

Impact of the COVID-19 Pandemic on Community-acquired Neonatal Pneumonia Admissions to a Tertiary Care Hospital During Respiratory Syncytial Virus Season

COVID-19 Pandemisinin Respiratuar Sinsityal Virüs Sezonunda Üçüncü Basamak Bir Hastanenin Toplum Kökenli Yenidoğan Pnömonisi Başvuruları Üzerindeki Etkisi

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ABSTRACT

Objective: Currently there are conflicting data about the incidence of community-acquired infections of common respiratory viruses during the pandemic caused by the novel Severe acute respiratory syndrome-Coronavirus-2.

Methods: The data of the patients, who were admitted to the neonatal intensive care unit for suspected community-acquired neonatal pneumonia during the respiratory syncytial virus (RSV) season in the pre-Coronavirus disease-2019 (COVID-19) pandemic era (October 2019-March 2020) and post-COVID-19 pandemic era (October 2020-March 2021) were retrospectively analyzed.

Results: A total of 869 patient records were screened. Seventy patients (22%) in the pre-COVID-19 pandemic era and 15 patients (6.8%) in the post-COVID-19 pandemic era met the selection criteria and were included in the analysis. In the pre- and post-COVID-19 pandemic era respectively, males accounted for 57.1% and 73.3% of patients ($p=0.245$), the mean gestational age at birth was 37 ± 2 and 35 ± 3 weeks ($p=0.007$), the mean birth weight was 3045 ± 601 and 2386 ± 840 g ($p=0.001$), the mean postnatal age at admission was 9 ± 3 and 7 ± 1 days ($p=0.177$), and the mean length of hospital stay was 10 ± 3 and 8 ± 2 days ($p=0.023$). RSV was detected in 42 (60%) patients in the pre-COVID-19 pandemic era compared to 2 (13.3%) patients in the post-COVID-19 pandemic era ($p=0.001$).

Conclusion: A 3-fold decrease in hospitalizations due to community acquired pneumonia was observed in the post COVID-19 era. Strict compliance with the rules such as mask use, hand washing, and social distancing and lockdown during the COVID-19 pandemic could explain the decrease in neonatal pneumonia.

Keywords: Neonate, respiratory syncytial virus, community-acquired pneumonia, COVID-19, pandemic

ÖZ

Amaç: Halihazırda, yeni Şiddetli Akut Solunumsal Sendrom-Koronavirüs-2'nin neden olduğu pandemi döneminde toplum kaynaklı enfeksiyonlara neden olan solunum yolu virüslerinin insidansı hakkında çelişkili veriler bulunmaktadır.

Yöntem: Bu çalışmaya, Koronavirüs hastalığı-2019 (COVID-19) pandemisi öncesi dönemde (Ekim 2019-Mart 2020) ve COVID-19 pandemisi sonrası dönemde (Ekim 2020-Mart 2021) respiratuar sinsityal virüs (RSV) mevsiminde şüpheli toplum kökenli yenidoğan pnömonisi nedeniyle yenidoğan yoğun bakım ünitesine kabul edilen hastaların verileri retrospektif olarak değerlendirildi.

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Bulgular: Toplam 869 hasta kaydı tarandı. COVID-19 pandemisi öncesi dönemde 70 hasta (%22) ve COVID-19 pandemisi sonrası dönemde 15 hasta (%6,8) seçim kriterlerini karşıladı ve analize dahil edildi. COVID-19 pandemisi öncesi ve sonrası dönemde sırasıyla hastaların %57,1 ve %73,3'ünü erkekler oluşturuyordu ($p=0,245$), doğumdaki ortalama gebelik yaşı 37 ± 2 ve 35 ± 3 haftaydı ($p=0,007$), ortalama doğum ağırlığı 3045 ± 601 ve 2386 ± 840 g ($p=0,001$), doğum sonrası ortalama başvuru yaşı 9 ± 3 ve 7 ± 1 gün ($p=0,177$), hastanede kalış süresi ortalama 9 ± 3 ve 7 ± 1 gün idi ($p=0,023$). COVID-19 pandemisi öncesi dönemde 42 (%60) hastada, COVID-19 pandemisi sonrası dönemde 2 (%13,3) hastada RSV tespit edildi ($p=0,001$).

