Factors Associated With Readmission in Late-Preterm Infants: A Matched Case-Control Study

abstract

OBJECTIVE: The goal of this study was to evaluate risk factors for readmission among late-preterm (34–36 weeks’ gestation) infants in clinical practice.

METHODS: This was a retrospective, matched case-control study of late-preterm infants receiving care across 8 regional hospitals in 2009 in the United States. Those readmitted within 28 days of birth were matched to non-readmitted infants at a ratio of 1:3 according to birth hospital, birth month, and gestational age. Step-wise modeling with likelihood ratio tests were used to develop a multivariable logistic regression model. A subgroup analysis of hyperbilirubinemia readmissions was also performed.

RESULTS: Of 1861 late-preterm infants delivered during the study period, 67 (3.6%) were readmitted within 28 days of birth. These were matched to 201 control infants, for a final sample of 268 infants. In multivariable regression, each additional day in length of stay was associated with a significantly reduced odds ratio (OR) for readmission (0.57, \( P = .004 \)); however, for those infants delivered vaginally, there was no significant association between length of stay and readmission (adjusted OR: 1.08, \( P = .16 \)). A stronger inverse relationship was observed in subgroup analysis for hyperbilirubinemia readmissions, with the adjusted OR associated with increased length of stay 0.40 (\( P = .002 \)) for infants born by cesarean delivery but 1.14 (\( P = .27 \)) for those delivered vaginally.

CONCLUSIONS: Infants born via cesarean delivery with longer length of hospital stay have a decreased risk for readmission. As hospitals implement protocols to standardize length of stay, mode of delivery may be a useful factor to identify late-preterm infants at higher risk for readmission.

Late-preterm infants, defined as infants born at 34 to 36 weeks’ gestation,\(^1\) have an increased risk of morbidity and complications compared with term infants (born at \( \geq 37 \) weeks’ gestation).\(^2\)–\(^7\) Previous studies demonstrated that late-preterm infants may be up to 3 times more likely to be readmitted than term infants,\(^5\)–\(^9\) most commonly for hyperbilirubinemia, sepsis evaluation, and feeding difficulties,\(^1\)–\(^13\) with the overall readmission rate progressively increasing as gestational age decreases from 40 weeks.\(^14\) It is estimated that >250,000 late-preterm births occur in the United States each year.\(^15\) Given this contribution to neonatal hospitalizations and health care spending, as well as the significant variability in late-preterm readmissions attributed to lack of standardized care,\(^7\)–\(^16\) reduction of hospital readmission for this population represents an important area for potential improvements in hospital care quality.

Infant factors associated with increased readmission risk among late-preterm infants are well described and include being the first-born child, male gender, maternal
delivery complications, initial discharge from the normal newborn nursery rather than an ICU, breastfeeding, Asian/Pacific Island descent, and public insurance status. However, there is limited evidence to support models of discharge care that effectively mitigate this outcome. In fact, some evidence suggests that over time, readmission rates have increased for this population. One challenge to developing a standardized approach to discharge may be difficulty in appropriately identifying infants at highest risk for readmission in real time, before discharge. With birth weights often comparable to term infants, many late-preterm infants receive routine newborn hospital care postpartum and may not present with feeding inadequacy or other complications until after discharge. However, previous studies of both late-preterm and term infants have failed to demonstrate that longer length of stay actually reduces readmission risk. In addition, given that the most common indication for neonatal readmission, hyperbilirubinemia, generally develops after the first 2 days of life, any benefit from delaying hospital discharge on readmission risk may be differentially observed for this diagnosis compared with other indications for readmission.

The present study takes advantage of access to a regionally defined, population-based cohort of late-preterm readmitted and non-readmitted infants. Our objective was to evaluate risk factors for neonatal readmission, adjusting for variation in care across multiple hospitals, with the goal of informing more effective approaches for risk stratification in clinical practice.

