EVALUATION OF PANDEMIC INFLUENZA A (H1N1) CASES IN VAN REGION

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ABSTRACT

Objective: *Influenza viruses have retained their importance throughout history by creating pandemics since the segmental structure of the RNA undergo frequent genetic changes. The purpose of this study was to investigate the pandemic influenza A (H1N1) cases detected our region.*

Material and Method: *Totally 570 patients were registered with pre-diagnosis of Pandemic Influenza A (H1N1) infection in five different hospitals located in Van region between 15 October 2009 - 15 January 2010. After nasopharyngeal/throat swab samples were taken from patients, they were sent to Refik Saydam Hygiene Center (RSHC) in accordance with the rules of biosafety, and specimens were investigated for Pandemic Influenza A(H1N1) 2009 by using Real-Time PCR method.*

Results: *Pandemic Influenza A (H1N1) was determined by RSHC as positive for 220 patients. 36 of these patients were in intensive care conditions, 85 were hospitalized and 16 passed away. 109 patients, who were diagnosed with Pandemic Influenza A (H1N1), were within range of 6-25 years. All patients in this age range were treated and discharged. The most common symptoms of patients who were hospitalized were defined as cough and fever. In these patients, the most common risk factors were as follows; being <5 years, having the cardiovascular disease, using immunosuppressive drugs and having lung disease.*

Conclusion: *Pandemic influenza A (H1N1) infections are more frequent in young adults and patients without risk factor, unlike seasonal flu. When examining its effect on the society, Pandemic Influenza A (H1N1) 2009 constitutes a good opportunity in terms of preparation of inevitable struggling with pandemics in the future.*

Keywords: *Pandemics, Influenza A virus, H1N1 subtype, polymerase chain reaction* ***Nobel Med 2014; 10(3): 36-40***

VAN BÖLGESİNDE PANDEMİK İNFLUENZA A (H1N1) OLGULARININ İRDELENMESİ

ÖZET

Amaç: İnfluenza virüsleri, parçalı RNA yapısının sık genetik değişime uğraması sonucu pandemiler oluşturarak tarih boyunca önemlerini korumuşlardır. Çalışmada, bölgemizde tespit edilen Pandemik İnfluenza A (H1N1) olgularının irdelenmesi amaçlanmıştır.

Materyal ve Metod: Bölgemizdeki beş farklı hastaneye, 15 Ekim 2009-15 Ocak 2010 tarihleri arasında Pandemik İnfluenza A (H1N1) enfeksiyonu ön tanılı 570 hasta başvurmuştur. Hastalardan nazofaringeal/boğaz sürüntü örnekleri alınmış, Refik Saydam Hıfzısıhha Merkezi'ne (RSHM) biyogüvenlik kuralları içerinde ulaştırılarak Real-Time PCR yöntemi ile etkenin Pandemik İnfluenza A (H1N1) 2009 olup olmadığı araştırılmıştır.

Bulgular: RSHM tarafından yapılan PCR testi ile 220 hastada Pandemik İnfluenza A (H1N1) pozitif bulunmuştur. Bu hastaların 36'sı yoğun bakım şartlarında olmak üzere 85'i hastaneye yatırılmış ve 16'sı yaşamını yitirmiştir. Pandemik İnfluenza A (H1N1) tanısı alan hastaların 109'unun 6-25 yaş aralığında olduğu görülmüştür. Bu yaş aralığında tüm hastalar tedavi edilerek şifa ile taburcu edilmiştir. Yatarak tedavi gören hastalarda öksürük ve ateş en sık bulunan semptomlar olarak belirlenmiştir. Yatan hastalarda <5 yaş, kardiyovasküler hastalık, immünsupresif ilaç kullanımı ve akciğer hastalığı en sık rastlanan risk faktörleri olarak gözlenmiştir.

Sonuç: Pandemik influenza A (H1N1) enfeksiyonu, mevsimsel gribin aksine genç erişkin ve risk faktörü olmayan hastalarda daha sık oranda görülmektedir. Toplum üzerindeki etkisi irdelendiğinde, 2009 İnfluenza A (H1N1) pandemisi, gelecekte kaçınılmaz pandemilerle mücadeleye hazırlık açısından iyi bir fırsat oluşturmuştur.

