

# Avian influenza A(H5N1) in humans: lessons from Egypt

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Highly pathogenic avian influenza A(H5N1) has ravaged the Egyptian poultry population. Ninety human cases, including 27 fatalities have been recorded by 30 December, 2009. However, epidemiological information on the infection in humans in Egypt is scarce. We analysed the first three years of highly pathogenic avian influenza A(H5N1) in Egypt between 20 March 2006 and 31 August 2009) and found that more cases occurred in females than males, especially in 2006 and 2007. Women in the age group 20-39 years had the greatest tendency to be infected. It took an average of one day and 18 hours to seek medical assistance in patients who recovered and of six days in fatal cases. Children sought treatment much earlier than adults. On average, a patient died 11 days after the onset of symptoms. Exposure to infected poultry remained the most important risk factor.

## Introduction

On 17 February 2006, highly pathogenic avian influenza A(H5N1) was first reported in the poultry population in Egypt [1]. Since that time, the infection had affected at least 21 governorates forcing over 1.5 million individuals to loose their source of livelihood [1]. Overall, 370 backyard poultry flocks, 850 farms, and four zoos have been affected, and more than 36 million birds (mainly chickens) have died or have been culled in Egypt at an enormous cost to the country [1]. Currently, the virus is endemic in the Egyptian poultry population.

The first human case of avian influenza A(H5N1) in Egypt occurred on 17 March 2006 [2], and to date (30 December 2009), the statistics of human infection and fatalities continue to rise. Specifically, 90 human cases (approximately one fifth of the total global count), including 27 fatalities (approximately one eleventh of the global count) have been recorded in Egypt as of 30 December 2009 [2]. These numbers rank Egypt third in the list of recorded human cases and fatalities in the world, after Indonesia and Vietnam, and remain by far the highest in Africa. The World Health Organization (WHO) had previously stated that “countries around the world had improved their defenses against bird flu, but the situation remained critical in Egypt and Indonesia where the risk of the H5N1 virus mutating into a major human threat remains high” [3].

Worrisome with the situation in Egypt is the frequency with which women and young people are being infected and the very current trend of rising infections in children: in 2009 alone, 79% of all infected individuals were under 10 years old. Between January and December 2009, 17 of the 34 recorded cases involved children between 12 and 30 months-old. Similarly, at the time of this report, human cases of 2009 pandemic influenza A(H1N1) had also been confirmed in the Egyptian population, which raises the possibility of co-infection and the emergence of reassortant viruses.

While the situation in Egypt remains critical, empirical evaluation of its peculiarities seem to be lacking, except for a very recent report by Dudley [4]. Assessment of the scientific literature and epidemiological data returned little or no concrete evidence from Egypt. However, the country has provided adequate records to international organisations like the WHO and the World Organization for Animal Health (OIE) and these reports have improved significantly since the first submission in terms of spatial and temporal data, and clinical records of affected persons.

In this study, we analysed the records on avian influenza A(H5N1) in Egypt between 20 March 2006 and 31 August 2009 and explain the epidemiological significance of our findings.

## Materials and Method

The Egyptian government reports to the WHO, available on the WHO website [2], were the primary source of data for these analyses. We considered all laboratory-confirmed human cases of avian influenza A(H5N1) reported to the WHO from Egypt between 20 March 2006 and 31 August 2009. All positive samples reported and used in these analyses had earlier been confirmed by microneutralisation assay on serum or by PCR on respiratory tract specimens as reported [5]. Similar confirmatory tests were done in the Egyptian national reference laboratory and at the WHO reference laboratories for diagnosis of influenza A(H5) infection, including the United States Naval Medical Research Unit 3 in Cairo, Egypt [4].

The parameters included in our analysis were: date of exposure, date of onset, course of symptoms, and time

from hospitalisation until death/recovery, as listed in the WHO situation reports on avian influenza [6].

In the absence of complete information, reports were based on approximate dates and times from the reports. However, in cases of ambiguity arising from the records, such data were excluded from the calculations. In total, 85 confirmed cases were reported during the study period, of which 27 were fatal. After the exclusion of ambiguous data, only 63 of the 85 reported cases and 20 of the 27 fatal cases were evaluated for symptoms and hospitalization; and 44 of the 58 cases who recovered or were stable were analysed for symptoms and recovery. Analyses were performed using StatGraphics v2.0. Distributions were compared using chi-square test, and medians were compared using Fisher's exact test.

## Results

### Demographic characteristics

In the period under analyses, 85 cases were evaluated, 32 of whom were male and 53 were female. Eighteen cases had been reported in 2006, 25 in 2007, eight in 2008 and 34 to date (31 August) in 2009, including a total of 27 human fatalities over the three and a half-year period.

