Paediatrica Indonesiana

VOLUME 50 July • 2010 NUMBER 4

Original Article

Cognitive outcome in late preterm babies

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Abstract

Background Late preterm babies are at risk for delayed cognitive outcome, but little attention has been paid on this issue. There has been a general assumption that this group of babies will have the same development as full-term babies.

Objective To compare the cognitive development between late preterm babies and full-term babies.

Methods A prospective cohort study was conducted at the Department of Child Health Medical School of Udayana University/Sanglah Hospital. Babies with 34 to 42 weeks of gestational age who were born in Sanglah Hospital between November 1st 2007 and December 31st 2008, were recruited to the study. Cognitive development of each baby was measured by Mullen Scale's of Early Learning twice, at 7 days and 3 months of age. We used corrected age for late preterm babies and chronological age for fullterm babies.

Results The incidence of under-average development for late preterm babies at three months corrected age was 47.8% compared to 4.1% among fullterm babies ($P < 0.0001$). The relative risk for under-average development among late preterm babies was 11.8 (95%CI 9.95 to 13.75). Multivariate analysis revealed late preterm influenced cognitive significantly with OR 17.01 (95%CI 1.15 to 32.87).

Conclusions Cognitive outcome of late preterm babies was delayed compared to full-term babies. **[Paediatr Indones. 2010;50:239-244]**.

Keywords: *cognitive outcome, late preterm babies, Mullen Scale of Early Learni ng*

Late preterm babies, who are born within 34 to < 37 weeks of gestational age (GA), are at risk for deterioration because of organ immaturation, medical intervention and its complications, and the effect of condition that cause the prematurity.[1] One of the important effect of the deteriorations is delayed cognitive outcome of survived preterm babbies.[2-7] Most of the studies on cognitive outcome of preterm babies were conducted on high risk preterm baby group.[8-13] Only few studies were conducted on late preterm babies even though this subgroup constituted 70% of the survived preterm babies.[14-16] This subgroup also had a little attention in the following observation because of general assumption that this group had a little risk to develop abnormally.[17]

Intervention for delayed development would have the best result, if conducted as early as possible. One study in Bali reported that stimulation for low birth weight infant already showed result at three

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months corrected age.[18] Based on this, we conducted our study to compare cognitive outcome between late preterm and full-term babies at three months corrected age.

Methods

This was a prospective cohort study on babies born within 34 to 42 weeks of gestational age, in Sanglah Hospital between November 1st 2007 and December 31st 2008. Inclusion criteria were singleton with birth weight appropriate to gestational age, mother aged 20 to 35 years, and live permanently in Denpasar. Exclusion criteria were major anomaly congenital, severe asphyxia, traumatic delivery at head region, early neonatal complication (convulsion, apneu, hyperbilirubinemia, hypoglicemia, respiratory distress). Drop out criteria were clinically sepsis or positive microorganism in blood culture, severe head trauma, and death before the end of the study. The babies were recruited by consecutive sampling.

Written informed consent was asked from parent/guardian of every baby who met the eligibility criteria within 48 hours after birth. Measurement of gestational age were performed using Dubowitz score, birthweight (BW) with DS Pediatric Examining Table produced by Atom Medical Corp., head cirumference (HC) with plastic tape, and blood glucose (Optium Xceed). Some demographic data such as parent's education, family income, the number of family members were collected by questionnaire.

By the age of seven days, parents were asked to take their babies to children outpatient clinic at Sanglah Hospital. History taking and physical examination were conducted to identify any signs of early neonatal complications. Babies who had any clinical sign of early neonatal complication were turned out from the study. Cognitive outcome of was measured using Mullen Scale of Early Learning (MSEL).

At three months of age, corrected age for late preterm babies and chronological age for fullterm babies, data about babies' intake, caretaker and education were collected by history taking to the parent. We also measured the weight, length, HC, and cognitive development with MSEL. MSEL measures cognitive development from five different domains: gross and fine motoric, visual receptive, receptive and expressive language; and it can be used largely to diagnose developmental delay in our setting. The measurement was conducted by two research assistants with an interobserver agreement of 0.67. The doctor and the research assistants were blinded. The doctor did not know the result of cognitive measurement and the assistants did not know whether the baby was late preterm or full-term. At the end of sampling, the whole data were analyzed by computer program. Ethical approval of this study was obtained from Research and Development Committee of Faculty of Medicine, Udayana University, Denpasar.

