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Original Article

# Preterm and low birth weight as risk factors for infant delayed development

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## Abstract

***Background*** In developed countries, birth weight of less than 1,500 g contributes in infant delayed development. It might be different in developing countries.

***Objective*** This study aimed to determine whether preterm infants with birth weight of 1,500 to 2,499 g are risk factors for delayed development at 7-10 months of age.

***Methods*** We analyzed singleton infants at 7-10 months of corrected age, born with birth weight of 1,500 to 2,499 grams, preterm-appropriate for gestational age (or LBW group), and at 7-10 months of chronological age, born with birth weight >2,500 g-term-appropriate for gestational (non-LBW group) in a hospital-based retrospective cohort study. Data were taken from medical records in Hasan Sadikin Hospital, Bandung, from September 2003 to May 2004. We excluded infants with major congenital anomalies, hyaline membrane disease, assisted ventilation, or exchange transfusion. Multiple regression logistic analysis was performed for data analysis.

***Results*** The percentage of delayed development in LBW group was higher than in non-LBW group (17.1% vs. 1.6%). Logistic regression analysis revealed that low birth weight was a risk factor for delayed development (RR=5.13, 95%CI 1.55;16.96, P=0.007). Other biological risk factors for delayed development are hyperbilirubinemia (RR=3.32, 95%CI 1.29;8.54, P=0.013) and sepsis (RR=2.74, 95%CI 1.15;6.52, P=0.023).

***Conclusions*** Preterm-appropriate for gestational age with birth weight of 1,500 to 2,499 g are risk factors for infant delayed development after being adjusted to other biological risk factors. **[Paediatr Indones 2008;48:1-4]**.

***Keywords:*** *Preterm, low birth weight, appropriate for gestational age, delayed development, Bayley Infant Neurodevelopment of Screener (BINS)*

Birth weight and gestational age are critical factors in determining developmental outcomes. Low birth weight (LBW) and preterm infants have an increased risk for neurodevelopment disabilities; short gestational period and LBW correlate with greater risk level of neurological deficits. They are are also susceptible to organ injury because of premature organ functions.[1,2]

The incidence of LBW (birth weight <2,500 g) is quite high in developing countries;[3] the overall incidence of LBW in Indonesia is about 14%, i.e., 10.5% in rural and 20% in urban area.[4] In 2003, the LBW incidence in Hasan Sadikin General Hospital was 22.7% and the incidence of preterm infants was 12.3%.[5] The survival of babies born with low birth weight has been increasing; consequently many babies may have the risk for delayed development. Many studies published in developed countries explore the relationship between degrees of LBW and subsequent outcome, up to such infants reach the school age.[6] Such studies are scare in Indonesia.[7]

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Early identification and intervention may improve prognosis and reduce secondary disability. We need a screening tool for identifying delayed developmental process; without screening, 70% of developmental delayed children are not identified, but with a screening tool 70-80% are identified.[8] One of developmental screening tools used is BINS (*Bayley Infant Neuro-development of Screener)* that identifies the risks for delayed development in infants, born with biological risk factors. Our previous study on infants aged <7 months could not define that LBW as a risk factor for delayed development.[8] We aimed to determine whether preterm-appropriate for gestational age are risk factors for delayed development in infants at 7-10 months of age.

## Methods

This hospital based retrospective cohort study was carried out in Bandung, West Java. Study subjects were singleton infants at 7-10 months of corrected age, born with birth weight of 1,500 to 2,499 g, preterm-appropriate for gestational age (LBW group). For control we used 7-10 months of chronological age infants, born with birth weight of >2,500 g-term-appropriate for gestational (non-LBW group). Data were taken from medical records of Perinatology Division, Hasan Sadikin Hospital Bandung, from September 2003 to May 2004. Biological risk factors in prenatal and infancy periods were noted. We excluded subjects who had major congenital anomalies, hyaline membrane disease, assisted ventilation, or exchange transfusion.

We designed the study to evaluate the biological risks that theoretically associated with developmental delay, i.e., mother's obstetric history (mother's age, maternal medical history, parity, and obstetric history), history of delivery (spontaneous, cesarean section or others, maternal delivery complications), neonatal and infant's conditions (severe asphyxia, sepsis, hyper-bilirubinemia, frequent URTI, frequent diarrhea, anemia), and nutrition (exclusive breast-feeding). Sample size was determined using hypothesis testing for two proportions and risks for delayed development.

The BINS screening test was performed to determine risks for delayed development. Four conceptual areas of ability were assessed by the BINS, i.e.: 1) basic neurological functions, 2) receptive functions, 3) expressive functions, and 4) cognitive process. We classified the outcomes as dichotomous (high or low).

Bivariate and multivariate (logistic regression) analysis were performed. For all analyses, SPSS for Windows, Release 10.00 (SPSS Inc, Chicago, Illinois, USA) was used. This study had been approved by the Medical Ethics Committee of Hasan Sadikin General Hospital Bandung.

## Results

One hundred and eighty nine infants fulfilled the inclusion criteria. Among these infants, 37 were excluded bacause 2 (1.0%) out of them have died, 6 (3.1%) infants lived out of city, and 29 (15.3%) infants could not be located. The remaining 152 LBW infants had the mean birth weight of 2,082 (SD 275) g, and born at a mean gestational age of 34 (SD 1.4) weeks. Their mean of age when they were screened by BINS was 8.4 (SD 1.2) months. Seventy-two infants (47.4%) were screened at Child Growth and Developmental Clinic, and in the rest 80 (52.6%) infants the BINS was measured at home.

