Abstract

Respiratory virus detection in critically ill patients with severe pneumonia: epidemiology and clinical implications

Hyung-Jun Kim

College of Medicine, Department of Clinical Medical Sciences

The Graduate School

Seoul National University

Introduction: Viral pneumonia is associated with high morbidity and mortality in critically ill patients. Considering various kinds of antiviral agents and vaccines, it is important to reveal prevalence of each virus, and furthermore announce clinical impact of such detection. Our study aimed to report viral pathogens in patients admitted to the intensive care unit (ICU) due to severe pneumonia, and further analyze their clinical implications.

Methods: We evaluated patients with severe viral pneumonia admitted to a medical ICU between January 2008 and December 2015. Patients underwent reverse transcription polymerase chain reaction (RT-PCR) for 8 different respiratory viruses when viral pneumonia was suggested. Baseline clinical

characteristics, laboratory results, results of microbiological detection, and the clinical outcomes including hospital stay and mortality were obtained.

Results: Among the 2,347 patients admitted to the medical ICU over the 8 years, 519 patients were suspected of viral pathogen, and 69 of them had positive results from the RT-PCR. Detection rate was highest during the winter seasons; with respiratory syncytial virus was most common pathogen. Clinical characteristics and laboratory results did not differ among viral pathogens, however, such detection led to change of patient management in 33.3%. Bacterial coinfection was detected in 27 (39.1%) patients, but specific types of viral and bacterial pathogens did not show significant correlation with one another.

Conclusions: Viral pathogens were detected in severe pneumonia not infrequently and such detection can lead to positive change of clinical managements in considerable cases.

Keywords: Pneumonia, viruses, critical illness, reverse transcription

Student number: 2015-22246

CONTENTS

LIST OF TABLES AND FIGURES

INTRODUCTION

Respiratory viruses are common pathogens among hospitalized adults with pneumonia, and are more frequently detected than bacterial pathogens in a certain group of patients (1). Detected respiratory virus is not only a bystander but likely to be pathogenic, and is associated with high mortality (2, 3). Among them, influenza is a well-known respiratory viral pathogen, and others including respiratory syncytial virus (RSV) and parainfluenza virus are also common (4-6).

Such viral pathogens are not easy to distinguish according to clinical findings alone (7). Therefore, it is suggested that reverse transcription polymerase chain reaction (RT-PCR) be performed in patients when viral pathogen is suspected (8). Such testing for respiratory viruses can decrease use of inappropriate antibiotics and other medical resources (9). Considering different antiviral agents and vaccines, it is necessary to reveal the general prevalence of viral pathogens, and furthermore announce clinical impacts of such detection.

Viral pneumonia is also a major cause of patient deterioration in the intensive care unit (ICU) (10). Respiratory viruses are well known for their high prevalence among community acquired pneumonia patients with milder forms of clinical presentations (11, 12). Furthermore, its role as a nosocomial pathogen in a more severe group of patients is recently being highlighted (13, 14). However, it is not established if such detection rates differ among each pneumonia groups, or whether such detection leads to change in clinical management or patient outcomes.

In this study, we aimed to reveal common respiratory viral pathogens with severe pneumonia admitted to the ICU including CAP, healthcare-associated pneumonia

(HCAP), and also HAP, in a longer period of time. In addition, we aimed to analyze clinical impact of such detection.

MATERIALS AND METHODS

1. Study design and patients

This study evaluated patients over the age of 19 with severe pneumonia admitted to a 22-bed medical ICU in a tertiary teaching hospital between January 2008 and December 2015. Patients' respiratory specimens underwent RT-PCR for respiratory viral pathogens when they did not respond to empirical antibiotics or when radiological findings suggested viral pneumonia.

The multiplex respiratory viral RT-PCR kit of our institution detected 12 respiratory viral pathogens using a combined method of RT-PCR and electrophoresis from 2007 to 2014 (RV12; Seegene, Seoul, South Korea), and 16 pathogens using multiplex real-time PCR from 2015 until now (RV16; Seegene, Seoul, South Korea). However, due to national medical insurance policy in South Korea, only 8 pathogens were reported to the attending physicians. Reported respiratory viruses were: influenza A, influenza B, parainfluenza 1, parainfluenza 2, parainfluenza 3, RSV A, RSV B, and adenovirus.

Type of sampling for the RT-PCR was decided according to the attending physician, which included invasive (bronchoalveolar lavage [BAL]) and noninvasive (nasopharyngeal swab, sputum, or endotracheal aspirate) methods. Patients with detected viral pathogen were included in the analysis.

