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Household transmission of 2009 H1N1 influenza virus in Yazd, Iran

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Summary
Objectives: The 2009 pandemic influenza A (H1N1) virus is a public health challenge. Notably, laboratory-confirmed cases do not represent the age group most susceptible to infection. To characterize the age distribution of all cases of H1N1 influenza, we studied the personal contacts of confirmed cases to identify the age group at the highest risk.
Methods: We investigated the family members of 162 laboratory-confirmed cases of 2009 H1N1 in Yazd, Iran. Family members were retrospectively asked whether they had ≥2 respiratory symptoms within 7 days of the last contact with the associated index cases. The ages and symptoms of the patients as well as the interval between diagnosis and the onset of symptoms among household contacts were determined using a questionnaire.
Results: We identified 596 family members of index cases, 83 (13.9%) of whom developed acute respiratory illness. No acute respiratory illness was found in 104 families (64%); however, there were 2 cases in 15 families (9.3%) and ≥3 cases in 4 families (24%). Household contacts from 5 to 18 years old were more susceptible to acute respiratory illness than those who were ≥51 years old (RR = 3.174, 95% CI 1.313—7.675 *P*-value = 0.01).
Conclusion: Individuals ≤18 years old were most susceptible to infection by the H1N1 virus. Therefore, in low-income populations, prevention of the spread of H1N1 to this age group should be emphasized.

Introduction

The 2009 pandemic influenza A (H1N1) virus has turned to represent a new challenge for health care providers [1]. Globally, based on documented cases, it caused 18,000 deaths prior to May 30,

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2010 [2]. Although the risk of household contact-mediated transmission of 2009 influenza A (H1N1) during the recent pandemic was evaluated in recent studies [3—7], more studies are necessary due to the variable quality of domestic facilities in different countries. Children and young adults seem to be affected more frequently, and individuals older than 60 years are infected less frequently. The data on the rate of secondary attack are controversial [8]. To our knowledge, no study has examined the infectivity rate of 2009 influenza A (HINI) in Iran to date. Due to limitations in terms of the diagnostic reagents available, laboratory-confirmed cases likely represent a biased sample, with cases at the beginning of the outbreak and cases that are more severe being over represented. We conducted a survey regarding the intra-familial contacts of documented cases to identify the age group at highest risk; this age group should be targeted in future interventions.

Materials and methods

This study, which was of the form of a retrospective descriptive-analytic cross-sectional investigation, was conducted in Yazd city, which has a population of 566,152.

Study population

Between April 21, 2009 and March 26, 2010, we enrolled all family members of confirmed 2009 A (H1N1) influenza cases in Yazd in the study.

Information was gathered up to 3 months after the confirmation of index cases. The secondary attack rate was defined as the proportion of household contacts for which the onset of symptoms occurred within 7 days before or within 7 days after the onset of symptoms in the index case [4]. Acute respiratory illness was defined as at least 2 of the following symptoms: fever or feverish sensation, cough, sore throat and rhinorrhea. An intern surveyed all family members of confirmed 2009 A (H1N1) cases who were registered at the Yazd district health center by telephone. Cases were confirmed by the I.R. Iran's Ministry of Health. When no response was received from a given family, they were contacted repeatedly. We interviewed parents instead of their children. Information was gathered from index cases via a questionnaire comprising the following parameters: age, gender, symptoms (fever, or feverish sensation, cough, rhinorrhea, sore throat, diarrhea or vomiting), hospital history or ICU admission, underlying condition and a history of taking *oseltamivir* or *zanamivir*. The questionnaire included questions about the family contacts regarding the interval between the appearance of symptoms in the index case and in the family member(s), age, gender, symptoms (cough, fever, sore throat, diarrhea, vomiting, rhinorrhea, myalgia and headache) occurring in a period beginning from 7 days prior to confirmation of the index case and ending 7 days after confirmation. We selected those household individuals who became ill up to 7 days after the index cases and analyzed them separately. The Yazd health center did not plan to perform RT-PCR on all contact cases. However, one family was tested at the beginning of the epidemic. Four (80%) out of five family members had laboratory-confirmed cases of infection with the 2009 H1N1 virus.

