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The analysis of patients under mechanical ventilation support in ıntensive care unit with the diagnosis of H1N1 infection: retrospective study

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Abstract
The aim of this study is to analyze the demographic data of the patients followed in intensive care unit, under mechanical ventilation support, with a proved diagnosis of H1N1 infection. Our secondary aim is to determine the similarities and differences of these data with previous outbreaks. Seventeen patients followed in anesthesiology and reanimation intensive care unit under mechanical ventilation support due to H1N1 infection were conducted in the study. The diagnosis was proved with reverse transcription polymerase chain reaction and virus culture. Patients' ages, comorbidities, vaccination stories, complications, mechanical ventilation period and pathological laboratory results were retrospectively recorded. Nine of the patients were male and mean age was calculated as 58.6 ± 19.4. Most common comorbidities were chronic obstructive pulmonary disease, hypertension and diabetes mellitus. Mean duration for onset of respiratory insufficiency was 9.2 ± 3.9 days. The duration was significantly lower in elderly patients. Most frequently seen complication at mechanically ventilated patients was acute respiratory distress syndrome and septic shock. Mean period for mechanical ventilation support was calculated as 15.9 ± 9.2 days. There was a weak correlation between age and mortality. When we analyzed the laboratory results, all patients' creatine kinase levels were found to be high. We found our patients to have a long mechanical ventilation period. Older patients were shown to have a higher risk for mortality. The risk groups should be well known and vaccination programmes should be increased to prevent complications.

Keywords: Influenza A, intensive care unit, mechanical ventilation

Introduction

Influenza A virus (H1N1) was first time detected in two children in 2009 [1]. After this year, the disease has spread rapidly worldwide and disease activity reached to the highest level at October and November 2009 [2].

Although most of the infected patients recovered without any complications, intensive care need as high as 30% was reported in some countries during the pandemia of 2009. Most common complications were; acute respiratory distress syndrome (ARDS) with respiratory insufficiency and refractory hypoxemia, secondary bacterial superinfection, septic shock, renal failure, multi organ failure, myocarditis, encefalitis and worsening of underlying disease [3].

In the recent months, a significant increase has been detected in the number of patients with symptoms like H1N1 infection. These symptoms were accepted as a part of seasonal influenza. Some of these patients have required intensive care.

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The aim of this study is to analyse the demographic data of the patients who were followed in intensive care unit under mechanical ventilation, with a proved diagnosis of H1N1 infection. Our secondary aim is to determine the similarities and differences of these data with previous outbreaks.

Material and Metod

After receiving hospital ethic committee approval and patients' informed consent, we have conducted the study in Muğla Sıtkı Koçman University Training and Research Hospital. Seventeen patients were admitted to Anesthesiology and Reanimation Intensive Care Unit (AICU) between December 2015 and March 2016. All the patients were diagnosed with H1N1 infection in the emergency service or infectious diseases clinic and transferred to AICU. The validity of diagnosis was proved by reverse transcription polymerase chain reaction and virus culture. After approval of the disease, patients' age, comorbidities, vaccination histories, complications, mechanical ventilation duration and pathological laboratory results were retrospectively recorded from the patients' files.

Statistical Analysis

Statistical evaluation was performed using the Statistical package for Social Science, version 18.0 (SPSS Inc.

Chicago, IL). The descriptive data of the study was specified with mean, standard deviation, and percentage. Normality of the variables were analyzed by Kolmogornow-Smirnov test and homogeneity was analyzed by Levene's test. Student's t test was used to evaluate continuous variables. Pearson correlation was used to show correlation. The p value <0.05 was considered statistically significant.

Results

There were totally 17 patients in the study; nine of them were male and eight of them were female. Mean age of the patients was 58.6±19.4 (minimum 36 and maximum 86). Ten of the patients were under 65 years old. The demographic data of the patients are listed in Table 1.

Table 1. Demographic data of the patients

Mean age	58.6±19.4
Age > 65/ Age < 65	7/10
Comorbidity	17/17
Vaccination	0/17

All of the patients had one or more underlying chronic diseases. Most common comorbidities were chronic obstructive pulmonary disease (COPD), hypertension (HT) and diabetes mellitus (DM). Others were chronic renal failure, congestive heart disease, cerebrovascular disease, Parkinson's disease**,** morbid obesity, Alzheimer's disease and interstitial lung disease. Ten of the patients had more then one chronic disease.

The shortest period between onset of first symptom and occurance of respiratory insufficiency was four days, and the longest period was 14 days. The mean period for occurance of respiratory insufficiency was 9.2±3.9 days. Mean period was 11.2±3.2 days for patients under 65 years old, while it was only 6.4±3 days for patients over 65 years old. The difference was statistically significant (p = 0.007).

When we analyze the complications seen during the follow-up of mechanically ventilated patients, the most common complication was ARDS. Septic shock was detected in seven of the patients and acute renal failure was seen in five of the patients.

The mean duration needed for mechanical ventilation support was found as 15.9±9.2 days for all patients. This period was 18.1±9.8 days for patients over 65 years old, while it was 14.3±8.9 days for patients under 65 years old. The difference was not statistically significant (p=0.414). The shortest mechanical ventilation support period was five days and the longest was 32 days. Two of the patients under 65 years old and four of the patients over 65 years old died during the therapy. There was a weak correlation between "increasing age" and "mortality" with a Pearson coefficient of 0.415.

Creatine kinase was found to be high in all patients at the admittance to ICU. C-reactive protein (CRP) was high in 14 of the patients and lactate dehydrogenase was high in 11 of the patients at admittance to ICU. The pathological laboratory results of the patients are listed in Table 2.

None of the patients were reported to be vaccinated by their relatives.

Table 2. Pathological laboratory results of the patients

	n	Mean	
Creatine Kinase	17	2074.6	U/L
CRP	14	168.8	mg/dL
Laktate dehydrogenase	12	573.6	U/L
Hypoalbuminemia	11	2.94	gr/dL
Leukocytosis	7	15700/mm3	
Hyponatremia	4	132	mmol/L
Leukopenia	4	2400 /mm3	
Trombocytopenia	4	81000/mm3	

CRP: C reactive protein

Discussion

In the current study, we retrospectively analyzed the files of patients who had aggresive H1N1 infection and followed with mechanical ventilation support in the Anesthesia and Reanimation ICU.

Influenza A virus caused severe infections first time in April 2009 and spread rapidly worldwide. Thus, it was described as "pandemia" by World Health Organization (WHO) in June 2009 [4]. Pregnancy, obesity, chronic diseases, age under two years old and age over 65 years old are accepted as risk factors for H1N1 infection [5].

There were three presentations of infections during the pandemia; Non severe infections involved nonspesific symptoms such as uncomplicated fever, cough, sorethroat, nasal discharge, muscle pain, fatigue, nausea and vomiting [6]. In the moderate form, infection presentation started with uncomplicated symptoms and worsened in a short time. Severe form, complicated cases has involved severe hypoxemia, tachypnea, cyanosis and respiratory insufficiency. These patients should be treated in intensive care units [7]. In the current study, all the patients were entubated and they were under mechanical ventilation support. Our patients had progressed respiratory insuffiency during their treatments in the wards or they had directly applied to emergency services with respiratory difficulty. So, all of the patients' disease presentations were "severe" H1N1 infection.

WHO reported that half of the complicated cases during the pandemia of 2009 had underlying chronic diseases. Moreover, only one third of the patients treated in ICU were reported to be a healthy person before pandemia [3]. In the current study, all the patients had one or more chronic diseases. There are two possible reasons for this; AICU is a third level intensive care unit, most severe

patients are referred to this ward and patients under 18 years old age are not admitted to AICU, they are followed in Pediatric ICU. Besides, Wiesen et al. analyzed the postpandemic influenza outbreak of 2013-2014 in America and detected that affected population was older and had more chronic diseases than the affected population in 2009 pandemia. The authors suggested that younger population has gained immunity against Influenza A at the 2009 pandemia and the patients in risk groups were poorly vaccinated during the outbreak of 2013-2014 [8].

In the current study, the period between first symptom onset and occurance of respiratory insufficiency was significantly shorter in geriatric group. Geriatric people are well known to be more susceptible to infection, due to age-related dysfunction of the immune system resulting from low-grade chronic inflammation. This is called 'inflamm-ageing'. The immune system of older people exhibits a diminished ability to respond to microbial threats and clear infections[9].

Webb et al. reported that mean mechanical ventilation support duration was eight days in the 2009 outbreak [10]. Franquiz et al. analyzed both 2009 and 2013 pandemia in their hospital and they reported mean mechanical ventilation support duration as eight days in 2009 outbreak and nine days in 2013 outbreak [11]. This duration was 15.9±9.2 days and significantly longer in our study. The most possible reason is that affected patients in postpandemic period had more chronic pulmonary and cardiac diseases which makes weaning from mechanical ventilation more difficult. Wiesen et al. detected that affected patients in the postpandemic period required higher positive end expiratory pressure and had lower PaO2/FiO2 ratio, which means patients had a higher tendency for severe hypoxemia [8]. The results of the previous study may explain why our patients had difficulty in weaning from mechanical ventilation support.

In our study, patients under 65 years old has remained under mechanical ventilation support for 14.3±8.9, while patients over 65 years old has remained for 18.1±9.8 days. The difference was not significant. There are two possible reasons: The patients who had the longest mechanical ventilation period (32 days) was a morbidly obese, young woman. It is well known that ventilation of obese patients is more difficult and the use of both PEEP and periodic recruitment maneuvers during mechanical ventilation is almost mandatory [12]. Secondly, more patients in the geriatric group died during their treatments and mechanical ventilation period remained shorter. We found a weak correlation between increasing age and mortality. It is not suprising that older patients with more chronic diseases have a tendency to worse outcomes. Geriatric population has reported to have higher baseline levels of proinflammatory factors such as C-reactive protein, tumour necrosis factor -α, interleukin −1β and interleukin-6 and higher levels of these mediators are shown to be related with disease-associated mortality [13,14].

In the current study, none of the patients had a story of vaccination. However, Minchole et al. reported that even young people should be vaccinated if they have any risk factors for infection [15].

Conclusion

In the current study, patients with H1N1 infection was found to have a longer mechanical ventilation period when compaired with previous outbreak [10,11]. Older patients had a higher risk of mortality. Influenza A infection frequently seen in the last months are still considered as a part of seasonal influenza and epidemiology strategies have not been put into practice. The risk groups should be well known and vaccination programmes should be increased to prevent complications.

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