This study was conducted in accordance with the amended Declaration of Helsinki. It was reviewed by the local institutional review board (protocol number: H-1603-

106-750). The informed consent was waived because all data were de-identified before starting the analysis.

2. Variables and data collection

Baseline characteristics such as age, gender, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Charlson Comorbidity Index (CCI), and underlying pulmonary conditions were investigated. Laboratory results including C-reactive protein and procalcitonin closest but not after the respiratory viral RT-PCR were included in the analysis. Microorganisms were considered as pathogens when blood cultures, respiratory tract specimen cultures, or urine pneumococcal antigens showed positive results. It was considered as a coinfection if both virus and bacteria were detected. Clinical outcomes including hospital days, ICU days, change of management, and in-hospital mortality were analysed. Causes of in-hospital mortality were also obtained retrospectively from the medical records.

3. Definition

Pneumonia was diagnosed by the attending physician, with combination of new lung infiltrate plus clinical evidence including the new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation (15). It was divided into CAP, HCAP, and HAP, according to the American Thoracic Society and Infectious Disease Society of America guidelines (15, 16). Underlying chronic lung disease included chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis,

and pneumoconiosis (17-19).

4. Statistical analysis

Patients with proven respiratory viral pathogen were described. Categorical variables were reported as number and percentage, and continuous variables were reported as median and interquartile range (IQR) or mean and standard deviation (SD), considering their type of distribution. Viral pathogens according to the period of detection were illustrated. Furthermore, patients with viral infection were divided into two groups: with and without bacterial coinfection. They were compared considering baseline characteristics, laboratory results, and clinical outcomes. Virus detection rate according to categories of pneumonia or types respiratory samplings were compared as well. All statistical analyses and graphing were performed using SPSS software (version 22.0; SPSS Inc., Chicago, IL) and Prism 5 software (GraphPad software, San Diego, CA).

RESULTS

Baseline and clinical characteristics

During the 8-year study period, 2,347 patients admitted to the medical ICU due to severe pneumonia. Among them, 519 patients underwent RT-PCR for respiratory viruses suspecting viral pathogen. Total of 69 patients had positive results from the RT-PCR (Figure 1).

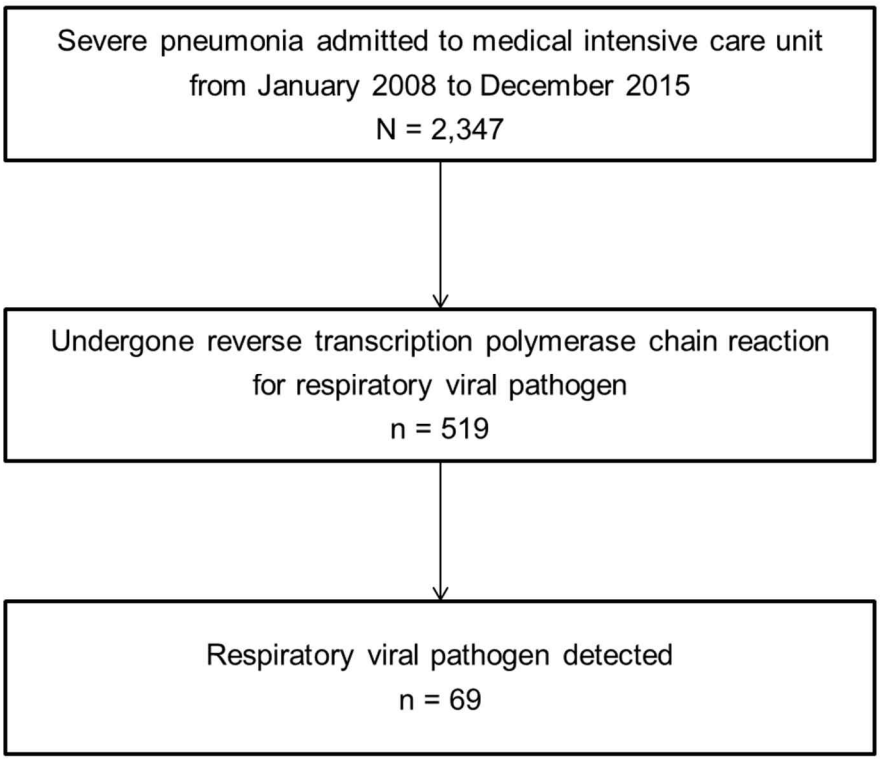

Figure 1. Flowchart of patient selection.

