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THE CIRCULATION OF HIGHLY PATHOGENIC AVIAN INFLUENZA VIRUSES (HPAI) IN NON-HUMAN MAMMALS WORLDWIDE DURING THE PERIOD 01.01.2019 – 04.30.2024

CIRCULAȚIA VIRUSURILOR GRIPALE AVIARE ÎNALT PATOGENE (HPAI) LA MAMIFERE NON UMANE LA NIVEL MONDIAL ÎN PERIOADA 01.01.2019 – 30.04.2024

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ABSTRACT | REZUMAT

The paper presents the circulation of highly pathogenic avian influenza viruses (HPAIV) among non-human mammals globally in correlation with the evolution of the disease in domestic and wild bird populations as a result of the analysis of confirmed events and recorded in the Empres-i+ database. The data analysis carried out during the period 01.01.2019 – 30.04.2024 have showed that, in 2019, the events caused by circulating HPAI viral serotypes were in small number and did not cause events in non-human mammals. In 2020, an event caused by the H5N8 HPAI virus serotype was recorded in a fox in the UK. In 2021, an event determined by the H5N1 HPAI serotype was recorded in a fox in Estonia. As of 2022, the viral serotypes leading to events in non-human mammals were H5N1 HPAI and HPAI, which circulated widely (Africa,Europe, Asia, and America). There were 4 fox events in Belgium, one cat event in France, one fox event in Asia, and 88 non-human mammal events in the Americas. In 2023, the circulating viral serotypes affecting non-human mammals were H5N1 HPAI, H5 HPAI, and H5N5 HPAI. The events increased compared to the previous period, and were recorded in Europe, Asia, and the Americason a wide range of animals. In the first quarter of 2024, events in non-human mammalian species caused by serotype H5N1 HPAI were reported in Europe and the Americas in a wide range of mammals.

Keywords: avian influenza in mammals epidemiology, H5N1 HPAI

În lucrare este prezentată circulația virusurilor gripale aviare înalt patogene (HPAIV) în rândul mamiferelor non-umane la nivel global în corelație cu evoluția bolii în populațiile de păsări domestice și sălbatice, ca rezultat al analizei evenimentelor confirmate și înregistrate în baza de date Empres-i+. Analiza datelor a fost efectuată pentru perioada 01.01.2019–30.04.2024 și a scos în evidență faptul că în anul 2019 evenimentele determinate de serotipurile virale HPAI circulante au fost în număr mic și nu au determinat evenimente la mamifere non umane. În anul 2020 a fost înregistrat un eveniment determinat de serotipul viral H5N8 HPAI la vulpe în Marea Britanie. În 2021 a fost înregistrat un eveniment determinat de serotipul H5N1 HPAI la vulpe în Estonia. Începând cu 2022 serotipurile virale care au dus la evenimente în rândul mamiferelor non umane au fost serotipurile H5N1 HPAI și HPAI, care au circulat pe zone extinse (Africa, Europa, Asia, America) și au fost 4 evenimente la vulpe în Belgia, un eveniment la pisică în Franța, un eveniment la vulpe în Asia și 88 de evenimente în America, la mamifere non umane. În anul 2023, serotipurile virale circulante care au afectat mamiferele non umane au fost H5N1 HPAI, H5 HPAI și H5N5 HPAI, evenimentele au fost în creștere față de perioada anterioară, și au fost înregistrate în Europa, Asia și America, la o gamă largă de animale. În primul trimestru al anului 2024, au fost înregistrate evenimente la specii de mamifere non umane, determinate de serotipul H5N1 HPAI în Europa și în America, la o gamă largă de mamifere.

Cuvinte cheie: gripa aviară în epidemiologia mamiferelor, HPAI H5N1

Avian influenza viruses belong to the genus *Alphainfluenzavirus* of the family *Orthomyxoviridae*. They contain a segmented, negative-sense, single-stranded RNA genome (8 segments) and are classified into subtypes based on glycoproteins on their surface, hemagglutinin (HA), and neuraminidase (NA). The viral serotypes are combinations of the 16 types of HA and 9 subtypes of NA (15). HA recognises and binds the virus to target cells and is a determinant factor of AIV virulence, while NA has the role of releasing the viral particles into the infected cell. The HA cleavage is a prerequisite for the virus to be infectious. Highly pathogenic viral serotypes (HPAI) have the HA polybasic cleavage motif and are cleaved by ubiquitous proteases; they can replicate systemically and cause severe

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disease. Low pathogenic viral serotypes (LPAI) possess a monobasic amino acid motif in the HA cleavage site; they are recognized by trypsin-like proteases located in some mucosal tissues; and the replication of LPAIV is limited to the respiratory and intestinal tracts where these enzymes are present (14).

A large number of bird species are susceptible to infection with the avian influenza virus (AIV), with wild waterfowl representing the natural reservoir of the virus and playing a decisive role in its circulation. The increased reassortment capacity of avian influenza viruses, when they co-infect the same cell in the host organism, causes the occurrence of new viruses with pandemic potential. Genetic and antigenic variation is driven by the combination of a high mutation rate and a segmented genome that provides the ability to change and adapt to new hosts. Influenza virus genome segmentation facilitates genetic recombination by reassorting segments in hosts that are infected with two different influenza viruses at the same time, leading to mutation in a form that can easily cross between mammalian species, including humans.

