Preventive Veterinary Medicine 103 (2012) 170–177

Contents lists available at SciVerse ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

Spatio-temporal epidemiology of highly pathogenic avian influenza (H5N1) outbreaks in Nigeria, 2006–2008

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ARTICLE INFO

Article history:
Received 31 December 2010
Received in revised form
11 September 2011
Accepted 1 October 2011

Keywords:
Highly pathogenic avian influenza
H5N1
Epidemiology
Spatio-temporal pattern
Outbreaks
Nigeria

ABSTRACT

From 2006 to 2008, outbreaks of highly pathogenic avian influenza A (HPAI) virus of the H5N1 subtype occurred among poultry in Nigeria. We described the spatio-temporal patterns of the HPAI H5N1 outbreaks in Nigeria. Data of suspected and laboratory confirmed outbreaks maintained at the National Veterinary Research Institute Vom was analyzed using descriptive and exploratory analyses, GIS mapping, global and local spatial statistical analyses using the Cuzick–Edwards' (C–E) test and SaTScan Space-Time Scan Statistic. A total of 1654 suspected outbreaks were reported from 32 of the 36 States and the Federal Capital Territory (FCT), 299 were confirmed HPAI H5N1 positive from 27 states and FCT. The outbreaks occurred as three distinct epidemic waves with peak periods of January–March mainly in the North-West, North-Central and North-East regions during 2006 and 2007 and July–September in the South-West and South-South regions in 2007. Three spatio-temporal clusters were identified extending across States and international borders, consistent with disease transmission occurring through local and long-distance spread. This calls for enhanced strategies by the states and regional authorities to improve surveillance, prevention and control measures at the states, national and international levels.

1. Introduction

The first outbreak of the highly pathogenic avian influenza A (HPAI) subtype H5N1 occurred in mid-January 2006 in a commercial poultry farm in Jaji, Igabi local government area (LGA) of Kaduna state, North-West Nigeria with a report of high mortality in chickens, geese and ostriches reared on the same premises (Joannis et al., 2006; De Benedictis et al., 2007). A similar outbreak with onset traced to mid-January 2006 was confirmed on another commercial poultry farm in Ogun state, south west Nigeria during February 2006. Since the first introduction, the outbreak has spread among backyard poultry and local and wild birds in different parts of the country resulting in over 1.2 million deaths of domesticated birds including those culled to stop its spread (Meseko et al., 2010). By October 2007, two hundred and ninety four (294) outbreaks had been recorded in 25 of the 36 states in Nigeria and the Federal Capital Territory (FCT). In January 2007, Nigeria experienced the only human case of H5N1 avian influenza A in a 22-year old woman from Lagos state, western Nigeria

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0167-5877/$ – see front matter
doi:10.1016/j.prevetmed.2011.10.001

(Ekong et al., 2007; WHO, 2008) with a history of exposure to infected bird.

During these HPAI outbreaks, the Nigerian government instituted various preventive and control measures to contain the outbreak. These included intra- and inter-states restriction of bird movement, rapid stamping out of all laboratory confirmed cases, thorough decontamination of all infected premises and education of farmers on the need to adopt strict bio-security measures.

The first step in controlling the spread of HPAI virus is to understand the infection dynamics of the virus in the environment and have insight into the causes of the disease process. An understanding of the complex epidemiological system that involves the frequent interactions between the various infection reservoirs and hosts is needed to be able to break the transmission cycle. Clustering of disease events provides clues to the causes of the disease process, and may assist in formulating disease prevention and control programs.

The objectives of this study therefore were (1) to describe the spatial and temporal patterns of the HPAI H5N1 outbreaks reported between January 2006 and December 2008; and (2) to assess spatio-temporal clusters and possible factors responsible for its spread in Nigeria. This information may be useful in planning prevention, surveillance and control strategies in HPAI virus high-risk areas and also to direct future research into HPAI epidemiology in the country.

