

Evaluation of The Seroprevalence of H1N1 IgG Antibodies Between Healthcare Workers and Outpatients*

Sağlık Çalışanlarında ve Poliklinik Hastalarında H1N1 IgG Antikor Sıklığının Karşılaştırılması*

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ABSTRACT

Aim: The aim of the present study was to compare the seroprevalence of pandemic H1N1 IgG antibodies between health care workers and patients presenting with upper airway symptoms suggestive of H1N1 influenza infection who are admitted to the outpatient clinics during pandemic H1N1 influenza infection.

Material and Methods: The present study comprised 82 subjects unvaccinated with influenza A (H1N1) vaccination, including 53 health care workers (33 females, 20 males, 15 doctors; median age: 38 years), 16 nurses (median age: 26.5 years), 22 auxiliary health care workers (median age: 32 years), and 29 outpatients (14 females, 15 males; median age: 38 years). The presence of symptoms suggestive of pandemic influenza infection was questioned in the health care providers and outpatients. Serum H1N1 IgG antibody levels were determined in the health care workers and outpatients using the ELISA method. The statistical analyses were performed using the SPSS software package. ANOVA (analysis of variance) was used to evaluate the significance of difference between the groups, and the Kruskal-Wallis test was used to evaluate the significance of difference in terms of median values. The nominal variables were analyzed using Pearson's chi-square test or Fisher's exact test. A p value of < 0.05 was considered statistically significant.

Results: The seroprevalence of H1N1 IgG antibody positivity for health care workers and outpatients were %43.3 and %6.9, respectively.

H1N1 IgG antibody seropositivity did not show a significant relation with gender and mean age (p=0.87 and p=0.657, respectively). There was a statistically significant difference between health care workers and outpatients in terms of H1N1 IgG antibody seropositivity (p<0.001). The prevalence of H1N1 IgG antibody seropositivity was significantly higher in health care providers compared to outpatients.

The intra-group comparison of health care workers shows a significant difference in terms of H1N1 IgG antibody positivity. The prevalence of H1N1 IgG antibody positivity among the doctors was higher compared to nurses and auxiliary health care workers (p<0.001).

Conclusion: Exposure to the H1N1 virus and the prevalence of the H1N1 antibody positivity among health care workers during pandemic influenza infection was higher compared to outpatients presenting with upper airway symptoms suggestive of an influenza infection. Therefore, health care workers who are at risk of acquiring influenza infection encouraged through training about immunization.

Key words: Health care workers, outpatients, H1N1, seroprevalence, IgG, ELISA

Özet

Amaç: Pandemi influenza döneminde sağlık çalışanlarında H1N1 influenza virüsü IgG antikor sıklığının H1N1 döneminde üst solunum yolu semptomları ile müracat eden ve olası pandemi H1N1 enfeksiyonu olan poliklinik hastaları ile karşılaştırılması idi.

Gereç ve Yöntemler: Çalışmaya 53 sağlık personeli [15 doktor (, 16 hemşire , 22 yardımcı sağlık personeli ile 29 poliklinik hastası olmak üzere influenza A (H1N1) aşısı uygulanmamış 82 kişi dahil edildi. Sağlık çalışanlarında ve poliklinik hastalarında influenzaya yönelik semptomların varlığı sorgulandı. Sağlık personeli ve hasta grubunda H1N1 IgG antikor düzeyleri ELISA yöntemiyle belirlendi. İstatistiksel analizler SPSS programında yapıldı. $p < 0,05$ için sonuçlar istatistiksel olarak anlamlı kabul edildi.

Bulgular: Sağlık çalışanlarında ve poliklinik hastalarında H1N1 IgG antikor pozitiflik oranları sırasıyla; %43.3 ve %6.9 idi. H1N1 IgG antikor pozitifliği açısından cinsiyete ve yaş ortalaması açısından anlamlı farklılık saptanmadı (p değerleri sırasıyla cinsiyet için $p: 0.87$, yaş ortalaması için $p: 0.657$) H1N1 IgG antikor pozitifliği açısından sağlık personeli ile poliklinik hastaları arasında istatistiksel olarak anlamlı farklılık vardı ($p < 0.001$). Sağlık çalışanlarında H1N1 IgG antikor pozitifliği oranı poliklinik hastalarından daha yüksekti. Sağlık çalışanları kendi arasında karşılaştırıldığında H1N1 IgG antikor pozitifliği açısından farklılık saptandı. Doktorlarda H1N1 IgG antikor pozitifliği oranı, hemşire ve sağlık personelinden daha yüksekti.

