Communicability of H1N1 and seasonal influenza among household contacts of cases in large families

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Background Quantitative knowledge of the transmissibility of influenza is crucial to its prevention and control.

Objectives To quantify the transmission of influenza A (H1N1) and seasonal influenza in household contacts of patients with influenza diagnosed in a large university hospital.

Patients /Methods A prospective study was conducted between September and October 2009 in which all confirmed cases of influenza diagnosed at King Khalid University Hospital were included. All household contacts were followed by telephone calls every other day for 12 days. They were asked about the development of influenza symptoms in addition to their age and nationality.

Results Overall, 432 household contacts of 69 influenza A (H1N1) cases and 417 contacts of 91 seasonal influenza cases were included. Suspected influenza was diagnosed in 16.9% and 4% of household contacts of H1N1 and seasonal influenza patients, respectively. Household reproduction numbers were 1.06 (0.84–1.28) for H1N1 and 0.66 (0.51–0.81) for seasonal influenza. Children in households were more susceptible than were adults (22.2% versus 13.7%, respectively). Evidence of coughing in the index case tripled the risk of infection in households afflicted with the H1N1 influenza [relative risk (RR) = 3.28, CI = 1.24–8.69], while evidence of a runny nose doubled it (RR = 1.89, CI = 1.19–2.92).

Conclusions Communicability of influenza in households in Riyadh is comparable to that in other countries. Children are more susceptible to influenza infection. The presence of a cough or runny nose in the index cases increases the risk of infection.

Keywords Influenza, reproduction number, secondary attack rate.

Introduction Known human influenza dates back to the 12th century, but most lessons about its epidemiology have been learned from the three well-documented pandemics of the 20th century that occurred during 1918–1919, 1957–1958, and 1968–1969.1

Influenza pandemics occur when a novel influenza virus emerges because of an antigenic shift, against which the vast majority of the world’s population has no immunity.2 Influenza A (H1N1) virus circulated from 1908 onward.3 The 2009 pandemic is known to have been due to H1N1 virus related to swine influenza in 1918–1919, a process referred to as antigenic recycling. It has since spread worldwide.4

Natural influenza transmission in humans occurs over short distances, primarily via droplets and by contact. Artificially aerosolized swine flu virus in air samples on chick embryos survived for 16 h.5

During influenza infection, the virus is shed in nasal and pharyngeal secretions and dispersed through sneezing and coughing. A recent review of experimental influenza studies in volunteers found that viral shedding peaked on the 2nd day of inoculation and stopped completely by the 6th or 7th day.6 However, viral shedding level and duration can be reduced by treatment. On the other hand, patients with seasonal influenza may be able to infect others 1 day before symptoms appear and up to 5 days after they appear.7

The United States Centers for Disease Control and Prevention (US CDC) have estimated that the incubation period of influenza A could be between 1 and 7 days but is more likely to be between 1 and 4 days.8 A study in Japan indicates that most secondary cases are probably infected around the time of symptom onset of the index case (IC).9
The World Health Organization (WHO) reported that the current estimates of the secondary attack rate (SAR) of influenza A (H1N1) was 22–33%, while that of seasonal influenza was 5–15%. Factors affecting SAR are different both between and within countries. Follow-up studies to measure the communicability of influenza A (H1N1) is a priority for its prevention and control. The objective of this study is to quantify influenza transmission in household contacts of cases attending King Khalid University Hospital in Riyadh, Saudi Arabia.

**Methods**

This is a prospective study conducted between August and October 2009 and involved all reverse transcriptase-polymerase chain reaction-confirmed cases of influenza diagnosed at King Khalid University Clinics and confirmed as influenza A/H1N1 or seasonal influenza. Only cases wherein the patient was the first person in his or her household to be affected by the disease were identified as the IC.

A list of all household contacts was requested from the patient or his or her companions. On assumption that the attack rate is 25% (20–30%) among household contacts, the required number of household contacts to satisfy the study objectives was 288. Considering the average family size to be five persons and a response rate of 80%, 73 households were required. A complete history of the clinical picture and the history of exposure to suspected sources of infection were obtained for each case.