The patients had a mean age of 62.3 years, with 82.6% of male predominance (Table 1). The mean APACHE II score was 27.23, and the median CCI was 2. HCAP was the most common

Viral pathogen

Among the 69 patients, RSV A was the most common viral pathogen, followed by influenza A, parainfluenza 3, RSV B, adenovirus, influenza B, and parainfluenza 1 (Table 2). Influenza A/B and RSV A were more commonly detected after the year 2012, and parainfluenza 3 was not detected after the year 2013. The other pathogens did not show much predominance over a certain period of time (Figure 2). Detection rate of RT-PCR for respiratory viral pathogens differed according to the tested season. The rate was highest during the winter seasons including February (35.6%) and January (26.7%), while it was lower in September (2.5%) and May (2.7%). Details are shown in Figure 3.

Detection of viral pathogen led to change in patient management in 33.3% of patients (Table 3). Twelve patients (17.4%) added antiviral therapy such as oseltamivir and ribavirin, while 3 (4.3%) patients decreased or stopped the use of immunosuppressant agents including steroids. Some patients stopped using antibiotics (2.9%), while others continued (2.9%) or extended (2.9%) the empirical use of antiviral agents.

Table 1. Baseline characteristics

Variables		Values
Age		62.30±15.79
Gender, male		57 (82.6)
APACHE II		27.23±9.55
Charlson comorbidity index		2 (1–4)
Pneumonia category		
	Healthcare-associated pneumonia	28 (40.6)
	Community acquired pneumonia	24 (34.8)
	Hospital acquired pneumonia	17 (24.6)
Underlying condition		
	Hypertension	24 (34.8)
	Recent chemotherapy	19 (27.5)
	Hematologic malignancy	19 (27.5)
	Solid organ malignancy	15 (21.7)
	Immune suppressants	15 (21.7)
	Diabetes mellitus	13 (18.8)
	Chronic kidney disease	13 (18.8)
	Arrhythmia	6 (8.7)
	Liver cirrhosis	5 (7.2)
	Chronic lung disease	5 (7.2)
RT-PCR specimen		
	BAL fluid	61 (88.4)
	Endotracheal aspirate	16 (23.2)
	Sputum	10 (14.5)
	Nasopharyngeal swab	6 (8.7)
Laboratory results		
	C-reactive protein	15.53±9.52
	BAL fluid segmented neutrophil	49.38±33.33
	BAL fluid lymphocyte	10.00 (3.00–26.50)
	BAL fluid CD4/CD8 ratio	0.87±0.63

Values are shown as numbers (%), median (interquartile range), or mean±standard deviation. APACHE II, Acute Physiology and Chronic Health Evaluation II; RT-PCR, reverse transcription polymerase chain reaction; BAL, bronchoalveolar lavage

manifestation, and HAP was the least. About 7% of the patients had underlying chronic lung disease. Most of the patients had undergone bronchoscopy to obtain BAL fluids, but noninvasive samplings were also not rare (i.e. endotracheal aspirate 23.2%, sputum 14.5%, and nasopharyngeal swab 8.7%).

Table 2. Distribution of viral pathogen according to pneumonia categories

Pneumonia categories	Viral pathogen	Values
CAP (n = 24)		
	RSV A	8 (33.3)
	Influenza A	8 (33.3)
	Parainfluenza 3	3 (12.5)
	RSV B	3 (12.5)
	Influenza B	2 (8.3)
	Adenovirus	1 (4.2)
HCAP (n = 28)		
	RSV A	9 (32.1)
	Influenza A	7 (25.0)
	Parainfluenza 3	5 (17.9)
	Adenovirus	3 (10.7)
	RSV B	2 (7.1)
	Parainfluenza 1	2 (7.1)
	Influenza B	1 (3.6)
HAP (n = 17)		
	RSV A	4 (23.5)
	Parainfluenza 3	4 (23.5)
	RSV B	4 (23.5)
	Influenza A	3 (17.6)
	Adenovirus	3 (17.6)

Values are shown as numbers (%). Percentages (%) refer to percentages in each categories of pneumonia (i.e. CAP, HCAP, and HAP). AP, community acquired pneumonia; HCAP, healthcare-associated pneumonia; HAP, hospital acquired pneumonia; RSV, respiratory syncytial virus.

