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# Comparative analysis of croup severity and treatment in pediatric patient: a study of COVID-19 positive vs. negative cases during peak Omicron

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## Abstract

**Background** The Omicron variant of SARS-CoV-2 has been associated with unique clinical presentations in children, including croup-like symptoms such as barking cough, hoarseness, and respiratory distress. This study aimed to compare the clinical, laboratory, and treatment characteristics of hospitalized pediatric patients with croup who tested positive or negative for COVID-19 during the Omicron wave.

**Methods** A retrospective, descriptive-analytical study was conducted on 111 pediatric patients hospitalized with croup at Bahrami Children's Hospital and the Children's Medical Center in Iran from January 21 to March 20, 2022. Patients were categorized into two groups: PCR-positive (Omicron group,  $n=30$ ) and PCR-negative (non-Omicron group,  $n=81$ ). Data on demographics, clinical severity, laboratory indices, treatments, and outcomes were extracted and analyzed using SPSS version 20.

**Results** The mean age of the Omicron group was significantly younger ( $16.93 \pm 24.80$  months) compared to the non-Omicron group ( $32.58 \pm 37.26$  months;  $p=0.049$ ). Symptom severity was higher in the Omicron group, with moderate to severe symptoms observed in 73.4% of patients, compared to 32.1% in the non-Omicron group ( $p=0.001$ ). The Omicron group had longer hospital stays ( $2.59 \pm 3.93$  vs.  $2.11 \pm 2.75$  days;  $p=0.016$ ) and required more nebulized epinephrine ( $2.47 \pm 1.27$  vs.  $1.77 \pm 1.003$  days;  $p=0.003$ ) and repeat corticosteroid doses (83.3% vs. 38.3%;  $p=0.0001$ ). Laboratory findings showed no significant differences between the groups (all  $p > 0.05$ ).

**Conclusion** Children with croup during the Omicron surge exhibited increased symptom severity, required more intensive treatment, and experienced longer hospital stays compared to those without COVID-19. These findings emphasize the need for heightened clinical awareness and tailored management strategies for Omicron-related croup in pediatric populations.

**Keywords** Croup, COVID-19, Omicron variant, Children, Hospitalization, Pediatric respiratory illness

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## Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has profoundly altered the landscape of global health since its emergence in December 2019 in Wuhan, China. Initial cases presented with symptoms including fever, dry cough, and shortness of breath, predominantly involving the lower respiratory tract [1, 2]. As of November 2024, the global impact of the COVID-19 pandemic has been immense [3]. Cumulative reports indicate over 774 million confirmed cases and more than 7 million deaths worldwide. These numbers continue to reflect the scale and persistence of SARS-CoV-2's impact, with variations in reporting and public health measures affecting the trends across regions [4, 5].

Since its declaration as a pandemic in March 2020, SARS-CoV-2 has undergone several genetic mutations, resulting in the emergence of new variants with varying degrees of transmissibility, pathogenicity, and immune evasion [6, 7]. Among these, the Omicron variant (B.1.1.529), first identified in South Africa in November 2021, has been particularly concerning [8]. The WHO classified it as a variant of concern (VOC) due to its extensive mutations, especially in the spike (S) protein, which facilitate increased transmissibility and partial resistance to immunity from prior infections or vaccinations. Within weeks of its emergence, Omicron led to unprecedented global case surges, with over 15 million cases reported worldwide in a single week. Its subvariants, including BA.1, BA.2, and BA.5, quickly became dominant in various regions, underscoring Omicron's adaptability and potential to outcompete earlier variants [9, 10].

Although Omicron is associated with generally milder disease in comparison to the Delta variant, it has not been without consequence. Pediatric populations, particularly unvaccinated children under the age of five, have experienced a rise in hospitalizations during the Omicron wave [11, 12]. This trend has been attributed to the variant's heightened transmissibility and the increased vulnerability of children lacking prior immunity or vaccination coverage. Clinical manifestations in children infected with Omicron often mimic those of previous SARS-CoV-2 variants, including fever, cough, and respiratory distress. However, unique presentations, such as croup-like symptoms, have garnered significant attention from clinicians and researchers [13, 14].

