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The Scope and Impact of Early and Late Preterm Infants Admitted to the PICU with Respiratory Illness

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Abstract

Objective—To determine the clinical course and outcomes of children born early preterm (EPT, <32 weeks), late preterm (LPT, 32–35 weeks), and full term (FT, ≥36 weeks) who were subsequently admitted to the pediatric intensive care unit (PICU) with respiratory illness.

Study design—Retrospective chart review of patients less than 2 years old admitted to a tertiary PICU with respiratory illness.

Results—271 patients met inclusion criteria: 17.3% were EPT, 12.2% were LPT, and 70.5% were FT. Lower respiratory tract infection was the most common diagnosis (55%) for all groups. Median PICU length of stay was longer for EPT (6.3 days) and LPT infants (7.1 days) compared with FT infants (3.7 days; $p < 0.03$ for both comparisons). EPT and LPT infants had longer hospital stays (median, 11.7 and 13.8 days, respectively) compared with FT infants (median, 7.1 days; $p < 0.03$ and $p = 0.004$, respectively). Median hospital charges were also greater for EPT (\$85,151) and LPT (\$83,576) groups compared with FT group (\$55,122; $p < 0.01$ and $p < 0.02$, respectively).

Conclusion—EPT and LPT infants comprise a considerable proportion of PICU admissions for respiratory illness and have greater resource utilization than FT infants.

Keywords

pediatric intensive care; preterm birth; respiratory illness; resource utilization

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Premature birth is associated with respiratory morbidities such as chronic lung disease (CLD) and a high risk for respiratory infections in the first years of life, which may lead to rehospitalization (1). Up to 50% of preterm infants with CLD are readmitted to the hospital during the first or second year of life, with respiratory disease as the most common reason for rehospitalization (2-4). Rehospitalization results in significant resource utilization, large financial burden, and increased stress for families who have already experienced infants' initial neonatal intensive care admission, especially if the rehospitalization involves admission to the pediatric intensive care unit (PICU). Although the rate of rehospitalization of preterm infants with CLD and their clinical course has been described, the impact of preterm infants admitted specifically to the PICU with respiratory disease has not been sufficiently evaluated. One study evaluating the impact of PICU admissions attributable to respiratory syncytial virus (RSV) infection found that 30% of the children admitted with RSV were preterm infants (5). Yet, there are limited data about the resource utilization and financial burden of premature infants admitted to the PICU with respiratory disease.

Previous studies evaluating rehospitalization of preterm infants have focused either on early preterm (EPT) infants (< 32 weeks' gestational age at birth) or on preterm infants with bronchopulmonary dysplasia (BPD). However, it is becoming increasingly evident that preterm infants born at later gestational ages and those early preterm infants without the diagnosis of BPD have increased morbidity and mortality compared with term infants (6-12). Because late preterm (LPT) infants (> 32 weeks' gestation age at birth) comprise 84% of all preterm deliveries (13), morbidities incurred by this group may require significant utilization of health resources.

Characterization of late morbidities incurred by preterm infants associated with admission to the PICU for respiratory illness may guide allocation of health service resources and the design and implementation of appropriate preventive strategies. Therefore, the aim of this study was to determine the proportion of children under the age of two admitted to the PICU with respiratory illness that were born preterm. To test the hypothesis that LPT infants consume PICU resources to a similar degree as EPT infants, we evaluated the differences in resource utilization and outcomes between children that were born EPT, LPT, and full term (FT).

