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Modeling the spread of bird flu and predicting outbreak diversity

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Abstract

Avian influenza, commonly known as bird flu, is an epidemic caused by H5N1 virus that primarily affects birds like chickens, wild water birds, etc. On rare occasions, these can infect other species including pigs and humans. In the span of less than a year, the lethal strain of bird flu is spreading very fast across the globe mainly in South East Asia, parts of Central Asia, Africa and Europe. In order to study the patterns of spread of epidemic, we made an investigation of outbreaks of the epidemic in one week, that is from February 13–18, 2006, when the deadly virus surfaced in India. We have designed a statistical transmission model of bird flu taking into account the factors that affect the epidemic transmission such as source of infection, social and natural factors and various control measures are suggested. For modeling the general intensity coefficient \( f(r) \), we have implemented the recent ideas given in the article \textit{Fitting the Bill}, \textit{Nature} [R. Howlett, Fitting the bill, Nature 439 (2006) 402], which describes the geographical spread of epidemics due to transportation of poultry products. Our aim is to study the spread of avian influenza, both in time and space, to gain a better understanding of transmission mechanism. Our model yields satisfactory results as evidenced by the simulations and may be used for the prediction of future situations of epidemic for longer periods. We utilize real data at these various scales and our model allows one to generalize our predictions and make better suggestions for the control of this epidemic.

\textit{MSC}: 37N30; 37N25

\textit{Keywords}: Bird flu; Mathematical model; Epidemiology; Predicting outbreak diversity

1. Introduction

Bird flu also known as avian influenza is an infection caused by a virus known as \textit{orthomyxoviridae} in virus classification [55]. Influenza virus has only one species in it, which is called influenza A virus. These influenza viruses occur naturally among birds. Wild birds worldwide carry these viruses in their intestine but usually do not get sick from them. However, avian influenza is very contagious among birds and can make some domesticated birds including chickens, ducks and turkeys very sick and kill them [20,24,30,43]. Infected birds shed influenza viruses from their saliva, nasal secretions, etc. Susceptible birds become infected when they come in contact with the contaminated surfaces. Domesticated birds may become infected with avian influenza viruses through direct contact with infected waterfowl or other infected poultry [24,28,38] or through contact with surfaces (such as dirt or cages) or materials (such as water or food) that have been contaminated with the virus [1,15,39,45,49].

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Infection with bird flu viruses in domestic poultry causes two main forms of disease that are distinguished by low and high extremes of virulence. The “low pathogenic” form may go undetected and usually causes only mild symptoms (such as ruffled feathers). However, the highly pathogenic form spreads more rapidly through flocks of poultry. This form may cause diseases that affect multiple internal organs and has a mortality rate that reaches 90–100% often within 48 hours [8].

In 2006, the High Security Animal Disease Laboratory in Bhopal confirmed genetic signatures of the virus in eight samples of dead poultry tissues that it had received from Navapur in Nandurbar district near the Maharashtra–Gujarat border. For more than two years, the virus has ravaged poultry and caused human illness and death in many Southeast Asian countries and China. Between April and June 2005, a large number of wild water birds at Qinghai Lake in western China perished after being infected by the virus. During, July–August 2005, outbreaks involving the virus were reported from Mongolia, Siberia and Kazakhstan. The virus reached Turkey, Croatia, Romania and Greece by October 2005. The virus was infecting chicken and humans in northern Iraq by January 2006. In early February 2006, Nigeria became the first African nation to report the bird flu virus, with an outbreak at a large commercial poultry farm. In February 2006, many European countries, Egypt and Iran found wild birds infected with H5N1 virus [12,14,15,23,26,40,42].

Avian influenza or bird flu can result in immediate and severe disaster, for example, the outbreak in USA [48] in 1983–1984 led to destruction of more than 17 million birds at a cost of nearly US $56 million [21]. Similar case again happened in Hong Kong in 1997–1998 [12,15,38,39,42]. Therefore rapid and effective measures must be taken to stop the spread of epidemics. The most effective measures to prevent the transmission of bird flu are rapid destruction of all infected or exposed birds, proper disposal of carcasses and excrement, the quarantining and rigorous disinfectioning of farms and timely use of vaccine [4,25,35,36,50]. The information relating to the spread of this epidemic in Canada may be obtained from the website [3].