Croup, or laryngotracheobronchitis, is a common upper respiratory condition in young children caused primarily by viral infections such as parainfluenza. Characterized by a barking cough, hoarseness, stridor, and varying degrees of respiratory distress, croup is generally self-limiting and managed in outpatient settings. Severe cases may require hospitalization, oxygen support, and treatment with nebulized epinephrine or corticosteroids.

During the Omicron surge, several studies and case reports observed an increased incidence of croup among children with confirmed COVID-19, suggesting a potential link between the variant and upper respiratory tract inflammation [15].

These findings underscore the need for a deeper understanding of the clinical characteristics and treatment outcomes in children affected by this dual pathology [16].

This study seeks to address these gaps by conducting a comparative analysis of children hospitalized with croup during the Omicron surge, examining differences in clinical, laboratory, and therapeutic outcomes between COVID-19-positive and COVID-19-negative cases. By providing insight into the interplay between Omicron and croup, this research aims to inform clinical practice and optimize management strategies for children affected by these concurrent conditions.

## Method

### Study design

This study employed a descriptive-analytical design with a practical aim, conducted through a retrospective review of patient records at two major pediatric hospitals: Bahrami Children's Hospital and the Children's Medical Center in Iran. The research sought to compare clinical, laboratory, and treatment outcomes between children hospitalized with croup during the Omicron variant surge who tested positive versus negative for SARS-CoV-2 by polymerase chain reaction (PCR). The study design was retrospective and descriptive-analytical, utilizing data extracted from medical records. Verbal and written informed consent was obtained from the parents for the use of medical records and participation in a brief questionnaire, which gathered additional demographic information not readily available in the medical charts. The questionnaire was used solely for the purpose of capturing family-related demographic data and did not involve any medical interventions.

### Study population and sample

The study included all pediatric patients diagnosed with croup and admitted to the aforementioned hospitals during the peak of the Omicron wave (January 21 to March 20, 2022). Inclusion criteria were:

1. A clinical diagnosis of croup based on typical symptoms such as barking cough, stridor, and respiratory distress.
2. Availability of a nasopharyngeal PCR test result for SARS-CoV-2 (either positive or negative).

Exclusion criteria were:

1. Incomplete or missing clinical and demographic data in medical records.
2. Cases managed solely on an outpatient basis without hospitalization.

A total of 111 patients were included after applying these criteria. The study cohort was divided into two groups:

- **PCR-positive group:** 30 patients with confirmed SARS-CoV-2 infection.
- **PCR-negative group:** 81 patients without evidence of SARS-CoV-2 infection.

### Data collection

Data were extracted retrospectively from patient medical records using a structured data extraction form. The form captured the following variables: demographic data, clinical presentation, treatment and interventions, and hospital course. Vaccination status was not included as a variable due to the limited vaccination coverage for children under five years of age during the study period in the region, making it unlikely to provide meaningful differentiation between groups.

In this retrospective study, patients were tested for SARS-CoV-2 using nasopharyngeal PCR during the Omicron variant wave. The study specifically focused on SARS-CoV-2 due to the predominant role of the virus during this time and the availability of PCR testing for SARS-CoV-2. While we acknowledge that other respiratory viruses such as Parainfluenza, Influenza, and RSV

are common in pediatric respiratory illnesses, testing for these viruses was not included in this study due to limited resources and the primary focus on COVID-19. Future studies may consider broader viral panels to provide a more comprehensive understanding of the pediatric respiratory illness landscape during the pandemic.

### Ethical considerations

All stages of this study adhered to the Declaration of Helsinki and were approved by the Institutional Review Board (IRB) of the Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1402.135). This study involved a retrospective review of medical records; thus, no new consent was obtained. However, all patients included in the analysis had already provided verbal and written informed consent as part of routine hospital admissions or prior clinical protocols, ensuring their data could be used for research purposes. The confidentiality of patient data was strictly maintained.