Anahtar Kelimeler: Pandemik, İnfluenza A virüsü, H1N1 alt tip, polimeraz zincir reaksiyonu **Nobel Med 2014; 10(3): 36-40**

INTRODUCTION

Influenza viruses are respiratory tract infection factors that have an acute onset, show a rapid spread in society and are characteristically encountered as an epidemy.[1,2] The antigenic changes observed on virus surface proteins due to the feature of being mutated and genetic reunions obstruct the control of influenza viruses.[3,4]

Following the explanation of Centers for Disease Control and Prevention (CDC) concerning the identification of the Influenza A (H1N1) virus originating from the swine in 2009, it apparently spread in many areas of the world in a short time and the World Health Organization (WHO) explained that there was a 6th stage pandemia for the Influenza A (H1N1) virus.[5,6] The purpose of this study was to determine the patients who applied to five different hospitals in our region and were accepted as the suspects of Pandemic Influenza A (H1N1) according to the criteria of WHO and to examine the cases with Pandemic Influenza A (H1N1) in our region.

MATERIAL and METHOD

570 patients with the pre-diagnosis of Pandemic Influenza A (H1N1) infection applied to five different hospitals in our region between 15 October 2009-15 January 2010. Nasopharyngeal/throat swab specimens were received from the patients and sent to Refik Saydam Hygiene Center (RSHC) in accordance with biosafety rules and then the existence of Pandemic Influenza A (H1N1) was investigated with the Real-Time PCR method.

Patients with the suspicion of Influenza A (H1N1) were selected according to the protocol determined by WHO. Accordingly, patients with a fever of >38°C and/or epidemiological criteria accompanied by at least two acute respiratory tract symptoms were clinically accepted as the suspects of Pandemic Influenza A (H1N1) 2009.[7] While investigating the risk factors for influenza in inpatients, chronic medical conditions such as cardiovascular, pulmonary, renal, hepatic, neuromuscular, hematological and metabolic disorders, as well as immune deficiency that are documented in many countries have been also investigated.[8-10]

The obtained specimens were taken in the viral transport medium (Universal Transport Medium, Copan, USA) with the suggestion of the reference laboratory of RSHC and were immediately sent to the RSHC laboratory within a convenient container in accordance with cold chain and biosafety rules. →

Table 1: Distribution of patients diagnosed with Pandemic Influenza A (H1N1) according to their ages and the number of inpatients, intensive care patients and deceased patients.

Age range	Total number of patients	Number of inpatients	Number of intensive care patients	Number of deceased patients
< 1	14	11	5	3
1-5	11	7	-	-
6-15	66	5	4	-
16-25	43	11	2	-
26-35	42	27	13	5
36-45	18	11	4	4
46-55	13	7	5	3
56-65	7	3	-	-
65<	6	3	3	1
Total	**220**	**85**	**36**	**16**

Table 2: Ages and risk factors of deceased patients

Patients	Age	Risk Factor
1	75	Congestive heart failure, chronic renal failure
2	53	Immunosuppressive use (pemphigus vulgaris)
3	51	Immunosuppressive use (temporal arteritis)
4	46	Hepatic cirrhosis, HBV (+) and HCV (+)
5	44	Acute myeloblastic leukemia (M2)
6	39	No risk
7	37	Postpartum Period
8	36	Chronic renal failure
9	32	No risk
10	32	No risk
11	32	No risk
12	28	No risk
13	28	COPD, Neuromuscular disease
14	7 months	<1 year
15	4 months	<1 year, Common variable immunodeficiency, heart failure
16	4 months	<1 year

COPD: Chronic obstructive pulmanary disease

The specimens were studied through targeting the protected gene area of the influenza virus. RSHC determined diagnosis of the Pandemic Influenza A (H1N1) by using the Real-Time PCR protocol that was suggested by CDC and the reagents that were provided by the same institution.[11] The data evaluated in this study was approved by the Clinical Research Ethical Committee of The Medical Faculty of Yüzüncü Yıl University (Date: 09.05.2013, Number: 36).

RESULTS

570 patients with the suspicion of Pandemic Influenza A (H1N1) infection were evaluated in our region according to the criteria of WHO. 283 of these patients were female and 287 were male.

