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International Journal of Infectious Diseases

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

Consequences and global risks of highly pathogenic avian influenza outbreaks in poultry in the United Kingdom

The first case of the ongoing highly pathogenic avian influenza (HPAI) outbreaks in poultry in the United Kingdom (UK) was detected on October 01, 2022 [1]. Between October 01, 2022, and January 13, 2023, a total of 162 cases of HPAI were detected in the UK; 143 in England, 15 in Scotland, three in Wales, and one in Northern Ireland [1]. The outbreaks have resulted in the culling of more than 4.6 million birds as of January 13, 2023 [2]. In the preceding year between 2021 and 2022, Europe also experienced the largest HPAI outbreaks [3]. A total of 6614 HPAI cases were detected in 37 countries resulting in the deaths or culling of more than 50 million birds [3]. The current UK outbreaks carried important consequences which are beginning to unfold, both epidemiologically, economically, and in global health contexts.

Avian influenza A viruses (AIV) are divided into two groups [4]. The most virulent HPAI virus can infect domestic poultry, other birds, and several mammalian species, causing as high as 100% fatality in chicken flocks. Low pathogenic avian influenza (LPAI) virus causes relatively mild respiratory or no clinical diseases in poultry [4,5]. AIVs are classified by 18 hemagglutinin (HA) and 11 neuraminidase (NA) surface proteins that make up a large variety of subtypes ($H_{1-18} N_{1-11}$) [4–7]. HPAI are restricted to the subtypes H5 and H7 although not all H5 and H7 are HPAI [4,5]. Both HPAI and LPAI occasionally infect humans which can be fatal [5]. From January 2003 to January 2023, a total of 868 cases of human infection with HPAI A/H5N1 have been detected in 21 countries with 457 fatal cases (Case-fatality ratio [CFR] of 53%) [8,9] (Table 1). In 2013, an LPAI virus A/H7N9 emerged in humans in China that caused more than 230 deaths among approximately 680 laboratory-confirmed human infections (CFR: 26%) [5,10].

Human infection of zoonotic influenza viruses, including HPAI A/H5N1 and A/H9N2, is acquired through direct contact with infected birds or animals or a contaminated environment. However, the transmission of the HPAI A/H5 virus between humans is limited by a lack of receptor binding properties (sialic acid- α 2,3-galactose) in humans [7,11]. Between October to December 2022, two human cases of HPAI infection were recorded in Spain (one A/H5N1, and one A/H5N6), one in Vietnam (A/H5NX), and one in China (A/H9N2) [3]. An individual in the UK was infected with HPAI A/H5N1 in January 2022. The person was the owner of the Muscovy duck flock of approximately 125 birds that were infected with the HPAI A(H5N1) virus, with two birds that died and the rest showing clinical signs of illness and were subsequently culled [12]. The sample was taken as part of a routine investigation of the contact person of the infected premises, who had received prophylac-

Table 1

Cumulative number of confirmed human cases of avian influenza A(H5N1) reported to World Health Organization, 2003–2022 (until 25 Nov 2022). Adapted from World Health Organization [9].

Country	Cases	Deaths	Case-fatality ratio (%)
Azerbaijan	8	5	62.5
Bangladesh	8	1	0.12
Cambodia	56	37	66.1
Canada	1	1	100.0
China	54	32	59.3
Djibouti	1	0	0.0
Egypt	359	120	33.4
India	1	1	100.0
Indonesia	200	168	84.0
Iraq	3	2	66.7
Lao People's Democratic Republic	3	2	66.7
Myanmar	1	0	0.0
Nepal	1	1	100.0
Nigeria	1	1	100.0
Pakistan	3	1	33.4
Spain	2	0	0.0
Thailand	25	17	68.0
Turkey	12	4	16.0
United Kingdom	1	0	0.0
United States	1	0	0.0
Vietnam	127	64	50.4
Total	868	457	52.6

tic Oseltamivir (75 mg once per day) and showed no clinical signs [12]. The virus isolated from the infected individual was identical to the virus of his ducks and had a similar profile as other UK HPAI A/H5N1 viruses with no affinity for humans and contained no mutation conferring antiviral resistance to Oseltamivir or amantadine [12]. Currently, various influenza A (H5) subtypes continue to be detected in birds in Asia, Africa, Europe, and North America and sporadic human cases are detected in countries with higher HPAI A(H5) cases [13]. However, the current epidemiologic and virologic evidence suggest that influenza HPAI A/H5 viruses have not yet acquired the ability of sustained transmission in humans [13].

Although direct zoonotic infection by HPAI is rare, novel human influenza derived from the human-animal interface, especially from poultry and/or pigs, and mixing in the industrial and global farming systems with virus exposure and evolution implies a high risk of potential human infections. This was evidenced by the last H1N1 pandemic in 2009, caused by the H1N1 pdm09 virus [14] when a new influenza virus spilled over from pigs to humans,

which was transmitted quickly to cause an initial outbreak in Mexico and then became a pandemic [14]. The virus had reassorted between the influenza viruses of pigs, poultry, and humans in Asia, Europe, and North America [15]. The three influenza pandemics recorded in the last century – the 1918 H1N1 Spanish pandemic, the 1957 H2N2 Asian pandemic, 1968 H3N2 Hong Kong pandemic – were all results of the adaptation of animal-origin viruses which infected humans who continued the transmission via aerosol or respiratory droplets (airborne transmission) [7]. The receptor binding preference of currently circulating HPAI A/H5 viruses can be altered by only a few amino acid replacements in the HA protein [7,11].

