Original Article

Retrospective evaluation of laboratory-confirmed and recovered cases of influenza A(H1N1)v

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Aim: To retrospectively evaluate patients that were diagnosed with H1N1 and recovered from the disease in the initial period of an influenza A(H1N1)v epidemic in the province of Diyarbakir. It is estimated that 34-67 million individuals around the world have been infected by influenza A(H1N1)v, that 154,000-303,000 individuals have been hospitalized, and that 7000-13,000 individuals have lost their lives.

Materials and methods: We were able to include 250 of 362 cases (69.0%) of confirmed influenza A(H1N1)v, from which the patients recovered, from the samples received between 19 October and 3 December 2009 after a pandemic alarm was given in the province of Diyarbakır. Patients with laboratory-confirmed cases were reached by telephone 15 days after the onset of influenza symptoms.

Results: In terms of demographics, 44.8% of patients were between the ages of 0-14, 51.6% were male, and 44.0% were students. In 77.6% of the cases, fever was observed, while 53.2% had coughs and 18.4% had vomiting problems. It was determined that patients older than 45 years old, pregnant women, and individuals with chronic diseases were hospitalized more frequently than the young, nonpregnant women, and individuals without a chronic disease. The secondary attack rate within the clinic was 24.6%.

Conclusion: Children and individuals with chronic diseases are important risk groups. It is believed that precautions such as hand-washing, limiting visits, and ensuring proper ventilation within houses will reduce in-house infectivity and the secondary attack rate.

Key words: Influenza (H1N1)v, retrospective study, Diyarbakır

Laboratuvar olarak doğrulanmış ve iyileşmiş influenza a(H1N1)v vakalarının retrospektif değerlendirilmesi

Amaç: Dünyada 34-67 milyon kişinin influenza A(H1N1)v ile enfekte olduğu, 154-303 bin kişinin bu nedenle hastaneye yattığı, 7-13 bin kişinin ise öldüğü tahmin edilmektedir. Beş yaş altı çocukların, gebelerin ve astım, kalp hastalığı gibi herhangi bir kronik hastalığı olanların influenza A(H1N1)v gribi açısından risk altında oldukları belirtilmektedir. Bu araştırmada, Diyarbakır İli'ndeki influenza A(H1N1)v salgınının ilk dönemlerinde H1N1 pozitifliği doğrulanmış ve iyileşmiş vakaların retrospektif olarak değerlendirilmesi amaçlanmıştır.

Yöntem ve gereç: Diyarbakır İli'nde pandemi alarmı verildikten sonraki 19 Ekim-3 Aralık 2009 tarihleri arasında alınan numunelerden influenza A(H1N1)v doğrulanmış ve iyileşmiş olan 362 vakanın 250'si (% 69,0) araştırmaya dahil edilebilmiştir. Doğrulanmış vakalara semptomlarının başlangıcından 15 gün sonra telefon aracılığı ile ulaşılmıştır.

Bulgular: Vakaların % 44,8'i 0-14 yaş grubunda, % 51,6'sı erkek, % 44,0'ı ise öğrencidir. Vakaların % 77,6'sında ateş, % 53,2'sinde öksürük, % 18,4'ünde kusma görülmüştür. 45 yaş ve üstü vakaların diğer yaş gruplarına, gebe olanların olmayanlara, kronik hastalığı olanların olmayanlara göre daha fazla hastaneye yattıkları saptanmıştır. Vakaların klinik hane içi sekonder atak hızı % 24,6'dır.

Sonuç: Çocuklar ve kronik hastalığı olanlar influenza A(H1N1)v açısından önemli risk gruplarıdır. Hane içinde el yıkama, ziyaretlerin kısıtlanması ve havalandırma gibi önlemlerin, hane içi bulaştırıcılığı ve sekonder atak hızını azaltacağı düşünülmektedir.

Anahtar sözcükler: İnfluenza (H1N1)v, retrospektif çalışma, Diyarbakır

Introduction

Influenza A viruses are negative-stranded RNA viruses of the family Orthomyxoviridae (1). Influenza A(H1N1)v is a triple-reassortant influenza virus, containing genes from human, swine, and avian influenza A viruses (2-4). The new influenza A (H1N1)v was first defined by the CDC in April 2009; it was reported then that 60.0% of the population of one Mexican town was infected in the month of March and that 2 residents of the town died as a result (5). The CDC declared the influenza A(H1N1)v epidemic a public health emergency in April of 2009 (6), whereas the WHO declared it pandemic in June of 2009 (7-10).

