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HPAI Epidemic in Egypt: Evaluation, Risk Factors and Dynamic of Spreading

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Abstract: On 17 February 2006, the Egyptian government confirmed that bird flu had broken out in the nation's poultry in Egypt. In this work Trials were carried out to determine: The transmission parameter ß (i.e., the average rate at which infected flocks infect susceptible flocks) and the infectious periods (T) between various districts. *Rh* was calculated as the product of the estimates of the transmission parameter and the infectious period. Results revealed that, the infection was spread to 21 governorates, 5 of them with a high density of poultry farms. In all, 826 districts containing commercial flocks became infected during a period of 4 months. Suggested geographic maps for the spread of HPAI virus that had been stroked Egypt 2006 were constructed. The transmission parameters varied in-between the districts in the various governorates. It was ranged from 23 days to 87 days. Governorates of heavy density (number of poultry farms per km^2) have less periods for the transmission of the virus from district to another. It was found a negative correlations between the number of the infected farms of the governorate and (T) parameter of transmission ($r = -0.415$ at $P < 0.05$) and a negative significant one between the number of infected districts and parameter (T) ($r = 0.51$ at $P < 0.05$). Also there was a significant correlation between the number of infected districts and the activity of the transporting traffic of poultry between the districts of the same governorate and to other governorates ($r = 0.66$ at $P<0.05$). Parameter (T), it was ranged from 0.36 day to 27.6 days. Rh between-districts transmission decreased significantly after virus detection, it was still > 1 ($R = 1.2$ for both areas) suggested that the control measures were inadequate to interrupt the chain of infection. The association between the presence of the migratory birds and the occurrence of AI infection, was determined, where the relative risk was 1.17 and the magnitude of this association = 0.12 (attributable risk) i.e. 12 % of infection probably owing to migratory birds.

Key words: Avian influenza, transmissibility, migratory birds and risk factors

Introduction

In recent years, several large epidemics have occurred with serious socioeconomic consequences (Spackman *et al*., 2002 and Boender *et al*., 2007) as, in the case of highly pathogenic avian influenza viruses of the H5 and H7 subtypes, also with possible public health implications (Munster *et al*., 2005). Improved understanding of the factors facilitating the introduction and subsequent spread of these viruses is crucial for effective control. Over the past decade, the emergent HPAI viruses have shifted to increased virulence for chickens (Saad *et al*., 2007). HPAI viruses typically produce a similar severe, systemic disease with high mortality in chickens and other gallinaceous birds. However, these same viruses usually produce no clinical signs of infection or only mild disease in domestic ducks and wild birds.

On 17 February 2006, the Egyptian government confirmed that bird flu had broken out in the nation's poultry. With the international spotlight beaming upon it, the government did not want to look unprepared or, worse, at fault. So it immediately responded by blaming migratory birds and traditional poultry practices. In less than a month, the Egyptian government effectively destroyed its multi-billion dollar poultry industry, the livelihoods of millions of Egyptians and its ancient poultry practices and biodiversity. Approximately 70 percent of all broilers are produced by medium- to large-scale commercial enterprises. The rest is produced by small-scale, essentially noncommercial, village farms. More than one-third of Egypt's farmers keep a flock of about 20 birds. Farmers raise local chicken breeds which are well adapted to low nutritional standards, summer heat, and harsh environment.

In this paper we have presented an analysis and suggestion of the spatial transmission dynamics of the highly pathogenic avian influenza virus in Egypt. As the main source (s) and the specific transmission route responsible for infection are unknown, especially for all of the infected farms in the governorates. We have adopted a phenomenological approach, trying to investigate the dynamic of the epidemic occurrence.

Materials and Methods

A striking characteristic of the 2006 epidemic was that most of the infected farms were spread to 21 governorates, 5 of them with a high density of poultry farms. In all, 826 districts containing commercial flocks

became infected during a period of 4 months (Fig. 1). The industry estimates that 50% of the commercial farms in the country have been infected and that over 25 million chickens have been slaughtered.

Methods

1 For estimation of the model parameters, we use the data set that was collected during the outbreaks the of highly pathogenic H5N1 avian influenza virus in the Egyptian Governorates in 2006 (Egyptian reference laboratory, Ministry of Agriculture).