Sonuç: COVID-19 sonrası dönemde toplum kökenli pnömoni nedeniyle hastaneye yatışlarda 3 kat azalma gözlemlendi. COVID-19 pandemisi sırasında maske kullanımı, el yıkama, sosyal mesafe ve sokağa çıkma yasağı gibi kurallara sıkı sıkıya uyulması neonatal pnömonideki azalmayı açıklayabilir.

Anahtar Kelimeler: Yenidoğan, respiratuvar sinsiyyal virüsü, toplum kökenli pnömoni, COVID-19, pandemi

INTRODUCTION

Neonatal pneumonia is among the major causes of neonatal morbidity and mortality, especially in developing countries. Annually, 750.000 to 1.200.000 neonatal deaths and numerous stillbirths worldwide are attributed to pneumonia, which shows seasonal variation in prevalence and has multiple etiologies.¹ The most common bacterial causes of community-acquired neonatal pneumonia (CANP) are *Escherichia coli*, group B streptococci, and *Listeria monocytogenes*; viral causes are respiratory syncytial virus (RSV), rhinovirus, influenza, parainfluenza, adenovirus, and metapneumovirus.²⁻⁴ Pneumococci have also been shown to be the most common agent in co-infections with viral infections.⁵

The Coronavirus disease-2019 (COVID-19) pandemic caused by the Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) has swept across the world. Neonates are particularly indefensible to this viral infection compared with older children and healthy young adults, with individual challenges in their management. In several previously published articles, it has been reported that the epidemiology of the common respiratory viruses has been dramatically changed.⁶ Social distancing and public health measures settled to prevent pandemic spread of COVID-19 pandemic had a substantial effect on all respiratory virus transmissions and related diseases with a partial exception of rhinovirus published in a few reports.⁷

The study aimed to conduct a comparative analysis of newborns who visited pediatric emergency and neonatal outpatient clinics and were hospitalized to the neonatal intensive care unit (NICU) for CANP before and during the COVID-19 pandemic eras.

METHODS

Our hospital, which includes 180 bed tertiary NICU served as a referral hospital during the pandemics for all age of patients.

This retrospective study included patients who were presented to the pediatric emergency and neonatal outpatient clinics with upper and lower respiratory tract infection symptoms (fever, nasal discharge, nasal congestion, cough, wheezing, tachypnea, feeding

difficulties) during the RSV season and were admitted to the NICU for suspected community-acquired pneumonia in a pre-COVID-19 pandemic era (October 2019-March 2020) and post-COVID-19 pandemic era (October 2020-March 2021). The study was approved by the Ankara State Hospital Local Clinical Research Ethics Committee (date: 24.02.2021, protocol no: E2-21-207).

Patients with neonatal septicemia, urinary tract infection, and positive SARS-CoV-2 polymerase chain reaction (PCR) test were excluded from the study. The infants' gestational age, birth weight, sex, age at presentation, presenting symptoms, length of hospital stay, duration of respiratory support, auscultation findings at admission, admitting hematological and biochemical parameters, respiratory virus screening results, radiological findings, and inhalant treatments were obtained from patient charts and the hospital database.

Respiratory viruses were screened by QIAstat-Dx[®] Respiratory Panel system for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs. Real-time PCR was performed on QIAstat-Dx[®] Analyzer 1.0 (QIAGEN), for each reaction 300 μ L volume was used. The following organism types and subtypes are determined using the QIAstat-Dx[®] Respiratory Panel: Adenovirus, Coronavirus 229E, Coronavirus NL63, Coronavirus HKU1, Coronavirus OC43, Influenza A, Influenza A H1, Influenza A H3, Influenza A H1N1/pdm09, Influenza B, Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Parainfluenza virus 4, Human Metapneumovirus A+B, RSV A+B, Rhinovirus/Enterovirus, *Mycoplasma pneumonia*, *Chlamydomphila pneumonia* and *Bordetella pertussis*. An internal control was implicated in each sample to check both extraction efficiency and PCR inhibition. In every run, a negative control was used to observe carry-over contamination and a positive control to check the PCR reaction. The results were analyzed automatically using QIAstat-Dx[®] Analyzer 1.0 software (QIAstat-Dx[®] Analyzer V1.0, Hilden, Germany).

