A comparison of the characteristics and outcomes of children with COVID-19 infections and children with other respiratory tract viral infections requiring high-flow nasal cannula

Dorukhan Besin (dorukhanbesin@gmail.com)
Dr. Behcet Uz Children's Hospital
Elif Böncüoğlu
Dr. Behcet Uz Children's Hospital
Elif Kıymet
Dr. Behcet Uz Children's Hospital
Ela Cem
Dr. Behcet Uz Children's Hospital
Miray Yilmaz Çelebi
Dr. Behcet Uz Children's Hospital
Mine Düzgöl
Dr. Behcet Uz Children's Hospital
Şahika Şahinkaya
Dr. Behcet Uz Children's Hospital
Anil Er
Dr. Behcet Uz Children's Hospital
Hursit Apa
Dr. Behcet Uz Children's Hospital
Aybüke Akaslan Kara
Dr. Behcet Uz Children's Hospital
Süleyman Nuri Bayram
Dr. Behcet Uz Children's Hospital
Ilker Devrim
Dr. Behcet Uz Children's Hospital

Research Article

Keywords: Covid19, high-flow nasal cannula, nasal high flow, pneumonia

Posted Date: September 6th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3298972/v1

Abstract

Background

The aim of this single-center retrospective cohort study was to compare the clinical and laboratory differences, response, and outome of the patients requiring HFNC between two distinct groups, children with SARS-CoV-2 infection and children infected with other types of respiratory tract viruses during the COVID-19 pandemic.

Methods

This single-center cross-sectional study was conducted in the Pediatric Infectious Disease Ward and COVID-19 pademic wardç Data of the patients was collected from medical records including information on demographic characteristics (age, gender, and medical history); underlying diseases or co-morbidities, indications for HFNC and physical examination findings. If present laboratory examinations taken from the submissions were recorded. The indication and duration of HFNC, the length of hospital stay, admission or transfer to the PICU each patient's stay in the hospital and if present the mortality rates by group were recorded..

Results

During the study period a total of 171 patients were followed-up under HFNC. Among them, 8 patients were excluded from the study due to absence of arterial blood gas results before HFNC and 6 patients were excluded due to absence of PCR testing for COVID-19. At the final analysis, 157 patients under HFNC treatment were included including 22 COVID-19 PCR positive (group I) and 135 COVID-19 PCR negative patients(Group II).

Conclusions

This study, patients with COVID-19 infections had longer durations of HFNC and hospital stay, in addition to high rate of transmission to PICU, suggesting a worser clinical outcome compared to infections with other viruses.

Background

High-flow nasal cannula (HFNC) oxygen therapy for patient ventilation is a non-invasive ventilation device in which warmed and humidified oxygen is administered to the patient at various flows via a nasal cannula [1]. In recent years, there has been an increase of interest in using HFNCs for the treatment of respiratory infections. Through the nasal cannula, it provides a heated, humidified air-oxygen combination[2],[3]. The majority of the HFNC studies include respiratory infections such as bronchiolitis and pneumonia, especially in pediatric wards and emergency departments where it is used as first-line treatment [4], [5]. Nasal high-flow provides some positive airway pressure and reduces the effort of breathing [6], [7] and the use of HFNC found to be well tolerated by children [8].

High-flow nasal cannula was widely used in adult patients with COVID-19 who were followed up in intensive care units (ICUs) or in wards other than the ICUs. which were the ICU's or adults with non-eligible for intensive care unit care. However there are limited studies concerning HFNC use in children with COVID-19. Although COVID-19 was initially introduced with milder symptoms and a lower risk of life-threatening complications in children, it was later discovered that children may also experience severe clinical symptoms and even an unfavorable outcome [9]. Indeed, in the United States, a significant number of children have required acute or critical hospital care. [10] .

The aim of this single-center retrospective cohort study was to compare the clinical and laboratory differences, response, and outome of the patients requiring HFNC between two distinct groups, children with SARS-CoV-2 infection and children infected with other types of respiratory tract viruses during the COVID-19 pandemic.