HPAI, especially serotype H5N1, have recently been notable for expanding the range of affected non-avian hosts due to the acquisition of the ability to cross the interspecies barrier and multiply outside the respiratory organs (12). The increase in the number of confirmed cases in an ever-growing number of mammalian species indicates that they have acquired a widened tissue tropism, which leads to the damage of more tissues and organs, and the evolution of the disease at a systemic level. and, consequently, a high mortality rate (5, 6, 7, 8). Starting with 2022, the number of non -human mammal species affected by highly pathogenic avian viral serotypes has increased compared to infection episodes prior to the analysed period, and the geographic area has expanded. The plausible explanation is the close contact with infected birds.

RESULTS AND DISCUSSIONS

Data on avian influenza virus events were collected from the Empres-i+ database developed by the Food and Agriculture Organisation of the United Nations (FAO). We selected the data represented by confirmed and recorded events caused by HPAI avian influenza virus strains that have evolved globally and identified events that affected non-human mammalian species in correlation with the evolution of avian influenza virus in bird populations, taking into consideration that the natural reservoir of the virus is represented by wild waterfowl. For the analysis, we used descriptive statistics and took into account the major epidemiological determinants, represented by the host animals and the other affected species, as well as the causative agents represented by the HPAI viral serotypes, to create an overview of the evolution in time and space of strains of the HPAI avian influenza virus. The data recorded between 01.01.2019 and 04.30.2024 were selected by year and analysed for each continent. Following the analysis of confirmed and recorded data in 2019, globally, a small number of events caused by HPAI avian influenza viruses have affected the population of domestic and wild birds, and no events were recorded in wild or domestic non-human mammals.

At the continental level, the situation regarding the circulation of HPAI viral serotypes was as follows: in Europe, a number of 12 events determined by the viral serotypes H5N8 HPAI, H5N6 HPAI, and H5 HPAI were recorded, the predominant ones being those determined by H5N8 HPAI that affected the populations of domestic birds. Regarding the viral serotype H5N6 HPAI, only one event was recorded in the wild bird population (Fig. 1). 173 events caused by virus serotypes H5 HPAI, H5N1 HPAI, H5N2 HPAI, H5N5 HPAI, H5N6 HPAI, and H5N8 HPAI were recorded in Asia, which predominantly affected the domestic bird population, and serotype H5N2 HPAI caused the largest number of events. The serotype H5N1 HPAI was confirmed only in Asia and most cases were in birds from the domestic area (30 events) compared to the wild environment, where 2 events were recorded (Fig. 2). In the African continent, 27 events were recorded and were determined by the viral serotypes H5N2 HPAI, H5N6 HPAI, H5N8 HPAI - which was the most important, causing 18 events in domestic birds and 6 events in wild birds (Fig.3). In America, 43 events were recorded in domestic birds, caused by H7N3 HPAI (Fig. 4).

In 2020, the HPAI avian influenza viruses' circulation trend increased, and a number of 1351 events were registered in Europe, with the predominant circulating serotype being represented by H5N8 HPAI, which evolved at an increased level both in the wild bird population (689 events) and in the domestic bird population (557 events), as well as in captive birds (8 events). Of the 689 events in wild animals by H5N8 HPAI, one event was recorded in Great Britain in the red fox (Fig. 5). In Asia, a number of 420 events were recorded; the main circulating viral serotype was H5N8 HPAI, with the highest incidence in the domestic bird population (124 events); other types were represented by H5 HPAI, H5N1 HPAI, H5N2 HPAI, H5N5 HPAI, and H5N6 HPAI (Fig. 6). In the African continent, there were 6 confirmed and recorded events; the circulating HPAI viral serotype was represented by H5N8 HPAI (4 events) and H5N1 HPAI (2 events). No events were recorded in non-human mammals (Fig. 7). In Northern America, a single event determined by the viral serotype H7N3 HPAI was recorded in domestic birds (Fig. 8). In Oceania, 3 events were recorded in domestic birds, determined by the viral serotype H7N7 HPAI (Fig. 9).