The gestational age was determined in weeks, based on Dubowitz score. Late preterm was defined as gestational age of 34 to < 37 weeks and full-term as 37 to 42 weeks. Cognitive outcome was a composite standard score (CSS) appropriate with MSEL and divided into two categories: a) average if CSS was 85 to 115 and b) below average if CSS was less than 85. Nutritional status at 3 m.o was assessed based on WHO Z score of weight to length calculated. It was defined as normal if the Z score within -2 to +2 standard deviation (SD) and as malnutrition if the Z score was < -2 SD. Family income was assessed based on parent's report. It was considered as adequate if the income was more than minimum regional income of Bali Province year 2007 to 2008 and not adequate if less than that.

Numerical data was analyzed by independent t-test if the distribution was normal and Mann-Whitney test if the distribution was not normal. Categorical data was analyzed by chi-square test. Multivariate analysis with stepwise logistic regression was done to identify the association between gestational age and cognitive outcome.

Results

During the period of November 1st 2007 to December 31st 2008 there were 161 babies who met the inclusion criteria. Thirteen of them were excluded because of neonatal sepsis and five babies were lost to follow up. The total subject until the end of the study was 143 babies, consisted of 69 late preterm and 74 fullterm babies.

The baseline characteristics of two groups were similar, except for birthweight and weight at 3 months of age (Table 1).

The cognitive outcome based on MSEL is presented in Table 2. Late preterm babies were more common to have the result of MSEL of below average than that in full-term babies, both at 7 days dan 3 months of age. The relative risk of below average cognitive development in late preterm babies was 11.8 (95%CI 9.95 to 13.75).

The mean CSS of late preterm babies was lower than that of full-term babies (Table 3). However, the developmental rate which is the different CSS between 7 days and 3 months of age was not different, both in the late preterm and full-term babies.

Delayed development was occurred in all developmental domain as reflected by lesser t-score of each developmental domain in the late preterm babies **(Table 4)**.

A proportion of late preterm babies experienced development category alteration from below average to average which was not occured in fullterm babies **(Table 5)**.

Table 1. Characteristics of late preterm and fullterm groups

Characteristic	Late preterm (n = 69)	Fullterm (n = 74)
Birthweight, g, median (range)	2300 (1900 to 2500)	3175 (2600 to 4000)
Head circumference, cm, median (range)	32 (29 to 34)	33 (30 to 38)
Weight at 3 m.o, g, median (range)	6100 (5000 to 7700)	6800 (5000 to 8000)
Head circumference at 3 m.o, cm, median (range)	39 (33 to 46)	40 (37 to 43)
Male (%)		
malnutrition at 3 month (%)	40 (58)	40 (54)
	2 (2.9)	1 (0.4)
Father's education, (%)		
Elementary school	8 (11)	3 (4)
Junior high school	16 (23)	15 (20)
Senior high school	38 (55)	46 (62)
Academician degree-holder	7 (10)	10 (13)
Mother's education, (%)		
Elementary school	12 (17)	10 (13)
Junior high school	23 (33)	16 (21)
Senior high school	31 (44)	43 (58)
Academician degree-holder	3 (4)	5 (6)
Adequate family income (%)	42 (60)	49 (66)
Breastfed within 3 mo (%)	40 (58)	39 (52)
Cared by parent (%)	58 (84)	5 (74)
Caretaker's education (%)		
Elementary school	18 (26)	21 (28)
Junior high school	24 (34)	23 (31)
Senior high school	26 (37)	28 (37)
Academician degree-holder	1 (1)	2 (2)

Table 2. MSEL descriptive category in late preterm and full-term babies

Age	Gestational age	Mullen Scale Descriptive Category		Total	RR	95%CI	P
		Below average	Average				
7 d.o	Late preterm, n(%)	51 (74)	18 (26)	69	18.23	15.33 to 21.24	<0.0001¶
	Fullterm, n (%)	3 (4)	71 (96)	74			
3 m.o	Late preterm, n(%)	33 (48)	36 (52)	69	11.80	9.95 to 13.75	<0.0001¶
	Fullterm, n (%)	3 (4)	71 (96)	74			

¶ x^2 test

Table 3. Mean composite standard score of late preterm and fullterm babies

Age	Mean composite standard score (SD)		Mean difference (95%CI)	P
	Late preterm	Fullterm		
7 d.o	83.2 (SD 3.5)	87.8 (SD 1.2)	4.6 (3.7 to 5.4)	<0.0001†
3 m.o	87.0 (SD 3.3)	91.6 (SD 2.4)	4.6 (3.6 to 5.5)	<0.0001†

† Mann-Whitney test

Table 4. t-score of each developmental domain of MSEL for fullterm and late preterm babies at 3 months of age