In general, the influenza virus or flu virus can be classified into three categories: types A, B and C, which are distinguished by differences in two major internal proteins. Influenza virus type A is the most significant epidemiologically and the most interesting from an ecological and evolutionary stand point, because it is found in a wide variety of bird and mammal species [9,41] and can undergo major shifts in immunological properties. Type B is largely confined to humans and very little is known about type C. Type A virus is responsible for causing bird flu, which was first found in Italy in 1878. Type A virus is further divided into subtypes based on differences in membrane proteins HA and NA, which are the most important targets for the immune system. The notation H_hN_n is used to refer to the subtype comprising the _hth discovered HA proteins and the _nth discovered NA protein. The subtype H5N1 virus of type A virus is the main cause of the bird flu [12,15,23,31,42]. Subtype is further divided into strains; each genetically distinct virus isolated is usually considered to be a separate strain [11,33].

According to the research of World Health Organization (WHO), the transmission mode of bird flu can be divided into following two types [21]:

- spread from one farm to another within a country and
- spread from country to country.

Generally, the virus resides in bird droppings, contaminated soil and airborne virus. Contaminated equipments, vehicles, food, cages and clothing like shoes can carry the viruses from farm to farm. Some evidence suggests that flies can also act as mechanical vectors [18]. Wet markets where live birds are sold under crowded and sometimes unsanitary conditions can be another source of spread. These constitute the main cause of the former transmission. Export and import of poultry products are the main cause of the latter transmission, since they can carry the viruses for long distances freely when artificial factors are prevented. Migratory birds can also be a cause of transmission between the countries [5,27]. Efforts have been made on the study of avian influenza and most of the recent papers focus on topics such as the route of transmission, physiological and biological properties, etc. The bird flu virus of low pathogenicity can mutate into highly pathogenic one after a short time; the virus is sensitive to temperature change (it was found that the virus survives for shorter time at a higher temperature). This kind of influenza is able to transmit to humans under some circumstances (http://www.who.int/mediacentre/factsheets/fs277/en/) [6,7,21,44,47,52]; however, no sufficient and clear evidences of human-to-human transmission have been found up to now [21]. Among these researches, an important approach to study bird flu is to establish a statistical transmission model, from which the general trends of epidemics can be predicted, and the effect of various control measures can be assessed
To cite successful examples, model for foot-and-mouth disease has successfully controlled the epidemic in 2001 in UK [46]. In 2003, model for severe acute respiratory syndrome (SARS) has reached the similar objectives [16,34]. Likewise, we expect our statistical transmission model of bird flu will also reach its objective.

In order to study the patterns of the spread of epidemic, we have made an investigation of outbreaks of the epidemic in one week during February 13–18, 2006 till it reached India.

2. Investigation of bird flu in a week

The actual data for outbreaks of bird flu in a week have been taken from an article of The Indian Express published on February 19, 2006. On February 18, 2006 the lethal strain of H5N1 virus surfaced in India in the trivial pocket of Navapur in Nandurbar district of Northern Maharashtra. It was the sixth day of our study. On Monday, the first day, outbreaks occurred in five countries of Africa and Eastern Europe namely Nigeria, Greece, Slovenia, Romania and Bulgaria. On the second day bird flu hit four nations of Southeast Asia, Central Asia and Europe namely Indonesia, Iran, Austria and Germany. On the third day, outbreaks took place in two European countries, Hungary and Italy. On Thursday, new cases of bird flu were found in three European and African countries, Switzerland, Denmark and Egypt. Reaching France on Friday, bird flu, at last, on Saturday surfaced in India (Fig. 1).

We investigated many related reports on bird flu and collected some important information that became a base for our model, which is described below.

In general, the outbreak of an infectious disease is dependent upon three necessary conditions as the source of an infection, the route of transmission and the herd susceptibility [21]. Other social and natural factors also play an important role in the transmission of infection, for example, the control measures and the change in temperature. The source of infection that led to the outbreak is not clear. In some researcher’s view migratory birds are thought to be carrying the virus [5,27]. If migratory birds had brought the virus one would have expected outbreaks well before February as bird’s migrations were over by around November. So we consider in our problem the source of outbreaks of bird flu to be the transportation of infected poultry as globalization has turned the chicken into the world’s number one migratory bird species. We have assumed that it is mainly the human activities of commerce and trade that this epidemic has spread. For implementing this we have considered the concerns expressed by scientists from Max Plank Institute for Dynamics and Self Organization, Germany [19]. They have recognized the statistical characteristics of

![Fig. 1. Outbreaks of bird flu in a week during February 13–18, 2006.](image-url)
human travel independent of the means of transportation people use for the modeling of the spread of epidemics as published in the article [19].