The youngest cases were one year of age (two boys), and the oldest case was a 75 year-old woman. The median age of all confirmed cases was six years. The age of the cases ( $n=85$ ) ranged from 12 months to 75 years, with a mean of 13 years and two months. The median age of all fatalities ( $n=27$ ) was 25 years (range: four to 75 years) and the mean was 26 years and three months. The median age of the female cases ( $n=53$ ) was 15 years, (range: 14 months to 75 years) and the mean was 16 years and 10 months, while the median age of the male cases ( $n=32$ ) was four years (range: two months to 32 years) and the mean seven years and two months (Table, Figures 1 and 2).

The overall sex ratio (male:female) was 0.6 and the annual sex ratios were 0.4 (2006), 0.4 (2007), 1.0 (2008) and 0.9 (2009). By age, the sex ratios (male:female) were 1.1 (<10 years), 0.3 (10-19 years), 0.1 (20-29 years), 0.2 (30-39 years), 0 (40-49 years; no case) and 0 (>50 years; all cases female), with  $x=11.87$  in Pearson's chi-square test,  $p=0.001$  in Fisher's exact test, and degree of freedom (DF)=1 (see Table).

### Intervals

The number of days from onset of symptoms to hospitalisation (S-H) for all cases was calculated for 63 of the 85 cases. The median was two days (range: 12 hours to 11 days), the mean was two days and 19 hours. For the fatal cases (17 of 27 were included in the analysis), the median (S-H) was six days (range: two to 11 days) with a mean of six days. Among the recovered cases (47 of 58 were included in the analysis), the median (S-H) was one day (range: 12 hours to five days), and the mean was one day and 18 hours.

The time from onset of symptoms to death had a median of nine days (range: five to 30 days) and a mean of 11 days, while the time from hospitalisation to death had a median of four days (range: one to 25 days) and a mean of six days. The S-H in children and teenagers between the ages of 10 and 19 years ( $n=51$ ) had a median of one day (range: 12 hours to eight days) and a mean of two days and 12 hours, in contrast to the adults over 20 years of age ( $n=12$ ), in whom the median was four days (range: 12 hours to 11 days) and the mean was four days. Many (19) of the adults did not present with full hospital records and were not included in the analysis for hospitalisation.

### Mortality

The overall case fatality rate was 32% (27/85). It was much lower in male (3/32) than in female (24/53) cases. According to age, the case fatality was two of 49 in the under 10-year-olds, eight of 13 in the 10-19-year-olds, seven of nine in the 20-29-year-olds, eight of 12 in the 30-39-year-olds, and two of two in the over 50-year-olds (there were no cases among the 40-49-year-olds). In the years under review, the case fatality was 10 of 18 for 2006, nine of 25 for 2007, four of eight for 2008 and four of 34 for 2009, with  $x=10.81$  in Pearson's chi-square test and DF=4).

### Discussion

This study is subject to some limitations. We conducted our analyses based on the limited data available for scrutiny. We suspect that cases have been missed because of the current surveillance system in humans which targets only severe infections backed by laboratory confirmation [7]. If this is so, Egypt may have had many more cases and possibly fatalities than reported and used in this work. People trying to avoid hospitalisation, especially among the adults, may also have contributed to underreporting.

In this analysis, the female cases had a wider age window (14 months to 75 years) than the male cases (12 months to 32 years). Since exposure to poultry remains the most important risk factor for human infection in Egypt, this may reflect the fact that across all age groups, more women than men are involved in poultry-related activities. All infected individuals with the exception of three (whose exposure status was uncertain) had been exposed to infected poultry or poultry products or to slaughtered or defeathered infected birds. In children and young adults, however, infection was more prevalent among males, although it is not clear why. Although infections in children peaked in the years 2007 and 2009, the reason for this is not yet clearly understood. Strong peaks of infection usually appear to follow periods of relaxation of preventative measures [7].

It also appears that especially in the group of the 20-39-year-olds, women had a greater tendency to be infected and more women died post infection. Fifteen of 21 infected women in this age group died.

