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Children hospitalized with respiratory syncytial virus infection in Saskatchewan pediatric tertiary care centers, 2002-2005

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Abstract: Objective To describe the epidemiology and severity of illness of children hospitalized with respiratory syncytial virus (RSV) infection, including those who received palivizumab prophylaxis, at Royal University Hospital (RUH), Saskatoon and Regina General Hospital (RGH) from July 2002 to June 2005. **Methods** Children hospitalized for ≥ 24 hours with laboratory-confirmed RSV infection were enrolled, and their health records were retrospectively reviewed for patient demographics and referral patterns, use of palivizumab prophylaxis, severity of infection (length of hospitalization, need for and duration of pediatric intensive care and mechanical ventilation) and outcome of infection. **Results** A total of 590 children (324 males) were hospitalized over the three years. The median chronological age at admission was 5.3 months, and median hospital stay was 4.0 days. Gestational age at birth was ≥ 36 weeks in 82.4% of patients. RSV disease severity was mild to moderate in 478 patients (81.0%) and severe in 110 (18.6%). Thirty-nine patients (6.6%) required pediatric intensive care unit admission, for a median of 5.0 days. Twenty-two of these patients (56%) were mechanically ventilated for a median of 6.0 days. Two children died, not attributed to RSV infection. Twenty-two patients had received palivizumab prophylaxis before hospital admission, with 18 completing at least 2 of the monthly doses. Most of these children (17/22) had mild to moderate illness. **Conclusions** RSV causes significant morbidity in Saskatchewan, affecting predominantly term infants. The majority of illness is mild to moderate. Some patients who have received palivizumab may still develop significant RSV disease.

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Key words: Respiratory syncytial virus; Palivizumab; Child

2002~2005 年期间萨斯喀彻温省儿科三级医疗中心因呼吸道合胞病毒感染住院的儿童病例分析

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中文概要：呼吸道合胞病毒（RSV）是 2 岁以下儿童呼吸道感染最常见的病原体，也是引起婴儿病毒感染所致死亡的主要原因。到目前为止，尚未见加拿大萨斯喀彻温省 RSV 流行病学的研究报道。本研究的目的是描述 2002 年 7 月至 2005 年 6 月期间在萨斯喀彻温省的两个儿科三级医疗中心，即皇家大学医院（RUH）和萨斯卡通和里贾纳总医院（RGH），因 RSV 感染住院的儿童的流行病学特点及疾病严重程度，其中部分患儿有帕利珠单抗（palivizumab）预防史。

在上述 2 个医疗中心住院时间≥ 24 h 的儿童（年龄：从出生到 16 岁 11 个月）经实验室病毒鉴定确诊为 RSV 感染的儿童纳入本研究。在 RUH 中心，患儿鼻咽部分泌物经直接荧光抗体（DFA）检测阳性者确诊为 RSV 感染。如果 DFA 为阴性，则对该标本进行病毒培养。在 RGH 中心，所有患儿鼻咽部分泌物标本均进行 DFA 检

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测和病毒培养。确诊后对患儿的健康记录进行回顾性分析，内容包括患儿的人口统计信息、转诊模式、帕利珠单抗预防史、感染严重程度及转归。目前尚无统一的感染严重程度的判断标准，本研究根据住院时间、是否需要小儿重症监护及持续时间、是否机械通气等进行评估。在研究期间，萨斯喀彻温省的帕利珠单抗预防的标准与加拿大儿科学会（CPS）的建议一致。