Influenza A(H1N1)v spread in North American within weeks and began to be detected in different parts of the world. It is estimated that 34-67 million individuals around the world have been infected by influenza A(H1N1)v, that 154,000-303,000 individuals have been hospitalized, and that 7000-13,000 individuals have lost their lives (11).

It is known that the first group to be infected by influenza A(H1N1)v was travelling adults and that the fast transition of the virus among humans by means of adults caused the pandemic (12,13). The infectivity rate in Mexico was reported to be 1.0%-2.0%, while the mortality rate was reported as 0.2%-0.6% (14,15). Influenza A(H1N1)v has affected 80.0% of individuals under 25 (16). Children under the age of 5, pregnant women, and individuals with chronic diseases such as asthma and cardiac diseases are particularly at risk for influenza A(H1N1)v (5,17-19).

In a person that has contact with the virus, clinical symptoms and findings are observed approximately 2 days (ranging from 1 to 4 days) later. The symptoms of influenza A(H1N1)v are fever, sore throat, nasal flow, widespread body ache, headache, cold, and weakness, which are seen in approximately the third day of the infection (1). It was also stated that diarrhea and vomiting are seen in 25.0% of cases (5,12).

The clinical attack rate of influenza A(H1N1)v was calculated as lower than 20.0%. While this value is higher than the attack rate of seasonal influenza, it is lower than those of previous pandemics. The reasons for this are partial immunity in the elderly, the asymptomatic and/or light course of the disease, and the variety in the definitions of cases reported by different countries (8). In the H1N1 case management scheme prepared by the Ministry of Health of the Republic of Turkey, a possible case is defined as the "presence of at least one of the symptoms of widespread body ache, sore throat, headache, nose flow, cough, or respiration difficulty with fever or fever history exceeding 38 °C (armpit) that cannot be explained with any other reason." Confirmed cases of influenza A(H1N1)v are defined as follows: a "possible case in which pandemic influenza A(H1N1)v is detected in one of the reference laboratories determined by the Ministry of Health with real-time PCR or virus culture" (20).

The aim of this study was to retrospectively evaluate the cases in which H1N1 positivity was confirmed and from which patients recovered in the first stage of an influenza A(H1N1)v epidemic in Diyarbakır.

Materials and methods

Pandemic influenza (H1N1) was observed for the first time in the samples taken in the month of September in Diyarbakır. The intensity of control efforts against pandemic influenza in the province

increased from that date onward. After an obvious increase was detected in H1N1 cases in the province of Diyarbakır, this study was established, comprising 362 cases of confirmed influenza A(H1N1)v, for which the patients applied to health centers between 19 October and 3 December 2009 and from which the patients later recovered. In this definitive-type study, the researchers tried to reach all patients via telephone.

The cases were evaluated according to age, gender, patients' complaints at the time of applying to the health centers, recovery period, working status, pregnancy, presence of chronic disease, hospitalization and duration of hospitalization, status of travelling, size of household, and number of persons with similar complaints within the same house.

It was planned to reach the laboratory-confirmed patients by telephone 15 days after the onset of influenza symptoms. Telephone numbers of 52 of the 362 patients (14.4%) could not be found, 60 patients (16.6%) whose telephone numbers were known were called 2 times a day but did not answer, and thus 250 cases (69.0%) could be included in the study.

Analyses were carried out with SPSS version 15.0. In the analyses, percentage distributions, chi-square tests, Fisher's exact tests, one-way ANOVA, t-tests, and 95% confidence interval odds ratios (OR) were used. A P-value of <0.05 was considered statistically significant.

Results

For this retrospective study of confirmed cases of influenza A(H1N1)v from which patients recovered, some of the characteristics of the 250 cases are presented in Table 1.

Of the 250 participants, 43.9% were in the 0-14 age group (median age = 16), 51.6% were male, and 30.4% had a chronic disease. It was determined that 23.6% of the confirmed influenza A(H1N1)v cases required hospitalization, while 3.6% of patients stated that they had travelled recently (Table 1).

When patient complaints were evaluated, the following common complaints were found: fever in 77.6% of cases, cough in 53.2%, weakness in 33.2%, vomiting in 18.4%, and diarrhea in 9.2% (Table 2).

