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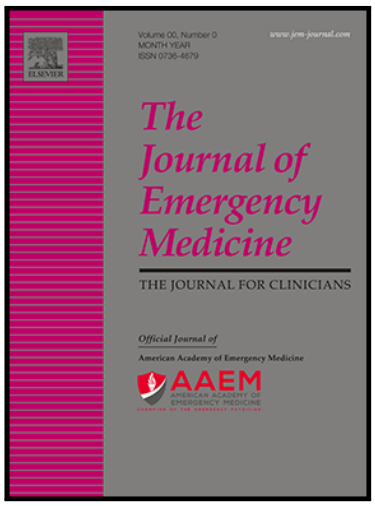

Research Brief: COVID-19 croup is observed in older children during the Omicron wave in New York City

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Research Brief: COVID-19 croup is observed in older children during the Omicron wave in New York City

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Clinical Trial Registration (if any): N/A

Abbreviations: Coronavirus Disease 2019 (COVID-19)

Contributors' Statement Page

Nisha Narayanan, Karen Acker, and Deborah Levine conceptualized and designed the study, coordinated and supervised data collection, drafted the initial manuscript, and reviewed and revised the manuscript.

Samantha Langer, Will Simmons, and Alan Wu designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript.

Steven Rosenblatt, Erika Abramson, Zachary Grinspan, and Jin-Young Han conceptualized and designed the study and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

STRUCTURED ABSTRACT

Background:

The Omicron variant of SARS-CoV2 has a predilection for the upper airways, causing symptoms such as sore throat, hoarse voice, and stridor.

Objective:

We describe a series of children with COVID-19-associated croup in an urban multicenter hospital system.

Methods:

We conducted a cross-sectional study of children ≤ 18 years presenting to the ED during the COVID-19 pandemic. Data were extracted from an institutional data repository comprised of all patients tested for SARS-CoV2. We included patients with a croup diagnosis by ICD-10 code and a positive SARS-CoV2 test within 3 days of presentation. We compared demographics, clinical characteristics, and outcomes for patients presenting during a pre-Omicron period (March 1, 2020- December 1, 2021) to the Omicron wave (December 2, 2021-February 15, 2022).

Results:

We identified 67 children with croup, ten (15%) pre-Omicron and 57 (85%) during the Omicron wave. The prevalence of croup among SARS-CoV-2 positive children increased by a factor of 5.8 (95% CI, 3.0, 11.4) during the Omicron wave compared to prior. More patients

were ≥ six years in the Omicron wave than prior (19% vs 0%). The majority were not hospitalized (77%). More patients ≥ six years received epinephrine therapy for croup during the Omicron wave (73% vs 35%). Most patients ≥ six years had no prior croup history (64%) and only 45% were vaccinated against SARS-CoV2.

Conclusion:

Croup was prevalent during the Omicron wave, atypically affecting older patients ≥ six years old. COVID-19- associated croup should be added to the differential diagnosis of children with stridor, regardless of age.

KEYWORDS

SARS-CoV2; croup; laryngotracheitis; COVID-19

INTRODUCTION

Understanding how COVID-19 affects children is important, as is understanding the changing clinical landscape as new variants of the virus emerge. Compared to previous variants of SARS-CoV-2, the Omicron variant has shown a predilection for the upper airways, manifesting as sore throat and hoarse voice in adults and croup in children [1,2]. Croup is a clinical syndrome characterized by inspiratory stridor, barking cough, and hoarseness due to the added narrowing of small subglottic airways by viral-induced inflammation. It typically occurs in children between six months and three years of age, and is rare in children over six years old due to their larger airway diameters[3,4]. Here, we describe the clinical characteristics and disease course of a pediatric case series of COVID-19-associated croup from a multi-

center hospital system in a large urban center during the COVID-19 pandemic in New York City (NYC).

METHODS

We conducted a cross-sectional study of patients ≤18 years old who presented to three affiliated urban pediatric emergency departments (ED) during the COVID-19 pandemic. This study was approved by the Weill Cornell Medicine (WCM) Institutional Review Board. Data were extracted from the WCM COVID-19 Institutional Data Repository (IDR), which aggregates data on patients tested for SARS-CoV-2 from electronic health records of New York-Presbyterian/ Weill Cornell Medical Center[5]. Patients were divided into pre-Omicron (March 1, 2020 to December 1, 2021) and Omicron waves (December 2, 2021 to February 15, 2022). Cohort date ranges were selected based on the prevalence of SARS-CoV-2 variants as reported by the NYC Department of Health and Mental Hygiene data[6]. We included ED patients with a croup diagnosis within 24 hours of presentation (ICD 10: J05.0, R06.1, 464.2, J04.2)[7], and a positive nasopharyngeal reverse transcription polymerase chain reaction SARS-CoV-2 test within three days of presentation. Repeat visits within three days of a prior visit were considered one clinical course. Abstracted data was corroborated with manual chart review. We reported patient demographic and clinical characteristics, including age, sex, race, ethnicity, vaccination status, and medical complexity as defined using the Pediatric Medical Complexity Algorithm[8]. We also reported clinical outcomes such as disposition, medication administration, and need for respiratory support.

