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Risk of developmental delay: Comparison of late preterm and full term Canadian infants at age 12 months

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ABSTRACT

Background: Late preterm ($34^{0/7}$ to $36^{6/7}$ weeks gestation) infants may experience developmental delays greater than those found in term (≥ $37^{0/7}$ weeks gestation) infants.
Aim: The aim of this study was to compare the risk of developmental delay between late preterm and full-term Canadian born infants at age 12 months, and to determine infant and maternal factors associated with risk of delay.
Methods: A descriptive comparative study was conducted from data available from the All Our Babies community-based, prospective, pregnancy cohort in Calgary, Alberta. Participants were a sample of mothers of 52 infants born late preterm and 156 randomly selected mothers of term infants, matched for infant sex; eligible infants were singleton births. Mothers completed a developmental screening tool, the Ages and Stages Questionnaire, version 3 (ASQ-3), when their infant was age 12 months. Corrected age (CA) was used for preterm infants.
Results: Both late preterm and term infants who required neonatal intensive care (NICU) were more likely to demonstrate risk of developmental delay. Compared to term infants, there was a trend for late preterm infants to be at risk of communication and gross motor delay at age 12 months CA that was attenuated to the null when adjustments were made for NICU admission and other covariates.
Conclusions: Infants born between 34 and 41 weeks who are admitted to NICU are at increased risk of developmental delay. Early identification of risk provides an opportunity for referral for developmental assessment and early intervention programming.

1. Introduction

Worldwide in 2010, 11.1% of live births were preterm (< $37^{0/7}$ weeks gestation), an estimated 14.9 million infants [1]. In Canada, 7.7% of live births were preterm [2]. Approximately 75% of preterm infants were born between $34^{0/7}$ to $36^{6/7}$ weeks gestation [3], or late preterm (LP) [4]. Based on recent reviews [5–9], LP infants have a greater risk of short- and longer-term morbidity as compared to their term counterparts (≥ $37^{0/7}$ weeks gestation). During the birth hospitalization, LP infants have greater risk of respiratory distress syndrome (relative risk [RR], 17.3), apnea (RR, 15.7), feeding difficulties (RR, 6.5), hypoglycemia (RR, 7.4), hyperbilirubinemia (RR, 2.8), sepsis (RR, 5.6), and intraventricular hemorrhage (RR, 4.9) [6], which are attributed to physiological immaturity [10]. These morbidities are associated with increased rates of admission to NICU [11], increased length of hospital stay [4,12] and re-hospitalization [4,13,14]. Compared to their full term counterparts, LP infants are suggested to be at increased risk of poorer longer-term outcomes [7,8,15,16]. Under the age of 6 years, evidence suggests that children born LP are at increased risk of developmental delay [17–19], cerebral palsy [20], and behavioral and emotional problems [21]. At school age, LP children are more likely to have poorer cognitive, language and mathematics scores [15,22], be enrolled in special education programs [23–25], and have cerebral palsy [26] and behavioral problems [15]. At school start, the risk of poor school achievement increased as gestational age decreased [25,27]. However, one recent review suggests that school age outcomes for these children may be more varied than previously believed [15]. A large USA study that followed 1298

Abbreviations: LP, late preterm; NICU, neonatal intensive care unit; ASQ-3, Ages and Stages Questionnaires 3rd edition; CA, corrected age.

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children ($n = 53$ LP) from birth to age 15 years found no significant differences between children born LP and full term on cognitive, achievement, social, behavioral, and emotional outcomes [21]. Similarly, in a retrospective USA cohort, there were no differences between children born LP ($n = 256$) versus full term ($n = 4419$) in the incidence of learning disabilities and attention deficit/hyperactivity disorder followed to age 19 years [28].

Despite what is known about the increased risk of potentially adverse outcomes during perinatal, preschool and school ages, there is limited research focused on the early development of LP infants up to 12 months of age in more contemporary cohorts. Studies that addressed development at this age present ambiguous results using prospective cohort [29] and comparison study designs [30–34]. Ambiguous results may be related to inconsistent use of corrected age (CA; chronological age minus the number of weeks born early). For example, studies that compared LP and term infants reported no developmental differences when using CA [30–32], but found significant differences [31,32] when using chronological age at 12 month assessment. Results were further limited by (1) heterogeneity of outcomes, (2) small sample sizes, (3) use of developmental screeners versus assessments, and (4) failure to control for covariates. When LP infants and very preterm infants (≤ 32 weeks) who required NICU admission were compared, no significant differences in developmental outcomes [34] were reported after controlling for co-morbidities and the risk of requiring developmental intervention at age 12 months was the same [33]. Yet, required NICU admission as a predictor of increased developmental risk for LP infants as compared to term or very preterm infants has not been fully investigated [7]. Also poorly understood are the factors and comorbidities associated with early developmental delay in LP infants. Further investigation of the early risks and predictors of developmental delay in LP infants is warranted to inform early intervention and improve outcomes.