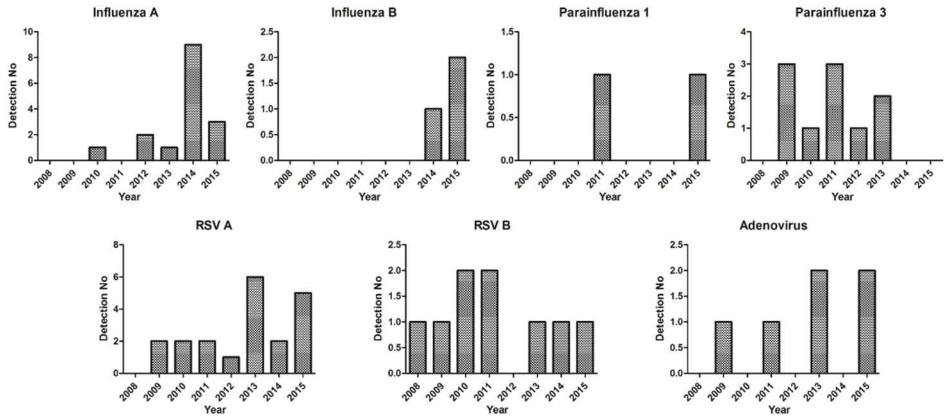

Figure 2. Detection of respiratory viruses according to each year.

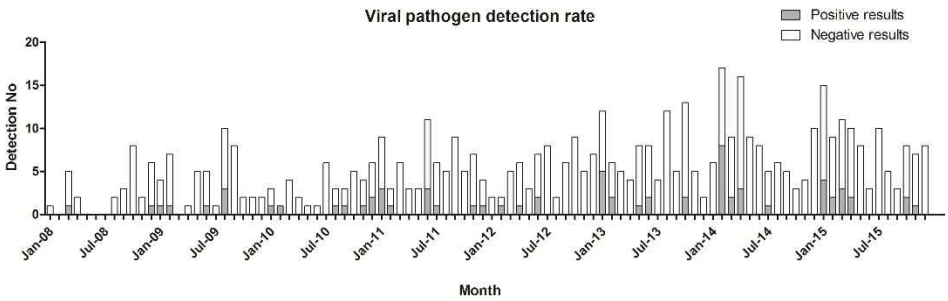

Figure 3. Detection rate of each viral pathogen according to year and month.

Table 3. Change in management after detection of viral pathogen

Variables	Values
Addition of antiviral therapy	12 (17.4)
Reduction or cessation of immunosuppressant	3 (4.3)
Stop antibiotics	2 (2.9)
Continue empirical antiviral therapy	2 (2.9)
Extend duration of antiviral therapy	2 (2.9)
Change antiviral agent	1 (1.4)
Stop antiviral agent	1 (1.4)
No change	46 (66.7)

Values are shown as numbers (%).

Bacterial coinfection

Bacterial coinfection was detected in 27 patients, and they were compared against patients without coinfection (n = 42). The patients did not differ in age, gender, CCI, and APACHE II scores. Patients with bacterial coinfection had higher rates of underlying chronic lung disease, although the difference did not show statistical significance. BAL fluid analysis showed higher percentages of segmented neutrophils and lower percentages of lymphocytes in the coinfection group. Clinical outcomes such as hospital days, ICU days, and in-hospital mortalities did not show significant difference (Table 4).

Specific pathogens of coinfection are described in Table 5. Influenza A was the most common viral pathogen, and *Staphylococcus aureus* was the most common bacterial pathogen of coinfection. However, specific types of viral and bacterial pathogens did not show significant correlation with one another.

Table 4. Comparison between patients with and without bacterial coinfection

Variables		With Coinfection n = 27	Without Coinfection n = 42	*P*
Age		64.33±13.91	61.00±16.92	0.376
Gender, male		20 (74.1)	37 (88.1)	0.134
CCI		2 (1–4)	2 (1–4)	0.984
APACHE II		29.74±9.66	25.62±9.24	0.084
Pneumonia category				
	Healthcare-associated pneumonia	11 (40.7)	17 (40.5)	0.999
	Community acquired pneumonia	10 (37.0)	14 (33.3)	0.799
	Hospital acquired pneumonia	6 (22.2)	11 (26.2)	0.781
Chronic lung disease		4 (14.8)	1 (2.4)	0.073
Laboratory results				
	C-reactive protein	16.97±10.97	14.58±8.45	0.342
	Procalcitonin	0.75 (0.24–2.46)	0.69 (0.31–6.64)	0.999
	BAL fluid segmented neutrophil	70.36±25.91	38.89±31.96	0.002
	BAL fluid lymphocyte	7 (2.5–12.00)	17 (3–35.75)	0.026
	BAL fluid CD4/CD8 ratio	0.54±0.55	0.98±0.62	0.100
Hospital days		30 (19–50)	31.5 (22.75–46.00)	0.685
ICU days		14.78±10.69	13.86±12.60	0.746
In hospital mortality				
	Overall	17 (63.0)	25 (59.5)	0.775
	Pneumonia related	12 (44.4)	16 (38.1)	0.600

