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Brief Report

Laboratory-based surveillance of hospital-acquired respiratory virus infection in a tertiary care hospital

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Of 7,772 laboratory-confirmed cases of respiratory viral infection among hospitalized patients, 22.8% were categorized as having hospital-acquired infection. The overall incidence of hospital-acquired respiratory viral infection was 3.9 (95% confidence interval, 3.7-4.1) cases per 1,000 admitted patients. Rhinovirus was the most common virus (30.3%), followed by influenza virus (17.6%) and parainfluenza virus (15.6%).

The human respiratory viruses include adenovirus, bocavirus, human coronaviruses, enterovirus, influenza viruses, human metapneumovirus, parainfluenza virus, respiratory syncytial virus, and rhinovirus. Although respiratory viruses are mainly recognized as causes of community-acquired infections, they can also cause serious hospital-acquired respiratory infections[1] and may be responsible for hospital outbreaks.[2-4] Their relatively short incubation times and efficient transmission via small droplets among comorbid patients highlight the need for better understanding of respiratory viral infections in hospital settings. However, very limited published data are available on the overall epidemiologic characteristics of hospital-acquired infection caused by respiratory viruses, especially by viruses other than influenza viruses. Therefore, using laboratory-based surveillance, we investigated the overall incidence and related factors of hospital-acquired respiratory virus infections.

METHODS

This study was performed at a 2,700-bed, tertiary care, university-affiliated hospital between January 2012 and December 2015. All admitted patients who had positive test results for respiratory virus polymerase chain reaction (PCR) were prospectively identified and monitored until their discharge or release from isolation. Performance of the PCR test for respiratory viruses was at the discretion of the attending physician. Outpatients and patients discharged in the emergency room were not included. Respiratory viruses were detected by multiplex reverse-transcription PCR assay using a Seeplex RV15 ACE Detection kit (Seegene, Seoul, Korea) (January 2012-October 2013) or Anyplex II RV16 Detection kit (Seegene) (November 2013-December 2015). The performance of those PCR kits used in this study has been evaluated in a published study.[5] The overall sensitivities of Seeplex RV15 ACE detection kit and Anyplex II RV16 Detection kit were 93.3% and 95.2%, respectively. The specificity of the kits for each virus ranged from 98.6%-100%. These kits simultaneously detect influenza virus A and B, respiratory syncytial virus A and B, parainfluenza virus types 1-4, human metapneumovirus, adenovirus, coronaviruses 229E/NL63 and OC43/HKU1, rhinovirus, and enterovirus.

PCR-positive cases were categorized as hospital-acquired infection if the respiratory virus was newly identified beyond the maximum incubation period from the time of admission

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(adenovirus >14 days, bocavirus >4 days, enterovirus >6 days, human coronaviruses 229E/NL63 and OC43/HKU1 >5 days, human metapneumovirus >5 days, influenza virus >4 days, parainfluenza virus >6 days, respiratory syncytial virus >8 days, and rhinovirus >3 days).[6,7]

The proportion of hospital-acquired respiratory viral infections was calculated for all viruses. The incidence of such infections was calculated as the number of cases per 1,000 admissions and as cases per 10,000 patient days. This study was approved by the Institutional Review Board of Asan Medical Center.

RESULTS

During the study period, there were 453,075 admissions, and a total of 21,288 respiratory viral PCR tests were conducted. Table 1 shows the variation of the number of study subjects from year to year. A total of 7,772 nonduplicative PCR-positive cases were identified. Of these, 1,770 (22.8%) were categorized as having hospital-acquired infections. A total of 1,888 viruses were identified: 2 viruses were identified in 101 patients, 3 viruses were identified in 7 patients, and 4 viruses were identified in 1 patient. Of the 1,888 viruses identified, 573 (30.3%) were positive for rhinovirus, 333 (17.6%) were positive for influenza virus comprising 254 with influenza A and 79 with influenza B, 294 (15.6%) were positive for parainfluenza virus, 240 (12.7%) were positive for respiratory syncytial virus, 230 (12.2%) were positive for human coronavirus, 91 (4.8%) were positive for human metapneumovirus, 54 (2.9%) were positive for bocavirus, 43 (2.3%) were positive for adenovirus, and 30 (1.6%) were positive for enterovirus. The proportion of hospital-acquired infections was highest in human coronavirus (30.2%), followed by parainfluenza virus (29.8%), influenza virus (28.1%), rhinovirus (24.5%), respiratory syncytial virus (21.4%), bocavirus (21.1%), human metapneumovirus (20.5%), enterovirus (14.0%), and adenovirus (9.1%). The median length of hospital stay prior to contracting a respiratory viral infection was 16 days (interquartile range, 9-32 days).

