Hospital admissions for acute respiratory tract infections among infants from Nunavut and the burden of respiratory syncytial virus: a 10-year retrospective cohort study

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Summary

Background Nunavut is a northern Canadian territory where a high proportion of infants are admitted to hospital with acute respiratory tract infection (ARI). Previous studies have been limited in regional and/or short duration of coverage. This study aimed to estimate the incidence rate, microbiology and outcomes of ARI hospitalizations in Nunavut infants.

Methods We conducted a retrospective cohort study of infants aged <1 year from Nunavut hospitalized for ARI at two regional and four tertiary pediatric hospitals in Canada, January 1, 2010, to June 30, 2020. One regional hospital was located in Nunavut; others were located across Canada. Descriptive statistics and multivariable logistic regression were performed.

Findings We identified 1189 ARI admissions, with an incidence rate of 133.9 per 1000 infants per year (95% confidence interval (CI): 126.8, 141.3). Of these admissions, 56.0% (n = 666) were to regional hospitals alone, 72.3% (n = 860) involved hospitalization outside of Nunavut, 15.6% (n = 185) were admitted into intensive care, and 9.2% (n = 109) underwent mechanical ventilation. Among 730 admissions with a pathogen identified, 45.8% had respiratory syncytial virus (RSV; n = 334), for a yearly incidence rate of 37.8 RSV-associated hospitalizations per 1000 infants (95% CI: 33.9, 42.1). Among RSV-associated hospitalizations, 41.1% (n = 138) were infants 0–2 months of age and 32.1% (n = 108) were >6 months. Compared with non-RSV admissions, infants with RSV had higher odds of admission into intensive care, oxygen therapy, CPAP/BiPAP respiratory support and length of hospital stay over a week.

Interpretation Understanding the high burden of ARI among Nunavut infants can inform health policy and serve as a baseline for assessing the impact of any new interventions targeting infant ARIs.

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Research in context

Evidence before this study

Respiratory syncytial virus (RSV) is the most common cause of severe acute respiratory tract infection (ARI) in infants worldwide and may contribute 30–41% of ARI hospitalizations among infants from Nunavut. We used PubMed and Google Scholar, to probe the burden of ARI hospitalizations among infants from Nunavut, a territory in northern Canada. The literature was searched up to May 22, 2024, and search terms included "infants", "hospitalization", "Nunavut", "acute respiratory tract infection" and "respiratory syncytial virus". Although there have been improvements in the management of children requiring admission to hospital with ARIs, previous studies from Nunavut have documented infant ARI hospitalization rates among the highest in the world. However, previous studies were limited to only certain regions in Nunavut, a single illness season, or only those air transferred to tertiary pediatric hospitals, which presents an incomplete understanding of the overall burden.

Added value of this study

Our study covered 10 years of ARI hospital admissions (2010–2020) to all contracted referral hospitals that children from Nunavut are admitted (four tertiary care sites and two territorial hospitals), which is the largest review of the burden among infants from Nunavut. Our study comprehensively covered both tertiary and regional hospitals, the latter of which have not always been included. Our study also featured a unique collaboration of researchers and clinicians from Nunavut and across Canada, Nunavut Public Health and the involvement of Nunavut Tunngavik Incorporated (NTI) to help guide this study from conceptualization to interpretation of the results. This study examined the rate, microbiology results, and outcomes of ARI hospitalizations among infants from Nunavut and showed that nearly 1 in 6 infants in the territory were admitted with ARIs over a 10 year period, with respiratory syncytial virus (RSV) as the leading pathogen identified.

Implications of all the available evidence

These findings highlight the heavy burden of ARIs among infants in Nunavut and the unique health care challenges facing families and health providers in resource-limited health settings within remote communities in Northern Canada. These data can help support health policy decision-making and serve as a baseline for understanding the impact of potential interventions targeting ARI in infants. These data suggest that ongoing, systematic ARI hospitalization surveillance in Nunavut to optimize effective, feasible and culturally appropriate prevention approaches is warranted.

Introduction

Nunavut, the largest region in Inuit Nunangat, is a northern Canadian territory where approximately 85% of the population identifies as Inuit. Although there have been improvements in the management of children requiring admission to hospital with acute respiratory tract infection (ARI),[1] a high proportion of infants in the territory have historically been hospitalized due to these infections.[2–4] The 2007–2008 Nunavut Inuit Child Health Survey reported 33% of children younger than two years experienced a severe lower respiratory tract infection, of which 81% resulted in hospitalizations.[5] Respiratory syncytial virus (RSV) is the most common cause of severe ARI in infants worldwide and globally, an estimated 1.4 million infants younger than 6 months old were hospitalized due to RSV-associated acute lower respiratory infections in 2019.[6] Studies from Nunavut indicate that RSV may contribute 30–41% of ARI hospitalizations among infants.[7,8] Due to the remoteness of communities (all are fly-in, without road access) and complex referral pathways in Nunavut, infants admitted to hospital with RSV and other respiratory pathogens often require transport out of territory and a high rate of intensive care admission has been documented among transferred cases.[5] A review of paediatric urgent air transfers for children across Northern Canada found 54% of cases originated from Nunavut; an estimated 40.7 per 1000 infants from Nunavut are air transported to tertiary paediatric hospitals for severe ARIs annually.[8] A study from Alberta found high hospital resource use and parental time burden, out of pocket costs, lost work productivity and significant parental stress associated with infant RSV-associated hospitalizations,[9] which is heightened with additional complexities of accessing care in remote Nunavut communities. Transport outside of their home community is disruptive to the whole family, which is magnified with transport out of territory.