It was determined that the healing process of males and individuals without a chronic disease was faster than those of females and those with a chronic disease (2.2 days, from a range of 1.1-4.6 days, compared to 2.9 days, from a range of 1.4-5.7 days) (Table 3).

Patients older than 45 were 6.5 times more likely to be hospitalized than those in the 0-14 age group, pregnant women were 8.7 times more likely to be hospitalized than nonpregnant women, those with chronic diseases were 4.4 times more likely to be hospitalized than those without such a disease, those with a lung disease were 3.3 times more likely to be hospitalized than those without such a disease, and overweight individuals were 6.9 times more likely to be hospitalized than those who were not overweight (Table 4).

The average recovery period for females and those with a chronic disease was longer compared to those of males and those without a chronic disease; this difference was found to be statistically significant (Table 5).

The number of individuals living in the same house as the studied influenza patients was found, as was the number of individuals with similar complaints. The clinical in-house secondary attack rate was calculated as 24.6%.

Discussion

In this study, it was seen that the majority of patients were from the 0-14 age group (44.8%); the median age was 16. In a study from the United States, it was demonstrated that 60.0% of patients from 642 confirmed cases were 18 years old or younger (16). Similarly, in a retrospective study conducted by Echevarria-Zuno et al., the median age of confirmed patients was 16 (14). In a study conducted by Castro-Jimenez et al. on 183 confirmed cases, the majority of patients were young (21). One of the influenza A(H1N1)v risk groups comprises children and the young.

It was determined in the present study that in 44.0% of the confirmed 250 cases, the patients were students, the largest demographic category in

Table 1. The distribution of some characteristics of confirmed cases of influenza A(H1N1)v (October-December 2009, Diyarbakır).

	n	%
Age (n = 250)		
0-14	112	44.8
15-24	65	26.0
25-44	63	25.2
≥45	10	4.0
Mean ± sd = 18.0 ± 12.0	Median = 16.0	Min-max = 1-54
Sex (n = 250)		
Male	129	51.6
Female	121	48.4
Employment (n = 250)		
Student	110	44.0
Housewife	36	14.4
Teacher	11	4.4
Health staff	4	1.6
Other*	89	35.6
Pregnancy (n = 77)**		
Yes	18	23.4
No	59	76.6
Chronic Diseases (n = 250)		
No	174	69.6
Yes	76	30.4
Chronic pulmonary diseases	21	27.6
Chronic nephropathy	10	13.2
Overweight	6	7.8
Chronic cardiac diseases	6	7.8
Hypertension	4	5.2
Diabetes mellitus	3	3.9
Immunodeficiency	2	2.6
Other***	28	36.8
Hospital stay (n = 250)		
No	191	76.4
Yes	59	23.6
Intensive care unit	13	22.0
Mechanical ventilation	-	-
Duration of hospital stay (n = 249)		
≤3	52	20.9
4-6	130	52.2
≥7	67	26.9
Mean ± sd = 5.5 ± 2.6	Median = 5.0	Min-max = 1-22
Travelling (n = 250)		
No	241	96.4
Yes	9	3.6
Size of household (n = 249)		
≤3	52	20.9
4-5	85	34.1
≥6	112	45.0
Mean ± sd = 5.5 ± 2.6	Median = 5.0	Min-max = 1-22

* Jobless, <7 years;   **Women 15-49 years old;
***Chronic gastrointestinal diseases, cancer, infectious diseases, rheumatic diseases

Table 2. The distribution of complaints for confirmed influenza A(H1N1)v cases (October-December 2009, Diyarbakır).

Symptoms	n	%
Fewer	194	77.6
Cough	133	53.2
Exhaustion	83	33.2
Headache	62	24.8
Sore throat	51	20.4
Vomiting	46	18.4
Nausea	44	17.6
Nasal flow	44	17.6
Diarrhea	23	9.2
Common muscle aches	20	8.0
Dyspnea	19	7.6
Abdominal pain	14	5.6

terms of employment status. In the retrospective study conducted by Echevarria-Zuno et al., females, children, and the 10-19 age group were found to be at risk of influenza A(H1N1)v infection, while babies, individuals older than 60, and individuals with chronic diseases were found to be at risk of serious diseases (14). Since students are both children and present in communal places, they are very important in terms of in-school spreading of infection (22).