This study resulted from a thesis approved by the ethical board of the Shahid Sadoughi Medical University. Participants were informed that they were going to be involved in a telephone survey. The data were processed using SPSS and analyzed with chi-square and Fisher exact tests. *P* values of 0.05 were considered significant.

Theory

Immune status varies among individuals in different communities. Therefore, a survey of the close contacts of patients may more precisely reveal the age groups that have the highest risk of contracting influenza. Because resources in developing countries are limited, prophylactic measures can be focused on these age groups.

Results

One hundred and eighty-one confirmed H1N1 cases were registered at the Yazd district health center from the beginning of the epidemic (April 21, 2009) until March 26, 2010 (Fig. 1). Telephone interviews led to the selection of 162 (89.5%) cases. Within the 162 households, we identified 596 exposed family members, which included all of the family members in contact with the index cases.

Confirmed 2009 influenza A (H1N1) cases

The mean age of patients was 32.76 ± 23.8 (1—89) years; 88 patients (54%) were male; the age group most commonly affected was 19—50 years old (38%). Ninety-seven (60%) of the patients were admitted to the hospital, and 33 (31%) of the

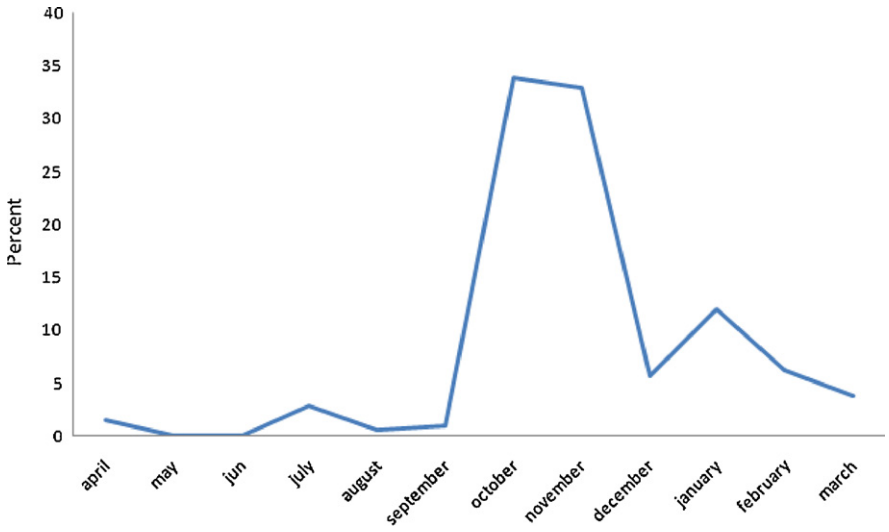

Figure 1 Distribution of pandemic H1N1 2009—2010 influenza virus in Yazd, Iran.

hospitalized patients were admitted to the ICU. The mortality rate was 11.7% (19 cases). The symptoms of the confirmed cases are presented in Table 1.

Among the 596 family members exposed to the confirmed cases, 286 (48%) were male and 310 (52%) were female. Their mean age was 31 ± 17.94 years (3 months to 83 years). The mean number of individuals in contact with each confirmed case was 3.7.

No acute respiratory illness was found in 104 families (64.2%). One case per family was found in 39 families (24.1%), two cases per family were found in 15 families (9.3%), three cases per family were found in two families (1.2%), and four cases per family were found in another two families (1.2%). In total, there were 83 cases in 58 families (out of 162 families of confirmed cases).

Individuals aged 5—18 years old in household contact with confirmed cases were more likely to report an illness than household contacts of ≥51 years old (RR = 3.174, 95% CI 1.313—7.675 $P = 0.01$) (Tables 2 and 3).