Material-methods

This single-center cross-sectional study was conducted in the Pediatric Infectious Disease Ward and COVID-19 pademic ward at the University of Health Sciences Dr Behcet Uz Children's Hospital with a 360-bed tertiary care hospital in Izmir, Turkey, from 11, 2020, to 11, 2022. This hospital is a pediatric referral center in the Aegean Region of Turkey with annual approximately 600,000 outpatients and 24,000 hospitalizations. The study included all children who required HFNC upon admission or during follow-up. Patients were split into two groups: Group 1 included the patients who tested positive for SARS-CoV-2, group 2 included the patients who tested and found negative for SARS-CoV-2

COVID-19 infection was diagnosed using quantitative real-time reverse transcriptase-PCR positivity with detection of double targets, N-gene and ORF ab1 region at cycling threshold value under 35 cycles [SARS-CoV-2 (2019-nCoV) qPCR Detection Kit, Bio-Speedy, Turkey][11]. The respiratory viruses were detected using a multiplex real-time PCR test (Bosphore Respiratory Pathogens Panel Kit V4,Anato lia Geneworks, Turkey) that is capable of identifying viral pathogens including influenza viruses (influenza A, pandemic H1N1 influenza A, seasonal H1N1 influenza A, and influenza B), parainfluenza viruses (PIVs; PIV-1, PIV-2, PIV-3, and PIV-4), human coronaviruses (CoV OC43, CoV NL63, CoV HKU1, and CoV 229E), RSV A/B, rhinovirus, hMPV, enterovirus, bocavirus, adenovirus, and parechovirus. For detection of respiratory viruses' specific master mix reagents which include targeted genomic regions of microorganisms were used and cycling threshold values under 35 cycles was considered as positive[12]

Data collection:

Data of the patients was collected from medical records including information on demographic characteristics (age, gender, and medical history); underlying diseases or co-morbidities, indications for HFNC and physical examination findings. If present laboratory examinations taken from the submissions were recorded, including complete blood count (total lymphocyte count, absolute lymphocyte count, hemoglobin, and platelet count), levels of serum coagulation parameters (PT, aPTT, INR, fibrinogen, and D-dimer), C-reactive protein (CRP), procalcitonin, and troponin I/T. The arterial venous parameters such as pH (mmHg), PCO2 (mmHg), PaO2 (mmHg), HCO3 (mmol/L), Lactat (mmol/L), So2(%), and FiO2(%)were also recorded from medical records.

Respiratory distress is typically characterized by signs of increased work of breathing, such as tachypnea, use of accessory muscles, nasal flaring, and/or retractions. The diagnosis of respiratory failure requires at least two clinical signs of respiratory distress and one laboratory criterion (arterial PaCO2 > 50 mmHg and PaO2 < 50 mm Hg in room air; PaCO2 >50 mm Hg and pH 60 mmHg and PaO2 < 60 mm Hg when FiO2 0.60 in patients without cyanotic heart disease; oxygen saturation. Oxygenation of the patients was monitored by pulse oximetry and lower than 94% was accepted as hypoxemia [13]

The indication and duration of HFNC, the length of hospital stay, admission or transfer to the PICU each patient's stay in the hospital and if present the mortality rates by group were recorded. On high-flow, children received high-flow at weight specific flows (Table-1) delivered via age-appropriate OptiflowTM Junior 274 Nasal Interfaces, OptiflowTM Junior 2+ Nasal Interfaces or Adult cannula and a high-flow delivery system, AirvoTM 2 System (Fisher&Paykel Healthcare, Auckland, New Zealand) [14]. Inspired oxygen fraction (FiO2) was adjusted to obtain oxygen saturation between 92 and 98%.

Statistical analysis

The descriptive properties (mean, median, number, and percentage) of the variables were determined. The numeric variables were checked for fit with normal distribution. While comparing the two groups, the Student's t-test was used for numeric variables with normal distribution. The Mann-Whitney U test was performed for numeric variables not normally distributed. The chi-square test was performed to compare categorical variables between group I and group II. A *p*-value < 0.05 was considered statistically significant. Statistical Package for the Social Sciences (SPSS) version 17 (Chicago, Illinois, USA) software was used to analyze the results.