METHODS
Setting and Study Population
The setting for this study was a regional, population-based clinical newborn service across 8 hospitals provided by the Cincinnati Children’s Hospital Medical Center Division of Neonatology. Providers serve all newborn infants requiring intensive care in greater Cincinnati and ~85% of all healthy infants born in the region. With >30,000 annual regional births, distributed across high- and low-volume academic and community hospitals, this service is one of the largest and most comprehensive programs of care for newborns in the United States managed by a single academic clinician group. Of the 8 hospitals included in our study, 5 incorporate Level I and II nurseries, 2 have Level I and IIIB nurseries, and 1 freestanding children’s hospital has a Level IIIC NICU.

The target population was late-preterm infants born January 1, 2009, to December 31, 2009, and admitted to 1 of these 8 area hospitals. All infants who met condition eligibility criteria (gestational age 34 0/7 through 36 6/7 weeks) were included for potential selection into the study sample. At the time this study was conducted, no institutional policy for late-preterm infant care had been implemented. Discharge decisions regarding length of stay, attained weight, or feeding criteria were at the treating physician’s discretion, and policies regarding criteria for Level II or Level III nursery admission varied according to each hospital.

Institutional human subjects review board approval was obtained from all participating study hospitals. The study was determined to pose minimal risk to the participants as a retrospective chart review.

Data Sources and Study Design
Data for this retrospective, matched case-control study were derived from maternal and infant birth hospitalization records as well as readmission records. First, all late-preterm infants readmitted within 28 days of birth (case subjects) were identified through manual chart review for each study hospital. A control population of non-readmitted late-preterm infants for each hospital was then chosen by using birth certificate data provided by the Ohio Department of Health. Cases were then matched to a sample of control infants who were not readmitted within 28 days. For each case infant, a pool of control infants matched on birth hospital and gestational age was defined. To account for seasonal variation in readmissions, control infants were also matched to case subjects based on month of birth. From this matched pool of controls, 3 control infants were selected for each case infant by using random number sequencing. In the situation in which there were not 3 control births in the relevant month, the month before or after was used.

Analytic Variables and Outcomes
For both case and control subjects, data were abstracted from maternal and infant hospital records. Variables were selected a priori based on their availability in the data sources and their potential relevance for readmission: birth hospital, maternal age, race, type of insurance, marital status, parity, infant gestational age at time of delivery, mode of delivery, pregnancy and delivery complications, maternal and infant blood type, infant gender, birth and discharge weight, Apgar scores, feeding method, performance of bilirubin screening, and length of hospital stay. Because bilirubin screening was not performed for all infants, and because in many cases the
transcutaneous bilirubin level was not documented in the medical record, we only assessed whether any screening was performed. For those readmitted infants, age and weight at readmission were also obtained. Indications for readmission were ascertained based on chart review and grouped into categories similar to those in previous studies (ie, hyperbilirubinemia, feeding difficulties, hypothermia, sepsis evaluation). Categories were not mutually exclusive, such that >1 category were assigned to some infants.

Data Analysis

Sample size determinations were based on the probability of exposure in the control subjects, assuming a fixed α level of 0.05, power of 80%, and an estimated correlation coefficient for exposures between case and control subjects of 0.2. First, data distributions were assessed by using means ± SDs and/or medians with ranges and interquartile ranges, frequencies, and proportions. Bivariate analyses were then conducted by using unadjusted (simple) conditional logistic regression, which tested for differences between the matched case and control subjects. Step-wise modeling with covariates deemed to be empirically or statistically important (P < .20) was used to develop a parsimonious multivariable conditional logistic regression model. Due to large observed differences in readmission according to mode of delivery, we made a decision to test the effect of an interaction term between mode of delivery and length of stay in the model; this finding was statistically significant (P < .05) and was retained in the final model. Finally, we conducted a subgroup analysis of control and case infants readmitted for hyperbilirubinemia only, as this diagnosis was associated with a shorter mean length of stay and younger mean age at readmission compared with other readmission diagnoses. The Akaike information criterion and -2 log-likelihood values were used to help assess the fitness of the model.

All statistical tests were 2-sided, and statistical significance was defined as P < .05. Analyses were performed by using SAS version 9.3 (SAS Institute, Inc, Cary, NC).

