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Review Article

Risk factor modelling of the spatio-temporal patterns of highly pathogenic avian influenza (HPAIV) H5N1: A review

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ABSTRACT

Highly pathogenic avian influenza virus (HPAIV) H5N1 continues to impact on smallholder livelihoods, to constrain development of the poultry production sector, and to cause occasional human fatalities. HPAI H5N1 outbreaks have occurred in a variety of ecological systems with economic, agricultural and environmental differences. This review aimed to identify common risk factors amongst spatial modelling studies conducted in these different agro-ecological systems, and to identify gaps in our understanding of the disease's spatial epidemiology. Three types of variables with similar statistical association with HPAI H5N1 presence across studies and regions were identified: domestic waterfowl, several anthropogenic variables (human population density, distance to roads) and indicators of water presence. Variables on socio-economic conditions, poultry trade, wild bird distribution and movements were comparatively rarely considered. Few studies have analysed the HPAI H5N1 distribution in countries such as Egypt and Indonesia, where HPAIV H5N1 continues to circulate extensively.

1. Introduction

Highly pathogenic avian influenza virus (HPAIV) type H5N1 causes a highly contagious disease of poultry that was first observed in the province of Guangdong, China, in 1996 (Xu et al., 1999). For several years, it was only recorded in China and Hong Kong where it resulted in human morbidity and fatality (Claas et al., 1998). During late 2003 and 2004, the virus spread extensively and caused new outbreaks in China, but also in several other Asian countries including Vietnam, Thailand, Lao, Cambodia, Indonesia, Japan and South Korea. In summer 2005, it spread westwards and outbreaks were reported from Kazakhstan and Russia. This was soon followed in autumn 2005 and winter 2005/2006 by outbreaks reported in many European countries, and in several African countries. All together, and over the entire period 2003–2011, the virus was reported in over 60 countries distributed across Asia, Europe and Africa (FAO, 2009; World Organization for Animal Health, World Animal Health Information Database (WAHID), 2011). In many countries where it was introduced, HPAIV H5N1 only persisted for a few months, and was soon eradicated. However, to date it persists endemically or shows occasional resurgence in a limited number of countries including Bangladesh, Cambodia, China, Egypt, India, Indonesia, Japan, South Korea, Russia, Vietnam (FAO, 2009; World Organization for Animal Health, World Animal Health Information Database (WAHID), 2011).

Considering its geographical distribution, its socio-economic impact on poultry farming and smallholder livelihoods, and the mortality caused in the wild avifauna in some particularly spectacular outbreaks, the HPAI H5N1 panzootic has no known precedent. HPAIV H5N1 has hence been subject to considerable fundamental and applied research aimed at studying the disease from the perspective

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of many disciplines. The number of published studies on HPAIV H5N1 ranged between 23 and 56 publications per year prior to the panzootic. It increased to 1098 publications in 2010 (see Fig. 1, ISI Web of science search 19th September 2011 on "H5N1" term). This is, however very modest, compared with, for example, "climate change", that generated >25,000 papers in 2010.

A fraction of this abundant literature has focused on the epidemiology of HPAIV H5N1, and more specifically on the factors associated with its presence in various regions and countries. Various approaches have been used, including qualitative and descriptive studies investigating the conditions of HPAIV H5N1 introduction and spread, empirical studies based on HPAI H5N1 distribution data, and more theoretical work focusing on the exploration of disease control scenarios.

This literature review focuses on studies that have studied explicitly the spatial distribution of HPAI H5N1 based on empirical data. These studies that fall under the general definition of *spatial epidemiology* (Ostfeld et al., 2005; Pfeiffer et al., 2008) have analysed disease distribution data with the aim to characterise their spatial or temporal pattern (e.g. clustering of cases), to identify spatial predictors associated with disease presence, and in some instances to map disease risk over large geographical areas. Case-control studies carried out at the farm or market level were also included in this review, provided that some spatial variables (e.g. distance to road, local human population density) were considered as potential risk factors.