2002 年 7 月至 2005 年 6 月 3 年期间，总共有 590 名 RSV 儿童（包括 324 名男童）住院治疗，共 602 次住院记录，其中 12 名儿童住院 1 次以上。入院时患儿中位实足年龄为 5.3 个月，平均住院时间为 4.0 d（范围：<1 d 至 121.2 个月）。82.4%的患儿出生时胎龄≥ 36 周，7.5%为 33~35 周，9.5%≤ 32 周。RSV 感染住院情况呈现季节性模式，其中大部分发生在三月和六月。患儿最常见的临床表现为细支气管炎（70.2%），38.1%表现为肺炎，17.3%为上呼吸道感染，0.5%表现为哮吼（患儿可能同时有 1 个以上的临床表现）。478 例（81.0%）为 RSV 轻度至中度感染，110 例（18.6%）为重度感染。25.1% 的患儿有继发性细菌感染。共有 39 例（6.7%）需要入住儿科重症监护病房（PICU），中位入住时间为 5.0 d。其中，22 例重症患儿（56%）需要机械通气（通气时间中位数 6.0 d），14 例重症患儿（36%）有继发性细菌感染。与入住普通病房的患儿比较，PICU 患儿大多有如下情况：入院时年龄较小（P<0.01），有潜在的肺部疾病（P<0.01）或先天性心脏疾病（P=0.01），有两个或更多潜在的疾病（P<0.01），与其他儿童共同居住（P=0.02）。在本研究过程中，2 例儿童死亡，但均与 RSV 感染无关。

本研究有 22 例患儿在入院前接受过帕利珠单抗预防 RSV 感染，其中 18 例已完成至少 2 个月的剂量，17 例（77%）有 1 个或以上的慢性疾病，14 例（64%）出生时胎龄不超过 32 周。入院时中位实足年龄为 5.6 个月（范围 0~27.5 个月），中位住院时间为 9.5 d（范围 2~271 d）。大多数儿童（17/22）为轻度至中度 RSV 感染。

小结：RSV 在萨斯喀彻温省保持较高的发病率，男性、实足年龄小于 1 岁的足月儿或晚期早产儿发病率较高。细支气管炎是最常见的临床表现。大多数患儿呈轻度至中度感染，但约 7%的患儿需要重症监护。较小的实足年龄、潜在的肺部或心脏疾病或多个潜在疾病等因素均有可能导致患儿需要重症监护。此外，与其他孩子同住也有可能是导致患儿需要重症监护的一个因素。需要重症监护的患儿往往胎龄大于 35 周。虽然部分接受过帕利珠单抗预防的患儿也感染了 RSV，但是其大部分患儿的病情为轻度至中度。这些曾接受过帕利珠单抗预防的患儿更可能有潜在疾病，并且出生时胎龄往往小于 32 周。在本研究中，无一例因 RSV 感染而引起的死亡病例。本研究尚浅，需要开展更深入的研究，以进一步确定 RSV 患儿，特别是 PICU 患儿以及曾接受过帕利珠单抗预防却仍然受到 RSV 感染的患儿的特征。

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［关键词］ 呼吸道合胞病毒；帕利珠单抗；儿童

Introduction

Respiratory syncytial virus (RSV) is the most common cause of respiratory tract infection in children under age 2 worldwide[1], with 90% of children infected by their second birthday[2]. Up to 40% of these children will have an acute lower respiratory tract infection (LRTI)[3]. In Canada, RSV is responsible for many of the 12 000 hospitalizations annually for bronchiolitis in children under the age of two[4]. RSV is still a leading viral cause of death in infants[5]. In the United States, RSV is responsible for 100-500 deaths each year, with most of them being in children under one year-of-age[6]. Nair et al[5] estimate that 66 000-199 000 children under age 5 died from RSV associated LRTIs worldwide in 2005. Health care spending for RSV related hospital admissions in Canada is $18 million (US) annually[7].

Premature infants <35 weeks gestation and those with chronic lung disease or hemodynamically significant congenital heart disease are at the highest risk of morbidity and mortality from RSV[1,8]. Infants with chronic lung disease related to prematurity have high rates of hospitalization for LRTI, and have increased vulnerability to severe RSV disease[9]. High risk groups, including the above and those with other comorbid conditions such as neurologic impairment, are at higher risk of death during RSV hospitalization[10]. In Canada, infants in remote and northern communities and those of aboriginal descent are thought to be at increased risk for RSV[11]. Palivizumab, a humanized monoclonal RSV antibody, has been shown to be well tolerated and to decrease the risk of RSV-related hospitalizations in high risk children, including premature infants up to 35 weeks gestation at birth[12-13].