Values are shown as numbers (%), median (interquartile range), or mean±standard deviation. CCI, Charlson Comorbidity Index; APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; BAL, bronchoalveolar lavage

Table 5. Pathogens of coinfection

Category	Pathogen	Values
Virus		
	Influenza A	11 (40.7)
	RSV A	7 (25.9)
	Parainfluenza 3	4 (14.8)
	Adenovirus	3 (11.1)
	RSV B	2 (7.4)
	Influenza B	1 (3.7)
Bacteria		
	MSSA	4 (14.8)
	MRSA	4 (14.8)
	Enterococcus faecium	4 (14.8)
	Klebsiella pneumoniae	4 (14.8)
	IRAB	2 (7.4)
	Pseudomonas aeruginosa	2 (7.4)
	Escheria coli	1 (3.7)
	Klebsiella oxytoca	1 (3.7)
	Staphylococcus epidermidis	1 (3.7)
	Streptococcus viridans	1 (3.7)
	Corynebacterium striatum	1 (3.7)
	Moraxella catarrhalis	1 (3.7)
	Stenotrophomonas maltophilia	1 (3.7)

Values are shown as numbers (%). MSSA, Methicilin susceptible *Staphylococcus aureus*, MRSA, Methicillin resistant *Staphylococcus aureus*, IRAB, Imipenem resistant *Acinetobacter baumannii.*

.

Detection rate of viral pathogens

We compared the detection rate of respiratory viral pathogens according to different categories. When they were divided into three pneumonia categories (CAP, HCAP, and HAP), viral detection rate was significantly higher with CAP

(18.6%), and lower with HAP (9.1%). The details are described in Table 6.

Table 6. Detection of viral pathogen according to each categories of pneumonia

Categories	Viral pathogen detected n = 69	Viral pathogen not detected n = 451	*P*
Community acquired pneumonia	24 (18.6)	104 (81.4)	0.033
Healthcare-associated pneumonia	28 (13.8)	175 (86.2)	0.789
Hospital acquired pneumonia	17 (9.1)	171 (90.9)	0.032

Values are shown as numbers (%).

Furthermore, the patients were divided into groups according to their sampling types (invasive and noninvasive). Among the 69 patients, 36 of them underwent invasive respiratory specimen sampling (BAL), 8 patients retrieved viral pathogen from noninvasive sampling (endotracheal aspirate, nasopharyngeal swab, and sputum), and the remaining 25 patients underwent both types of sampling (Table 7). Viral detection rate was the highest among the patients who had undergone both types of sampling (30.5%), and was the lowest among the patients who had undergone invasive sampling only (9.2%). Furthermore, among the 25 patients who had undergone both invasive and noninvasive samplings, only 7 patients obtained new information from invasive sampling: 8 patients had positive results from noninvasive specimens only, and 10 patients had same results of noninvasive and invasive samplings.

Table 7. Viral detection rates according to types of respiratory sampling

Variables	Viral pathogen detected n = 69	Viral pathogen not detected n = 451	*P*
Invasive specimen only	36 (9.2)	354 (90.8)	<0.001
Noninvasive specimen only	8 (17.0)	39 (83.0)	0.430
Both	25 (30.5)	57 (69.5)	<0.001

Values are shown as numbers (%). Both refer to both invasive and noninvasive specimens.

DISCUSSION

In our study, we revealed viral pathogens from severe pneumonia patients admitted to the medical ICU over a longer duration (8 years) compared to previous reports, regardless of their pneumonia categories (CAP, HCAP, or HAP). Such detection rate was 13.3%, and led to change of management among one-third of patients. Bacterial coinfection rate was 39.1%, although the patients with coinfection did not show different clinical outcomes compared to patients without sole viral infection. This is the first adult study to reveal the rates of change in management among severe viral pneumonia patients. There were previous studies about children with respiratory illnesses, however, children have much higher rates of respiratory viral illnesses compared to adults and needs to be discussed separately (9, 20-22). Among the 23 patients with change in management, change regarding antiviral agents was the most common (n = 18). Currently, anti-influenza agents are the only antiviral agents used actively, and ribavirin is the only antiviral treatment option for non-influenza respiratory viruses (23). Our study results can help emphasize the development of novel antiviral agents for respiratory viruses. Apart from antiviral agents, respiratory viral detection in critically ill patients led to reduction or cessation of immunosuppressant in 3 patients. Use of high-dose steroids is known to be associated with higher mortality and longer viral shedding in influenza A patients (24). Therefore it can be helpful to reduce the use of immune modulating agents including steroids to improve patient outcome. Two other patients stopped using empirical antibiotics, and focused on respiratory viruses as pathogens. Long term use of antibacterial in viral pneumonia patients is known to increase the risk

of multidrug resistant pathogens and *Clostridium difficile* infection rather than to improve clinical outcomes (25, 26). Our study supports that detection of viral pathogens in severe pneumonia patients reduces unnecessary antibiotics.

