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Investigation of the Effect of the COVID-19 Pandemic on Viral Respiratory Tract Infections in the Neonatal Intensive Care Unit

Yenidoğan Yoğun Bakım Ünitesinde COVID-19 Pandemisinin Viral Solunum Yolu Enfeksiyonlarına Etkisinin Araştırılması

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ABSTRACT

Introduction: *This study aimed to compare the incidence of non-COVID-19 viral respiratory tract infections (RTI) in the neonatal intensive care unit (NICU) before and during the pandemic period.*

Materials and Methods: *The viral RTI diagnoses followed up in the NICU of our hospital during the pre-pandemic period (PPP, March 10, 2019-March 10, 2020) and the pandemic period (PP, March 11, 2020-March 11, 2021) were analyzed retrospectively. The incidence of viral RTIs was compared between the two periods, and the data were statistically evaluated.*

Results: *A total of 1550 newborns were observed during PPP, and 1109 newborns were monitored during the PP. There were 24 (1.54%) positive viral respiratory tract samples in the PPP and 3 (0.27%) positive viral respiratory tract samples in the PP (p= 0.0011). While there were 18 Respiratory syncytial virus infections in the PPP, only two were detected in the PP (p= 0.004).*

Conclusion: *Mask use, physical distancing, increased hygiene practices, and various restrictions implemented during the COVID-19 pandemic reduce the incidence of viral RTIs in newborns. Experience gained throughout this pandemic may serve as a guide to lowering the incidence of RTIs in newborns.*

Key Words: *COVID-19; Respiratory tract infections; Viral infections; Newborn*

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ÖZ

Yenidoğan Yoğun Bakım Ünitesinde COVID-19 Pandemisinin Viral Solunum Yolu Enfeksiyonlarına Etkisinin Araştırılması

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Giriş: *Bu araştırmada bir yenidoğan yoğun bakım ünitesinde (YYBÜ) pandemi öncesi ve pandemi döneminde gelişen COVID-19 dışı viral alt solunum yolu enfeksiyonlarının (ASYE) sıklığının karşılaştırılması amaçlanmıştır.*

Materyal ve Metod: *Bu araştırmada hastanemiz YYBÜ izlenen, pandemi öncesi dönem (PÖD; 10 Mart 2019-10 Mart 2020) ve pandemi dönemindeki (PD; 11 Mart 2020-11 Mart 2021) viral ASYE tanı sıklığı geriye dönük incelendi. İki dönem arasındaki viral alt solunum yolu örneklerinin sıklığı karşılaştırıldı. Veriler istatistiki olarak değerlendirildi.*

Bulgular: *PÖD'de 1550 ve PD ise 1109 yenidoğan izlendi. PÖD'de 24 (%1.54) ve PD'de üç (%0.27) viral solunum yolu örneği pozitifliği tespit edildi (p= 0.0011). PÖD'de 18 respiratuar sinsityal virüs enfeksiyonu (RSV) varken PD'de iki RSV enfeksiyonu tespit edildi (p= 0.004).*

Sonuç: *COVID-19 salgını sırasında uygulanan maske, fiziksel mesafe, artmış hijyen uygulamaları ve çeşitli kısıtlamalar yenidoğanlarda görülen viral ASYE'yi azaltmaktadır. Bu salgındaki tecrübeler yenidoğanlardaki bulaşıcı ASYE sıklığını azaltmak için yol gösterici olabilir.*

Anahtar Kelimeler: *COVID-19; Respiratuvar sinsiyal virüs; Viral enfeksiyonlar; Yenidoğan*

INTRODUCTION

Respiratory tract infections (RTIs) are an important reason for hospitalization in infants[1]. Respiratory syncytial virus (RSV), rhinovirus, parainfluenza virus, orthomyxovirus, and adenovirus are the leading causes of viral RTIs during early childhood[2,3]. Generally accepted transmission routes for viruses that can cause RTIs are direct contact with droplets or indirect contact through an intermediary surface/object[4]. Standard infection control measures, avoidance of crowds, rapid detection of new cases, and contact isolation are essential to prevent viral RTI. In order to prevent the effects of epidemics in the neonatal intensive care unit (NICU), it is necessary to enhance hygiene measures, especially in winter, and to control visitors during the epidemic period[5]. Placing viral RTI patients in isolation rooms, washing hands before and after contact with such patients, using gowns, gloves, and protective masks, and limiting visitor entrance and exit is critical in preventing the spread of these infections[6].