RESULTS

Of 1861 late-preterm infants delivered at 8 hospitals during the study period, 67 were readmitted within 28 days of birth, resulting in a late-preterm readmission rate of 3.6%. The percentage of infants readmitted varied 3.5-fold between hospitals, ranging from 2.0% to 6.9%. The majority of readmissions (75%) occurred due to hyperbilirubinemia, with 34% of readmissions categorized as relating to feeding problems, 12% as hypothermia, and 4% as suspected infection. The average age at readmission was 7.3 days; however, age varied according to infant’s readmission diagnosis. The mean age at readmission was the youngest (4.5 days) for those infants with hyperbilirubinemia, whereas the mean age at readmission for feeding problems, hypothermia, and suspected infection was 10.4, 9.3, and 13.0 days, respectively (Table 1). Matching all 67 readmitted infants to control infants at a ratio of 1:3 resulted in a final analytic sample size of 268 late-preterm infants.

Bivariate Analysis

There were no statistical differences between the case and control groups regarding birth weight, gender, or singleton versus multiple birth (Table 2). Bivariate comparisons demonstrated a statistically significant association between mode of delivery and readmission status, with readmitted infants more likely to be delivered vaginally compared with non-readmitted infants (75% vs 55%; P = .003). In bivariate analyses, feeding method also differed significantly according to readmission status, with 49% of non-readmitted infants versus 34% of readmitted infants receiving formula exclusively (P = .03).

Other significant differences according to readmission status included mean length of stay (P = .04) and performance of screening bilirubin (P = .009) before nursery discharge. In both groups, most mothers received prenatal care, were non-Hispanic white, multiparous, and had private insurance. There was no statistical difference between case and control subjects in maternal parity, admission status after delivery (NICU versus normal newborn nursery), or discharge weight.

Multivariate Analysis for all Readmissions

As stated earlier, an interaction term between delivery mode and length of stay was tested and was statistically significant.

<table>
<thead>
<tr>
<th>Indication for Readmission</th>
<th>Age at Initial Discharge</th>
<th>Age at Readmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperbilirubinemia, n = 50</td>
<td>2.4 ± 1.3</td>
<td>4.5 ± 2.2</td>
</tr>
<tr>
<td>Feeding difficulty, n = 23</td>
<td>5.5 ± 5.2</td>
<td>10.4 ± 8.1</td>
</tr>
<tr>
<td>Hypothermia, n = 8</td>
<td>6.3 ± 6.3</td>
<td>9.3 ± 7.3</td>
</tr>
<tr>
<td>Suspected infection, n = 16</td>
<td>5.3 ± 4.3</td>
<td>13.0 ± 7.4</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD in days. Diagnostic categories are not mutually exclusive.
Among vaginally delivered infants, the mean length of stay was 3.5 days, with a median of 2 days and a range of 1 to 37 days. Among those born via cesarean delivery, mean length of stay was 5.8 days, with a median of 3.5 days and a range of 0.5 to 26 days. The multivariable conditional logistic regression model derived through stepwise modeling is shown in Table 3 and included birth weight, bilirubin screening before discharge, admission to a NICU/special care nursery, and the interaction term between delivery mode and length of stay. Adjusting for all covariates, each additional day in length of stay was associated with a significantly reduced odds ratio (OR) for readmission (0.57 [95% confidence interval (CI): 0.39–0.84]); however, this association was only observed for infants born by cesarean delivery. For those delivered vaginally, there was no significant association between length of stay and readmission (adjusted OR: 1.08 [95% CI: 0.97–1.20]).

**Subanalysis for Hyperbilirubinemia**

Based on differences in length of stay and age at readmission for infants admitted for hyperbilirubinemia, a subgroup analysis was performed for 46...
Discharge age for cesarean delivery 0.57 0.39–0.84 .004
Discharge age for vaginal delivery 1.08 0.97–1.20 .16

Study design adjusts for matching characteristics of gestational age, birth hospital, and month of birth.