2. Materials and methods

2.1. Study area and study period

Nigeria is a federal constitutional republic located in West Africa between latitudes 4–14° N and longitudes 2–16° E. It occupies a land area of 917,156 km^2 and is divided into six geo-political zones (region), 36 states, one federal capital territory (FCT) and 774 local government areas (LGAs) (Fig. 1). It is the most populous country in Africa with a population of over 140 million (Joannis et al., 2008). Agriculture plays an important role in the Nigerian economy contributing 38% of the gross domestic product (GDP), only second to the petroleum sector, accounting for 40% of the GDP. The poultry population in Nigeria is estimated to be 140 million of which 25% is kept in the commercial production system, 15% in the semi-commercial and 60% as backyard or rural poultry (Ortiz et al., 2007). The bulk of commercial poultry is based in South-West Nigeria especially the states close to Lagos, the industrial capital of Nigeria. In this regard, it is estimated that over 65% of Nigeria's commercial poultry is located in the 5 states of Lagos, Ogun, Oyo, Osun and Ondo; another 25%

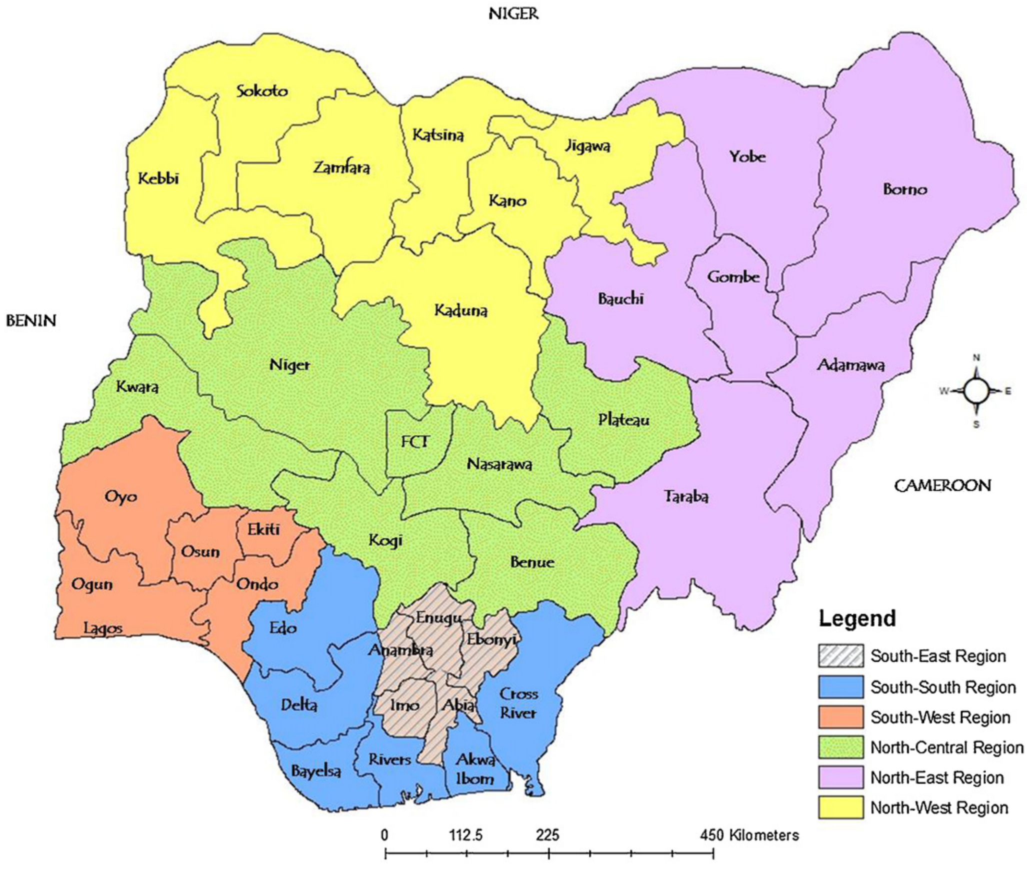

Fig. 1. Map of Nigeria showing the six (6) geopolitical zones. (For interpretation of the references to color in this figure, the reader is referred to the web version of the article.)

is based in the South-South and South-East geo-political zones. The balance of 10% or less of Nigeria's commercial poultry is based in the 15 North-Central, North-West and North-East states. The backyard production system is subsistent and mostly extensive, consisting of multiple species with both local and improved breeds. The rural poultry production system is largely practiced in the North (Adene and Oguntade, 2006)

In February 2004, the Federal government of Nigeria established a risk assessment committee on HPAI in Nigeria following the continuous outbreaks of HPAI in Asia and the growing threat of its spread to Africa (Maina, 2007). Immediate surveillance for HPAI was incorporated into the existing surveillance system. An emergency preparedness plan was produced in 2005. Targeted surveillance on wild fowl and migrating birds was conducted at the Nguru-Hadejia wetlands between September and November 2005 and in selected farming areas and live poultry market in Nigeria but failed to detect H5 or H7 avian influenza virus (Joannis et al., 2008). Sero-surveys of poultry samples collected in other studies during 1999–2004 were all negative for avian influenza antibodies (Owoade et al., 2006). The study period therefore is from the first outbreak and detection of avian influenza H5N1 in mid January 2006 to December 31, 2008.