Methods

After Institutional Review Board approval, we performed a retrospective chart analysis of all patients under the age of two admitted to a single institution tertiary 26 bed PICU for respiratory illness from January 2006 through December 2007. Our institution has a separate 16 bed cardiac intensive care unit, and patients admitted to that unit were not included in this study. Patients were identified from an admission database, and the medical records were subsequently reviewed to confirm the presence or absence of respiratory illness as the primary reason for the PICU admission. There were no exclusion criteria. The primary PICU admission diagnosis as assigned by the treating physicians was categorized into one of six types of respiratory illness: lower respiratory tract infection, non-infectious airway compromise, infectious airway compromise, non-infectious pulmonary disease, respiratory insufficiency, and pulmonary hypertension. Lower respiratory tract infection was defined as proven or suspected infection that affected structures of the lower airways and lungs including diagnoses such as bronchiolitis and pneumonia. Non-infectious airway compromise was defined as a non-infectious cause of upper or central airway obstruction such as anatomic airway anomaly or large foreign body aspiration. Infectious airway compromise was defined as proven or suspected infectious illness leading to upper or central airway obstruction such as croup or parapharyngeal abscess. Non-infectious pulmonary disease was defined as a primary lung disease that was non-infectious in nature, such as interstitial lung disease or hydrocarbon pneumonitis. Respiratory insufficiency was defined as a non-pulmonary condition that impaired effective ventilation, including

neurodegenerative disease, scoliosis, and excessive sedation. Finally, pulmonary hypertension was defined as elevated pulmonary artery pressure as determined by the treating physicians.

The following data were collected from the medical records: gestational age at birth, sex, chronologic age at PICU admission, chronic disabilities and non-pulmonary diseases, oxygen therapy and other respiratory support prior to admission and at hospital discharge, medications prior to admission and at hospital discharge, and organisms responsible for infectious illnesses. In addition, utilization of resources during the hospital stay were also recorded including length of mechanical ventilation during the PICU stay; echocardiograms, cultures, and radiological studies ordered; repeat admission to the PICU during the hospitalization; PICU and hospital lengths of stay (LOS); and total hospital charges. Patients were stratified into one of three groups by gestational age at birth: EPT (< 32 weeks' gestation), LPT (32 - 35 6/7 week's gestation), and FT ($\geq$ 36 weeks' gestation).

Statistical analysis

Group frequencies were tested using a Chi-square or Fisher exact test where necessary. Multivariate categorical data were analyzed using a weighted least squares approach in SAS Proc Catmod, using contrasts to test specific group differences. ANOVA was used to compare continuous variables between groups in the case of normal distributions and ANOVA was used on the ranks of the variables in the case of non-normal distributions, and contrasts were used to specific group differences. Poisson regression was employed to assess differences in counts, adjusted for hospital LOS. A level of significance was set at 0.05. All statistical analyses were performed using SAS v 9.1.3 (Cary, NC).

Results

During the two year period of this study, 2,336 patients were admitted to the PICU, of which 720 were less than 2 years old at the time of admission. Of these, 271 (38%) patients were identified as having an acute respiratory illness and were included in this study (Table I). Preterm infants (PT) comprised 80 (30%) of the 271 patients requiring PICU admission for respiratory disease. Of these, 47 (17%) were EPT and 33 (12%) were LPT. Males were significantly overrepresented in both the EPT and LPT groups compared with the FT group ($p < 0.05$). Prior to admission, a significantly greater proportion of EPT infants (70%) were receiving chronic oxygen therapy compared with LPT infants (42%; $p < 0.02$) and both EPT and LPT infants' oxygen use was greater than FT infants (11%; $p < 0.0001$). More EPT infants had an existing tracheostomy compared with FT infants (19% versus 2%; $p < 0.0001$) indicating that a greater proportion of preterm infants had chronic respiratory disease. In addition, more EPT and LPT infants had non-respiratory illnesses or chronic disabilities (45% for both groups), compared with FT infants (19%; $p < 0.02$).

Lower respiratory tract infection constituted the majority of admissions (55%) in all age groups (Table I). Noninfectious airway compromise was the second leading diagnosis affecting 21% of all patients. The admission diagnoses were not significantly different among the groups for most respiratory illnesses except EPT infants had significantly lower instances of infectious airway disease ($n = 0$; $p < 0.01$) and were the only group to have patients admitted primarily for pulmonary hypertension ($n = 4$; $p < 0.001$). RSV was the primary cause of lower respiratory tract infection in all three groups, responsible for 28%, 48%, and 45% in the EPT, LPT, and FT groups, respectively. There were no significant differences between the gestational age groups in these or other etiologic agents responsible for lower respiratory tract infection (Table II; available at www.jpeds.com).

