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Transmissibility of seasonal and pandemic influenza in a cohort of households in Hong Kong in 2009

Brendan Klick[1], **Hiroshi Nishiura**[1,2,3], **Sophia Ng**[1], **Vicky J. Fang**[1], **Gabriel M. Leung**[1], **J. S. Malik Peiris**[4], and **Benjamin J. Cowling**[1]

[1]School of Public Health, The University of Hong Kong, Pokfulam, Hong Kong Special Administrative Region, China [2]PRESTO, Japan Science and Technology Agency, Saitama 332-0012, Japan [3]Theoretical Epidemiology, University of Utrecht, Yalelaan 7, 3584 CL Utrecht, The Netherlands [4]Department of Microbiology, The University of Hong Kong, Pokfulam, Hong Kong Special Administrative Region, China

Abstract

Background—The household secondary attack proportion is commonly used to measure the transmissibility of an infectious disease.

Methods—We analyzed the final outbreak distributions of pandemic A(H1N1), seasonal A(H1N1) and A(H3N2) infections identified in paired sera collected from members of 117 Hong Kong households in April and August-October 2009.

Results—The estimated community probability of infection overall was higher for children than adults; the probability was similar for pandemic A(H1N1) and seasonal A(H3N2) influenza. The household secondary attack proportion for pandemic A(H1N1) was higher in children than adults, whereas for seasonal A(H3N2) it was similar in children and adults. The estimated secondary attack proportions were similar for seasonal A(H3N2) and pandemic A(H1N1) after excluding persons with higher baseline antibody titers from analysis.

Conclusions—Pandemic and seasonal influenza A viruses had similar age-specific transmissibility in a cohort of initially uninfected households after adjustment for baseline immunity.

The household secondary attack proportion is often used to characterize the transmissibility of an infectious disease. This measure is defined as the probability that a susceptible person will be infected by someone in their household who has already been infected.[1,2] Estimates of the secondary attack proportion for 2009 pandemic influenza A(H1N1) ranged from 9% to 30% depending on age, study location, household size and method of ascertainment.[3-11] Estimates for seasonal influenza A and B have varied from 5% to 60%.[11-19] There are few direct comparisons of the transmissibility of pandemic and seasonal influenza. In a previous study, we conducted a transmission study in 99 households in Hong Kong, each including an index case with confirmed influenza. We found similar estimates of the secondary attack proportion for seasonal and pandemic influenza based on laboratory and clinical

Benjamin J. Cowling, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Units 624-7, Cyberport 3, Pokfulam, Hong Kong. Tel: +852 3906 2011; Fax: +852 3520 1945; bcowling@hku.hk.

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outcomes.[11] In that study, however, index cases were recruited following presentation in an outpatient setting, and selection bias could have led to overestimates of the household secondary attack proportion.

We report here on 117 households followed through the summer 2009 influenza season and the pandemic in Hong Kong.[20] We use estimates of infection status of persons clustered within households to infer and compare the risk of infection with seasonal influenza A(H1N1) (sH1N1) and A(H3N2) (sH3N2) and pandemic A(H1N1) (pH1N1) from the community versus within households.

METHODS

In October-December 2008 we recruited 119 families to a randomized trial of the direct and indirect benefits of influenza vaccination.[20] One child in each household was randomized to receive seasonal influenza vaccine or placebo control. We collected baseline sera from everyone aged 6 years or older, and further sera from all participants in April 2009 and then during the period from August 2009 to October 2009. Household report of acute respiratory illnesses (defined as at least two of temperature ≥37.8°C, cough, headache, sore throat, phlegm or myalgia) was obtained by telephone interviews at biweekly intervals. When illness was reported via a study hotline or biweekly interviews, a study nurse visited the household to collect nose and throat swabs for confirmation of influenza virus infection. All analyses reported here are based on the follow-up period from April 2009 through August-October 2009, which included a period of seasonal influenza circulation followed by the pandemic.[20] We collected sera from 425 people in 117 of the 119 families during this period.

Paired sera were tested for antibody responses to A/Brisbane/59/2007 (sH1N1) and A/Brisbane/10/2007 (sH3N2) by hemagglutination-inhibition (HI) assays, and for antibody responses to A/California/04/2009 (pH1N1) by viral microneutralization assays using standard methods.[20] VN tests rather than HI tests were used for pH1N1 based on studies showing that the former could better discriminate pH1N1 infection.[11,20,21] A 4-fold or greater rise in antibody titers was considered to indicate influenza infection.[22,23] Both pH1N1 and sH3N2 were widely circulating in Hong Kong during the summer of 2009.[20] Rises in antibody titers against more than one strain could be associated with cross-reactive antibody responses to a single infection, or with infection by more than one strain during the follow-up period of 4-6 months. Twelve persons with a 4-fold or greater rise in antibody titer to more than one strain were classified as having only one infection based on corresponding laboratory confirmation, infections in other family members, and dates of acute respiratory illnesses (eAppendix Table 1, http://links.lww.com).