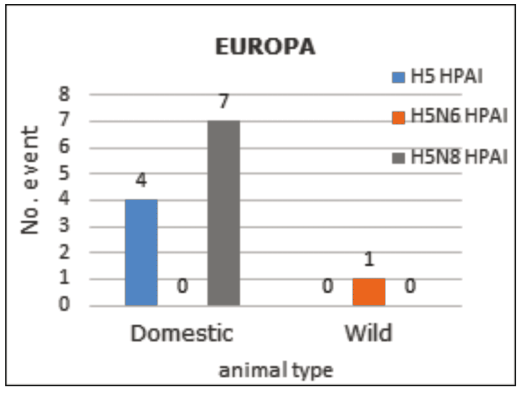

Fig. 1. 2019 – Europe Evolution of HPAI viral serotypes

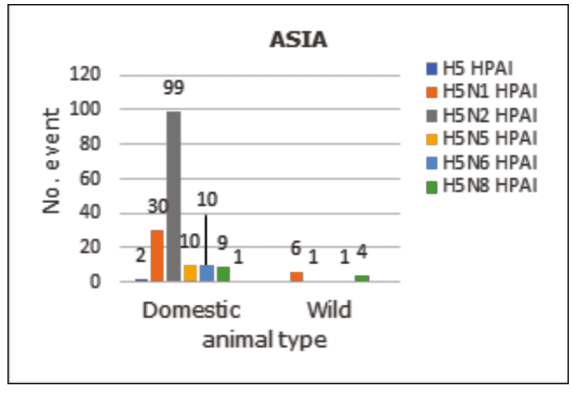

Fig. 2. 2019 –Asia Evolution of HPAI virus serotypes

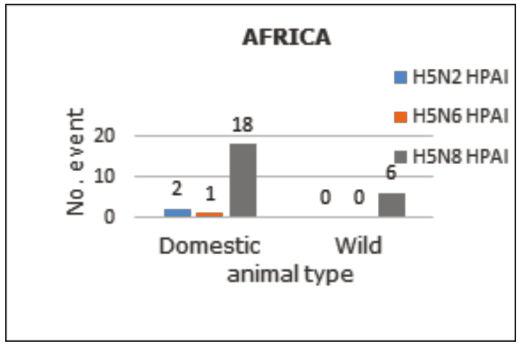

Fig. 3. 2019 – Africa Evolution of HPAI virus serotypes

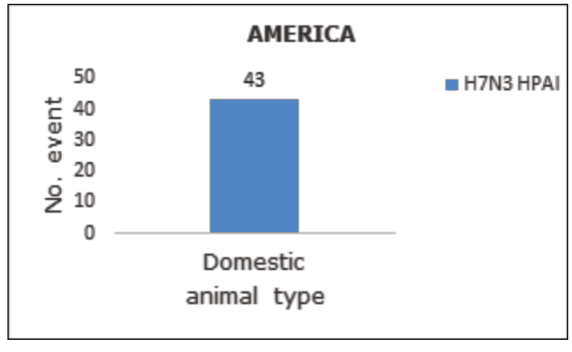

Fig. 4. 2019 – America Evolution of HPAI virus serotypes

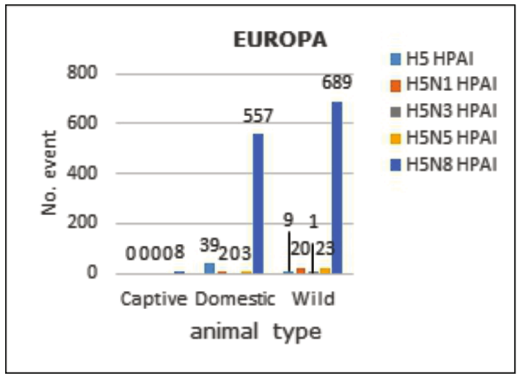

Fig. 5. 2020 – Europe Evolution of HPAI virus serotypes

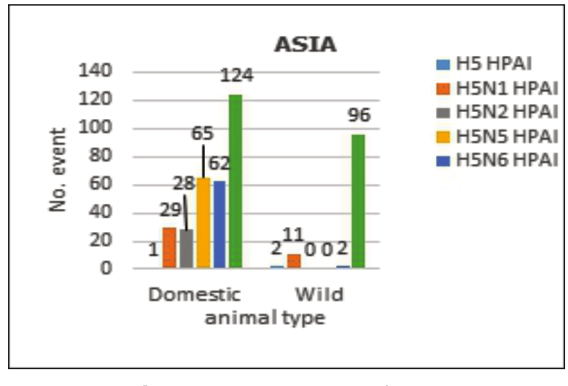

Fig. 6. 2020 – Asia Evolution of HPAI virus serotypes

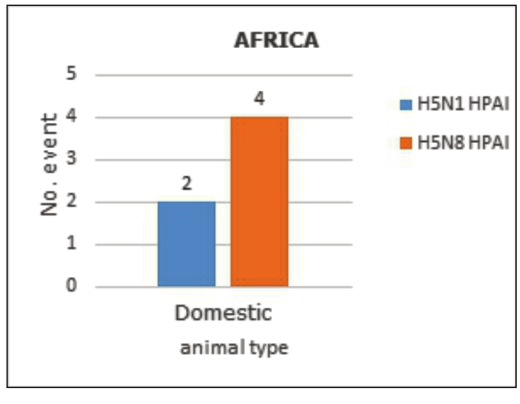

Fig. 7. 2020 – Africa Evolution of HPAI virus serotypes

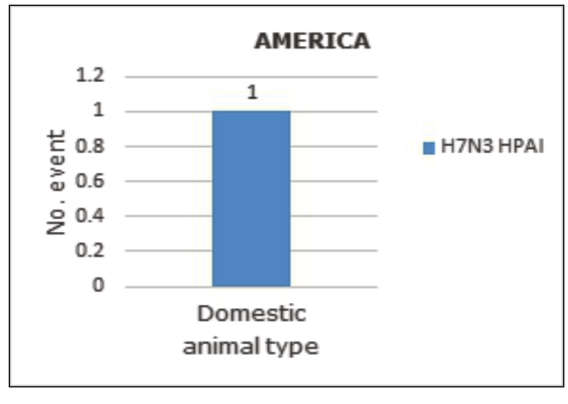

Fig. 8. 2020 – America Evolution of HPAI virus serotypes

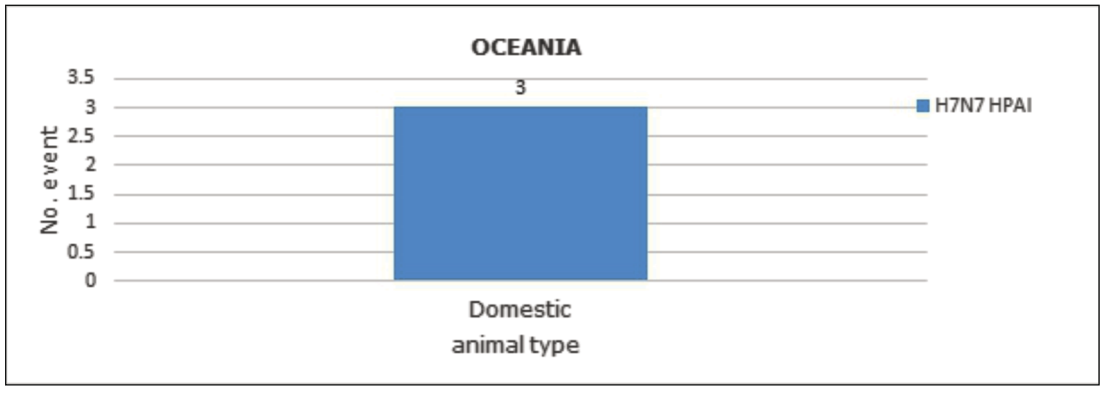

Fig. 9. 2020 - Oceania - Evolution of HPAI virus serotypes

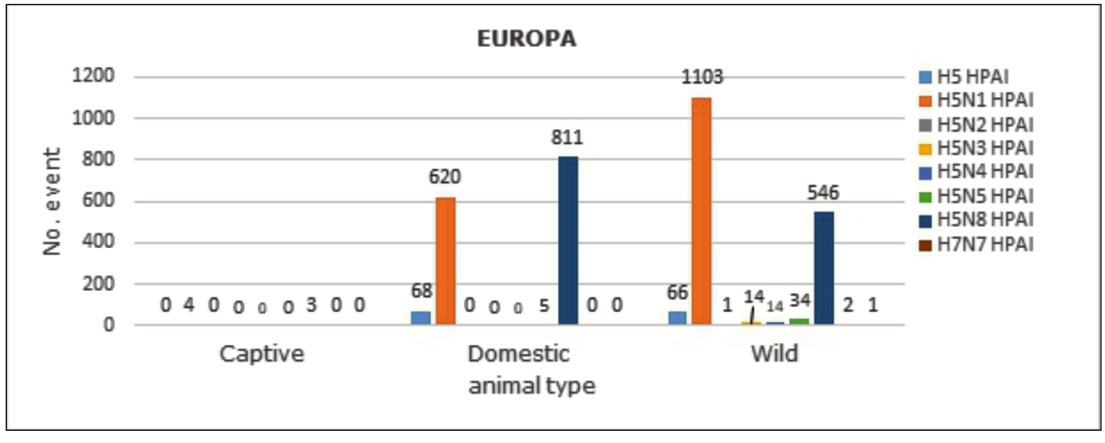

Fig. 10. 2021 Europe - Evolution of HPAI virus serotypes

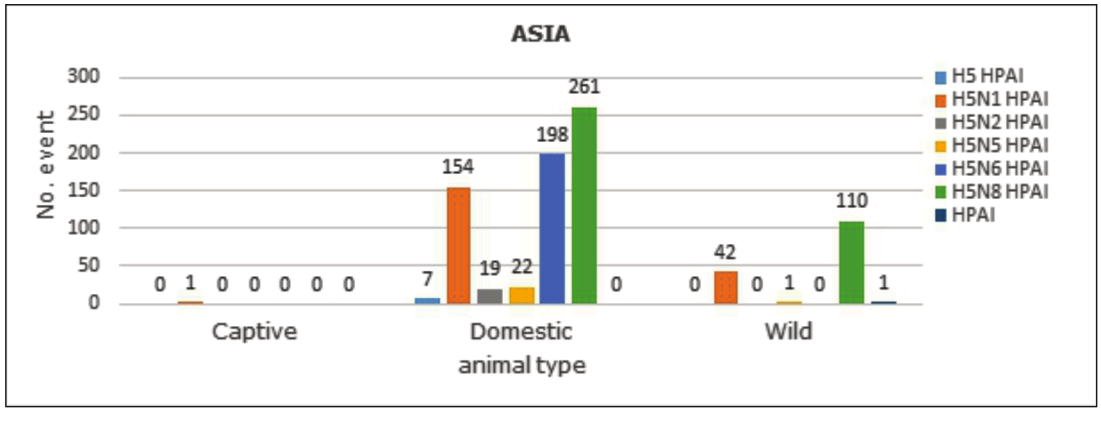

Fig. 11. 2021 Asia - Evolution of HPAI virus serotypes

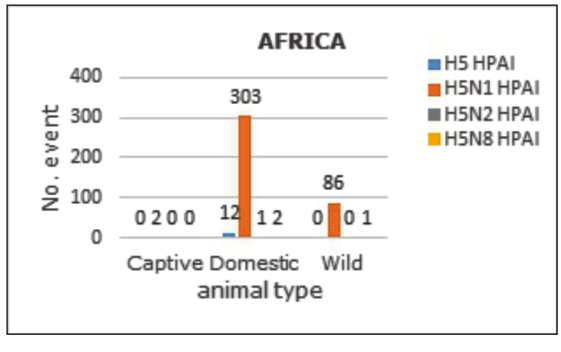

Fig. 12. 2021 Africa - Evolution of HPAI virus serotypes

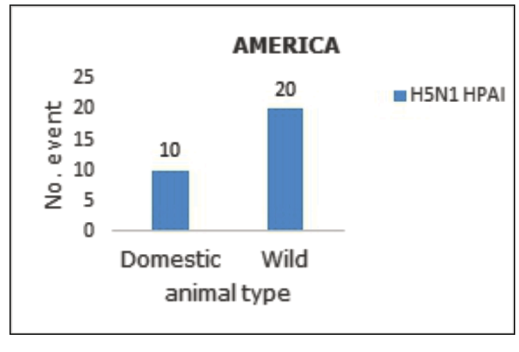

Fig. 13. 2021 America - Evolution of HPAI virus serotypes