The objective of this review was twofold. First, given the variation in ecological systems in which HPAI H5N1 cases have occurred, it would be useful to compare risk factor patterns. Any consistencies in such patterns would strengthen associated causal interpretations and potentially lead to improved control or prevention policies. Conversely, factors found significant in some circumstances and not in others, may reflect differences in transmission patterns between countries, but may also be indicative of spurious statistical relationships.

Second, synthesizing the knowledge generated by spatial epidemiological studies on HPAI H5N1 also aimed at identifying any gaps in relation to risk factors, countries, or epidemiological conditions, and towards which future research could be directed.

2. Materials and methods

We searched the ISI Web of Science (1996–end 2010) and CAB abstracts (1996 »–end 2010) with the terms «avian influenza» combined with the terms «Spatial», «Risk», «Cluster», «Map» or «Distribution». The search was conducted on April, 16th 2010, and updated on August, 9th 2011. Based on these results, we performed a first selection including all papers with explicit reference to spatial data on avian influenza. The reference list of these papers was then carefully checked to identify other papers that had not been identified through the initial searches. These references were then grouped into six categories: (i) papers where the main focus was the statistical analysis of disease distribution data; (ii) papers that analysed or discussed HPAI H5N1 risk, but from the perspective of wild birds: this includes papers that have attempted to predict the risk of HPAIV H5N1 introduction through wild migratory birds, and papers that have primarily analysed wild bird migration data but in relation to the location of HPAI H5N1 outbreaks: (iii) papers that analysed HPAI H5N1 risk in relation to poultry trade: this includes risk assessments of introduction by trade, or trade network analysis in the context of HPAIV H5N1 prevention strategies; (iv) papers using mathematical modelling to quantify transmission parameters, or to test disease control scenarios; (v) phylogenetic studies with a strong emphasis on the spatial dimension, and (vi) review papers.

Only papers from the first category, i.e. focussing primarily on the statistical analysis of HPAI H5N1 disease and infection data, were included in this review, and we restricted our selection to papers on disease and infection caused by HPAIV subtype H5N1.

These studies were classified based on several criteria: the study area, the unit of analysis, the analysis methods, the type of factors considered, grouped into nine categories: (i) farming practice and local biosecurity, (ii) poultry and livestock census data, (iii) anthropogenic variables, (iv) socio-economic variables, (v) variables indicative of the presence or abundance of wild birds, (vi) variables indicative of the presence or abundance of rivers, lakes or wetlands, (vii) eco-climatic variables obtained using weather station data or remote sensing, (viii) land-use and cropping variables, and finally (ix) topography. For each of the factors identified as significant in the different studies, we noted the significance ($p < 0.05$; $p < 0.01$; $p < 0.001$) and signs of the association with HPAI H5N1 presence in the case-control and cross-sectional studies. When a factor was tested in both a uni- and multi-variate model, the significance and sign of the factor in the multivariate model was used.

3. Results

The first selection resulted in 115 references relevant to avian influenza and spatial epidemiology in their widest sense. Of these, 55 reported results of empirical studies on AI distribution, 29 papers pertained primarily to wild bird migration patterns in relation to AI risk, eight papers focussed on AI risk assessment based on poultry trade patterns, 12 papers had a primary focus on mathematical modelling, six papers were phylogenetic studies with a strong spatial dimension, and five were review papers. Out of the 55 papers based on empirical AI data, 47 papers pertained to HPAIV subtype H5N1.

These 47 can be grouped into four main study categories. First, descriptive studies ($n = 9$) that included descriptive statistics on HPAI H5N1 distribution data without explicit statistical hypothesis testing (e.g. maps of cases, epidemic curves), with discussion of spatial and/or temporal patterns. Second, spatio-temporal pattern studies ($n = 10$) where the spatial and/or temporal distribution of HPAI H5N1 cases was studied using statistical hypothesis testing in order to characterise their space and/or time clustering. Third, case-control studies with farms, markets