A The presence of influenza A specific RNA was detected through the reverse transcription-polymerase chain reaction (RT-PCR) which targets fragments of the M gene, the most highly conserved genome segment of influenza viruses (Boender *et al*., 2007 and Stegeman *et al*., 2004), or the nucleocapsid gene. When a positive result is obtained, RT-PCRs amplifying fragments of the haemagglutinin gene of subtypes H5 and H7 are run to detect the presence of notifiable AIVs (Stegeman *et al*., 2004). PCRs and other DNA techniques are being designed for the detection of Asian lineage H5N1 strains (Halvorson, 2002). Non-H5/H7 subtypes can be identified by a canonical RT-PCR and subsequent sequence analysis of the HA-2 subunit (Lisa *et al*., 2006 and Lee *et al*., 2006).

2 To explain the observed patterns of infection of highly pathogenic avian influenza virus between governorates, and to be able to evaluate the potential effectiveness of control measures, we adopt a modeling approach similar to those have been used in modeling studies of the interfarm spread and the effectiveness of control measures during the HPAI epidemic in the Netherlands in 2003, with required modification (Boender *et al*., 2007.

A The transmission parameter ß (i.e., the average rate at which infected flocks infect susceptible flocks in a population consisting almost exclusively of susceptible flocks) according to: (Becker, 1989 and Sturm-Ramirez *et al*., 2004) with required modification.

B. The infectious periods (T) between various districts were calculated as described above, on the basis of the moment of detection and the moment of culling or stamping out. Rh was calculated as the product of the estimates of the transmission parameter and the infectious period:

Results and Discussion

Time spreading pattern of epidemic, Egypt 2006: The infection was spread to 21 governorates, 5 of them with a high density of poultry farms. In all, 826 districts containing commercial flocks became infected during a period of 4 months (Fig.1).

Foci of infection

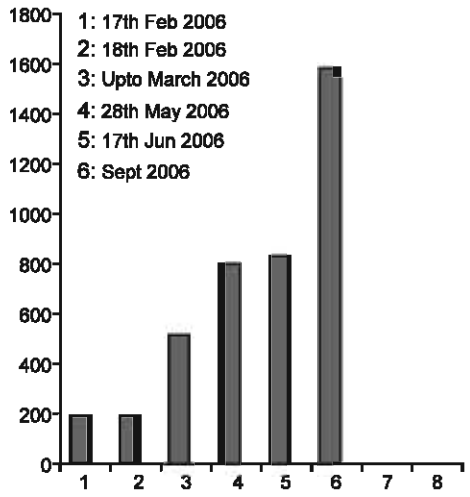

Fig. 1: Time spreading-pattern

Geographic maps for the spread of highly pathogenic avian influenza virus had been stroked Egypt 2006 (Fig.2): The present study allows us to produce suggested geographic maps for the spread of highly pathogenic avian influenza virus had been stroked Egypt 2006. These maps are based on the calculation of a local reproduction number, and are constructed so as to apply to a given intervention strategy.

Trial for quantification the between-flock transmission characteristics (infectious period and transmissibility) of the HPAI H5N1 strain of the first outbreak of AI in Egypt in 2006.

We carried out a trial for quantification the between-flock transmission characteristics (infectious period and transmissibility) of the HPAI H5N1 strain of the first outbreak of AI in Egypt in 2006. Virus transmission apparently not decreased considerably during the outbreak and there is a strong indication that the infectious period increased after the culling of infected flocks. As a consequence, *Rh* increased quite strongly during such period of AI, This increase is probably a consequence of the control measures implemented. Unfortunately, it was not possible to establish the contribution of individual measures to the overall reduction of virus transmission.

Due to the late effective control measures less effective farm biosecurity measures gotten failure in reducing transmission, the estimates of the reproduction ratio were still more than 1. This suggests that the control measures were probably not sufficient to halt the epidemic. In fact, containment of the epidemic may have been due to the depletion of susceptible flocks as a result of culling rather than to a decrease in the transmission rate. Therefore, the main value of the control measures may be in preventing the spread of

