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Viral acute respiratory infections in neonatal intensive care healthcare workers: a nine-month point-prevalence cohort study

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SUMMARY

Background: Healthcare-acquired viral acute respiratory infections (ARIs) are a common problem in neonatal care. Health-care workers may transmit viruses to neonates when having a symptomatic or asymptomatic ARI.

Aim: This prospective nine-month repeated point-prevalence cohort study aimed to investigate the occurrence and aetiology of asymptomatic and symptomatic ARIs in health-care employees in a tertiary neonatal intensive care unit (NICU).

Methods: Flocked nasal swabs were collected on every second Tuesday in a NICU from all personnel working on that day. Additionally, in the case of ARI symptoms, a nasal swab was self-collected by the study subjects.

Findings: A virus was detected in 16 (3.3%) of the asymptomatic subjects. Altogether 36 symptomatic ARIs (mean 0.5 per person) were reported.

Conclusion: Our data suggests that ARIs are not uncommon among NICU health-care workers and moreover are commonly asymptomatic. It is noteworthy that these individuals may transmit.

Introduction

Healthcare-acquired viral acute respiratory infections (ARIs, 'common cold') are a significant but underappreciated problem in hospitals [1]. Healthcare-acquired ARIs are associated with higher risk of morbidity and with a longer length of stay in hospital in all age groups. In neonates and hospitalized newborns, the incidence of hospital-acquired ARIs is higher than in older children and adults [1]. The source of ARIs in newborns is often unknown, but viruses are transmitted either from infected family members, staff members or other patients [2]. Extensive research catalysed by the COVID-19 pandemic has demonstrated that a significant number of ARIs are asymptomatic and that transmission of viruses from asymptomatic individuals, especially among healthcare workers, is more common than earlier understood [3]. Epidemiologic observations suggest that at any time 5–10% of adults and 50% of children less than 5 years of age are virus positive [4,5]. Our prospective nine-month point-prevalence cohort study aimed to investigate the occurrence and aetiology of

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asymptomatic and symptomatic ARIs in tertiary neonatal intensive care unit (NICU) healthcare employees.

Methods

This nine-month repeated point-prevalence cohort study was conducted in a level III NICU in Turku University Hospital between 1st September 2019 and 6th June 2020. The whole NICU personnel (including nurses ($N = 65$), doctors ($N = 17$), and other staff ($N = 3$)) being in regular close contact with infants) was eligible to participate in the study.

Our NICU is the only tertiary-level NICU in south-west Finland serving a population of about 870,000. An average of 500—600 infants are admitted to the NICU annually, resulting in approximately 5000 patient care days per year. At the time of the current study, 11 of 12 patient rooms accommodated up to two patients. One room accommodated up to four patients and it was used for short-term admission of full-term infants. The average census was 14.3 patients (per day) in 2019—2020. As twins always shared a room, the majority of preterm patients and full-term infants staying longer than two days were cared for in a single-family room. However, in situations with high census, the two-patient rooms were shared by two unrelated families with one baby each.

Parents were encouraged to stay with their infants and healthy siblings were allowed to access NICU, except during the respiratory syncytial virus (RSV) outbreak in the community (between 19th December 2019 and 26th May 2020) when siblings under school age were not allowed to visit. Neither parents nor visitors were allowed to enter the NICU with respiratory tract infection symptoms. The COVID-19 pandemic did change the visitation policies in our NICU from 3rd April 2020, when no sibling visits were allowed. Parental visits were not restricted.

Before the COVID-19 pandemic the general staff instruction was to stay home if having a febrile ARI. Otherwise, the decision to take sick leave when having symptoms of ARI was based on individual assessment of the severity of the symptoms. Prior to March 2020 (pre-pandemic period), there was no specific masking protocol in our NICU. Symptomatic employees rarely used masks, and the decision was based on individual assessment. During the COVID-19 pandemic, the implementation of common masking did not occur in Finland until October 2020.

ARI was defined as the acute onset of at least one of the following symptoms lasting at least one day: sore throat, rhinorrhoea, nasal congestion, cough, and fever ($\geq$37.8 °C). A four-point severity scale (0 = absent, 1 = mild, 2 = moderate, and 3 = severe) was used. The total symptom score was calculated for sore throat, rhinorrhoea, nasal congestion, cough, hoarseness, lethargy, and muscle soreness (max 105 points) over the first five days of illness.