While previous studies in Nunavut highlighted infant RSV as a concern of high priority, understanding the burden of ARI hospitalizations has been limited by

studies with only certain regions,[4,10] a single illness season,[7,10] or only those air transferred to tertiary paediatric hospitals.[8] Particularly given the potential of new interventions to prevent severe RSV disease in infancy,[11] the objective of our study is to comprehensively estimate the burden of ARI hospitalizations in infants from Nunavut over 10 years (2010–2020), including determining the rate, microbiology and outcomes of ARI hospitalizations.

Methods

Study design and population

This study is part of the larger Burden Ethnographic Modelling Evaluation Qaujilisaaqtuq (BEMEQ) RSV initiative to estimate the burden of RSV, perceptions and potential impact of preventive interventions. We conducted a retrospective chart review at all six referral hospitals serving Nunavut's population, including two regional hospitals and four tertiary care hospitals. There is only one regional hospital in Nunavut, Qikiqtani General Hospital (QGH) in Iqaluit, the capital of Nunavut. The other regional hospital was Stanton Territorial Hospital (STH) located outside of Nunavut. Nunavut has three regions: for the Kitikmeot region, out-of-territory referrals flow to Northwest Territories (to STH) and Alberta (Stollery Children's Hospital, SCH); for the Kivalliq region, to Manitoba (Winnipeg Children's Hospital, WCH); and for the Qikiqtaaluk/Qikiqtani region, to QGH and Ontario (Children's Hospital of Eastern Canada, CHEO) (Fig. 1,[12]). Montreal Children's Hospital (MCH) in Quebec was also included because it was an overflow referral hospital for the Qikiqtaaluk/Qikiqtani region. During the study, laboratory testing for respiratory pathogens were available at tertiary care sites; molecular tests were not available on site at regional hospitals (QGH and STH) and were sent out for testing. With our focus on hospital admissions, this study did not capture outpatient primary care visits to health centres in Nunavut communities, including Rankin Inlet.

Our study included all children <12 months of age who were residents of Nunavut with suspected or proven community-onset ARI as the reason for hospitalization admitted between January 1, 2010 and the end of the 2019–2020 RSV season (June 30, 2020). Nunavut residency was confirmed by postal code. ARIs were defined as a new illness (<14 days duration) with respiratory symptoms suspected to be caused by infection. Hospitalizations were defined as admissions of at least 24 h at the hospital centre. Hospital visits less than 24 h (i.e. emergency room visits) were excluded.

Data collection and analysis

Hospital charts were identified using respiratory ICD-10 codes (Supplementary File 1) extracted from hospitalization databases at tertiary hospitals. At regional hospitals, all admissions of infants from Nunavut apart from birth hospitalizations were reviewed. All retrieved charts were reviewed by trained members of the study team in each hospital to determine eligibility. Relevant data were extracted by a trained research assistant/nurse at each site using a modified version of the previously utilized Urgent Air Transfer data collection form[8]; data were quality checked by a research coordinator and queries were reviewed with site investigators and/or the principal investigator. Demographics, clinical history, transportation to the study hospital, all microbiology results and clinical procedures during the admission, and patient outcomes were extracted from hospital records. Prematurity was defined as <37 weeks gestation and low birthweight was defined as <2500 g. When more than one pathogen was identified, the site investigator adjudicated the likely primary pathogen based on timing, site of detection and the clinical picture. Data from tertiary sites from 2010 to 2014 were already collected during the Urgent Air Transfer study and the current BEMEQ study added to the dataset by collecting 2015–2020 data. Regional hospitals were not included in the Urgent Air Transfer study so data were collected for 2010–2020. Records of infants transferred from regional to tertiary hospitals were linked using health care numbers, names, date of birth and admission/transfer records in their hospital charts.

The data was stored in REDCap (Research Electronic Data Capture), managed at the BC Children's Hospital Research Institute. Descriptive statistics were conducted to present the demographics, underlying comorbidities, clinical care during admissions, and the identified microbial aetiologies. Nunavut Bureau of Statistics population data were used to calculate the incidence of infant ARI and RSV-associated hospitalization rates, based on an annual average of admissions by population over 2010–2019.[13] We did not calculate the incidence for 2020 due to a truncated year ending after the 2019–2020 RSV season in June and the potential influence of the COVID-19 pandemic. Logistic regression analysis was used to investigate associations between demographic characteristics and clinical outcomes firstly, among admitted infants with laboratory confirmed RSV versus other respiratory viral pathogens, and secondly, among admitted infants with RSV only versus RSV with documented coinfections (other respiratory viruses). We present result as odds ratios (ORs) and 95% confidence intervals adjusted for confounders: age, time period 2010–2014/2015–2020, preterm birth (yes/no), and region of residence. These were identified *a priori* by clinicians in the study team as key confounders with reliable data sourced from health records. Analyses were conducted using R statistical software.