The overall incidence of hospital-acquired respiratory virus infections was 3.9 cases per 1,000 admissions (95% confidence interval, 3.7-4.1) and 4.9 cases per 10,000 patient days (95% confidence interval, 4.7-5.2). The incidences of such infections according to the year, sex, age group, ward, and virus type are summarized in Table 1. The incidences ranged from 3.6-4.3 cases per 1,000 admissions, with the highest incidence in the year 2015. Patients ≤15 years were more likely to develop hospital-acquired respiratory virus infections. The incidence of such infections was highest in intensive care units (ICUs), followed by medical wards and surgical wards. Of the ICU cases, the median days of ICU stay before viral infection was 4 days (interquartile range, 1-12). All-cause 30-day mortality, 60-day mortality, and in-hospital mortality were 11.3%, 16.5%, and 12.9%, respectively.

The seasonal distribution of hospital-acquired respiratory viruses among hospitalized patients was similar to that of community-acquired infections (Supplementary Fig S1).

DISCUSSION

We found that hospital-acquired respiratory viral infections commonly occurred in a tertiary care hospital. Despite the inherent limitations of laboratory-based surveillance, which underestimated the disease burden, >20% of respiratory viral infections of hospitalized patients were categorized as hospital-acquired events, and various respiratory viruses were responsible. Our study is notable in that we included year-round data from 4 consecutive years and provided the admission days–adjusted incidence for each infection.

Table 1
Study subjects and incidence of hospital-acquired respiratory virus infection

Variable	Admissions	Conduction of respiratory virus PCR	Positive PCR	Incidence (95% CI) of HA-RV infection per 1,000 admissions	Incidence (95% CI) of HA-RV infection per 10,000 patients days
Total	453,075	21,288	1,770	3.9 (3.7-4.1)	4.9 (4.7-5.2)
Year					
2012	110,929	4,751	418	3.8 (3.4-4.1)	4.6 (4.2-5.1)
2013	111,128	4,536	404	3.6 (3.3-4.0)	4.5 (4.1-5.0)
2014	114,023	5,429	440	3.9 (3.5-4.2)	4.9 (4.5-5.4)
2015	116,995	6,572	508	4.3 (4.0-4.7)	5.7 (5.2-6.2)
Sex					
Male	231,174	12,573	1,028	4.5 (4.2-4.7)	5.2 (4.9-5.5)
Female	221,901	8,715	742	3.3 (3.1-3.6)	4.6 (4.3-4.9)
Age group					
≤15 y	47,167	3,474	455	9.7 (8.8-10.5)	12.9 (11.7-14.1)
>15 y	405,908	17,814	1,315	3.2 (3.1-3.4)	4.1 (3.8-4.3)
Ward					
Medical ward	297,746	14,071	1,253	4.2 (4.0-4.4)	5.5 (5.2-5.9)
Surgical ward	139,461	2,737	266	1.9 (1.7-2.1)	2.5 (2.2-2.8)
Intensive care unit	15,868	4,480	251	15.8 (13.9-17.8)	9.8 (8.6-11.0)
Virus*					
Rhinovirus				1.26 (1.16-1.37)	1.60 (1.47-1.73)
Influenza virus				0.73 (0.66-0.81)	0.93 (0.83-1.03)
Influenza A				0.56 (0.49-0.63)	0.71 (0.62-0.80)
Influenza B				0.17 (0.14-0.21)	0.22 (0.17-0.27)
Parainfluenza virus				0.65 (0.57-0.72)	0.82 (0.73-0.91)
Respiratory syncytial virus				0.53 (0.46-0.60)	0.67 (0.58-0.75)
Human coronavirus OC43/HKU-1 or 229E/NL63				0.51 (0.44-0.57)	0.64 (0.56-0.72)
Human metapneumovirus				0.20 (0.16-0.24)	0.25 (0.20-0.31)
Bocavirus				0.12 (0.09-0.15)	0.15 (0.11-0.19)
Adenovirus				0.09 (0.07-0.12)	0.12 (0.08-0.16)
Enterovirus				0.07 (0.04-0.09)	0.08 (0.05-0.11)