Also, we acquired some of the important information about bird flu such as, the virus H5N1 is sensitive to temperature changes, and the virus survives for shorter time at a high temperature. Also there are many effective control measures to block the virus transmission such as compulsory vaccination, culling of all infected or exposed birds [2]. Indeed, in the absence of such control mechanisms this avian influenza may pose a big threat to global health care [10,17,29,32,37,51,53,54].

3. Modeling bird flu

We know the major factors that play an important role in the transmission of bird flu are the way the infected poultry products are transported, air temperature, the control measures (for example, culling the poultry in the infected form, introducing compulsory vaccination to enhance the resistibility of poultry in the non-infected farms forbidding live birds being sold under crowded and unsanitary conditions, etc.), migratory birds and other infected transportation vehicles (which means the vehicles carry infected poultry or bird dropping or contaminated soil, etc.). Also there are some other factors not considered in our model, viz. bird flu transmitting to human beings, viruses of low pathogenicity mutating into high pathogenicity after some time, etc. since these elements will not contribute much to the usual transmission of bird flu [22].

How do these factors affect the transmission? The infected animals are the source of the infection, higher air temperature can drastically cut down the lifetime of the virus, and transportation of infected poultry is the route of transmission. Control measures such as active and effective actions play an important role in preventing and destroying the epidemics, which can effectively block the route of transmission of the infection, diminish the source of infection and promote the resistibility of susceptible poultry [21]. So we must take all the major factors into account in the formulation of our transmission model.

These factors may be reflected in the following parameters:

- $N(n)$ is the total number of regions of outbreak on the $n$th day.
- $D(n)$ is the lifetime of the virus regarding the $n$th day since the beginning of the epidemic which implicitly corresponds to air temperature.
- $I(n)$ is the resistibility of the poultry on the $n$th day since from the beginning of the epidemic many of the above control measures objectively promote the resistibility of poultry and even human beings.
- $f(r)$ is the distribution of the probability that infected poultry products are transported a distance $r$.

The following are necessary assumptions for our model:

Let $P(n, r)$ represent the probability for a new outbreak to take place, then

$$P(n, r) \propto N(n),$$

$$P(n, r) \propto D(n),$$

$$P(n, r) \propto 1/I(n),$$

$$P(n, r) \propto f(r).$$

Considering the above assumptions, we obtain our proposed model for transmission of bird flu as under:

$$P(n, r) = f(r) \cdot R \cdot D(n) \cdot N(n) \cdot \frac{1}{I(n)},$$

where

$$f(r) = r^{-(1+\beta)}.$$

$\beta$ is taken close to 0.6 [22] and $R \in [0, 1]$ is a random float number.
4. Methodology

In this section, we have discussed the methodology that we have used for simulation experiments. We first discuss, one by one the various parameters taken in our model. Also we explain, how we have computed these parameters and finally how we have given the methodology used to predict a new outbreak with the help of a flowchart suggested by Li et al. [21].

- In our model, we have used the random float number \( R \) which we have generated in our program by using random number generator. Why do we need \( R \) in our model? As we know the outbreak of bird flu is a probabilistic instance and not a deterministic one, even though \( f(r) \), \( D(n) \), \( N(n) \) contribute much to \( P(n, r) \), we cannot definitely assure that there will be a certain outbreak of bird flu in a region but can only say that there is enormous possibility or danger for an outbreak to take place. So an additional random parameter \( R \) is introduced to reflect the uncertainty.

- \( D(n) \) denotes the lifetime of the virus of bird flu on the \( n \)th day. As a matter of fact we only have the data of survival duration of the virus obtained from the website (http://www.who.int/asr/don/2004_02_18/en/). The H5N1 virus can survive at cool temperatures in contaminated manure for at least three months; in water, the virus can survive for up to 30 days at 0°C; about four days at 22°C; about 3 hours at 56°C and only 30 min at 60°C [21]. By means of fitting the above data by curve fitting method, we obtained an approximate formula as follows:

\[
D(t) = e^{3.4 - 0.0915t^{1.1}},
\]

where \( t \) represents the air temperature.

