Human infections with avian influenza A(H7N9) virus in China: preliminary assessments of the age and sex distribution

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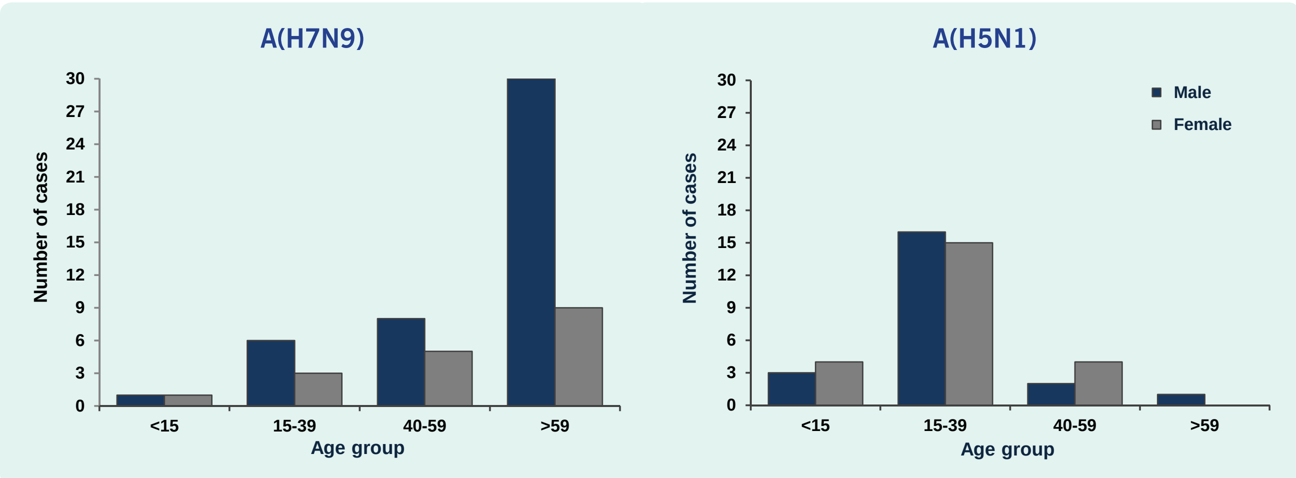
Since 31 March 2013, the Government of China has been notifying the World Health Organization (WHO) of human infections with the avian influenza A(H7N9) virus,[1] as mandated by the International Health Regulations (2005).[2] While human infections with other subgroups of H7 influenza viruses (e.g. H7N2, H7N3 and H7N7) have previously been reported,[3] the current event in China is of historical significance as it is the first time that A(H7N9) viruses have been detected among humans and the first time that a low pathogenic avian influenza virus is being associated with human fatalities.[4] In this rapidly evolving situation, detailed epidemiologic and clinical data from reported cases are limited—making assessments challenging—however, some key questions have arisen from the available data. Age and sex data, as one of the first and most readily available data, may be an important proxy for gender-specific behaviours/conditions and an entry point for response.[5,6] Here, we describe the age and sex distribution of the human cases of avian influenza A(H7N9) to better inform risk assessments and potential next steps.

Between 31 March and 16 April 2013, there were 63 reported cases of avian influenza A(H7N9). The median age was 64 years (range 4–87), and 45 cases (71%) were male. Notably, 39 of the 63 cases (62%) were ≥ 60 years of age. When stratified by age and sex, elderly men were the most affected demographic group (**Figure 1**). This is different to the Chinese population which has a large proportion of young and middle-aged adults and a greater number of women among the

Figure 1. **Age group and sex distribution of reported human infections with avian influenza A(H7N9) and A(H5N1) viruses, China, as of 16 April 2013**



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elderly.[7] Although the case fatality rate (CFR) in all males at 22% (10/45) was similar to females at 22% (4/18), when restricted to elderly cases ≥ 60 years of age, the CFR in males was 20% (6/30) compared to no deaths in females (0/9). The case distribution of current avian influenza A(H7N9) cases is also different to reported avian influenza A(H5N1) cases in China (N=45), where the majority were young working age adults (median: 26 years; range 2–62), with no difference in gender (**Figure 1**).[8] Hence, two questions naturally arise – Why are we seeing the current age and sex distribution, and what key questions can we ask to allow public health practitioners to respond in an efficient and effective manner?

