ORIGINAL ARTICLES

Developmental Delay in Moderately Preterm-Born Children with Low Socioeconomic Status: Risks Multiply

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Objective To assess separate and joint effects of low socioeconomic status (SES) and moderate prematurity on preschool developmental delay.

Study design Prospective cohort study with a community-based sample of preterm- and term-born children (Longitudinal Preterm Outcome Project). We assessed SES on the basis of education, occupation, and family income. The *Ages and Stages Questionnaire* was used to assess developmental delay at age 4 years. We determined scores for overall development, and domains fine motor, gross motor, communication, problem-solving, and personal-social of 926 moderately preterm-born (MP) (32-36 weeks gestation) and 544 term-born children. In multivariable logistic regression analyses, we used standardized values for SES and gestational age (GA).

Results Prevalence rates for overall developmental delay were 12.5%, 7.8%, and 5.6% in MP children with low, intermediate, and high SES, respectively, and 7.2%, 4.0%, and 2.8% in term-born children, respectively. The risk for overall developmental delay increased more with decreasing SES than with decreasing GA, but the difference was not statistically significant: OR (95% CI) for a 1 standard deviation decrease were: 1.62 (1.30-2.03) and 1.34 (1.05-1.69), respectively, after adjustment for sex, number of siblings, and maternal age. No interaction was found except for communication, showing that effects of SES and GA are mostly multiplicative.

Conclusions Low SES and moderate prematurity are separate risk factors with multiplicative effects on developmental delay. The double jeopardy of MP children with low SES needs special attention in pediatric care. *(J Pediatr 2013;163:1289-95)*.

Worldwide, 1 in 10 live births ends before 37 weeks of gestational age (GA).[1] Although children born at less than 32 weeks of gestation face the greatest risk of mortality and morbidity, more than 85% of preterm children are born beyond 32 weeks' of gestation.[2] Every week, therefore, that a child is born closer to term decreases the risk of mortality and morbidity,[3] but it increases the impact on public health because of the much larger number of children involved.[4]

In the long-term, moderately preterm-born (MP) children (32-36 weeks gestation) face significantly more developmental problems than term-born children (38-42 weeks gestation).[5-8] In MP children aged 4 years, the risk of developmental delay is twice the risk of term-born children and one-half the risk of very preterm children (<32 weeks gestation).[6] Huddy et al reported that up to one-third of MP children will have difficulties functioning at school.[7] Specifically fine motor skills and handwriting seem to be affected.[6,7-9]

Recent evidence indicated that differences in socioeconomic status (SES) may (partially) explain the association of moderate prematurity with developmental delay.[5,10] Additionally, low SES may further increase the effects of moderate prematurity on development. Nevertheless, the role of SES in the relationship between moderate prematurity and developmental delay is unclear. Our aim was to assess the separate and joint effects of moderate prematurity and low SES on developmental delay in early childhood.

Methods

Data for this study are from the Longitudinal Preterm Outcome Project (Lollipop), a large prospective cohort study designed to investigate growth, development, and general health of preterm-born children, with a special focus on MP children (32^0 to 35^6 weeks of gestation) in The Netherlands.[6] Lollipop

ASQ	*Ages and Stages Questionnaire*
GA	Gestational age
Lollipop	Longitudinal Preterm Outcome Project
MP	Moderately preterm-born
PCH	Preventive child healthcare
SES	Socioeconomic status

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consists of a community-based sample of preterm children and a random sample of term-born controls (38^0 to 41^6 weeks of gestation). At the time in which the study was designed, MP children concerned those children born at 32-35 weeks gestation and therefore children born at 36^0-36^6 weeks gestation were not included. Participants were recruited from 13 randomly selected preventive child healthcare (PCH) centers from across the country, covering urban and rural areas. Together, the 13 centers monitored 45 446 children (25% of all 4-year-old children monitored by Dutch PCH centers). In The Netherlands, 90%-95% of children are seen regularly and free of charge by PCH doctors for well-child care from birth up to 4 years.[11] PCH professionals monitor mental and physical development through structured interviews with parents, general physical examinations, and standardized screening procedures, all of which are documented in PCH files. Lollipop was approved by the local institutional review board, and written informed consent was obtained from all parents.