In our simulation, we studied the epidemic for one week till it reached India, that is for a short duration. Hence the temperature change may be taken as a linear approximation regarding the epidemic duration, that is,

\[
t(n) = t_1 + t_2n,
\]

in which \( t_1 \) and \( t_2 \) are two constants that can be determined by fitting the average temperature of the various countries through which the virus reached India. In this model \( t_1 = 0.2 \) and \( t_2 = 2.2286 \) (started on February 13, 2006). So the relation between the lifetime of the virus and the epidemic duration shall be a compound form of (2) and (3) as

\[
D(n) = e^{3.4 - 0.0915(0.2 + 2.2286n)^{1.1}}.
\]

- \( I(n) \) stands for the resistibility of poultry on the \( n \)th day. Obviously the resistibility will increase with the artificial interventions and the control measures. We assume the increase abides by law similar to Sigmoid function \( 1/(1 + e^{-x}) \). Thus \( I(n) \) assumes the following form:

\[
I(n) = \frac{B}{1 + (B - 1)e^{-n/C}}.
\]

Apparently, this is a modified sigmoid form. When \( n = 0 \), \( I(0) = 1 \), and when \( n = \infty \), \( I(n) = B \); which indicates the resistibility is impossible to approach a very big number [21].

- \( f(r) \) is the distribution of the probability that infected poultry products are transported a distance \( r \). The basic idea for taking the above mentioned form of \( f(r) \) stems from Howlett [19]. The researchers at Max Planck Institute for Dynamics and Self Organization have used the dispersal of dollar bills within the United States as a proxy measurement of human movement (since people cannot be tracked while banknotes travel with the people). They analyzed the data on the peregrinations of more than half-a-million US dollar bills recorded over a five-year period on an online bill-backing system (http://www.wheresgeorge.com) and give a simple model that only depends upon two parameters. Since the poultry products are also imported and exported very frequently, to various countries, we can assume its transport to be very similar to the human movement. So the probability that

\[
f(r) = r^{-(1+\beta)}
\]
infected poultry product is transported from the farm may assume a distance \( r \), for \( r \) larger than 10 km with \( \beta \) close to 0.6.
This distribution behaves like a power law. This function decreases as \( r \) grows larger, meaning that transportation of poultry over a long distance is less common than short ones. However, it does not decrease as fast as other common probability distributions, which means that transportation over long distances are still common enough to have a significant effect. Poultry products make many short journeys, but the occasional long haul ensures that they disperse widely.
• A threshold value \( S \) is necessary which acts as a criterion: when \( P(n, r) \) is greater than \( S \) there will be an outbreak; otherwise not. However, how to determine the possible number of outbreaks per day denoted by \( K(n) \)? Intuitively, \( K(n) \) shall be in direct proportion to \( N(n) \); however, since only the nearest several outbreaks have notable contribution to the probability of a new outbreak a number of distant outbreaks contribute little, so dependent relation of \( K(n) \) upon \( N(n) \) is of the form [21]

\[
K(n) = AN(n)^b,
\]

where \( A \geq 1 \) and \( 0 < b \ll 1 \), that is, \( K(n) \) increases slowly with the augment of \( N(n) \).

Thus the method for predicting an outbreak is explained with the help of an algorithm given in Fig. 2.

We provide a short description of the algorithm. Suppose the epidemic has begun, we compute the number of actual outbreaks on the \( r \)th day. First we generate \( K(n) \) according to (6). Then we calculate each \( P(n, r) \) according to (1); when \( P \geq S \), a new outbreak will take place, otherwise not. So, the total number of new outbreaks is always less than \( K(n) \).

In our model, there are six parameters \( \beta, A, b, B, C \) and \( S \) which are all adjustable. So one may argue that too many adjustable parameters may not be an advantage for a “good” model. However, we must analyze independence of these parameters. Here \( S \) is not an independent parameter, rather dependent on \( f(r) \), hence on \( \beta \). Parameter \( A \) controls the initial possible number of outbreaks the epidemic may abort if \( A \) is too small and overflow if \( A \) is large. So there shall be a proper intermediate value for \( A \). \( b \) denotes the general trend of the outbreaks, the total number of outbreaks will grow too rapidly to be practical if \( b \) is a big number and may be too flat if \( b \) is too small. \( B \) determines the ultimate resistibility, which reflects the final degree of stringency of artificial interventions; the greater \( B \) is the more stringent the interventions are. As of \( C \), it reflects the average degree of stringency throughout the epidemics; the smaller \( C \) is the more stringent the control measures are. In other words, \( B \) determines the final height of the curve \( I(n) \) and \( C \) controls the shape or the process of \( I(n) \).