We specified a statistical model that explicitly accounted for the probabilities of influenza infection from the community and from within the household.[19,24,25] We extended the model to differentiate the risk of infection for adults aged 15 years or older, and children aged 14 years or younger. The model allowed estimation of the community probability of infection, which can be interpreted as the probability of infection from the community during the period from April to October 2009.[12] The model estimated the community probability of infection and the secondary attack proportion for both children and adults, based on the possible transmission chains that could have led to the observed final infection status of each person within a household. Additional technical details of our statistical methods including the likelihood function used and justification for the choice of priors are provided in the eAppendix (http://links.lww.com).

We included data on infections with pH1N1, sH1N1 and sH3N2 during the follow-up period, and fitted separate transmission parameters for each strain. We fitted the models using Markov Chain Monte Carlo methods.[26,27] We used semi-informative beta(1.5,6) priors for the secondary attack proportions, beta(1.2, 6) for the community probability of infection with pH1N1 and sH3N2 (which were prevalent during the study period),[20] and beta(1.5,30) for the community probability of infection with sH1N1 (which was less prevalent in the community during the study period) (eAppendix, http://links.lww.com).[20] Those missing one or both sera specimens were considered to have unknown infection status; this was explicitly incorporated into the modeling algorithm.[28]

Since the model assumed that everyone was susceptible to infection, additional analyses were performed to examine how reduced susceptibility might affect the results. Antibody titers of 1:40 or higher by HI have been associated with 50% protection against infection.[29-31] For each strain we therefore fitted the model on two subgroups, those with baseline titers 1:160 or higher, and those 1:40 or higher, assuming that persons with elevated titers were immune to infection.

We performed three sensitivity analyses. First, we excluded everyone who had received seasonal vaccine. Second, because seasonal influenza circulated before pH1N1 and we had previously found some evidence consistent with broad temporary immunity,[20] we assumed that those infected with seasonal influenza were immune to pH1N1 and excluded them from the model. Third, we repeated analyses permitting anyone with more than one four-fold or greater rise in antibody titer to have had more than one infection.

RESULTS

Table 1 shows the baseline characteristics of the study population and the proportion of influenza infections in each group. eAppendix Table 2 (http://links.lww.com) shows the numbers of infections in children and adults overall, and in the subgroups with lower baseline antibody titers. There were high levels of baseline antibody against both sH1N1 and sH3N2, particularly among children; 64% of children had baseline antibody titers higher than 1:40 against sH1N1 and 63% against sH3N2. Four adults and no children had baseline antibody levels above 1:40 against pH1N1. eAppendix Figures 1-3 (http://links.lww.com) show the prior and posterior distributions for model parameters in these three analyses.

Table 2 shows the subtype-specific estimates of community probabilities of infection and secondary attack proportions for children and adults. For pH1N1, estimates were higher in children than adults for both the community probability of infection (0.18 vs 0.06) and the secondary attack proportion (0.15 vs 0.07). Among children, the community probability of infection and secondary attack proportion was lower for sH3N2 than pH1N1 (0.09 vs 0.18 for the community probability of infection and 0.07 vs 0.15 for the secondary attack proportion [p-value=0.02 and >0.27 respectively]). However, when only those with lower levels (≤1:160 and ≤1:40) of baseline antibody were considered susceptible to infection, there was little evidence of differences between secondary attack proportions for pandemic and seasonal viruses in either children or adults. Chi-square goodness-of-fit tests indicate that all models had satisfactory fit (all p-values>0.1).

When we performed sensitivity analysis by restricting our analysis to only those with antibody titers less than 1:160 and 1:40 and who did not receive seasonal vaccine, parameter estimates were similar to those using the entire sample (eAppendix Table 3, http://links.lww.com). Moreover, when we restricted analysis to those who had not been infected with seasonal influenza, parameter estimates for pH1N1 were similar to those using the entire sample (eAppendix Table 4, http://links.lww.com). When individuals (eAppendix

Table 2, http://links.lww.com) were allowed to have more than one infection rather than classifying them to one infection, all estimates of the community probability of infection and SAP were similar (eAppendix Table 5, http://links.lww.com).