### Statistical analysis

The sample size was determined using the formula for differences in proportions between two independent groups, with a power of 80% ( $Z1-\beta=0.84$ ) and a confidence level of 95% ( $Z1-\alpha/2=1.96$ ). Based on prior studies, expected proportions were set at 56.3% (P1) and 12.4% (P2), resulting in a calculated minimum sample size of 42. Data were entered and analyzed using SPSS version 29. Descriptive statistics were employed to summarize demographic and clinical characteristics. Quantitative variables were reported as means with standard deviations (SD), while qualitative variables were presented as frequencies and percentages. Kolmogorov-Smirnov tests to assess the distribution of quantitative data. Also, Independent samples t-tests for continuous variables and Chi-square tests for categorical variables. A p-value of < 0.05 was considered statistically significant.

## Results

### Demographic and clinical characteristics

A total of 111 children diagnosed with croup were included in the study, comprising 30 patients with positive PCR results for SARS-CoV-2 (Omicron group) and 81 patients with negative PCR results (non-Omicron group). The mean age of patients in the Omicron group was significantly younger at  $16.93 \pm 24.80$  months, compared to  $32.58 \pm 37.26$  months in the non-Omicron group ( $p=0.049$ ). Gender distribution was comparable between the groups, with 66.7% male and 33.3% female in the Omicron group versus 65.4% male and 34.6% female in the non-Omicron group ( $p=0.903$ ) (Table 1).

**Table 1** Clinical characteristics of 111 children hospitalized for croup in Omicron peak

Characteristics	group		P value
	Pcr positive	Pcr negative	
No. of patients	30	81	
Age, mon (median $\pm$ sd)	$24.80 \pm 16.93$	$37.26 \pm 32.58$	0.049
Sex No.(%)			0.903
Male	20 (66.7)	53 (65.4)	
Female	10 (33.3)	28 (34.6)	
Severity of Croup symptoms			
Mild	8 (26.6)	55 (67.9)	0.001
Mod	16 (53.4)	19 (23.5)	
Severe	6 (20.0)	7 (8.6)	
Length of stay in hospital, day	$3.93 \pm 2.59$	$2.75 \pm 2.11$	0.016
ICU admission No.(%)	4 (13.3)	4 (4.9)	0.129
Length of stay in ICU, day	$0.6 \pm 1.75$	$0.2 \pm 1.08$	0.150
mechanical ventilation No.(%)			
mask	26 (86.7)	78 (96.3)	0.064
intube/niv	4 (13.3)	3 (3.7)	
epinephrine nebulizer, day	$2.47 \pm 1.27$	$1.77 \pm 1.003$	0.003
repeat dose of corticosteroids	25 (83.3)	31 (38.3)	0.0001

Corresponding Westley scores for level of severity would be 0 to 2 for mild croup, 3 to 5 for moderate croup, 6 to 11 for severe croup

### Symptom severity and Westley croup scores

Symptom severity, assessed using the Westley Croup Score, demonstrated significant differences between the groups. Moderate to severe symptoms were more common in the Omicron group, with 53.4% classified as moderate and 20% as severe. In contrast, the majority of the non-Omicron group (67.9%) exhibited mild symptoms, with only 23.5% classified as moderate and 8.6% as severe ( $p = 0.001$ ).

### Hospitalization and treatment indicators

The length of hospital stay was significantly longer in the Omicron group, averaging  $2.59 \pm 3.93$  days, compared to  $2.11 \pm 2.75$  days in the non-Omicron group ( $p = 0.016$ ). Similarly, the use of nebulized epinephrine was more intensive in the Omicron group, with a mean duration of  $2.47 \pm 1.27$  days versus  $1.77 \pm 1.003$  days in the non-Omicron group ( $p = 0.003$ ).

The need for repeat corticosteroid doses was significantly higher among the Omicron group, with 83.3% requiring additional doses compared to 38.3% in the non-Omicron group ( $p = 0.0001$ ).

### Intensive care unit (ICU) admission and respiratory support

Although ICU admission rates and duration of ICU stay were not statistically different between the groups ( $p = 0.129$  and  $p = 0.150$ , respectively), trends suggested a higher frequency of ICU admission in the Omicron group (13.3% vs. 4.9%). Similarly, while the need for mechanical ventilation or non-invasive ventilation (NIV) did not differ significantly ( $p = 0.064$ ), the Omicron group exhibited a slightly higher rate of intubation.