Ethical considerations and stakeholder engagement

The study received ethics approval from the University of British Columbia Children's and Women's Research Ethics Board (H19-03793), the University of Alberta Health Research Ethics Board (Pro 00103234),

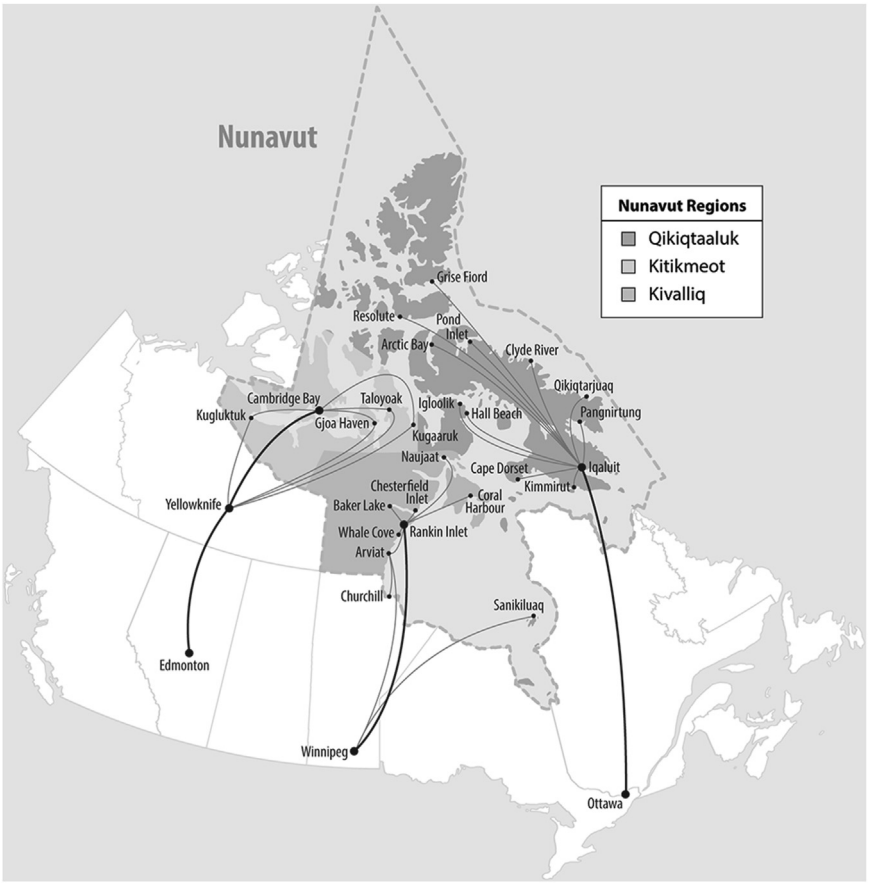

Fig. 1: Map of Canada depicting the air links between Nunavut communities and the locations where residents may be flown if they cannot receive needed health care in their own community.[12]

University of Manitoba Health Research Ethics Board (H2021:259), the Children's Hospital of Eastern Ontario Research Ethics Board (21/18×), and the Paediatric Panel of the Research Ethics Board of the Research Institute of the McGill University Health Centre (2021–6256). In addition to ethical approvals, Scientific Research Licences from the Northwest Territories (16,813) and Nunavut (01 011 23 R-M) were obtained following territorial policies. Exact numbers in data categories with less than five patients were not reported to protect confidentiality. Our project involved the collaboration and engagement of partners from Nunavut Tunngavik Incorporated (NTI), a representative organization for Inuit in Nunavut, and Nunavut Department of Health, including public health stakeholders and clinicians. Partners were involved throughout the study in project planning, project updates and interpretation of results, to ensure alignment with Nunavut priorities and needs.

Role of the funding source

This work was supported by the Canadian Immunization Research Network (CIRN) through a grant from the Public Health Agency of Canada and the Canadian Institutes of Health Research (CNF 151944). The funders had no role in the study design, analysis, interpretation of the results, or decision to publish.

Results

Of the 1352 patient charts identified and assessed for eligibility, 1189 ARI admissions among infants from Nunavut were included for review after removal of duplicate and ineligible charts and linking transferred admissions (Fig. 2). Of these, 666 (56.0%) to regional hospitals alone (QGH and STN), 494 (41.5%) to tertiary hospitals alone, and 29 (2.4%) were first admitted at a regional hospital before being transferred to a tertiary hospital. 329 infants' (27.7%) were admitted to QGH, the only hospital within the territory, while the other 860 (72.3%) admissions involved hospitalization outside of Nunavut. Of the 1189 admissions, 534 (44.9%) were from the Qikiqtaaluk/Qikiqtani region, 379 (31.9%) from the Kitikmeot region, and 276 (23.2%) from the Kivalliq region.

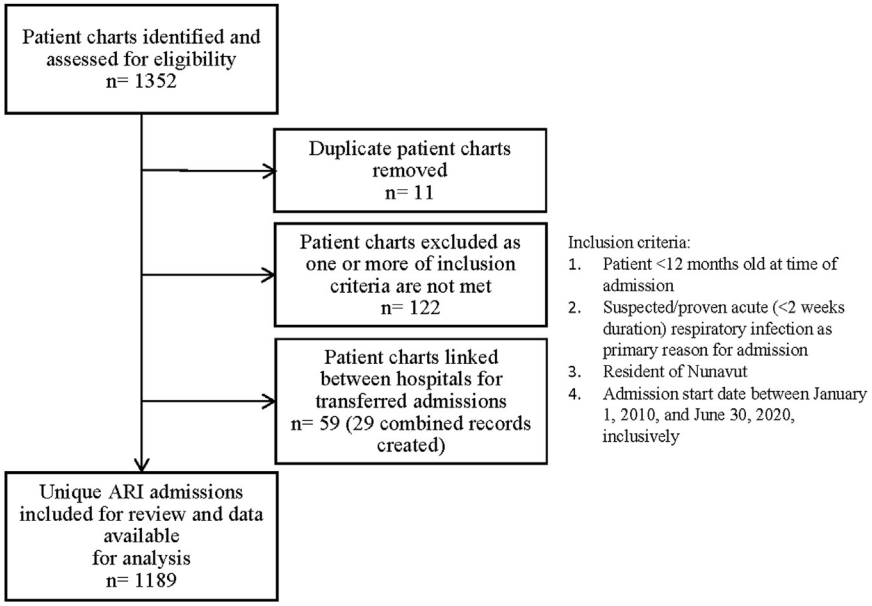

Fig. 2: Flow diagram of patient charts.

