

Rapid communications

CASES OF INFLUENZA A(H1N1)v REPORTED IN TURKEY, MAY-JULY 2009

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Following the declaration by the World Health Organization (WHO) of human cases of infection with a new influenza A(H1N1)v virus of swine origin, the Turkish Ministry of Health launched a case-based reporting of influenza A(H1N1)v throughout the country on 27 April 2009. The index case was detected on 15 May 2009. As of 17 July 2009 the number of laboratory-confirmed cases of influenza A(H1N1)v totalled 128 of whom 38 were indigenous cases.

Introduction

Since the detection of the first human case of infection with a triple reassortant influenza A(H1N1)v virus in mid-April in California, United States [1], human cases of infection with this variant have been reported from countries throughout the world [2].

Here we report the first 128 cases of influenza A(H1N1)v identified in Turkey along with control measures taken by the Ministry of Health (MoH) for containment of the epidemic from 27 April to 17 July 2009.

Methods

Surveillance

Sentinel surveillance for seasonal influenza has been conducted in Turkey since 2003 in 14 out of 81 provinces. On 27 April 2009, after the official declaration of the first human case of new influenza A(H1N1)v by the World Health Organization, the Turkish MoH

implemented a case-based reporting of influenza A(H1N1)v that was extended throughout the year and included all 81 provinces of the country and the Turkish community in Cyprus. In this case-based reporting system the local health authorities (LHAs) were supplied by the MoH with case definition and patient information forms to be disseminated to all healthcare institutions in their province. LHAs in each province designated hospitals and clinics where all suspected cases were directed to, in order to better track and contain the infection. These designated hospitals and clinics were asked to take samples from patients who fulfilled the case definition criteria and send them for confirmation to the designated reference laboratories.

Laboratories

Turkey has two national influenza reference laboratories, the Refik Saydam National Public Health Agency (RSHM) that is located in Ankara and the National Influenza Reference Laboratory (NIRL) at Istanbul Faculty of Medicine that is located in Istanbul. Both reference laboratories were prepared for testing influenza A(H1N1)v with the real-time RT-PCR protocol and reagents supplied by the United States Centers for Disease Control and Prevention (CDC). The reference laboratory in Ankara was assigned 58 out of 81 provinces whereas the reference laboratory in Istanbul was assigned the remaining 23 provinces for testing samples from suspected cases. These 23 provinces include the cities that harbour major

TABLE 1

Case definition for influenza A(H1N1)v, Turkey, 2009

Clinical criteria	Any person with one of the following two symptoms: <ul style="list-style-type: none">• Fever >38°C with symptoms of acute respiratory infection• Infections accompanied with respiratory distress
Epidemiological criteria	<ul style="list-style-type: none">• Travel to a country within the past 7 days where human to human transmission of influenza A(H1N1)v has been confirmed.• Close contact with persons of confirmed influenza A(H1N1)v within the past 7 day.
Laboratory criteria	Positive results with one of the following: <ul style="list-style-type: none">• RT-PCR• Viral culture (in BSL3 facilities)• Fourfold increase in influenza A(H1N1)v virus specific neutralizing antibody titer.
Case definition	<ul style="list-style-type: none">A. Probable case• Any person meeting the clinical and epidemiological criteriaB. Confirmed case• Any person meeting the laboratory criteria

air and sea ports and resort towns. Laboratories report the results directly to the MoH immediately after the results are obtained. The MoH then informs the LHAs who contact the physicians and give necessary guidance to the physicians for the care of the patients.

Patients and samples

A probable case with influenza A(H1N1)v is defined as a person with high fever (≥ 38 °C) and/or at least two acute respiratory symptoms along with epidemiological criteria listed in the case definition protocol published by WHO [2]. Table 1 summarises the case definition that was prepared in light of the information released by WHO. However, during the first month of the pandemic, in addition to probable cases, samples were also taken from individuals with no detectable symptoms but with either travel history to areas of high prevalence and/or close contact with a confirmed case, who presented in hospitals and asked to be tested. Nasal and/or nasopharyngeal samples along with patient information forms from suspected cases were transported to reference laboratories in a viral transport medium (Virocult, Medical Wire&Equipment, UK). A total of 977 samples from suspected cases were sent to the reference laboratories between 27 April and 17 July 2009 from various cities in Turkey (n=899) and from the Turkish Cypriot community (n=78).

