Communication Impairments in Early Term and Late Preterm Children: A Prospective Cohort Study following Children to Age 36 Months

Stene-Larsen, Kim; Brandlistuen, Ragnhild Eek; Lang, Astri M; Landolt, Markus A; Latal, Beatrice; Vollrath, Margarete E

Abstract: OBJECTIVE To investigate the risk of communication impairments at age 18 and 36 months in children born early term (gestational weeks 37-38) and late preterm (gestational weeks 34-36). STUDY DESIGN A total of 39 423 children and their mothers participated in the Norwegian Mother and Child Cohort Study. The sample included 7109 children (18%) born early term and 1673 (4.2%) born late preterm. Information on gestational age and prenatal and postnatal risk factors was obtained from the Medical Birth Registry of Norway. Information on communication impairments was assessed using standardized questionnaires filled out by the mothers. Stepwise logistic regression analysis was applied to explore the associations between early term/late preterm birth and communication impairments at age 18 and 36 months. RESULTS Compared with children born at term, children born early term and late preterm had an increased risk of communication impairments at age 18 and 36 months. In early term, the aOR was 1.27 (95% CI, 1.12-1.44) at 18 months for communication impairments and 1.22 (95% CI, 1.07-1.39) at 36 months for expressive language impairments. In late preterm, the aOR was 1.74 (95% CI, 1.41-2.14) at 18 months and 1.37 (95% CI, 1.09-1.73) at 36 months. CONCLUSION Not only children born late preterm, but also those born early term, are at increased risk for communication impairments. Given the large number of children potentially affected, this may result in significant health care costs.

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Study design A total of 39,423 children and their mothers participated in the Norwegian Mother and Child Cohort Study. The sample included 7,109 children (18%) born early term and 1,673 (4.2%) born late preterm. Information on gestational age and prenatal and postnatal risk factors was obtained from the Medical Birth Registry of Norway. Information on communication impairments was assessed using standardized questionnaires filled out by the mothers. Stepwise logistic regression analysis was applied to explore the associations between early term/late preterm birth and communication impairments at age 18 and 36 months.

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Conclusion Not only children born late preterm, but also those born early term, are at increased risk for communication impairments. Given the large number of children potentially affected, this may result in significant health care costs. (J Pediatr 2014;□:□-□).
This prospective study examines communication impairments in both children born late preterm and those born early term. The study follows children born late preterm or early term within a large epidemiologic cohort with repeated assessments measuring level and development of communication skills up to age 36 months. The large sample size of the study permits detection of small effects. We hypothesize that children born early term and late preterm are at increased risk for communication impairments at age 18 and 36 months.

Methods

This study is based on data from the Norwegian Mother and Child Cohort Study (MoBa), a prospective population-based pregnancy cohort study that sought to survey all pregnant women in Norway between 1999 and 2008 (http://www.fhi.no/morogbarn). Pregnant women attending more than 50 hospitals across Norway for their first prenatal ultrasound examination (which is offered without charge by the Norwegian Antenatal Healthcare system) were invited by letter (usually at gestational week 17-18). Of the invited women, 38.7% agreed to participate in the study. The cohort now includes roughly 109,000 children and 91,000 mothers. The mothers completed questionnaires at the 17th and 30th weeks of pregnancy and when their children were age 6, 18, and 36 months. The response rates in the mothers who consented to join the study were 95% at gestational week 17, 92% at gestational week 30, 87% at child age 6 months, 77% at child age 18 months, and 62% at child age 36 months. In addition, information on maternal age, duration of pregnancy, and prenatal and postnatal risk factors was retrieved from the Medical Birth Registry of Norway (MBRN). The study was approved by the Regional Committee for Medical Research Ethics in Norway.

The inclusion criteria for this study were a complete set of questionnaires from gestational week 17 (n = 101,624), child age 18 months (n = 64,970), and child age 36 months (n = 45,125). Of the 45,125 children who met the inclusion criteria, we excluded those with severe malformations or syndromes (n = 1,350), severe hearing deficits (n = 148), and cerebral palsy (n = 54). We also excluded children with gestation longer than 41 6/7 weeks or shorter than 33 6/7 weeks (n = 4,150). The final sample comprised 39,423 children, of whom 16,73 (4.2%) were born late preterm and 7,109 (18%) were born early term.