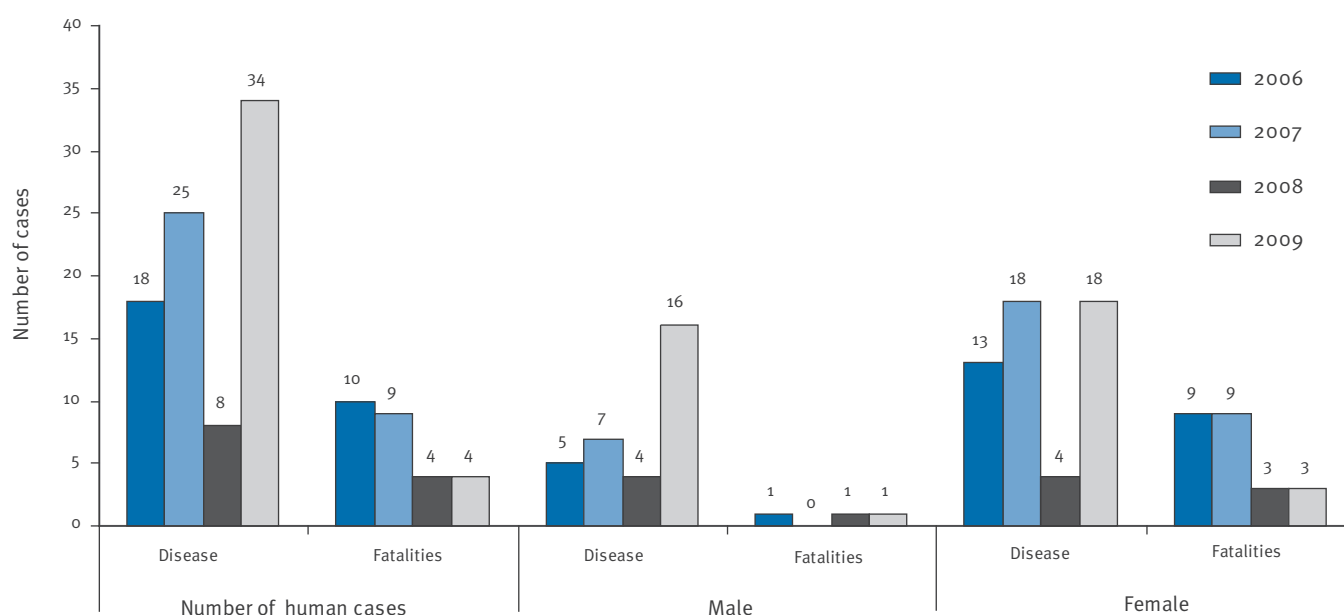
**TABLE**

Human cases and fatalities associated with avian influenza A(H5N1) in Egypt, 20 March 2006–31 August 2009 (n=85)

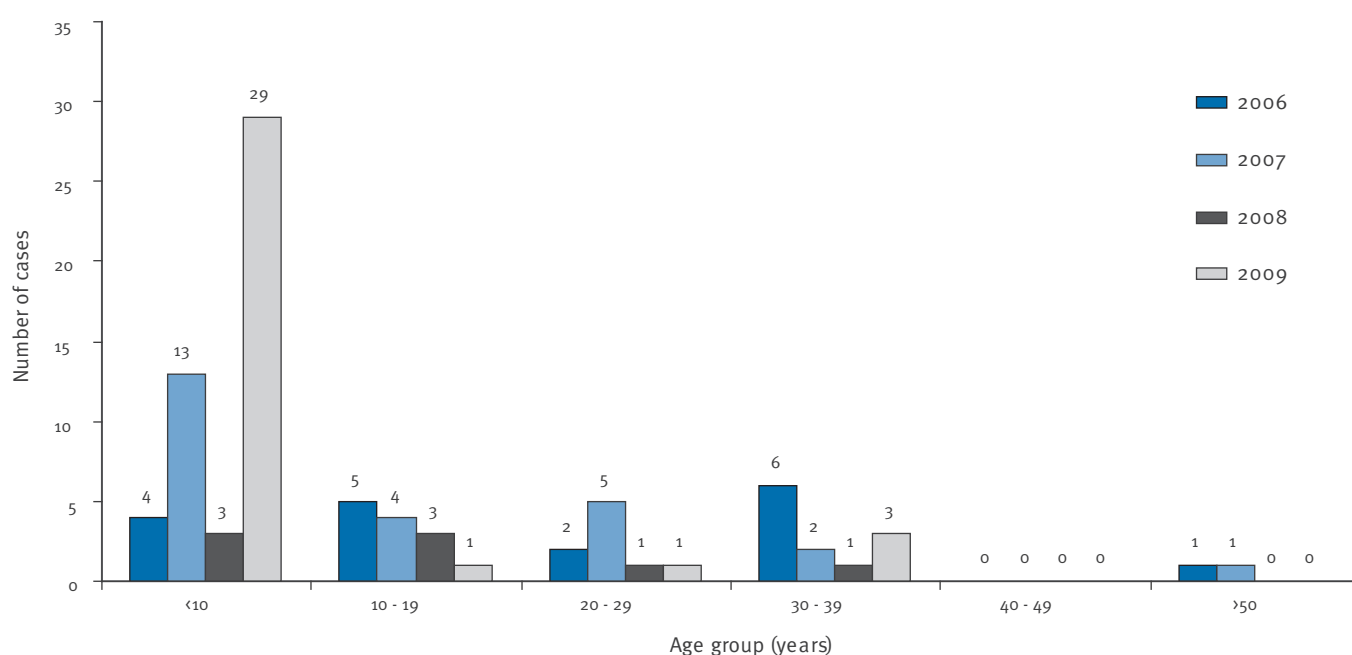
Year	Human cases and fatalities distributed according to sex						Human cases (disease) distributed according to age					
	Number of human cases						Age range of human cases (years)					
	Total		Male		Female							
	Disease	Fatalities	Disease	Fatalities	Disease	Fatalities	<10	10-19	20-29	30-39	40-49	>50
2006	18	10	5	1	13	9	4	5	2	6	0	1
2007	25	9	7	0	18	9	13	4	5	2	0	1
2008	8	4	4	1	4	3	3	3	1	1	0	0
2009	34	4	16	1	18	3	29	1	1	3	0	0
<b>Total</b>	<b>85</b>	<b>27</b>	<b>32</b>	<b>3</b>	<b>53</b>	<b>24</b>	<b>49</b>	<b>13</b>	<b>9</b>	<b>12</b>	<b>0</b>	<b>2</b>