Being 1 year younger increased the susceptibility to acute respiratory illness by 1.02-fold. The risk susceptibility decreased by 0.731 from one age group to the next older group (95% CI 0.568—0.958).

The symptoms of the household contacts are presented in Tables 2 and 3. Acute respiratory illness was observed in 83 family members of confirmed cases (13.9%). After omitting previous infections and infections that occurred concomitantly with the infections of the index cases, 68 family members of confirmed cases with acute respiratory illness (11.8%) were identified.

The interval between the onset of symptoms in confirmed cases and symptom onset in their family contacts varied from no delay (symptoms started on the same day) to 15 days; the mean interval was 4.69 ± 3.61 days. In 50% of secondary cases, symptoms occurred within 4 days.

There was a statistically significant association between age and the frequency of acute respiratory illness (Table 2) (*P*-value 0.021).

There were no differences between women and men with respect to the likelihood of contracting acute respiratory illness ($P = 0.36$). Sore throat and rhinorrhea were more common among secondary (household contact) cases, whereas

Table 1 Clinical findings of confirmed H1N1 cases according to age group.

Clinical findings No. (%)	Total 162	<2 years 3	2—4 years 4	5—18 years 49	19—50 years 63	≥51 years 43	*P*-value
Fever	151(93)	2(66)	4(100)	49(100)	57(90)	39(90)	0.035
Cough	114(70)	2(66)	3(75)	33(67)	48(76)	28(43)	0.75
Sore throat	48(29)	0(0)	1(25)	21(43)	23(36)	5(12)	0.016
Rhinorrhea	39(24)	1(33)	1(25)	14(28)	16(25)	7(16)	0.81
Vomiting	33(20)	0(0)	1(25)	14(28)	12(19)	6(14)	0.61
Diarrhea	15(9)	0(0)	1(25)	5(10)	6(9)	3(7)	0.88

Table 2 Clinical findings of household contacts of confirmed H1N1 cases according to age group.

Clinical findings No. (%)	Total $N = 596$	<2 years $N = 13$	2—4 years $N = 14$	5—18 years $N = 123$	19—50 years $N = 356$	≥51 years $N = 86$	*P*-value
Fever	75(12)	1(7)	4(22)	22(17)	40(11)	8(9)	0.079
Cough	64(11)	1(7)	3(17)	23(19)	33(9)	4(5)	0.107
Sore throat	48(8)	0(0)	0(0)	15(12)	28(8)	5(6)	0.024
Rhinorrhea	42(7)	1(7)	4(22)	15(12)	20(6)	5(6)	0.002
Vomiting	7(1)	0(0)	0(0)	3(2)	2(0.5)	1(1.16)	0.33
Diarrhea	3(0.5)	0(0)	1(5)	2(1.6)	1(0.2)	0(0)	0.30
Acute respiratory illness in contacts	83(13.5)	1(7.7)	4(22.2)	27(22)	44(12.4)	7(8.1)	0.024
Relative risk (95% CI)		0.940(0.106—8.332)	3.224(0.833—12.483)	3.174(1.313—7.675)	1.562(0.691—3.668)	1	
P-value for relative risk		0.956	0.09	0.01	0.275		

Table 3 Clinical findings of household contacts of confirmed H1N1 cases occurring after index cases according to age group.

Clinical findings No. (%)	Total 575	<2 years 13	2—4 years 18	5—18 years 117	19—50 years 344	≥51 years 83	*P*-value0.73
Fever	68(11.84)	1(7.7)	4(22)	20(17.09)	36(10.47)	7(0.84)	0.151
Cough	58(10.8)	1(7.7)	3(16.6)	19(16.2)	31(9)	4(4.8)	0.065
Sore throat	38(6.6)	0(0)	0(0)	12(10.25)	22(6.4)	4(4.8)	0.270
Rhinorrhea	35(6.08)	1(7.7)	4(22)	14(12)	15(4.3)	4(4.8)	0.002
Vomiting	6(1.04)	0(0)	1(5.5)	2(1.7)	2(0.6)	1(1.2)	0.170
Diarrhea	4(0.69)	0(0)	0(0)	2(1.7)	2(0.6)	0(0)	0.448
Acute respiratory illness in contacts	68(11.84)	1(7.7)	4(22)	21(18)	36(10.4)	6(7.22)	0.073
Relative risk (95% CI)		1.069(0.118—9.677)	3.667(0.916—14.683)	2.807(1.080—7.299)	1.500(0.610—3.688)	1	
P-value for relative risk		0.641	0.165	0.022	0.217		