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences version 22.0 (IBM

Corp, Armonk, NY). Results are expressed as number, mean±standard deviation and percentage. Student's t-test, Mann-Whitney U test, Fisher's exact test and χ^2 test were used to compare categorical and parametric variables. P values <0.05 were accepted as statistically significant.

RESULTS

Data about 869 patients were reviewed. Of these, 70 patients (22%) in the pre-COVID-19 pandemic era and 15 patients (6.8%) in the post-COVID-19 pandemic era met the selection criteria and were included in the analysis (Figure 1). Ten SARS-CoV-2 PCR-positive infants were excluded from the study. In the pre- and post-COVID-19 pandemic eras, respectively, males accounted for 57.1% and 73.3% of the patients (p=0.245), the mean gestational age at birth was 37±2 and 35±3 weeks (p=0.007), the mean birth weight was 3045±601 and 2386±840 g (p=0.001), the mean postnatal age at admission was 9±3 and 7±1 days (p=0.177), and the mean length of hospital stay was 9±3 and 7±1 days (p=0.023).

The patients' presenting symptoms, physical examination and radiological findings, hematological and biochemical parameters at admission, and results from respiratory viral panel screening are summarized in Table 1. During the pre-COVID-19 pandemic era, respiratory tract viral panel indicated RSV infection in 42 patients (p=0.001) and rhinovirus with influenza or metapneumovirus co-infection in 2 patients. During the post-COVID-19 pandemic era metapneumovirus was detected in three patients. When the incidence rates within each group are compared, a 3-fold decrease in babies with RSV was seen between the post-COVID-19 pandemic and pre-COVID-19 pandemic eras. Influenza, enterovirus and adenovirus were not found in patients during the post-COVID-19 pandemic era. There was no statistical difference between pre-COVID-19 pandemic and post-COVID-19 pandemic eras in terms of other viruses (Table 2).

The length of hospital stay, and the need for invasive and noninvasive respiratory support were higher in patients in the pre-COVID-19 pandemic era (p=0.014 and p=0.004). One patient with metapneumovirus infection died in the post-COVID-19 pandemic era. Patients in both groups were most frequently treated with ampicillin and gentamicin/amikacin for suspected bacterial superinfection or co-infection. Oseltamivir was administered to five patients who were tested positive for influenza infection.

DISCUSSION

Our results demonstrated that RSV was the most common viral cause of NICU admissions due to CANP before the COVID-19 pandemic; the hospitalizations for RSV pneumonia decreased 3-fold during the COVID-19 pandemic, which we attributed to public healthcare measures such as maintaining social distance, hand washing, and mask use, avoiding crowded places, the lockdown of the schools in Turkey.

Respiratory tract viral infections are the major cause of emergency admissions and hospitalization in pediatric patient groups.⁸ Of these viral infections, RSV and influenza are the most common which were also confirmed with our results before pandemics.⁴ In our study, we can explain the prolonged respiratory support need and the longer hospital stay of the patients during the pre-COVID-19 pandemic, with the lack of protective measures before the pandemic, and as a result, higher viral load and a more severe course of lower respiratory tract diseases. However, during the COVID-19 pandemic, the epidemiology of common respiratory viruses dramatically changed. Binns et al.⁹ reported a significant reduction in both influenza and bronchiolitis during usual peak seasons in Australia and New Zealand. Data from early months of winter in Europe are showing similar trends.⁷ ; Chiara Vittucci et al.¹⁰,

