1113.9)	-2.92	0.005
Length, mean $\pm$ SD	71.9 (3.5)	73.8 (2.6)	-2.66	0.01
Head circumference, mean $\pm$ SD	44.2 (1.7)	45.0 (1.5)	-2.04	0.05
MDI, mean $\pm$ SD	87.7 (8.6)	102.2 (5.5)	-8.95	<0.001
range	66-112	93-120		
PDI, mean $\pm$ SD	83.8 (10.0)	95.2 (7.6)	-5.77	<0.001
range	65-105	81-109		

SD: Standard Deviation; MDI: Mental Developmental Index; PDI: Psychomotor Developmental Index

**Table 2:** Growth parameters and neurodevelopment assessment of late preterm and term infants at 12 months of age.

## Discussion

This study found that neurodevelopmental assessment scores of late preterm infants by the BSID-II, at the chronological age of 12 months were significantly lower than those of term infants. This means that late preterm infants, even without major neurological deficits, have not caught up regarding their overall development at 12 months of age yet. However, when the tests were administered by adjusting for prematurity, the mean MDI and PDI scores were not statistically different from those of term infants. The use of this correction in preterm infants had been viewed as controversial when assessing cognitive functions [12,29]. The findings in this study were similar to the study by Morag et al who reported that at 6 and 12 months, late preterm infants performed significantly lower than term infants on all subscales of the Griffiths Mental Development Scales, but with post conception age adjustment, developmental scores were similar in both groups [30]. Similar findings of late preterm infants at 12 and 18 months of age were reported [20]. Infants born moderately/late preterm had similar Bayley-II cognitive scores similar to term infants [31].

Previous studies found that late preterm infants were at a similar stage of development to term infants [16,20]. One study found that the intelligence quotient of late preterm infants at the age of 5 years was within the normal range [22]. Another study showed that uncomplicated late preterm infants did not affect their development at preschool age [17]. However, it was found that at 2 years of age, late preterm infants had lower developmental scores than term infants [23]. In a study that children were followed through 6 years of age, late preterm infants were found to have lower intelligence quotients when they were assessed whilst controlling other factors such as maternal education and socioeconomic status [21]. As cognitive problems may be reported in late infancy or at preschool age in late preterm infants, our findings raise the issue on whether the results obtained by using scores for chronological age may allow early identification the infants who will be at risk of cognitive difficulties and early intervention could be provided.

At 12 months of age, the mean weight and length of late preterm infants were lower than those of term infants. Only the mean head circumference was not significantly different between the two groups (44.2 vs 45.0 cm in late preterm and term infants, respectively). The head circumference is among the growth parameters that can be

caught up earlier, so that it has been suggested that the head circumference be adjusted for prematurity until the age of 18 months [32]. Weight and height may be adjusted until the age of 24 and 40 months, respectively.

This present study used BSID-II to assess neurodevelopment in late preterm and term infants. All participants were born and followed up at a tertiary medical care center. However, there were some limitations in the study. Firstly, the number of late preterm samples was small because of this study's objective to evaluate infants without major perinatal complications, as those would affect their development. Some parents of these infants chose not to participate in the study and opted to be followed-up at other local hospitals. Secondly, the assessment was carried out in infants until 12 months of age and a study of a longer duration would have provided more information. However, this study aimed to identify developmental problems in late preterm infants early, especially those who had not caught up their development yet, in order to provide appropriate intervention for them. Those with low MDI and PDI scores were referred for further assessment and received early intervention. Thirdly, the factors associated with developmental disabilities could not be analyzed due to the small sample size. There were some reports that infants of male gender, with lower maternal education, and delivered by emergency cesarean section, were at increased risk of low developmental scores [30]. Lastly, the BSID-II was used in this study. The separate scores of cognitive, gross motor, fine motor, and language development of Bayley-III would add more information.

The findings in this study revealed that at 12 months of age, the neurodevelopment and the growth of late preterm were not the same as those of term infants. In general developmental assessments of preterm infants need to be and are adjusted for prematurity until 2 years of age. At 1 year of age, some late preterm infants may have caught up regarding their development but those who have not caught up with term infants regarding their development, should be monitored closely so that their developmental problems are not underestimated and appropriate intervention can be provided for these infants.

## Acknowledgment

We would like to thank staff in the High-Risk and Child Health Clinics. We also extend our gratitude to the patients and their families for their participation in this study.

## Ethical approval

The study was approved by the Ethics Research Committee of the Faculty of Medicine, Chiang Mai University.

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