Table 1 summarizes the demographics of patients by hospital and overall. There were 804 (67.6%) infants less than six months of age and 385 (32.4%) six months or older. Among those admitted only to regional hospitals, 36.3% (242 of 666) were six months or older, compared to 27.3% (143 of 523) of those admitted to or transferred to the four tertiary hospitals. The median age of admission was three months, with an interquartile range of two to seven months. Almost all (968 of 972; 99.6%) infants with ethnicity recorded in their hospital charts were Inuit, 679 (57.1%) were male, and 264 (22.7%) were born premature. The median gestational age for premature infants was 35 weeks (late preterm). Underlying chronic medical conditions were reported in 205 (17.2%) cases, including 53 (4.5%) with significant cardiac and/or respiratory condition.

Table 2 summarizes admissions and outcomes by hospital. Of the 1189 admissions, 185 (15.6%) were admitted into intensive care and 109 (9.2%) were intubated and underwent mechanical ventilation. The median length of stay was five days, with lengthier stays reported at tertiary hospitals, and 381 (32.0%) were hospitalized for over a week. Pneumonia and bronchiolitis were the primary diagnosis in 1035 (87.0%) admissions. Almost all infants (1167 of 1189; 98.1%) were discharged home, though 96 (8.1%) were

	Regional hospitals		Tertiary hospitals				Transferred admissions[a]	Total
	QGH (n = 329)	STN (n = 337)	SCH (n = 27)	WCH (n = 367)	CHE (n = 96)	MCH (n < 5)	(n = 29)	(n = 1189)
Age								
0–2 months	115 (35.0%)	126 (37.4%)	13 (48.1%)	165 (45.0%)	48 (50.0%)	<5	13 (44.8%)	484 (40.7%)
3–5 months	94 (28.6%)	89 (26.4%)	7 (25.9%)	99 (27.0%)	22 (22.9%)	0 (0.0%)	9 (31.0%)	320 (26.9%)
6–8 months	55 (16.7%)	70 (20.8%)	<5	61 (16.6%)	12 (12.5%)	0 (0.0%)	<5	203 (17.1%)
9–11 months	65 (19.8%)	52 (15.4%)	5 (18.5%)	42 (11.4%)	14 (14.6%)	0 (0.0%)	<5	182 (15.3%)
Preterm birth[b] <37 weeks gestation	73 (23.0%)	49 (14.9%)	8 (30.8%)	85 (23.2%)	46 (48.4%)	<5	<5	264 (22.7%)
Low birthweight[c] <2500 g	44 (16.1%)	21 (7.14%)	<5	59 (18.8%)	24 (32.9%)	<5	<5	153 (15.2%)
Underlying chronic medical condition								
Any chronic condition	52 (15.8%)	34 (10.1%)	7 (25.9%)	82 (22.3%)	22 (22.9%)	<5	7 (24.1%)	205 (17.2%)
Significant cardiac or respiratory condition	7 (2.1%)	10 (2.97%)	<5	22 (6.0%)	10 (10.4%)	0 (0.0%)	0 (0.0%)	53 (4.5%)

QGH, Qikiqtani General Hospital; STN, Stanton Territorial Hospital; SCH, Stollery Children's Hospital; WCH, Winnipeg Children's Hospital; CHE, Children's Hospital of Eastern Ontario; MCH, Montreal Children's Hospital. [a]Transferred admissions include QGH to CHE, QGH-WPG, and STN to SCH. [b]Out of 1136 cases with preterm birth data (QGH n = 317, STN n = 329, SCH n = 26, WCH n = 366, CHE n = 95, MCH n = 3). [c]Out of 978 cases with birthweight data (QGH n = 274, STN n = 294, SCH n = 21, WCH n = 314, CHE n = 73, MCH n = 2).

Table 1: **Summary of demographics for Nunavut acute respiratory infection infant admissions between 2010 and 2020.**

	Regional hospitals		Tertiary hospitals				Transferred admissions[a]	Total
	QGH (n = 329)	STN (n = 337)	SCH (n = 27)	WCH (n = 367)	CHE (n = 96)	MCH (n < 5)	(n = 29)	(n = 1189)
Admission into intensive care	0 (0.0%)[b]	0 (0.0%)[b]	21 (77.8%)	78 (21.3%)	65 (67.7%)	<5	17 (58.6%)	185 (15.6%)
Highest respiratory support								
Oxygen only	153 (46.5%)	226 (67.1%)	10 (37.0%)	206 (56.1%)	18 (18.8%)	0 (0.0%)	13 (44.8%)	626 (52.6%)
CPAP/BiPAP	0 (0.0%)	0 (0.0%)	0 (0.0%)	27 (7.4%)	22 (22.9%)	<5	<5	52 (4.4%)
Mechanical ventilation/HFOV	0 (0.0%)	<5	16 (59.3%)	39 (10.6%)	37 (38.5%)	<5	11 (37.9%)	109 (9.2%)
Antimicrobial therapy	212 (64.4%)	237 (70.3%)	25 (92.6%)	230 (62.7%)	80 (83.3%)	<5	26 (89.6%)	814 (68.5%)
Median length of stay [IQR]	4.0 [3.0; 6.0]	5.0 [4.0; 8.0]	12.0 [9.0; 15.0]	5.0 [3.0; 9.0]	12.0 [7.0; 20.0]	16.0 [13.0; 18.5]	14.0 [11.0; 22.0]	5.0 [3.0; 9.0]
Length of stay >7 days	47 (14.3%)	85 (25.2%)	22 (81.5%)	125 (34.1%)	70 (72.9%)	<5	28 (96.6%)	381 (32.0%)
Primary discharge diagnosis								
Pneumonia	61 (18.5%)	87 (25.8%)	<5	86 (23.4%)	24 (25.0%)	0 (0.0%)	8 (27.6%)	269 (22.6%)
Bronchiolitis	187 (56.8%)	218 (64.7%)	18 (66.7%)	273 (74.4%)	49 (51.0%)	<5	17 (58.6%)	766 (64.4%)
Hospital readmission within 30 days	31 (9.4%)	20 (5.9%)	0 (0.0%)	31 (8.5%)	10 (10.4%)	0 (0.0%)	<5	96 (8.1%)