**FIGURE 1**

Distribution of human cases of avian influenza A(H5N1) by sex, Egypt, 20 March 2006–31 August 2009 (n=85)

**FIGURE 2**

Distribution of human cases of avian influenza A(H5N1) by age group, Egypt, 20 March 2006–31 August 2009 (n=85)



These groups face the highest risk of exposure as it is mainly they who are involved in home slaughtering and defeathering of chicken and preparation of food, farm work and visits to infected farms. A recent study has analysed the age and sex bias with regards to the situation in Egypt [4], and it has been reported that farmers from other infected African countries believe that there is little or no risk of infection from culling, defeathering, home slaughtering and visit to infected premises [8,9]. In addition, failure of the government to pay compensation in Egypt for culled birds and the practice of keeping of poultry on rooftops and in close association with humans may have played a role. Although no association has yet been established between the level of exposure to avian influenza A(H5N1) and fatalities in Egypt, reports on workers in Asia showed that a high prevalence of infection in the poultry population is associated with a higher incidence of infection in humans, and that controlling such outbreaks of H5N1 influenza in the poultry flocks can stop human infection [7,10,11]. In addition, genetic characterisation of viruses from both the human and avian populations in Asia revealed that the viruses from both species were very similar [9,10].

According to our analysis, early hospitalisation following infection increased the chances of recovery. Children tend to be hospitalised earlier than adults and this may have contributed to the significantly lower death rate in the children (only two cases in children under the age of 10 years were fatal). Similarly, although 62 of the 85 cases were under 19 years old, this does not represent national demography since only approximately 32% of the population are 15 years and younger [12]. In most parts of Africa, people are known to visit a hospital less frequently as they advance in age, and supposedly non life-threatening conditions such as seasonal influenza are often treated at home and therefore underreported [8].

The overall case fatality in this study was 32% (27/85). This percentage may appear small when compared with statistics from other places, for example 82% in Indonesia (115/141), 68% in Thailand (17/25), 66% in China (25/38) and 50% in Vietnam (56/111). Nevertheless, with the exceptional surge in number of cases (especially in children) arising in Egypt in 2009 and the recent reoccurrence of human cases of avian influenza A(H5N1) in China and Vietnam despite an intensive control programme in the poultry populations, the pandemic potential of this virus is still very evident. Case fatality was significantly higher in females compared with males, but whether this is related to exposure dose can not be confirmed in this analysis.

As previously suggested by Briand and Fukuda [9], public health guidelines in Egypt will need to be tailored to meet the local situation taking into consideration the agricultural practices and the people's perceptions. It will also be necessary to conduct more studies on

human H5N1 influenza infection in Africa to evaluate the situation of asymptomatic carriers and unreported cases.

Finally, as evident in this analysis, exposure to infected poultry remains the only common denominator and an important risk factor for the spread of avian influenza A(H5N1) in humans in Egypt. Other workers had identified and reported the same risk factor exposure to sick poultry previously [10,11].

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