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Pediatric sepsis during the COVID-19 pandemic

Population-level preventive measures for limiting the spread of infectious diseases, such as those implemented during COVID-19, will have the greatest effect on reducing pediatric sepsis morbidity and mortality.

ABSTRACT

Background: Approximately half the global cases of sepsis, a life-threatening condition, occur in children. Infectious diseases such as influenza, pneumonia, and respiratory syncytial virus are common causes of pediatric sepsis. We assessed changes in pediatric sepsis incidence and severity following the implementation of COVID-19 health protocols.

Methods: We conducted a retrospective observational cohort study using data on pediatric sepsis cases that were admitted to the pediatric ICU at BC Children's Hospital during five periods: March 2018–March 2019, March 2019–March 2020, March 2020–March 2021, March 2021–March 2022, and March 2022–March 2023. March 2018–March 2020 were considered pre-COVID-19 years; the following 3 years were considered COVID-19 years.

Results: We assessed 514 cases. The number of admissions decreased by 24.5% in the first 2 years of COVID-19 compared with the pre-COVID-19 years. However, between March 2022 and March 2023, the number of admissions

increased more than in any other year. Influenza and pneumonia cases similarly declined by 48.8% in the initial 2 years of COVID-19 yet were 44.2% higher between March 2022 and March 2023 than during the pre-COVID years' average.

Conclusions: Overall, there was an initial decrease in infection-related admissions to the pediatric ICU during the first 2 years of the COVID-19 pandemic, but the number of cases increased during the third year. Adaptations to provincial health and safety guidelines made in response to the pandemic may be related to these trends.

Background

Sepsis is a life-threatening condition that involves systemic inflammation and organ dysfunction due to a suspected infection.¹ It is estimated that there are upward of 45 million sepsis cases globally each year, approximately half of which occur in children.² Sepsis can result from either a bacterial or viral infection; pneumonia is the most common cause in children and adolescents.³ Preventive measures to reduce the burden of sepsis are crucial, given that there are limited specific therapies aside from supportive care and antibiotics.

In response to the COVID-19 pandemic in Canada, dramatic changes to social behaviors and regular hygiene practices have been made in an effort to reduce the spread of infection.⁴ In British Columbia, various levels of province-wide restrictions have been employed since March 2020, when

the number of community-transmitted COVID-19 cases began to increase. This has included closure of nonessential services, limits to the number of individuals permitted to gather in indoor and outdoor spaces, and routine wearing of masks. A number of restrictions have also been imposed specifically among children and adolescents, including periodic closures of BC schools and public playgrounds and changes to contact sports rules. These measures not only have limited the spread of COVID-19 but also have the potential to reduce the spread of other infectious diseases, such as influenza, respiratory syncytial virus, and other common causes of pediatric sepsis. The removal of these measures has had the capacity to alter the spread of transmission due to increased contact among individuals as they have resumed normal activities.

We conducted this analysis to determine whether there have been changes in the incidence, severity, and outcome of pediatric sepsis cases in the BC Children's Hospital pediatric ICU, a large referral ICU for children across BC, during the COVID-19 pandemic.

Methods

Study design

In this retrospective observational cohort study, we collected data on pediatric sepsis cases that were admitted to the pediatric ICU of BC Children's Hospital between March 2018 and March 2023. Cases were identified through critical care records using

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the International Statistical Classification of Diseases and Related Health Problems (ICD) code system. Our definition of sepsis included any child who had an infection that required hospitalization and admission to the pediatric ICU as an indication of organ dysfunction and suspected infection. Because nearly all children in mainland BC who require advanced critical care would be admitted to this ICU, this study serves as a surrogate for population-level disease incidence during the study period. There were no exclusion criteria.

Data collection

Data were collected using a REDCap database of information and included demographics, comorbidities, ICD code, Pediatric Risk of Mortality (PRISM) score, vital signs, symptoms, laboratory data, pathogen testing, and final outcome. The presence of comorbidities was defined as having acute diabetes, an oncology diagnosis, or a cardiovascular disease. Data were collected from information documented in patient charts. Fever was defined as a temperature of at least 38.5 °C, and rapid breathing and rapid heart rate were assessed using the pediatric systemic inflammatory response syndrome, sepsis, and septic shock criteria, based on the child’s age.⁵

Data analysis

Data from five periods were compared: March 2018–March 2019, March 2019–March 2020, March 2020–March 2021,

March 2021–March 2022, and March 2022–March 2023. March 2018–March 2020 were considered pre-COVID-19 years; the following 3 years were considered COVID-19 years. Descriptive analyses were conducted to assess any quantifiable changes in the incidence, severity, and source of infection of sepsis between time periods. The PRISM score is calculated based on a pediatric patient’s most severe vitals and lab values within the first 4 hours of pediatric ICU care to predict risk of mortality.⁶ Having a higher risk of mortality was used as a surrogate for higher illness severity in this study. The main outcomes were duration of stay in the pediatric ICU and ICU disposition.