The study protocol was approved by local ethical committee.

RESULTS

During the study period a total of 171 patients were followed-up under HFNC. Among them, 8 patients were excluded from the study due to absence of arterial blood gas results before HFNC and 6 patients were excluded due to absence of PCR testing for COVID-19. At the final analysis, 157 patients under HFNC treatment were included including 22 COVID-19 PCR positive (group I) and 135 COVID-19 PCR negative patients(Group II).

Among the COVID-19 negative patients, nasopharyngeal multiplex PCR results were present at 80.8 % (n=126) and in the 86 patients (68.3%), yielded viral pathogens. Most isolated virüs was rhinovirus (n=50, 39.6**%**); RSV (n=23, 18.2%), followed by enterovirus (n=5, %3.9), influenza (n=4, %3.1), parainfluenza (n=2, 1.5%), human metapneumovirus (n=1, 0.7 %), coronavirus 229 (n=1, 0.7 %)

Demographic comparison of the two groups

The median age of the patients was 8 years (min:2 month, max: 14 years) in the COVID-19 PCR positive group and 9 months (median 9 months, min:1 month, max:10 years) in the COVID-19 PCR negative group, and significantly higher in the COVID-19 positive group (p<0.001).There was no statistical difference between these two groups regarding gender (p >0.05).. The rate of underlying disease in the COVID-19 group and COVID-19 negative group was 9.1%(n=2) and 19.3% (n=26) consequetively, and no significant difference was present(p>0.05). The rate of pneumonia was 86.4% in the COVID-19 positive group, while the rate of pneumonia was 58.6% in the COVID-19 negative group, and significantly higher in the COVID-19 group, and the rate of acute bronciolitis was significantly higher in the COVID-19 negative group(p=0.013)(table-2). The distribution of socio-demographic characteristics of the case and control group was summarized in Table-2

Comparion of clinical findings and arterial gas parameters

The rate of patients who have hypoxia, tachypnea and tachycardia was significantly higher in the COVID-19 positive group compared to COVID-19 PCR negative group (p=0.045, p= 0.001, p<0.001 consecutively). The rate of patients who had pH< 7.30 and lactat level >2 was not significantly different between the groups(>0.05). Table-3 summarizes the clinical findings. The arterial blood gas analysis revealed no significant difference between the groups regarding pH, PCo2, Hco3, Lactat, So2, FiO2, levels(p>0.05), while the partial oxygen pressure was significantly higher in the COVID-19 positive group compared to COVID-19 PCR negative group (p=0.005)(Table-4). Table-4 summarizes the comparision of arterial gas parameters between the groups.

Comparison of the outcome between COVID-19 PCR positive and COVID-19 PCR negative groups.

The average duration under HFNC treatment was 5.5±1.8 days(ranging from 2 days to-10 days) in the COVID-19 positive group and 4.4±1.8 days (ranging from 1 to 10 days) in the COVID-19 PCR negative group, and significantly longer in the COVID-19 positive group (p=0.012). Transfer rate to the PICU under HFNC was 59.1%(n=13) in the COVID-19 positive group and 13.5% (n=17) in the COVID-19 PCR negative group, and significantly higher in the COVID-19 positive group(p< 0.001). The rate of endotracheal entubation was 4.5% in the COVID-19 positive group and 1.6% in the in the COVID-19 PCR negative group, and no significance was present (p>0.05).The average hospital stay was 11.8 ± 5.3 days(median 10, ranging from 4 to 24 days) in the COVID-19 positive group and 7.7 ± 4.1 days (median 7, ranging 1 to 30 days) in the COVID-19 PCR negative group, and significantly longer in the COVID-19 positive group (p<0.001)