Resource Utilization

Utilization of resources by each of the study groups is listed in Table III (available at www.jpeds.com). Fifty-nine percent of all patients required mechanical ventilation during their PICU stay, and this was not significantly different between the gestational age groups. Among patients requiring mechanical ventilation, the median ventilator days were 9, 10, and 5 days for EPT, LPT, and FT groups, respectively, $p = 0.13$. A greater proportion of EPT infants had at least one echocardiogram (47%) compared with FT (20%) infants ($p < 0.001$). We evaluated the number of respiratory cultures and viral studies ordered during the hospitalization, adjusting for LOS, and found no significant differences between the three groups. However, after adjusting for LOS, EPT infants had more non-respiratory cultures obtained compared with FT infants ($p = 0.03$). After adjusting for LOS, there were no significant differences in the number of specific radiological tests (e.g. chest X-ray, abdominal X-ray, head CT, etc.) or in the total number of radiological studies ordered between the groups (data not shown).

Median PICU LOS was longer for both EPT and LPT infants (6.3 and 7.1 days, respectively) compared with FT infants (3.7 days; Figure 1). The median hospital LOS for both EPT and LPT infants (11.7 and 13.8 days, respectively) were longer compared with FT infants (7.1 days). The median total hospital charges were also significantly greater in both the EPT and LPT groups compared with FT group (Figure 2). After adjusting for LOS, the difference in total hospital charges remained significant between LPT and FT groups ($p = 0.03$), but not between EPT and FT groups ($p = 0.09$).

Analyses of the measures were repeated controlling for preadmission oxygen use (Table I). Overall, infants without preadmission oxygen use had shorter median PICU LOS (3.8 days) and hospital LOS (7.2 days) compared with infants with preadmission oxygen use (7.2 days, $p < 0.0005$ and 15.4 days, $p < 0.0001$, respectively). Infants without preadmission oxygen use also had lower median hospital charges (\$56,808) compared with infants with preadmission oxygen use (\$116,504, $p < 0.001$). These findings were consistent in subgroup analysis for the EPT infants (PICU LOS $p = 0.05$, total hospital LOS $p < 0.002$, hospital charges $p < 0.005$) and FT infants (PICU LOS $p < 0.02$, total hospital LOS $p < 0.04$, hospital charges $p = 0.06$), but there were no significant differences between infants with and without preadmission oxygen use in the LPT group (PICU LOS $p = 0.38$, total hospital LOS $p = 0.61$, hospital charges $p = 0.80$). There were no significant differences in these measures between gestational age groups for patients with or without preadmission oxygen use.

We also evaluated these measures controlling for pre-existing non-respiratory illnesses/disabilities (Table I). Infants without pre-existing non-respiratory illnesses/disabilities had shorter median PICU LOS (3.7 days) and total hospital LOS (7.1 days) compared with infants with non-respiratory illnesses/disabilities (median PICU LOS = 6.5 days, $p < 0.0005$; median hospital LOS = 14.7 days, $p < 0.0001$). However, in sub-group analyses these differences were only significant for FT infants (PICU LOS $p = 0.0095$, total hospital LOS $p < 0.0003$). Furthermore, among patients without non-respiratory illnesses/disabilities, LPT infants had longer median PICU LOS (7.1 days) and hospital LOS (11.7 days), compared with FT infants (median PICU LOS = 3.5 days, $p < 0.02$; median hospital LOS = 6.9 days, $p < 0.05$) and EPT median LOS in the PICU (4.8 days) and the hospital (9.0 days) were not significantly different from either LPT or FT infants. Among infants that did have non-respiratory illnesses/disabilities prior to admission, no differences were identified in PICU or hospital LOS between gestational age groups.