Results

In total, 514 cases that met the criteria for infection and ICU admission were included in this study. Baseline characteristics of patients are presented in **Table 1**.

The number of sepsis cases was 200 (~100/year) pre-COVID and 314 (~105/year) during COVID, which represents a 5% increase per COVID year. However, the majority of admissions (51.9%) during COVID occurred between March 2022 and March 2023. Between March 2020 and March 2022, the number of sepsis cases declined by 24.5% relative to the pre-COVID years. The trends in admissions to the pediatric ICU during the study period are shown in the **Figure**.

Changes between years in ICD codes,

respiratory interventions at any point during admission, severity, and final outcomes are presented in **Table 2**. The number of ICD code diagnoses categorized as influenza and pneumonia declined from 43 (21.5/year) in the pre-COVID years to 22 (11.0/year) in the first 2 years of COVID-19. Between March 2022 and March 2023, there was an increase to 31 cases. The greatest number of total pediatric ICU admissions during COVID-19 occurred between September 2022 and January 2023 (97 cases), a trend that was also observed across Canada and around the world.⁷⁻⁹ A similar trend was observed in the “Other viral disease” category, in which the number of cases declined by 50% in the initial 2 years of COVID relative to each of the pre-COVID years but increased by 214.3% in the third year of COVID.

The ICD code for COVID-19 took effect 1 April 2020. During all 3 years of COVID-19, a total of 46 admissions to the pediatric ICU were attributable to COVID-19.

Respiratory interventions were assessed as a proportion of the number of cases in each year [**Table 2**]. The proportion of respiratory interventions exhibited a decrease in invasive respiratory interventions (6.9%) and non-invasive respiratory interventions (16.9%) in the initial 2 years of COVID. Once again, there was a subsequent increase the following year (37.4% invasive, 43.3% non-invasive) relative to the pre-COVID years’ average.

TABLE 1. Baseline characteristics of patients admitted to the BC Children’s Hospital pediatric ICU, March 2018–March 2023.

	March 2018– March 2019 (n = 110)	March 2019– March 2020 (n = 90)	March 2020– March 2021 (n = 58)	March 2021– March 2022 (n = 93)	March 2022– March 2023 (n = 163)
Age (mean ± SD) (months)	76.81 (± 64.90)	78.84 (± 62.73)	87.10 (± 74.11)	95.37 (± 94.32)	76.55 (± 64.11)
Sex					
Male	60 (54.55%)	54 (60.00%)	31 (53.45%)	52 (55.91%)	100 (61.35%)
Female	50 (45.45%)	36 (40.00%)	27 (46.55%)	41 (44.09%)	63 (38.65%)
Previous ICU admission	10 (9.09%)	8 (8.89%)	6 (10.34%)	6 (6.45%)	8 (4.91%)
Comorbidity	22 (20.00%)	19 (21.11%)	14 (24.14%)	22 (23.66%)	25 (15.34%)

The PRISM scores throughout all pre-COVID and COVID years remained relatively unchanged, staying within the lowest score group ≤ 9 with a $< 10\%$ risk of mortality.¹⁰

The median duration of stay in the pediatric ICU for children with sepsis increased in the first COVID-19 year with a 15.5-day median, whereas the remainder of COVID years and pre-COVID years had medians ranging from 7.6 to 9.8 days.

Discussion

Between March 2018 and March 2022, there was an initial decline in the number of sepsis cases in the pediatric ICU at BC Children’s Hospital and, by proxy, across BC. Between March 2022 and March 2023,