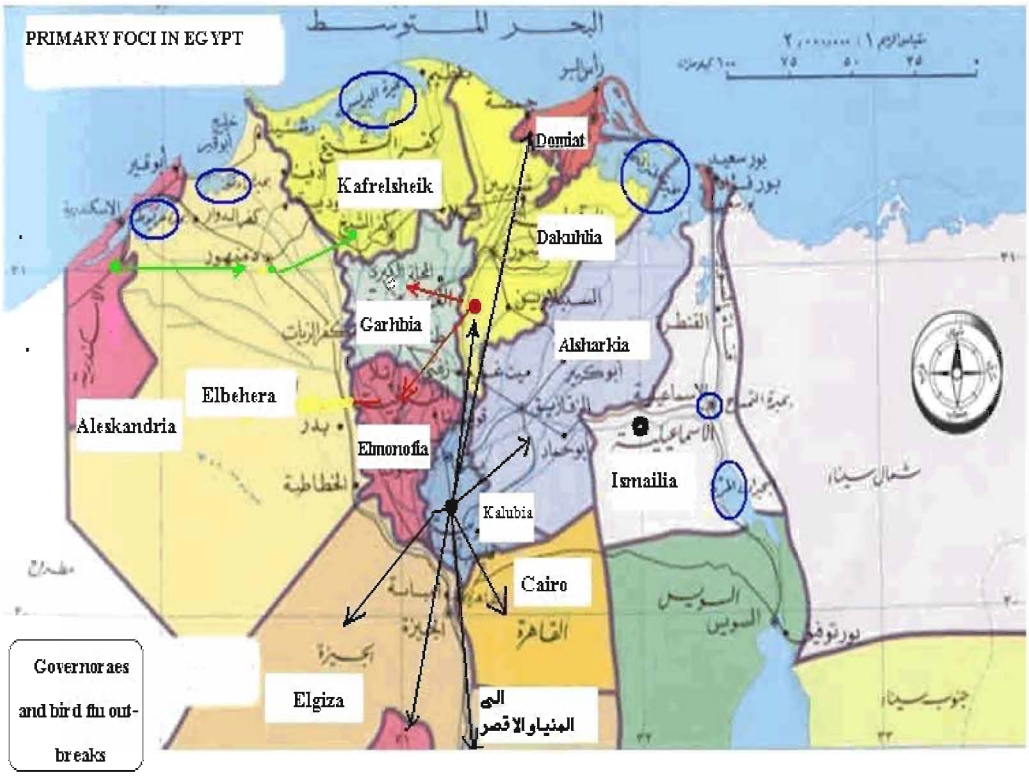

Fig. 2: Geographic maps for the spread of highly pathogenic avian influenza virus had been stroked Egypt 2006

virus to unaffected areas rather than in preventing the spread of virus within an area. This may be especially significant for areas with a high flock density, such as El-Qualubia , Al-Sharkia El-Giza ---- (mean flock density, more than 8 flocks / km^2), where an epidemic may be impossible to stop once it has taken off specially in the absence of effective biosecurity and transport banning. In Italy, where an outbreak of HPAI H7N1 virus spread quickly and extensively and could be controlled only by the depopulation of nearly all flocks in the affected area of 5500 km^2 (Thompson *et al.,* 2002).

The transmission parameters ß varied in-between the districts in the various governorates. It was ranged from 23 days to 87 days. Governorates of heavy poultry farms density have less periods for the transmission of the virus from district to another. Qualubia governorate had lowest transmission period (2 , 3 days) followed by Dukahlia and El Sharkia governorates 7, 3 and 7, 7 respectively .

It was found a non-significant correlation between the square area of the governorate and parameter ß of transmission (r = 0.055). Also there was a positive significant correlation between such parameters and the activity of the transporting traffic of poultry between the districts of the same governorate and to other governorates (r = 0.66 at P<0.01) (Fig. 3) .

Concerning the parameter (T), it was ranged from 0. 36 day to 27.6 days. But these parameters depend on the density of the farms in the districts or the governorate. i.e. when the density of the farms increases ,the infectious period in-between flocks or farms increases as well in the same district or governorate as in case Qualubia , Sharkia and Giza where the T parameter was 0.55 ,0.36 and 0.79 respectively.

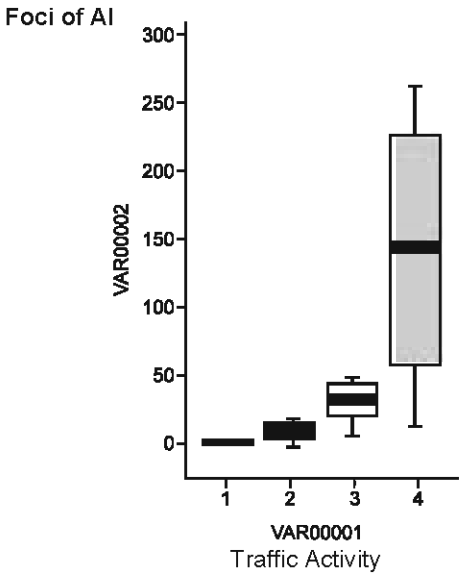

Fig. 3: Correlation between traffic activity and transmissibility of foci of AI

Table 1: The transmission parameter (ß), infection period (T) and reproductive ratio (Rh) of Governorates