No difference was seen in respect to the occurrence rate between the genders, while it was determined that the recovery period of females was longer than that of males. In the study by Echevarria-Zuno et al., it was proved that the occurrence rate and seriousness of the disease were not related to gender (14). It was found that those without a chronic disease recovered faster compared to those with chronic diseases. The higher percentage of females with a chronic disease compared to males might be a reason for the longer recovery periods of females.

It was found that 30.4% of confirmed cases in this study also exhibited a chronic disease, and that the most frequently cited chronic disease was lung disease (27.6%). In a study conducted by Mangtani et al., chronic diseases such as asthma, diabetes mellitus, morbid obesity, and diseases affecting the immune system were present in more than 70.0% of the cases (23). In a study conducted by Jain et al., on the other hand, it was found that the most frequent underlying chronic disease in both adults and children was asthma (24). Individuals with chronic diseases are important risk groups for influenza A(H1N1)v.

The most frequently cited symptoms were, respectively, fever, cough, weakness, and headache. In the retrospective evaluation of confirmed cases by Echevarria-Zuno et al., similarly, the most frequently cited symptoms were fever, cough, and headache (14). In other studies, it was reported that the most frequently cited symptoms were, respectively, fever, cough, and sore throat (16,21). Vomiting was observed in 18.4% of cases while diarrhea was observed in 9.2%. In a study conducted by the Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team, diarrhea and vomiting were observed in one-fourth of the cases, different from other studies (16). Although there is a difference among countries in respect to clinical symptom percentages, the order of occurrence frequency is similar.

It was determined that 23.6% of confirmed cases were hospitalized. In the study conducted by the Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team, the hospitalization rate for 642 cases was reported as 9.0% (16), while in the study by Castro-Jimenez et al., the rate of hospitalization for 183 cases was reported as 14.2% (21). Moreover, it was determined that the hospitalization rates for

Table 3. Distribution of recovery time for confirmed influenza A(H1N1)v cases in accordance with age, sex, pregnancy, and chronic diseases (October-December 2009, Diyarbakır).

	Recovery Time				P	OR (95% CI)
	≤7 days		>7 days			
	n	%	n	%		
Age						
0-14	97	89.8	11	10.2	0.085	ref
15-24	50	80.6	12	19.4		2.1 (0.8-5.6)
25-44	47	77.0	14	23.0		2.6 (1.0-6.8)
≥45	7	70.3	3	30.0		3.8 (0.7-20.1)
Sex						
Male	110	88.7	14	11.3	0.023	ref
Female	91	77.8	26	22.2		2.2 (1.1-4.6)
Pregnancy**						
No	47	81.0	11	19.0	0.103	ref
Yes	10	58.8	7	41.2		2.9 (0.9-9.6)
Any other chronic diseases						
No	149	88.2	20	11.8	0.002	ref
Yes	52	72.2	20	27.8		2.9 (1.4-5.7)
Hypertension						
No	198	83.5	39	16.5	0.519*	ref
Yes	3	75.0	1	25.0		1.7 (0.2-16.7)
Diabetes mellitus						
No	201	84.5	37	15.5	0.004*	-
Yes	-	-	3	100.0		
Chronic cardiac disease						
No	197	83.5	39	16.5	1.000*	ref
Yes	4	80.0	1	20.0		1.3 (0.1-11.6)
Chronic pulmonary disease						
No	189	84.4	35	15.6	0.171*	ref
Yes	12	70.6	5	29.4		2.3 (0.7-6.8)
Chronic nephropathy						
No	197	84.0	37	16.0	0.220*	ref
Yes	7	70.0	3	30.0		2.2 (0.6-9.1)
Overweight						
No	198	84.3	37	15.7	0.059*	ref
Yes	3	50.0	3	50.0		5.4 (1.0-27.5)

*Fisher's exact test
**Women 15-49 years old

Table 4. Distribution of hospital stay for confirmed influenza A(H1N1)v cases in accordance with age, sex, pregnancy, and chronic diseases (October-December 2009, Diyarbakır).