Laboratory diagnosis (real-time RT-PCR)

Both laboratories used the same "in-house" real-time PCR protocol provided by CDC for detection of influenza A(H1N1)v. RNA extraction was done with QIAamp viral RNA mini kit (Qiagen, Valencia, CA, USA) or with a High Pure Viral RNA isolation kit from Roche. Real-time RT-PCR was performed on ABI 7000 and/or 7500 [3]. NA, HA and M genes of the isolate from the index case were partially sequenced and the resulting sequences were analysed by CLC Main Workbench 4.1.1 Software program (Denmark).

Control measures and patient management

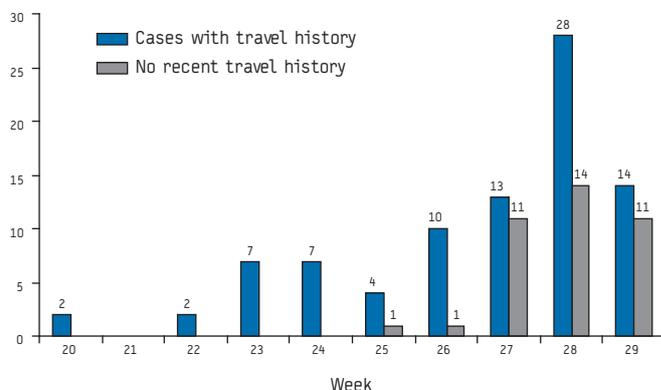
After the declaration of the pandemic by WHO on 11 June, the MoH held a meeting with its scientific advisory committee for revision of the pandemic plan. Revisions included the pandemic vaccination strategies (e.g. determining the priority order for vaccination), antiviral stockpiling and other measures. Two million doses of oseltamivir and 113,000 doses of zanamivir were distributed to all local healthcare centres. Four hundred thousand protective healthcare kits (each containing masks, gloves, hand disinfectant, goggles and foot covers) were distributed to healthcare providers, giving priority to those working at designated hospitals and clinics.

Special attention was given to the country points of entry such as airports and seaports. A thermal camera system was installed at airports and seaports in order to detect probable cases entering the country from regions of high prevalence. All travellers from abroad were requested to declare their health status and those captured by thermal camera system were further examined by physicians and suspected cases were isolated for transfer to the designated hospitals. Co-travellers sitting at close proximity (three seat lines in the front and back and on the sides) to confirmed cases were contacted by phone, informed about the situation and offered guidance on what they needed to do in case they developed symptoms and supplied with prophylactic doses of oseltamivir.

Two million pamphlets providing information on the flu pandemic were distributed to all flight crews and made available to travellers at airports and seaports. In addition, informative posters were posted at prominent places at ports and all public hospitals.

FIGURE 1

Figure 1. Number of travel-associated and indigenous cases of influenza A(H1N1)v, by week of laboratory confirmation, Turkey, May-July 2009 (n=125*)

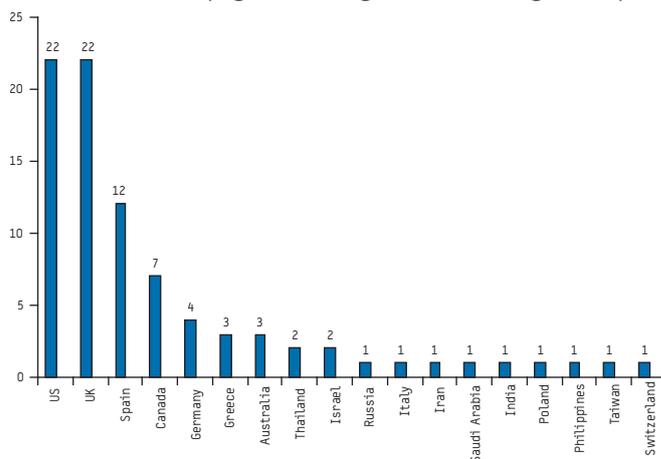


*Number of cases with available date of the laboratory confirmation. Case numbers collected by the Turkish Ministry of Health include cases from the Turkish Cypriot community.