Governorate rate	No. of infected districts	No. of infected flocks	β	T	Rh
Al-monofia	8	33	9.70	2.60	
Al-Gahrbia	8	49	8.75	1.43	
Alexanderia	3	10	24.30	7.30	
Luxor	1	2	22.00	11.00	
Cairo	5	8	12.40	7.75	
Beni-Sweif	1	1	5.00	5.00	
Al-Fayoum	5	19	13.00	3.42	
Sohage	3	3	27.70	27.60	
Dammeiata	3	11	17.00	6.64	
El-Behhera	8	25	9.60	3.10	
Al-Dukahlia	8	44	10.60	1.93	
Al-Sharkkia	13	267	7.30	0.36	
El-Giza	11	107	7.70	0.79	
Kafer-Elsheikh	4	16	11.00	2.75	
Al-Qualubia	7	183	14.40	0.55	
Al-Issmailia	3	6	3.20	1.16	
Assuite	4	3	8.75	11.70	
Quena	1	1	87.00		
Asswan	1	1	8.00		
El-Mainia	6	30	13.60	2.73	

Rh >1

In the Gelderse Vallei, for AI epidemic in Netherlands 2003, the infectious period decreased from 13.8 days (95% CI, 9.9–17.6 days), for the 5 flocks suspected to have AI on the first day of detection, to 7.3 days (95% CI, 3.4–11.1 days), for the period after detection. In Limburg, the infectious period for the first 2 affected flocks was 7 and 9 days. During the period after detection, the average infectious period was 6.9 days (95% CI, 3.9–9.9 days). Rh between-flock transmission decreased significantly after virus detection, was still <1 (R =1.2 for both areas) suggested that the control measures were inadequate to interrupt the chain of infection. The containment of the epidemic was, therefore, probably due to the reduction in the number of susceptible flocks caused by depopulation of the infected areas rather than to the reduction of the transmission level by the other control measures (Sturm-Ramirez *et al.*, 2004; Thompson *et al.*, 2002 and Boender *et al.*, 2007).

Our results indicate that outbreaks of HPAI viruses are difficult, if not impossible, to control with usual measures in poultry-dense areas (Council of the European Communities, 1992), and effective control could be achieved only by depopulation of the whole affected area. Moreover, new outbreaks appeared, because AI virus strains are became endemic in Egypt (Alexander, 2000). It might be worthwhile to consider reducing the flock density of commercial flocks, to reduce the probability of another epidemic of this size, or to consider vaccinating poultry, as an additional control measure. Vaccination was used in outbreaks of LPAI in Italy in 2000–2002 (Capua and Marangons , 2003) and in Utah in 1995 (Gilsdorf *et al.*, 2003) and in an outbreak of HPAI in Mexico in 1994 (Arriola , 2000). Vaccination significantly reduces the excretion of virus, which may reduce virus spread in an infected area, thereby reducing the risk of human exposure. The risk of the introduction of AI virus into poultry from wild waterfowl might be reduced by keeping poultry indoors. However, this might be unacceptable to the general public, which prefers the idea of free-range poultry for (presumed) welfare reasons.

On the one hand, it is highly unlikely that vaccination can be effective once a highly pathogenic virus has successively been introduced in a densely populated poultry region. The reason is that it takes at least a week to vaccinate all susceptible poultry and an additional 7-14 d before a vaccine produces effective protection against infection and subsequent transmission. This time span would give the virus ample opportunity to spread throughout the area.

On the other hand, vaccination is increasingly being considered as a possible tool to prevent the successful introduction of the disease in certain high- risk areas in case a highly pathogenic virus has been detected at a certain distance from the area of out-break.

1 Infection probabilities increased towards other governorates of active poultry transports (i.e., from Qualubia to Sharkia) but not due to the factor of the distance between the governorates.
2 The probability of infection is strongly increases: I) In districts of the same governorates when the poultry farm density of heavy character as in case of Qualubia and Sharkia governorates. ii) Probability of infection is strongly decreased in governorates of low poultry farm density as in case of Quena, Aswan, and Sohage - governorates.