QGH, Qikiqtani General Hospital; STN, Stanton Territorial Hospital; SCH, Stollery Children's Hospital; WCH, Winnipeg Children's Hospital; CHE, Children's Hospital of Eastern Ontario; MCH, Montreal Children's Hospital; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; IQR, interquartile range; HFOV, high-frequency oscillatory ventilation. [a]Transferred admissions include QGH to CHE, QGH-WPG, and STN to SCH. [b]Intensive care was not available at QGH and STN.

Table 2: **Hospital admission and outcomes.**

readmitted at a hospital within 30 days of discharge. Two infant deaths at tertiary hospitals were reported.

Table 3 summarizes the microbiology of ARI admissions. Of the 730 (61.4%) admissions with laboratory confirmation of aetiology, RSV was the leading primary pathogen with 334 (45.8%) cases. There were two admissions that reported RSV as a concurrent infection to the primary pathogen. Other major pathogens reported include influenza A and B, parainfluenza, hMPV, coronavirus, adenovirus, rhinovirus, enterovirus and *Haemophilus influenzae*. Other viruses and bacteria reported (15 cases, 2.1%) included *Streptococcus pneumoniae*, *Staphylococcus aureus -methicillin resistant*, *Bordetella pertussis*, and HSV Type 1. There were 220 (18.5%) admissions with documented co-infections.

The incidence rate of infant RSV-associated hospitalizations in Nunavut was 37.8 per 1000 infants per year (95% confidence interval [CI]: 33.9–42.1), with an overall rate of ARI hospitalizations at 133.9 per 1000 infants per year (95% CI: 126.8–141.3) (Supplementary File 2). Fig. 3 illustrates that there was variability in the number of hospitalizations and the rate of RSV compared to all other ARI hospitalizations by season (Supplementary File 3). The seasonality of RSV in Nunavut over the 10-year period presented as the total monthly cases aggregated across years is reported in Supplementary File 4.

Table 4 compares demographic characteristics and clinical outcomes by infants with laboratory confirmed RSV and other respiratory viral infections. In infants admitted for an ARI, the odds of testing RSV positive was similar for older age cohorts compared to the comparison group (0–2 month old). Compared to infants with other respiratory viral infections, RSV positive infants had lower odds of prematurity status (aOR 0.59, 95% CI: 0.41–0.86, p = 0.006). Clinical outcomes were generally worse amongst RSV positive cases. For example, those with RSV had higher odds of admission into intensive care (aOR 1.65, 95% CI: 1.13–2.41, p = 0.009) and oxygen therapy (aOR 2.24, 95% CI: 1.59–3.17, p < 0.001). Antimicrobial therapy was lower in those with RSV (aOR = 0.59, 95% CI: 0.42–0.82, p = 0.002). RSV positive infants had higher odds of hospital stays over a week in length (aOR = 1.40, 95% CI: 1.03–1.90, p = 0.03).

Table 5 compares demographic characteristics and clinical outcomes for infants with RSV only versus those with RSV and concurrent infections. Concurrent infection rates were similar by infant age. Rates of low birthweight and cardiac or respiratory condition were also similar between groups. Mechanical ventilation (aOR = 2.50, 95% CI: 1.25–4.97, p = 0.009) and hospital readmission within 30 days (aOR = 3.18, 95% CI: 1.15–8.84, p = 0.024) were more frequent in those with concurrent infection. Adjusted analyses also produced point estimates suggesting higher odds of intensive care, antimicrobial therapy, oxygen therapy but all estimates had wide confidence intervals compatible with both large increases and decreases.

Discussion

We found a high rate of ARI admissions among infants from Nunavut, with RSV being the leading pathogen identified, though fortunately with a relatively low rate of in hospital mortality in the ten-year period. The incidence rate of RSV-associated hospitalizations among Nunavut infants were substantially higher than global estimates and estimates from other provinces in Canada (Nunavut: 37.8 per 1000 infants [95% CI: 33.9–42.1]