Discussion

In this study, we shared our expericence with HFNC at COVID-19 positive and negative patients. The age of the patients who required HFNC were older in the COVID-19 positive group and had significantly higher rate of pneumonia compared to COVID-19 negative group. Despite no sigificant difference was present at the arterial blood gas parameters, the COVID-19 patients tended to be under HFNC treatment one day longer compared to COVID-19 negative patients, and rate of transfer to the PICU under HFNC was higher in the COVID-19 patients. In addition COVID-19 infections required longer hospital stay compared to COVID-19 negative patients

In the current study, the age of the patients who required HFNC were older in the COVID-19 positive group and had significantly higher rate of pneumonia compared to COVID-19 negative group. In line with other studies in the literature, the median age of our COVID-19 patients was similar [15], [16]. On the contrary the study on epidemiological characteristics of 2143 pediatric patient shown that infants made up the highest proportion of severe or critical disease (32%) with preschool ages (1–5 years) next with 28.8%.[15]. In the currrent study, the age of the patients who required HFNC were older in the COVID-19 positive compared to COVID-19 negative patients under HFNC. Despite children of all ages can be infected with COVID-19, younger children and infants were reported to more infected[17]. Despite all ages were affected, Kara et al reported that an association between increased age and worse outcomes in their study, in addition to previous studies indicating that younger age has no protective effect on preventing SARS-CoV-2 infection from developing COVID-19 pneumonia in children[18] [19]. In addition Böncüoğlu et al, reported that the mean age was not dfferent at children with or without pulmonary involvement confirmed by CT scan [20].

In a recent study comparing children with COVID-19 infection and those with H1N1pdm09 virus infection, found that age was significantly higher in the COVID-19 patients' group compared to the pandemic influenza group. In the COVID-19 negative group, most common isolated viruses were rhinovirus and RSV which formed the first and second frequent cause of bronchiolitis especially during the first year of age [21]–[24]. Moreover a rate of up to %50 of infants who were hospitalized with the diagnosis of the bronchiolitis were reported to be infected with RV, suggesting the lower age in the COVID-19 negative group[25]. In another study, comparing COVID-19 pneumonia and other viral pathogens also reported higher age in the COVID-19 group, supporting our findings[26]

In our study, the rate of pneumonia was significantly higher in the COVID-19 group, whereas the rate of acute bronchiolitis was significantly higher in the COVID-19 negative group. In the previous reports the prevalence of pneumonia in SARS-CoV-2 infection was 62.5% [26], and compared to be higher than that of H1N1 influenza (11%) and many other viruses[26]. Despite the early reports of COVID-19 is had a much more favorable outcome, later before the new mutations at SARS-COV-2, Currently, pediatric patients with severe manifestations of the disease are increasing [27]; pneumonia is the most common respiratory entity, and acute respiratory distress syndrome (ARDS) is the critical form [28]. Despite reports of the lower rate of severe pneumonia in COVID-19 penumonia cohort comparing to viral

pneumonia [26], our findings suggested indirectly the rate of pneumonia requring HFNC was higher in the COVID-19 group, in addition HFNC stay time is longer in the COVID-19 group comparing to the COVID-19 PCR negative group.

In the literature compared to COVID-19 versus seasonal respiratory agents cases were associated with a higher proportion of inpatient admissions but were similar in ICU admission and death rates in hospitalized pediatric patients [29]. In our study, the COVID-19 patients had one day longer HFNC duration in addition rate of transfer to PICU was high in the COVID-19 group, reflecting more serious illness compared to COVID-19 negative group. It has been shown that most children testing positive for COVID-19 are asymptomatic, and only 2% of pediatric patients require intensive care [32] In our study %59.1 of COVID-19 patients were transferred to intensive care. Our rate is higher; it could be related to age factor because of difficulty adherence to nasal flow treatment, in addition to the high rate of presence of pnuemonia in the COVID-19 patients compared to patients infected with other viruses.