Three main reasons may be considered for the current case distribution: (1) differential exposure between males and females due to gender-associated practices and norms; (2) biological differences between males and females in the clinical course post exposure/infection; and (3) differential health care-seeking/access behaviour between male and females, leading to surveillance/detection bias.

Assessing whether the current distribution is due to differential exposures is difficult. The same is true with many other field investigations of acute outbreaks due to the lack of detailed case-based exposure information. Despite this, limited information among current cases point to poultry-related exposure such as live bird markets (LBMs) as a potential risk factor.[9] LBMs have been the primary site where avian influenza A(H7N9) virus has been detected in poultry and environmental samples in the affected areas,[9] although age- and sex-specific LBM visit patterns are unknown.Elderly Chinese men are also well-known to be hobbyists of ornamental pet songbirds and take frequent and extended walks with their caged birds, congregating together in parks.[10] As the source and mode of infection remain unknown, control and prevention efforts are difficult. A better understanding of the social norms and behaviours among elderly Chinese men in affected areas may better guide us in the investigation (e.g. by identifying hypotheses for case-control studies).

Biological characteristics particular to elderly men may also be a possible explanation for the observed age and sex distribution. A defining feature of seasonal influenza is its severe morbidity and mortality among the elderly, due to higher biological susceptibility to severe outcomes from influenza infection among this age group.[11,12] While poultry exposure appears to be a common risk factor in the current event, the age distribution among reported cases also raises the question why so few young adults (i.e. those of working age exposed to poultry as vendors/LBM workers/breeders/transporters) have been reported. This suggests not only greater exposure among elderly men but also a possible greater biological susceptibility to more severe outcomes. The number of cases and the CFR is higher among elderly men relative to elderly women (although this may be a function of dose response due to greater or more frequent exposure). Serologic investigations among close contacts and other subpopulations in the area will assist with our understanding of the clinical spectrum of this infection, information regarding smoking, underlying medical conditions and other risk factors among the current case series would help to elucidate some of these issues.

Health care-seeking behaviour and access also need to be considered as an explanatory factor. If elderly men are more likely to access health care, be detected or reported, surveillance bias may occur such that the distribution of the reported cases does not reflect the underlying distribution of disease occurrence in the population. However, given the high severity among the majority of the reported cases to date, the current high awareness level in both the public and the health care community and the nationwide implementation of enhanced influenza-like illness and severe acute respiratory illness surveillance activities, it seems unlikely that elderly men are being overly selected.

At this time, it is clear that there are more questions than answers. Based on the basic age and sex distribution, we identify several critical questions and options to guide the ongoing investigation:

- What are the societal norms and common social practices among elderly men in the affected provinces? Qualitative approaches and involvement of anthropologists/sociologists specializing in the sociology of health of the Chinese population may be beneficial.

- What is the age and sex distribution of severe acute respiratory illnesses and key risk factors for respiratory illness (e.g. smoking) in the underlying population in the affected provinces? While detailed case-based clinical information is pending, data from the general population may be helpful for initial assessments.

- What is the age and sex distribution of health care utilization in the Chinese population in the affected provinces? Ruling out any possible selection bias will be an important initial step in understanding both the clinical and epidemiologic spectrum of infection.

In these situations, it is easy to dismiss preliminary epidemiologic assessments as being too low in numbers or with too few variables of interest. There is a need for further case-based information, such as zoonotic exposures and underlying medical conditions. However, for public health workers engaged in rapid response to acute events, it is essential to operate as observational scientists and assess available information to help formulate the next steps. Following age and sex distributions closely over time may detect important changes in the epidemiology of this virus, and with better understanding, high-risk populations, targeted interventions (e.g. gender-specific risk communication messages), prevention and control measures (e.g. vaccination) and treatment options (e.g. antivirals) may be identified. While this brief and rapid communication cannot offer answers, we hope that public health practitioners involved in similar responses – at various capacities around the world – may consider these key concerns and questions to help respond to not only the current virus but also other emerging infectious threats.

Conflicts of interest

None declared.

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