The Department of Environment, Food and Rural Affairs (DEFRA), UK Health Security Agency (UKHSA), and the Food Standards Agency (FSA) conducted a risk assessment for exposure and infection of HPAI A/H5 infection in the wild, captive, and commercial birds, humans, and food consumers, respectively [1]. The risk of HPAI A/H5 exposure in poultry in Great Britain is assessed as high for farms with poor biosecurity i.e., event occurs very often with low uncertainty, and the risk of HPAI A/H5 exposure in poultry is medium for the farms with good biosecurity, i.e. event occurs regularly with high uncertainty [1]. The UKHSA advises that avian influenza is primarily a disease of birds and the risk to the general public's health is very low [1]. The FSA cautioned that avian influenza poses a very low food safety risk for UK consumers and that properly cooked poultry and poultry products, including eggs, are safe to eat [1]. This is also supported by regulatory agencies in other jurisdictions, for example, the United States Centers for Diseases Control and Prevention and European Food Safety Authority as the animal-to-human transmission of AIV occurs primarily through direct contact with birds or contaminated environments, and intermediate host (e.g., pigs) and there is no evidence of transmission through consumption of contaminated poultry product [3,16].

Annually, people in the UK consume 13.5 billion eggs of which 11.3 billion eggs are produced in the country [17]. Overall, there are about 38 million laying chickens reared commercially in the UK [18]. The UK has culled more than 4.6 million birds between 1 Oct and January 13, 2023 [2]. As a guideline for HAPI, a 3 km protection zone, and 10-km surveillance zone is set up for every HPAI case. All the poultry of the infected premises are required to be killed and buried, and all other free-range poultry within the protection zone are forced to be kept indoors [1]. The culling of chickens resulted in a serious shortage of eggs in major supermarkets in the UK and some countries in Europe [19,20]. Several supermarkets have started rationing eggs per person [18,19]. The shortage also resulted in a more than 50% increase in eggs price in the UK in November 2022 [21]. This price hike exaggerates the unaffordability of economically vulnerable people in the UK. Children and elderly people are especially dependent on egg-based nutrition. The increased price of eggs and a sudden shortage of supplies could hamper nourishment for children of economically vulnerable families.

In human society, free-range chickens are a source of income, recreation, and family nutrition for many people. Free-range chickens share 63.7% of the eggs market in the UK [17]. The current ongoing HPAI outbreak risks the future of free-range chicken farming, a sector that was the major animal production system before industrial expansion and the current wave of epidemics and pandemics. HPAI has been circulating in poultry and wild birds in the UK throughout the year including the summer months in 2022 [1,3]. This means that the farmers must keep the chickens indoors for prolonged periods in unsuitable conditions and thus the free-range nature of rearing the chicken is lost leading also to increased costs from the artificial feed. This situation is compounded by increased poultry feed prices because of the ongoing Russia-Ukraine

war [22]. DEFRA recommended following strict biosecurity measures in the captive and free-range premises to reduce the chance of HPAI infection through wild and migratory birds [1]. Whether this strategy is realistic in the long term is questionable and it may create a paradox, as reliance on intensive and closed environment poultry carries the significant potential risk for the evolution of novel pathogens [23,24].

HPAI has become a global issue since the massive expansion of the poultry industry, especially in Asia where fatal pathogens have emerged from poultry of a different character than hitherto. An example of this is HPAI A/H5N1 which has developed the capacity to infect wild birds and cause severe disease in these normally resistant populations [25]. This increased risk of virus reassortment has indeed occurred in the past [14]. Epidemiologically, the UK outbreaks could increase the risk of zoonotic transmission and the potential for mixing of the influenza viruses of other species, the situation of which can facilitate the emergence of a novel reassorted detrimental virus to cause human diseases. Sentinel surveillance, joint epidemiological research, and global collaboration are crucial in enhancing preparedness against HPAI outbreaks. Economically, the disruption of chicken egg supplies in the supermarkets has resulted in an increase in the price of eggs and potentially reduced nourishment for children of poor families while supplies of free-range chicken, which are the source of family income and nutrition are becoming scarce. Similar problems may emerge in other parts of the world as HPAI continues to evolve. Another key question is whether industrialization of poultry farming is a sensible and or viable option given the risk and consequences. An alternative and more resilient poultry system is needed. This might be possible by reverting to genetically resistant stock and a less globally and more locally integrated industry with higher welfare standards. This will have mostly positive consequences on One Health for humans and wild and domestic animals.

Declaration of competing interest

The authors have no competing interests to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics

This study does not include any individual-level data and thus does not require any ethical approval.

Acknowledgments

NH, RK and AZ are members of The Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET) funded by the European (EU) and Developing Countries Clinical Trials Partnership, supported by the EU Horizon 2020 Framework Programme. We acknowledge Dr Sharifa Nasreen, University of Toronto, for reading and commenting on this article. AZ is in receipt of a UK-National Institute for Health and Care Research Senior Investigator award and is a Mahathir Science Award and EU-EDCTP Pascoal Mocumbi Prize Laureate.

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