Flocked nasal swabs (553C, Copan, Brescia, Italy) from a depth of 4—5 cm were taken by the study nurse collectively on every other Tuesday in the NICU from all the personnel working on that day if the study subject was asymptomatic and had been a minimum of seven days asymptomatic after the last symptomatic ARI. Additionally, in the case of ARI symptoms, a nasal swab was self-collected by the study subjects at home on days 1—3 of the illness. A nasal swab was also taken from infants treated in our NICU if they presented with any possible symptoms of ARI. Swabs were inserted into dry test tubes and transported to the laboratory for storage at -80 °C. For nucleic acid extraction, 1 mL of phosphate-buffered saline was added into tubes, vortexed and 550 μL of the suspension was processed with BioMerieux Nuclisense easyMAG extractor with an elution volume of 55 μL.

The virus surveillance was made by the Department of Virology of the University of Turku during the spring 2024. Laboratory testing was carried out for respiratory syncytial type A and B viruses, adenovirus, influenza A and B viruses, rhinovirus, enterovirus, parainfluenza type 1—4 viruses, human coronaviruses 229E, OC43, and NL63, human bocavirus, and human metapneumovirus (Allplex Respiratory Panels 1—3, Seegene, Seoul, South Korea). In addition, a more sensitive in-house triplex polymerase chain reaction (PCR) assay was used for rhinovirus (non-coding region), enterovirus (non-coding region), and respiratory syncytial virus (fusion protein gene). SARS-CoV-2 virus was detected using a using a laboratory-developed PCR assay with WHO-recommended primers and probe targeting the E gene.

This study complied with the Declaration of Helsinki as revised in 2000 and all study-related activities were conducted according to Good Clinical Practice. The study protocol was approved by the Ethics Committee of the Hospital District of Southwest Finland (ETMK Dnro: 56/1801/2018). Written informed consent was obtained from all study subjects.

Results

A total of five people (all nurses) declined to participate in the study, the final number of participants being 80 (94.1% of total personnel). The first 29 weeks of the follow-up period (from 1st September 2019 to 12th March 2020, i.e., the pre-pandemic period) were normal regarding virus epidemiology, however, the last 12 weeks of the follow-up period (from 13th March to 6th June 2020) was influenced by the COVID-19 pandemic; this included the lockdown period (in Finland from 13th March to 15th June 2020) (Figure 1).

Overall, 525 nasal swabs were tested for viruses as follows: 489 asymptomatic samples and 36 samples taken at the beginning of ARI symptoms. In total, there were 20 Tuesdays (Figure 1, I—XX) with asymptomatic sample collections in the NICU and on average 24 samples were taken on one Tuesday. The mean (range) number of asymptomatic samples per person during the nine-month study period was 6.1 (1—15). A virus was detected in 16 (3.3%) of the 489 asymptomatic samples (Figure 1). Rhinovirus was the most commonly detected virus ($N = 11$, 64.7%), followed by human bocaviruses ($N = 3$, 17.6%) and seasonal human coronaviruses (CoVNL63 $N = 1$, CoVOC43 $N = 1$, 11.8%). In one sample two different viruses were detected simultaneously. Three samples were positive after ($\geq$7 days) a preceding ARI caused by the same virus. After 12th March 2020 (COVID-19 lockdown), only one virus positive asymptomatic episode was detected (Figure 1).

