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SARS-CoV-2 Infection of Young Infants during the Omicron Wave: A Case Series

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Established Facts

- The emergence of Omicron variant of the severe acute respiratory syndrome coronavirus 2 has caused significant public health concern due to its virulence and higher transmissibility.
- Milder forms of disease in neonates and infants infected with previous variants of SARS CoV-2 have been reported, although severe illness can occur.

Novel Insights

- We describe the clinical course of 4 infants including three premature neonates who presented during the emergence of Omicron variant and were tested positive for SARS-CoV-2 on PCR.
- Our experience with these infants provides evidence for a severe form of disease and varied clinical presentation in neonates and young infants who were likely infected with Omicron variant.

Keywords
SARS-CoV-2 · Omicron · Neonate · Infant

Abstract
We describe the clinical course of 4 infants infected with severe acute respiratory syndrome coronavirus 2. All were admitted to our tertiary care neonatal intensive care unit during the Omicron variant wave in our region. All 4 infants, who were less than 3 months of age, including three born prematurely, presented with critical illness. However, their clinical presentation varied considerably. Of them, two infants presented with apnea, one with respiratory distress, and one with gastrointestinal manifestation. Our experience with these four infants provides evidence for a severe form of disease and varied clinical presentation in neonates and young infants speculated to be infected with Omicron variant.

Introduction

The emergence of the Omicron variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused significant public health concern due to its higher transmissibility and the reduced protection against

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Table 1. Demographic, clinical, and laboratory characteristics of 4 cases

Characteristics	Case 1	Case 2	Case 3	Case 4
Age at presentation, days	69	63	6	25
Gestational age at birth, weeks	26	26	35	37
Birth weight, kg	1.02	0.92	2.57	3.8
Sex	Male	Male	Female	Female
Exposure with confirmed SARS-CoV-2 positive contact	Yes, mother	Yes, mother	Both parents asymptomatic and PCR negative	Both parents asymptomatic and PCR negative
Symptoms of COVID-19 infection				
Lethargy	Yes	Yes	No	Yes
Poor feeding	Yes	Yes	Yes	Yes
Resp. distress	Yes	Yes	Yes	No
Apnea	Yes	Yes	No	No
Vomiting	No	No	No	Yes
Diarrhea	No	No	No	Yes
Laboratory findings on the day of admission				
Hemoglobin, g/L	100	93	163	147
WBC, 10^9/L	6.96	4.11	10.7	23.25
Platelets, 10^9/L	303	177	76	397
Blood culture	No growth	No growth	No growth	No growth
CSF culture	Not done	Not done	No growth	No growth
Urine culture	No growth	No growth	No growth	No growth
SARS-CoV-2 PCR	Positive	Positive	Positive	Positive
PCR for other respiratory viruses	Negative	Negative	Negative	Negative
CRP, mg/L	2.9	36.7	1.7	52.2
X-ray chest	Coarse interstitial markings, focal opacity in left retrocardiac region	Coarse interstitium with diffuse reticular markings Repeated after 12 days: bilateral patchy opacities	Patchy granular opacities with reduction in left lung volume	Not done
Respiratory support during hospitalization	Endotracheal intubation and ventilation for 2 days, HHFNC 2 days, LF 3 days	Endotracheal intubation and ventilation for 2 days, CPAP and HHFNC for 16 days	NIPPV for 4 days, CPAP for 28 days	None
Maximum fraction of inspired oxygen during hospitalization	0.3	0.4	0.45	None
Treatment during hospitalization				
IV fluids	Yes	Yes	Yes	Yes
Antibiotics	Yes for 48 h	Yes for 48 h	Yes for 48 h	Yes for 48 h
Dexamethasone	No	Yes	Yes	No
Remdesivir	No	No	Yes	No
Total hospital stay for SARS-CoV-2 illness, days	9	20	36	10

it afforded by current vaccines [1–3]. Most current evidence indicates that young children infected with the SARS-CoV-2 have a milder course than older children and adults [4], but little is known about the presentation and clinical course in infants less than 3 months of age, particularly if they were born prematurely. We review here the clinical course of 4 young infants infected with SARS-CoV-2, admitted to our neonatal intensive care unit (NICU) in January 2022, during the Omicron wave in our region.