Due to the COVID-19 pandemic, people have preferred to maintain physical distance and avoid crowded environments. Other respiratory viral agents have also been prevented while observing mask-distance-hygiene measures to prevent severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) transmission. Reports from France and Finland have shown a significant decline in the incidence of viral RTIs after implementing the measures[7].

Have viral RTIs in neonatal units also decreased? There is still a lack of data on this issue. This study aimed to compare the incidence of viral RTIs during the pandemic period (PP) and the pre-pandemic period (PPP).

MATERIALS and METHODS

Center

Sakarya University Faculty of Medicine, Department of NICU, is a tertiary care unit that serves a population of around a million.

Study Periods

In this study, it was aimed to retrospectively examine the proportion of patients diagnosed with viral RTI and followed up in the NICU during PP and PPP. This study was conducted in accordance with the guidelines of the Helsinki Declaration

and was approved by the Non-Invasive Clinical Research Ethics Committee (30.03.2021-E.21469) of Sakarya University Faculty of Medicine.

PPP: Patients who were followed up in the NICU owing to viral RTI between March 10, 2019, and March 10, 2020, were included in the study.

PP: Records of patients who were followed up in the NICU due to viral RTI between March 11, 2020, and March 11, 2021, were included in the study.

The clinical and laboratory findings of the patients included in the study were obtained retrospectively from the records on the automation system.

Criteria for Hospitalization

Newborns meeting at least one of the following criteria were admitted to the hospital.

A. Symptoms of respiratory distress: Tachypnea (respiratory rate >60/min) and/or hypoxemia (peripheral oxygen saturation <90%) and cough, wheezing, retraction and/or apnea (respiratory arrest for at least 20 seconds)

B. Feeding difficulties in an infant with respiratory symptoms

C. Signs of circulatory failure (such as tachycardia and hypotension)

Exclusion Criteria

- Having been diagnosed with COVID-19, positive COVID-19 reverse transcription-polymerase chain reaction (RT-PCR) test, or a history of contact with an individual infected with COVID-19
- Congenital respiratory anomaly
- Bronchopulmonary dysplasia
- Congenital heart disease
- Infants with bacterial growth in blood culture

Collection and Processing of Samples

Nasopharyngeal swab samples were collected with a sterile dacron swab immediately after admission of infants with clinical findings of RTI. The samples were placed in the viral transport medium and delivered to the laboratory.

Patients hospitalized in our NICU with acute respiratory infection symptoms were routinely tested for the following (non-SARS-CoV-2) viruses: Influenza A and B, coronavirus 229E, coronavirus HKU1, coronavirus NL63, coronavirus OC43, parainfluenza 1, parainfluenza 2, parainfluenza 3, parainfluenza 4, RSV, human metapneumovirus, adenovirus, bocavirus, rhinovirus/enterovirus by multiplex RT-PCR. The tests were carried out according to the manufacturer's procedure.

Statistical Analysis

Statistical analysis was performed using Epi Info ver 6.0 (CDC Atlanta). The rates and absolute numbers for cumulative viral respiratory tract infections from 2019 to 2020 were compared with those for the same length of time from 2019 to 2020. This study was performed at a single pathogen level using Fisher's exact test. All tests applied were two-tailed, and a p-value of <0.05 was considered significant.

RESULTS

A total of 1550 patients were monitored for 12.248 patient-days during PPP, and 1109 patients for 10.331 patient-days during PP in the NICU (Table 1).

Mean gestational week of the newborns followed up with a diagnosis of RTI was 37.90 during PPP and 38.66 weeks during PP (p= 0.26). Mean birth weight was 3110.29 g during PPP and 3504.66 g during PP (p= 0.09).

When clinical complaints of the patients hospitalized due to RTI were examined, respiratory distress and cough were the most common symptoms both during PPP and PP. The demographic data, delivery information, and respiratory complaints of the newborns during both periods are shown in Table 2.

During the study period, samples were collected from 40 newborns with a diagnosis of respiratory tract infection during PPP and from 7 newborns during PP. RT-PCR tests of 24 patients during PPP and three patients during PP were viral positives. When the bacterial distribution of the agents isolated in the respiratory tract samples

Table 1. Number of hospitalized patients, patient days and respiratory tract sample pre-pandemic and pandemic period

Parameter	Pre-pandemic period	Pandemic period	P
Patients n	1.550	1.109	NA
Patient days n	12.248	11.331	NA
Hospital infections n (%)	29 (1.87)	21 (1.89)	0.96
Number of newborns hospitalized with a diagnosis of respiratory tract (non-COVID-19) infections n (%)	40 (2.58)	7 (0.63)	0.00016
Number of positive viral respiratory samples (non-COVID-19) n (%)	24 (1.54)	3 (0.27)	0.0011

NA: Not applicable.

