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Clinical Characteristics of Hospitalized Patients with Viral Pneumonia Between October 2017 and April 2018

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ABSTRACT

Respiratory viruses are among the potential seasonal causes of community-acquired pneumonia (CAP) and can lead to severe diseases and deaths in patients at risk. In this study, we aimed to present the clinical features of hospitalized patients who underwent RT-PCR during the seasonal period of October 2017-April 2018.

One hundred patients (male, 61%; mean age, 58.37±16.8) were included in the study. Demographic data and clinical and laboratory findings of patients were evaluated retrospectively using medical records.

Multiplex RT-PCR test was positive in 76 (76%) patients. The most found virus type was Influenza A (H1N1). Pneumonia was present in 68 of 100 patients. Bilateral infiltration was significantly higher in pneumonia patients ($p<0.001$). Influenza A(H1N1) was found to cause pneumonia significantly higher than other viruses, ($p<0.001$). Mortality in all pneumonia patients and those with positive viral cultures was 13.3% and 7.9%, respectively. Viral agents were high in the etiology of CAP causing hospitalization in the seasonal period. Influenza A (H1N1) is seen as the most common cause of viral pneumonia. Bilateral lung infiltration was radiologically observed as the predominant finding of viral pneumonia. Early etiological diagnosis can be achieved with multiplex RT-PCR.

Keywords: Influenza A (H1N1), Pneumonia, Reverse Transcriptase Polymerase Chain Reaction, Viral infection

Introduction

Viral infections are usually characterized by acute-onset fever (AOF), myalgia, and respiratory symptoms. While healing without complications in healthy individuals in general, viral infections lead to an increase in neuromuscular, cardiac, and pulmonary complications and hospitalizations among those at risk (1,2). Pulmonary complications include the exacerbations of pneumonia and chronic lung diseases and are a leading cause of mortality and morbidity (3). Although viral pneumonia can be seen throughout the year, the frequency of viral pneumonia increases in seasonal periods and plays an important role in adult community-acquired pneumonia (CAP)(4). During the peaks of seasonal viral infections, most of the hospitalizations are seen in patients <2 and >65 years of age and in those with such comorbidities as diabetes mellitus (DM), pulmonary, cardiovascular, and neurological diseases (5-7).

Viral pathogens are vital in the etiology of lower respiratory tract infections; however, viral pathogens require appropriate samples for the differential diagnosis from other pathogens due to similar clinical symptoms. As well as conventional methods in diagnosis, molecular methods such as polymerase chain reaction (PCR) with high sensitivity have come to the fore in recent years (8,9). With the increasing use of PCR tests in recent years, the detection rates of viral pathogens have also elevated in the etiology of CAPs. Detailed information on the etiology of CAP is necessary to define the treatment approaches and preventive measures (10). Therefore, the present study aimed to determine the significance and clinical features of the viruses in the etiology of CAP by retrospectively investigating the patients hospitalized and undergoing the reverse-transcriptase PCR (RT-PCR) test.

Materials and Methods

The present study was carried out in the departments of chest diseases and the emergency room of Konya Training and Research Hospital at Health Sciences University. Admitted to the outpatient clinic of chest diseases and the emergency department with complaints of the respiratory tract between 1st October 2017 and 1st April 2018, the patients hospitalized by a pulmonologist and undergoing the multiplex RT-PCR test were included in the study. The patients <18 years of age and those deprived of

