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ORIGINAL ARTICLE

Medical retrieval and needs of infants with bronchiolitis: An analysis by gestational age

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Aim: Viral bronchiolitis is the most common lower respiratory tract infection in children less than 12 months of age. Prematurity is an independent risk factor for disease severity. Many infected infants require hospitalisation and those living in regional centres frequently require transfer to metropolitan hospitals capable of providing assisted ventilation.

Method: We reviewed infants with bronchiolitis transported by the Victorian Newborn Emergency Transport Service between January 2003 and June 2007. We compared the clinical presentation and treatment required by infants born preterm with those of their term counterparts.

Results: Of the 192 infants transported, 92 were born preterm. Preterm infants were younger at time of transport (mean post-menstrual age 41 weeks vs. 45 weeks) and were more likely to require invasive ventilation (60% vs. 32%, $P < 0.001$) and to receive a fluid bolus (47% vs. 34%, $P = 0.04$) when compared with infants who had been born at term. Apnoea, either as a presenting symptom or in combination with respiratory distress, was more common in the preterm group (70% vs. 36%, $P < 0.001$).

Conclusion: Higher illness severity should be anticipated in ex-preterm infants who present with bronchiolitis. Preterm infants with bronchiolitis are more likely to require invasive ventilation and fluid resuscitation than term infants, suggesting the need for a lower threshold for referral and medical retrieval.

Key words: general paediatric; infectious disease; intensive care; neonatology; respiratory.

What is already known on this topic

1 Approximately 1–3% of infants who develop bronchiolitis require hospital admission.
2 Underlying conditions such as congenital heart disease and prematurity increase the likelihood of hospitalisation.
3 Prematurity is an independent risk factor for progression to severe disease.

What this paper adds

1 Preterm infants who develop bronchiolitis (even those without lung disease) are more likely to present with apnoea and to require any form of invasive respiratory support and fluid resuscitation when compared with infants born at term.
2 Preterm infants present with symptomatic bronchiolitis at an earlier "corrected age" than infants born at term.
3 A history of prematurity should prompt paediatricians, especially those in rural settings, to seek advice earlier in an infant's illness.

Bronchiolitis is a common lower respiratory tract infection of infants and is usually of viral origin. It is characterised by acute inflammation, oedema and necrosis of epithelial cells lining the small airways, increased mucous production and bronchospasm.[1] It is estimated that up to 90% of infections are caused by the respiratory syncytial virus (RSV) though many other viruses can cause infection including bocavirus, human metapneumovirus, adenovirus, influenza, parainfluenza, coronavirus and enterovirus.[2] Ninety per cent of children are infected with RSV in the first 2 years of life and up to 40% of these children will have lower respiratory infection.[1,3,4]

Severe bronchiolitis is defined by the American Academy of Pediatrics as 'signs and symptoms associated with poor feeding and respiratory distress characterised by tachypnoea, nasal flaring and hypoxemia'.[1] Epidemiological evidence shows that premature birth (less than 37 weeks) and young age (less than 6–12 weeks) at the start of the bronchiolitis season are associated with an increased risk of severe disease.[5–7] Underlying conditions that have been associated with an increased risk of progression to severe disease or mortality include haemodynamically significant congenital heart disease, chronic lung disease of prematurity and the immunocompromised infant.[5,8,9]

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Hospital admission rates for children with bronchiolitis vary between 1 and 3% and it is estimated that approximately 10% of hospitalised infants will require admission to intensive care.[10–12] About 10–15% of infants with chronic lung disease of prematurity are re-hospitalised with bronchiolitis, but 5–10% of all preterm infants (<35 weeks) without lung disease also require admission.[13] For infants who are admitted to intensive care and who require assisted ventilatory support, the mean duration of ventilation is also longer for infants with pre-existing disorders.[14] Although overall bronchiolitis-associated mortality remains low (1.82/100 000 for children in the United Kingdom[15]), mortality rates for ex-preterm infants, especially in association with RSV infection, can be considerably higher.[16]

The aim of this study was to compare preterm and term infants with bronchiolitis who were retrieved from regional Victorian hospitals with respect to their demographic characteristics at time of referral and treatment requirements during the retrieval process.