Table 4 Frequency of clinical findings in confirmed cases versus household contact cases.

Clinical findingsNo. (%)	Confirmed cases $N = 162$	Household contacts $N = 83$	*P*-value
Fever	151(93.2)	75(90.4)	0.43
Cough	114(70.4)	64(17.1)	0.26
Sore throat	48(29.6)	48(57.8)	0.001
Rhinorrhea	38(23.5)	42(50.6)	0.001
Vomiting	32(19.9)	7(8.5)	0.022
Diarrhea	15(9.3)	3(3.7)	0.109

Table 5 Frequency of clinical findings in confirmed cases versus household contact cases occurring after index cases.

Clinical findingsNo. (%)	Confirmed cases 162	Household contacts 68	*P*-value
Fever	151(93.2)	62(91.2)	0.591
Cough	114(70.4)	55(80.9)	0.099
Sore throat	48(29.6)	38(55.9)	<0.001
Rhinorrhea	38(23.5)	32(40.06)	<0.001
Vomiting	32(19.9)	6(8.82)	0.042
Diarrhea	15(9.3)	2(2.94)	0.097

vomiting was more common among confirmed H1N1 cases (Tables 4 and 5). We found no significant difference in the results after omitting cases that occurred before or concomitant with index cases ($P = 0.022$) (Tables 3 and 5).

Discussion

In the present study, the risk of secondary cases occurring among household contacts was 13.9%, which is similar to the value reported by a study conducted in the USA at the beginning of the pandemic [4]. This previous study was the source from which we adopted the period of 7 days prior to 7 days after the index case as the period of intrafamilial transmission.

These two studies were similar with regard to the methodology. The risk reported herein is lower than that (26%) found in studies based on RT-PCR analysis of throat samples [5,9].

Other studies have revealed rates of secondary cases ranging from 8% up to 33% [10,11]. This variation may be due to different methodologies and differences in terms of house crowding. Sixty percent of our confirmed cases had been admitted to hospitals during the first week of their illness, which decreased the extent of respiratory contact with their families. Therefore, the attack rate may have been underestimated. A serologic survey showed preexisting antibodies to H1N1 among the older study participants; these antibodies were rarely detected in children [12]. To account for the period when influenza is contagious, we also included those who have had acute respiratory illness 7 days before the index case [4].

The average interval between the onset of symptoms of confirmed cases and the onset of symptoms in household contacts was 4.69 (0—15) days. This interval ranged from 2.6 to 4 days in other studies [3—6]. Intervals longer than 10 days in this study were observed in families with $\geq$2 cases, which may be due to the transmission of infections from a second case to a third case.

The age distribution of confirmed cases is not representative of the age distribution of the susceptible population because confirmation was limited to selected cases (e.g., more severe cases and cases identified during the initial phase of the outbreak). Therefore, secondary cases represent the age distribution more accurately.

In the present study, individuals $\leq$18 years old were among the age group most strongly affected by acute respiratory illness ($P = 0.01$). We found no significant difference in the results after omitting cases that occurred before or concomitant with index cases ($P = 0.022$).

Two other studies showed that children younger than 5 years are the most susceptible [3,13].

One study did not reveal any difference in the susceptibility of individuals as related to age [5]. Due to immunity acquired during the previous

pandemic, individuals ≥51 years old were the least susceptible age group.