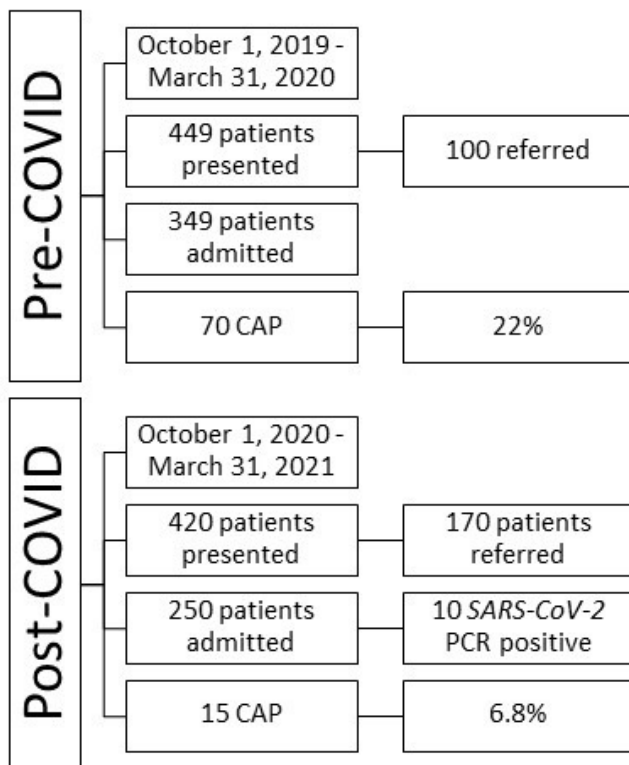


Figure 1. Summary of patients presenting, admitted, and diagnosed as having CAP before and during the COVID-19 pandemic eras

COVID-19: Coronavirus disease-2019, CAP: Community-acquired pneumonia, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2

Table 1. Comparison of patients admitted for community-acquired neonatal pneumonia before and during the COVID-19 pandemic era

	Pre-COVID-19 pandemic era (n=70)	Post-COVID-19 pandemic era (n=15)	p value
Patient characteristics			
Male sex	57.1%	73.3%	0.245
Gestational age (weeks)	37±2	35±3	0.007
Birth weight (g)	3045±601	2386±840	0.001
Postnatal age at presentation (days)	9±3	7±1	0.177
Presenting symptoms			
Wheezing	21.4%	46.7%	0.056
Tachypnea	14.3%	13.3%	0.644
Rales	64.3%	53.3%	0.427
Infiltration	58.6%	73.4%	0.064
Admitting hematological and biochemical parameters			
White blood cells (x10 ⁶ /L)	9275±3251	10399±3830	0.243
Neutrophils (x10 ⁶ /L)	3153±1857	3082±1731	0.891
Lymphocytes (x10 ⁶ /L)	4284±1824	5070±2475	0.160
Hemoglobin (g/dL)	13.3±3.1	11.6±3.1	0.071
Hematocrit (%)	40.5±9.9	35.5±9.9	0.096
Plateletcrit (%)	0.3±0.1	0.3±0.1	0.310
Platelets (x10 ⁶ /L)	400700±146566	431066±154203	0.472
Delta neutrophil index (%)	1.2±2.4	2.0±5.5	0.359
Large unstained cells (x10 ⁶ /L)	0.4±0.2	0.5±0.3	0.083
Neutrophil to leukocyte ratio	0.8±0.6	0.8±0.7	0.926
Systemic inflammatory index	347413±276541	392116±447742	0.617
C-reactive protein (mg/L)	10.3±15.2	6.6±8.2	0.368
pH	7.4±3.0	7.4±3.0	0.883
pCO ₂ (mmHg)	32±19	30±16	0.646
pO ₂ (mmHg)	34±23	33±19	0.758
HCO ₃ (mmol/L)	18±10	18±9	0.907
Base excess (mmol/L)	9±3	7±1	0.467
Lactate (mmol/L)	2.3±1.9	2.0±1.3	0.485
SpO ₂ (%)	94±2	95±1	0.885
Treatment and outcomes			
Length of ICU stay (days)	10±3	8±2	0.023
MV duration (days)	0.6±2.0	0±0	0.014
NIV duration (days)	1.7±2.1	0.6±1.2	0.004
Salbutamol inhalation therapy	38.6%	13.3%	0.061
Budesonide inhalation therapy	10.0%	13.3%	0.498
3% saline inhalation therapy	7.1%	6.7%	0.715
Mortality	0%	1.4%	*NS
*NS: Not significant. Values are presented as mean±standard deviation or percentage.			
ICU: Intensive care unit, MV: Mechanical ventilation, NIV: Non-invasive ventilation, COVID-19: Coronavirus disease-2019			

demonstrated a significant decrease especially in RSV cases moreover, they reported that rhinovirus cases were declined, but to a lesser extent compared to RSV cases. Besides they did not detect any influenza cases during pandemics.