Table 3: Multivariable Conditional Logistic Regression Model for All Readmissions Within 28 Days, aOR, and 95% CIs (N = 268)

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant birth weight, g&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.07</td>
<td>0.995–1.16</td>
<td>.07</td>
</tr>
<tr>
<td>Discharge bilirubin data available</td>
<td>3.39</td>
<td>1.64–7.00</td>
<td>.001</td>
</tr>
<tr>
<td>Level II or III nursery care</td>
<td>2.52</td>
<td>1.03–6.17</td>
<td>.04</td>
</tr>
<tr>
<td>Age at discharge by mode of delivery&lt;sup&gt;b&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Discharge age for vaginal delivery</td>
<td>1.08</td>
<td>0.97–1.20</td>
<td>.16</td>
</tr>
<tr>
<td>Discharge age for cesarean delivery</td>
<td>0.57</td>
<td>0.39–0.84</td>
<td>.004</td>
</tr>
</tbody>
</table>

Study design adjusts for matching characteristics of gestational age, birth hospital, and month of birth.

Table 4: Multivariable Conditional Logistic Regression Model for Hyperbilirubinemia Readmissions, aOR, and 95% CIs (N = 46)

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant birth weight, g&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.19</td>
<td>1.02–1.40</td>
<td>.03</td>
</tr>
<tr>
<td>Bottle-fed only</td>
<td>0.27</td>
<td>0.08–0.86</td>
<td>.03</td>
</tr>
<tr>
<td>Discharge bilirubin data available</td>
<td>8.76</td>
<td>2.54–30.25</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age at discharge by mode of delivery&lt;sup&gt;b&lt;/sup&gt;</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Discharge age for vaginal delivery</td>
<td>1.14</td>
<td>0.90–1.45</td>
<td>.27</td>
</tr>
<tr>
<td>Discharge age for cesarean delivery</td>
<td>0.40</td>
<td>0.22–0.72</td>
<td>.002</td>
</tr>
</tbody>
</table>

Study design adjusts for matching characteristics of gestational age, birth hospital, and month of birth.

Table 3: Multivariable Conditional Logistic Regression Model for All Readmissions Within 28 Days, aOR, and 95% CIs (N = 268)

Table 4: Multivariable Conditional Logistic Regression Model for Hyperbilirubinemia Readmissions, aOR, and 95% CIs (N = 46)

Case infants with hyperbilirubinemia and their matched 138 control subjects. Four additional infants admitted for both infection and hyperbilirubinemia were omitted from this analysis. The multivariable conditional logistic regression model derived through stepwise modeling for this subgroup is shown in Table 4 and included birth weight, feeding method, bilirubin screening before discharge, and the interaction term between delivery mode and length of stay. As with the multivariable analysis results for the full sample, an association between increased length of stay and adjusted OR of readmission was only observed for infants born by cesarean delivery (adjusted OR: 0.40 [95% CI: 0.22–0.72]). For those delivered vaginally, there was no significant association between increasing length of stay and readmission (adjusted OR: 1.14 [95% CI: 0.90–1.45]).

**DISCUSSION**

Readmissions during the neonatal period account for >100 000 hospitalizations each year, and they are increasingly recognized as an outcome of importance to families, hospital, and payers. Late-preterm infants represent a population that is particularly at risk; in fact, recent evidence suggests that in the immediate weeks after discharge, they are perhaps even more vulnerable than infants born at earlier gestational ages due to a combination of immature physiology and lower intensity of hospital and follow-up services. Despite extensive previous literature demonstrating the increased risk of late-preterm infants for readmission, there remains limited evidence to guide the development of hospital-based approaches to discharge management for this population. Length of stay in particular has been evaluated for its potential effect on neonatal readmissions, with previous studies of both term and late-preterm infants failing to demonstrate any independent association with reduced readmission risk. Results from our current study using a population-based matched cohort demonstrate a significant modifying effect of delivery mode on the association between length of stay and readmission risk. Methodologic differences may explain some of the discrepancies with findings of previous studies (ie, time period of measurement for readmission, all late-preterm infants versus vaginally delivered only). However, given the high percentage of late-preterm infants affected by cesarean delivery, as well as the considerable variation in their length of stay, we felt that this population was important to include for analysis. We found that each additional day in length of stay was associated with a significantly reduced likelihood of late-preterm infant readmission but only for those delivered by cesarean delivery; no effect of length of stay was demonstrated for late-preterm infants delivered vaginally. Additional factors that were significantly associated with readmission included having a screening bilirubin test before discharge and admission to a Level II or Level III nursery (presumably an indicator of additional morbidity during hospitalization).