Our study revealed that, the COVID-19 patients under HFNC stayed longer under HFNC and also had longer hospital durations compared to COVID-19 negative patients. In contrary; another study comparing infections due to COVID-19 and other respiratory viruses except COVID-19 agents reported that infections with other respiratory viruses required much more oxygen therapy than COVID-19 patients[16]. Since SARS-CoV-2 is a new virüs, the experience and therefore the well-designed guidelines were limited, while the treatment modalities of the common viral pathogens were well-known, thus the studies including treatment of COVID-19 infections might show different results.

non-COVID viruses are more virulent in children, increasing the rates of morbidity, mortality, and PICU hospitalizations, need for conventional mechanical ventilation was higher in non-covid patients

Due to the study's design, it has limitations. First the data were collected retrospectively from the hospital's medical records and computerized data storage system. Secondly, all the cases in this study lack the multiplex PCR, in addition the distribution of the viruses were not homogenous in the COVID-19 negative group, thus we could not compare subgroups of viruses. In addition, we included only the patients under HFNC treatment, and could not give general infromation of the clinical course of total COVID-19 infections at general population.

In conclusion, in our study, patients with COVID-19 infections had longer durations of HFNC and hospital stay, in addition to high rate of transmission to PICU, suggesting a worser clinical outcome compared to infections with other viruses.

Declarations

Funding

There is no funding for his research.

Authors' contributions

DB, ID, and EB carried out the treatment, collected and analyzed the data, and wrote the manuscript. EK, EC, MYC, MD, SS, AE, HA ,AAK, NB and DB conceived of the study and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by local ethical committee accordance statement with a named standard research was carried out in line with named Behcet uz Hospital ethics commitee. Approval protocol number is 515.

Consent for publication

Each patient gave written informed consent for their data to be used for research and publication.

Competing interests

The authors declare that they have no competing interests.

References

1. A. Kawaguchi, Y. Yasui, A. deCaen, and D. Garros, “The Clinical Impact of Heated Humidified High-Flow Nasal Cannula on Pediatric Respiratory Distress.,” *Pediatr. Crit. care Med. a J. Soc. Crit. Care Med. World Fed. Pediatr. Intensive Crit. Care Soc.*, vol. 18, no. 2, pp. 112–119, Feb. 2017, doi: 10.1097/PCC.0000000000000985.
2. J. Lin, Y. Zhang, L. Xiong, S. Liu, C. Gong, and J. Dai, “High-flow nasal cannula therapy for children with bronchiolitis: a systematic review and meta-analysis.,” *Arch. Dis. Child.*, vol. 104, no. 6, pp. 564–576, Jun. 2019, doi: 10.1136/archdischild-2018-315846.