Outcomes

Patient outcomes are listed in Table IV. There was no difference in hospital mortality between the three groups (4% of all patients). During the hospitalization, there was no difference

between the three groups in the number of patients requiring repeat admission to the PICU (12% of all patients). Discharge medications in following categories were evaluated: supplemental oxygen, bronchodilators, inhaled steroids, systemic steroids, diuretics, acid blockers, and antibiotics. After adjusting for pre-admission usage, we found significant differences between the groups for only 2 of these medications upon hospital discharge. LPT infants more often received new prescriptions for diuretics than both EPT and FT infants ($p < 0.01$), and EPT infants more often received new prescriptions for acid blocker therapy compared with both LPT and FT infants ($p < 0.01$).

Discussion

Preterm infants are at high risk for rehospitalization due to respiratory illness. We found that 30% of children under the age of two admitted to the PICU for respiratory diseases were born prematurely. Although a larger proportion of these infants were classified as early preterm (17%), late preterm infants also accounted for a significant proportion (12%) of admissions. Males were overrepresented in both the EPT and LPT groups compared with the FT group, which is similar to the sex disparity described for chronic lung disease of prematurity (14). Lower respiratory tract infection accounted for over 50% of admissions in all three groups, with RSV being the most common infectious organism. Preterm infants had longer PICU and hospital lengths of stay, utilized more hospital resources, and incurred higher total hospital charges compared with FT infants. Remarkably, LPT infants had similarly high lengths of stay and hospital charges as EPT infants, suggesting that resource utilization was similar between for EPT and LPT infants admitted to the PICU.

These findings are important because our data show that not only do children born preterm comprise a substantial proportion of admissions to the PICU for respiratory illness in the first years of life, but they consume considerably more hospital resources and incur more charges than full term infants. The fact that preterm infants represented almost one-third of respiratory admissions to our PICU is significant considering that in 2004, preterm infants accounted for 12.5% of all births (13). In addition, the proportion of preterm infants in this study represents an estimation of late morbidity rather than early morbidity because our institution frequently admits premature infants less than 44 weeks post-conceptional age back to the neonatal intensive care unit, and those infants were not included in this study. The fact that preterm infants are at high risk for rehospitalization has been well-reported in the literature (2,4) but few studies have examined the morbidity incurred once admitted, or the clinical course. It is notable that among the infants admitted to the PICU, LPT infants had similarly high morbidity as did EPT infants, which appears contrary to the commonly held assumption that LPT infants have a morbidity risk profile more closely approximate to that of FT infants. This information should be utilized for both preventive strategies and prognostication, and provides more evidence for labeling infants in this gestational age group as late preterm rather than near-term.

Recent studies have also found that LPT infants are a population at risk for increased morbidities, cost, and rehospitalization when compared with FT infants. Khashu et al reported that perinatal respiratory morbidity among LPT infants was 4.4 times greater than in FT infants and that infections were 5.2 times more common (9). Another study evaluating morbidity in the first year of life found that 15.2 % of LPT infants were rehospitalized compared with 7.9% of FT infants (15). Respiratory illness was the most common reason for rehospitalization among both groups. In addition, infants born 35 to 36 weeks' gestation were more likely than infants born ≥ 37 weeks' gestation to be rehospitalized 15 to 182 days after birth (8). Our data support the findings of these previous studies that the LPT population should be considered a group at considerable risk for future morbidities including rehospitalization and PICU admission, and should not be considered to have risk similar to that of FT infants.