Table 2. Characteristics of the patients with a positive viral respiratory tract sample (non-COVID-19)

Characteristics	Pre-Pandemic Period n= 24 (%)	Pandemic Period n= 3 (%)	P
Sex (female)	12 (50)	1 (33.33)	0.685
Length of hospital stay	8.6 ± 6.62	7.3 ± 3.05	0.272
Gestational week	37.9 ± 2.12	38.6 ± 0.57	0.26
Birth weight (g)	3110.29 ± 819.21	3504.66 ± 50.64	0.09
1500-2500 gr	5 (20.84)	0	NA
>2500 gr	19 (79.16)	3 (100)	0.381
Fever	2 (8.33)	0	NA
Cough	16 (66.66)	3 (100)	0.233
Respiratory distress	21 (87.5)	2 (66.6)	0.338
Mechanical ventilation support	3 (12.50)	0	NA
Influenza A	0	0	NA
Influenza B	2 (8.33)	0	NA
Coronavirüs 229E	0	0	NA
Coronavirüs HKU1	0	0	NA
Coronavirüs NL63	2 (8.33)	0	NA
Coronavirüs OC43	0	0	NA
Parainfluenza 1	0	0	NA
Parainfluenza 2	0	0	NA
Parainfluenza 3	0	0	NA
Parainfluenza 4	0	0	NA
Respiratory syncytial viruses A/B	18 (75)	2 (66.66)	0.004
Human metapneumoviruses A/B	0	0	NA
Adenovirus	0	0	NA
Bocavirus	0	0	NA
Rhinovirus/Enterovirus	2 (8.33)	1 (33.33)	0.76

NA: Not applicable.

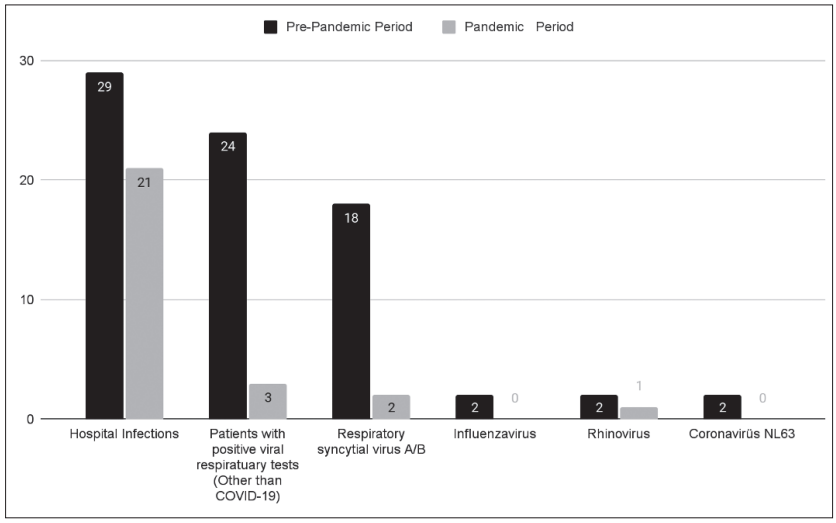

Figure 1. Viral respiratory infections and hospital infections pre-pandemic and pandemic period.

was examined, four (10%) [*Bordetella pertussis* (n= 3) and *Staphylococcus aureus* (n= 1)] bacterial agents were found during PPP. No bacterial RTI agent was detected during PP. When the distribution of viral agents was examined, the most common cause of RTI during both PPP and PP was RSV A/B (n= 18, n= 2, respectively) (Figure 1).

When evaluated by months, a total of 24 cases [December 2019 (2), January 2020 (10), February 2020 (11), only 1 case in March 2020] were detected during PPP, while three cases were found during PP (1 in December 2021 and 2 in February 2021).

DISCUSSION

The immune systems of newborns are not sufficiently mature. Many infants hospitalized in the NICU are susceptible to infections due to repeated invasive procedures. Many presentations in previous years, which were roughly defined as viral respiratory tract infections, can be defined currently at the species level, thanks to the developments in PCR techniques. Therefore, we can demonstrate the effect of the pandemic on the epidemiology of RTI in NICU.