In this study population, there were 36 symptomatic ARIs reported altogether (mean 0.5, range 0—4/per person) (Figure 1). A viral aetiology was identified in 17 (47.2%) samples. Rhinoviruses ($N = 8$, 47.1%) and seasonal coronaviruses ($N = 3$, 17.6%) were the most common viruses detected (Figure 1). In two samples, two different viruses were detected simultaneously. No SARS-CoV-2-positive findings were detected. After 12th March 2020 (COVID-19 lockdown), only two symptomatic ARIs were reported, and one sample was virus

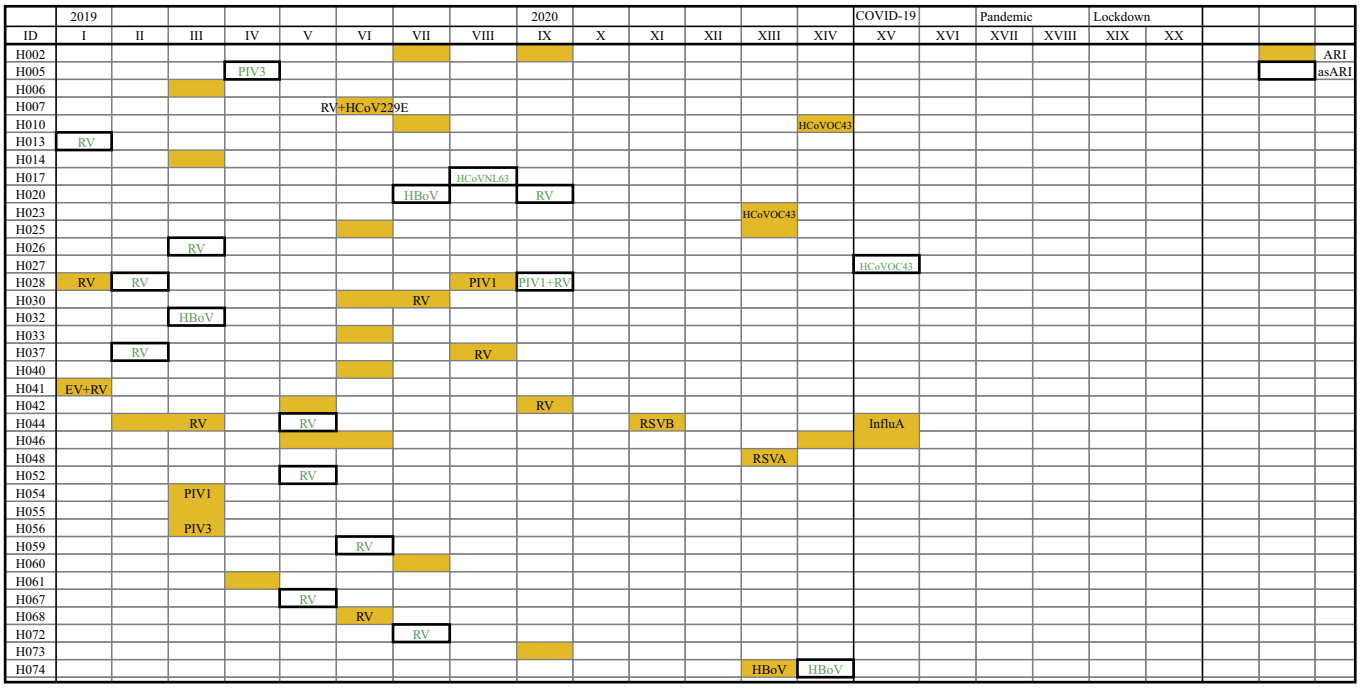

Figure 1. Occurrence and aetiology of acute respiratory illnesses (ARIs) in the neonatal intensive care unit (NICU) healthcare workers during the nine-month study period (between 1st September 2019 and 6th June 2020). I—XX, sample collection days in NICUs. Orange cell, ARI — symptomatic ARI (including virus finding, if positive); uncoloured cell, asARI — asymptomatic ARI. EV, enterovirus; HBoV, human bocavirus; HCoV, human coronaviruses 229E, OC43, and NL63; InfA, influenza A virus; PIV, parainfluenza type 1 and 3 viruses; RSV, respiratory syncytial type A and B viruses; RV, rhinovirus.

positive (Figure 1). Symptom diaries were available for 26 (72%) ARI episodes. The mean duration of the symptoms was seven (range 1—23) days. The total mean severity score was 24 (range 3—64). Six febrile illness episodes were reported.

The mean (standard deviation) Ct-value of asymptomatic and symptomatic virus positive samples was 36.6 (4.6) and 30.1 (5.0), $P<0.001$, Mann—Whitney U-test). There were five subjects with a high viral load (Ct-values <27), all being symptomatic. No significant correlation was detected between Ct-values and duration or severity of symptoms.