The households of the IC were contacted by telephone every other day for 12 days. For all, personal data (age and sex), relationship to the IC, and underlying diseases were collected in the first contact. Inquiries about influenza-like symptoms were made during each telephone call. An individual with acute respiratory illness, fever (reported or documented) and cough, sore throat, shortness of breath, difficulty in breathing, or chest pain was suspected to have H1N1 influenza. On the other hand, a suspected case of seasonal influenza is defined by the presence of fever >38°C; feverishness when the temperature was not taken; or at least two of the following symptoms: cough, sore throat, nasal congestion, rhinorrhea, sneezing, fatigue, headache, stiffness, or myalgia.

**Statistical analysis**

Data were analyzed using SPSS version 17 (SPSS Inc., Chicago, IL, USA). SAR was calculated as the number of H1N1 cases among the household contacts divided by the total number of household contacts. Reproduction number was calculated as the number of secondary cases generated by the IC during its period of infectiousness. The chi-square test was used to test the association between categorical variables and the occurrence of suspect cases among contacts. Relative risk (RR) and its 95% confidence interval (CI) were used to assess the association between manifestations of IC and infection among contacts.

**Results**

The study included 69 cases of H1N1 influenza and 91 cases of seasonal influenza. Patients with H1N1 influenza were significantly younger (22.8 ± 9.4 years) than those with the seasonal flu (31.9 ± 13.5 years). Men constituted 57.8% of the total sample. While one-third of seasonal influenza patients were non-Saudi nationals, only 5.8% of H1N1 cases were non-Saudi nationals (P = 0.000). Cough was the most common symptom (89.9%) followed by sore throat (78.3%) and fever (73.9%) in the case of H1N1. Cough and runny nose occupied the same rank (80.2%), followed by sore throat (78%) in seasonal influenza (Table 1).

As shown in Table 2, there were a total of 849 household contacts, 432 H1N1 cases, and 417 seasonal cases. A total of 15.7% household contacts, 16.9% H1N1 contacts, and 14.4% seasonal influenza contacts satisfied the suspected influenza criteria.

The household reproduction number of H1N1 influenza among household contacts was 1.06 (0.84–1.28) (73.69), but it was only 0.66 (0.51–0.81) (60.91) among household contacts of patients with seasonal influenza. Table 3 reveals that among H1N1 influenza contacts, the incidence of infection was the highest among children 1–5 years of age (31%), followed by children 6–15 years of age (25.8%) and adults >15 years of age (11.9%). Pre-school children also had the highest incidence among seasonal influenza contacts (22.2%). Men and women contacts had more or less the same incidence in both H1N1 (17.4% and 16.4%, respectively) and seasonal influenza (14.3% and 14.5%, respectively). Non-Saudi nationals had a higher incidence of both H1N1 and seasonal influenza than that of Saudi nationals (37.5% versus 16.5% and 24.7% versus 11.4%, respectively).

Table 4 shows that the risk of infection was nearly twice as high in contacts of H1N1 cases with runny noses compared with cases without runny noses (RR = 1.86, 95% CI = 1.19–2.92). This risk increased to 3-fold in cases with coughing (RR = 3.28, 95% CI = 1.24–8.69). The risk of the infection of seasonal influenza contacts did not differ significantly in the presence of runny nose or cough (RR = 1.13, 95% CI = 0.63–2.04 and RR = 0.63, 95% CI = 0.37–1.06, respectively).

**Discussion**

Knowledge of influenza pandemic transmissibility estimates is crucial in the development of effective mitigation strategies. This study investigated influenza transmissibility in households. Households have historically comprised the
best-defined setting and lend themselves to natural laboratories for the study of transmission rates.\textsuperscript{16,17}

The reproduction number is a quantitative measure of pathogenic transmissibility.\textsuperscript{18} In this work, it was $R_0 \approx 0.06 (0.84–1.28)$ for H1N1 and $0.66 (0.51–0.81)$ for seasonal influenza, indicating that H1N1 is more infectious than seasonal influenza, but may also reflect the effect of media, which was more concerned about H1N1 and insisted the strict application of control measures in all the community including households. Chowell \textit{et al.} applied the epidemic model to weekly indicators of influenza mortality data from the USA, France, and Australia and reported that an epidemic may occur if the reproduction number is $>1$.