In this study, no significant change was found in the incidence of nosocomial infections detected in the NICU during PPP and PP. However, considering the incidence of infants hospitalized with the diagnosis of RTI, it was found that respiratory tract infections significantly decreased during the PP. With the pandemic, measures such as hand cleaning, physical distancing, obligatory temporary closure, school closure, and wearing face masks became widespread both among healthcare professionals and in the community. However, the widespread use of masks and personal protective equipment in the community and among healthcare professionals has changed the dynamics at NICU. We found that RTIs during PP were 5.7 times (7/40) less common when compared to PPP (p= 0.00016). Moreover, we found that the number of viral infections detected during the same length of time decreased significantly during PP. We believe that the awareness of contact isolation raised both among healthcare professionals and in the community has a significant impact. Non-pharmaceutical interventions represent a cost-effective approach to prevent the spread of viral respiratory agents. Until pharmaceutical therapies that may be used widely become available, such interventions may be a practical approach for limiting the pandemic[8].

During the PP, there was a significant decrease in the number of patients tested for respiratory tract infections other than SARS-CoV-2. Hence, the simplest and cheapest method that reduces the risk of transmission of viral respiratory infections is good hand hygiene and avoidance of contact. It is essential to avoid crowds and

passive smoking, pay attention to hygiene in nurseries and kindergartens, and help healthcare professionals and families acquire handwashing habits. Similar findings have been reported in different countries. There was an unprecedented decrease in hospitalizations for RSV in Alaska[9]. We believe that the main reasons for this decline were the widespread use of face masks and visors, avoidance of close contact due to concerns about virus transmission, and enhanced hand hygiene.

Respiratory viruses such as influenza, RSV, and SARS-CoV-2 are transmitted in similar ways. Therefore, major social efforts to prevent the spread of SARS-CoV-2 in the community have also had an impact on the epidemiology of influenza and RSV[10]. The incidence of both RSV and influenza increases in the autumn and winter months. At the beginning of the COVID-19 pandemic, concurrent infections with influenza, RSV, and COVID-19 were highly feared. However, according to our data, there is a significant decrease in viral respiratory tract infections during the COVID-19 pandemic period. Non-pharmaceutical measures such as mask-wearing and physical distancing for COVID-19 greatly reduce the incidence of many other diseases, including RSV, influenza[11,12]. This reduction in the number of cases can be interpreted as a positive impact of preventing COVID-19[13]. In addition, curfews and restrictions on transportation, especially the ban on long-distance travel, have prevented the spread of agents[14].

Schools are critical areas in the spread of viral agents in society. Respiratory viruses spread rapidly in closed environments such as schools. Unfortunately, many schools had to be closed in the early stages of the COVID-19 pandemic. School closures have also occurred in other viral infections (e.g. RSV, influenza and SARS-CoV-2)[15,16]. It is possible to reduce viral respiratory tract infections and their damage by early implementation of critical measures such as masks, distance and vaccination[17].

All probable or laboratory-confirmed neonates with SARS-CoV-2 should be isolated[18]. Visitor restriction policies should be enforced[19]. Asymptomatic newborns born to mothers negative for SARS-CoV-2 can be housed together. It has been shown that the risk of infection is the same for babies who are temporarily separated from their mothers compared to babies who stay in the same room with their mothers. Therefore, it is recommended that mothers and newborns stay in the same room[20].

Our study has certain limitations that need to be considered. Patients may be self-medicating at home under the stress of the pandemic. Hence, we may not have evaluated outpatients who did not present to our center. The retrospective nature of our study is another limitation.

More information is needed on the epidemiology of SARS-CoV-2 infection. Extensive efforts are underway to explore its impact on maternal and neonatal outcomes. We believe that the decline in the number of common viral respiratory infections was a result of the interventions implemented during the COVID-19 PP. Our pandemic experience might be also used to prevent future viral epidemics that may occur in the NICUs.

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ETHICS COMMITTEE APPROVAL

The approval for this study was obtained from Sakarya University Faculty of Medicine Non-invasive Clinical Research Ethics Committee (Decision no: E.21469 Date: 30.03.2021).

CONFLICT of INTEREST

No conflicts of interest to be declared concerning the publication of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: MK

Data Collection or Processing: MK

Analysis/Interpretation: MK

Literature Search: MK

Writing: MK

Final Approval: MK

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