In the study, a total of 220 patients, who were determined by RSHC to have positive Pandemic Influenza A (H1N1), were investigated according to various features. 111 (50%) of these patients were female, 109 (50%) were male and the ages were between 0-90.

In our region where the first case was determined in 19 October 2009, the number of confirmed patients increased rapidly and the pandemia peaked at the 46th week. Pandemic Influenza A (H1N1) infection started to decrease afterwards and only observed as sporadic cases.

85 (38.6%) of 220 patients diagnosed with pandemic influenza A (H1N1) were hospitalized and 36 (16.3%) were followed under intensive care conditions. However, 16 (7.2%) of the patients died.

Examining the distribution of patients diagnosed with pandemic influenza A (H1N1) according to their ages; in the <1 group, 79% of patients received an in-patient treatment, 5 were taken into the intensive care and 3 of them died. The fact that all the patients in the age group of 36-45 that were treated under intensive care conditions died was considered an important finding of the study. All the patients in the age groups of 1-5, 6-15 and 16-25 that were diagnosed with pandemic influenza A (H1N1) were treated, and discharged with full recovery (Table 1).

A total of 85 patients diagnosed with pandemic influenza A (H1N1) were hospitalized. Among the inpatients, 41 were female and 44 were male. It was determined that 43 of these patients had no disease in the risk group and 42 had at least one disease in the risk group. The most frequent risk factors in inpatients involved being a child younger than 5, chronic cardiovascular disease, immunosuppressive drug use and chronic lung disease. 76 of inpatients received the antiviral treatment, which was preferred as oseltamivir.

From the 16 deceased patients, 8 were female and 8 were male; 5 of deceased patients were healthy individuals aged between 32 and 39 who had no risk factors. Other deceased patients, on the other hand, had at least one of the following risk factors: immunity disorder, heart disease, lung disease, being an infant or an elder.

It was observed that the patients generally died within the first week following hospitalization. 15 of these patients received antiviral treatment. Only one patient died before the antiviral treatment soon after the hospitalization. Even though 16 deceased →

patients who were aged between 0-75 had various risk factors, 5 patients had no risk factors at all (Table 2). The most frequent symptoms in inpatients were determined as cough (87%) and fever (86%). Apart from classic influenza symptoms such as throat ache, nasal discharge; some patients had diarrhea, vomiting and stomach ache.

DISCUSSION

Epidemic influenza virus infections occur regularly. The severity of this epidemia varies according to different gene segments of the virus. Pandemic influenza A (H1N1) is the last example of the influenza virus epidemia.[11,12]

It is reported that even though the rates of getting the influenza virus during childhood and adolescence are high, the disease has a fatal course especially in elders. It was determined that as well as elders, individuals with a chronic disease had a higher mortality rate during the influenza pandemia. Being defined as the risky group in influenza epidemia, the chronic lung disease, ischemic heart disease, chronic liver disease, diabetes or chronic renal disease, neurological diseases and malignancies were also found to be valid for pandemic influenza.[13,14]

Patients having asthma and other lung diseases, diabetes, morbid obesity, immune system disorders, neurological or cardiovascular disorders and receiving the immunosuppressive treatment were indicated to be in the risky group for Pandemic Influenza A (H1N1).[15] Echevarría-Zuno et al. stated that the pandemic influenza infection was more frequently encountered in individuals with a chronic disease such as hypertension, diabetes and obesity.[16] In our study, we intensively encountered with these risk factors in patients receiving an in-patient treatment. Among diseases that were indicated as the risky group with a rate of 51%, at least one was found in our patient.

The confirmed cases are reported to generally consist of young adults. In their study that was conducted with 9,459 patients with a positive pandemic influenza A (H1N1), Ertek et al. examined the age groups.[17] Accordingly, the patients were observed to be mostly in the age group of 5-14, 15-24 and 25-44. Distribution of the patients diagnosed with pandemic influenza A (H1N1) with the help of PCR according to their ages in this study examined as parallel with the data in Turkey; it was observed that the patients were mostly in age groups of 6-15, 16-25 and 26-35 according to the frequency in this study. However, this range in age groups varied in inpatients, intensive care patients and deceased patients. It was observed that the inpatients were mostly in the age group of 26-35, which required a greater intensive care. Similarly, the deceased patients were mainly in this age group. 6-25% of patients who were treated at the hospital due to the Pandemic Influenza A (H1N1) infection were followed up under intensive care conditions.[18,19] 36 (16.3%) out of 220 patients diagnosed with pandemic influenza in our region were followed up under intensive care conditions, which was found to be in parallel with the literature knowledge.