The objectives of the current study were to compare the risk of developmental delay between LP and term Canadian infants at age 12 months, and to determine infant and maternal factors associated with risk of delay. The research questions were: (1) Compared to term infants, do LP infants have a greater risk of developmental delay as measured by the domains (Communication, Gross Motor, Fine Motor, Problem-Solving, and Personal-Social) on the Ages and Stages Questionnaires 3rd edition (ASQ-3) (35) at age 12 months CA? (2) Controlling for infant and maternal characteristics selected based on the literature, what is the association between LP birth status and risk of delay at age 12 months CA?

2. Methods

2.1. Participants

A descriptive comparative study design was used with data collected for the All Our Babies (AOB) community-based, prospective, pregnancy cohort [36]. Women in the AOB study were recruited between May 2008 and December 2010 at <25 weeks gestation in Calgary, Alberta. Eligible women were ≥ age 18 years, understood spoken and written English, and had a singleton pregnancy. The response rate was 85% (McDonald et al., 2013b). In the current study, the sample was 52 LP infants and 156 out of 1185 randomly selected term infants, matched 1:3 on infant sex, with mother-completed questionnaires at age 12 months CA ± 2 weeks. Exclusion criteria applied to both groups were: (1) infant born small for gestational age (< 10th percentile,) and/or with a genetic disorder or congenital anomaly, and (2) non-English speaking mother.

2.2. Procedures

Mothers completed mailed questionnaires at <25 weeks, between 34 and 36 weeks, and postnatal ages 4 and 12 months. Maternal demographic characteristics were collected at intake. For infants, the ASQ-3 was administered at 12 months (± 2 weeks) using CA for preterms and chronologic age for terms. The gestational age of LP infants was verified against health records. Term and LP infants were matched on sex because being a male has been associated with poorer developmental outcomes [37]. This study was approved by the Conjoint Health Research Ethics Board at the University of Calgary. Participants provided consent at enrolment.

2.3. Measures

2.3.1. Ages and Stages Questionnaire - Third Edition (ASQ-3) (35)

This parent-completed screening instrument for children aged 1 to 66 months has 30 age-appropriate items that address five developmental domains: communication, gross motor, fine motor, problem-solving, and personal-social. Each item describes a skill, ability, or behavior to which a parent responds "yes" (10 points), "sometimes" (5), or "not yet" (0). A score is calculated for each domain and categorized as: (1) above cut-off (typical development), (2) monitoring zone (score between one and two standard deviations below the mean), and (3) referral zone (score less than two standard deviations below the mean). Between 2% and 7% of children in the normative population of 18,572 American children scored in the referral zone. Families approximated American census proportional estimates for education, economic and ethnic diversity in the normative sample. The American normative sample is the best available evidence for North American comparisons given there is no Canadian normative sample. For preterm infants, ASQ developers recommend using CA up to 24 months. The ASQ-3 was written at a 5th grade level and takes 10 to 15 min to complete. Intra-parental agreement was 92% over a 2-week interval. Parent and trained examiners agreement was 93%. Cronbach's alphas across age intervals and developmental domains ranged from 0.51 to 0.87. The ASQ-3 has moderate to high agreement with delay classifications on the Battelle Developmental Inventory [38] and moderate agreement with the Bayley-III [39] in term and preterm infants. In the 2 to 12 month age band, sensitivity was 0.85 and specificity was 0.91 [35]. In addition to strong psychometric properties, the ASQ-3 screener was selected because of its ease of use, low cost, and widespread adoption within the local community.

2.4. Statistical analyses

Up to two missing values on a domain were replaced by the mean score for that infant [35]. Infants were classified in the monitoring/referral zone when they scored <1 standard deviation below the mean of the normative ASQ data in accordance with the user's manual [35]. Frequencies and percentages were used to describe maternal and infant demographic characteristics and birth outcomes. Sample characteristics were compared for LP versus term infants using Pearson's chi-square test (or Fisher's exact test when expected cell counts were <5). Bivariate associations between maternal and infant characteristics, including term status (LP versus term) and ASQ-3 domain classifications were conducted using Pearson's chi-square test (or Fisher's exact test when expected cell counts were <5) and unadjusted odds ratios (uOR) and 95% confidence intervals (CI).

Multivariable logistic regression was used to estimate adjusted differences in each ASQ-3 domain between LP and term infants (aOR). Co-linearity was evaluated prior to analysis and all correlations were deemed adequate. All multivariable models controlled for potential confounders identified in the literature including maternal education, method of delivery, NICU admission or non-admission, and breastfeeding status to allow comparison with other research studies [37], [40,41]. Matching on infant sex allowed for control of this confounding variable in the design stage. Significance was set at $p < 0.05$. Analyses were conducted with Statistical Package for Social Sciences (SPSS) – Version 22 (IBM Corp., Armonk, New York, USA).