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Epidemiology and etiology of influenza-like-illness in households in Vietnam; it's not all about the kids!

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ABSTRACT

Background: Household studies provide opportunities to understand influenza-like-illness (ILI) transmission, but data from (sub)tropical developing countries are scarce.
Objective: To determine the viral etiology and epidemiology of ILI in households.
Study design: ILI was detected by active case finding amongst a cohort of 263 northern Vietnam households between 2008 and 2013. Health workers collected nose and throat swabs for virus detection by multiplex real-time RT-PCR.
Results: ILI was detected at least once in 219 (23.7%) of 945 household members. 271 (62.3%) of 435 nose/throat swabs were positive for at least one of the 15 viruses tested. Six viruses predominated amongst positive swabs: Rhinovirus (28%), Influenza virus (17%), Coronavirus (8%), Enterovirus (5%), Respiratory syncytial virus (3%), Metapneumovirus virus (2.5%) and Parainfluenza virus 3 (1.8%). There was no clear seasonality, but 78% of episodes occurred in Winter/Spring for Influenza compared to 32% for Rhinovirus. Participants, on average, suffered 0.49 ILI, and 0.29 virus-positive ILI episodes, with no significant effects of gender, age, or household size. In contrast to US and Australian community studies, the frequency of ILI decreased as the number of household members aged below 5 years increased ($p = 0.006$).
Conclusion: The findings indicate the need for tailored ILI control strategies, and for better understanding of how local childcare practices and seasonality may influence transmission and the role of children.

1. Background

Acute respiratory illnesses (ARIs) are a leading global cause of morbidity and mortality [1], commonly caused by viruses such as Influenza (Inf), Rhinoviruses (Rhino) and other Enteroviruses (Entero), Coronaviruses (Corona), Respiratory syncytial virus (RSV), Human Metapneumovirus (MPV), Parainfluenza virus (PIV) 1–4, and Adenoviruses (Adeno) [2–5]. Influenza-like-illness (ILI) represents a subset of ARI patients, being variably defined as fever with at least one respiratory symptom, usually cough, which are common in patients presenting with other viral causes of ARI [3,6,7], and not specific for influenza [8,9].

Household cohort studies are fundamental for understanding respiratory virus transmission [10]. There is a wealth of information regarding influenza virus transmission in households [11,12], but relatively few studies characterize non-influenza virus transmission. In 2007, we established a household cohort in Ha Nam, northern Vietnam, and have conducted active ILI surveillance to

Abbreviations: ILI, influenza like illness; ARI, acute respiratory illness; Inf, influenza virus; Rhino, rhinoviruses; Entero, enteroviruses; Corona, coronaviruses; RSV, respiratory syncytial virus; MPV, human metapneumovirus; Boca, bocavirus; PIV, parainfluenza viruses; Adeno, adenoviruses.

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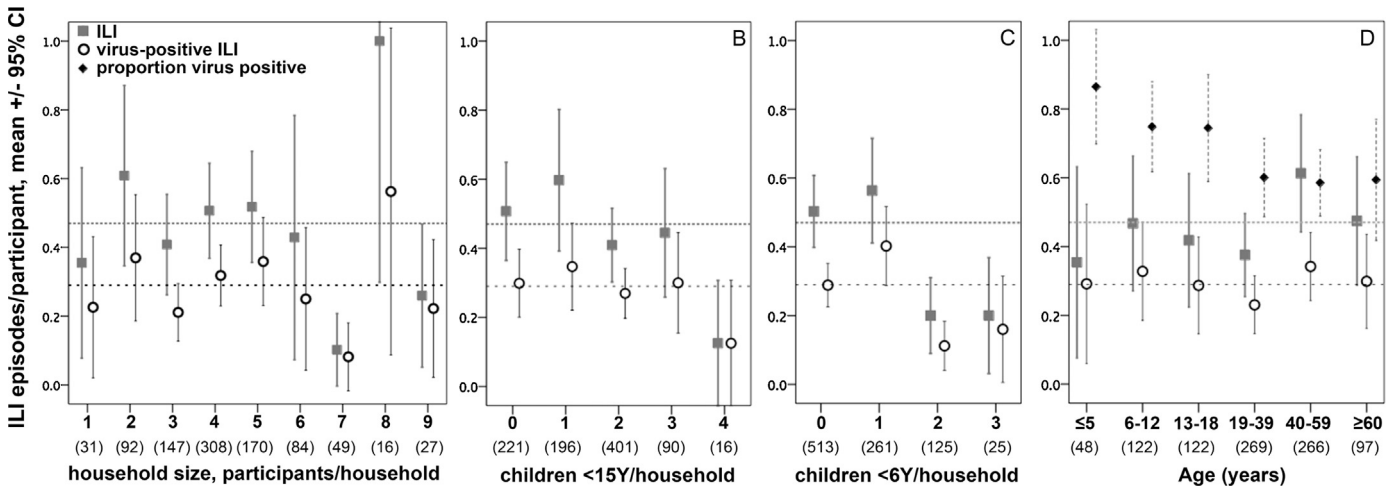