CI, confidence interval; *HA-RV*, hospital-acquired respiratory virus; *PCR*, polymerase chain reaction.
*Some patients had ≥2 viruses. The maximum incubation period was defined as follows: rhinovirus (3 days), influenza virus (4 days), parainfluenza virus (6 days), respiratory syncytial virus (8 days), human coronavirus (5 days), human metapneumovirus (5 days), bocavirus (4 days), adenovirus (14 days), and enterovirus (6 days).

Data on hospital-acquired respiratory virus infections are still very scarce, mostly confined to influenza virus infections. A Canadian group reported that among hospitalized patients in 51 Canadian hospitals, 23.2%-23.6% of influenza virus infections were health care–associated infections.[8] A German group recently reported the proportion of hospital-acquired influenza virus infection as 20.5%-24.6%.[9] Our rate of such infections (28.1%) was somewhat higher than prior reports. Our inclusion of pediatric patients may have been responsible for this. Of note, the influenza virus was responsible for only 13.9% of all hospital-acquired respiratory viral infections. That is, most cases were caused by respiratory viruses other than the influenza virus and which have received much less attention. These findings highlight the importance of year-round surveillance and infection control measures for various respiratory viruses beyond the influenza virus.

According to our results, the incidence of hospital-acquired respiratory virus infections has increased in recent years. We speculate that increased numbers of prescriptions for PCR tests for hospitalized patients are responsible for this finding. That means that clinicians are increasingly aware of respiratory viral infection as one of the important causes of hospital-acquired infection. The use of more sensitive PCR kits in recent years may also have affected the incidence of respiratory viral infection. However, because the reported sensitivities of the 2 assays (93.3% and 95.2%, respectively) are similar,[5] the impact of changes in the PCR kits is not likely to have been substantial. Surprisingly, the incidence of respiratory virus infections was highest in ICUs. Considering the brevity of ICU stays (median, 4 days) before the detection of viruses, it is probable that most of the cases were hospital-acquired lower respiratory tract infections that occurred in wards, not in the ICUs. These findings are consistent with those of a Spanish group, which showed that during the influenza season, 29.5% of critical patients with suspected lower respiratory tract infections had influenza, 42% of which were hospital acquired.[10] It has also been reported that respiratory viruses were responsible for 22.5% of cases of severe hospital-acquired pneumonia requiring ICU admission in adults.[11] These results strongly suggest that hospital-acquired infections caused by respiratory viruses could lead to serious consequences.

This study had several limitations. First, it was performed at a single, large tertiary care hospital. Our study population included a substantial number of immunocompromised patients who were susceptible to infection, which likely biased our results. Second, some patients categorized as having hospital-acquired infections may have been already carrying respiratory viruses at the time of admission. Finally, the indications for conducting PCR tests for respiratory viruses were not standardized across the hospital, and the detailed significance of PCR-positive cases was not analyzed.

In conclusion, hospital-acquired respiratory viral infections are commonly encountered among hospitalized patients. Hospital surveillance of respiratory viruses should be considered to identify infected patients early and to prevent intrahospital transmission of respiratory viruses.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajic.2017.01.009.

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