Sonuç: Sağlık çalışanlarında pandemi influenza döneminde H1N1 ile karşılaşma sıklığı ve antikor pozitifliği oranı, influenza ile uyumlu üst solunum yolu semptomları olan poliklinik hastalarından daha yüksekti. Sağlık çalışanları influenza enfeksiyonu açısından risk grubundadır bu nedenle sağlık çalışanları aşılama konusunda eğitim verilerek teşvik edilmelidir.

Anahtar Kelimeler: Sağlık çalışanları, poliklinik hastaları, H1N1, seroprevalans, IgG, ELISA

Introduction

Pandemic influenza A (H1N1) virus with commonly used alias was first seen in Mexico in April 2009 and it spread throughout the world. The World Health Organization (WHO) raised influenza A (H1N1) pandemic alert level to 6, caused a great public panic about this virus infection in the world (1-3). Despite this concern, anxiety and uncertainty was experienced in the administration of p H1N1 vaccine developed against the virus all over the world as well as in our country. Since the healthcare workers especially became biased against the vaccine, the vaccination rates among the healthcare workers were well below the expected in the world and in our country (1,4-6). However, when the outbreak-related mortality and morbidity is taken in the consideration, it is a fact that the side effects of the vaccine can be ignored and this approach of the medical staff is extremely risky.

According to the Ministry of Health, 207,580 healthcare workers were vaccinated in the 2009 outbreak in our country. However the number of healthcare personnel was 609,900 in 2009 in our country which corresponds to vaccinated staff numbers of 34% of the total healthcare personnel (7)

Purpose of this study is to determine the levels of IgG antibodies against influenza A (H1N1) and epidemiological data associated with seropositivity in outpatients and healthcare workers with clinical findings and symptoms suggestive of influenza A (H1N1).

Material and Method

Patient and healthcare worker group: During 2009 influenza A (H1N1) period, the study included possible cases with symptoms and clinical findings suggestive of influenza A (H1N1) admitted to Infectious Disease Influenza Outpatient Clinic in Ankara Training and Research Hospital, 29 outpatients with symptoms and clinical findings suggestive of the influenza A

(H1N1), and 53 healthcare workers unvaccinated with influenza A (H1N1) vaccination with the same symptoms and clinical signs. Consent from patients and ethics committee approval was obtained for the study. Possible case was defined with fever above 38 ° C degrees (axillary) or history of fever unexplainable with any other reason, and presence of at least one of the following complaints: widespread body pain, sore throat, headache, runny nose, cough, difficulty breathing.

Outpatients group: Twenty -nine outpatients unvaccinated with influenza A (H1N1) vaccination with symptoms and clinical findings suggestive of the influenza A were included the study.

Demographic characteristics of outpatients and healthcare personnel are given in Table 1.

Blood samples of outpatients and healthcare personnel were taken during the period of 4-8 weeks after the symptoms of H1N1 started. Voluntary consent form from patients and healthcare professionals and the ethics

committee approval for the study from Ankara Hospital was obtained.

H1N1 IgG assays in serum samples: Serum samples were analyzed with influenza A (H1N1) IgG commercial ELISA kit (Genzyme VIROTECH, Germany) in accordance with the manufacturer's recommendations. In the study, IgG antibody titers of > 11 arbitrary units (AU) was considered to be positive.

IgG antibody titers of <9 AU was considered as negative, IgG titers of 9 - 11 AU was considered to be the threshold (8).

Statistical Analysis: Statistical analyzes were recorded in SPSS program. ANOVA variance analysis was used to evaluate statistical differences between the groups, where to Kruskal-Wallis test was used evaluate the differences in terms of median values. As for the numerical variables, Pearson's Chi-Square test or Fisher's exact test was performed. $p < 0.05$ was considered statistically significant.

Results

Influenza A (H1N1) IgG antibody positivity rates of healthcare personnel were determined as 73.3% (11/15) in doctors, 50% (8/16) in nurses, and 16% (4/22) in auxiliary healthcare staff. The H1N1 IgG positivity rate in outpatients was 6.9% (2/29). H1N1 IgG seropositivity rate in entire health care personnel was determined as 43.3% (23/53). This ratio was significantly higher in terms of statistically than 6.9% rate that found in outpatients (approximately 7 times).