The control group included 522 infants born with weight of >2,500 g and gestational age of >37 weeks. Among these, at the age of 7-10 months three (0.1%) had died, 67 (12.8%) lived out of city, and 146 (27.8%) could not be located. The control group thus included 246 infants with a mean birth weight of 3,117 (SD 355) g, and born at a mean gestational age of 39 (SD 1) weeks. The mean age when this control group underwent BINS screening was 8.4 (SD 1.2) months. Sixty-eight infants (27.6%) were screened at Child Growth and Developmental Clinic and the rest 178 (72.4%) infants were screened at home. In total, 398 infants were included in the analysis consisted of 152 LBW and 246 non-LBW infants. The percentage of delayed develop-ment in LBW group was higher than that in non-LBW group (17.1% vs. 1.6%) (**Table 1**).

Univariate analysis revealed that the following variables were significantly associated with the high risk for delayed development: LBW, severe asphyxia, sepsis, hyperbilirubinaemia, non-exclusive breastfeed-ing, frequent diarrhea, and anemia. Biologically, the

predominant causes of delayed development were sepsis (p<0.001), hyperbilirubinaemia (p<0.001), LBW (p<0.001), severe asphyxia (p=0.012), anemia (p=0.022), non-exclusive breastfeeding (p=0.033), and frequent diarrhea (p=0.030).

In multivariate analysis, those 7 variables were included in the initial multivariable model using a backward elimination strategy. After final adjustment, only three variables were found to be independent predictors of high risk for delayed development, i.e., LBW (RR=5.13, 95%Cl 1.55;16.97, p=0.007), hyperbilirubinaemia (RR=3.32, 95%CI 1.29;8.54, p=0.013), and sepsis (RR=2.74, 95%CI 1.15;6.52, p=0.023). This means that that occurrence of infant delayed development in LBW group was approxi-mately 5 times higher than non-LBW group, 3 times higher in hyperbilirubinaemia in than non-hyperbi-lirubinaemia infants, and twice higher in sepsis infants than non-sepsis infants.

**Table 1.** Result of BINS measurement in LBW and non-LBW group

| Risks for delayed developmet | LBW group | | Non-LBW group | | P value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| High | 26 | 17.1 | 4 | 1.6 | |
| Moderate* | 19 | 12.5 | 6 | 2.4 | P=0.000 |
| Low* | 107 | 70.4 | 236 | 95.9 | |

*Note: moderate and low risk for delayed development in this study were enrolled as low risk group for delayed development

## Discussion

This study shows that low birth weight, hyperbilirubinemia, and sepsis, are contributing factors for infant delayed development at 7-10 months of age. Most studies in developed countries demonstrates that LBW is consistently associated with the risk for delayed development. The difference between this study and the previous studies is that we analyzed preterm-appropriate for gestational age infants with birth weight of 1,500 to 2,499 g and adjusted for covariates which evaluate the combine effects of more biological risk factors. The LBW infants had 5 times higher risk for delayed development than the non-LBW infants, supporting the results of previous studies which found that LBW infants had 2 to 5 times higher risk for delayed development than non-LBW. This is because the preterm infant was born during critical period of rapid fetal brain growth and maturation.[9-12]

Hyperbilirubinaemia, both increased levels of direct or indirect bilirubin, is a risk factor for delayed development.[2] Investigators have suggested that moderate hyperbilirubinaemia (13-20 mg/dL) may be associated with milder forms of central nervous system dysfunction and sequel, including the sensory motor function. Minor neurological dysfunction has been observed in such infants in the first year of life.[13,14]

In infants with sepsis, we had to be careful for the possibility of bacterial meningitis. Clinically, they are difficult to differentiate. In infants who survived, 40 to 50% could be having late complications, such as cerebral palsy, epilepsy, hearing impairment, or hydrocephalus.[15,16]

This study focused on LBW as a risk factor for delayed development. Other biological risk factors that theoretically associated with delayed developmental, seemed could not give significant results. It means we have to increase the sample size.

Developmental screening is a process of examining infants by a standardized procedure to identify if they need further assessment. One of the widely used standardized developmental screening tests is BINS. BINS is used to asses and identify the development process of infants aged 3 to 24 months, and this had been used to study hospitalized infants. The BINS has some advantages, i.e.,[17] 1) conceptual areas of ability are assessed: neurological functions, receptive functions, expressive functions, and cognitive processes, 2) direct examination, 3) takes only 10 to 15 minutes, 4) good test-retest and inter-rater reability, 5) 75-86% sensitivity and specificity, and 6) well-suited for a biologically at-risk population. Therefore, the BINS is a satisfactory screening tool for LBW infants when used in conjunction with biological risk factors

In analyzing the outcome of BINS develop-ment study, we divided developmental delay into 2 groups, i.e.[1] 1) high risk developmental delay, and 2) low risk developmental delay (included median and low risk). This approach looks consistent with previous studies. In particular, Aylward[17] had analyzed that this kind of categorization was better than the grouping as follow: 1) high risk develop-mental delay (included high and moderate risk), and 2) low risk developmental delay.

To sum up, the results of this study show that preterm-appropriate for gestational age with birth weight of 1,500 to 2,499 g is an independent risk factor for delayed development. This should draw our attention that early screening needs to be done to assess all infants with biological risk factors. Proper management is needed for high risk infants with examination to establish diagnosis, and finally intervention to improve the overall prognosis of the patients. It requires multidisciplinary approach involving area of neuropediatrics, growth and development, ear-nose-and throat, ophthalmology, psychiatry, medical rehabilitation, psychology departments, and other relevant area.

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