Measures

Predictors. Information on gestational age based on ultrasound examination was retrieved from the MBRN. In accordance with definitions suggested in the recent literature, for the purpose of the present study we chose to discriminate between early term birth (gestational age 37 0/7 weeks to 38 6/7 weeks) and term birth with a gestational age of 39 0/7 weeks to 41 6/7 weeks. Late preterm birth was defined as a gestational age of 34 0/7 weeks to 36 6/7 weeks.

Outcome Variables at Age 18 Months. Child communication impairments at age 18 months were measured using 3 specifically selected items from the Ages and Stages Questionnaire (ASQ). Two of these items assess receptive communication skills, and the other item assesses expressive communication skills. Typical items of the ASQ are: “Does your child say 8 or more words in addition to ‘mama’ and ‘dada’?” and “Without showing him first, does your child point to the correct picture when you say ‘show me the kitty’ or ask ‘where is the dog?’” (the child needs to identify only 1 picture correctly). The selection of items for the MoBa study was performed a priori by specialists in clinical and developmental psychology. Mothers were asked to find time to observe the child and rate the extent to which the child would typically show mastery of the skill in question, using the response categories “yes” (1), “very often” (2), “not yet” (3), and “I don’t know” (missing). To identify those children at risk for clinically significant communication impairments, we set a cutoff at 2 SD above the cohort mean, as suggested by Squires et al. To explore the reliability of the scale, we used a 2-parameter item response theory analysis. The average factor loading was 0.75, indicating high reliability.

Outcome Variables at Age 36 Months. Child communication impairments at age 36 months were assessed using 6 items from the ASQ measuring expressive (3 items) and receptive (3 items) communication skills. Typical items of the ASQ for this age are: “When you ask your child to point to her nose, eyes, hair, feet, ears, and so forth, does she correctly point to at least 7 body parts?” (she can point to parts of herself, you, or a doll), and “Without giving your child help by pointing or using gestures, ask him to ‘put the book on the table’ and ‘put the shoe under the chair.’ Does your child carry out both of these directions correctly?” Mothers were asked to rate the extent to which their child mastered the skill using the same response categories as on the ASQ at age 18 months. To identify the children at risk for clinically significant communication impairments, we set a cutoff of 2 SD above the cohort mean. To explore the reliability of the scale, we performed a 2-parameter item response theory analysis. The average factor loading was found to be 0.82, indicating high reliability.

Expressive language impairment at age 36 months was measured using the parent-based assessment of grammar abilities of Dale et al. This measure has been validated against scores on the Communication domain of the Vineland Adaptive Behavior Scale in a subsample of children with autism spectrum disorders in the MoBa study. The measure consists of 1 item with 6 alternate answer categories. Mothers are asked to select which category best describes how their child talks: (1) child is not yet talking; (2) child is talking, but not yet understandably; (3) child is talking in single-word utterances, such as “milk”; (4) child is talking in 2- to 3-word phrases, such as “Me got ball”; (5) child is talking in fairly complete sentences, such as “Can I go outside?”; and (6) child is talking in long and complicated sentences, such as “When I went to the park, I went on the swings.”
In line with previous recommendations,18 we dichotomized the Dale measure so that a score of ≥5 was coded 0 and a score of ≤4 was coded 1.

**Control Variables.** An index of prenatal risk was coded by counting the number of the following risk factors present in the child: maternal gestational diabetes, preeclampsia/HELLP syndrome (severe preeclampsia), multiple gestation, and small for gestational age (SGA) status. SGA was coded by combining the infant’s birth weight and gestational age according to established norms.19 Information on prenatal risk factors was retrieved from the MBRN.

Information on cesarean delivery (elective and emergency) was retrieved from the MBRN. In our analyses, only emergency cesarean delivery was included as a risk factor, because this mode of delivery is the factor most closely associated with an increased risk of complications.20 Emergency cesarean delivery was defined as procedures that needed to be done rapidly (within 8 hours) to protect the health of the mother or infant.

An index of postnatal risk was determined by counting the number of the following risk factors present in the child: 5-minute Apgar score ≤6, diagnosis of respiratory distress or intracranial bleeding, and use of mechanical ventilation after birth. Information on all postnatal risk factors was retrieved from the MBRN.