There was not a significant difference in H1N1 IgG antibody positivity in terms of gender and mean age (p values for gender and mean age were $p: 0.87$ and $p: 0.657$, respectively).

H1N1 IgG antibody positivity rates in healthcare workers and outpatients are shown in the Table.

Table. H1N1 IgG antibody positivity rates in healthcare workers and outpatients

Groups	H1N1 IgG Positive Number	(%)	H1N1 IgG Negative Number	(%)	P value
Doctor (n: 15)	11	73.3	4	26.7	$p < 0.001$
Nurse (n:16)	8	50	8	50	$p < 0.001$
Auxiliary healthcare workers (n: 22)	4	16	18	81.8	$p < 0.001$
Outpatients (n:29)	2	6.9	27	93.1	$p < 0.001$
Total (n: 82)	25	30,5	57		

Discussion

Clinical signs have a wide spectrum in swine flu, with or without fever signs ranging from mild viral respiratory tract infections to exacerbations of underlying clinical picture can be seen. There is not a specific finding to distinguish influenza A (H1N1) from seasonal flu; H1N1 clinical symptoms are similar to seasonal influenza. Symptoms such as fever, fatigue, malaise, headache, myalgia, cough, sore throat are seen. Unlike seasonal influenza, diarrhea, and vomiting can be seen especially in children. Different from seasonal influenza, if a patient has leukopenia, concomitantly relative lymphopenia, / thrombocytopenia can be also seen (2,3).

Influenza vaccine has the utmost importance in protection of healthcare personnel during influenza (flu) pandemic and outbreaks in the winter. In contrast, rates of H1N1 vaccination for both public and healthcare personnel was found at very low levels during H1N1 pandemic in all over the world and our country in 2009 (1,4-6)

In a study conducted by Budak et al. (4) in Istanbul, pandemic influenza A (H1N1) vaccine was administered to 669 volunteers from a total of 1,185 medical personnel. When percentages of vaccination that were accepted by staff analyzed, the rate was found to be 84.3% (291/345) in physician group, 52.9% (198/374) in nurses group, and 38.6% (180/466) in auxiliary healthcare personnel. Personnel were actively tracked for 14 days and 1 year following the vaccination with passive surveillance based on reporting. A total of 261 (38.6%) side effects associated with the vaccine were detected. 62 (9%) of the vaccinated staff reported only local side effects, where 89 (13.3%) reported local and systemic reactions. Pain in the site of the vaccination (17.3%), fatigue (7.6%) and headache (6.7%) were the most common side effects. None of the vaccinated personnel has developed life-threatening severe side effects. As a result, due to the low rate of vaccination in healthcare personnel, authors came to a conclusion that preventing prejudice towards the vaccine by advising and training the healthcare personnel better in case of an epidemic threatening the public health could raise the compliance to vaccination.

Ormen et al. (5) 2009 investigated the safety and observed side effects of the vaccine, and healthcare workers' opinion about the vaccination after pandemic influenza A (H1N1) vaccination in Izmir Atatürk Training and Research Hospital. Pandemic influenza vaccination of the hospital staff was conducted in December 2009 at the location where the research was done, the rate of vaccination was observed as 40% (800/2000) in the study. Four months after vaccination, a survey was conducted about opinions of the hospital staff who agree to participate in the study (staff



vaccinated and not vaccinated) regarding vaccination and the side effects observed after vaccination in vaccinated group. A total of 332 volunteers participated in the survey; 247 participants (74.4%) were in vaccinated, 85 (25.6%) of them were in the unvaccinated group. Vaccination rates; in the older age groups compared to the young adults, in men compared to women and in patients with children compared to those without children was found to be significantly higher.

However, vaccination rates were higher in staff from non-healthcare professional group (cleaning staff, administrative staff, etc.) (57.5%) compared to doctors (29.1%) and nurses (13.4%); and higher in employees of intensive care unit, emergency service and administrative department (54.7%) compared to those working in the internal medicine (22.3%) and surgical clinic (23.1%). It was observed that "being afraid of the side effects of the vaccine" (69.4%) and "no confidence in vaccine efficacy" (56.4%) were the most important reasons for the refusal to be vaccinated. It was determined that "not to pass on the disease to one's family" (60.3%) and "being in the risk group" (54.3%) were the leading reasons to accept vaccination. In the vaccinated group, rate of local reactions observed after vaccination (pain, swelling, redness in vaccination area) was 43.3% where the rate of systemic reactions (malaise, fatigue, myalgia, flu-like symptoms etc.) was determined as 43.7%; there were no vasculitis, neuritis, encephalomyelitis, Guillain-Barre syndrome, and serious side effects such as anaphylactic reactions in any of the case. Study results showed that concerns regarding safety of the vaccine adversely affect the vaccination