### Laboratory findings

No statistically significant differences were observed between the groups in laboratory indices, including white blood cell count (WBC), lymphocyte percentage, neutrophil count, hemoglobin, platelet count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels (all  $p > 0.05$ ) (Table 2).

### Discussion

This study provides valuable insights into the clinical presentation, severity, and management outcomes of children hospitalized with croup during the peak of the Omicron variant surge. By comparing PCR-positive and PCR-negative cases, we identified several critical differences that underscore the unique impact of the Omicron variant on pediatric croup.

The length of hospital stay was significantly longer in the Omicron group, which also required more intensive treatments, including nebulized epinephrine and repeat corticosteroid doses. This observation may reflect the increased severity of symptoms in the Omicron group,

**Table 2** Laboratory indices evaluated in the two groups

Lab tests	Group		P.value
	Positive	Negative	
WBC	$10.74 \pm 5.49$	$10.96 \pm 6.44$	0.865
Neu	$66.20 \pm 13.40$	$29.01 \pm 17.42$	0.305
Lym	$24.93 \pm 12.35$	$44.71 \pm 142.38$	0.242
Hb	$11.59 \pm 0.99$	$11.93 \pm 1.25$	0.186
plt	$321.77 \pm 93.60$	$291.65 \pm 88.8$	0.121
ESR	$15.87 \pm 9.71$	$16.41 \pm 10.84$	0.811

as indicated by their higher need for interventions. However, due to the retrospective nature of this study, it is not possible to determine whether the longer hospital stay was influenced by government-mandated quarantine policies or solely due to symptom persistence requiring prolonged medical care. This uncertainty is acknowledged as a limitation of our study, and future prospective studies should explore the impact of quarantine advisories on hospitalization duration to better delineate this relationship.

Our findings demonstrated that children in the Omicron group were significantly younger than those in the non-Omicron group. This observation aligns with global reports suggesting that younger children, particularly those under five years old, are at higher risk of hospitalization during the Omicron wave [17, 18]. The Omicron variant's tropism for the upper respiratory tract may exacerbate airway inflammation in this vulnerable age group, leading to increased croup severity [19].

It is also worth noting that vaccination coverage in children under five years of age was minimal during the study period due to limited vaccine availability and recommendations for this age group. As a result, vaccination status was not included as a variable in this analysis. While it is unlikely to have played a significant role in this younger population, its absence represents a limitation of the study. Future research should consider vaccination status to better understand its potential impact on disease severity and hospitalization rates in pediatric populations.

The increased frequency of moderate and severe symptoms in the Omicron group, as indicated by higher Westley Croup Scores, highlights the variant's potential to intensify upper airway inflammation. Previous studies have reported similar findings, suggesting that Omicron-related croup is associated with more pronounced stridor, respiratory distress, and a longer recovery time compared to croup caused by traditional viruses such as parainfluenza [20, 21]. In line with our findings, Lam et al. in a descriptive study among the pediatric population in Hong Kong found that the COVID-19 incidence among patients with croup was significantly higher in the COVID-19 Omicron group than in the COVID-19 pre Omicron group [22].

Hospitalization duration was significantly longer in the Omicron group, which also required more intensive treatments, including nebulized epinephrine and repeat corticosteroid doses. These findings mirror the observations of Scribner et al. (2023), who reported higher rates of prolonged hospital stays and recurrent corticosteroid use in Omicron-associated croup [23]. The prolonged inflammatory response triggered by SARS-CoV-2 infection may account for these increased treatment demands [24, 25].

The greater reliance on nebulized epinephrine suggests a need to address airway inflammation more aggressively in Omicron-related croup cases. This aligns with the findings of Narayanan et al. (2023), who emphasized the elevated use of racemic epinephrine during the Omicron period [24, 26]. Although ICU admission and mechanical ventilation rates were not statistically significant between groups, trends indicated a higher proportion of ICU admissions in the Omicron group. This is consistent with global data showing increased ICU utilization during severe cases of Omicron-associated croup [26, 27]. These cases may be driven by a combination of severe airway obstruction and systemic inflammation.