DISCUSSION

Our results suggest similar patterns of household infection and transmission for sH3N2 and pH1N1 viruses in Hong Kong during the summer and early fall of 2009.[11] The estimated secondary attack proportions for pH1N1 were consistent with estimates of confirmed infection in the literature.[5,6,9-11] While unadjusted community probability of infection and secondary attack proportion estimates were lower for seasonal influenza than for pandemic influenza, the estimates for the sH3N2 and pH1N1 viruses generally were similar once we restricted our analysis to a subgroup with low immunity to seasonal influenza. This suggests that the household transmission potential of pH1N1 and sH3N2 would not differ greatly in equally susceptible populations (Table 2). Secondary attack proportion estimates in adults were slightly lower for pH1N1 compared with sH3N2, although in the subgroup analyses excluding those with high-baseline antibody levels, this difference was inconsistent. A number of other studies have demonstrated decreasing risk of pH1N1 infection with increasing age.[4,10,11,21,32,33]

One limitation of our study is that the models assumed that everyone included in analyses were susceptible to infection. We conducted sub-analyses assuming that persons with higher levels of baseline antibody were immune to infection. Due to the study design, one child in some families received influenza vaccine in September-October 2008 and a small proportion of other household members also reported receipt of vaccine.[20] Of the children who had received vaccine, 70% had baseline titers higher than 1:40 against sH1N1 in April 2009, and 74% had elevated titers against sH3N2; they thus were removed from at least one subgroup analysis. Although humoral antibody is imperfectly correlated with immunity,[20] it is plausible that models restricting the analysis to the subgroup with low baseline antibody titers (≤1:40) should represent a group largely susceptible to infection.

Three other technical issues should be noted. First, the study ended before the end of pH1N1 circulation in Hong Kong;[34] and some pH1N1 infections may have occurred after the end of our study, potentially leading us to underestimate the community probability of infection for pH1N1. Second, the HI and VN assays have imperfect sensitivity and specificity,[35] and infection status may have been misclassified.[11] Finally, while the community probability of infection and secondary attack proportion have straightforward epidemiologic interpretations, the risk of community infection in the adopted model is separately estimated from that in households. Further work is needed to link estimates of household transmissibility with more detailed transmission dynamics.[36]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Risk of influenza virus infection by individual characteristics in 425adults and children.

Characteristic		Pandemic H1N1	Seasonal H1N1	Seasonal H3N2
	No.	No. (%[a])	No. (%[a])	No. (%[a])
Age (years)				
0-14	183	35 (22)	4 (2)	13 (8)
15-59	234	19 (9)	4 (2)	14 (6)
≥60	6	0 (0)	0 (0)	0 (0)
Sex				
Male	199	27 (15)	4 (2)	8 (5)
Female	226	27 (13)	4 (2)	19 (9)
Received 2008-09 seasonal influenza vaccine	97	17 (19)	0 (0)	4 (4)

[a]Proportions calculated based on all individuals with paired antibody titers available.

Table 2

Estimates of the Community Probability of Infection and the Secondary Attack Proportion for children and adults

Persons assumed to be susceptible	Influenza A subtype	Cumulative community probability of infection (per season)				Secondary attack proportion			
		Children probability (95%CI)		Adults probability (95%CI)		Children probability (95% CI)		Adults probability (95% C1)	
All persons	pH1N1	0.18	(0.12- 0.25)	0.06	(0.03- 0.11)	0.15	(0.05- 0.28)	0.07	(0.00- 0.15)
	sH1N1	0.03	(0.01- 0.06)	0.02	(0.01- 0.04)	0.06	(0.00- 0.19)	0.07	(0.00- 0.19)
	sH3N2	0.09	(0.0-, 0.14)	0.05	(0.02- 0.08)	0.07	(0.00- 0.17)	0.09	(0.03- 0.18)
Persons with antibody ≤1:160	pH1N1	0.18	(0.12- 0.25)	0.07	(0.03- 0.11)	0.18	(0.05- 0.33)	0.08	(0.02- 0.15)
	sH1N1	0.04	(0.02- 0.08)	0.02	(0.01- 0.05)	0.10	(0.00- 0.31)	0.08	(0.00- 0.23)
	sH3N2	0.13	(0.08- 0.20)	0.05	(0.02- 0.08)	0.14	(0.02- 0.35)	0.11	(0.03- 0.22)
Persons with antibody ≤1:40	pH1N1	0.18	(0.11- 0.24)	0.07	(0.03,-0.11)	0.18	(0.05- 0.31)	0.08	(0.02- 0.16)
	sH1N1	0.06	(0.02- 0.12)	0.02	(0.01- 0.05)	0.25	(0.00- 0.83)	0.07	(0.00- 0.21)
	sH3N2	0.16	(0.08- 0.28)	0.06	(0.03- 0.09)	0.18	(0.02- 0.46)	0.12	(0.02- 0.26)

CI = credibility interval.

1A(H3N2).