Lower respiratory tract infection was the leading cause of admission in our study with relatively few PICU admissions in preterm infants attributed to infectious airway compromise compared with FT infants. One possible explanation for this finding is that infections causing airway compromise in these groups also caused lower respiratory tract infection, and patients were primarily labeled as such in the medical record. Previous studies have found that RSV is a common etiologic agent for lower respiratory tract infection and rehospitalization in preterm infants with chronic lung disease (16,17), and this was the case among the infants admitted to the PICU. Carbonell-Estrany et al found that 20% of infants born less than 32 weeks' gestation without defined chronic lung disease were rehospitalized for respiratory disease, with RSV being the causative agent in nearly 50% (17). Additionally, preterm infants were found to constitute 30% of PICU admissions for RSV (16% EPT, 14% LPT) in Israel (5). Because RSV is an important cause of rehospitalization and morbidity in EPT infants with or without CLD, RSV prophylaxis with palivizumab has been recommended for EPT infants and other infants with cardiac or chronic lung disease in an effort to reduce severe respiratory illness (18). Although our study suggests that LPT infants represent a significant proportion of infants admitted to the PICU with RSV and have similar morbidities to EPT infants once admitted, we do not have admission rate data for this group of infants in order to determine the cost-benefit ratio for providing palivizumab to LPT infants. McLaurin reported that RSV was the most common cause of admission among the 15.2% of LPT infants rehospitalized in the first year of life (15). Because morbidity is high for LPT infants who are admitted to the PICU with RSV, further studies evaluating risk factors for ICU admission in LPT infants should be performed to determine which of these infants might benefit from palivizumab prophylaxis.

These data suggest that the increased resource utilization and hospital charges, at least among LPT infants, are independent of LOS. Several areas of increased resource utilization among the PT infants were identified including increased length of ventilation (although this did not reach statistical significance), and increased orders for echocardiograms and non-respiratory cultures. The reasons for higher resource utilization in these groups may stem from the fact that many children in the EPT and LPT groups required significant medical support for both chronic respiratory and non-respiratory conditions prior to hospitalization. Greater surveillance of these special needs children including adherence to RSV prophylaxis, improved monitoring of oxygen requirement (both awake and asleep), nutritional status, and ensuring optimal home environments may help prevent late PICU admission, but requires further study. Among children without non-respiratory disorders, LPT infants had significantly greater LOS compared with FT infants which suggests that additional factors beyond these conditions influence morbidly risk. We speculate that some of these LPT infants may have had subtle health impairments that may have been under appreciated prior to rehospitalization. More specific identification of these risk factors for resource utilization after admission would allow more targeted intervention strategies for these groups.

There are several limitations to our study. First, there are inconsistent reports in the literature of the proper age definitions of early and late preterm infants. Although newer definitions of LPT infants have limited infants in this group to 34-36 weeks' gestational age birth, we chose to define early preterm as < 32 weeks' gestational age because this is the age group at greatest risk for chronic lung disease. However, we were unable to identify with certainty those infants who were diagnosed with BPD during their neonatal intensive care unit (NICU) admission because we did not have access to data from the NICU course for most patients. In addition, for many of the patients, gestational age at birth was obtained from the PICU admission history and physical, which may not be completely accurate. Due to the inconsistent recording of gestational age for infants ≥ 36 weeks' gestational age in the medical record, we chose to classify these infants as full term. Because FT infants represented a much higher proportion of study patients, there was greater power to detect differences between each of the preterm groups and the FT group than between the two preterm groups. Finally, children with non-respiratory

chronic disease accounted for a large proportion of PICU admissions (nearly 50% in EPT and LPT groups), which may be responsible for some of the morbidities seen in these groups. Unfortunately, further detail of these disabilities and their impact on morbidity risk could not be obtained as part of this study.

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List of Abbreviations

EPT	Early preterm
LPT	Late preterm
FT	Full term
PICU	Pediatric Intensive Care Unit
CLD	Chronic Lung Disease
RSV	Respiratory Syncytial Virus
BPD	Bronchopulmonary Dysplasia
LOS	Length of Stay
NICU	Neonatal Intensive Care Unit

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Figure 1.

Preterm infants had longer lengths of stay in the PICU and the hospital compared with full term infants. Length of stay in both the PICU and the hospital are displayed by gestational age at birth. Solid circles represent total hospital days, and open circles represent PICU days. Straight bars represent median values. Significant differences between the groups are shown with the p-values.

Figure 2.

Preterm infants incurred greater hospital charges than term infants. Hospital charges are displayed by gestational age at birth. Straight bars represent median values. Significant differences between the groups are shown with the p-values.