3. S. O’Brien, S. Craig, F. E. Babl, M. L. Borland, E. Oakley, and S. R. Dalziel, “‘Rational use of high-flow therapy in infants with bronchiolitis. What do the latest trials tell us?’ A Paediatric Research in Emergency Departments International Collaborative perspective.,” *J. Paediatr. Child Health*, vol. 55, no. 7, pp. 746–752, Jul. 2019, doi: 10.1111/jpc.14496.
4. L. Piper, E. L. Stalets, and A. M. Statile, “Clinical Progress Note: High Flow Nasal Cannula Therapy for Bronchiolitis Outside the ICU in Infants.,” *J. Hosp. Med.*, vol. 15, no. 1, pp. 49–51, Jan. 2020, doi: 10.12788/jhm.3328.
5. S. J. Kotecha, D. Vick, M. Delgado-Thompson, J. West, and M. O. Edwards, “Establishing paediatric ward high-flow nasal cannula usage for infants with bronchiolitis.,” *Acta paediatrica (Oslo, Norway : 1992)*, vol. 111, no. 3. Norway, pp. 638–639, Mar. 2022. doi: 10.1111/apa.15527.
6. J. L. Hough, T. M. T. Pham, and A. Schibler, “Physiologic effect of high-flow nasal cannula in infants with bronchiolitis.,” *Pediatr. Crit. care Med. a J. Soc. Crit. Care Med. World Fed. Pediatr. Intensive Crit. Care Soc.*, vol. 15, no. 5, pp. e214-9, Jun. 2014, doi: 10.1097/PCC.0000000000000112.
7. C. Milési *et al.*, “Is treatment with a high flow nasal cannula effective in acute viral bronchiolitis? A physiologic study.,” *Intensive Care Med.*, vol. 39, no. 6, pp. 1088–1094, Jun. 2013, doi: 10.1007/s00134-013-2879-y.
8. H. Nair *et al.*, “Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis.,” *Lancet (London, England)*, vol. 381, no. 9875, pp. 1380–1390, Apr. 2013, doi: 10.1016/S0140-6736(12)61901-1.
9. Y. Dong *et al.*, “Epidemiology of COVID-19 Among Children in China.,” *Pediatrics*, vol. 145, no. 6, Jun. 2020, doi: 10.1542/peds.2020-0702.
10. E. B. Pathak, J. L. Salemi, N. Sobers, J. Menard, and I. R. Hambleton, “COVID-19 in Children in the United States: Intensive Care Admissions, Estimated Total Infected, and Projected Numbers of Severe Pediatric Cases in 2020.,” *J. Public Health Manag. Pract.*, vol. 26, no. 4, pp. 325–333, 2020, doi: 10.1097/PHH.0000000000001190.
11. Y. T. Tok *et al.*, “Detection of SARS-CoV-2 RNA in Upper Respiratory Swap Samples by Pooling Method.,” *Balkan Med. J.*, vol. 39, no. 1, pp. 48–54, Jan. 2022, doi: 10.5152/balkanmedj.2021.21135.
12. E. Kıymet *et al.*, “Distribution of spreading viruses during COVID-19 pandemic: Effect of mitigation strategies.,” *Am. J. Infect. Control*, vol. 49, no. 9, pp. 1142–1145, Sep. 2021, doi: 10.1016/j.ajic.2021.06.002.
13. F. Kamit Can *et al.*, “Predictive factors for the outcome of high flow nasal cannula therapy in a pediatric intensive care unit: Is the SpO2/FiO2 ratio useful?,” *J. Crit. Care*, vol. 44, pp. 436–444, 2018, doi:

https://doi.org/10.1016/j.jcrc.2017.09.003.

14. D. Franklin *et al.*, “High flow in children with respiratory failure: A randomised controlled pilot trial - A paediatric acute respiratory intervention study.,” *J. Paediatr. Child Health*, vol. 57, no. 2, pp. 273–281, Feb. 2021, doi: 10.1111/jpc.15259.
15. C. Eastin and T. Eastin, “Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China: Dong Y, Mo X, Hu Y, et al. Pediatrics. 2020; doi: 10.1542/peds.2020-0702.,” *The Journal of Emergency Medicine*, vol. 58, no. 4. pp. 712–713, Apr. 2020. doi: 10.1016/j.jemermed.2020.04.006.
16. O. Perk, S. Ozcan, S. Emeksiz, E. Uyar, and B. Gulhan, “Comparison of Clinical Findings in SARS-CoV-2 with Other Respiratory Viruses in Critically Ill Children during the COVID-19 Pandemic.,” *J. Trop. Pediatr.*, vol. 67, no. 6, Dec. 2021, doi: 10.1093/tropej/fmab102.
17. G. Vidya, M. Kalpana, K. Roja, J. A. Nitin, and M. Taranikanti, “Pathophysiology and Clinical Presentation of COVID-19 in Children: Systematic Review of the Literature.,” *Maedica*, vol. 16, no. 3. Romania, pp. 499–506, Sep. 2021. doi: 10.26574/maedica.2020.16.3.499.
18. A. A. Kara *et al.*, “Evaluation of predictors of severe-moderate COVID-19 infections at children: A review of 292 children.,” *J. Med. Virol.*, vol. 93, no. 12, pp. 6634–6640, Dec. 2021, doi: 10.1002/jmv.27237.
19. G. Chen *et al.*, “Clinical and immunological features of severe and moderate coronavirus disease 2019,” *J. Clin. Invest.*, vol. 130, no. 5, pp. 2620–2629, May 2020, doi: 10.1172/JCI137244.
20. E. Böncüoğlu *et al.*, “Can laboratory findings predict pulmonary involvement in children with COVID-19 infection?,” *Pediatr. Pulmonol.*, vol. 56, no. 8, pp. 2489–2494, Aug. 2021, doi: 10.1002/ppul.25452.
21. R. Turunen *et al.*, “The first wheezing episode: respiratory virus etiology, atopic characteristics, and illness severity,” *Pediatr. Allergy Immunol.*, vol. 25, no. 8, pp. 796–803, 2014, doi: https://doi.org/10.1111/pai.12318.
22. A. Kotaniemi-Syrjänen, T. M. Reijonen, K. Korhonen, M. Waris, R. Vainionpää, and M. Korppi, “Wheezing due to rhinovirus infection in infancy: Bronchial hyperresponsiveness at school age,” *Pediatr. Int.*, vol. 50, no. 4, pp. 506–510, 2008, doi: https://doi.org/10.1111/j.1442-200X.2008.02620.x.
23. T. Jartti and J. E. Gern, “Role of viral infections in the development and exacerbation of asthma in children,” *J. Allergy Clin. Immunol.*, vol. 140, no. 4, pp. 895–906, Oct. 2017, doi: 10.1016/j.jaci.2017.08.003.
24. D. Lo, J. L. Kennedy, R. C. Kurten, R. A. Panettieri, and C. J. Koziol-White, “Modulation of airway hyperresponsiveness by rhinovirus exposure,” *Respir. Res.*, vol. 19, no. 1, p. 208, 2018, doi: 10.1186/s12931-018-0914-9.
25. T. Jartti, P. Lehtinen, T. Vuorinen, and O. Ruuskanen, “Bronchiolitis: Age and Previous Wheezing Episodes Are Linked to Viral Etiology and Atopic Characteristics,” *Pediatr. Infect. Dis. J.*, vol. 28, no. 4, 2009, [Online]. Available: https://journals.lww.com/pidj/Fulltext/2009/04000/Bronchiolitis__Age_and_Previous_Wheezing_Episodes.11.aspx
26. G.-L. Ren *et al.*, “Comparison of acute pneumonia caused by SARS-COV-2 and other respiratory viruses in children: a retrospective multi-center cohort study during COVID-19 outbreak,” *Mil. Med. Res.*, vol. 8, no. 1, p. 13, 2021, doi: 10.1186/s40779-021-00306-7.
27. K. Yuki, M. Fujiogi, and S. Koutsogiannaki, “COVID-19 pathophysiology: A review.,” *Clin. Immunol.*, vol. 215, p. 108427, Jun. 2020, doi: 10.1016/j.clim.2020.108427.
28. T. H. de Souza, J. A. Nadal, R. J. N. Nogueira, R. M. Pereira, and M. B. Brandão, “Clinical manifestations of children with COVID-19: A systematic review.,” *Pediatr. Pulmonol.*, vol. 55, no. 8, pp. 1892–1899, Aug. 2020, doi: 10.1002/ppul.24885.
29. X. Song, M. Delaney, R. K. Shah, J. M. Campos, D. L. Wessel, and R. L. DeBiasi, “Common seasonal respiratory viral infections in children before and during the coronavirus disease 2019 (COVID-19) pandemic.,” *Infect. Control Hosp. Epidemiol.*, vol. 43, no. 10, pp. 1454–1458, Oct. 2022, doi: 10.1017/ice.2021.430.