Gurbuz et al. (6) studied the approach of healthcare workers towards influenza vaccine after 2009 influenza A (H1N1) pandemic began and causes of rejection were examined. In the study, a survey was administered to 570 people among 2803 staff working in Diskapi Training and Research Hospital to determine their approach toward seasonal influenza vaccine and H1N1 vaccine by sampling using stratified random sampling method due to the diverseness of profession and education. While 42.3% of respondents expressed that they wanted to be vaccinated with seasonal vaccine, 39.6% of them wanted to be vaccinated with H1N1 Influenza A (H1N1) vaccine, the percentage of people who wanted to be vaccinated with both vaccines was determined as 37.2%. While the most important causes of the one's unwillingness to be vaccinated with seasonal vaccine were not to believe in the necessity of the vaccine (79.4%) and to prefer other methods of protection (70.5%); vaccine not being sufficiently tested became prominent (83.1%) as the cause for unwillingness to be vaccinated with influenza A (H1N1) vaccine. The authors came to the conclusion on there is a need for more training

activities to persuade hospital staff to be vaccinated with influenza vaccine.

Pathirana et al. (9) investigated the effectiveness of the influenza A (H1N1) vaccine containing adjuvant on healthcare workers in their study in Norway. In the study, they investigated post-vaccination IgG titers of 15 healthcare workers with low response to vaccine and 25 control group healthcare workers. They detected that protective hemagglutination inhibition titers were positive in (≥ 40) 97% two weeks after the vaccination, but this was detected as 16% in poor responders and protective response was not sustained for 90 days in poor responders.

Low IgG levels were reported in poor responders compared to control group on day 7, while decrease in virus-specific IgG levels were reported on 21st day. In this study, for the long-term protection in poor responders, necessity for booster vaccination with H1N1 was emphasized.

Cifci et al. (10) investigated the frequency of H1N1-Ig G antibodies in total of 68 healthcare workers including 53 vaccinated and 15 unvaccinated healthcare workers with the H1N1 vaccine.

In this study, IgG antibody titers were positive in 16 (30%) of 53 vaccinated healthcare workers (while > 11 arbitrary units (AU) were detected negative in 17 (32%) and intermediate values were detected in 20 (37.7%) of them; it was positive only in 1 (6.6%) of the 15 unvaccinated healthcare workers, negative in 11 (73%), and intermediate values in 3 (20%) of them). There was not a significant difference detected in antibody positivity in terms of gender and mean age in unvaccinated and vaccinated healthcare personnel.

In our study, the rates for H1N1 IgG antibody positivity in healthcare workers were 73.3% (11/15) in doctors, 50% (8/16) in nurses, 16% (4/22) in auxiliary healthcare workers. H1N1 IgG positivity rate in outpatients was 6.9% (2/29). H1N1 IgG seropositivity rate in all healthcare staff was detected as 43.3% (23/53). This higher rates were statistically significant than the rate of 6.9% found in outpatients (approximately 7 times). There was not a significant difference in H1N1 IgG antibody positivity in terms of gender and mean age (p values for gender and mean age were p: 0.87 and p: 0.657, respectively).

This result was in compliance with Cifci ve et al.'s (10) data. There was a statistically significant difference between healthcare workers and outpatients in terms of H1N1 IgG antibody seropositivity ($p < 0.001$). The prevalence of H1N1 IgG antibody seropositivity was higher in healthcare workers compared to outpatients.

The intra-group comparison of healthcare workers show a significant difference in terms of H1N1 IgG antibody positivity. The prevalence of H1N1 IgG antibody positivity

among the doctors was higher compared to nurses and auxiliary health care workers.

As a result, exposure to the H1N1 virus and the prevalence of the H1N1 antibody positivity among healthcare workers during pandemic influenza infection was higher compared to outpatients presenting with upper airway symptoms and physical examination findings suggestive of an influenza infection. Therefore, we believe that healthcare workers who are at risk of acquiring influenza infection encouraged through training about immunization.

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