Table 1**Clinical Characteristics of Study Patients**

Gestational Age	Early Preterm	Late Preterm	Full term
Patients, n (%)	47 (17.3)	33 (12.2)	191 (70.5)
Gestational age at birth, weeks	27.2 ±2.3	34 ±1.1	≥36 weeks
Chronological age at admission, months	9.9 ±6.2	8.8 ±6.4	7.0 ±7.5
Sex, male/female	30 / 17*	23 / 10*	91 / 100
Status prior to admission	n (%)	n (%)	n (%)
Chronic oxygen therapy	33 (70.2) ^{§†}	14 (42.4) [§]	22 (11.5)
Tracheostomy	9 (19.1) ^{§†}	1 (3.0)	4 (2.1)
Nonrespiratory chronic disability/illness	21 (44.7) [‡]	15 (45.4)*	38 (19.9)
PICU Admission Diagnosis			
Lower Respiratory Tract Infection	25 (53.2)	23 (69.7)	100 (52.4)
Non-infectious Airway Compromise	11 (23.4)	6 (18.2)	40 (20.9)
Infectious Airway Compromise	0 (0) [‡]	2 (6.1)	30 (15.7)
Non-infectious Pulmonary Disease	3 (6.4)	1 (3.0)	15 (7.9)
Respiratory Insufficiency	4 (8.5)	1 (3.0)	6 (3.1)
Pulmonary Hypertension	4 (8.5) [§]	0 (0)	0 (0)

Values are mean ± SD unless otherwise noted.

* $P < 0.05$ compared to full term

[†] $P < 0.05$ compared to late preterm

[‡] $P < 0.01$ compared to full term

[§] $P < 0.001$ compared to full term.

Table 2

Etiology of Lower Respiratory Tract Infections

	Early	Late	Full Term	
	n (%)	n (%)	n (%)	<i>P</i>
Respiratory Syncytial Virus	7 (28)	11 (48)	45 (45)	NS
Culture Negative	8 (32)	4 (17)	23 (23)	NS
Moraxella Catarrhalis	2 (8)	2 (9)	11 (11)	NS
Haemophilus Influenza	1 (4)	3 (13)	7 (7)	NS
Human Metapneumovirus	1 (4)	3 (13)	5 (5)	NS
Influenza A virus	0 0	1 (4)	7 (7)	NS
Streptococcus Pneumoniae	0 0	1 (4)	7 (7)	NS
Parainfluenza	2 (8)	1 (4)	3 (3)	NS
Other	8 (32)	6 (26)	11 (11)	NS

Note: multiple organisms were recovered from some patients.

NS = not significant

Table 3

Utilization of Resources

	Early Preterm	Late Preterm	Full Term
Required Ventilation (%)	30 (64)	19 (58)	110 (58)
Multiple Intubations (%)	3 (6)	7 (21)	23 (12)
Ventilator days, median (range)	9 (1-40)	10 (1-23)	5 (1-211)
Patients Undergoing Echocardiogram (%)	22 (47) [‡]	9 (27)	39 (20)
Respiratory Cultures/Viral Studies Ordered, median (IQR) [*]	2 (0-4)	1 (1-2)	1 (0-2)
Nonrespiratory Cultures Ordered, median (IQR) [*]	1 (0-4) [‡]	1 (0-2)	1 (0-2)

IQR = intraquartile range.

^{*} Analysis adjusted for length of stay.

[‡] $P < 0.05$ compared to full term

[‡] $P < 0.001$ compared to full term.

Table 4

Outcome Data

	Early Preterm n (%)	Late Preterm n (%)	Full Term n (%)
Repeat ICU Admission During Hospitalization	5 (11)	7 (21)	19 (10)
Survived Hospitalization	45 (96)	31 (94)	184 (96)
Discharged on Oxygen	35 (74) [†]	18 (54) [*]	54 (28)
Newly Prescribed Oxygen at Discharge	4 (9)	8 (24)	38 (20)

* $P < 0.01$ compared to full term

[†] $P < 0.001$ compared to full term.