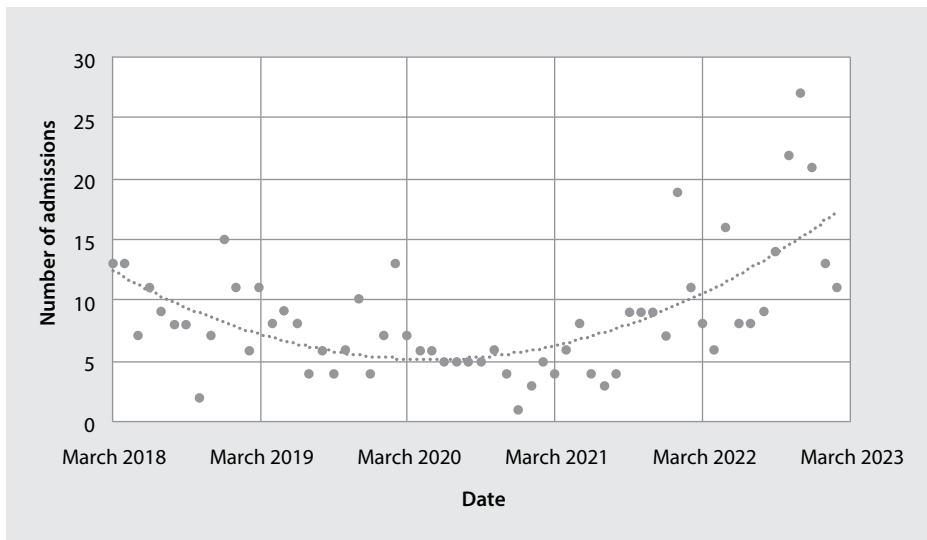


FIGURE. Monthly admissions to the BC Children’s Hospital pediatric ICU due to sepsis, March 2018–March 2023.

TABLE 2. Outcomes for patients admitted to the BC Children’s Hospital pediatric ICU, March 2018–March 2023.

	March 2018– March 2019 (n = 110)	March 2019– March 2020 (n = 90)	March 2020– March 2021 (n = 58)	March 2021– March 2022 (n = 93)	March 2022– March 2023 (n = 163)
<i>ICD-10 codes</i>					
Other bacterial diseases (A30–A49)	7 (6.4%)	10 (11.1%)	4 (6.9%)	9 (9.7%)	18 (11.0%)
Other viral diseases (B25–B34)	7 (6.4%)	7 (7.8%)	4 (6.9%)	3 (3.2%)	44 (27.0%)
Bacterial, viral, and other infectious agents (B95–B98)	27 (24.5%)	12 (13.3%)	5 (8.6%)	6 (6.5%)	14 (8.6%)
Severe sepsis with or without septic shock (R6520, R6521)	29 (26.4%)	21 (23.3%)	21 (36.2%)	23 (24.7%)	27 (16.6%)
Influenza and pneumonia (J09–J18)	20 (18.2%)	23 (25.6%)	7 (12.1%)	15 (16.1%)	31 (19.0%)
COVID-19 (U07.1)	N/A	N/A	4 (6.9%)	23 (24.7%)	19 (11.7%)
Other ICD codes	20 (18.2%)	17 (18.9%)	13 (22.4%)	14 (15.1%)	10 (6.1%)
<i>Respiratory intervention during admission</i>					
Invasive ventilation	54 (49.1%)	43 (47.8%)	28 (48.3%)	39 (41.9%)	99 (60.7%)
Non-invasive ventilation	51 (46.4%)	39 (43.3%)	22 (37.9%)	34 (36.6%)	83 (50.9%)
<i>Severity</i>					
Median Pediatric Risk of Mortality score	3.0	4.0	3.5	3.0	3.0
<i>Final outcomes</i>					
Median duration of stay in the pediatric ICU (days)	7.6	9.8	15.5	8.8	7.5
Discharged alive	102 (92.7%)	86 (95.6%)	57 (98.3%)	89 (95.6%)	152 (93.3%)
Death	8 (7.3%)	4 (4.4%)	1 (1.7%)	4 (4.3%)	11 (6.7%)

a resurgence in cases resulted in increased admissions to the pediatric ICU. These findings align with those from pediatric ICUs around the world, which showed an initial decline in cases in 2020 compared with previous years, particularly for respiratory syncytial virus and influenza admissions.¹¹⁻¹³ In addition, a subsequent rebound has been observed globally due to co-circulation of COVID-19, respiratory syncytial virus, and influenza as health and safety protocols have gradually returned to practices that are more like those that were in place pre-COVID.^{7-9,14} Therefore, sepsis has been observed to be a preventable disease with population-level interventions.

At the beginning of the pandemic, the Canadian federal and provincial governments made health recommendations and regulations to limit the spread of COVID-19.⁴ By encouraging mask wearing, social distancing, and increased handwashing, individuals were also preventing the spread of other common childhood illnesses that can ultimately lead to sepsis.¹² School closures and the cancellation of contact sports also reduced the opportunity for the spread of illness among children and adolescents. It is unclear which measures had the greatest impact in reducing the incidence of sepsis cases that required pediatric ICU admission. However, as mandates were gradually removed between March 2022 and March 2023, rates of admission to the pediatric ICU increased, particularly between September 2022 and January 2023, which coincided with influenza and respiratory syncytial virus season. In the coming years, it will be beneficial to observe how the trends in sepsis cases change with varying public health measures and whether rates will return to baseline pre-COVID years.