During the study period 60 nasal samples were taken from neonates treated in our NICU due to a suspicion of ARI for viral analysis. No virus-positive findings in neonates were detected.

Discussion

Outbreaks of all common respiratory viruses among birth hospitalized infants with respiratory symptoms have been described [6]. Respiratory viruses have also been detected from asymptomatic infants in whom the infection was clinically unrecognized [6]. Although the clinical course of a respiratory virus infection in a neonate is usually mild, viruses can also cause significant morbidity and potentially fatal illnesses in otherwise healthy infants [7]. Early-life viral respiratory infections have been shown to be associated with increased morbidity and mortality, length of hospital stay, unnecessary antimicrobial exposure, subsequent lung function abnormalities, particularly recurrent wheeze and asthma, and neurodevelopmental sequalae at follow-up [7].

Hospital personnel, family members, and visitors may transmit viruses to neonates when they have symptomatic or asymptomatic ARIs [3]. In a pioneer study examining on-duty healthcare workers, nasal swabs were collected biweekly from November until April from healthcare workers. Seven samples (3.5%) of 200 asymptomatic subjects were virus positive [4]. Our corresponding proportion was the same, 3.3%. This is comparable with 3—10% reported in the normal adult population [5]. Interestingly, in a study with healthy young adults a single point analysis of naso-/oropharyngeal samples revealed that up to 17% of the individuals were asymptomatically infected with a respiratory virus [8]. It is well established that SARS-CoV-2 Ct values of <27 generally demonstrate an infectious virus, but infectiousness has not been studied in other viruses. In our study population, the mean Ct-value in asymptomatic virus-positive episodes was 37.

Enhanced isolation precautions have been shown to reduce the overall rate of healthcare-acquired respiratory virus infections [2]. The COVID-19 pandemic provided evidence that multi-layered, high-level mitigation measures against transmission of respiratory viruses are also effective at the community level. Public health preventive measures and personal countermeasures dramatically reduced the occurrence of non-COVID respiratory viral infections, especially influenza and respiratory syncytial virus infections [9]. Our findings are consistent with those observations, and the study found that the mitigation protocols efficiently reduced the occurrence of ARI episodes as well as virus-positive asymptomatic episodes.

Respiratory pathogens spread through small respiratory aerosols and spread especially in closed environments, crowded indoor spaces and close-contact settings [10]. In a study examining on-duty healthcare workers, 46% of the subjects reported working while being ill [4]. The results of this study

showed that, in our NICU we did also have continuously virus-positive staff and thus putatively transmittable personnel on duty. Interestingly, although personnel in our NICU were not wearing masks before the COVID-19 pandemic, a good message is that they did not seem to transmit a disease to infants. It must be acknowledged that all asymptomatic infants were not systematically studied in this survey. Thus, differences in infection units' mitigation policies, adherence to those policies, and surveillance strategies, are likely to play a major role in the transmission of ARIs in NICUs.

In conclusion, our data suggests that ARIs are not uncommon among healthcare workers and moreover can be asymptomatic. It is noteworthy that these individuals are potential infectors of vulnerable patients with respiratory viruses. However, no symptomatic ARIs were detected in infants treated in our NICU during the study period indicating a sufficiently efficient enough institutional mitigation policy. The risk for viral ARI transmission can further be reduced by avoiding patient care duties during the first days of symptomatic ARI or at least by using a mask when symptomatic [9]. However, unknown asymptomatic but putatively infectious respiratory viral infections make prevention challenging.

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Author contributions

All of the authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by R.L. and M.V. The first draft of the manuscript was written by R.L. and O.R., and all the authors commented on previous versions of the manuscript. All of the authors read and approved the final manuscript.

Conflict of interest statement

All authors report no conflicts of interest relevant to this article.

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Ethics statement

This study complied with the Declaration of Helsinki as revised in 2000 and all study-related activities were conducted according to Good Clinical Practice. The study protocol was approved by the Ethics Committee of the Hospital District of Southwest Finland (ETMK Dnro: 56/1801/2018). Written informed consent was obtained from all study subjects.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2025.05.019.

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