There have been no studies reviewing the epidemiology of RSV infection and its burden to

society in Canada within a defined population and over a specific time period. Further, there is very little information on those infants who contract RSV disease after prophylaxis. The purpose of this study was to describe the epidemiology of children hospitalized due to RSV in the province of Saskatchewan, with a population of one million, as well as determine the severity of RSV infection in those who required hospitalization despite palivizumab prophylaxis.

Materials and methods

Patients

The Canadian Paediatric Society (CPS) recommends palivizumab for children <24 months of age with chronic lung disease (CLD) of prematurity who require ongoing medical therapy within the six months preceding the RSV season, and children <24 months of age with hemodynamically significant heart disease. For preterm infants, the CPS recommended palivizumab to infants born at <32 weeks (rather than <35 weeks) gestation who are <6 months old at the start of the RSV season (includes those with or without CLD), and included children born at <36 weeks gestation who reside in northern or rural remote communities and Inuit infants if they are <6 months of age at the beginning of RSV season[8]. These CPS recommendations were implemented and received funding from Saskatchewan Health between 1999 and 2005.

This study included all children (from birth to 16 years and 11 months) hospitalized with known RSV infection for greater than 24 hours at the only two tertiary pediatric care centers in the province of Saskatchewan, Royal University Hospital (RUH) in Saskatoon, and Regina General Hospital (RGH) in Regina, during the study period (July 2002 to June 2005). These two tertiary pediatric centers serve the entire province, with a population of approximately 970 000 during the study period[14]. Patients were identified using virology records. For patients admitted at RUH, RSV was deemed to be present if there was a positive Direct Fluorescent Antibody (DFA, SimulFluor RSV/Flu A Kit, Millipore, Billerica, MA) result performed on a nasopharyngeal aspirate (NPA). Viral culture was only performed on DFA negative specimens in Saskatoon. For patients admitted at RGH, RSV was deemed to be present if there was a positive DFA (SimulFluor Respiratory Screen) and/or viral culture (HEp-2 cells) for RSV performed on nasopharyngeal swabs (nylon-flocked tips, microRheologics, Copan Diagnostics, Corona, CA) at the provincial Laboratory.

Once patients were identified, hospital records were retrospectively reviewed for the following demographic criteria: gender, ethnicity, and residence/community. Past medical history was noted for: chronological age at admission, gestational age at birth, presence of underlying medical conditions, need for home oxygen prior to admission, and whether the patient has received palivizumab prophylaxis prior to admission. The course in hospital was reviewed for: mode of transportation to hospital, type and severity of RSV infection, total duration of hospital admission, need for and duration of pediatric intensive care, need for and duration of intubation and mechanical ventilation, secondary bacterial infections, and outcomes, including RSV related deaths.

As there were no available case definitions measuring severity of RSV disease requiring hospitalization, we developed our own. Mild illness was defined as no change in oxygen requirement, hospitalized for <48 hours and no secondary complications. Moderate illness included those who were hospitalized for 2-6 days, had increased oxygen requirement for at least 12-24 hours (based on an oxygen saturation less than 92% in room air), and no more than 5% dehydration (still able to feed, but may have some vomiting or diarrhea). Severe illness was defined as those with respiratory distress requiring PICU admission, and/or intubation and ventilation, complications such as pneumothorax, secondary bacterial infection (pneumonia, pleural effusion, sepsis) requiring antibiotic treatment, a total hospital

duration (including PICU) of 7 days or more, or death. Secondary bacterial infection was defined as having a positive blood, NPA, or sputum culture.

Eligibility criteria for palivizumab prophylaxis in Saskatchewan during the study period were consistent with the recommendations of the CPS, first published in 1999[15-16]. From 2004 on, the CPS further recommended that children < 2 years of age with hemodynamically significant cyanotic or acyanotic congenital heart disease (requiring corrective surgery or on cardiac medication for hemodynamic considerations) also receive palivizumab prophylaxis.