Table 1. Characteristics of cases of influenza in Riyadh in 2009 included in the study

| Characteristic          | H1N1 influenza | Seasonal influenza | Total  | $P$    |
|-------------------------|----------------|-------------------|--------|-------|
| Age in years            |                |                   |        |       |
| Mean                    | 22.8           | 31.9              | 27.8   | 0.000 |
| Standard deviation      | 9.4            | 13.5              | 12.9   |       |
| Sex                     |                |                   |        |       |
| Male                    | 39 (56.5)      | 53 (58.2)         | 92 (57.8) | 0.828 |
| Female                  | 30 (43.3)      | 38 (41.8)         | 68 (42.5) |       |
| Nationality             |                |                   |        |       |
| Saudi                   | 65 (94.2)      | 61 (67.0)         | 126 (78.8) | 0.000 |
| Non-Saudi               | 4 (5.8)        | 30 (33.0)         | 34 (21.2) |       |
| Manifestations          |                |                   |        |       |
| Running nose            | 38 (55.1)      | 73 (80.2)         | 111 (69.4) | 0.0006 |
| Cough                   | 62 (89.9)      | 73 (80.2)         | 135 (84.4) | 0.097 |
| Fever                   | 51 (73.9)      | 65 (71.4)         | 116 (72.5) | 0.728 |
| Sore throat             | 54 (78.3)      | 71 (78.0)         | 125 (78.1) | 0.971 |
| Shortness of breathing  | 8 (11.6)       | 20 (22.0)         | 28 (17.5) | 0.088 |
| Difficulty in breathing | 5 (7.2)        | 10 (11.0)         | 15 (9.4) | 0.423 |
| Chest pain              | 8 (11.6)       | 12 (13.2)         | 20 (12.5) | 0.763 |

Table 2. Suspected cases of influenza among contacts of H1N1 and seasonal influenza cases in large families in Riyadh in 2009

| Status                  | H1N1 influenza | Seasonal influenza | Total  | $P$    |
|-------------------------|----------------|-------------------|--------|-------|
| Suspected influenza      | 73 (16.9)      | 60 (14.4)         | 133 (15.7) |       |
| Healthy                 | 359 (83.1)     | 357 (85.6)        | 716 (84.3) | 0.345 |
| Total                   | 432 (100)      | 417 (100)         | 849 (100) |       |

Table 3. Characteristics of H1N1 and seasonal influenza contacts and the occurrence of suspected influenza among them in large families in Riyadh in 2009

| Characteristic          | H1N1 influenza contacts | Seasonal influenza contacts | $P$    |
|-------------------------|-------------------------|-----------------------------|-------|
| Age in years            | H1N1 influenza suspects | Healthy | Seasonal influenza suspects | Healthy | $P$    |
| ≤5                      | 29 (69.0) | 13 (31.0) | 42 (77.8) | 12 (22.2) | 0.003 |
| 5–15                    | 72 (74.2) | 25 (25.8) | 89 (88.1) | 12 (11.9) | 0.19 |
| >15                     | 258 (88.1) | 35 (11.9) | 226 (86.3) | 36 (13.7) | 0.954 |
| Sex                     | H1N1 influenza suspects | Healthy | Seasonal influenza suspects | Healthy | $P$    |
| Male                    | 181 (82.6) | 38 (17.4) | 174 (85.7) | 29 (14.3) | 0.799 |
| Female                  | 178 (83.6) | 35 (16.4) | 183 (85.5) | 31 (14.5) |       |
| Nationality             | H1N1 influenza suspects | Healthy | Seasonal influenza suspects | Healthy | $P$    |
| Saudi                   | 354 (83.5) | 70 (16.5) | 287 (88.6) | 37 (11.4) | 0.117 |
| Non-Saudi               | 56 (62.5) | 3 (37.5) | 70 (75.3) | 23 (24.7) | 0.001 |
Table 4. Manifestations of influenza index cases and occurrence of suspected influenza among contacts in large families