In 2021, 3,292 events determined by highly pathogenic viral serotypes were confirmed and recorded in Europe, of which 1,360 were determined by H5N8 HPAI (811 in birds from the domestic environment and 546 from the wild environment). The events caused by the H5N1 HPAI serotype increased considerably compared to 2020: 1727 events, of which 1102 in wild birds and one confirmed event in foxes (Estonia), 620 in domestic birds, and 4 in captive birds. The serotype H5 HPAI caused 134 events in both wild and domestic birds. H5N2 HPAI caused one event, H5N3 HPAI caused 14 events, H5N5 HPAI caused 39 events, and H7N7 HPAI caused two events (Fig. 10). In Asia, there were 816 events caused by the following viral serotypes: H5 HPAI (7), H5N1 HPAI (197), H5N2 HPAI (19), H5N5 HPAI (23), H5N6 HPAI (198), H5N8 HPAI (371), and HPAI (1). No events were recorded in non-human mammals (Fig. 11). In Africa, a total of 407 events were recorded and 391 of them were caused by the H5N1 HPAI serotype. No events were recorded in mammals (Fig. 12). On the American continent, in 2021, the viral serotype H5N1 HPAI circulated, with 30 events confirmed and recorded; no events in non-human mammals were recorded.

In 2022, in Europe, 4025 events caused by avian HPAI viral serotypes, 3985 caused by H5N1 HPAI serotype were confirmed and recorded in the database, of which two fox events in Ireland, 4 fox events in Belgium and one event in a cat, in France; another event in the fox, in Belgium, was determined by HPAI (Fig. 14). In Africa, a total of 228 events were recorded, of which 226 were caused by the H5N1 HPAI virus serotype, but no cases were recorded in mammals (Fig. 15). In Asia, the events increased considerably in 2022, with a total of 885 events recorded, of which 798 were caused by the H5N1 HPAI virus serotype and one case recorded in a fox (Fig. 16). In America, 1696 events were recorded, of which 1571 were determined by H5N1 HPAI serotype, of which 88 events were identified in non-human mammals (lynx,fox, leopard, cougar, grizzly bear, coyote, mink, cat, and seal) (Fig. 17).

In 2023, 2954 events caused by highly pathogenic avian viral serotypes were recorded in Europe in both birds and non-human mammals (123 events out of the total number of recorded events), H5N1 HPAI caused a number of 2887 out of the total number of events; in non-human mammals caused by H5N1 HPAI there were 110 events in different species of mammals (lynx, cat, dog, fox, mink, arctic fox, and red fox) in Belgium, Finland, Germany, and Italy; other events in