The study was approved by the Biomedical Ethics Research Board for the University of Saskatchewan.

Statistical analyses

Descriptive statistics (i.e. proportions, medians) were obtained using SPSS 17.0. Since patients admitted at RUH and RGH were similar, we combined data from the two centers for analysis. The Mann-Whitney test was applied for comparing medians and for categorical data, the Pearson Chi-Square statistic was used to test associations and Fisher's exact test if expected cell frequencies were less than five.

Results

A total of 590 children (324 males) accounted for 602 hospital admissions for RSV infection over the 3 years, with twelve children having two hospitalizations each. The characteristics of these patients are summarized in Table 1. Three-hundred and twelve children (53.2%) were hospitalized at RGH and 278 children (47.1%) at RUH. Thirty-six (6.1%) patients required transportation by air ambulance to the tertiary care center, while 97 (16.4%) required ground ambulance transport. The median chronological age at admission was 5.3 months (range <1 day-121.2 months). The gestational age at birth was ≥ 36 weeks in 82.4%, 33-35 weeks in 7.5%, and ≤ 32 weeks in 9.5% of patients.

The distribution of cases throughout the months based on date of RSV positive test can be seen in Figure 1. RSV cases followed a seasonal pattern, with the majority of cases occurring in the winter months. In 2004, the RSV season was slightly delayed, with more cases occurring from March to June.

Table 1 Demographics and patterns of referral for 590 subjects

Characteristics	*n* (%)
Male	324(54.9)
Year (season) admitted	
July 1 2002 – June 2003	234(39.7)
July 1 2003 – June 2004	155(26.3)
July 1 2004 – June 2005	201(34.1)
Hospital	
Regina General Hospital	312(53.2)
Saskatoon Royal University	278(47.1)
Patient residence*	
Local health region (SHR or RQHR)	354(60.0)
Other health region	235(39.8)
Transport to tertiary care centre*	
Air ambulance	36(6.1)
Ground ambulance	97(16.4)
Used own transportation	437(74.1)
Gestational age at birth*	
≤ 29 weeks	42(7.1)
30-32 weeks	14(2.4)
33-35 weeks	44(7.5)
≥36 weeks	486(82.4)
Chronological age at admission	5.3 months(<1 day-121.2 months)#

Note: SHR: Saskatoon Health Region; RQHR: Regina-Qu'Appelle Health Region. #Chronological age at admission is expressed as "median (range)". *Some data is missing and only available data are reported.

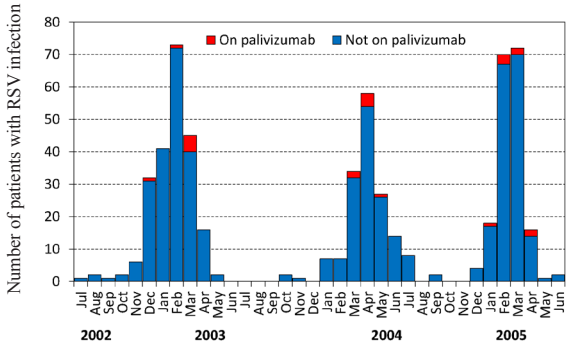

Figure 1 Children hospitalized with RSV infection at Royal University Hospital and Regina General Hospital, Saskatchewan-2002-05

Clinical characteristics of patients

Clinical presentation at time of hospitalization included bronchiolitis (70.2%), pneumonia (38.1%), upper respiratory infection (URI) (17.3%) and croup (0.5%) (Table 2, patients may have more than one clinical presentation). Infections were classified as mild to moderate in 478 patients (81.0%), while 110 (18.6%) were considered severe. The median duration of hospitalization was 4 days (range 2-367 days). The vast majority of patients, 548 (92.9%), required general pediatric ward stay only, with 39 (6.6%) requiring PICU care. Nineteen patients (3.2%) required mechanical ventilation. Twenty-five percent of patients had a secondary bacterial infection. No deaths were attributed to RSV infection. Although the majority of the patients had infections that had resolved or were improving from the infection at hospital discharge, 36 patients (6.1%) required prolonged hospitalization, all for non-RSV related reasons.