| Serotype | Manifestations of index case | Disease status | RR (95% CI) |
|----------|-----------------------------|----------------|-------------|
|          |                             | Sick           | RR          |
| H1N1     | Runny nose                  |                |             |
|          | Present                     | 49 (67.1)      | 1.86 (1.19–2.92) |
|          | Absent                      | 24 (32.9)      | 182 (50.7)  |
|          | Cough                       |                |             |
|          | Present                     | 69 (94.5)      | 3.28 (1.24–8.69) |
|          | Absent                      | 4 (5.5)        | 65 (18.1)   |
| Seasonal | Runny nose                  |                |             |
|          | Present                     | 48 (80.0)      | 1.13 (0.63–2.04) |
|          | Absent                      | 12 (20.0)      | 80 (22.4)   |
|          | Cough                       |                |             |
|          | Present                     | 45 (75.0)      | 0.63 (0.37–1.06) |
|          | Absent                      | 15 (25.0)      | 57 (16.0)   |

RR, relative risk.

Whereas transmission cannot be sustained if it is <1,14 H1N1 was a pandemic at the time of the study. The same authors calculated the reproduction number of seasonal influenza in the USA, France, and Australia and found it to be 1.3 for each with substantial inter-annual variability.14 This may indicate that the influenza virus is more transmissible in cold weather in the Northern hemisphere than in the hot weather in The Kingdom of Saudi Arabia.

Yang et al.15 in the USA reviewed the literature and reported that the best estimate of the SAR in USA was 27.3% among H1N1 influenza contacts. This figure is higher than these study findings. However, recent studies investigating the transmissibility of H1N1 influenza in Japan, the UK, and the USA reported that the overall percentage of infected non-IC ranged from <5% to >25% with infection rates of 8–11% and 13% in the largest studies.19-21 One of the findings of this study was that the SAR is higher among young children contacts than adult contacts. One biological explanation for this finding is that younger children are less likely to be protected by prior immunity. Viboud et al.13,22 concluded that children are more susceptible than older age groups and that they contribute more extensively to spreading the virus across populations. Reichert et al.19 collected case data from 11 countries mid-July 2009. They compared sequence data for the hemagglutinin of novel H1N1 with sequences of H1N1 viruses from 1918 to the present. In their composite, over 75% of confirmed cases of novel H1N1 occurred in persons ≤50 years old, with peak incidence in the age range, 10–19 years. Less than 3% of cases occurred in persons over 65, with a gradation in incidence between ages 20 and 60 years. The sequence data indicate that novel H1N1 is most similar to H1N1 viruses that circulated before 1943.23

We used the clinical WHO definition of influenza without laboratory testing to define influenza in contacts. This may be considered as a study limitation. However, studies have reported that 75–80% of household transmission occurs directly from the influenza-positive index patient or from the same source of infection as the IC.24,25 Another limitation of the current study was that we could not identify asymptomatic cases; as a result, the role of asymptomatic transmission was not investigated. Also the calculated reproduction numbers are actually SARs within families, which do not represent the reproduction numbers for the population as a whole; the possible role of community in estimates of the reproduction number at the household level could not be excluded. Studies conducted on the genetic sequences of influenza viruses recovered in families in the USA and Canada suggested that transmission from community sources was rare in families in which an index patient had tested positive for influenza A.26

We calculated a SAR of 16.9% among household H1N1 contacts and 14.4% among seasonal influenza contacts. Children in families are at higher risk of infection. Cough and a runny nose increased the risk of infection with H1N1 influenza.

Preventive measures should be applied in households, particularly for children and contacts of cases presenting with cough or a runny nose. Further research is needed to explain the propagation of seasonal influenza with an apparent reproduction number <1.

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