Methods

This retrospective cohort study used data collected on infants transported by Newborn Emergency Transport Service Victoria (NETS VIC), between January 2003 and July 2007. All infants with a clinical diagnosis of bronchiolitis recorded on the NETS database were eligible for inclusion. The Royal Women's Hospital Research and Research Ethics Committee confirmed that this study meets the Australian Health and Medical Research Council's requirements for quality assurance/audit projects.

Baseline demographic variables included sex, weight, prematurity (<37 weeks post-conceptional age), reason for referral (increased work of breathing/respiratory failure, apnoea or both) and the transport platform used. Clinical parameters included blood gas analysis at initial assessment, use of fluid boluses and inotropes, other drugs administered (methylxanthine or sedatives), transcutaneous carbon dioxide (Linde, Switzerland) and fraction of inspired oxygen (FiO_2) at the beginning and end of each retrieval. The use of RSV prophylaxis (palivizumab) was not obtainable as it is not routinely administered to all preterm infants in Victoria.

Data were entered into a Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA) and results were analysed using GraphPad QuickCalcs (GraphPad Software Inc., San Diego, CA, USA). Dichotomous outcomes were compared using two-tailed Fisher's exact test and continuous outcomes using unpaired Student's *t*-tests.

The NETS VIC is one of the largest providers of neonatal transport in Australia and serves a region of 5 million people covering 225 000 km^2. The retrieval team consists of a nurse with at least 2-year experience in a neonatal intensive care unit and training in retrieval medicine, and a senior registrar (usually training in either general paediatrics or neonatology) who has a minimum of 6 months neonatal intensive care experience and has passed the Royal Australasian College of Physicians Paediatric examinations. Approximately 1100 infants are transported each year as emergency retrievals. Transport by fixed and rotary wing aircraft accounts for 15% of transfers.

NETS VIC guidelines for management of bronchiolitis: NETS transfers infants up to approximately 6 months of age and under 6 kg at the time of referral. Assisted mechanical ventilatory support (continuous positive airway pressure (CPAP) or intermittent mandatory ventilation (IMV)) is generated by the Stefan Reanimator 120 ventilator (Stephen GMBH, Gackenbach, Germany) and is considered for any infant with (i) severe apnoea (requiring frequent stimulation), (ii) respiratory acidosis (pH < 7.25) or (iii) an oxygen requirement > 80% to maintain saturations > 93%. Blood gases are measured by either capillary or arterial samples using the i-STAT analyser (Abbot, Princeton, NJ, USA). The transport team consists of a neonatal transport nurse and transport fellow. All transports are triaged and supervised by consultant neonatologists on call exclusively for transport.

Results

Between January 2003 and July 2007, 192 infants with a clinical diagnosis of viral bronchiolitis were referred to NETS VIC for medical transport. One hundred of these infants had been born at term and 92 were preterm. Of the 92 infants born preterm, 43 (47%) were born at ≤32 weeks.

The majority of infants (80%) were transported by NETS road ambulance with 15% transferred by fixed wing aircraft and 5% by helicopter. Forty-six per cent of infants were transferred to a paediatric intensive care unit, 17% to a neonatal intensive care unit and the remainder to the emergency department for assessment and ongoing care.

Baseline demographic details of both groups are shown in Table 1. Infants born preterm were significantly younger (post-menstrual age) and weighed less at the time of referral when compared with term infants.

Clinical presentation at time of referral differed between the groups. Infants who were born preterm were more likely to

Table 1 Baseline demographics of preterm and term infants

	Preterm	Term	*P* value
Male : Female	48:44	55:45	NS
Median (IQR) gestation at birth	33 (24–36)	40 (37–42)	$P < 0.0001$
Mean age (SD) at referral	67 days (41)	38 days (29)	$P < 0.0001$
Median post-menstrual age at referral	41 weeks (35–55)	45 weeks (39–70)	$P < 0.0001$
Mean weight	3480 g (867)	4236 g (921)	$P < 0.0001$

IQR, interquartile range; NS, not significant; SD, standard deviation.