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the criteria investigated in the study and without the radiological examination findings and multiplex RT-PCR test results were not included in the study. Approval was obtained from the Clinical Research Ethics Committee of the institution (Date: 13/12/2018 with the number: 48929119/ 774). The patients' demographic and clinical data, radiological and laboratory findings, comorbidities, and treatment modalities were obtained from the medical records in the hospital archive system. The viral panel of the patients was also analyzed from nasopharyngeal swab samples through the multiplex RT-PCR test. The sputum and blood culture methods were used to perform the bacteriological examination. Additionally, the radiologic examinations of the patients were also performed through the posteroanterior (PA) chest X-ray and thorax computed tomography (CT) techniques. Thorax CT investigations of the patients were performed using a 128-slice multidetector CT (MDCT) scanner (Philips Ingenuity 128 NT, Philips Healthcare, Netherlands). The administration of influenza antiviral therapy and the onset time of the treatment were obtained from patients' files. The onset of early antiviral treatment was considered to be the time within the first two days of the hospitalization. In addition, the combinations of antibiotics received by the patients and the onset time were also evaluated. The cases were divided into groups with positive and negative multiplex RT-PCR test, and with and without pneumonia. The groups were compared in terms of the distributions of virus types, clinical, laboratory and radiological findings, comorbidities, stay in the intensive care unit (ICU), and length of hospital stay.

Statistical Analysis: Continuous variables were described as mean and (±) standard deviation (SD), while the categorical variables were defined as numbers and percentages. The independent t-test was used to compare the numerical variables. To compare categorical variables between groups, the chi-square test was utilized, and Fisher's exact test was preferred depending on data distribution and sample size. By performing the logistic regression analysis, the odds ratios (OR) were calculated for the pneumonia-related variables. The statistical analyses were performed using the Statistical Analysis System (SAS) University Edition (SAS® University Edition V. 6p.2, SAS Institute Inc., Cary, NC, USA.), and a p-value <0.05 was considered significant.

Results

One hundred patients hospitalized and undergoing the RT-PCR test were included in the study. Of 100 patients, 39 and 61% were female and male, and the mean age was found as 58.37±16.8, ranging between 18-89 years of age. The most common symptoms in the patients were found to be cough (92%), shortness of breath (89%), and fever (80%). In 88% of the patients, the most remarkable laboratory finding was the elevated values of CRP. 66% of patients had at least one comorbid disease, most commonly chronic obstructive pulmonary disease (COPD) (42%). Multiplex RT-PCR test was positive in 76% of the patients. Pneumonia was determined in 68% of all the patients (Table 1). Blood cultures and sputum cultures were obtained from 43% and 66% of the patients, respectively. However, no bacteriological agent was detected.

Comparison of the PCR positive and negative patients: Multiplex RT-PCR test was positive in 76 of the patients and negative in 24. Ten different types of viruses were detected, and more than one type of virus existed in 16 patients. Among all patients, the types of the viruses, from the most common to the least, were detected as *Influenza A* 45% (new *H1N1* 44% and seasonal *H1N1* 1%), *Respiratory syncytial virus-B (RSVB)* 23%, *RSVA* 10%, *Rhinovirus* 5%, *Parainfluenza-3* 4%, *Bocavirus* 3%, *Coronavirus* 2%, *Metapneumovirus* 2%, *Parainfluenza-4* 2%, and *Influenza B* 1%.

When it comes to the comparisons between the patients with positive and negative multiplex RT-PCR test findings, the presence of pneumonia (75%), elevated CRP (92.11%), findings of bilateral infiltrations (68.42%), and duration of hospital stay >7 days (72.36%) were found to be significantly higher among those with the multiplex RT-PCR test positivity (p <0.001, p=0.035, p=0.028 and p=0.016) (Table 2).

When patients' characteristics were evaluated regarding the virus types, the existence of pneumonia (88.89%), bilateral lung infiltration (84.45%), and staying time of hospitalization>7 days (64.44%) were also detected to be significantly higher in *influenza A H1N1*, compared to other virus types and the group with unknown etiology (p<0.001, p=0.003 and p=0.010) (Table 3).

Comparison of the patients with and without Pneumonia: Pneumonia was present in 68 of 100 patients. Comparisons of laboratory values of patients with and without pneumonia are shown in the Table 4. The levels of CRP, procalcitonin, leukocyte and sedimentation were significantly higher in the pneumonia group (p=0.001, p=0.026, p=0.020 and p=0.001).

The distribution of types of viruses, clinical symptoms, and radiological features in patients with and without pneumonia are given in Table 5. *Influenza*

Table 1: Demographic and Clinical Features of All the Study Participants (n=100)

Characteristics	Values
Age (mean±SD)	58.37 ± 16.83
Sex (n, %)	
Male	61 (61%)
Female	39 (39%)
Symptoms (n, %)	
Cough	92 (92%)
Shortness of breath	89 (92%)
Acute onset fever	80 (80%)
Sore throat	42 (42%)
Headache	31 (31%)
Rhinorrhea	27 (27%)
Nausea-vomiting	23 (23%)
Laboratory Findings (n, %)	
Elevated CRP	88 (88%)
Elevated Sedimentation	42 (42%)
Anemia	32 (32%)
Elevated procalcitonin	25 (25%)
Leukocytosis	49 (49%)
Leukopenia	5 (5%)
Thrombocytosis	19 (19%)
Thrombopenia	9 (9%)
Comorbidity (n, %)	
COPD	42 (42%)
CHF	13 (13%)
Asthma	11 (11%)
Diabetes Mellitus	10 (10%)
Immunosuppression	7 (7%)
Virus Diagnosis (n, %)	
RT-PCR positive	76 (76%)
RT-PCR negative	24 (24%)
Clinical Findings (n, %)	
Pneumonia	68 (68%)
Others (COPD and asthma attacks, ARF, etc)	32 (32%)

n: Frequency, (%): Percentages, SD: Standard Deviation.
ARF: Acute renal failure, CHF: Congestive Heart Failure, COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, RT-PCR: Reverse transcriptase polymerase chain reaction

A H1N1 was determined in 40 (58.82%) of the patients with pneumonia, and the finding was highly significant, compared with those without pneumonia ($p<0.001$). The types of *Influenza A* were detected as new *H1N1* in 39 and seasonal *H1N1* in one case. *RSVB* and *RSVA* were found as the most common viruses after *Influenza A*; however, there was no significant difference between the groups. While no significant difference was found in terms of clinical symptoms between the two groups, a significant difference was seen in terms of radiological findings between both ($p<0.001$). The most common radiological finding encountered in those with pneumonia was bilateral infiltration (86.77%). Even so, other findings were single lung multilobar (8.82%) and single lobe infiltrations (4.41%). Among those without pneumonia, there were radiological findings related to the underlying diseases, such as COPD, congestive heart failure (CHF), and acute renal failure(ARF). Considering the comparisons of the

Table 2: Characteristics of Patients with Negative and Positive Viral Cultures

	Viral cultures positive n=76		Viral cultures negative n=24		P-values
	n	%	n	%	
Clinical Findings					
Pneumonia	57	75.00	11	45.83	
COPD attacks	15	19.74	4	16.67	<0.001**
Asthma attacks	4	5.26	3	12.50	
Others (alveolar hemorrhage, pulmonary edema, ARF, etc.)	0	0.00	6	25.00	
Laboratory Findings					
CRP	70	92.11	18	75.00	0.035**
Procalcitonin	19	25.00	6	25.00	1.000*
Sedimentation	34	44.74	8	33.33	0.323*
Radiological Findings					
Due to underlying disease	18	23.68	11	45.83	
Bilateral infitration	52	68.42	9	37.50	0.028**
Single lobe infiltration	2	2.63	2	8.33	
Multilobar unilateral infiltration	4	5.26	2	8.33	
Comorbidity	52	68.42	14	58.33	0.363*
Hospitalization time >7 days	55	72.36	11	45.83	0.016*
Stay in ICU					
No	62	81.57	20	83.33	
Oxygen Treatment in ICU	6	7.90	0	0.00	
NIMV	2	2.63	0	0.00	0.299**
IMV	6	7.90	4	16.67	
Clinical Outcomes					
Exitus	6	7.90	3	12.50	0.430*
Discharge with good health	70	92.10	21	87.50	

*Chi-square, **Fisher's exact test.
ARF: Acute renal failure, COPD: Chronic obstructive pulmonary disease, ICU: Intensive care unit, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation

patients in terms of comorbidities, no significant difference was found between the groups (p=0.395) (Table 5).

The early antiviral therapy was initiated in 50 (73.53%) patients with pneumonia on admission and in 2 (2.94%) patients within the first 48 hours. In addition, corticosteroid therapy was also administered in 5 (7.35%) of the pneumonia patients due to the existing disease and in 28 (41.18%) due to an underlying disease (p=0.020). All patients received the empirical dual antibiotic therapy. However, 16 (23.53%) of the patients with pneumonia received treatment with more than 2 antibiotic agents (p=0.001). While 18 (26.4%) patients in the pneumonia group required admission to ICU, 10 (%14.74) were seen to need invasive mechanical ventilation (IMV) (p=0.001). Of 68 patients with pneumonia, 59 (86.76%) were discharged with good health, and 9 (13.24%) resulted in deaths (Table 6).

A logistic regression model was constructed to identify factors that could potentially influence the occurrence of pneumonia. The most notable risk factors for the development of pneumonia in hospitalized patients were the *H1N1* virus type (Odds ratio: 14.37, 95% CI: 3.07-67.02, p=0,001), and elevated values of procalcitonin (Odds ratio: 7.09, 95% CI: 1.30-38.6, p=0,023) and CRP (Odds ratio: 1.01, 95% CI: 1.004-1.023, p=0,004).

Discussion

The potential importance of the viruses, especially in adult CAP has been better understood with the use of more sensitive and rapid diagnostic tests, such as

Table 3: Patient Characteristics According to the Types of Viruses

	Influenza A H1N1 (New n=45		Other Viruses n=31		No Viruses n= 24		P-values
	n	%	n	%	n	%	
Clinical Findings							
Pneumonia	40	88.89	17	54.84	11	45.83	<0.001*
Others (COPD-asthma attacks, alveolar hemorrhage, pulmonary edema, ARF, etc.)	5	11.11	14	45.16	13	54.17	
Laboratory Findings							
CRP	42	93.33	28	90.32	18	75.00	0.100**
Procalcitonin	12	26.67	7	22.58	6	25.00	0.921*
Sedimentation	21	46.67	13	41.94	8	33.33	0.565*
Anemia	15	33.33	9	29.03	8	33.33	0.913*
Leukopenia	1	2.22	2	6.45	2	8.33	0.796**
Thrombocytopenia	3	6.67	4	12.90	2	8.33	0.909**
Radiological Findings							
Due to underlying disease	5	11.11	13	41.94	11	45.83	
Bilateral infitration	38	84.45	14	45.16	9	37.50	0.003**
Single lobe infiltration	0	0.00	2	6.45	2	8.33	
Multilobar unilateral infiltration	2	4.44	2	6.45	2	8.33	
Comorbidity	29	6.44	23	74.19	14	58.33	0.448*
Hospitalization time >7 days	29	64.44	26	83.97	11	45.8	0.010*
Stay in ICU							
No	34	75.56	28	90.32	20	83.33	
Oxygen Treatment in ICU	4	8.89	2	6.45	0	0.00	0.309**
NIMV	2	4.44	0	0.00	0	0.00	
IMV	5	11.11	1	3.23	4	16.67	
Clinical Outcomes							
Exitus	5	11.11	1	3.23	3	12.50	0.438**
Discharge with good health	40	88.89	30	96.77	21	87.50	

*Chi-square, **Fisher's exact test

ARF: Acute renal failure, COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, ICU: Intensive care unit, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation

PCR, in recent years. While identified as the culprits in CAP at a lower rate in previous studies, the viruses were stated at such higher rates as 25-56% in studies evaluating the etiology of respiratory tract infections through PCR (11-14). In determining the viral etiology, especially the multiplex RT-PCR test has been specified as a method with high clinical diagnostic sensitivity, in which many viruses can be investigated simultaneously in a single mixture (8,9). In the study by Liolios et al., it was found that the multiplex RT-PCR test was a much more sensitive method than the viral culture and immunofluorescence methods in the detection of respiratory viral pathogens, and reported the specificity and sensitivity of the multiplex RT-PCR test as 93 and 100% (8). In our study, the multiplex RT-PCR test was used for the diagnosis, and viral pathogens were detected in 76 (76%) of 100 patients. Viruses were shown as the causative pathogen in 57 of 68 pneumonia patients. We consider that the high rate of detecting viruses as the cause of pneumonia was due to the hospitalization of all patients during the seasonal period and the RT-PCR test performed in all patients before the antiviral treatment.

The rates of detecting the agents in CAP were reported as 33-88% in previous studies (15,16). Although the sputum culture is important in detecting the bacterial agents in cases with pneumonia, the

Table 4: Laboratory Characteristics of Patients with and without Pneumonia

	Those with pneumonia n=68		Those without pneumonia n=32		P-values
	Mean	SD	Mean	SD	
Age (years)	57.30	16.65	60.62	17.23	0.368
Leukocyte	12.60	6.32	10.12	4.05	0.020
Hgb	12.85	2.77	13.58	2.03	0.142
Thrombocyte	270.1	114.5	256.9	77.44	0.498
CRP	125.2	89.55	47.53	62.00	0.001
Procalcitonin	0.67	1.11	0.24	0.78	0.026
Sedimentation	31.96	19.47	17.31	11.49	0.001

Independent t-test was applied. SD: Standart deviation, CRP: C-reactive protein, Hgb: Hemoglobin

Table 5: Distribution of Types of Viruses, Clinical Symptoms, Radiological Features, and Comorbidity in Patients with and without Pneumonia

	Those with Pneumonia n =68		Those without Pneumonia n=32		P-values
	n	%	n	%	
Types of Viruses					
Influenza A (H1N1)	40	58.82	5	15.63	<0.001*
RSVB	15	22.06	8	25.00	0.744*
RSVA	6	8.82	4	12.50	0.722**
Rhinovirus	3	4.41	2	6.25	0.653**
Parainfluenza 3	3	4.41	1	3.13	1.000**
Parainfluenza 4	2	2.94	0	0.00	1.000**
Bocavirus	3	4.41	0	0.00	0.549**
Coronavirus	2	2.94	0	0.00	1.000**
Metapneumovirus	2	2.94	0	0.00	1.000**
Influenza B	1	1.47	0	0.00	1.000**
Symptoms					
Cough	61	89.71	31	96.88	0.430**
Shortness of breath	59	86.77	30	93.75	0.430**
AOF	56	82.35	24	75.00	0.391*
Sore throat	28	41.18	14	43.75	0.808*
Headache	19	27.94	12	37.50	0.335*
Rhinorrhea	16	23.53	11	34.38	0.254*
Nausea-vomiting	18	26.47	5	15.63	0.229*
Radiological Findings					
Radiological findings related to the underlying disease	0	0.00	29	90.63	<0.001**
Bilateral infiltration	59	86.77	2	6.25	
Multilobar unilateral infiltration	6	8.82	0	0.00	
Single lobe infiltration	3	4.41	1	3.12	
Comorbidity	43	63.24	23	71.88	0.395*

*Chi-square, **Fisher's exact test
AOF: Acute-onset fever, RSVA: Respiratory syncytial virus-A, RSVB: Respiratory syncytial virus-B

Table 6: Clinical Course and Treatment Outcomes of Patients with and without Pneumonia

	Those with pneumonia n=68		Those without pneumonia n=32		P-values
	n	%	n	%	
Antiviral Treatment					
On admission	50	73.53	21	65.63	
Within 48 hours	2	2.94	1	3.13	0.759**
After 48 hours	16	23.53	10	31.25	
Use of Corticosteroids					
No	35	51.47	6	18.75	
On admission iv	5	7.35	1	3.13	0.002**
Due to the underlying disease	28	41.18	25	78.13	
Antibiotic Therapy					
Dual antibiotic therapy	51	75.00	32	100	
Antibiotic therapy >2	16	23.53	0	0.00	0.001**
Hospitalization >7 days	43	63.24	23	71.88	0.395*
Stay in ICU					
No	50	73.53	32	100	
Oxygen Treatment in ICU	6	8.82	0	0.00	0.006**
NIMV	2	2.94	0	0.00	
IMV	10	14.71	0	0.00	
Clinical Outcomes					
Exitus	9	13.24	0	0.00	0.054**
Discharge with good health	59	86.76	32	100	

*Chi-square, **Fisher's exact test

ICU: Intensive care unit, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation

value of sputum culture was found lower in guiding the diagnosis and treatment due to such reasons as the initiation of empirical antibiotics, inability to obtain quality samples of sputum and delayed results between 24-48 hours (11,17).

In our study, sputum and blood cultures were obtained from 66 and 43% of the patients respectively, However, the cultures were found to be negative. No causative agent was detected in 11 of our 68 patients with pneumonia. Bacterial diagnostic tests could not be performed in all patients, and most of the patients received antibiotic treatment during accumulating the cultures. We consider that antibiotic treatment given at the time of culture collection prevented the detection of bacteriological agents.

The most common agents of viral pneumonia have been reported as primarily *Influenza A,* and then *RSV, Adenovirus, Parainfluenza virus (type 1, 2,* and *3), Coronavirus, Rhinovirus,* and *Influenza B* (18,19). In our study, viral pathogens were detected as 10 different viruses in 76 patients (76%). The most common viral pathogen was *Influenza A* (45%) as *new H1N1* 44% and *seasonal H1N1* 1%. *Influenza A* was, in turn, followed by *RSVB* (23%) and other virus types. In line with the findings in previous studies, *Influenza A (H1N1)* was detected as the most common virus in our results. Among the hospitalized patients with pneumonia, the causative rate of *Influenza A* was 58.82%, and the rate was found to be significantly higher, compared to those without pneumonia. Also, in the patients with COPD, it was observed that the virus leading to pneumonia was *Influenza A H1N1* at a high rate, but other viruses (*Rhino, RSVA, RSVB*, etc.) were the cause of the COPD attacks.

Many risk factors have been identified, playing a role in the development of CAP. Especially the advanced age and accompanying chronic diseases have been accepted as significant risk factors for contracting and a more severe course of the condition (15,19,20). The patients hospitalized due to influenza were witnessed to be individuals >65 years of age more commonly (21). In our study, the mean age of the patients was 58.37±16.8. However, the existence of comorbidity demonstrated no significant difference between the

Tablo 7: Factors Affecting Pneumonia Occurrence

Parameter	OD	95% CI	P-values
New H1N1 Virus Subtype (+/-)	14.369	3.071-67.232	0.001
Elevated Procalcitonin (+/-)	7.088	1.301-38.626	0.023
Elevated CRP (+/-)	1.013	1.004-1.023	0.004

Logistic Regression was applied. OD: Odds ratio, CI: Confidence interval

patient groups in terms of pneumonia and RT-PCR positivity. In this study, virus positivity, subtypes of viral agents (*H1N1*), procalcitonin, and CRP elevation were found as significant markers in indicating pneumonia.

Fever, cough, dyspnea, and fatigue were reported as the most common presenting symptoms of viral pneumonia (22,23). In our study, cough, fever, and shortness of breath were detected as common symptoms, as well. Although leukopenia remains at the forefront of laboratory findings in viral pneumonia, both leukopenia and leukocytosis have commonly been reported among hospitalized patients in several studies (24). In our study, leukocytosis was prominent, and sedimentation, CRP, and procalcitonin values of the patients with RT-PCR positivity and those with pneumonia were also found to be significantly higher.

Radiologically, in viral pneumonia, such appearances as multifocal ground-glass opacities, mixed ground-glass-consolidation opacities, interlobular septum thickenings, peripheral distributions, and multilobar involvements have been described in several studies (20,25). In some studies conducted during the 2009 *H1N1* pandemic, the localizations of the infiltration distributions in those with pneumonia findings were found as bilateral in 66%, single lobe-limited in 26%, and unilateral multilobar in 6% of the cases (26,27). In our study, parenchymal infiltrates were also evaluated under the localizations of distributions, and bilateral infiltration was detected in 86.77% of the patients with pneumonia, and the finding was significantly higher in the patients with pneumonia and viral test positivity than those without pneumonia. In addition, *H1N1* was observed to lead to a higher rate of bilateral infiltration than other viruses.

Albeit the administration of vaccines and effective antibiotics, CAP remains an infection with high mortality and morbidity (19). In different studies, the factors associated with mortality in pneumonia have been emphasized as advanced age, extensive lung involvement, need for mechanical ventilation, and long hospital stay (19,27). In our study, the hospitalization rates >7 days were significantly higher in patients with pneumonia and viral culture positivity. In previous studies, the mortality rates are reported as 1-5% in outpatients, the average mortality rate is 12% in hospitalized patients and rises to 40%, especially in those requiring support in ICU (18,28). In our study, the mortality rate was determined as 13.23% in all patients with pneumonia. Patients with influenza-associated pneumonia have an increased risk of admission to ICU, need for mechanical ventilation, and deaths, compared to those without pneumonia. In the case series investigating the outcomes of the 2009 *H1N1* pandemic, the rates of hospitalization in ICU (36-58%), respiratory failure (10-67%), and deaths (7-39%) were detected to be higher (29,30). Based on the literature, the data on seasonal influenza-associated pneumonia and its serious consequences are seen to be limited further. In an observational study where 101 patients with acute pulmonary disease were hospitalized due to influenza during 1999-2003, it was reported that 16 (16%) were admitted to ICU, 10 (10%) required mechanical ventilation, and six (6%) resulted in deaths(31). Of 76 patients with viral test positivity in our study, 57 (75.0%) were found to have pneumonia, 14 (18.43%) required admission to ICU, and 6 (7.9%) resulted in deaths. Given the evaluation of virus types, it was detected that 40 (88.89%) of 45 patients with *H1N1* had pneumonia, 11 (24.44%) were hospitalized in ICU, and five (11.11%) cases resulted in deaths. Considering the virus type of *H1N1*, the rates of pneumonia, stay in ICU and deaths were significantly higher, compared to the other types of viruses and the group with uncertain etiology.

In the pharmacological management of influenza, the treatment with oseltamivir and zanamivir is recommended under the criteria released by the World Health Organization (WHO), as soon as the symptoms develop in those at risk for pneumonia (32). Although sensitive to the two neuraminidase inhibitors oseltamivir and zanamivir during the 2009 outbreak, the *H1N1* virus infection was resistant to amantadine and rimantadine (22,33). The benefits of antiviral therapy are emphasized as the initiation of the treatment within 48 hours from the onset of the disease. However, there are also studies demonstrating a decrease in mortality in the treatments launched after 48 hours (34-35). In the present study, the therapy with oseltamivir and

empirical antibiotic therapy had been initiated in all patients on admission. We believe that early antiviral treatment improves the rates of amelioration and prevents the condition from turning into severe pneumonia; however, we did not compare any group not receiving antiviral treatment in the study.

The current research has some limitations. Our study was composed of fewer participants, the study group could not be compared with another not receiving treatment, and no comparisons were carried out with the patients not hospitalized and the cases with pneumonia where bacterial agents were determined.

Viral agents were found higher in the etiology of pneumonia bringing about hospitalization in the seasonal period. The pneumonia-induced potential of *Influenza A H1N1* was observed to be more prominent than other viruses. The multiplex RT-PCR test was also shown to be beneficial as an effective and sensitive method in the early etiological diagnosis. Bilateral lung infiltration was observed radiologically as the predominant finding of viral pneumonia, especially in the cases of *Influenza A* (*H1N1*). We consider that further studies including larger populations and are needed to elucidate the roles of viruses in the etiology of pneumonia in hospitalized adult patients and the results of early antiviral therapy.

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Conflict of Interest: The authors declare that there is no conflict of interest

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