It has been reported that patients who had died because of pandemic influenza A (H1N1) infection are in the adult age group in general. It was determined in the same study that about 65% of deaths occurred in patients who were 25 years old or older.[20] In our area, 16 patients died who were followed up under intensive care unit conditions with pandemic influenza diagnosis. Thirteen of these mortality cases were in the age group of 25 and older.

Seasonal influenza mostly affects the elderly patients with co-morbidities. However, mostly young adults were affected from pandemic influenza and patients with co-morbidities were affected less as compared to seasonal influenza.[21] Only one of the patients (75 years old) who died in our area was found to be in the elderly patient group with co-morbidities. In our study, we found that 5 out of the 16 deaths were in the young adult group without any risk factors; it was also found out that 4 patients out of these 5 patients were in the range of 26-35 years of age. This situation has shown that in contrast with the seasonal influenza, pandemic influenza A (H1N1) has a greater mortality in young adults without any co-morbidities.

The most frequent symptoms of pandemic influenza have been reported as cough and fever in all the studies carried out globally and in our country. In addition, headache, sore throat, nasal discharge, chills and muscular pain were noted as the other symptoms frequently seen in pandemic influenza infection.[22-24] Apart from these symptoms, nausea, shortness of breath, articular pain or stomach ache were found in some of the patients.[25] It has also been reported that diarrhea develops in some pandemic influenza infections as a peculiarity.[22,26]

Akıncı et al. reported the frequency of the pandemic influenza symptoms in the following order: cough, fever, fatigue, headache and muscular pain.[14] In another study, Akçay-Ciblak et al. determined the pandemic influenza symptoms similarly with the order of cough, fever, sore throat, headache, post-nasal discharge and muscular pain.[7] The most →

frequent symptoms in patients diagnosed with pandemic influenza in our region were found as cough and fever consistently with other studies originating from our country and from abroad. The symptoms we have encountered were found as sore throat, nasal discharge, shortness of breath, headache and muscular symptoms according to the order of frequency.

CONCLUSION

Virulence of pandemic influenza A (H1N1) is similar to that of the seasonal flu viruses. When its effects on the population are analyzed, the 2009 influenza A (H1N1) pandemics constitute a good opportunity to prepare against the unavoidable pandemics of the future. Contrary to the seasonal flu, pandemic influenza A (H1N1) infection is more frequently seen in the young adults without any risk factors. It must be born in mind that these results obtained in the year of onset of the pandemics can change in relation with the possible changes in the clinical features of pandemic influenza A (H1N1) virus after becoming established as a causative organism of seasonal influenza.

* The authors declare that there are no conflicts of interest.