2.2. Data sources, case and control definition

Data on HPAI H5N1 virus outbreaks between January 2006 and December 2008 were obtained from the disease-reporting database maintained by the Central Diagnostic Laboratory at the National Veterinary Research Institute (NVRI), Vom, Nigeria. The data included case history of suspected outbreaks, dates, localities with their geographic coordinates, LGAs and states where the outbreak occurred. We used the date of onset of clinical signs in a flock as the start of the outbreak. In the absence of this information we used the date the outbreaks were reported to the laboratory. All HPAI suspicions were reported to the NVRI where they were confirmed as either positive or negative by virus isolation (VI) and/or polymerase chain reaction (PCR). A digital map of Nigeria was obtained from the customised Transboundry Animal Disease Information System (TADinfo®) database for Nigeria (TADinfo-Nigeria, 2006). Geographic coordinates for premises with unspecified coordinates were obtained using the TADinfo® and visualized using a geographic information system (GIS) (ArcMap 9.0, ArcGIS, ESRI, Redlands, CA). Cases for this study were defined as poultry premises with history of sudden and unusually high mortality in bird(s) with signs which included cyanosis of combs and wattles, reddish shank, swollen face and wattles and or post mortem lesions of HPAI and confirmed by at least two laboratory tests. Controls were defined as poultry premises that had at least 1 HPAI suspect based on clinical signs and or post mortem lesions but were subsequently negative by virus isolation or PCR test.

2.3. Data analyses

The data analyses have three major components: statistical and exploratory data analysis, GIS mapping, and spatial methods. The epidemic curves were created in Microsoft Excel (Microsoft Inc., Seattle, WA) and the percentage and 95% confidence intervals were calculated using MedCalc (SAS Institute Inc., Cary, NC). The spatial data was visualized using ArcGIS (ESRI Inc.). The cluster analyses were conducted using SSTAT, an add-in to Excel and using SaTScan (http://www.satscan.org/).

2.4. Affected bird types

For each year in the study period, we calculated the percentage of the HPAI outbreaks and the exact binomial 95% confidence intervals for the different bird types affected during the outbreaks.

2.5. Temporal analyses

The total number of confirmed cases per day was plotted as a function of time in an epidemic curve. Onset of control measures and dates of Christmas and New Year celebrations were superimposed on this plot to identify potential links between these activities and the HPAI outbreaks in Nigeria. The Christmas and New Year celebrations are associated with increased demand and trade of poultry.

2.6. Spatial cluster analyses

The Cuzick–Edwards' (C–E) test (Cuzick and Edwards, 1990) was used to identify global spatial clustering of HPAI outbreaks. Computations were performed using a spreadsheet add-in (SSTAT v470, University of California, Davis). To run the analysis, all controls were labeled as 0 and all cases were labeled as 1. The test examines the distribution of cases and determines whether more cases than expected are nearest neighbors (NNs), given the number of cases and controls in the population. Clustering was tested for one to six NNs. For example the first-level NN test is calculated by first identifying each case and then the status (case or control) of its NN. The total number of first NNs for all cases is then compared with what is expected if cases and controls were randomly distributed. The second-level NN test is calculated by first identifying each case and then the status (case or control) of its two NNs. The resulting total number of first or second NNs for all cases is then compared with what is expected if cases and controls were randomly distributed. A z-statistic was used to determine the statistical significance of the results.

2.7. Spatio-temporal cluster analyses

The scan statistic test (Kulldorff et al., 2009) was used to examine spatio-temporal clustering of HPAI outbreaks using SaTScan Space-Time Scan Statistic v8.0. The maximum cluster size was set to 50% of the population at risk. The Case-Control Bernoulli model was applied at the individual event location. Centroid of the LGAs was used as location information for both cases and controls. The scan statistic test imposed a circular window on the map and allowed its center to move over the whole area so that, at any given position, the window was centered on each of the several possible study sites throughout each region.

Table 1
Percentage of HPAI outbreaks in different geo-political zones (Region) in Nigeria stratified by year and overall through the study period.