Fig. 1. Frequency of ILI and virus-positive ILI according to characteristics of households and individuals. Results are presented as average episodes/participant in each x-axis category. Upper and lower dashed horizontal lines indicate averages for all participants combined for ILI and virus-positive ILI, respectively. The numbers of participants are shown below each category on the x-axis in parentheses.

describe influenza epidemiology [12–14]. Over 80% of swabs collected have been influenza-negative.

2. Objective

To determine the epidemiology and viral etiologies of ILI in Ha Nam households, and the effects of household and demographic factors on transmission.

3. Study design

3.1. Participants

The Ha Nam cohort was established in December 2007, and has been described previously [13]. Briefly, 270 households were selected randomly from a rural commune located 60 km from Hanoi, Vietnam. All participants provided written informed consent. Commune health workers visited houses weekly to identify ILI cases, and collected nose and throat swabs within 2 days of onset. Participants with ILI also self-presented to the commune health service. ILI was defined as an oral temperature of at least 38 °C together with cough or sore throat. The current study assessed ILI occurring between September 2008 and August 2013, but excluded the year between September of 2009 and 2010, when protocols were adjusted due to the 2009 H1N1 pandemic. 98 ILI episodes were detected during this pandemic period and 25% were H1N1 2009 pandemic strain positive.

3.2. Diagnostic testing

Internal RNA-virus control (equine arteritis virus) was added to 200 μl of combined nose and throat swab media, then RNA was extracted using MagNA Pure 96 Extraction kit (Roche, Germany). Influenza A/H1N1, A/H3N2 and B viruses were detected by real-time RT-PCR according to WHO/US CDC protocols, version 2007 for seasonal influenza and version 2009 for pandemic H1N1 (http://www.who.int/csr/resources/publications/swineflu/CDCRealtimeRTPCR_SwineH1Assay-2009_20090430.pdf).

A four-tube real-time multiplex PCR assay developed by Jansen and colleagues was used to detect 12 respiratory viruses: respiratory syncytial viruses (RSVs) A/B; Rhinoviruses A-C; Coronaviruses OC43/HKU1 and 229E/NL63; Adenovirus, Parainfluenza viruses 1–4; human Metapneumovirus; Enteroviruses; Bocavirus; and Parechoviruses [15]. Limits of detection are between 40 and 50 copies per reaction for each target [15].

3.3. Analysis and statistics

Participants were classified as children and young children if aged below 15 and 6 years, respectively. Results are presented as means or proportions with 95% confidence intervals. Poisson log-linear regression was used to investigate factors associated with the number of ILI and virus-positive ILI episodes per participant, including age, gender, household size, and number of children per household.

4. Results

4.1. Population characteristics

924 participants from 263 households were included in this analysis after excluding 63 participants who were absent the majority of the time, because they were away for work or study, or had moved out of the commune or died, were excluded. A further six participants who had incomplete data were excluded. None had received influenza vaccine. Four reported having a pre-existing chronic condition, involving lungs (n = 2), heart (n = 1), or liver (n = 1). Households had between one and nine inhabitants, averaging 3.5 (95% CI 3.3–3.7), with 1.1 (1.0–1.2) children, and 0.5 (0.4–0.5) young children (Supplemental Fig. 1a). Numbers of children and young children per household increased with household size, such that average participant age decreased with household size (Supplementary Fig. 1a). Most households had no children (n = 102), or two children (n = 90), giving a bimodal age distribution (Supplementary Fig. 1b). Females (n = 510, 55.2%) predominated slightly over males (n = 414, 44.8%).

Panel A shows mean age by household size (circles) with error bars representing 95% confidence intervals, as well as the numbers of children per household by household size (stacked bars). The histograms in panel B show the age and gender distribution of the 924 participants studied.

4.2. ILI and virus-positive ILI detection frequencies

435 ILI episodes were detected in 219 (23.7%) participants. On average households had 1.6 (1.2–2.1) ILI episodes, but the distribution was skewed, ranging from 0 to 32, and only 120 (45.6%)