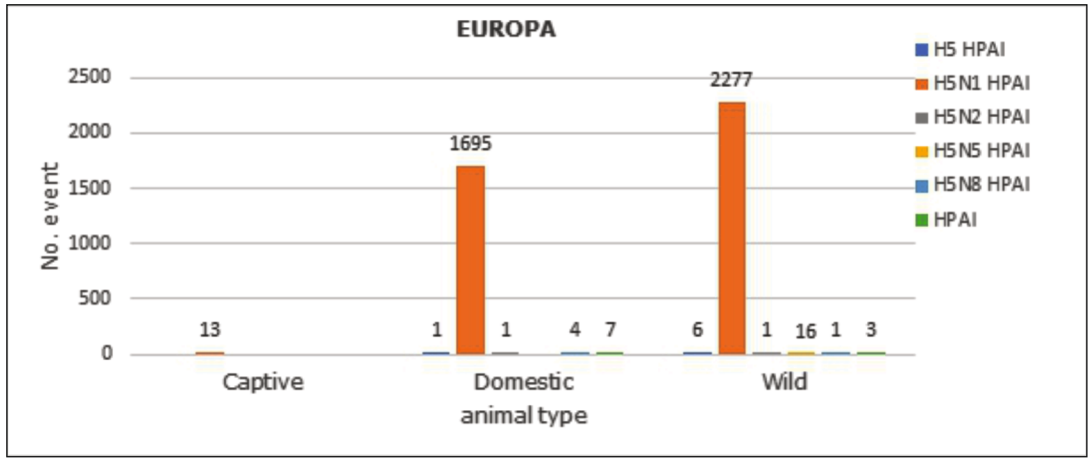

Fig. 14. 2022 - Europe - Evolution of HPAI virus serotypes

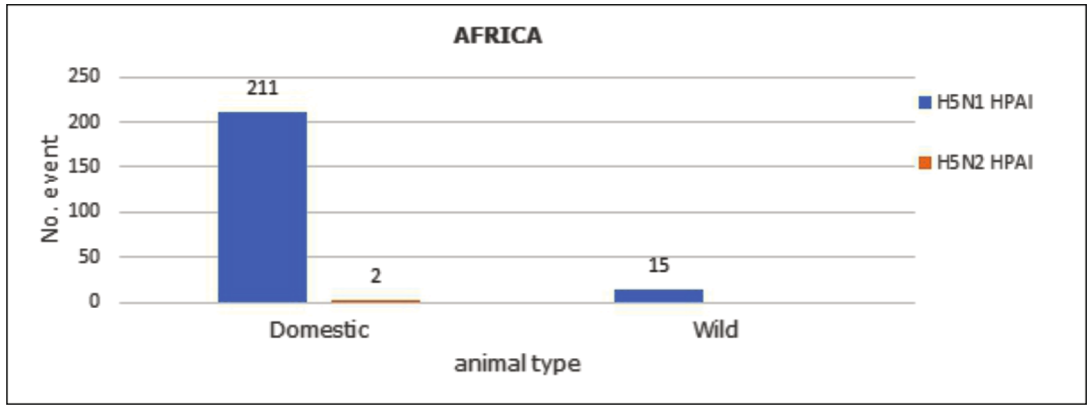

Fig. 15. 2022 - Africa - Evolution of HPAI virus serotypes

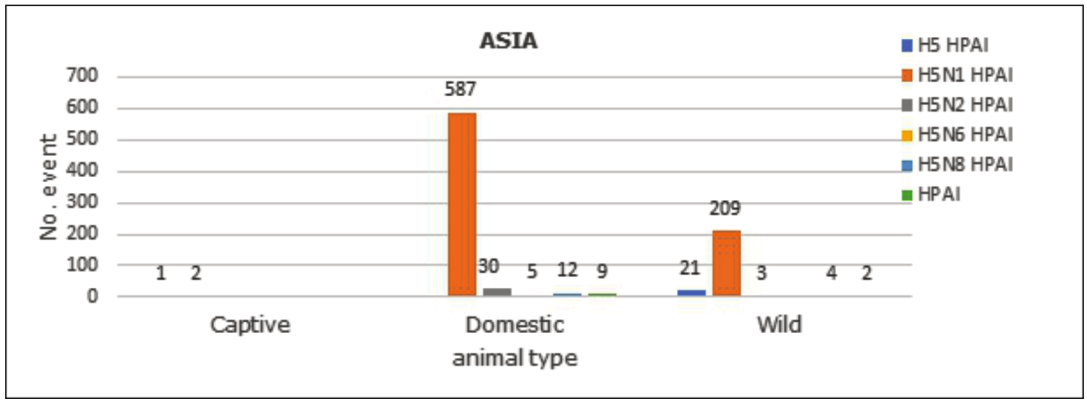

Fig. 16. 2022 - Asia - Evolution of HPAI virus serotypes

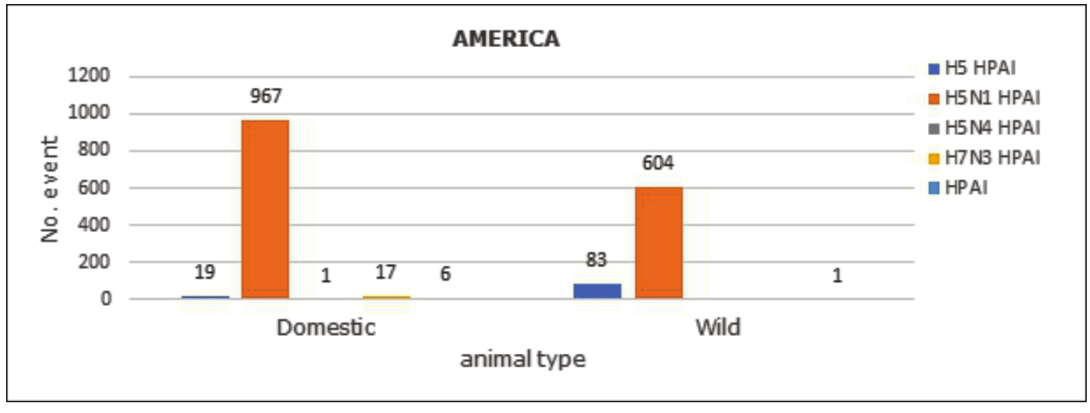

Fig. 17. 2022 - America - Evolution of HPAI virus serotypes

non-human mammals were caused by H5 HPAI, recorded in Belgium (4 events) in foxes, and by HPAI also in foxes in Belgium (Fig. 18). In Africa, no events were recorded in non-human mammals, the events recorded in domestic birds were caused by H5 HPAI, H5N1 HPAI, H7 HPAI, and H7N6 HPAI, and in wild birds were caused by H5HPAI and H5N1 HPAI (Fig. 19). In Asia, of the total of 407 events, the vast majority were caused by H5N1 HPAI (366), 2 events were recorded in cats, in Korea, and 2 events in foxes, in Japan (Fig. 20). In America, the number of events increased (1057), with the major viral serotype being H5N1 HPAI (741 events), but also H5 HPAI (281 events). Viral serotype H5 HPAI caused 57 events mainly in marine mammals (sea lion) from South America but also in otter (2 events) and Coati (1 event). The H5N1 HPAI virus serotype has caused 40 events in non-human mammals in North America (bear, lynx, cat, cougar, dog, polar bear, feral cat, fox, and one event in cattle), and 3 events in South America (Argentina), in a sea lion. The H5N5 HPAI serotype registered a number of 6 events, of which one event in fox (Fig. 21). In Antarctica, 8 events were recorded in wild birds, of which, 7 events were caused by serotype H5N1 HPAI and 1 event was caused by HPAI (Fig. 22).

In the first quarter of 2024, a number of 422 events were recorded in Europe, with the vast majority (399 events) being caused by the H5N1 HPAI serotype - the