Viral detection rate was higher in CAP and lower in HAP. This further supports the recommendation to use empirical therapy against influenza during the winter seasons among hospitalized CAP patients (27). On the other hand, viral pathogen can be less considered in severe HAP patients as reported in our study (9.1%). This is the first study to report such difference.

RSV was the most common pathogen of viral pneumonia. It is an important pathogen that can result in severe pneumonia, especially in the elderly (28, 29). Previous studies differed in detailed distribution of pathogens, but many have revealed common viral pathogens as influenza, parainfluenza, and RSV (13, 30, 31). As shown in Table 2, the prevalence of each viral pathogen did not differ significantly among each pneumonia categories. Detection rate of each pathogen was the highest in winter seasons as described in a previous review (10). Considering the limited strategies for treating and preventing respiratory viruses other than influenza, such distribution of various pathogens can further emphasize development of novel antiviral agents and vaccines.

Viral detection rate was highest in patients who had undergone both invasive and noninvasive samplings (n = 25), but only about 28% of patients benefited from further invasive samplings (n = 7). Noninvasive sampling was sufficient for the diagnosis of viral pathogen in the remaining 72% of the patients (n = 18). Details are shown in Table 8. Despite further studies are mandatory to announce the

clinical efficiency of invasive sampling in the settings of lower respiratory viral infection, potential harms of BAL in critically ill patients and low viral yield from BAL fluid should be thoroughly reviewed before the procedure. In addition, considering the recent preference of noninvasive sampling in the recent guideline for HAP, repeated noninvasive respiratory specimen could replace BAL in selected patients (15).

Table 8. Patients with virus from both invasive and noninvasive samples

Variables		Values
New information from IS		7 (28)
No additional information from IS		18 (72)
	Same results as NIS	10 (40)
	Negative results from IS	8 (32)

Values are shown as numbers (%). IS, invasive sampling; NIS, noninvasive sampling.

Our study has shown lower detection rates of respiratory viral pathogens compared to previous reports (30, 31). This may be due to the difference that we included HAP patients into analysis. Among 519 patients who underwent multiplex RT-PCR for respiratory viral pathogens, 188 (36.2%) of them were HAP patients. Detection rate was increased to 18.8% when only CAP patients were considered.
Bacterial coinfection rate was similar with previous reports (11, 32). It further supports the fact that patients with viral infection should be carefully examined for any additional infection with bacteria. Common bacterial pathogens of coinfection

were common colonizers in the nasopharynx (33). However we failed to show significant difference in mortality. This is also similar to previous reports, which have shown comparable results between patients with and without bacterial coinfection (34). Such difference with bacterial coinfection should be further studied in the future.

Our study has several limitations. First, this was a retrospective study performed in a single center. Second, we considered the detected microorganism as pathogens, and could not rule out bystanders. Third, multiplex RT-PCR of our center included only 8 viral pathogens, and did not include others including enterovirus or rhinovirus.

In conclusion, detection of viral pathogens in severe pneumonia can lead to significant change in clinical management. Such detection can be done by noninvasive sampling in many cases. Non-influenza respiratory viruses were common in all three pneumonia categories; therefore further studies are warranted for novel antiviral agents for non-influenza respiratory viruses.

REFERENCES

1. Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, Bramley AM, et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. The New England journal of medicine. 2015;373(5):415-27.

2. Crotty MP, Meyers S, Hampton N, Bledsoe S, Ritchie DJ, Buller RS, et al. Epidemiology, Co-Infections, and Outcomes of Viral Pneumonia in Adults: An Observational Cohort Study. Medicine. 2015;94(50):e2332.

3. Zhan Y, Yang Z, Chen R, Wang Y, Guan W, Zhao S. Respiratory virus is a real pathogen in immunocompetent community-acquired pneumonia: comparing to influenza like illness and volunteer controls. BMC pulmonary medicine. 2014;14:144.

4. Falsey AR, McElhaney JE, Beran J, van Essen GA, Duval X, Esen M, et al. Respiratory syncytial virus and other respiratory viral infections in older adults with moderate to severe influenza-like illness. The Journal of infectious diseases. 2014;209(12):1873-81.

5. Wiemken T, Peyrani P, Bryant K, Kelley RR, Summersgill J, Arnold F, et al. Incidence of respiratory viruses in patients with community-acquired pneumonia admitted to the intensive care unit: results from the Severe Influenza Pneumonia Surveillance (SIPS) project. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 2013;32(5):705-10.