Table 2 Clinical data and hospital care for 590 subjects

Characteristics	*n* (%)
Clinical presentation(may have >1 condition)	
Cold	102(17.3)
Bronchiolitis	414(70.2)
Croup	3(0.5)
Pneumonia	225(38.1)
Severity of RSV infection*	
Mild	122(20.7)
Moderate	356(60.3)
Severe	110(18.6)
Secondary bacterial infection	148(25.1)
Received ≥1 dose palivizumab prophylaxis	22(3.7)
On home oxygen before admission	7(1.2)
Required general pediatric ward stay only*	548(92.9)
Required PICU care*	39(6.6)
Required intubation/ventilation	19(3.2)
Median stay in PICU (days)	4.0#
Median ventilation (days)	6.0#
Duration of hospitalization	
Median (days)	4.0#
Range (days)	2-367#
Clinical outcome at discharge	
Infection clinically resolved	121(20.5)
Infection improved	422(71.5)
Extended hospital stay (not attributed to RSV)	36(6.1)
Death (not attributed to RSV)	2(0.3)

Note: #The results mean a duration (day), not "*n*(%)". *Some data is missing and only available data are reported.

Patients admitted to PICU

Of those 39 patients requiring PICU admission, 22 (56%) were male. The median duration of PICU stay was 5 days (range 0-92 days). Fourteen PICU patients (36%) had a secondary bacterial infection, the most common being *H. influenza* (36%), followed by *S. pneumoniae* (21%). Compared to patients admitted only to the general pediatric ward, those admitted to PICU were more likely to: be younger at admission (P<0.01), have an underlying lung disease (P<0.01) or congenital heart disease (P=0.01), have two or more underlying illnesses (P<0.01), and have other children residing in the household (P=0.02).

Nineteen of the children admitted to PICU (49%) were intubated and mechanically ventilated. The median length of intubation was 6 days (range 3-34 days). Pneumonia (P=0.02) and secondary bacterial infections (P=0.01) were more prevalent among ventilated patients than in those not ventilated, though no other statistically significant differences emerged.

Patients who had received palivizumab

Twenty-two patients had received palivizumab prophylaxis. Demographic, clinical and hospitalization data for these patients are shown in Tables 3 and 4. Only 12 patients (55%) had received >3 doses of palivizumab before being hospitalized.

Overall, 17 (77%) of these patients had one or more chronic medical illnesses. These included underlying lung, heart, and neurological/genetic conditions in 14 (64%), 7 (32%), and 4 (18%) patients, respectively. The median chronological age at admission was 5.6 months (range 0-27.5 months) and median duration of hospitalization was 9.5 days (range 2-271 days). Sixty-four percent (14/22) were <32 weeks gestation at birth. RSV illness was considered severe in 23% (5/22), with 14% (3/22) requiring PICU care for a median of 6 days (range 2-40 days); one child was intubated for 6 days. One death occurred, although not attributed to RSV.

Figure 1 also shows the distribution of RSV positive cases in those who had received palivizumab prophylaxis. These cases were distributed throughout the RSV season, with no cases in the summer months.