Table 2 Comparison of clinical presentation and respiratory parameters in preterm and term infants referred for retrieval

	Preterm, *n* (%)	Term, *n* (%)	*P* value
Clinical presentation			
RD	27	64	$P < 0.0001$ apnoea alone
Apnoea (alone)	16	10	or in combination with RD
RD and apnoea	49	26	
Frequency of apnoea in infants requiring invasive respiratory support (CPAP + IMV)	44/56	19/33	$P = 0.05$
Mode of respiratory support during retrieval			
Non-invasive support	36/92	68/100	$P < 0.0001$
Invasive (CPAP or IMV)	56/92	32/100	
FiO_2 at stabilisation (all infants)	0.57 (0.31)	0.54 (0.26)	$P = 0.58$
FiO_2 of infants needing assisted respiratory support (CPAP + IMV)	0.63 (0.31)	0.66 (0.27)	$P = 0.71$
FiO_2 of infants needing assisted respiratory support (IMV only)	0.75 (0.3)	0.67 (0.26)	$P = 0.46$
pH and pCO_2 of infants requiring invasive respiratory support (CPAP + IMV)			
pH mean	7.34 (0.12)	7.32 (0.08)	$P = 0.37$
pCO_2	52 (19)	56 (17)	$P = 0.47$
pH and pCO_2 of infants requiring IMV			
pH mean	7.36 (0.18)	7.29 (0.1)	$P = 0.26$
pCO_2	52 (27)	65 (20)	$P = 0.21$

CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen; IMV, intermittent mandatory ventilation; pCO_2, partial pressure of carbon dioxide; RD, respiratory distress.

Table 3 Comparing pH, pCO_2 and FiO_2 at stabilisation between infants needing assisted respiratory support (preterm and term infants) and those who did not

	No assisted ventilation (all infants)	Assisted ventilation (all infants)	*P* value
pH	7.33 (0.06)	7.33 (0.11)	$P = 0.99$
pCO_2	51 (10)	54 (18)	$P = 0.31$
FiO_2	0.42 (0.21)	0.64 (0.29)	$P < 0.0001$

All values are expressed as mean and standard deviation. FiO_2, fraction of inspired oxygen; pCO_2, partial pressure of carbon dioxide.

Table 4 Additional therapeutic and pharmacological interventions

	Preterm	Term	*P* value
Methylxanthines	44/92 (47%)	24/100 (27%)	$P = 0.004$
Cardiovascular support			
Mean blood pressure	63 (12) mmHg	65 (13) mmHg	NS
Fluid bolus	44/92 (47%)	34/100 (34%)	$P = 0.02$
Inotrope support	1/92	1/100	–
Proportion received antibiotics	63/92 (68%)	72/100 (72%)	0.63

–, inconclusive results; NS, not significant.

present with apnoea either alone or in combination with respiratory distress.

Preterm infants were significantly more likely to require any form of respiratory support (either CPAP or IMV) when compared with term infants. Among the preterm group, 35 infants (38%) were managed with CPAP and 21 (22%) with IMV. In the term group, 20 infants (20%) were managed with CPAP and 12 (12%) with IMV. Of the preterm infants requiring assisted ventilation, 25/56 (44%) were born between 24- and 32-week gestation. There were no differences seen in FiO_2, pH or partial pressure of carbon dioxide (pCO_2) between preterm and term infants who required assisted respiratory support (Table 2). For the study group as a whole, oxygen requirement at initial assessment appeared to best predict the need for assisted ventilatory support (Table 3).

In terms of additional treatment, more preterm infants received a fluid bolus and were treated with methylxanthines (aminophylline or caffeine) than their term counterparts. Most infants in both groups received antibiotic prophylaxis (Table 4).