6. Widmer K, Zhu Y, Williams JV, Griffin MR, Edwards KM, Talbot HK.

Rates of hospitalizations for respiratory syncytial virus, human metapneumovirus, and influenza virus in older adults. The Journal of infectious diseases. 2012;206(1):56-62.

7. Cunha BA, Corbett M, Mickail N. Human parainfluenza virus type 3 (HPIV 3) viral community-acquired pneumonia (CAP) mimicking swine influenza (H1N1) during the swine flu pandemic. Heart & lung : the journal of critical care. 2011;40(1):76-80.

8. Aramburo A, van Schaik S, Louie J, Boston E, Messenger S, Wright C, et al. Role of real-time reverse transcription polymerase chain reaction for detection of respiratory viruses in critically ill children with respiratory disease: Is it time for a change in algorithm? Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2011;12(4):e160-5.

9. Subramony A, Zachariah P, Krones A, Whittier S, Saiman L. Impact of Multiplex Polymerase Chain Reaction Testing for Respiratory Pathogens on Healthcare Resource Utilization for Pediatric Inpatients. The Journal of pediatrics. 2016;173:196-201 e2.

10. Nguyen C, Kaku S, Tutera D, Kuschner WG, Barr J. Viral Respiratory Infections of Adults in the Intensive Care Unit. Journal of intensive care medicine. 2016;31(7):427-41.

11. Choi SH, Hong SB, Ko GB, Lee Y, Park HJ, Park SY, et al. Viral infection in patients with severe pneumonia requiring intensive care unit admission. American journal of respiratory and critical care medicine. 2012;186(4):325-32.

12. Daubin C, Vincent S, Vabret A, du Cheyron D, Parienti JJ, Ramakers M, et al. Nosocomial viral ventilator-associated pneumonia in the intensive care unit: a prospective cohort study. Intensive care medicine. 2005;31(8):1116-22.

13. Hong HL, Hong SB, Ko GB, Huh JW, Sung H, Do KH, et al. Viral infection is not uncommon in adult patients with severe hospital-acquired pneumonia. PloS one. 2014;9(4):e95865.

14. Micek ST, Chew B, Hampton N, Kollef MH. A Case-Control Study Assessing the Impact of Nonventilated Hospital-Acquired Pneumonia on Patient Outcomes. Chest. 2016;150(5):1008-14.

15. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016.

16. American Thoracic S, Infectious Diseases Society of A. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. American journal of respiratory and critical care medicine. 2005;171(4):388-416.

17. Crestanello JA, Higgins RS, He X, Saha-Chaudhuri P, Englum BR, Brennan JM, et al. The association of chronic lung disease with early mortality and respiratory adverse events after aortic valve replacement. The Annals of thoracic surgery. 2014;98(6):2068-77.

18. Oliveira EC, Marik PE, Colice G. Influenza pneumonia: a descriptive study. Chest. 2001;119(6):1717-23.

19. Harris AM, Hicks LA, Qaseem A. Appropriate Antibiotic Use for Acute Respiratory Tract Infection in Adults: Advice for High-Value Care From the American College of Physicians and the Centers for Disease Control and Prevention. Annals of internal medicine. 2016;164(6):425-34.

20. Wei L, Liu W, Zhang XA, Liu EM, Wo Y, Cowling BJ, et al. Detection of viral and bacterial pathogens in hospitalized children with acute respiratory illnesses, Chongqing, 2009-2013. Medicine. 2015;94(16):e742.

21. Rhedin S, Lindstrand A, Rotzen-Ostlund M, Tolfvenstam T, Ohrmalm L, Rinder MR, et al. Clinical utility of PCR for common viruses in acute respiratory illness. Pediatrics. 2014;133(3):e538-45.

22. Rogers BB, Shankar P, Jerris RC, Kotzbauer D, Anderson EJ, Watson JR, et al. Impact of a rapid respiratory panel test on patient outcomes. Archives of pathology & laboratory medicine. 2015;139(5):636-41.

23. Waghmare A, Englund JA, Boeckh M. How I treat respiratory viral infections in the setting of intensive chemotherapy or hematopoietic cell transplantation. Blood. 2016;127(22):2682-92.

24. Cao B, Gao H, Zhou B, Deng X, Hu C, Deng C, et al. Adjuvant Corticosteroid Treatment in Adults With Influenza A (H7N9) Viral Pneumonia. Critical care medicine. 2016;44(6):e318-28.