Region	2006 (n = 144)		2007 (n = 156)		2008 (n = 4)		2006–2008 (n = 304)	
	N (%)	95% CI	*N* (%)	95% CI	*N* (%)	95% CI	*N* (%)	95% CI
North-Central	52 (36)	29–44	16 (10)	7–16	0	0–49	67 (22)	18–27
North-West	42 (29)	22–37	78 (50)	42–58	3 (75)	30–95	125 (41)	36–47
North-East	23 (16)	11–23	20 (13)	9–19	1 (25)	5–70	43 (14)	11–18
South-West	22 (15)	10–22	31 (20)	15–27	0	0–49	52 (17)	13–22
South-East	3 (2)	1–6	6 (4)	2–8	0	0–49	9 (3)	2–6
South-South	3 (2)	1–6	5 (3)	1–7	0	0–49	9 (3)	2–6

n: number of HPAI outbreaks; %: percentage of HPAI outbreaks; CI: confidence interval of %; N: number of outbreaks by region.

The radius of the circular window varied continuously from zero to maximum radius so that the window's coverage would not exceed 50% of the total population under study. To detect clusters, a likelihood function was applied to the windows, comparing the observed and expected number of cases inside and outside the window. The statistical significance of clusters was evaluated through Monte Carlo simulation (999 repetitions). The null hypotheses for the Cuzick–Edwards' and the scan tests were that the case flocks were randomly distributed in space and/or in time, after adjusting for the distribution of the underlying population at risk, or controls.

3. Results

Overall, 1654 suspected outbreaks were reported to NVRI from 32 states and FCT between 2006 and 2008, of which 299 were confirmed HPAI H5N1 positive from 27 states and FCT. This represents a total of 97 infected LGAs. From 2006 to 2008, the percentage of reported outbreaks increased from 29% (42/144) to 75% (3/4) in the North-West zone; 16% (23/144) to 25% (1/4) in the North-East zone and from 15% (22/144) to 20% (31/156) in the South-West zone from 2006 to 2007 (Table 1). In 2006, approximately 72% of infected flocks were small scale poultry flocks (flock size 2000 or less) and 28% large scale flocks (flock size >2000); in 2007, the ratio was 70% small scale to 30% large scale flocks.

3.1. Affected bird types

Throughout the epidemic, 75% (228/304) of affected bird type were exotic laying hens, 15% (46/304) were local chickens–hens, cocks and chicks, 6% (18/304) were ducks/geese and 4% (12/304) represents others. The percentage of outbreak that included exotic laying hens stayed constant around 75% in 2006 (105/144) and 2007 (120/156) and dropped to 25% (1/4) in 2008. The outbreaks in local chickens remained constant around 15% in 2006 (22/144) and 2007 (21/156) and rose to 50% (2/4) in 2008. Outbreaks in ducks/geese remained at 6% during 2006 (9/144) to 2007 (9/156), but rose to 25% (1/4) in 2008 (Table 2. *Note*: One outbreak could affect more than one bird type).

3.2. Temporal patterns

The epidemics in 2006–2008 took place during four distinct periods: January–October 2006; December 2006–April 2007; July–September 2007 and July 2008 (Fig. 2). Different reported dates of onset of the outbreaks were observed from all the regions (Fig. 3). However, the outbreaks were more concentrated in the three northern zones during the first phase of the epidemic, which started in January 2006 and peaked in February. The second phase had a similar pattern to the first phase, more evident in the northern zone (Fig. 3A–C). The onset was in late December 2006 and was at its peak in February 2007. The third phase was localized in the southern zone (Fig. 3D–F) with the largest number of outbreaks in the South-West zone (Fig. 3D). The epidemic reached its peak during June–September in the South-West zone in 2006, this pattern was also observed in 2007 (Fig. 3D). The fourth phase occurred in July 2008, about 10 months after the last outbreak (Fig. 3A and C).

3.3. Spatial and spatio-temporal cluster patterns

The Cuzick–Edwards test identified significant overall clustering of infected farms during the epidemic in all 6th

Table 2
Percentage of HPAI outbreaks recorded in different bird types in Nigeria stratified by year and overall through the study period. One outbreak could affect more than one bird type.