Additionally, the outcome of duration of stay appeared to show an increase in the first year of COVID (2020–2021), whereas the subsequent 2 years remained relatively stable within 2 days to the pre-COVID years. A prolonged duration of stay (12–20 days) in the pediatric ICU is associated with a higher risk of mortality.¹⁵ A trend in health care avoidance during the first

year of the pandemic may help explain the initial increase.¹⁶ Parents may not have been willing to bring their child to the hospital unless the illness was quite severe, thus increasing the duration of stay in those who were admitted. However, any explanation for this can only be hypothesized.

The potential impact on severity of illness was also explored through the measurement of PRISM scores and whether a

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patient required the use of a respiratory intervention. A higher PRISM score and use of respiratory intervention would indicate a more severe illness. The PRISM scores remained relatively the same throughout the study period with medians of < 10% risk of mortality in all years (scores ≤ 9). However, the number of respiratory interventions, both invasive and non-invasive, followed the trend of an initial decrease in the first 2 COVID-19 years and subsequent increase in the final year. It is uncertain whether this was a significant change, and further study of these differences should be explored after stratifying the cases by illness to determine whether one respiratory illness may have contributed more to the number of respiratory interventions than others.

In this study, the number of influenza and pneumonia cases declined by 48.8% during the first 2 years of COVID-19 compared with the 2 previous years. During the COVID-19 pandemic, caregiver attitudes toward influenza vaccinations for children in several countries shifted positively, and it was anticipated that there would be an increased distribution of influenza

vaccinations during the pandemic years.¹⁷ Because influenza is a common cause of pediatric hospitalization and a cause of pediatric severe sepsis, these rates may have also been affected by changes in health-seeking behaviors.¹¹ However, it is unclear whether the subsequent increase in influenza and pneumonia cases was related to alterations in hygiene practices as mandates changed or to changes in vaccination rates. Vaccine hesitancy has historically been a point of discussion among parents regarding their children, and the COVID-19 vaccinations generated some discourse that may have influenced other vaccination rates. COVID-19 vaccinations are one of the best ways to prevent other causes of sepsis, such as multisystem inflammatory syndrome in children, a life-threatening condition that may follow infection with SARS-CoV-2.^{18,19} Improving the delivery of vaccination information in terms of vaccine mechanism of action, importance, and availability may be an area of focus when considering methods to maintain relatively low rates of vaccine-preventable diseases.

Study limitations

This study had several limitations. First, our definition of sepsis included any child who had an infection that required hospitalization and admission to the pediatric ICU as an indication of organ dysfunction and suspected infection. However, the diagnosis of sepsis is based on a range of clinical signs and symptoms that are more typically diagnosed on a case-by-case basis.²⁰ For example, a symptom of fever may or may not be present when an individual has sepsis.²⁰ Therefore, it is uncertain whether our definition overrepresented or underrepresented the true incidence of sepsis. Additionally, it is unclear whether any differences in results would have been observed if more pediatric ICUs across Canada had been included in the study or if a longer time period had been assessed. Further study is needed to thoroughly assess any population-level changes in sepsis incidence. It is unclear whether our findings are significant or generalizable across Canada; however, because

this study involved a regionalized system, it likely represents province-level data on disease incidence. Additionally, because this was a retrospective observational cohort study, missing data in charts could not be collected. Some patient records did not include all vital sign measurements and laboratory results. Data on comorbidities were also collected at admission to the pediatric ICU, but they do not necessarily reflect trends throughout the duration of a patient's stay. Last, assessing the causality of public health measures on the incidence of sepsis in children who required pediatric ICU admission is difficult and any claims of a direct link are speculative; control groups in regions where there were different policy approaches would be required for that type of assessment.

Conclusions

The number of pediatric sepsis cases admitted to the pediatric ICU at BC Children's Hospital during the COVID-19 pandemic declined between March 2020 and March 2022 but increased between March 2022 and March 2023. New recommendations for hygiene practices and changes to social and health behaviors may have helped limit the spread of infection, which provides further proof that sepsis is a preventable disease and that population-level interventions will have the largest impact on reducing overall sepsis morbidity and mortality. However, the rapid increase in admissions during the process of removing public health measures also indicated that discussion is required regarding which hygiene practices may be practical long term and how recommendations can be best implemented within the pediatric population. ■

Competing interests

None declared.

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