Case 1

A 2.5-month-old boy presented to a local emergency room with poor feeding, breathing difficulty, and inconsolable cry. He was born at 26 weeks gestation and discharged home at 35 weeks gestational age without any complications, 1 week prior to this presentation. He was lethargic, apneic, and had shallow breathing for which he was intubated and transferred to the NICU. A septic workup was done, and intravenous antibiotics were started. A nasopharyngeal swab for respiratory multiplex (influenza A, influenza A subtype H1, influenza A subtype H3, influenza B, respiratory syncytial virus [RSV] A, RSV B, adenovirus, human metapneumovirus, enterovirus, para influenza virus 1, para influenza virus 2, para influenza virus 3, para influenza virus 4, bocavirus, rhinovirus, coronavirus 229E, coronavirus) and SARS-CoV-2 polymerase chain reaction (PCR) was sent. He tested positive for SARS-CoV-2 (Table 1). His mother had received two doses of SARS-CoV-2 vaccine. She developed fever 1 day prior to her infant's presentation, with no other symptoms. She subsequently also tested positive for SARS-CoV-2. He was extubated to humidified high-flow nasal cannula oxygen after 2 days and subsequently weaned off all respiratory support after another 3 days. Antibiotics were stopped after 48 h when his blood and urine cultures were negative. He was discharged home in a stable condition after 9 days of admission.

Case 2

A 2-month-old boy presented to a local emergency room with lethargy, poor perfusion, respiratory distress, and apnea. He was delivered at 26 weeks and 3 days gestational age and was discharged home at 35 weeks without any complications, 3 days prior to this presentation. He was lethargic, apneic, and had respiratory distress, for which he was intubated. He received one dose of dexamethasone and was then transferred to our NICU. Intravenous antibiotics were commenced after sending blood and urine cultures. His nasopharyngeal swab was also sent which tested positive for SARS-CoV-2 by PCR (Seegene) in which the targets used were *E* gene, *N* gene, RdRp, and *S* gene sequencing for N501Y. His mother was vaccinated and had no symptoms but was tested positive for SARS-CoV-2 by PCR. He was extubated to nasal continuous positive airway pressure (CPAP) 2 days later. Antibiotics were stopped after cultures were negative at 48 h. He received inhaled budesonide for a week and was subsequently weaned to low-flow oxygen given through nasal cannula. He remained stable until day 12 of admission when his respiratory condition worsened. CPAP via nasal prongs was reinstituted. Dexamethasone was started and continued for 10 days, and antibiotics were given for 7 days. He was weaned off respiratory support on day 18 and discharged home on day 20 of admission in a stable condition.

Case 3

A 6-day-old girl was transferred from a local hospital for poor feeding and increasing respiratory distress. She was born at 35 weeks of gestation in a community hospital where she was admitted for transient tachypnea of the newborn and treated with CPAP for the first 36 h of life. She remained stable until day 6 of life when she developed oxygen desaturations and respiratory distress. CPAP was restarted with a fraction of inspired oxygen of 0.45. Cultures of blood, cerebral spinal fluid, and urine were obtained, and intravenous antibiotics were started. A nasopharyngeal swab for respiratory multiplex panel and SARS-CoV-2 PCR was done. She tested positive for SARS-CoV-2 (Table 1). Both her parents subsequently had nasopharyngeal swabs sent for SARS-CoV-2 PCR which were negative. They were both vaccinated. Antibiotics were stopped after 48 h when blood, urine, and CSF cultures were negative. Her X-ray chest showed bilateral patchy granular opacities suggestive of pneumonia. She was given remdesivir for 5 days and dexamethasone for 10 days. She also presented with thrombocytopenia which resolved spontaneously. Chest radiograph repeated on day 13 of admission showed improved aeration in both lungs with hazy opacities in the right lung. She was given inhaled budesonide. She was transferred to a community hospital on nasal CPAP. She was successfully weaned to room air and discharged home on day 29 of life in a stable condition.

Case 4

A 25-day-old term baby girl presented to a local emergency room with lethargy and a 5-day history of vomiting and profuse diarrhea. She was exclusively formula fed. She had lost 15% of a recent body weight, sodium was167 mmol/L, and a venous sample showed pH of 6.94, bicarbonate 3 mmol/L, and a base deficit of 29 mmol/L. After fluid resuscitation and obtaining cultures of blood, urine, and cerebral spinal fluid, she was transferred to our NICU. Stool bacterial culture and multiplex PCR panel for gastrointestinal pathogens (*Salmonella*, *Shigella*, *Escherichia Coli*, *Campylobacter* species, *Yersinia*, *Clostridium difficile*, *Rotavirus*, *Norovirus*, Adenovirus, *Sapovirus*, Astrovirus) were negative. A nasopharyngeal swab for SARS-CoV-2 PCR (Seegene) was positive in which the targets used were *E* gene, N gene, RdRp, and *S* gene sequencing for N501Y. Nasopharyngeal swabs from the parents were negative for SARS-CoV-2 detected by PCR. Both parents were vaccinated. Antibiotics were stopped after 48 h. She was treated with intravenous fluids and had no further episodes of diarrhea. She was transferred to a community hospital on day 3 of admission, when she tolerated an elemental formula. She was discharged home without complications 5 days later. Nasopharyngeal swab 1 month after her initial presentation was negative for SARS-CoV-2 detected by PCR.