**Statistical Analyses**

SPSS version 20 (IBM, Armonk, New York) was used for all statistical analyses. Logistic regression analysis was applied to explore the association between early term/late preterm birth and communication impairments at age 18 and 36 months. Confounder adjustment was performed in 3 steps. We first adjusted for the prenatal risk factors only (M2), then for acute cesarean delivery (M3), and finally for the postnatal risk factors in addition to the prenatal risk factors and cesarean delivery (M4; Table I). For the majority of variables, the percentage of missing values was low (0.4%-2%); however, the percentage of missing values exceeded 5% for the variable maternal education. To substitute for the number of missing values in this variable, we performed a maximum likelihood imputation procedure using information from the highly correlated variables maternal and partner income.21

In the analyses presented herein, we restricted the confounders to the prenatal and postnatal variables for which we had information. However, to explore the impact of other confounders that potentially could influence a child’s communication development, such as child sex, maternal age, and maternal level of education, we also conducted analyses with these variables included in the regression equation. Furthermore, we adjusted for the children’s precise age in days when their mothers completed the questionnaire. For these specific analyses, we excluded children aged more than 6 months away from the target ages of 18 months (1%) or 36 months (0.8%). Finally, to evaluate the generalizability of our study cohort, we compared our sample with the cohort of women who did not return either the 18-month or 36-month questionnaire in terms of the variables maternal education, maternal age, child’s prenatal and postnatal risk factors, acute cesarean delivery, and child’s gestational age.

**Results**

Table II compares the children born early term/late preterm with those born at term on a range of background variables. In general, the early term and late preterm children differed from term children on most of the background variables; for example, a smaller proportion of mothers of children born early term and late preterm completed higher education (college or university degree) compared with mothers of children born at term (66% vs 69%), and the mothers of the late preterm children were slightly older than those of the term-born children (31 vs 30 years). In addition, the

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Table I. Logistic regression analysis showing ORs and 95% CIs for the associations among early term/late preterm birth, prenatal and postnatal risk factors, and child communication impairments at age 18 and 36 months

<table>
<thead>
<tr>
<th>Variables</th>
<th>Communication impairments at 18 mo</th>
<th>Communication impairments at 36 mo</th>
<th>Expressive language impairments at 36 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M1</td>
<td>M2</td>
<td>M3</td>
</tr>
<tr>
<td>Term early birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risks</td>
<td>Reference</td>
<td>1.27*</td>
<td>1.27*</td>
</tr>
<tr>
<td>Late preterm birth</td>
<td>(1.15-1.48)</td>
<td>(1.12-1.44)</td>
<td>(1.12-1.44)</td>
</tr>
<tr>
<td>Prenatal risk</td>
<td>2.04*</td>
<td>1.83†</td>
<td>1.78†</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>(1.67-2.48)</td>
<td>(1.49-2.24)</td>
<td>(1.45-2.19)</td>
</tr>
<tr>
<td>Postnatal risk</td>
<td>1.59*</td>
<td>1.34*</td>
<td>1.34*</td>
</tr>
<tr>
<td>Emergency cesarean delivery</td>
<td>(1.41-1.79)</td>
<td>(1.21-1.56)</td>
<td>(1.17-1.53)</td>
</tr>
<tr>
<td>Postnatal risk</td>
<td>1.56*</td>
<td>-</td>
<td>1.19</td>
</tr>
<tr>
<td>Postnatal risk</td>
<td>(1.34-1.82)</td>
<td>(0.99-1.44)</td>
<td>(0.98-1.42)</td>
</tr>
</tbody>
</table>

M1, unadjusted analysis; M2, adjusted for prenatal risk factors; M3, adjusted for prenatal risk factors and emergency cesarean; M4, adjusted for prenatal risk factors, emergency cesarean, and postnatal risk factors.

*P < .001.
†P < .01.
‡P < .05.
Table II. Characteristics of the sample (n = 39 423)