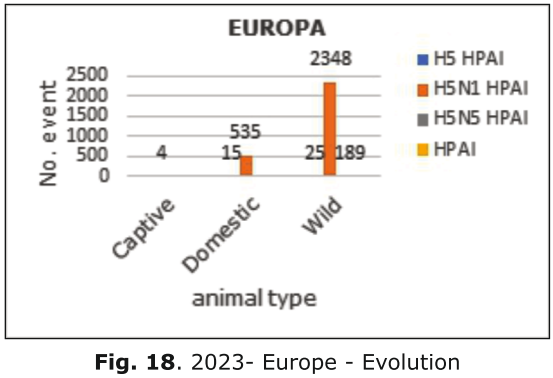

Fig. 18. 2023- Europe - Evolution of HPAI virus serotypes

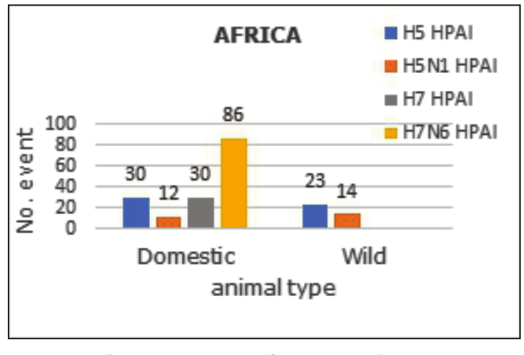

Fig. 19. 2023-Africa - Evolution of HPAI virus serotypes

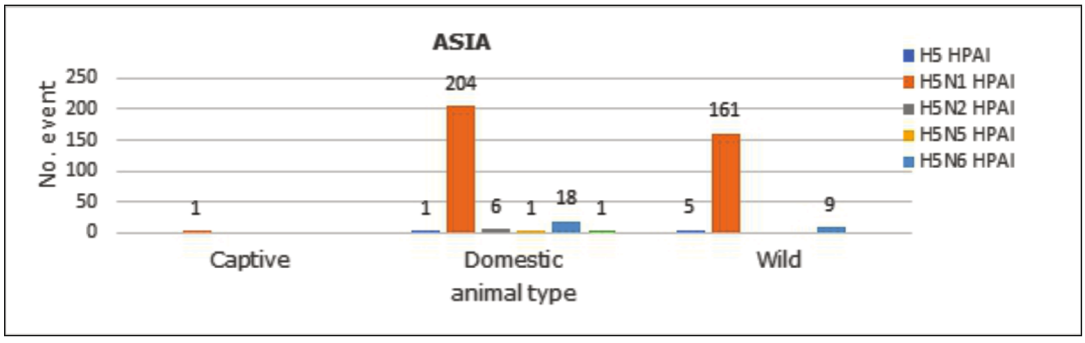

Fig. 20. 2023 - Asia - Evolution of HPAI virus serotypes

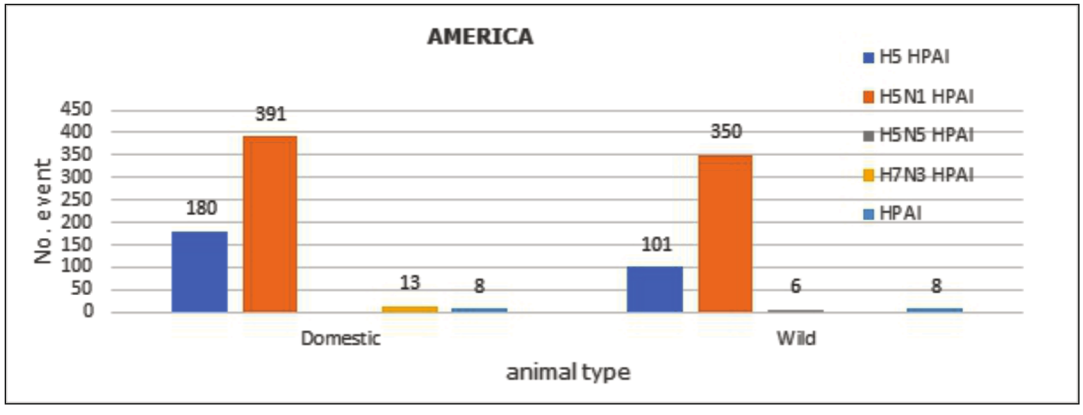

Fig. 21. 2023 - America - Evolution of HPAI virus serotypes

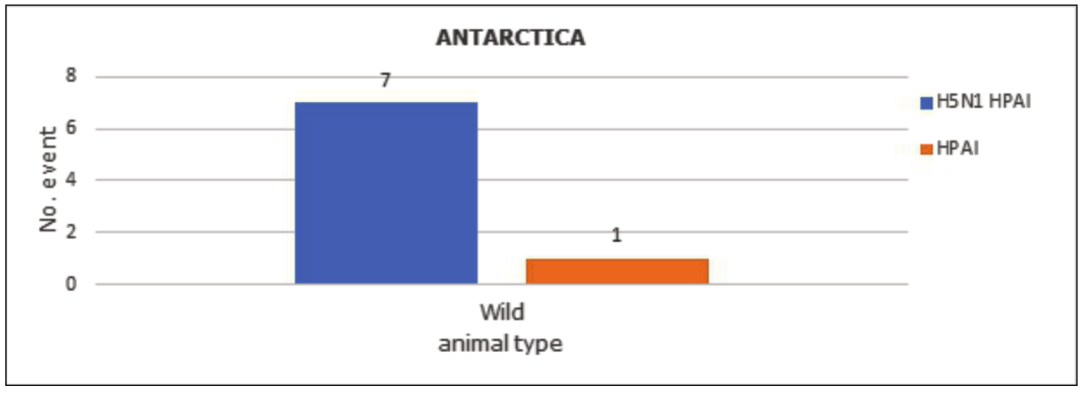

Fig. 22. 2023 - Antarctica - Evolution of HPAI viral serotypes

virus circulating mostly in the wild population (295 events). Of all events, 4 were recorded in foxes, 3 were caused by H5N1 HPAI and 1 event caused by HPAI (Fig. 23). In Asia a total of 174 events were recorded in domestic and wild bird populations, and no cases were recorded in non-human mammals (Fig. 24). In Africa, 6 events were recorded, mainly in domestic birds, and the circulating viral serotypes were H5 HPAI, H5N1 HPAI, H7N6 HPAI, and HPAI (Fig. 25). In America, the circulating serotype was H5N1 HPAI causing 140 of the 153 recorded events. Of all events, 52 were in non-human mammals of North America, and were caused by the H5N1 HPAI serotype, as follows: in lynx (2 events), cat (4 events), goat (1 event), mink (1 event), fox (3 events), and cattle (41 events) (Fig. 26). 14 events were recorded in wild birds, in Antarctica, and the circulating serotypes were H5 HPAI, H5N1 HPAI, and HPAI (Fig. 27).