Bird type	2006 (n = 144)		2007 (n = 156)		2008 (n = 4)		2006–2008 (n = 304)	
	N (%)	95% CI	*N* (%)	95% CI	*N* (%)	95% CI	*N* (%)	95% CI
Breeder	2 (1)	0–4	2 (1)	0–4	0	0–49	3 (1)	0–3
Exotic Laying hens	105 (73)	65–80	120 (77)	70–83	1 (25)	5–70	228 (75)	70–80
Local chicken	22 (15)	10–22	20 (13)	9–19	2 (50)	15–85	46 (15)	11–20
Duck; Geese	9 (6)	3–11	9 (6)	3–11	1 (25)	5–70	18 (6)	4–9
Turkey	3 (2)	1–6	6 (4)	2–8	0	0–49	9 (3)	2–6
Guinea fowl	4 (3)	1–7	3 (2)	1–6	0	0–49	9 (3)	2–6
Broiler	6 (4)	2–9	8 (5)	3–10	0	0–49	15 (5)	3–8
Ostrich	3 (2)	1–6	2 (1)	0–4	0	0–49	3 (1)	0–3

n: number of HPAI outbreaks; %: percentage of HPAI outbreaks; CI: confidence interval of %; N: number of outbreaks by bird type.

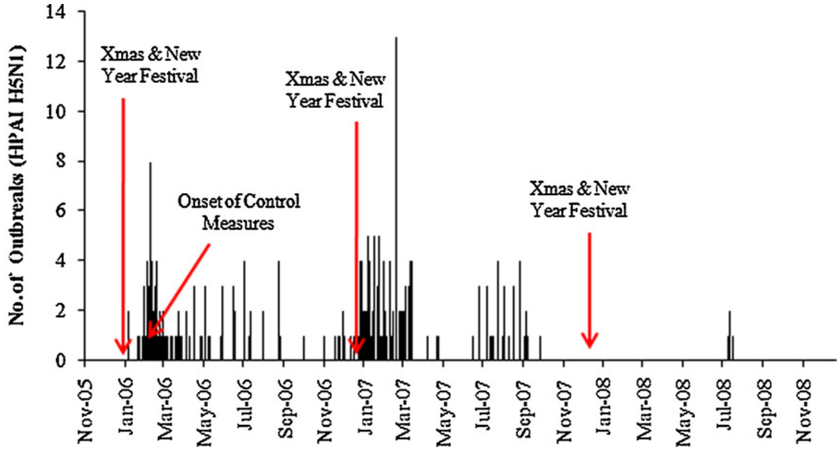

Fig. 2. Epidemic curve showing the daily number of HPAI H5N1 infection in Nigeria, 2006–2008, Christmas (Xmas) is celebrated on 25th December while New Year is celebrated on 1st January every year.

order NNs examined ($p < 0.001$). The space–time Bernoulli model identified 3 significant spatio-temporal clusters of HPAI infection. The first cluster (North-West zone) was detected between December 5, 2006 and March 26, 2007 ($p = 0.001$). It had a radius of 297.6 km from an infected farm at Zamfara state (centered at 12.99923°N, 6.48652°E), with 68 HPAI cases and 22 controls. It covered Kano, Kaduna, Katsina, Kebbi and Sokoto states, which borders the Niger and Benin Republics (Fig. 4). The observed/expected (O/E), log likelihood ratio (LLR) and relative risk (RR) for this cluster was 2.11, 33.67 and 2.47, respectively. The second cluster (South-West zone) was detected between July 3, 2007 and October 8, 2007 ($p = 0.001$). It had a radius of 379.5 km from an infected farm at Lagos state (centered at 6.47015°N, 3.3555°E), with 31 HPAI cases and 1 control. It covered all the south western states of Ogun, Oyo, Osun, Ekiti and Ondo. It also extended into Edo and Delta states, on the west border it extended into the Benin Republic. The O/E, LLR and RR for this cluster were 2.70, 28.92 and 2.92, respectively. The third cluster (North-East zone) was detected between January 31, 2006 and July 3, 2006 ($p = 0.021$). It had a radius of 317.1 km from an infected farm at Taraba state (centered at 8.83736°N, 11.61901°E), with 39 HPAI cases and 20 controls. It covered the Plateau and all north eastern states of Yobe, Borno, Bauchi, Gombe and Adamawa, which borders the North West province of Cameroon. The O/E, LLR and RR for this cluster were 1.84, 12.08 and 1.98, respectively.