<table>
<thead>
<tr>
<th></th>
<th>Term (77.7%; n = 30 641)</th>
<th>Early term (18.0%; n = 7109)</th>
<th>Late preterm (4.2%; n = 1673)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age, wk, median (range)</strong></td>
<td>40 (39-42)</td>
<td>38 (37-38)</td>
<td>36 (34-36)</td>
<td></td>
</tr>
<tr>
<td><strong>Maternal age, y, median (range)</strong></td>
<td>30 (16-47)</td>
<td>30 (14-46)</td>
<td>31 (16-44)</td>
<td>.023</td>
</tr>
<tr>
<td><strong>Higher education (college/university degree), %</strong></td>
<td>68.9</td>
<td>66.4†</td>
<td>66.1†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Male sex, %</strong></td>
<td>50.4</td>
<td>48.6†</td>
<td>51.3</td>
<td>.017</td>
</tr>
<tr>
<td><strong>Cesarean delivery, %</strong></td>
<td>9.7</td>
<td>23.0</td>
<td>29.5</td>
<td></td>
</tr>
<tr>
<td><strong>Emergency delivery, %</strong></td>
<td>58.5</td>
<td>33.1</td>
<td>72.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>One or more prenatal risk factors, %</strong></td>
<td>6.6</td>
<td>13.1†</td>
<td>30.3†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Gestational diabetes, %</strong></td>
<td>0.6</td>
<td>1.3</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td><strong>Preeclampsia, %</strong></td>
<td>2.6</td>
<td>6.1</td>
<td>16.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>HELLP syndrome, %</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Multiple gestation, %</strong></td>
<td>0.4</td>
<td>3.4</td>
<td>12.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>SGA status, %</strong></td>
<td>3.4</td>
<td>3.5</td>
<td>8.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>One or more postnatal risk factors, %</strong></td>
<td>1.0</td>
<td>1.0</td>
<td>5.1†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>5-min Apagar score &lt;6, %</strong></td>
<td>0.8</td>
<td>0.6</td>
<td>1.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Respiratory distress, %</strong></td>
<td>0.1</td>
<td>0.4</td>
<td>3.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Intracranial bleeding, %</strong></td>
<td>0.1</td>
<td>0.0</td>
<td>0.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Mechanical ventilation, %</strong></td>
<td>0.1</td>
<td>0.1</td>
<td>0.6</td>
<td></td>
</tr>
</tbody>
</table>

*P values were calculated using the χ² test for categorical variables and ANOVA for continuous variables.
†Group differs from controls (term birth) as measured by the Bonferroni post hoc test or χ² test.
‡Because of potential conflict with other MoBa projects, the effects of cesarean delivery, emergency cesarean delivery, and the specific prenatal and postnatal risk factors are not shown, following MoBa guidelines for publication (http://www.fhi.no/dokumenter/9f36b3e70.pdf).

Table III. Proportion of children with communication impairments at age 18 and 36 months according to term, early term, and late preterm birth status

<table>
<thead>
<tr>
<th>Variables</th>
<th>Term (n = 30 641)</th>
<th>Early term (n = 7109)</th>
<th>Late preterm (n = 1673)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child ASQ at 18mo ≥ 2 SD, n (%)</td>
<td>1133 (3.7)</td>
<td>341 (4.8)†</td>
<td>122 (7.3)†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Child ASQ at 36mo ≥ 2 SD, n (%)</td>
<td>1470 (4.8)</td>
<td>412 (5.8)†</td>
<td>105 (6.3)†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Child DALE at 36mo ≥ 2 SD, n (%)</td>
<td>1103 (3.6)</td>
<td>319 (4.5)†</td>
<td>92 (5.5)†</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

DALE, the parent based assessment of grammar abilities by Dale et al.17
*Group differs from controls (term birth) as measured by the χ² test.

Table I presents the results of logistic regression analyses with both the unadjusted and adjusted associations of early term birth and late preterm birth with communication and language impairments at age 18 and 36 months. The results from the fully adjusted logistic regression analyses (M4) showed that compared with term-born children, in the children born early term, the odds of communication impairments were 27% higher at 18 months and 18% higher at 36 months. The late preterm-born children had 74% greater odds of communication impairments at 18 months but no significantly increased odds at age 36 months. In terms of expressive communication, the associations between early term and communication impairments and between late preterm and communication impairments were significant after controlling for risk factors (22% and 37% increased odds, respectively). Further details on the logistic regression analysis and the specific effects of including each control variable are provided in Table I.

We obtained similar results when including child sex, maternal age, and maternal educational level in the regression analysis. The mean age of the children at completion of the 18-month questionnaire was 561 days (ie, 14 days older than 18 months), with a range of 365-730 days. At completion of the 36-month questionnaire, the mean age was 1114 days (ie, 19 days older than 36 months), with a range of 920-1278 days. Including the child’s age at completion of the parent questionnaires in the fully adjusted regression analyses did not yield different results than those already presented.

The mothers who did not return the questionnaires at 18 or 36 months were slightly overrepresented in terms of prenatal risk factors in the child (9.9% vs 9.2%), acute cesarean delivery (8.2% vs 7.9%), and postnatal risk factors in the child (3.0% vs 2.0%), and fewer had obtained a higher...
education 60.7% vs 68.4%. There were no differences in terms of child’s gestational age status or maternal age.