Each PCH center provided a sample of all preterm children born during a single year, either from January 2002-January 2003 or from June 2002-June 2003. Term-born children were sampled from the same PCH centers and belonged to the same age range as the preterm children. After the file of each second preterm child had been selected, the file of the next term-born child served as a control. In >95% of cases, GA was calculated by using the last date of menstruation, and confirmed by early ultrasound measurements. In The Netherlands, it is routine practice to assess GA with early ultrasound measurements between 10^0 and 12^6 weeks of gestation. Children were excluded if they had a congenital malformation or syndromes, if the GA could not be verified or was beyond the set range, or if families moved between sampling and inclusion. An overview of the sampling procedures of Lollipop previously was provided by Kerstjens et al.[6] In short, of the 1145 eligible MP children, 995 (86.9%) parents participated in the long-term follow-up part of the study and of the 674 eligible term-born children, 577 (85.6%) parents participated. Of all eligible children, response rates for the developmental questionnaire were 81.0% for MP children and 80.7% for term-born children. The total number of children in this study is 1470 (926 MP and 544 term-born children).

Assessment of SES

We determined SES on the basis of the 3 most frequently used measures: education, income, and occupation.[12,13] Data on the highest completed educational level of both parents were collected by a questionnaire when the children were 4 years old. The following categories were defined: primary school or less, low-level technical and vocational training (<12 years of education), high school or medium-level technical and vocational training (12-16 years of education), and university or high-level technical and vocational training (>16 years of education). Furthermore, parents were asked to give an indication of their net monthly household income in euros: ≤850 ($1087), 851-1150 ($1088-$1471), 1151-1750 ($1472-$2239), 1751-3050 ($2240-$3902), 3051-3500 ($3903-$4477), and >3500 ($4477). Data on occupational level were collected retrospectively from medical records kept by the PCH centers. We classified the occupational level of both parents according to the International Standard Classification of Occupations.[14] We assessed the composite SES score on the basis of five indicators: educational level of father, educational level of mother, family income, occupational level of father, and occupational level of mother. Information on each of the 5 indicators was available for 95%, 98%, 76%, 81%, and 71%, respectively, of the children participating in this study. We standardized each of the indicators and computed the mean per child of the indicators that were available for that child, resulting in one single SES score for each child. Then the SES scores were again standardized (ie, had a mean of 0 and a SD of 1).

Developmental Outcomes

Developmental outcomes were measured using the Dutch version of the 48-month form of the *Ages and Stages Questionnaire* (ASQ), which is a validated, parent-completed, developmental screening instrument.[15,16] We computed 5 developmental domains of the ASQ: fine motor, gross motor, communication, problem-solving, and personal-social skills.[16] Each domain consists of 6 questions on developmental milestones. For example, the domain communication problems consists of questions about the notion of categories, interpretation, meaning of objects, word conjugations, operating instructions, and the ability to form full sentences. Parents were asked to evaluate whether their child had achieved a milestone (yes, 10 points), had partly achieved a milestone (sometimes, 5 points), or had not yet achieved a milestone (no, 0 points). Furthermore, we computed the ASQ total score by taking the mean of the 5 domain scores. For the total score and the domains scores cut-offs for normal and abnormal scores were set at 2 SD below the mean score of the Dutch reference group.[15] In >95% of cases, the mother filled out the questionnaire.

Statistical Analyses

First, we assessed child and family characteristics across children with low, intermediate, and high SES. Second, we examined prevalence rates of ASQ scores in the abnormal range for term-born and MP children with low, intermediate, and high SES. Third, we performed univariate logistic regression analyses to assess the crude effect of SES and GA on developmental delay by using standardized scores for SES and GA, meaning that both have a mean of 0 and SD of 1. Finally, we assessed the effects of SES, GA, and the interaction between SES and GA on developmental delay in 3 consecutive multivariable logistic regression models. In the first model, we assessed separate effects of SES and GA, with mutual adjustment. Next, we assessed potentially synergistic effects of SES and GA by adding the SES*GA interaction (Model 2). In the final Model 3, we adjusted for the effect of potential confounders, which were identified on the basis of the literature and differences in background characteristics. We decided not to adjust for family composition and ethnicity of the mother to prevent over-adjustment for factors that