Interestingly, no significant differences were observed in laboratory indices, including WBC, lymphocyte percentages, and CRP levels, between the two groups. This suggests that while clinical severity is higher in Omicron-related croup, systemic inflammatory markers may not reliably differentiate between PCR-positive and PCR-negative cases. These results align with findings by Choi et al. (2022), who reported that laboratory indicators alone were insufficient to distinguish Omicron-associated respiratory illnesses [28]. The distinct clinical profile of Omicron-related croup underscores the need for heightened vigilance and a tailored approach to management. Prompt recognition of moderate and severe cases, combined with readiness for escalated treatments, including nebulized epinephrine and corticosteroids, is crucial. These findings also emphasize the importance of considering SARS-CoV-2 as a potential causative agent in croup cases presenting during pandemic waves [29].

This study was retrospective and limited to two centers, which may constrain the generalizability of the findings. Furthermore, some clinical data may have been incomplete or inconsistently documented in patient records. Future research should focus on prospective, multicenter studies to validate these findings and explore the long-term outcomes of children affected by Omicron-associated croup. Additionally, further investigation into the immunopathological mechanisms underlying the exacerbated upper airway inflammation observed in these cases is warranted.

## Conclusion

This study provides critical insights into the distinct clinical and treatment challenges posed by the Omicron variant in pediatric patients with croup. Children with Omicron-related croup were younger, exhibited more severe symptoms, and required intensified therapeutic interventions compared to their non-COVID-19 counterparts. These findings highlight the variant's unique impact on pediatric respiratory conditions, underscoring the importance of early recognition, vigilant monitoring, and tailored management strategies during pandemic surges. Future studies should focus on the long-term outcomes and pathophysiological mechanisms underlying these observations, paving the way for optimized care protocols and better preparedness for emerging variants.

## Abbreviations

BMI	Body Mass Index
COVID-19	Coronavirus Disease 2019
CRP	C-Reactive Protein
ESR	Erythrocyte Sedimentation Rate
ICU	Intensive Care Unit
NIV	Non-Invasive Ventilation
PCR	Polymerase Chain Reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
VOC	Variant of Concern
WBC	White Blood Cell

## Acknowledgements

We would like to extend our sincere gratitude to all the participants who participated in this study.

## Author contributions

FP conceived the study and SHM, FP and NGH, collected and analyzed the data. FP and SHM interpreted the statistical analyses and NGH wrote the first draft of the manuscript. FP contributed to manuscript revision and editing. All authors critically revised the manuscript. The authors (s) read and approved the final manuscript.

## Funding

No funding support was acquired for this project.

## Data availability

The data supporting the findings of this study are available upon request from the corresponding author. The data were not publicly available because of privacy or ethical restrictions.

## Declarations

### Ethics approval and consent to participate

All stages of this study were performed in studies involving human participants in accordance with the Declaration of Helsinki. Prior to enrollment, the study protocol was approved by the Institutional Review Board (IRB) and ethics committee of the Tehran University of Medical Sciences with the reference number IR.TUMS.MEDICINE.REC.1402.135. Prior to participation, verbal and written informed consent from parents were obtained, following a detailed presentation of the study's purpose and comprehensive explanations regarding the information sought in the questionnaire.

### Consent for publication

After explaining the purpose of the study, verbal and written informed consent was obtained from the parents of the students for the anonymous publication of their children's data.



### Competing interests

The authors declare no competing interests.

### Research involving human participants

The intervention conducted in this study was approved by the Tehran University of Medical Sciences (ethics code: IR.TUMS.MEDICINE.REC.1402.135), Tehran, Iran.

### Transparency declaration

The lead author asserts that this manuscript provides a truthful, precise, and transparent representation of reported studies. Furthermore, the lead author confirms that no significant elements of the studies have been excluded, and that any deviations from the originally intended studies have been adequately clarified.

### Clinical trial number

not applicable.

Received: 7 December 2024 / Accepted: 24 February 2025

Published online: 15 March 2025

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