Table 2: The association between the presence of the migratory birds and the occurrence of AI infection

Infection		No Infection			
A :Number of governorates	10	B :Number of governorates	2	Exposure	[Presence of Mig.birds]
C :Number of governorates	10	D :Number of governorates	4	Not Exposure	[Absence of Mig. birds]

Relative Risk = 1.17, Attributable Risk = 0.12, $\Omega = 3.3$

Table 2 reveals that, there was an association between the presence of the migratory birds and the occurrence of AI infection, where the relative risk was 1.17 and the magnitude of this association = 0.12 (attributable risk) i.e. 12 % of infection probably owing to migratory birds. On the other hand, Omega magnitude = 0.33 i.e. the probability of infection reduction will be decreased in a percentage of 33% in the absence of migratory birds.

The US Naval Medical Research Unit No. 3 and the Ministry of Environment of Egypt have collaborated since 2003 in obtaining samples from migratory birds to detect circulating influenza viruses. During the 2005–06 migratory birds season, 1,304 migratory birds were sampled from either live bird markets or cage birds trapped by fishermen in Port Said, Damietta, Fayoum, Arish, and Sharm el Sheikh (Promkuntod *et al*., 2006).

A total of 203 cloacal swab samples were positive for influenza A virus matrix gene when tested by real-time PCR, and 2 were also positive for the hemagglutinin 5 (H5) gene by using specific primers. Of the 2 migratory birds positive for the H5 gene, the first was a common teal (*Anas crecca*) captured in the Nile Delta region of Damietta in October 200). Sequencing of the H5 gene showed that this virus was an LPAI most closely related to strain A/mallard/Bavaria/1/2005(H5N2) (GenBank accession no. DQ387854 (Muramoto *et al*., 2006).

In January 2006, influenza A H5 virus (weak positive result) was detected in another common teal (trapped in a cage by a fisherman) sampled from the Damietta region in December 2005. The low viral load, coupled with the failure to isolate the virus, precluded the laboratory from conducting sequence analysis at the time on the basis of insufficient template material. After the outbreak of influenza A (H5N1) in poultry and humans in Egypt in February 2006, additional retrospective attempts to concentrate RNA were used to assess potential introduction scenarios. After multiple RNA extractions were conducted and the RNA was concentrated, this specimen was found to be positive for the neuraminidase 1 (N1) gene by real-time PCR. (Promkuntod *et al*., 2006 and Normile, 2006) suggested that an HPAI virus may have been introduced into Egypt through a migratory bird. Whether poultry were infected before mid-February or the teal was infected with influenza A (H5N1) virus by a domesticated species is not unknown.

Wild migratory birds are reservoirs for low pathogenic avian influenza (LPAI) viruses (Alexander, 2000), but their role in transmitting highly pathogenic avian influenza (HPAI) viruses is hotly debated and unclear (Muramoto *et al*., 2006; Swayne, 2007; Gasimov *et al*., 2006). Beginning in July 2005, a clade of HPAI (H5N1) viruses rapidly expanded from an apparent focus in western People's Republic of China and spread to the Middle East, Africa, and Europe (Van der Goot *et al*., 2005). Genetic analysis of HPAI virus isolates from dead wild birds along major flyways indicated that the strains were closely related to the Qinghai H5N1 A/bar-headed goose/Qinghai/65/2005 virus (clade II) (GenBank accession no. DQ095622). In addition to transmission to domestic poultry, HPAI (H5N1)–infected mute swans have been implicated in direct transmission to humans in Azerbaijan (Fouchier *et al*., 2003).

Our results, suggested that there were high risk factors contributed to the major epidemic of HPAI have been happened in Egypt 2006, summarizes as follows:

1 In high poultry –dense areas targeted control strategies (culling within a ring of 1-2 km around affected premises were unlikely to be effective or satisfactory in containing the epidemic.
2 Banning for poultry and their products between the different districts and governorates was taken after deletion.
3 Vaccination as targeted control strategies was strongly delayed as a prophylactic measure in free areas.
4 Moreover, the vaccinated strain (H5 N1) which used is confirmed to be unfavorable to freeze the spread of the epidemic. (H5N2) strain had to be used for vaccination instead of (H5N1).
5 Lack in the application of Biosecurity programs at the both levels Farms and Governorates.
6 During or at the beginning of the epidemic ,there were none or hardly any control measures in place, and detection of the infected farms was still imperfect and slow .

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