4. Discussion

The introduction and spread of H5N1 HPAI virus in Nigeria during 2006–2008 had serious consequences for

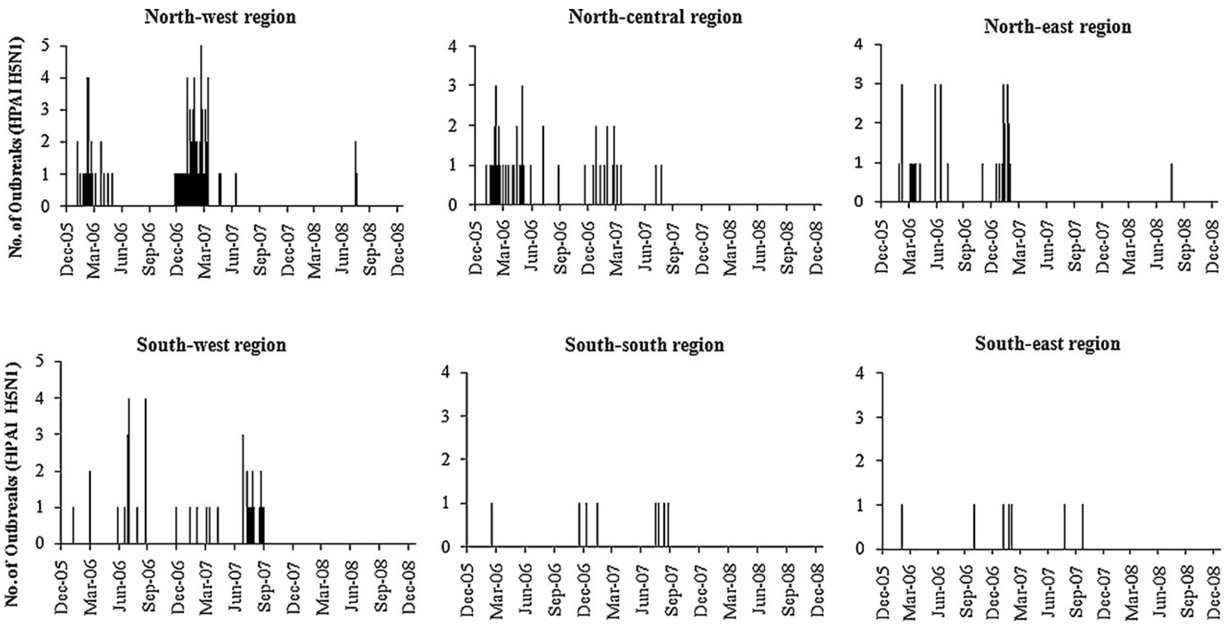

Fig. 3. Epidemic curves showing the daily number of HPAI H5N1 infection in the six geopolitical zones (regions) in Nigeria, 2006–2008.