FIGURE 2

Travel history of confirmed imported cases of influenza A(H1N1)v, Turkey, May-July 2009 (n=86*)

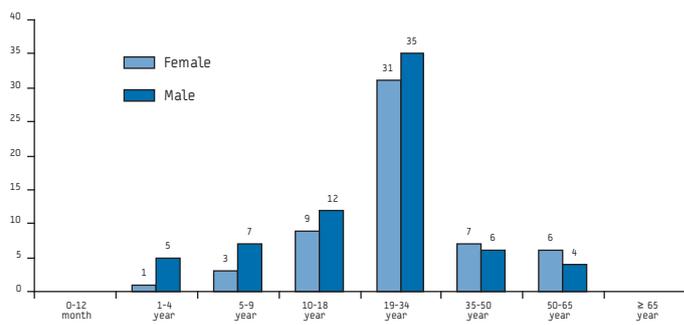
An interactive web page was designed to inform general public



*Number of cases with available data on travel history. Case numbers collected by the Turkish Ministry of Health include cases from the Turkish Cypriot community.

FIGURE 3

Age and sex distribution of confirmed cases of influenza A(H1N1)v, Turkey, May-July 2009 (n=126*)



*Number of cases with available data on age and sex. Case numbers collected by the Turkish Ministry of Health include cases from the Turkish Cypriot community.

and professionals about the pandemic influenza which included information on individual care for protection from contacting and transmitting influenza (www.grip.saglik.gov.tr). A telephone hotline was launched to serve public inquiries seven days a week 24 hours a day (Alo 184 SABİM). Television spots were prepared mainly to emphasise the importance of hand washing and usage of disposable tissue papers in protecting against contracting and transmitting the influenza virus. Daily press briefings were held during the first month of the pandemic to keep public informed about the pandemic status in Turkey.

Results

All samples received before the index case was detected on 15 May 2009 were processed immediately and results were reported to the MoH regardless of the time of arrival of the sample to the laboratory. After 15 May both laboratories provided results seven days per week. The average time between the swabbing to final diagnosis was 24 hours.

The index case was a United States resident travelling from Tennessee to Iraq through Ataturk Airport in Istanbul where his high temperature was captured by thermal camera. He was hospitalised in a designated hospital in Istanbul and treated with oseltamivir until laboratory tests were negative for influenza A(H1N1)v. By 17 July influenza A(H1N1)v was detected in 128 (13%) out of 977

samples tested. Of these 128 positive samples, 17 were from the Turkish Cypriot community*, the remaining 111 were from various provinces in Turkey. The number of samples positive for influenza A(H1N1)v increased remarkably from June onward. Figure 1 presents the number of travel-associated and indigenous cases of influenza A(H1N1)v, by week of laboratory-confirmation. Of the 111 confirmed cases in Turkey, 25 were domestic secondary cases. Of the 17 confirmed cases in the Turkish Cypriot community, 13 were indigenous. The travel history of the imported confirmed cases is summarised in Figure 2 and the age and sex distribution of all confirmed cases is shown in Figure 3.

The partial sequence analysis results of matrix, HA and NA segments were submitted to the National Center for Biotechnology Information (NCBI) GenBank with accession numbers GQ200600, GQ200598, and GQ200599 respectively. According to the topological phylogenetic analysis, results obtained from the partial nucleic acid sequencing isolate from the index case were closely related to isolates from the US and A/Catalonia/10/2009 (H1N1).

The majority of influenza A(H1N1)v-positive cases (n=80) were detected in samples received from Istanbul (Figure 4) which also included the majority of indigenous cases (n=22). The remaining three indigenous cases in Turkey were from Denizli, Antalya and Eskisehir. Two indigenous cases from Istanbul were detected in healthcare workers, one in a physician examining a laboratory-confirmed patient and another in a nurse responsible for taking the patient's sample in a private hospital setting. The physician and the nurse developed symptoms five days after contacting the patient; subsequent laboratory analysis confirmed these cases as influenza A(H1N1)v-positive.

Confirmed cases manifested moderate clinical symptoms. Three indigenous cases who contracted the virus from confirmed cases were asymptomatic. Clinical symptoms and their frequency in the confirmed cases are presented in Table 2.

The average time elapsed between the onset of the symptoms and the visit to the hospital (including those detected by thermal camera) was 1.68 days.

Of the 128 confirmed cases, 13 (10.2%) had received seasonal influenza vaccine in the past year. A similar proportion of vaccinated was found among patients who tested negative for influenza A(H1N1)v. All individuals who reported to the hospitals were closely monitored and those who were confirmed with influenza A(H1N1)v received antiviral treatment with oseltamivir. None of the confirmed cases developed any complications and no deaths occurred.