30. F. Zheng *et al.*, “Clinical Characteristics of Children with Coronavirus Disease 2019 in Hubei, China.,” *Curr. Med. Sci.*, vol. 40, no. 2, pp. 275–280, Apr. 2020, doi: 10.1007/s11596-020-2172-6.
31. C. Eastin and T. Eastin, “Clinical Characteristics of Coronavirus Disease 2019 in China: Guan W, Ni Z, Hu Y, et al. N Engl J Med. 2020 Feb 28 [Online ahead of print] DOI: 10.1056/NEJMoa2002032.,” *The Journal of Emergency Medicine*, vol. 58, no. 4. pp. 711–712, Apr. 2020. doi: 10.1016/j.jemermed.2020.04.004.
32. I. Liguoro *et al.*, “SARS-COV-2 infection in children and newborns: a systematic review.,” *Eur. J. Pediatr.*, vol. 179, no. 7, pp. 1029–1046, Jul. 2020, doi: 10.1007/s00431-020-03684-7.

Tables

Table-1: High flow age-specific flows according to the weights of the patients

Weight of the patients, kg	Flow rate
0–12	2 L/kg/min up to maximum of 25 L/min
13–15	30 L/min
16-30	35 L/min
31-50	40 L/min
>50	50 L/min

Table-2: Comparision of the demographic data and underlying disease in the COVID-19 PCR positive and negative groups

	COVID-19 PCR positive % (Number)	COVID-19 PCR negative % (Number)	P value
Age (months)	96(IQR=8)	9 (IQR=122)	<0.001
Gender			
Male	59.1%(13)	57.8% (78)	0.908
Female	40.9%(9)	42.2%(57)	
Total	100% (22)	100% (132)	
Patient Diagnoses*			
Pneumonia	86.4% (19)	58.6% (78)	<0.05
Acute bronchilitis	13.6% (3)	41.4% (55)	0.013
Total	100% (22)	100% (132)	
Underlying Disease			>0.05
Asthma	-	3.7%(5)	
Hydrocephalus	-	0.7%(1)	
Down Syndrome	-	1.5% (2)	
Acute Lymphoblastic Leucemia	-	0.7% (1)	
Hypotonic Infant	-	2.2% (3)	
Immun Deficiency	-	3.0%(4)	
Epilepsy	-	2.2% (3)	
Osephagus Atresia	-	0.7% (1)	
Atrial Septal Defect	-	1.3%(2)	
Ventriculer Septal Defect	9.1%(2)	1.5% (2)	
Metabolic Disease	-	1.4% (2)	
Total	9.1% (2)	19.3%(26)	
Duration of hospitalization (days)	11.8 ±5.3	7.8 ±4.2	<0.001

Table-3: Comparision of the clinical features of the COVID-19 PCR positive and negative groups

	COVID-19 PCR positive % (Number)	COVID-19 PCR negative Number (%)	P value
Presence of hypoxia	90.9%(20)	85%(113)	0.045
tachypnea	68.2%(15)	30.3%(40)	0.001
Tachycardia	72.7%(16)	29.3%(39)	0.000
PH <7.30	27.3(6)	19.4(26)	0.397
Lactat level >2 (mmol/L)	50%(11)	57.6%(76)	0.507
Total	22	135	

Table-4: Comparision of the arterial gas parameters, vital findings and oxygen saturation between the COVID-19 PCR positive and negative groups

	COVID-19 PCR positive Mean (min-max)	COVID-19 PCR negative Mean (min-max)	P value
pH(mmHg)	7.36±0.07(7.22-7.48)	7.30 ±0.52(7.35-7.63)	0.182
PCO2(mmHg)	38.2±8.73(21-56)	39.7±8.1(21-72)	non
PaO2(mmHg)	73.0±14.9(41.5-99.5)	62.8±17.3(25.1-117)	0.005
HCO3(mmol/L)	19.3±3.62(11.0-23.9)	20.3±2.69(14.7-26.5)	0.464
Lactat(mmol/L)	2.26±0.96(1.10-4.13)	2.40±1.73(0.60-18.5)	non
So2(%)	92.0±2.43(85.0-95.0)	91.4±2.98(78.0-98.0)	0.165
FiO2(%)	35.9±8.36(27.0-60.0)	39.4(21-60)	0.231
HR /min	139±23.3(100-180)	150± 16.2(110-120)	0.000
RR /min	39.0± 13.7(20-60)	50.7± 8.87(24-78)	0.028