Developmental domain	Median t-score (range)		P
	Late preterm	Fullterm	
Gross motoric	37 (31 to 37)	37 (31 to 37)	0.01
Fine motoric	34 (28 to 34)	34 (34 to 34)	<0.0001
Receptive visual	26 (20 to 40)	40 (20 to 40)	0.03
Receptive language	35 (27 to 35)	35 (35 to 35)	0.03
Expressive language	41 (31 to 41)	41 (41 to 41)	0.03

Table 5. Alteration category of development late preterm and fullterm babies at 7 d.o and 3 m.o

Gestational age	Proportion which experienced alteration from below average to average category		P
	Changed	Not changed	
Late preterm, n(%)	18 (26)	51 (74)	<0.0001
Fullterm, n (%)	0 (0)	74 (100)	

Table 6. Multivariate analysis (logistic regression) of factors associated with below-average cognitive outcome at 3 months corrected age

Variable	OR	95%CI	P
Late preterm	17.01	1.15 to 34.87	0.03
Low birthweight	1.00	1.00 to 1.03	<0.0001
Weight at 3 m.o	1.00	1.00 to 1.01	<0.0001

Stepwise regression logistic found that cognitive outcome was influenced by gestational age and weight **(Table 6)**.

Discussion

Late preterm infants are the largest survivors among preterm infants. These survivors are at risk of developmental delay. A study reported that delayed development of late preterm babies was 36% higher than that of fullterm babies.[17] Other study reported that one third proportion of babies born within 32 to 35 weeks GA would have learning problem at school age. [19]

Neuronal maturation started early in embryonal phase until few years after the baby born. There are several critical periods in brain development which need normal and healthy environment as well as enough time to produce normal brain. The cortical brain volume increases five time within 35 to 41 weeks GA. [20] At 34 weeks of GA, total brain weight was 65% of fullterm babies and cortical volume was 55%. This fact placed 34 to 37 weeks GA as a critical period for brain development and maturation. Other possible reason is neuron subplate was not formed yet before 36 weeks GA. An optimal neuron subplate was needed for continuity of axon from thalamus to higher cortical level. [21]

Development tasks for 7 days old babies are very few and could not be used as a predictor for cognitive development at later age. Large proportion of late preterm infants (26%) who progressed from below average to average cognitive development in this study proved that development was a dynamic process which was changed within time. Appropriate intervention plays a role to make a better achievement in shorter time.

This study found that delayed development in late preterm infants occured in all aspects of developmental domain. Fewer gross motoric ability would place a child to fewer chance for enviromental exploration and movement variation.[21,22] Visual disturbance would blocked a child to receive visual stimulation which would affect reading ability.[23,24] Several studies found deficit in language development in preterm babies which was similar to our study.[25,26] Deficit in language development would rise the risk of learning difficulties at school age.[27] Deficits in all aspect of developmental domain showed a need for intervention program for whole development aspect of late preterm babies.

From other studies, GA and bodyweight are frequently used as predictor of cognitive outcome. GA would reflect brain maturation.[28] Head circumference is also frequently associated with brain volume and intelligence quotient (IQ). Few good studies showed that the relationship of head circumference as predictor for child IQ was significant if it was measured at 9 m.o but not at birth.[29,30].

We control factors other than GA which may associate with cognitive outcome by excluding babies with early neonatal complications, sign of sepsis, major congenital anomaly, traumatic delivery in head area, and small nor large for GA babies.[31-35] Other factors such as parent's education, caretaker and caretaker's education, the adequancy of income, child nutritional status, and babies' intake were controlled by analysis.

Our study added that delayed development could be detected as early as 3 months of age. However, the very short observational time in this study limits us to report the impact of GA to cognitive outcome at school age. In addition, we could not identify the etiology of prematurity which lead to inability to associate it with the cognitive outcome. Brain traumatic injury was assumed from mode of delivery and not by head ultrasonography because this kind of measurement was not routinely done in our setting. Our study also could not define the quality of stimulation that was already given at home for our subjects. The result of this study emphasized on risk of delayed development in late preterm babies. It would be better to make a longterm follow up to late preterm babies. We should advice the parents to do more warm and responsive caregiving for the late preterm babies, and to start stimulation immediately because this might affect cognitive outcome.[40]

We conclude that cognitive outcome of late preterm babies is delayed in all aspects of developmental domain compared to fullterm babies. A longterm evaluation of child developmental should have been started as soon as 3 months of age, which will give a benefit for the parents and the babies.

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