25. Crotty MP, Meyers S, Hampton N, Bledsoe S, Ritchie DJ, Buller RS, et al. Impact of antibacterials on subsequent resistance and clinical outcomes in adult patients with viral pneumonia: an opportunity for stewardship. Critical care. 2015;19:404.

26. Shorr AF, Zilberberg MD. Going Viral: Importance of Viral Pathogens in Nonventilated Hospital-Acquired Pneumonia. Chest. 2016;150(5):991-2.

27. McCracken JP, Prill MM, Arvelo W, Lindblade KA, Lopez MR, Estevez A, et al. Respiratory syncytial virus infection in Guatemala, 2007-2012. The Journal of infectious diseases. 2013;208 Suppl 3:S197-206.

28. Falsey AR, Hennessey PA, Formica MA, Cox C, Walsh EE. Respiratory syncytial virus infection in elderly and high-risk adults. The New England journal of medicine. 2005;352(17):1749-59.

29. Martino R, Ramila E, Rabella N, Munoz JM, Peyret M, Portos JM, et al. Respiratory virus infections in adults with hematologic malignancies: a prospective study. Clin Infect Dis. 2003;36(1):1-8.

30. Tramuto F, Maida CM, Napoli G, Mammina C, Casuccio A, Cala C, et al. Burden and viral aetiology of influenza-like illness and acute respiratory infection in intensive care units. Microbes and infection / Institut Pasteur. 2015.

31. Das D, Le Floch H, Houhou N, Epelboin L, Hausfater P, Khalil A, et al. Viruses detected by systematic multiplex polymerase chain reaction in adults with suspected community-acquired pneumonia attending emergency departments in France. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2015;21(6):608 e1-8.

32. Falsey AR, Becker KL, Swinburne AJ, Nylen ES, Formica MA, Hennessey PA, et al. Bacterial complications of respiratory tract viral illness: a comprehensive evaluation. The Journal of infectious diseases. 2013;208(3):432-41.

33. Chertow DS, Memoli MJ. Bacterial coinfection in influenza: a grand rounds review. Jama. 2013;309(3):275-82.

34. Karhu J, Ala-Kokko TI, Vuorinen T, Ohtonen P, Syrjala H. Lower respiratory tract virus findings in mechanically ventilated patients with severe community-acquired pneumonia. Clin Infect Dis. 2014;59(1):62-70.

중증 바이러스 폐렴의 역학 및 임상 양상

국문 초록

김형준
의과대학 임상의과학과 석사 과정
서울대학교

서론: 호흡기 바이러스는 중증 폐렴의 중요한 원인이다. 원인 바이러스에 대한 정확한 역학조사는 물론, 이러한 바이러스 검출이 임상적으로 어떠한 영향을 미치는지 알아보는 것이 필요하다. 본 연구는 중증 폐렴으로 인해 중환자실에 입실한 환자들을 대상으로 하여 원인 바이러스들을 살펴보고 이들의 임상적 의미를 알아보고자 하였다.

방법: 2008년 1월부터 2015년 12월까지 내과계 중환자실에 입실한 폐렴 환자들을 분석하였다. 해당 환자가 바이러스 폐렴을 앓고 있을 것으로 추측이 되면, 담당 의사들은 역전사효소중합효소연쇄반응을 이용하여 8가지의 호흡기 바이러스에 대한 검사를 시행하였다. 환자들의 기저 질환, 각종 검사 결과, 그리고 재원 기간이나 사망률 같은 임상 양상들을 분석하였다.

결과: 8년의 기간 동안 2,347명의 환자들이 내과계 중환자실에 폐렴으로 입실하였고, 그 중에서 519명의 환자에서 호흡기 바이러스 감염이

의심되어 역전사효소중합효소연쇄반응을 시행하였다. 그 중에서 69명이 바이러스 양성 결과를 보였다. 겨울에 더 많이 검출되는 계절성을 보였으며, 그 중에서 호흡기세포융합바이러스가 가장 흔했다. 원인 바이러스에 따른 임상 양상 및 검사 결과를 비교해 보았으나 큰 차이는 없었으나, 원인 바이러스를 검출한 뒤에 그 검출 결과가 임상 결정에 영향을 미치는 경우는 33.3%로 적지 않았다. 27명(39.1%)의 환자에서 바이러스와 동반된 세균 감염이 있었으나, 특정한 바이러스가 특정 세균과의 연관성을 보이지는 않았다.

결론: 중증 폐렴에서 호흡기 바이러스의 검출률은 드물지 않고, 그러한 검출은 많은 경우에서 임상 결정에 영향을 줄 수 있다.

주요어: 폐렴, 바이러스, 중환자, 역전사효소중합효소연쇄반응

학 번: 2015-22246