Discussion

Increased illness severity among preterm infants who develop bronchiolitis following discharge from hospital is well described.[17] However, this is the first study of which we are aware comparing preterm and term infants with this condition who are referred for medical retrieval and their treatment requirements during that process. There are many factors that increase the risk of re-hospitalisation of preterm infants. Seasonal factors including time of discharge in relation to autumn and winter and physiological factors including the presence of pulmonary and neurological disability, as well as birthweight and young age at time of infection, all contribute to this increased risk.[17] Even in the absence of chronic lung disease, infants born preterm but at later gestation remain at increased risk of hospital re-admission.[18]

The need for assisted respiratory support (either CPAP or IMV) was greater in the preterm group. The main physiological difference seen among all infants requiring assisted support versus those who did not was their oxygen requirement at initial assessment. Within the group requiring assisted support, a large proportion of infants (56/89) were transported using CPAP. Non-invasive ventilation with CPAP has been used in paediatric and neonatal intensive care to manage patients with bronchiolitis since the 1970s.[19] There are many advantages to using non-invasive positive pressure ventilation in the management of bronchiolitis over endotracheal intubation. These include but are not limited to a reduced need for sedation and muscle relaxation, a reduction in ventilator-associated complications and trends towards reduction in supplemental oxygen therapy.[20]

The finding that apnoea was more common in premature infants is consistent with previous observational studies.[21] In fact, apnoea may be the first (and only) sign of the disease. The exact pathophysiology of bronchiolitis-related apnoea in infants remains unclear though immaturity of the respiratory control centre in the brain-stem is likely to play an important role. A further independent risk factor for the development of bronchiolitis-related apnoea includes young age at the time of infection.[22,23]

Preterm infants in this study were more likely to receive a fluid bolus. It is estimated that up to 30% of infants admitted to hospital with bronchiolitis will require fluid replacement therapy, the reasons for this include decreased oral intake and increased insensible losses through fever and increased respiratory rate.[24] For infants in this study, the stated reason for administering a fluid bolus in the majority of cases was decreased perfusion or prolonged capillary refill; however, this reason alone does not explain why more preterm infants in this cohort required fluid resuscitation. For infants requiring fluid replacement, consideration should be given to the potential complications of accidental water intoxication and electrolyte imbalances that may occur in association with this condition.[25]

Extrapulmonary manifestations may also occur in bronchiolitis caused by RSV infection. These include the following: endocrine abnormalities with increased production of anti-diuretic hormone; acute neurological signs such as depressed level of consciousness and seizures (due to inappropriate anti-diuretic hormone production and low sodium); and acute hepatitis and cardiac abnormalities including arrhythmias and hypotension (related to myocardial and/or hepatic infection and inflammation).[26–29] Previous studies have shown that hypotension associated with RSV infection frequently responds to fluid boluses with either crystalloid or colloid, followed by restricted maintenance fluids, and that inotropic support is less often required.[30]

Quite a high proportion of both preterm and term infants included for analysis were treated with antibiotics. This may be a result of antibiotics being commenced during initial management of infants who present with signs of systemic infection and then ceased when culture results are available. In general, when the diagnosis is clear and the infant does not have any coexisting morbidities, antibiotics are not considered useful in the management of bronchiolitis.[31,32] However, previous studies of infants admitted to paediatric intensive care units with severe disease have indicated that up to 40% of children may have secondary bacterial infection.[33] In this latter group, the ongoing use of antibiotics should be guided by surveillance of culture results, clinical condition and response to treatment.

We acknowledge that there are limitations to this study. Perhaps the most important of these is that the information collected and presented was retrospective in nature and relates to a brief period in the infant's illness. Subsequent course and follow-up data were not obtained. In addition, NETS retrieves infants who are less than 6 kg at the time of referral with bigger children retrieved by the Paediatric Emergency Transport Service based at the Royal Children's Hospital Melbourne and as such the cohort included in this study is selected on the basis of weight. As a result, some of the results may be skewed. It may be beneficial to review the older infants that Paediatric Emergency Transport Service retrieve to assess whether the same differences still exist in the ex-preterm infants who present at a later age and a greater weight.

Conclusion

In a cohort of infants with viral bronchiolitis who were referred for medical retrieval from regional to metropolitan hospitals, oxygen requirements in all infants predicted the need for assisted respiratory support. Infants born preterm were younger and lighter at the time of infection, were more likely to present with apnoea and were more likely to require invasive respiratory support and fluid resuscitation than infants born at term.

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