Therefore each parameter has a definite meaning and a specific role and has little overlap regarding the role, so the model is reasonable.

For conducting simulations we have assumed distances: \(< 500 \) miles as 10 units, 500–1000 miles as 11 units, 1000–1500 miles as 12 units and 1500–2000 miles as 13 units and so on.

5. Simulation results

The parameters are initialized as the beginning: \( N_0 = 6 \) refers to the total number of days (for which study is conducted) the epidemic lasts. \( N(1) = 5 \) means there are in all five cases of new outbreaks on the first day. The other parameters \( A, b, B, C \) and \( S \) will be determined in the simulation by comparing with the actual epidemic data.

Results of simulation are shown in Figs. 3 and 4. The values of the related parameters are

\[
\beta \approx 0.6, \quad A = 2, \quad b = 0.33, \quad B = 10, \quad C = 1.75, \quad S = 0.1.
\]

It is easy to see that the simulation is roughly in accordance with the actual situation. The parameters related to the artificial interventions include \( B \) and \( C \). If \( B \) is large, the epidemic can take place few times in most simulations; if \( B \) is very small, the epidemic can always happen and most times the overflow can happen. As for \( C \), if it is small enough, the epidemic hardly takes place, otherwise it can almost happen. Therefore the effective, powerful and stringent control measures are the key to stop the epidemics.

It should be pointed out that the parameters in the model are independent of each other, since each of them plays an independent role. These parameters have definite meaning, so the result of simulation can hardly coincide with the actual situation of the epidemic if the parameters cannot be adjusted to proper values.

Simulation results are presented in Table 1. It is clear from the table that the probability of new outbreak to occur decreases with the increase of distance from the source countries. The probability of occurrence of outbreak in India is very low because the flu virus reaches on the sixth day and also the country is far from the source country. The probability of occurrence of outbreak in Indonesia is also very low even on the second day. This is due to very large distance from the source country and also due to some other factors (like temperature). Figs. 3 and 4 show the pattern,
Fig. 3. Graph of probability of outbreak vs the distance from the source country.

Fig. 4. Graph of the probability of outbreak at a fixed distance vs number of days.

that the probability of outbreak to take place follows, depending upon the distance and number of days. These graphs show that the probability of outbreak is inversely proportional to the distance from the source country as well as the day on which the flu virus reaches the country.
Table 1

| Number of days (n) | Distance from source (r) | Probability of outbreaks (P) | Countries where outbreak occurred |
|--------------------|--------------------------|-----------------------------|----------------------------------|
| 2                  | 10                       | 0.94457699419187            | Austria, Germany,                |
|                    | 13                       | 0.391542652502286           | Iran                             |
|                    | 21                       | 0.143943139163055           | Indonesia                        |
| 3                  | 10                       | 0.87773439670344            | Italy                            |
|                    | 10                       | 0.814356026695878           | Hungary                          |
| 4                  | 10                       | 0.579586050504416           | Switzerland,                     |
|                    | 11                       | 0.333808020423165           | Denmark                          |
|                    | 11                       | 0.400400629162276           | Egypt                            |
| 5                  | 11                       | 0.37625988883904            | France                           |
|                    | 10                       | 0.292578722560819           | Bulgaria                         |
| 6                  | 16                       | 0.140831538038502           | India                            |

6. Conclusions and discussion

Bird flu is a highly pathogenic epidemic that can result in serious disaster in many areas. Immediate and effective control measures are of great importance in preventing the transmission of avian influenza. So it is challenging to study it from various angles, and develop statistical–mathematical transmission models [21]. In this research, we put forward a statistical transmission model, which exhibits satisfactory results verified through simulations. These results may be used for the prediction of the future situation of the epidemics. Meanwhile (as many control measures have been taken into account in the formulation of the model) if the actual effect of these measures are assessed, then useful and effective control measures can be proposed for the prevention of the epidemic. From Figs. 3 and 4, it is found that the probability of outbreak is inversely proportional to both the distance from the source country and the number of days at a fixed distance.

Our ongoing investigations relate to the question of how to assess the actual control measures and assign the parameters in the model with proper numerical values.

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