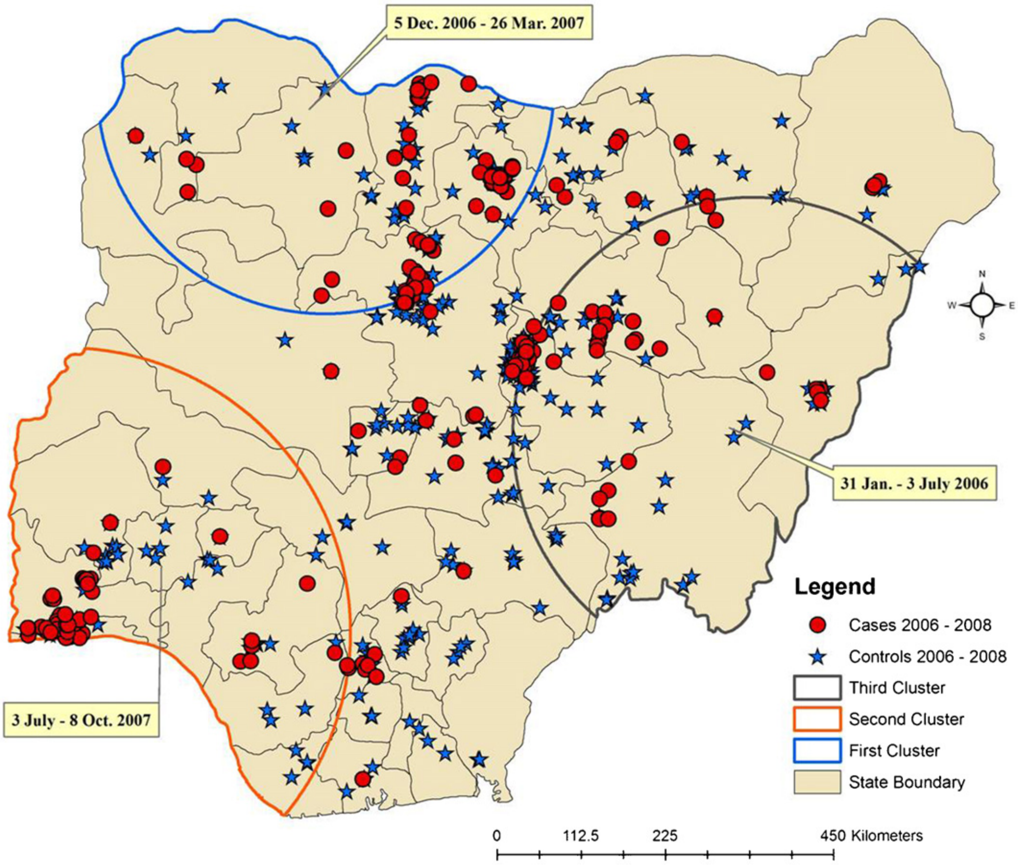

Fig. 4. Map of Nigeria showing the locations of HPAI infected and non-infected premises, areas with the result from the spatial scan statistic ($p < 0.001$) showing the first (most likely), second and third clusters and the time frame of each cluster. (For interpretation of the references to color in this figure, the reader is referred to the web version of the article.)

poultry production, human health and farmers' livelihood. The percentage of HPAI outbreaks recorded from the northern region was higher compared to the southern region. Although outbreaks were recorded in large scale commercial and poultry breeding farms, infections were predominantly present in backyard/small scale poultry flocks in 2006–2007. This supports the claim that backyard poultry production system is largely practiced in the north (Adene and Oguntade, 2006).

4.1. Affected bird types

There was an increasing percentage of outbreaks affecting exotic laying hens (chickens) during the HPAI H5N1epidemics in Nigeria, this pattern is similar to what was recorded in the Saudi Arabia HPAI H5N1 outbreak during 2007–2008 where 15 of the recorded 19 outbreaks in commercial poultry premises occurred in commercial layer farms (Lu et al., 2010). In Nigeria, exotic laying hens are the predominant bird type in the commercial farms and were mostly affected during the epidemics. In China, Indonesia, Thailand and Vietnam reports of the emergence of H5N1 viruses showed greater virulence in ducks (Sturm-Ramirez et al., 2005; Vascellari et al., 2007).

4.2. Temporal patterns

The temporal patterns of the reported HPAI outbreaks in Nigeria are shown in Figs. 2 and 3.

Analyses of the 2006–2008 HPAI H5N1 outbreaks indicated that the HPAI H5N1 epidemic in Nigeria emerged at different time in the northern and southern regions. This finding is consistent with the results of a genomic sequence analysis of the Nigerian virus isolates, which observed that the virus entered the country via three independent introductions (Ducatez et al., 2006; Ducatez et al., 2007).

The epidemic started in January 2006 while the last outbreak was recorded in July 2008. In 2006, the epidemic reached its peak between February and March; there was a decline in incidence from May to November. This decline may be related to the impact of the control measures of educating farmers on the need for strict bio-security measures on farms, restriction of poultry movement, preemptive slaughter of infected birds within and around infected farms, decontamination of infected premises and payment of compensation to farmers whose birds were depopulated as part of the outbreak containment and stamping out. The control measures were announced and implemented by the government following the first identification of the virus in February 2006. However, the virus continued to circulate and evolved within the poultry population giving rise to a reassortant virus (isolated in local bird populations in June 2006 in Taraba State) within seven months of its initial introduction (Salzberg et al., 2007; Monne et al., 2008). In 2007, the epidemic peaked in January–March and also in July–September. Phylogenetic analysis showed that the H5N1 virus circulating in Nigeria during 2007 was different from the one introduced in 2006 (Monne et al., 2008). This finding, in addition to increased reportage due to compensation paid to farmers, might account for the recorded higher incidence of the H5N1 in Nigeria in 2007 as compared to incidence in 2006. The predominance of a reassortant virus in Nigeria mimics the previously reported predominance of the Z genotype virus in Asia, although this genotype is believed to contain internal genes originating from non-H5N1 influenza viruses (Monne et al., 2008). The introduction of influenza virus (H5N1) of different clusters in Vietnam also resulted in the emergence of a reassortant strain (Nguyen et al., 2008; Wan et al., 2008). Unlike the Nigerian situation described here, the Vietnamese reassortant influenza virus (H5N1) did not become predominant in Vietnam (Monne et al., 2008). In 2008 a fresh outbreak was observed in a farm in Kano and Katsina states, 10 months after the last outbreak in 2007. Phylogenetic analysis of the virus isolated from a case detected in live bird market from Gombe state in July 2008 revealed a new sublineage which has never been previously detected in Africa (Fusaro et al., 2010). These findings call for improved preventive and control measures in Nigeria.