The difference between confirmed H1N1 cases and their household contacts regarding the occurrence of sore throat and rhinorrhea may be attributed to the occurrence of some cases of seasonal flu among the contacts; we did not confirmed that the respiratory illness was H1N1 influenza in the household contacts. Vomiting was observed more frequently in index cases.

There are some limitations of the present study. For example, recall bias may be a concern. Some of the participants had not been informed about their laboratory results until we called them, so they may not have paid sufficient attention to isolation precautions.

Our analysis did not consider some important effects on transmission, including isolation circumstances and treatment with anti-viral prophylaxis, although only four contact cases in the present study had received anti-viral prophylaxis (oseltamivir). This low number of cases should not have had a confounding effect. Another limitation was the lack of laboratory confirmation. Some of the contact cases might have had seasonal influenza rather than H1N1 influenza; however, some of the symptomatic patients who were not considered to have acute respiratory illness may have been infected with H1N1 influenza.

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Ethical approval: Not required.

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References

[1] Gordan Sm. Update on 2009 pandemic influenza A (H1N1) virus. Cleveland Clinic Journal of Medicine 2009;76(October (10)):577—82.

[2] World Health Organization. Pandemic (H_1N_1) 2009-update 104. www.who.int/entity/csr/don/2010_06_11/en/index.html [accessed 21.07.09].

[3] Morgan OW, Parks S, Shim T, Blevins PA, Lucas PM, Sanches R, et al. Household transmission of pandemic (H1N1) 2009, San Antonio, Texas, USA, April—May 2009. Emerging Infectious Diseases 2010;16(April (4)):631—7.

[4] Cauchemez S, Donnelly CA, Reed C, Ghani AC, Fraser C, KentCK, et al. House hold transmissibility and control of pandemic influenza A virus (H_1N_1) in the united state. New England Journal of Medicine 2009;361(December):2619—27.

[5] Sues T, Buchholz U, Dupke S, Grunow R, Heiden MAD, Heider A, et al. Shedding and transmission of novel influenza virus A/(H_1N_1) infection in household Germany 200. American Journal of Epidemiology 2010;171(11):1157—64.

[6] Sikora C, Fan S, Golonka R, Sturtevant D, Gratrix J, Lee BE, et al. transmission of pandemic influenza A (H_1N_1) 2009 within household: Edmonton Canada. Journal of Clinical Virology 2010;49:90—3.

[7] Doyle T, Hopkins R. Low secondary transmission of 2009 influenza A (H1N1) in households following an outbreak at a summer camp: a relationship to timing of exposure. Epidemiology and Infection 2010;21(June):1—7.

[8] Yang Y, Sugimoto JD, Halloran M.E., Basta NE, Chao DL, Matrajt L, et al. The transmissibility and control of pandemic influenza A (H_1N_1) virus. Science 2009;326:729.

[9] Tabu C, Sharif S, Okoth P, Kioko J, Nzioka C, Muthoka P, et al. Introduction and transmission of 2009 pandemic influenza A (H1N1) virus — Kenya, June—July 2009. MMWR Morbidity and Mortality Weekly Report 2009;54(October (41)):1143—6.

[10] Cowling BJ, Chan KH, Fang VJ, Lincoln LLH, So HC, Fung ROP, et al. Comparative Epidemiology of pandemic and seasonal Influenza A in Household. The New England Journal of Medicine 2010 June;362(23):2175—84.

[11] World Health Organization. Assessing the severity of influenza pandemic; May 11, 2009. http://who.int/csr/disease-swine flu/assess2009/index.html/ [accessed 12.05.09].

[12] Serum cross-reactive antibody response to a novel influenza (H1N1) virus after vaccination with seasonal influenza vaccine. MMWR Morbidity and Mortality Weekly Report 2009;58:521—4.

[13] France AM, Jackson M, Schrag S, Lynch M, Zimmerman C, Biggerstaff M, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York city April—May 2009. Journal of Infectious Diseases 2010;201:981—92.