RESULTS

Our cohort comprised 1,751 pediatric ED patients who tested positive for SARS-CoV-2, of which 865 (49%) were during the Omicron wave. We identified 67 of these children with croup; ten (15%) in the pre-Omicron period and 57 (85%) during the Omicron wave. The prevalence of croup among COVID-19-positive children increased by a factor of 5.8 (prevalence ratio = 5.8, 95% CI 3.0, 11.4) during the Omicron wave compared to the pre-Omicron period. Table 1 describes patient demographics and disposition. Median age was similar for both groups, but more patients ≥ six years old were in the Omicron group (0 vs. 19%). The majority of patients were not hospitalized (80% in pre-Omicron vs. 77% in Omicron wave). Comprehensive viral testing was performed in 34% of croup patients, with only 4 co-infections noted.

Table 2 describes the clinical characteristics of the 57 croup patients in the Omicron wave. The majority affected were under three years old (61%), and 19% were ≥ six years old. All patients ≥ six years old presented during the Omicron period. Though most children received steroids, more patients ≥ six years old received racemic epinephrine, suggesting a more severe initial presentation with stridor at rest than in the younger children (73% vs 35%). None were given Remdesivir. The most severe case was a ten-year-old who required multiple doses of racemic and intramuscular epinephrine, oxygen, and ICU admission. The majority of older patients (64%), including the aforementioned patient, had no prior croup history. All of these patients demonstrated significant improvement in their stridor with ED intervention and no additional work up such as x-ray, otolaryngology consult, or laryngoscopy was performed. In this ≥ six years old group, in which all patients were eligible for the COVID-19 vaccine, only 45% were fully vaccinated with two doses.

DISCUSSION

We found an increased prevalence of croup during the COVID-19 Omicron wave, notably among an older cohort of children than were affected in the pre-Omicron period. Most older children had no previous croup history and were under-vaccinated for COVID-19. Although few were hospitalized, the majority required steroids and racemic epinephrine, suggesting a more severe ED presentation than in younger children.

The association of the Omicron variant and croup has been previously described[2,9]. We identified an older subgroup of croup patients who, historically, have rarely been affected[3]. Animal models have demonstrated the Omicron variant's predilection for the upper respiratory tract compared to lung parenchyma[10]. This variant has also been associated with acute odynophagia and severe sore throat in adults[11]. It is unclear whether the variant's direct effects on the upper airways or a host inflammatory response accounts for the clinical presentation of croup in this unusual age group. Further investigations are needed to understand the mechanisms driving this association.

LIMITATIONS

The study is limited by its small sample size and data from a single urban health system. Although we cannot confirm the SARS-CoV-2 variant causing infection, the time periods in this study were based on NYC Omicron variant testing[6]. The impact of viral co-infection is unclear due to a lack of comprehensive viral testing. In addition, our database may not have captured all vaccination data external to our hospital system.

CONCLUSIONS

In summary, we found an increased prevalence of COVID-19-associated croup during the Omicron wave atypically affecting older children. COVID-19 associated croup should now be considered in the differential diagnosis of older children presenting with stridor. Further investigation is needed to elucidate the pathophysiology of COVID-19-associated croup to assist with diagnosis and management of these children.

ARTICLE SUMMARY

Why is this topic important?

Understanding how COVID-19 affects children is important, as is understanding the changing clinical landscape as new variants of the virus emerge. The Omicron variant of SARS-CoV-2 appears to cause croup in older children in which the disease rarely presents.

What does this study attempt to show?

This study describes the clinical characteristics and disease course of a pediatric case series of COVID-19 croup from a multi-center hospital system in a large urban center during the COVID-19 pandemic in New York City (NYC).

What are the key findings?

Older children >/=6 years old, in which croup is typically rare, presented with croup during the Omicron wave of SARS-CoV-2. The majority of this older cohort required steroids and racemic epinephrine, suggesting a more severe ED presentation than in younger children.

How is patient care impacted?

COVID-19-associated croup should now be considered in the differential diagnosis of older children presenting with stridor and/or respiratory distress.