Table 3 Demographic and clinical characteristics for 22 patients receiving palivizumab prophylaxis

Characteristics	*n* (%)
Male	15(68)
Age group	
0-6 months	12(55)
7-12 months	5(23)
13-24 months	4(18)
≥25 months	1(4)
Chronological age at admission	5.6 months (<1 day-27.5 months)#
Gestational age at birth	
≤ 32 weeks	14(64)
≤ 32 weeks	2(9)
≥36 weeks	6(27)
Doses of palivizumab prior to illness	
1 dose	4(18)
2 doses	6(27)
3 doses	5(23)
4 doses	1(5)
5 doses	6(27)
Aboriginal ancestry	11/20(55)
Home oxygen therapy	5(23)
Breastfeeding	5/20(25)
Smoking at home	4/16(25)
First degree relative with asthma	7/15(47)
Other children (<18 years) in house	18(82)
Underlying disease	
Pulmonary	14(64)
Cardiac	7(32)
Neurological/genetic	4(18)
At least one underlying illness	17(77)
Two or more underlying illnesses	7(32)
Secondary bacterial infection	4(18)

Note: #Chronological age at admission is expressed as "median (range)".

Table 4 Hospitalization, severity and outcomes for 22 patients receiving alivizumab prophylaxis

Characteristics	*n* (%)
Duration of hospitalization	
Median (days)	9.5#
Range (days)	2-271#
Required PICU care	3(14)
Duration of PICU course	
Median (days)	6#
Range (days)	2-40#
Required intubation/ventilation	1(4)
Median duration of intubation/ventilation (days)	6#
Severity of RSV infection	
Mild to moderate	17(77)
Severe	5(23)
Clinical outcome at discharge	
Infection improved	5(23)
Illness not resolved	11(50)
Extended hospitalization for non RSV illness	5(23)
Death (not attributed to RSV infection)	1(4)

Note: #The results mean a duration (day), not "*n*(%)".

Discussion

This is the first study to document the epidemiology of patients presenting with RSV to the only two tertiary care centers in Saskatchewan, Canada, and gives insight into overall burden of the disease. Typically all infants with moderate to severe LRTI are referred to these two centers therefore this is an accurate reflection of moderate to severe RSV disease in a defined population of one million.

These patients are more likely to be male, <1 year of age, and be >35 weeks gestation at birth, consistent with previous studies[8,17]. The most common presentation was bronchiolitis, most children had mild to moderate illness, and there was no mortality attributed to RSV infection. This is interesting to note, because the majority were late preterm and term infants, suggesting a shift of burden of disease from infants born preterm to infants born at later gestation.

Risk factors less consistently linked with RSV hospitalization include birth between October and December, birth weight less than 2 500 g, male sex, age less than 12 months, low socioeconomic status, daycare attendance, school-aged siblings, exposure to second hand smoke, congenital airway anomalies, and severe neuromuscular disease[8-9]. Recommendations were made to provide palivizumab prophylaxis to those born at 33-35 weeks gestation using a risk factor scoring system based on later studies[18-20], but were only implemented in Saskatchewan after 2005. The study period was chosen to reflect the epidemiology of RSV disease before eligibility for palivizumab prophylaxis was widened to include children born at 33-35 weeks gestation.

Prior to commencement of this chart review, definitions of severity of illness were not available in

the literature. The authors developed these definitions based on clinical experience. Although the definitions intuitively make sense, they have not been validated.

Twenty-five percent of 590 patients in this study had secondary bacterial infections, which is higher than that found in previous studies[21-22]. However, one of our two centers documented all positive blood cultures, which may have included contaminants, artificially elevating the secondary bacterial infection rate. For organisms isolated from sputum or endotracheal respiratory specimens, they may also reflect colonization, rather than true lower respiratory tract infections. Our data does not include timing of the diagnosis of secondary bacterial infection with diagnosis of the RSV infection, so we cannot determine which came first. One study in Japan found rates of respiratory bacterial co-infection of 43.6% based on sputum bacterial culture, though the clinical significance is unclear as not all patients required treatment with antibiotics[23].

Children admitted to PICU tended to be of younger chronological age, with a median age of 2.96 months. This is similar to other studies, specifically linking a chronological age of <6 weeks with ICU admission[24-25]. In this study, most patients admitted to the PICU (84%) were >35 weeks gestational age at birth. This is in keeping with other studies, and suggests that palivizumab prophylaxis is unlikely to have a significant effect on the burden of RSV disease in the intensive care setting[9,17,26-27].