	Regional hospitals		Tertiary hospitals				Transferred admissions[a]	Total
	QGH (n = 329)	STN (n = 337)	SCH (n = 27)	WCH (n = 367)	CHE (n = 96)	MCH (n < 5)	(n = 29)	(n = 1189)
Lab confirmation of pathogen	148 (45.0%)	217 (64.4%)	24 (88.9%)	242 (65.9%)	71 (74.0%)	<5	24 (82.8%)	730 (61.4%)
Primary pathogen identified								
RSV	63 (42.6%)	98 (45.2%)	7 (29.2%)	120 (49.6%)	31 (43.7%)	<5	13 (44.8%)	334 (45.8%)
Influenza A	9 (6.1%)	<5	0 (0.0%)	10 (4.1%)	<5	0 (0.0%)	0 (0.0%)	27 (3.7%)
Influenza B	<5	<5	0 (0.0%)	5 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (1.1%)
hMPV	13 (8.8%)	22 (10.1%)	<5	<5	5 (7.0%)	0 (0.0%)	0 (0.0%)	43 (5.9%)
Parainfluenza	12 (8.1%)	22 (10.1%)	6 (25.0%)	14 (5.8%)	<5	<5	<5	60 (8.2%)
Coronavirus[b]	6 (4.1%)	6 (2.8%)	0 (0.0%)	6 (2.5%)	<5	0 (0.0%)	<5	22 (3.0%)
Adenovirus	7 (4.7%)	<5	<5	18 (7.4%)	<5	0 (0.0%)	<5	34 (4.7%)
Rhinovirus/Enterovirus	30 (20.3%)	59 (27.2%)	9 (37.5%)	61 (25.2%)	12 (16.9%)	<5	6 (25.0%)	178 (24.4%)
Haemophilus influenzae	<5	<5	0 (0.0%)	<5	<5	0 (0.0%)	0 (0.0%)	9 (1.2%)
Laboratory confirmed concurrent infection	47 (14.3%)	63 (18.7%)	10 (37.0%)	69 (18.8%)	21 (21.9%)	0 (0.0%)	10 (34.5%)	220 (18.5%)

QGH, Qikiqtani General Hospital; STN, Stanton Territorial Hospital; SCH, Stollery Children's Hospital; WCH, Winnipeg Children's Hospital; CHE, Children's Hospital of Eastern Ontario; MCH, Montreal Children's Hospital; RSV, Respi17ratory syncytial virus; hMPV, Human metapneumovirus. [a]Transferred admissions include QGH to CHE, QGH-WPG, and STN to SCH. [b]HCoV-OC43, -NL63, -HKU1, -229 E.

Table 3: **Microbiology.**

versus global: 15.9 [12.6–21.2],[6] versus Ontario: 10.2 [10.0–10.4][14]). Seven in ten were hospitalized outside of Nunavut and approximately one in six admitted to intensive care. RSV admissions had heightened intensive care needs and longer hospital stays compared to infants admitted with other viral respiratory tract infections. RSV with another respiratory pathogen had higher rates of mechanical ventilation and hospital readmission compared to infants with RSV only. Similar to another contemporary study in Canada,[15] prematurity was not identified as a risk factor for RSV among infants Nunavut admitted with an ARI. In Nunavut there is ready availability of palivizumab for premature infants <36 weeks gestational age at birth and this may at least partially explain this finding.

Although RSV was the most commonly identified pathogen, our longer term study reports variability in rates from year to year, which may explain overall lower RSV admission rates than in previous one-year studies (134 versus 166 in the Qikiqtaaluk/Qikiqtani region[16] and 195 in the Kitikmeot region[7] per 1000 infants). However, we continue to report substantially higher infant RSV-associated hospitalization rates compared to global estimates [3.8% versus 1.6–1.8% global estimates[17–19]]. High rates of hospitalizations, frequently outside of territory, and intensive care admissions places a heavy burden on both the healthcare system and families. Language barriers are also a concern with hospitalizations outside of territory.

Previous studies concentrated on infant ARI admissions to tertiary care centres.[8,20] Our findings highlight the importance of studying admissions to regional hospitals where most hospitalizations occurred. Additionally, we found a higher proportion of infants six months or older at regional hospitals, compared to tertiary admissions. This may explain the larger proportion of RSV admissions with older infants in our study than previously reported. The IMPACT program at 13

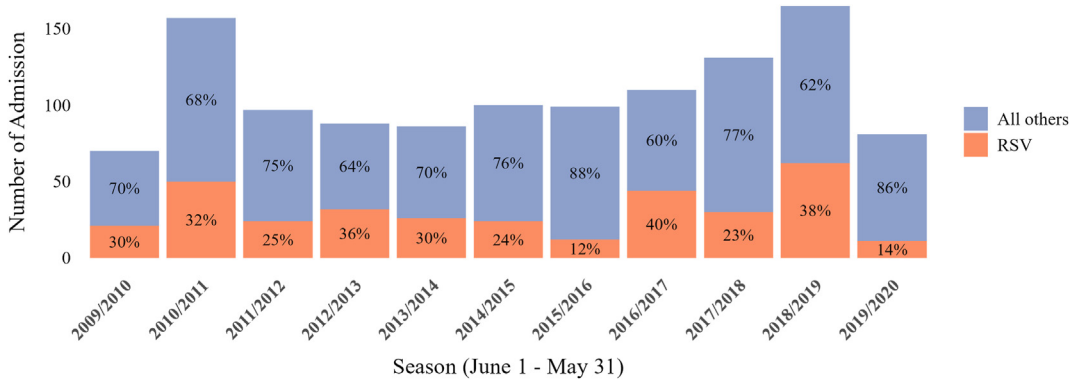

Fig. 3: Total acute respiratory infection admissions and admissions due to RSV over time.