**Discussion**

Our goal was to study the association between early term and late preterm birth and communication impairments in early childhood. In line with our hypothesis, we found that infants born early term or late preterm are at increased risk for communication impairments at age 18 and 36 months. We focused exclusively on communication impairments in early term and late preterm children. Our findings of impaired communication skills in these children are in line with previous studies reporting an increased risk of developmental problems in late preterm-born children.\(^2\) In terms of communication impairments, our findings differ from those reported by Baron et al,\(^10\) who did not find an increased risk of expressive or receptive communication impairments in children born late preterm. However, the sample of Baron et al comprised only 60 cases, which significantly limited that study’s statistical power to detect significant associations.

There could be several explanations for our findings. First, the linear association between the extent of developmental impairments and degree of prematurity\(^23,24\) is in line with the notion that the fetal brain develops continuously throughout all of gestation and remains vulnerable to interference (such as birth) before reaching a certain degree of maturity. Full cortical maturity might not be established by week 37 of gestation, as was previously assumed.\(^25\) This hypothesis is supported by findings showing higher rates of white matter brain injury in late preterm infants,\(^26\) and also by the increased risk of neurodevelopmental and cognitive impairments observed in these children.\(^24,27\) These findings suggest that the communication impairments seen in these children are not specific, but rather are part of a greater cerebral vulnerability.

Another possibility is that the association between early term or late preterm birth and communication impairments is related not to the duration of the pregnancy itself, but rather to an underlying medical condition causing both the early term/late preterm birth and the communication impairments. In other words, the relationship between early term or late preterm birth and communication impairments may be confounded by medical risk factors associated both with an earlier than normal delivery and with later neurologic impairment in the child. This hypothesis is weakened, however, by the fact that adjusting for the prenatal and postnatal risk factors only marginally decreased the OR between early term/late preterm and later communication impairments. The single exception to this pattern noted was the lack of a significant association between late preterm birth and child communication impairments at age 36 months in the adjusted models. Overall, the prenatal and postnatal risk factors appeared to be more important confounders in the association between prematurity and communication impairments in late preterm births than in early term births.

This finding is not surprising, given the greater severity and prevalence of both the prenatal and postnatal risk factors in the children born late preterm.

The present study has some limitations that should be kept in mind when interpreting our findings. First, the mothers participating in the MoBa study have higher educational attainment than the average mothers in the Norwegian population (69% vs 55%), and the size of the ethnic/linguistic cohorts are smaller than what is found in the general Norwegian population (7% vs 15%). The representativeness of the MoBa study has been thoroughly investigated,\(^25\) and some subpopulations, such as women younger than 25 years of age, women living alone, and smokers, were found to be underrepresented; however, the association between a list of exposure variables and a list of outcome variables was not biased when comparing the associations in the MoBa population with the same associations in all women giving birth in Norway, from information accessible through the MBRN. The degree of bias will depend on the variables of interest. Second, the study did not include a specific and direct test of communication abilities of the child, but rather was based on maternal ratings of the child on short versions of developmental scales. Clinical investigations are not feasible for a study of this size. Drawing subsamples from the entire cohort that are then submitted to in-depth clinical investigations of communication development could be an avenue for future research. On the other hand, mothers know their children best and are the only ones with the opportunity to observe the children every day in a range of different contexts.\(^15\) It also is important to keep in mind that the measures used in this study are screening tools, not diagnostic tools, for communication impairment. In addition, symptoms of communication impairments are often associated with several developmental disorders, including autism and attention-deficit hyperactivity disorder, about which we have no information. Considering our limited access to clinical data, we cannot rule out the possibility of insufficient adjustment of the prenatal and postnatal risk factors; for example, we had no information regarding intrauterine infections, such as chorioamnionitis, that potentially could explain both the early term/late preterm birth and the communication impairment in a child. Finally, it is important to keep in mind that the ORs presented in this article are point estimates, and the 95% CIs for some of the associations are relatively wide.

Health personnel should be aware of the increased risk of communication impairments in children born early term or late preterm. Roughly 30% of the children with problems at age 18 months continue to have problems at age 36 months, indicating long-lasting problems for a subgroup of children. Despite the moderate to small effect size of early term and late preterm birth on communication impairments, the large number of children born at these gestational ages represents a significant potential public health burden. If our findings can be replicated, procedures for screening children born early term for communication impairments could be of interest. Educating parents in providing optimal...
stimulation for language development could prove useful as well.29

We are grateful to all the families in Norway participating in this ongoing cohort study.

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