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REFERENCES

1. Schutten M, van Baalen C, Zoeteweij P, Fraaij P. The influenz virus: disease, diagnostics, and treatment. MLO MedLabObs 2013; 45: 38-40.
2. Obuchi M, Adachi Y, Takizawa T, Sata T. Influenza A(H1N1) pdm09 virus and asthma. Front Microbiol 2013; 4: 307.
3. Diaz A, Allerson M, Culhane M, Sreevatsan S, Torremorell M. Antigenic drift of H1N1 influenza A virus in pigs with and withou passive immunity. Influenza Other Respir Viruses 2013; 7: 52-60.
4. Velkov T, Ong C, Baker MA, et al. The antigenic architecture of the hemagglutinin of influenza H5N1 viruse. Mol Immunol 2013; 56: 705-719.
5. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team, Dawood FS, Jain S, Finelli L, et al. Emergence of a novel swine-origin Influenza A (H1N1) virus in humans. N Engl J Med 2009; 360: 2605-2615.
6. Alenzi FQ. H1N1 update review. Saudi Med J 2010; 31: 235-246.
7. Ciblak MA, Albayrak N, Odabas Y, et al. Cases of influenza A(H1N1)v reported in Turkey, May-July 2009, Euro Surveill 2009; 14: 19304.
8. National Center for Immunization and Respiratory Diseases. Use of influenza A (H1N1) 2009 monovalent vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. MMWR Recomm Rep 2009; 58: 1-8.
9. Fiore AE, Shay DK, Broder K, et al. Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. MMWR Recomm Rep 2009; 58: 1-52.
10. Mereckiene J, Cotter S, Nicoll A, et al. National seasonal influenza vaccination survey in Europe, 2008. Euro Surveill 2008; 13: 19017.
11. Kurtaran B. Influenza Epidemiology. Turkiye Klinikleri J Inf Dis-Special Topics 2010; 3: 5-14.
12. Van Kerkhove MD, Vandemaele KA, Shinde V, et al. Risk factors for severe outcomes following 2009 influenza A (H1N1) infection: a global pooled analysis. PLoS Med 2011; 8: e1001053.
13. Louie JK, Acosta M, Winter K, et al. California Pandemic (H1N1) Working Group. Factors associated with death or hospitalization due to pandemic 2009 influenza A(H1N1) infection in California, JAMA 2009; 302: 1896-1902.
14. Akıncı E, Kayaaslan B, Yetkin MA, et al. Analysis of 113 hospitalized patients with confirmed 2009 influenza A (H1N1) virus infection. Turk J Med Sci 2011; 41: 507-514.
15. Mangtani P, Mak TK, Pfeifer D. Pandemic H1N1 infection in pregnant women in the USA. Lancet 2009; 374: 429-430.
16. Echevarría-Zuno S, Mejía-Aranguré JM, Mar-Obeso AJ, et al. Infection and death from influenza A H1N1 virus in Mexico: A retrospective analysis. Lancet 2009; 374: 2072-2079.
17. Ertek M, Durmaz R, Guldemir D, et al. Epidemiological, demographic, and molecular characteristics of laboratory-confirmed pandemic influenza A (H1N1) virus infection in Turkey, May 15- November 30, 2009. Jpn J Infect Dis 2010; 63: 239-245.
18. Cerit GN, Özkiraz S, Asri S, Çetinkaya R. Risk Factors of severe outcomes among patients admitted to Hospital with Pandemic (H1N1) influenza. Türkiye Klinikleri J Anest Reanim 2011; 9: 196-201.
19. Itoh Y, Shinya K, Kiso M, et al. In vitro and in vivo characterization of news wine-origin H1N1 influenza viruses. Nature 2009; 460: 1021-1025.
20. Selvi Can Ö, Ünal N, Memikoğlu O, Tulunay M. Pandemic Influenza A (H1N1) 2009 Virus and Clinical Experience. Yoğun Bakım Derg 2010; 9: 1-12.
21. Evirgen Ö, Köksaldı Motor V, et al. Clinical characteristics of the patients with Pandemic Influenza A (H1N1). Ortadoğu Tıp Derg 2011; 3: 77-82.
22. Sullivan SJ, Jacobson RM, Dowdle WR, Poland GA. 2009 H1N1 Influenza. Mayo Clin Proc 2010; 85: 64-76.
23. Singh K, Vasoo S, Stevens J, Schreckenberger P, Trenholme G. Pitfalls in thediagnosis of Pandemic (Novel) A/H1N1 2009 Influenza. J Clin Microbiol 2010; 48: 1501-1503.
24. Lenzi L, Mello ÂM, Silva LR, Grochocki MH, Pontarolo R. Pandemic influenza A (H1N1) 2009: risk factors for hospitalization. J Bras Pneumol 2012; 38: 57-65.
25. Shinde, Bridges CB, Uyeki TM, et al. Triple-reassortant swine influenza A (H1) in humans in the United States, 2005-2009. N Engl J Med 2009; 360: 2616-2625.
26. Nayman Alpat S, Usluer G, Ozgunes I, Doyuk Kartal E, Erben N. Clinical and Epidemiologic Characteristics of Hospitalized Patients with 2009 H1N1 Influenza Infection. Influenza ResTreat 2012; 2012: 603989. doi: 10.1155/2012/603989.

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