CONCLUSIONS

After analysing the data on the global circulation of HPAI viruses during the period 2019-2024, we conclude that the circulation of HPAI avian influenza viruses has increased significantly in recent years. A variety of serotypes are involved in determining the events in non-human mammal populations. If, in 2019, the viral serotype H5N1 HPAI evolved only in Asia, causing a small number of events, starting from 2021 the number of events increased, so that in 2022, 2023 and in the first quarter of 2024, numerous events in domestic birds, wild birds and non-human mammals

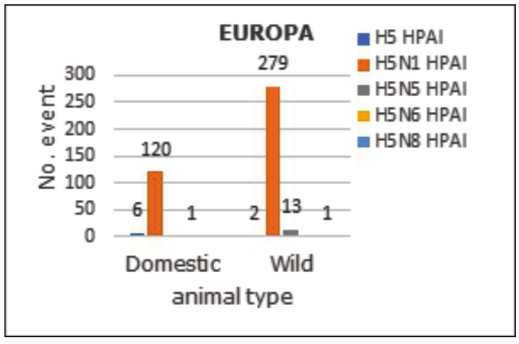

Fig. 23. 2024 - Europe - Evolution of HPAI virus serotypes

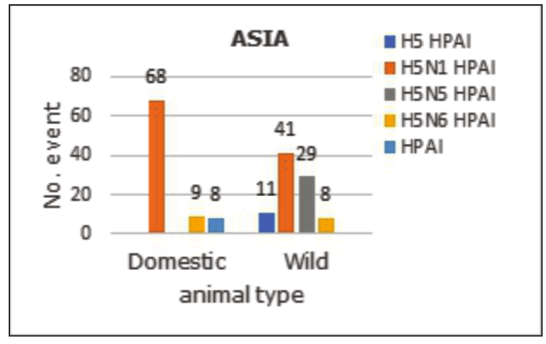

Fig. 24. 2024 - Asia - Evolution of HPAI virus serotypes

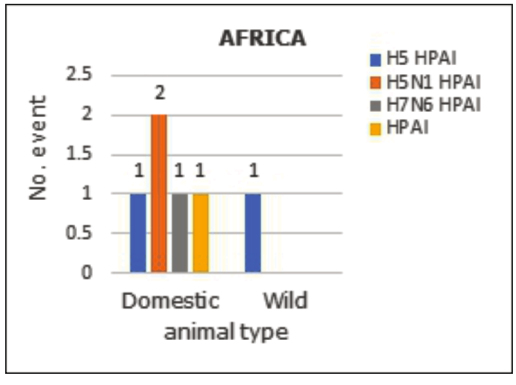

Fig. 25. 2024 - Africa - Evolution of HPAI virus serotypes

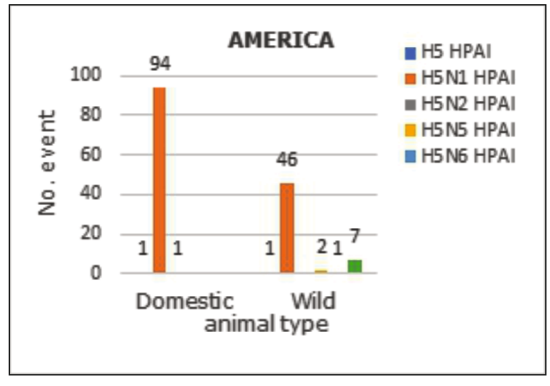

Fig. 26. 2024 - America - Evolution of HPAI virus serotypes

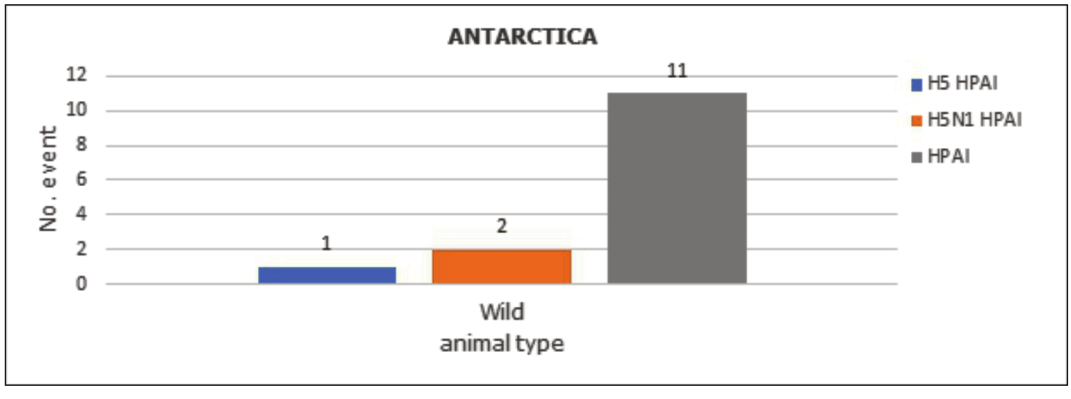

Fig. 27. 2024 - Antarctica - Evolution of HPAI viral serotypes

were recorded. The serotypes that caused events in non-human mammals, between 01.01.2019 and 04. 30.2024, were the following: H5N1 HPAI, H5N8 HPAI, H5 HPAI, H5N3 HPAI, H5N5 HPAI. Forecasting the possible evolution of diseases caused by AIV can help to identify and take early measures to limit the spread of the virus and control the risk of AIV dissemination.

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