	Other infection (n = 394)	RSV positive (n = 336)	Odds ratio (95% CI)	Adjusted odds ratio[a] (95% CI)	p-value
Demographics[b]					
Age					
0–2 months	171 (43.4%)	138 (41.1%)	Ref.	Ref.	–
3–5 months	111 (28.2%)	90 (26.8%)	1.00 (0.70, 1.44)	1.05 (0.73, 1.52)	0.777
6–8 months	58 (14.7%)	52 (15.5%)	1.11 (0.72, 1.72)	1.17 (0.74, 1.82)	0.502
9–11 months	54 (13.7%)	56 (16.7%)	1.28 (0.83, 1.99)	1.33 (0.84, 2.09)	0.22
Preterm birth[c] <37 weeks	99 (25.5%)	55 (17.0%)	0.60 (0.41, 0.86)	0.59 (0.41, 0.86)	0.006
Low birthweight[d] < 2500 g	55 (16.4%)	28 (10.1%)	0.57 (0.35, 0.93)	0.71 (0.4, 1.25)	0.244
Significant cardiac or respiratory condition	23 (5.84%)	8 (2.38%)	0.40 (0.16, 0.87)	0.45 (0.18, 0.99)	0.058
Clinical outcomes[e]					
Admission into intensive care	73 (18.5%)	82 (24.4%)	1.42 (0.99, 2.03)	1.65 (1.13, 2.41)	0.009
Oxygen therapy	244 (61.9%)	263 (78.3%)	2.21 (1.59, 3.09)	2.24 (1.59, 3.17)	<0.001
CPAP/BiPAP	32 (8.12%)	45 (13.4%)	1.75 (1.08, 2.84)	2.05 (1.24, 3.43)	0.005
Mechanical ventilation	49 (12.4%)	45 (13.4%)	1.09 (0.70, 1.68)	1.23 (0.78, 1.94)	0.362
Antimicrobial therapy	299 (75.9%)	218 (64.9%)	0.59 (0.43, 0.81)	0.59 (0.42, 0.82)	0.002
Median length of stay [IQR]	6.0 [4.0; 10.0]	7.0 [4.0; 10.0]	NA	NA	NA
Length of stay >7 days	149 (37.8%)	153 (45.5%)	1.37 (1.02, 1.85)	1.40 (1.03, 1.90)	0.03
Hospital readmission within 30 days	36 (9.14%)	19 (5.65%)	0.60 (0.33, 1.06)	0.62 (0.33, 1.1)	0.109

RSV, Respiratory syncytial virus; CI, confidence interval; ref, reference interval; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; IQR, interquartile range; NA, not applicable. [a]Adjusted for age, time period 2010–2014/2015–2020, preterm birth (yes/no), and region of residence. [b]For the demographic variables related to RSV status, the reference groups are 'Not Preterm,' 'Birthweight ≥2500 g,' and 'No Significant Cardiac/Respiratory Condition,' respectively. [c]Out of 712 cases with preterm birth data (Other infection n = 388, RSV positive n = 324). [d]Out of 612 cases with birthweight data (Other infection n = 335, RSV positive n = 277). [e]When examining the exposure of RSV on clinical outcomes, the reference group for RSV status is other respiratory viral pathogens.

Table 4: **Demographic and clinical outcomes in admitted infants with laboratory confirmed RSV compared to other respiratory viral infections.**

	RSV only (n = 243)	RSV with concurrent infection (n = 93)	Odds ratio (95% CI)	Adjusted odds ratio[a] (95% CI)	p-value
Demographics[b]					
Age					
0–2 months	98 (40.3%)	40 (43.0%)	Ref.	Ref.	–
3–5 months	69 (28.4%)	21 (22.6%)	0.75 (0.40, 1.37)	0.63 (0.33, 1.2)	0.166
6–8 months	37 (15.2%)	15 (16.1%)	1.00 (0.48, 2.00)	1.06 (0.5, 2.19)	0.878
9–11 months	39 (16.0%)	17 (18.3%)	1.07 (0.53, 2.10)	1.2 (0.57, 2.46)	0.626
Preterm birth[c] <37 weeks gestation	44 (18.8%)	11 (12.2%)	0.61 (0.28, 1.20)	0.62 (0.29, 1.24)	0.196
Low birthweight[d] < 2500 g	18 (9.09%)	10 (12.7%)	1.46 (0.61, 3.28)	2.78 (0.98, 8.25)	0.056
Significant cardiac or respiratory condition	6 (2.47%)	2 (2.15%)	0.91 (0.12, 4.19)	0.85 (0.12, 3.92)	0.849
Clinical outcomes[e]					
Admission into intensive care	56 (23.0%)	26 (28.0%)	1.30 (0.75, 2.22)	1.47 (0.82, 2.62)	0.191
Oxygen therapy	186 (76.5%)	77 (82.8%)	1.46 (0.81, 2.79)	1.72 (0.90, 3.44)	0.11
CPAP/BiPAP	34 (14.0%)	11 (11.8%)	0.83 (0.38, 1.68)	0.94 (0.42, 1.99)	0.876
Mechanical ventilation	26 (10.7%)	19 (20.4%)	2.14 (1.10, 4.09)	2.50 (1.25, 4.97)	0.009
Antimicrobial therapy	156 (64.2%)	62 (66.7%)	1.11 (0.67, 1.86)	1.11 (0.66, 1.91)	0.691
Median length of stay [IQR]	6.0 [4.0; 10.0]	8.0 [5.0; 15.0]	NA	NA	NA
Length of stay >7 days	105 (43.2%)	48 (51.6%)	1.40 (0.87, 2.27)	1.42 (0.86, 2.34)	0.173
Hospital readmission within 30 days	10 (4.1%)	9 (9.7%)	2.49 (0.95, 6.47)	3.18 (1.15, 8.84)	0.024

RSV, Respiratory syncytial virus; CI, confidence interval; ref, reference interval; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; IQR, interquartile range; NA, not applicable. [a]Adjusted for age, time period 2010–2014/2015–2020, preterm birth (yes/no), and region of residence. [b]For the demographic variables related to RSV status, the reference groups are 'Not Preterm,' 'Birthweight ≥2500 g,' and 'No Significant Cardiac/Respiratory Condition,' respectively. [c]Out of 324 cases with preterm birth data (RSV only n = 234, RSV with concurrent infection n = 90). [d]Out of 277 cases with birthweight data (RSV only n = 198, RSV with concurrent infection n = 79). [e]When examining the exposure of RSV with concurrent infections on clinical outcomes, the reference group is RSV only.