Conclusion

Influenza A(H1N1)v entered Turkey through travellers mainly coming from the United States and the United Kingdom. While the majority of confirmed cases in Turkey had a travel history to highly affected areas, confirmed cases from the Turkish Cypriot community* were mostly indigenous cases with no history of travel. The majority of the confirmed cases consisted of young adults as reported from other countries. This could be related to the frequency of travel among the young population [4]. The clinical manifestation of A(H1N1)v infection in the confirmed cases was similar to that observed in seasonal influenza. All cases manifested moderate clinical symptoms similar to those reported in other countries [5]. Cough was the most frequent symptom (68.7%) followed by fever >38°C (62.5%)*. None of the confirmed cases developed complications and no death was reported.

FIGURE 4
Geographical distribution of confirmed cases of influenza A(H1N1)v, Turkey, May-July 2009 (n=128)

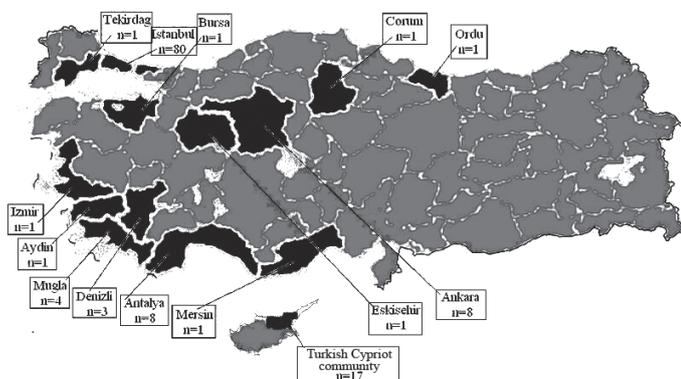


TABLE 2
Clinical characteristics of confirmed cases of influenza A(H1N1)v, Turkey, May-July 2009 (n=128)*

Symptoms	Number of cases with the symptom (%)
Cough	88 (68.7)
Fever ($\geq 38^{\circ}\text{C}$)	80 (62.5)
Sore throat	62 (48.4)
Headache	60 (46.8)
Coryza	59 (46.1)
Myalgia	56 (43.7)
Weakness	7 (5.5)
Pneumonia	3 (2.3)

*Case numbers collected by the Turkish Ministry of Health include cases from the Turkish Cypriot community.

Two confirmed indigenous cases were healthcare providers who contracted the disease in hospital while attending a confirmed case. This type of transmission in a hospital setting has been rare to date and it may require special attention [6].

After the detection of the index case on 15 May all confirmed cases were kept at the designated hospitals for treatment with oseltamivir and all contacts of these cases were traced and prophylactic oseltamivir doses were administered to these persons regardless of the symptoms. However, with increasing number of confirmed cases and individuals reporting to hospitals the MoH revised its policy on case investigation and management of the suspected cases on 5 June. With the new policy, confirmed patients with no signs of complications were put on oseltamivir therapy at home instead of hospitalisation, and prophylactic oseltamivir was no longer given to asymptomatic contacts of confirmed cases. Also, the practice of following up co-travellers of confirmed cases was ended by 5 June.

The amount of pandemic vaccine doses needed for vaccinating healthcare providers, public service providers and risk groups has been determined and necessary budget plans have been developed for purchasing 20 million doses to vaccinate 10 million individuals when the pandemic vaccine becomes available. Based on current knowledge of the pandemic, elderly people over 65 years were excluded from risk groups (in contrast with the seasonal vaccination recommendations) [7]. TV and radio spots have proven to be effective means of keeping the public calm and increasing awareness of pandemic influenza.

The MoH is planning to change its strategy and adopt measures for mitigation instead of containment of the pandemic in the coming weeks.

*Erratum: "Northern Cyprus" was replaced by "Turkish Cypriot community" throughout the text and the following information was added to the relevant tables and figures: Case numbers collected by the Turkish Ministry of Health include cases from the Turkish Cypriot community. These corrections were made on 17 August 2009.

**Author's correction: On request of the authors, the percentages in the sentence "Cough was the most frequent symptom (68.7%) followed by fever >38°C (62.5%)" were corrected on 20 August 2009.

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This article was published on 13 August 2009.

Citation style for this article: Ciblak MA, Albayrak N, Odabas Y, Basak Altas A, Kanturvardar M, Hasoksuz M, Sucaklı B, Korukluoglu G, Bal E, Ertek M, Badur S. Cases of influenza A(H1N1)v reported in Turkey, May-July 2009. *Euro Surveill.* 2009;14(32):pii=19304. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19304>