Discussion

Data on the severity of disease associated with the Omicron variant of SARS-CoV-2 in young infants are limited. This case series describes 4 infants less than 3 months of age, including three who were born prematurely, who tested positive for SARS-CoV-2 by PCR during the Omicron variant wave. They presented between 6 and 69 days of age which is consistent with earlier reports showing horizontal transmission as the commonest route of infection, although cases of transplacental acquisition have also been reported [5–7]. All 4 infants presented with severe symptoms and required admission in NICU. Throughout the previous waves of the pandemic spanning over 2 years, only 3 infants with SARS-CoV-2 infection were admitted to our tertiary care NICU. Of note, these four infants were admitted to our NICU within a span of 9 days (from January 7 to January 15, 2022). No other SARS-CoV-2-infected infants were admitted to NICU at the Hospital for Sick Children during the peak of the Omicron wave.

Clinical presentation of SARS-CoV-2 infection in young infants can vary considerably [8–11]. Milder forms of disease in infants infected with previous variants of SARS CoV-2 have been reported, although severe illness can occur [8, 9]. In a case series of 36 infants aged less than 90 days, 4 had severe illness with significant morbidity, including one death [4]. In a population-based cohort study of 66 SARS-CoV-2-infected young infants (50 term and 16 preterm) requiring hospitalization, apnea, lethargy, respiratory symptoms, poor feeding, and vomiting were commonly reported symptoms [11].

The two extremely preterm babies in our report presented with respiratory distress and apnea. Although RSV is the most common virus associated with apnea, many other viruses are also known to cause apnea in infants [12]. Premature infants with lower gestational age are more likely to develop apnea associated with viral respiratory tract infections [12]. This is consistent with the findings in our case series. The third infant who presented with isolated respiratory distress was treated with noninvasive ventilatory support.

Although much of the evidence about SARS-CoV-2 neonatal infections is focused on respiratory symptoms, gastrointestinal manifestations have also been described in literature [5]. In a systematic review incorporating 86 reports of SARS-CoV-2 neonatal infections, gastrointestinal symptoms have been described in 10% of neonates [5]. Consistent with this finding, our fourth case presented with gastrointestinal symptoms. Since this is a small case series, further surveillance is required to understand the full clinical spectrum of Omicron variant in young infants.

Limited information is available describing the clinical presentation in infants younger than 3 months of age, who were infected with the Omicron variant of SARS-CoV-2. The existing evidence regarding the clinical presentation of Omicron variant in pediatric population reports mild to moderate disease in children including neonates and infants over 3 months of age [13–15]. To our knowledge, only one case report is published to date which describes a severe clinical course in a term neonate infected with Omicron variant. He presented on day 29 of life with apnea and seizures requiring mechanical ventilation [16]. Our experience with these four infants provides evidence for a severe form of disease with varied clinical presentation in young infants. Given the likelihood for disease severity in young infants, this knowledge may guide clinicians in planning the allocation of health care resources and help them in developing an understanding about its management. Larger studies are required to explicate the severity and extent of this disease in neonates and young infants and to understand its effects on long-term outcomes. A limitation of this study is that SARS-CoV-2 genomic sequencing or probing for Omicron-associated mutations was not done on samples from these infants. However, it is highly likely that these infants were infected with the Omicron variant B.1.1.529 which accounted for 98.8% of all circulating SARS-CoV-2 variants during January 2022 [17]. In summary, this report expands our understanding of the range and severity of disease caused by the Omicron variant of SARS-CoV-2 in young infants.

Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from parents of all 4 infants to publish their infants' cases. The study protocol was reviewed and approved by the Hospital for Sick Children's research ethics board, approval number 1000079251.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Drs. Najmus Sehr Ansari, Douglas M. Campbell, Mohammed A. Sarhan, and Estelle B. Gauda conceptualized and designed the report, drafted the initial manuscript, and reviewed and revised the manuscript. Drs. Douglas Watson and Ari Bitnun, pediatric infectious disease specialist with expertise in assessment and treatment of infants with SARS-CoV-2, conceptualized and designed the report, provided content expertise, supervised the literature review, and critically reviewed the original and revised manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Data Availability Statement

All data related to this case series were extracted from the electronic medical record. Further inquiries can be directed to the corresponding author.

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