Table 5: **Demographic and clinical outcomes in admitted infants with laboratory confirmed RSV only compared to RSV with concurrent infection(s).**

Canadian tertiary paediatric hospitals reported 18.5% (1249 of 6737) of infant RSV-associated hospitalizations were infants older than five months[20] versus 32.1% (108 of 336) in our study. The age of RSV admissions is an important factor in designing RSV prevention programs.

Monoclonal antibodies specific to RSV, including palivizumab and nirsevimab,[21] have been developed and palivizumab has been implemented in Nunavut. Though our study recorded higher levels of prematurity and underlying chronic conditions than in the general population (22.7% preterm birth in our study versus 12.6% overall in Nunavut[22]), the majority of patients admitted with RSV were healthy, full-term infants not eligible for palivizumab. The recently developed longer acting monoclonal antibody, nirsevimab, is protective against RSV for both healthy late preterm and term infants for at least 150 days after birth,[23] including effectiveness findings from recent European infant-wide implementation programs.[24–26] A maternal vaccine has also recently been approved by regulatory authorities (including in Canada) with efficacy against RSV-associated hospitalizations until at least 180 days after birth.[27] These interventions have potential to support infant well-being in Nunavut, where our study has documented relatively high RSV burden. However, there is a need to understand factors that impact effectiveness, feasibility and acceptability within resource-limited remote health settings such as Nunavut. For example, the substantial rate of concurrent infections among infant ARI admissions from Nunavut may temper promising efficacy rates.[28] It will be helpful to assess impacts on patients/public, providers, costs, and outcomes in the context of stretched health systems, other illnesses and social determinants of health in Nunavut. Valuing Inuit expertise alongside Western biomedical approaches and ways of knowing is essential. Inuit have lived in this homeland for thousands of years, with rich culture and customs. Ongoing work to incorporate and align health services with the wisdom of *Inuit Qaujimajatuqangit* (Traditional Knowledge) is important for the territory and for the health and wellbeing of Inuit. Given the complexities of managing infant ARIs in Nunavut, a comprehensive approach is needed with medical therapies alongside continued strengthening non-invasive respiratory support, diagnostic tests, and on-site care from full-time paediatricians at regional hospitals, as well as action on prevention and social determinants of health.[8,29]

The primary strength of the study is the 10-year period of review and admissions to both tertiary hospitals and the smaller regional hospitals, allowing a better insight into the true burden of ARI hospitalizations in infants from Nunavut. The underlying reasons for these high rates of hospitalization are likely multifactorial and may include social determinants of health disparities, such as high levels of food insecurity[30] and crowded housing,[31] indoor air quality,[32] potential genetic determinants,[33] or challenges in geographically remote communities where thresholds for admission/transfer differ from southern centres. Poor reporting of social factors in medical charts limited the capacity of our study to explore the impacts of social determinants of health. Furthermore, rates of RSV and other pathogens are likely underestimates as laboratory testing was not always performed. Additionally, negative test results and readmission data beyond 30 days were not collected, which are limitations of our study. It was not possible to assess the opportunity costs or potential harms of focusing on RSV as opposed to other pathogens/health concerns. Future research is recommended to highlight the voices of impacted families and health system impacts, update dataset beyond June 2020 to understand the impact of the COVID-19 pandemic, concurrent infections, and durations of therapies for hospitalized infants to further understand the burden of diseases.

Conclusion

Our 10-year review of ARI hospital admissions is the largest among infants from Nunavut and included both tertiary and regional hospitals. Our findings document the heavy burden of respiratory tract infection among infants in Nunavut, with RSV as the leading infection. However, with high rates of concurrent infections and variability in terms of the RSV burden from year to year, these results highlight the value of RSV interventions alongside overall strengthening paediatric care in the region and further research into understanding underlying socio-demographic risk factors. Improved understanding of the infant ARI hospitalization burden can help support health policy decision-making as well as serve as a baseline for understanding the impact of any new interventions targeting ARI in infants in the region.

Contributors

DMG, JP, RJ, JE, and JR conceptualised the study and the methodology of the study with input from JA, JP, RD, LA, MS, HS, DS and AM. CW and IK conducted the investigation. DMG and MWK accessed and verified the overall data. YS and JNB conducted the statistical analyses and MWK wrote the first draft of the manuscript. All authors contributed to the interpretation and have read and approved the final manuscript.

Data sharing statement

Any summarised data could be made available rapidly, by emailing the corresponding author at david.goldfarb@cw.bc.ca. To obtain de-identified individual-level data (including a data dictionary), a specific request should be made to the same email address. The study investigators will work to provide the data in a timely manner, in accordance with our local regulations and assuming that permissions to share these data can be obtained by our Research Ethics Board.

Editor note

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Declaration of interests

Dr Papenburg reported grants from Merck, and personal fees from Enanta, outside the submitted work. Dr Robinson received an Honoria from the Alberta Pharmacists' Association (RxA) for a talk on RSV

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2025.101021.

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