While RSV and flu seems decreased, rhinovirus infections sustained and became prevalent, as previously reported by Wu et al.¹¹ Researchers speculated that nonpharmaceutical intervention, such as environment disinfection, had less effect on non-enveloped virus circulation, such as

Table 2. Comparison of viral agents' distribution of the patients before and during the COVID-19 pandemic era

	Pre-COVID-19 pandemic era (n=70)	Post-COVID-19 pandemic era (n=15)	p value
Respiratory syncytial virus	60%	13.3%	0.001
Rhinovirus	21.5%	46.7%	0.056
Influenza	7.1%	0%	0.581
Parainfluenza	4.3%	20%	0.065
Metapneumovirus	0%	20%	0.005
Enterovirus	5.7%	0%	0.453
Adenovirus	1.4%	0%	0.824

Values are presented as percentage.
COVID-19: Coronavirus disease-2019

rhinoviruses, which are comparatively ethanol-resistant containing antiseptic and survive longer on surfaces.^{12,13} Furthermore, Milton et al.¹⁴ reported that rhinoviruses mainly present in aerosol particles so, the effect of surgical mask on the spread of these viruses are less compared with viruses mainly presented in droplets such as influenza viruses. Confirming these findings, our results showed that the number of rhinovirus cases were comparable in both eras (21.5% vs. 46.7%). Surprisingly during pandemics 20% of CANP patients diagnosed as metapneumovirus infections, however there were no confirmed metapneumovirus cases in pre-COVID-19 pandemic era. Recently, Diesner-Treiber et al.¹⁵ reported that metapneumovirus infections disappeared during the pandemics along with influenza and RSV in children. A discrepancy of our results with this study may be due to the smaller number of cases.

Some published studies reported that the rates of RSV infection remained high and its epidemic season were similar to previous one. Du et al.¹⁶ stated that, RSV positivity rate from December 2020 to February 2021 was still quite high, possibly due to the susceptibility of those under 2 years old to RSV infection. Therefore, the gestational age and birth weight parameters of our patients, who were hospitalized during the post-COVID-19 pandemic were found to be lower. The respiratory tracts of these infants are not protected sufficiently by masks, and they have poor immune systems. Moreover, effective RSV vaccine has not yet been developed.

Study Limitations

The limitations of this study are; it involves only a limited number of cases from a single tertiary center and only newborn cases were studied. Therefore the results cannot be generalized for all children groups and all across the country. Multicenter, national larger studies must study

epidemiological changes in respiratory viruses in Turkey during COVID-19 pandemics.

CONCLUSION

Our results demonstrated that measures during COVID-19 pandemic suppressed the seasonal activity of RSV and influenza, but not of rhinovirus and metapneumovirus among neonates in a single tertiary center in the RSV season. However, these results need to be confirmed with national surveillance reports of the incidence of respiratory pathogens during the pandemics. Further research should focus on specific measure techniques, which may obligate the pathogen to disappear so, precise actions can be taken in future possible pandemic.

Ethics

Ethics Committee Approval: The study was approved by the Ankara State Hospital Local Clinical Research Ethics Committee (date: 24.02.2021, protocol no: E2-21-207).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.E., G.K.Ş., H.G.K.K., Design: S.E., F.E.C., H.G.K.K., Data Collection or Processing: S.E., A.Y., Analysis or Interpretation: F.E.C., G.K.Ş., H.G.K.K., İ.Ö., Literature Search: S.E., A.Y., Writing: S.E., H.G.K.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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