Similar to other studies, children requiring PICU were more likely to have other children in the house and were more likely to have an underlying illness[25,28]. Those with underlying illness were also more likely to be intubated and mechanically ventilated, again a known risk factor[29]. Secondary bacterial infections were more common in those admitted to PICU, particularly in those who were intubated and mechanically ventilated, consistent with other studies where rates of bacterial co-infection in patients with severe RSV disease have been reported of 20%-40%[30-31]. Most in this study were respiratory pathogens. The data does not allow for a differentiation between pneumonia and secondary bacterial infection associated solely with RSV and those infections associated with intensive care itself (i.e. ventilator associated pneumonia, bacteremia secondary to central line).

Some children who had received palivizumab prophylaxis still required hospitalization for RSV. Most were classified as mild to moderate illness, and only 14% of these children required PICU admission. This is consistent with previous studies, including a recent Cochrane review, which showed palivizumab to be effective at decreasing hospitalization and severity of RSV infection[12-3,32], as well as a comparison of two Canadian centers that showed a reduction of hospitalization of high risk infants for RSV infection from 7.3% to 3.0% in the center where prophylaxis was offered[4]. In the center where palivizumab was not offered, there was no reduction in the rate of hospitalization.

In this study, patients who received palivizumab had a younger gestational age at birth, not surprising as this is one of the major criteria to qualify for RSV prophylaxis. A large number had underlying pulmonary disease, again likely related to criteria for receiving palivizumab. CARESS (the Canadian Registry of Palivizumab) found that in Canada, patients were more likely to be hospitalized with RSV post-palivizumab prophylaxis if there was atopy in the immediate family, mother smoked in pregnancy, there were smokers in the home environment, 2 smokers in the household, siblings, higher birth weight, and if the infant had received fewer palivizumab injections[33]. This study did not look at most of these factors, though having siblings in the house was common. The distribution of RSV positive cases in those who had received palivizumab was seasonal, similar to the rest of the cases of RSV. Cases did not occur earlier in the season, suggesting that children who had received multiple doses still required hospitalization, though the numbers in this group are small so it is difficult to draw conclusions from this.

Saskatchewan has a proximately 15% aboriginal population, and in this study, 55% of children receiving palivizumab were of aboriginal descent, but we are unable to make comparisons with the other children included in the study as this piece of information was often missing from the data available in the chart.

Limitations of this study included the retrospective nature, and the fact that RSV hospitalization numbers do not reflect the population incidence of RSV. We cannot draw conclusions about the general population rates and demographic criteria of patients with RSV who are seen as outpatients, or in primary or secondary care centers. There may also have been children admitted to these tertiary care centers with bronchiolitis who were not tested, and therefore not included in the study. The standard practice in these two hospitals at the time of the study would suggest that most patients were tested, as would have occurred in all patients in the PICU, but some patients with mild to moderate illness may not have been. The two hospitals used different testing methods for RSV during the time of the study (RUH-viral culture only done if DFA negative, RGH-either viral culture or DFA), which may also have affected the results. These results are not generalizable to all patients admitted with RSV infection, as the study only included tertiary care sites, and not those admitted to primary or secondary sites. The numbers of patients requiring PICU care and those who had received palivizumab prophylaxis were small, making it difficult to draw any conclusions. We also do not have information available regarding the total number of children who received palivizumab prophylaxis, so cannot determine the percentage of children with palivizumab prophylaxis failure. It is possible that some children who received palivizumab prophylaxis were admitted to primary or secondary care sites, and so their admissions would not be included in this study. It appears that a disproportionate number of aboriginal infants are infected with RSV, but the lack of data surrounding the ethnic backgrounds of patients other than in the palivizumab group makes it difficult to interpret this. Further larger studies are needed to review the effects of ethnicity on RSV infection, as well as further characterize the demographic characteristics of patients requiring intensive care, and those who are hospitalized with RSV despite palivizumab prophylaxis.

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