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Table 1. Demographic characteristics of SARS-CoV-2 croup patients

Patients ≤18 years with 1+ ED visit* with (1) 1+ croup diagnosis within 24 hours after presentation, and (2) 1+ positive SARS-CoV-2 PCR lab(s) ±3 days from presentation.

Characteristic	Pre-Omicron, N = 10	Omicron, N = 57	p-value
Age [median (IQR)]	2.00 (1.00, 3.00)	2.00 (1.00, 5.00)	0.7
Age			
<3y	5 (50%)	36 (63%)	
3y to <6y	5 (50%)	10 (18%)	
6y to <12y	0 (0%)	11 (19%)	
Sex			>0.9
Female	3 (30%)	20 (35%)	
Male	7 (70%)	37 (65%)	
Race/Ethnicity			0.5
White	2 (20%)	21 (37%)	
Hispanic or Latino or Spanish Origin	3 (30%)	20 (35%)	
American Indian or Alaska Native	0 (0%)	1 (1.8%)	
Asian	2 (20%)	4 (7.0%)	
Black or African American	0 (0%)	2 (3.5%)	

Table 1. Demographic characteristics of SARS-CoV-2 croup patients

Patients ≤18 years with 1+ ED visit* with (1) 1+ croup diagnosis within 24 hours after presentation, and (2) 1+ positive SARS-CoV-2 PCR lab(s) ±3 days from presentation.

Characteristic	Pre-Omicron, N = 10	Omicron, N = 57	p-value
Other Combinations Not Described	1 (10%)	3 (5.3%)	
Unknown	2 (20%)	6 (11%)	
Admission status			0.5
Not admitted	8 (80%)	44 (77%)	
Admission to floor	1 (10%)	11 (19%)	
Admission to PICU	1 (10%)	2 (3.5%)	
Medical Complexity*			0.4
No chronic disease	9 (90%)	39 (68%)	
Non-complex chronic disease	0 (0%)	10 (18%)	
Complex chronic disease	1 (10%)	8 (14%)	

*Medical complexity defined using the Pediatric Medical Complexity Algorithm[8]

Table 2. Clinical characteristics of croup patients during Omicron wave

Patients ≤18 years with 1+ ED visit* with (1) 1+ croup diagnosis within 24 hours after presentation, and (2) 1+ positive SARS-CoV-2 PCR lab(s) ±3 days from presentation.

Characteristic	<6mo, N = 2	3y to <6y, N = 10	6mo to <3y, N = 34	6y to <12y, N = 11
Age	0.00 (0.00, 0.00)	4.00 (4.00, 5.00)	1.00 (1.00, 2.00)	8.00 (6.50, 9.00)
Vaccines				
0	2 (100%)	7 (70%)	34 (100%)	5 (45%)
1	0 (0%)	2 (20%)	0 (0%)	1 (9.1%)
2	0 (0%)	1 (10%)	0 (0%)	5 (45%)
History of Croup	0 (0%)	4 (40%)	3 (8.8%)	4 (36%)
Steroid	2 (100%)	10 (100%)	33 (97%)	11 (100%)
Racemic epinephrine	1 (50%)	2 (20%)	13 (38%)	8 (73%)
Racemic epinephrine doses				
1	0 (0%)	2 (100%)	6 (46%)	7 (88%)

Table 2. Clinical characteristics of croup patients during Omicron wave

Patients ≤18 years with 1+ ED visit* with (1) 1+ croup diagnosis within 24 hours after presentation, and (2) 1+ positive SARS-CoV-2 PCR lab(s) ±3 days from presentation.

Characteristic	<6mo, N = 2	3y to <6y, N = 10	6mo to <3y, N = 34	6y to <12y, N = 11
2	0 (0%)	0 (0%)	5 (38%)	0 (0%)
3	1 (100%)	0 (0%)	1 (7.7%)	0 (0%)
4	0 (0%)	0 (0%)	0 (0%)	1 (12%)
5	0 (0%)	0 (0%)	1 (7.7%)	0 (0%)
Intramuscular epinephrine	0 (0%)	1 (10%)	0 (0%)	1 (9.1%)
Respiratory support	0 (0%)	0 (0%)	2 (5.9%)	1 (9.1%)
Admitted	1 (50%)	2 (20%)	8 (24%)	1 (9.1%)
Admission location				
Floor	1 (100%)	2 (100%)	7 (88%)	0 (0%)
ICU	0 (0%)	0 (0%)	1 (12%)	1 (100%)
LOS inpatient (days)	1.10 (1.10, 1.10)	0.90 (0.50, 2.15)	1.20 (1.10, 2.60)	1.50 (1.50, 1.50)
LOS ICU (days)	NA (NA, NA)	NA (NA, NA)	4.1000 (4.1000, 4.1000)	NA (NA, NA)

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: