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Evaluation of prevalence and severity of acute respiratory distress syndrome in hospitalized patients due to H1N1 outbreak in Kerman, Iran

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ABSTRACT

Influenza is an acute respiratory viral disease which affects the upper and lower respiratory tract. The main cause of hospitalization was involvement of lower respiratory tract in the form of primary viral pneumonia due to direct invasion of lung tissue by virus. Primary pathological findings suggest extensive alveolar injury of interstitial hemorrhagic pneumonitis along with lymphocytic proliferation and relative neutrophil reduction in this tissue plus ARDS. Considering that there is no record of incidence and severity of ARDS in patients with H1N1 influenza in Iran, particularly in Kerman, this study seems to be necessary as a basic study for further preparation of possible future epidemics. This was a cross-sectional study conducted in the Afzalipour Hospital in Kerman in 2016. The sampling method was census-based; the studied population included patients admitted to the Afzalipur Hospital from March 21, 2015 to March 19, 2016 due to definitive development (PCR of sputum sample of H1N1-infected patients) of H1N1 influenza. After collecting data, data was analyzed by SPSS software, version 20. In patients with mild, moderate and severe ARDS, 18 (58.9%), 16 (76.42%) and 27 (79.41%) had underlying diseases. Frequency of ARDS severity was significantly different in terms of underlying diseases (p-value = 0.012); 22 (70.9%) of patients with mild ARDS, 15 (71.42%) of patients with moderate ARDS, and 24 (70.76%) of patients with severe ARDS were male. Frequency of ARDS severity was not significantly different in terms of gender (p-value = 0.112). The mean age was 51.54 ± 15.575 years in patients with mild ARDS, 53.98 ± 14.652 years in patients with moderate ARDS and 53.64 ± 14.942 years in patients with severe ARDS; no significant difference was observed in terms of age (p-value = 0.062). According to mortality results, there was a significant difference and mortality was significantly higher in patients with ARDS (p-value = 0.035). The results of this study showed that ARDS was higher in patients with underlying diseases and ARDS severity was higher in these patients than in other patients. Mortality rate also had a significant relationship with ARDS; most of mortalities were in these patients.

Keywords: Influenza, ARDS, Mortality

1. INTRODUCTION

Influenza is an acute respiratory viral disease which affects the upper and lower respiratory tract (Nasr Dadras et al., 2009; Yu et al., 2007). Influenza epidemics are commonly seen in the cold season and infect 5-15% of the population, causing 250000 to 500000 deaths each year or possibly causing death of millions by pandemics (WHO, 2009). Influenza virus, with partial and total antigenic changes (drift and shift), causes local and global epidemics, respectively (Roxas and Jurenka, 2007). Type A influenza virus has caused several pandemics in the twentieth century, causing millions of people to die in the past century (Kilbourne, 2006). Influenza virus A/H1N1 was first reported in April 2009 with a different form of pathogenicity from seasonal types in Mexico and several US states, then it quickly spread to most countries; in June 2009 (two months after the first report, the World Health Organization announced that it has become a global pandemic (Neumann et al., 2009; Lange et al., 2009). Over a short period after the outbreak, more than 17700 people died of this type of virus, according to the WHO report (2010). Based on a 6-month report in Iran (May to November 2009), 57 (2.18%) out of 2662 definitive cases of A/H1N1 influenza died (Gooya et al., 2010). In Canada, 37% and in the United States, more than 70% of hospitalized patients and 80% of died patients had at least one underlying disease. Severe cases of disease and mortality have occurred in pregnant women, particularly in the third trimester of pregnancy, which in some cases have resulted in intrauterine death or spontaneous abortion. Early reports from Chile and Canada show the relationship between obesity and fatal case of the disease and new reports from Michigan have supported this (WHO, 2009a). Most cases of the disease are mild and self-limiting and improve by outpatient treatments and a limited number of patients need to be admitted. All age groups may need to be hospitalized, but the number of admissions is more common in the age range of 15-45 years. In Japan, about 80% of the cases aged 10-19 years; in the Philippines, most cases aged 5-24 years; in England, the mean age of patients was 20 years and the male-female ratio was one-to-one in hospitalized cases (WHO, 2009b; WHO, 2010b). According to the latest WHO report in 2009, the highest incidence of disease was in adolescents and young people, but hospitalization rate was more in children to account for 1-10% of hospitalization cases, of which 10-25% need ICU (Intensive Care Unit) (Haghdoost et al., 2010; WHO, 2010b). Mortality of 0.5% of the affected population or 2-9% of admitted patients was due to the disease (WHO, 2009b; WHO, 2010b). In the first 400 confirmed cases in Iran, the highest incidence was at the age of 15-24 (45.61%), followed by 25-34 (16.2%) and 5-24 (15.3%). The number of males was higher, but the next study conducted in November 2009 showed no significant difference between genders (Hatami, 2009; Gooya et al., 2011). The main cause of hospitalization is involvement of the lower respiratory tract in the form of primary viral pneumonia due to direct virus invasion into the lung tissue. Primary pathologic findings indicate a widespread alveolar injury of interstitial haemorrhagic pneumonitis along with lymphocytic proliferation and relative neutrophil reduction in this tissue

plus ARDS. In some US hospitals, some patients with severe forms of pulmonary embolism have been reported with ARDS resistant to treatment. In some cases, viral pneumonia progresses quickly and leads to ARDS and does not respond unexpectedly to oxygen therapy. Respiratory failure caused by severe pneumonia and ARDS are the leading cause of death from A/H_1N_1 influenza worldwide (WHO, 2009a).

After a latency period of about 1-7 days, clinical symptoms of influenza appear, which is roughly like seasonal influenza, although gastrointestinal symptoms such as diarrhoea and vomiting are most commonly observed. The most common clinical symptoms are fever, cough, sore throat, fatigue and headache; in some patients, diarrhoea and vomiting are also seen. Chills, myalgia and arthralgia are common symptoms which are commonly seen with lower incidence (Beon et al., 1982; Price et al., 2018; Kormuth et al., 2019). At the time of the pandemic, 2-5% of the people with H1N1 influenza have complications, but considering that mild cases have never been seen by doctors or recorded, it seems that the incidence of complications is far less than this. In a US report, the incidence of complications has been reported to be about 0.3%. The most commonly reported complications include progressive pneumonia, respiratory failure, ARDS, empyema, necrotizing pneumonia, pneumonia associated with bacterial agents, and ventilator and convulsion pneumonia (Dawood et al., 2009).

ARDS is an acute syndrome within an inflammatory week which involves lung parenchyma in the form of bilateral synthesis in ARDS ($PaO_2/FiO_2<300$ mmHg), which is not due to inadequate cardiac function. Given that there is no record of the incidence and severity of ARDS in patients with H1N1 in Iran, and in particular in Kerman, this study seems necessary as a baseline study to prepare for next possible epidemics, because, as it has been observed, ARDS patients in the context of H1N1 influenza often do not respond to conventional ARDS treatments and may require more advanced treatments such as ECMO and more ICU beds to deal with future epidemics.

2. MATERIALS AND METHODS

This was a cross-sectional study conducted in 2016in the Afzalipour Hospital in Kerman.The study was approved by the Ethics Committee of Kerman University of Medical Sciences (IR.KMU.ACRS.REC.1396.1055). The sampling method was census-based; by collecting records of patients with H1N1 influenza and then extracting the data and inserting these data in a pre-prepared form, including gender, age, PAO_2/FIO_2 and the underlying disease, ARDS outbreak and then severity of ARDS were calculated based on $PAO_2/FIO_2$and finally, the percentage of people with mild, moderate and severe types was determined.

Mild: $200<PAO_2/FIO_2<300$

Moderate: $100<PAO_2/FIO_2<200$

Severe: $PAO_2/FIO_2<100$

The studied population consisted of patients admitted to the Afzalipur Hospital from March 21, 2015 to March 19, 2016 due to a definitive diagnosis of H1N1 influenza virus; the patients whose records were incomplete were excluded. This study examined the relationship between incidence and severity of ARDS and underlying diseases such as diabetes, heart failure, chronic obstructive diseases and other chronic pulmonary diseases, renal and hepatic failure, obesity and pregnancy. Upon data collection, data was analyzed by SPSS20.

3. RESULTS

The following table lists demographic data of patients (Table 1).

Table 1 demographic data of patients

Variable	N	%
Gender		
Male	315	54.3
Female	265	45.7
Underlying disease		
Yes	98	16.8
No	482	83.2
ARDS		
Yes	86	14.8
No	494	85.2

Mortality		
Yes	33	5.6
No	547	94.4
	Mean	SD
Age	53.85	15.965

The statistical tests used to achieve these results include chi-square test and ANOVA test in some cases. Regarding the results of ARDS frequency in both males and females, there was no statistically significant difference (p-value = 0.223) (Table 2).

Table 2 frequency of ARDS in terms of gender

Gender	ARDS		p-value
	Yes	No	
Male	51 (16.1)	264 (85.9)	0.223
Female	35 (13.2)	230 (82.8)	

The results showed a significant relationship between underlying diseases and ARDS (p-value=0.001) (Table 3) (Figure 1).

Table 3 frequency of ARDS in terms of underlying diseases

Underlying diseases	ARDS		p-value
	Yes	No	
Yes	61 (62.2)	17 (41.8)	0.001
No	25 (5.1)	457 (94.9)	

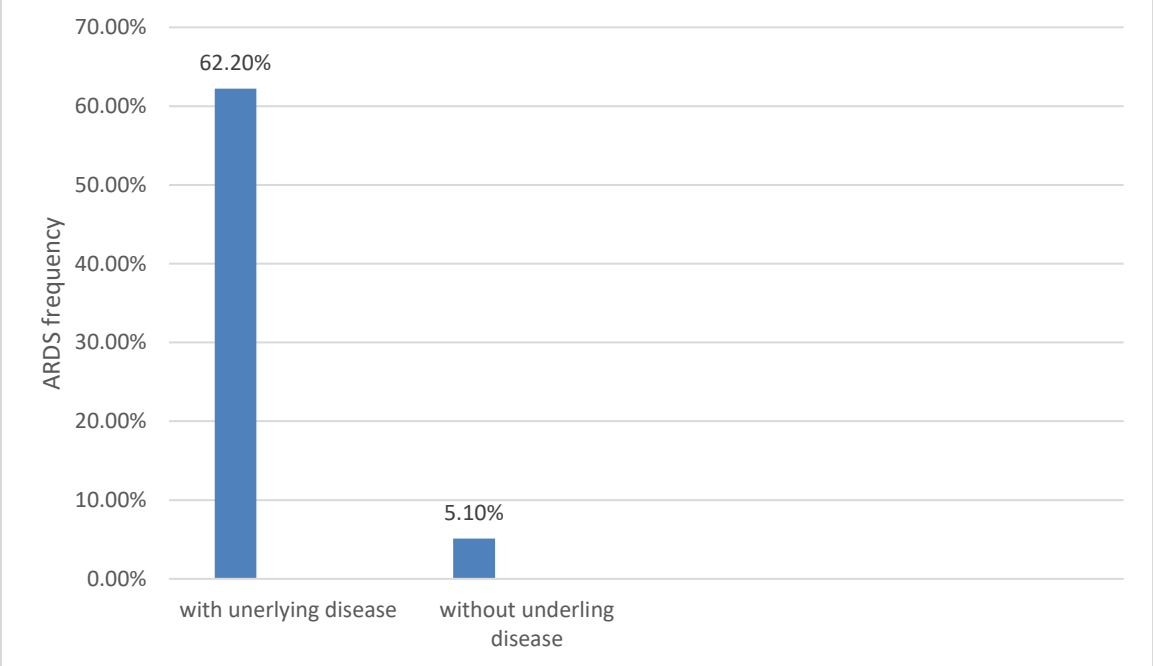

Figure 1 frequency of ARDS in term of underlying disease

There was no significant difference in mean age of patients with and without ARDS (p-value=0.124) (Table 4).

Table 4 frequency of ARDS in terms of age

Age	ARDS		p-value
	Yes	No	
Mean	54.52 ± 14.865	53.98 ± 15.684	0.124

The table below shows the severity of ARDS in terms of the prevalence of underlying diseases. In patients with mild, moderate and severe ARDS, 18 (58.9%), 16 (76.42%) and 27 (79.41%) had underlying disease, respectively. There was a significant difference in frequency of ARDS severity in terms of underlying diseases (p-value = 0.012) (Table 5) (Figure 2).

Table 5 frequency of ARDS severity in terms of underlying diseases

Severity	Underlying diseases		p-value
	Yes	No	
Mild	18 (58.9)	13 (41.1)	0.012
Moderate	16 (76.42)	5 (25.58)	
Severe	27 (79.41)	7 (20.59)	

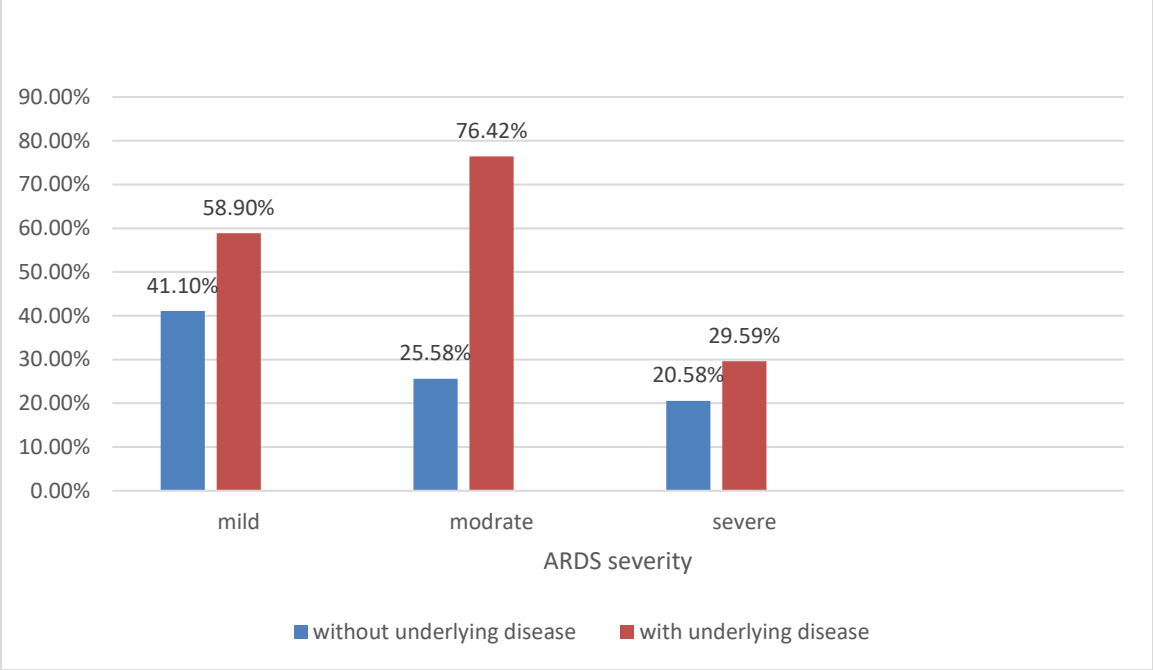

Figure 2 frequency of ARDS severity in term of underlying disease

In patients with mild ARDS, 22 (70.9%), in patients with moderate ARDS, 15 (71.42%), and in patients with severe ARDS, 24 (70.76%) were male. The frequency of ARDS severity was not significantly different in terms of gender (p-value = 0.112) (Table 6).

Table 6 frequency of ARDS severity in terms of gender

Severity	Gender		p-value
	Male	Female	
Mild	22 (70.9)	9 (29.1)	0.112
Moderate	15 (71.42)	6 (28.58)	
Severe	24 (70.76)	10 (29.24)	

The mean age was 51.54 ± 15.575 years in patients with mild ARDS, 53.98 ± 14.652 years in patients with moderate ARDS and 53.64 ± 14.942 years in patients with severe ARDS; no significant significance was observed in this regard (p-value = 0.062) (Table 7).

Table 7 frequency of ARDS severity in terms of age

Severity	Mean	p-value
Mild	51.54 ± 15.575	0.062
Moderate	53.98 ± 14.652	
Severe	53.64 ± 14.942	

According to mortality results, there was a significant difference and mortality was considerably higher in patients with ARDS (p-value = 0.035) (Table 8) (Figure 3).

Table 8 frequency of mortality in patients with ARDS

Mortality	ARDS		p-value
	Yes	No	
Yes	29 (87.87)	4 (12.13)	0.035
No	57 (10.42)	490 (89.58)	

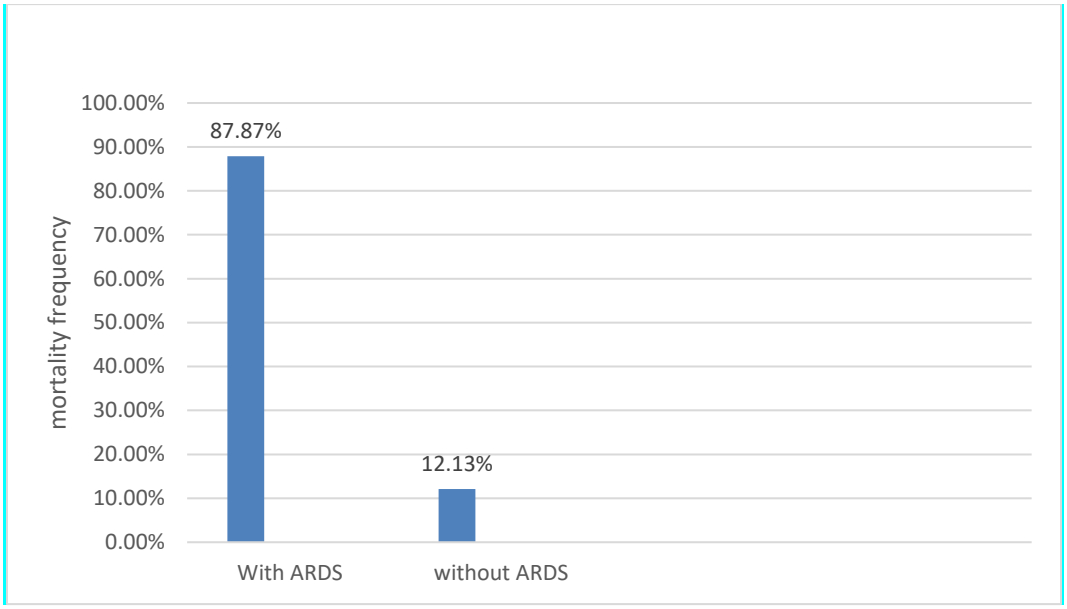

Figure 3 frequency of mortality in H1N1 patients with and without ARDS

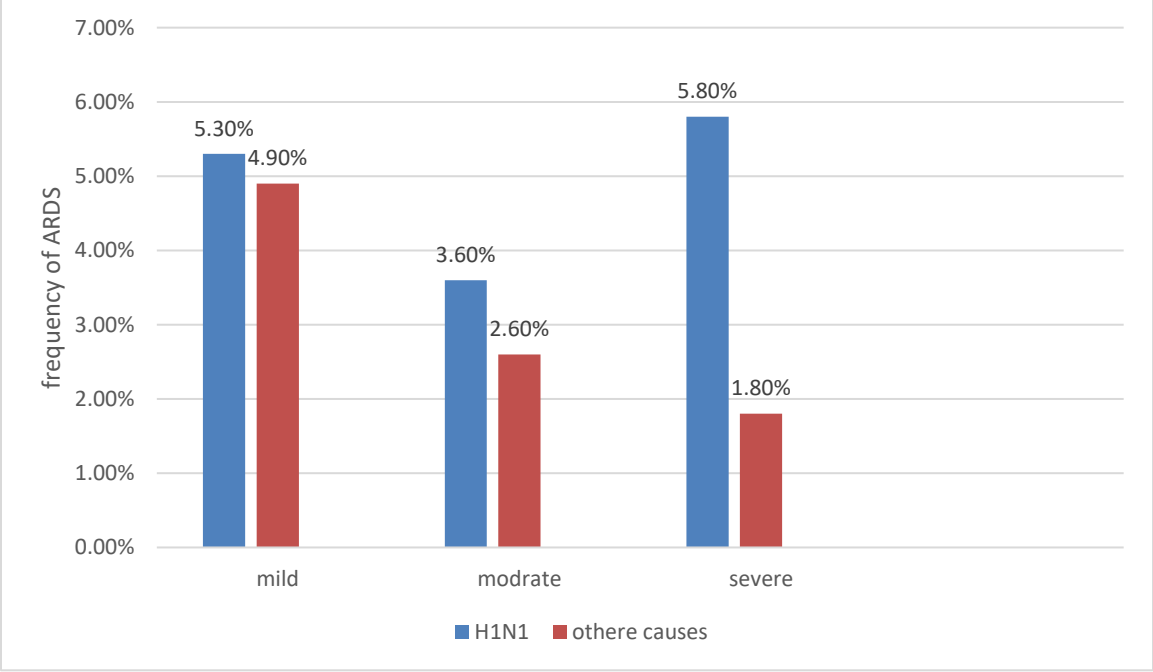

Figure 4 Frequency of different degree of ARDS in H1N1 and other causes

According to results of this study and incidence of ARDS, it was shown that the incidence of moderate and severe ARDS in H1N1 patients was significantly higher than the overall incidence of ARDS (p-value = 0.049) (Table 9) (Figure 4).

Table 9 comparison of prevalence of ARDS in H1N1 patients and its overall incidence

Incidence	ARDS severity			P-value
	Mild	Moderate	Severe	
H1N1 patients	5.3	3.6	5.8	0.049
Overall	4.9	2.6	1.8	

4. DISCUSSION

In this study, 580 cases of H1N1 influenza were examined; of 580 cases, 315 (54.3%) were male and 265 (45.7%) were female; 98 patients (16.8%) had underlying disease; 86 patients (14.8%) had ARDS, of which 31 (36%) had mild ARDS, 21 (24.4%) had moderate ARDS and 34 (39.6%) had severe ARDS. Of the 580 cases studied, 33 (5.6%) died; 87.77% of patients died had ARDS, which showed a statistically significant difference.

The results showed that in patients with ARDS, 51 (16.1%) were male and 35 (13.2%) were female, which was not significantly different. In patients with ARDS, 61 (62.2%) had an underlying disease; the results showed that ARDS was significantly higher in patients with underlying disease. However, the mean age of patients with ARDS was not significantly different from those who did not have ARDS.

In patients with mild ARDS, 18 (58.9%), in patients with moderate ARDS, 16 (76.42%) and in patients with severe ARDS, 27 (79.41%) had underlying disease. These results showed that ARDS severity was higher in patients with underlying disease and the severity of ARDS was moderate and severe in majority of patients with underlying disease. In patients with mild ARDS, 22 (70.9%), in patients with moderate ARDS, 15 (71.42%) and in patients with severe ARDS, 24 (70.76%) had underlying disease. The severity of ARDS was not significantly different in terms of gender. The mean age was 51.54 ± 15.575 years in patients with mild ARDS, 53.98 ± 14.652 years in patients with moderate ARDS and 53.64 ± 14.942 years in patients with severe ARDS; no significant difference was observed in terms of age.

In a study by Hubmayr and Farmer (2010) on 380 patients with H1N1, ARDS was higher in patients over the age of 70 and in pediatric patients; mortality rate was higher in patients with ARDS than in other patients. This study also found that mortality rate was higher in patients with ARDS.

In a study conducted by Ranieri et al. (1997) on 312 H1N1 patients, the results showed that ARDS was higher in patients with a history of underlying diseases, particularly pulmonary diseases (COPD and asthma). Mortality rates were higher in these patients. This is consistent with current study, so that the frequency of ARDS was higher in patients with underlying disease; moreover, mortality rate was higher in these patients.

In a study by Napolitano et al. (2014), the results showed that the incidence of ARDS was 19%in patients with H1N1, with 69% mortality in H1N1 patients with ARDS. The results of this study showed that 14.8% of patients had ARDS and 87.87% of them died, which is consistent with above study. The ARDS epidemic is 86 per 100000 in the world and the mild, moderate and severe ARDS epidemic is 18 per 100000, 29 per 100000, and 38 per 100000, which, in contrast to this study, showed that the ARDS outbreak was higher in terms of H1N1 disease and severe ARDS was also higher.

5. CONCLUSION

Finally, the results of this study showed that ARDS was higher in patients with underlying diseases, and ARDS severity was higher in these patients than in other patients. Mortality rates also had a significant relationship with ARDS and most of these mortalities were in these patients.

Conflict of interest

There was not any conflict of interest in this study.

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