Our findings build on previous research demonstrating a reduced likelihood of readmission associated with cesarean versus vaginal delivery. Our detection of an interaction between length of stay and mode of delivery in this population may reflect an intersection of differential level of support (ie, increased nursing care) during hospitalization based on delivery mode and higher morbidity associated with...
need for cesarean delivery. Results were even more pronounced when stratified according to readmission for hyperbilirubinemia, likely due to timing of bilirubin peak levels as well as establishment of breastfeeding. The importance of early breastfeeding support for this population as a whole is suggested by previous studies finding that almost 90% of those infants admitted for hyperbilirubinemia are breastfed.7 Our finding that infants born by cesarean delivery may be particularly vulnerable to the effects of less hospital support is consistent with biological evidence that both maternal and fetal stress during labor and delivery are associated with impaired lactogenesis.25

The interaction of delivery mode and length of stay on neonatal readmission risk is particularly relevant given recent shifts in obstetric practice regarding elective cesarean deliveries.26 In response to rising late-preterm birth rates over the last 2 decades, as well as increased recognition of the morbidity and mortality associated with these infants, statewide initiatives such as the Ohio Perinatal Quality Collaborative have focused on decreasing the rates of scheduled deliveries before 39 weeks that lacked documentation of a medical or obstetric indication. Through such improvement efforts, the rate of scheduled cesarean deliveries and labor inductions before 39 weeks declined from 25% to <5% in Ohio between 2008 and 2009.27 Although this approach has been demonstrated to be effective in reducing the incidence of late-preterm births, a consequence of this change in practice may mean that late-preterm cesarean births represent a “sicker” population compared with previous years, with prenatal or intrapartum complications that warrant a longer period of observation in the hospital and thus a longer hospital stay. This finding may have important implications for routine postpartum care of late-preterm infants, as current consensus-based guidelines do not categorically differentiate recommendations for length of stay based on mode of delivery.28 As hospitals and provider networks develop and implement protocols to standardize late-preterm infant management with the goal of optimizing outcomes, mode of delivery may be a critical factor in appropriately risk stratifying these infants and determining their discharge timing.

Our study has several limitations, primarily related to sample size. Covariates in our multivariable regression models were purposefully constrained based on the relatively small number of readmissions. As a result, more detailed factors reflecting morbidity associated with the decision to deliver by cesarean delivery were not included in final analyses. However, admission to a Level II or Level III nursery was included in the adjusted model and was significantly associated with increased odds of readmission; this factor likely serves as a proxy for higher morbidity in the absence of other clinical measures. An additional limitation is potential misclassification of infants who were readmitted to a hospital not included in this study. However, we believe this possibility is unlikely due to the region-wide practice of readmission to our regional children’s hospital or birth hospital. Although information bias (ie, differences in documentation between readmitted and non-readmitted infants) could also have theoretically affected results, we believe this bias is unlikely given that all predictor variable data used in this study were recorded as part of routine charting for the initial hospital discharge, before any of the infants were eventually readmitted. Finally, another limitation may be generalizability of findings given the regional population represented.

However, the late-preterm readmission rate in our cohort is consistent with other population-based studies. Limitations are offset by the strengths of this study, which include our ability to account for substantial variation in readmission rates across multiple hospitals, our reliance on manual chart review rather than administrative data, and the strength and significance of the effect sizes demonstrated for our predictors of interest.

CONCLUSIONS
In this matched cohort study of late-preterm infants receiving care at 8 regional hospitals, we found that neonatal readmission risk is independently associated with shorter length of stay after cesarean delivery but not after vaginal delivery. This effect was shown for all readmissions in the first 28 days of life but was particularly compelling for readmissions related to hyperbilirubinemia. Future research on this topic may evaluate a more comprehensive set of potential confounding variables as well as validate our findings in other late-preterm infant populations.

REFERENCES
3. Bird TM, Bronstein JM, Hall RW, Lowery CL, Nugent R, Mays GP. Late preterm infants:
birth outcomes and health care utilization in the first year. *Pediatrics.* 2010;126(2). Available at: www.pediatrics.org/cgi/content/full/126/2/e311.