The observed temporal pattern consisted of three distinct epidemic waves, the first started in January and peak in February, the second in December through March. This provides some interesting insights into the epidemic. These periods coincided with the long dry season months of October to early March in Southern Nigeria and October to mid-May in Northern Nigeria. This period is characterized by prevailing dry and dusty north-east winds, as well as the 'harmattan' (cold) conditions which peak in late December through early February across the country (Online Nigeria, 2002). The occurrence of the first two epidemic waves was likely associated with increased virus survival during this 'harmattan' months. However, the harmattan period during December–January is more intense and longer in the north than in the south, this could provide the evidence for the recorded higher incidence of the virus in Northern Nigeria compared to the Southern part during this period. Moreover, the first two epidemics coincided with the Christmas – New Year festival celebrations. There is increased demand and trade of poultry prior and during the Christmas – New Year festival period, which is a further probable explanation for the virus spread during the epidemic waves in 2006 and 2006–2007. This pattern is consistent with the epidemic of H5N1 in Vietnam where the epidemic waves coincided with the Tet festival period (Minh et al., 2009), but not with the lower temperatures of the winter months as the climatic conditions vary significantly between the North and South of Vietnam, whereas the temporal outbreak pattern was consistent across both parts of the country (Pfeiffer et al., 2007). However, observation in Thailand showed that high numbers of HPAI detections in 2004–2005 coincided with low temperatures from October to February (Tiensin et al., 2007).

The third wave corresponds with the rainy season in the Southern Nigeria. This period is characterized by wet conditions and a high humidity, especially during July and September, as a short dry period is experienced during the last two weeks in August.

4.3. Spatial and Spatio-temporal cluster patterns

The Cuzick–Edwards test statistic revealed clustering of infected farms up to the 6th order NNs examined, suggesting the existence of a large cluster. This cluster could have been related to movement of birds following the initial outbreak. The initial spread of the primary outbreak in Nigeria was strongly linked with movement of poultry and poultry products (Fasina et al., 2009). Reports of genetic relatedness of influenza virus (H5N1) isolates obtained from 7 Nigerian states in 2007 were linked to movement of infected birds across neighboring regions (Monne et al., 2008) and in 2008 to wild birds or the poultry trade (Fusaro et al., 2009). In Vietnam, long-distance movement of birds was given as likely explanation for some of the clusters found in the Red River and the Mekong River deltas (Minh et al., 2009). The space–time scan statistic identified 3 spatio-temporal clusters of HPAI infection. The first cluster covered the coldest (harmattan) period in the region. It might be related to the detection of HPAI H5N1 viruses among poultry in Niger and Benin Republics on 13 February 2006 and 7 November 2007 respectively (Brown, 2010). The second cluster centered in Lagos state might be the source of infection for the outbreak that started in Benin Republic on 7 November 2007. The third cluster coincided with the first detection and report of the HPAI H5N1 virus in domestic ducks in Cameroon in February–March 2006. Local movement and transportation of infected bird might be the most likely source of introduction of the virus across these borders as surveillance along these international borders is either lacking or insufficient. This calls for enhanced strategies by the states and regional authorities to improve surveillance, prevention and control measures at the states and international borders.

5. Conclusion

This study observed that the immediate challenge to HPAI H5N1 epidemic in Nigeria is the control of outbreaks in backyard/small scale poultry flocks. Backyard poultry greatly contribute to local meat consumption and subsistence agriculture in rural areas. An improved bio-security measure on all poultry farms is advocated in order to prevent and control the spread of avian influenza virus. Permanent surveillance programs should also be implemented in order to allow the prompt detection of HPAI H5N1infection followed by quick implementation of control policies.

Acknowledgement

We thank the National Veterinary Research Institute, Vom, Nigeria for providing the data.

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