	Hospital stay				P	OR (95% CI)
	Yes		No			
	n	%	n	%		
Age						
0-14	21	18.8	91	81.2	0.024	ref
15-24	18	27.7	47	72.3		1.7 (0.8-3.6)
25-44	14	22.2	49	77.8		1.2 (0.5-2.8)
≥45	6	60.0	4	40.0		6.5 (1.4-30.7)
Sex						
Male	27	20.9	102	79.1	0.305	ref
Female	32	26.4	89	73.6		1.4 (0.7-2.5)
Pregnancy**						
No	11	18.6	48	81.4	<0.005	ref
Yes	12	66.7	6	33.3		8.7 (2.7-28.4)
Any other chronic diseases						
No	26	14.9	148	85.1	<0.005	ref
Yes	33	43.4	43	56.6		4.4 (2.3-8.5)
Hypertension						
No	57	23.2	189	76.8	0.237*	ref
Yes	2	50.0	2	50.0		3.3 (0.5-24.1)
Diabetes mellitus						
No	56	22.7	191	77.3	0.013*	-
Yes	3	100.0	-	-		
Chronic cardiac disease						
No	56	23.0	188	77.0	0.145*	ref
Yes	3	50.0	3	50.0		3.3 (0.7-17.1)
Chronic pulmonary disease						
No	49	21.4	180	78.6	0.013*	ref
Yes	10	47.6	11	52.4		3.3 (1.3-8.3)
Chronic nephropathy						
No	55	22.9	185	77.1	0.252*	ref
Yes	4	40.0	6	60.0		2.2 (0.6-8.2)
Overweight						
No	55	22.5	189	77.5	0.029*	ref
Yes	4	66.7	2	33.3		6.9 (1.2-38.5)

*Fisher's exact test
**Women 15-49 years old

Table 5. Distribution of recovery time and duration of hospital stay of confirmed influenza A(H1N1)v cases in accordance with age, sex, pregnancy, and chronic diseases (October-December 2009, Diyarbakır).

	Recovery time (days) Mean ± sd	Duration of hospital stay (days) Mean ± sd
Age		
0-14	4.90 ± 3.72	6.60 ± 4.44
15-24	5.53 ± 3.20	6.89 ± 7.40
25-44	6.70 ± 5.90	8.71 ± 6.07
≥45	6.00 ± 3.49	9.00 ± 6.42
	F = 2.367 P = 0.072	F = 0.514 P = 0.674
Sex		
Male	4.71 ± 2.83	7.31 ± 6.30
Female	6.47 ± 5.31	7.56 ± 5.83
	t = 3.236 P = 0.001	t = 0.160 P = 0.874
Pregnancy*		
Yes	8.06 ± 6.68	7.83 ± 6.26
No	6.34 ± 5.23	7.64 ± 6.04
	t = 1.113 P = 0.269	t = 0.077 P = 0.940
Any other chronic diseases		
Yes	6.75 ± 5.19	8.67 ± 6.90
No	5.06 ± 3.77	5.84 ± 4.13
	t = 2.833 P = 0.005	t = 1.814 P = 0.075

*Women 15-49 years old
One-way ANOVA and t-test

patients older than 45, pregnant women, individuals with chronic diseases, individuals with lung diseases, and overweight individuals were higher compared to other groups. In a study conducted by Jamieson et al. that included 34 pregnant women between the ages of 15 and 44, it was estimated that hospitalization rates of pregnant women were higher compared to those of normal populations (18). The difference in the hospitalization rates of confirmed cases might have been caused by the difference of the frequency of chronic diseases of cases. It was found that approximately one-fifth of hospitalized cases needed intensive care. In a study conducted by Jain et al., it was stated that 25% of 272 confirmed and hospitalized cases required intensive care (24). The

hospitalization rates of confirmed cases were different than the data from the literature, whereas the rate of necessity for intensive care was similar. It would be useful to evaluate international case managements and hospitalization indications in order to explain the differences in hospitalization rates.

Particles contaminated with influenza A(H1N1)v are spread by means of coughing and sneezing. It is known that crowded environments are an important factor in the spread of influenza A(H1N1)v (25). In this study, the median number of individuals in a household was 5.0, whereas in-house infectivity was 24.6%. In a report published by Yang et al., the best determiner of infectivity was the secondary attack rate; this rate for influenza A(H1N1)v was 27.3%

(26). In that study, it was found that housewives were the second group in which influenza A(H1N1) v was seen most frequently. This might be due to the fact that children are in contact with housewives most regularly within the house, and housewives are present in the same environment for a very long time. It is believed that measures such as hand-washing, limiting visits, and ensuring proper ventilation within the house (5) will reduce in-house infectivity and the secondary attack rate.

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