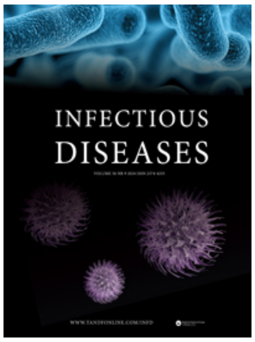

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On the avian influenza A (H7N5) outbreak: let's not underestimate the less famous subtypes

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COMMENT

On the avian influenza A (H7N5) outbreak: let's not underestimate the less famous subtypes

Avian influenza viruses are classified into two main categories: highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI). This classification is based on the severity of the disease in poultry. HPAI viruses cause severe disease and high mortality rates in infected birds, often leading to significant economic losses in the poultry industry [1]. LPAI viruses, on the other hand, typically cause mild or no symptoms in birds and are less likely to result in large-scale outbreaks. However, LPAI viruses can mutate into HPAI strains under certain conditions, making their monitoring crucial for preventing potential outbreaks [2]. Both HPAI and LPAI can infect a variety of bird species and have zoonotic potential, meaning they can sometimes infect humans, although this is rare [3]. H7N5 is a subtype of the avian influenza virus, but it is not commonly reported compared to other subtypes like H5N1 or H7N9. There is not much detailed information specific to H7N5 available in the scientific literature, suggesting that it has not been at the centre of significant outbreaks or public health concerns on a large scale. Regarding the classification as HPAI or LPAI, H7N5 strains could theoretically be classified into either category depending on their specific pathogenic characteristics. Like other H7 viruses, H7N5 could exist in both low pathogenic (LPAI) and highly pathogenic (HPAI) forms [4]. Determining pathogenicity would require a specific analysis of the viral strain and its ability to cause severe disease in poultry. In general, the classification of any avian influenza virus subtype as HPAI or LPAI is based on laboratory tests that evaluate the severity of the disease the strain causes in chickens and other birds. So far, there have been no significant reports of H7N5 causing major outbreaks or being a public health threat, but continuous monitoring and research are essential to track potential mutations and the pathogenicity of these viruses.

Even though the H7N5 subtype is not well known for being particularly virulent, we must not make the mistake of underestimating it and neglecting proper investigation. Among the recently re-emerged subtypes, H7 is present in the H7N9 reassortment [5]. However, this does not mean that it cannot undergo new reassortments or mutations that could transform it from being of low pathogenicity to highly pathogenic.

In early July, Germany has reported an outbreak of highly pathogenic H7N5 bird flu on a farm located in the western region of the country, close to the Netherlands border, according to the World Organisation for Animal Health (WOAH) (https://www.canadiancattlemen.ca/daily/germany-reports-rare-outbreak-of-h7n5-bird-flu-near-dutch-border/). The outbreak, detected on June 29 and confirmed on July 2 by the Friedrich Loeffler Institute's (https://www.fli.de/de/aktuelles/kurznachrichten/neues-einzelansicht/gefluegelpest-vom-subtyp-h7n5-bei-legehennen-in-niedersachsen-bestaetigt/) National Reference Laboratory for Avian Influenza (AI)/Fowl Influenza (FLI), prompted local authorities to take prescribed measures, including the culling of 6,000 birds out of a flock of 90,879 in the town of Bad Bentheim, Lower Saxony, as stated by WOAH. In addition, a protection zone (3 km) and a surveillance zone (10 km) were established. Two outbreaks of avian influenza occurred on farms in Lower Saxony in 2024: in January, the disease was detected on a turkey farm in the Emsland district and on a free-range laying hen farm in the Northeim district. Among wild birds, the last case in Lower Saxony was in March, when a gull was found infected in the Friesland region (Wangerooge). Despite these precedents, the early July outbreak represents the first case of H7N5 recorded in WOAH public records (https://wahis.woah.org/#/in-event/5745/dashboard), opening a new chapter on global animal disease outbreaks.

The phylogenetic tree shown in Figure 1 was created using sequences of the gene HA belonging to all H7N5 sequences available in GISAID over time (see Supplementary File S1). The main result of this analysis

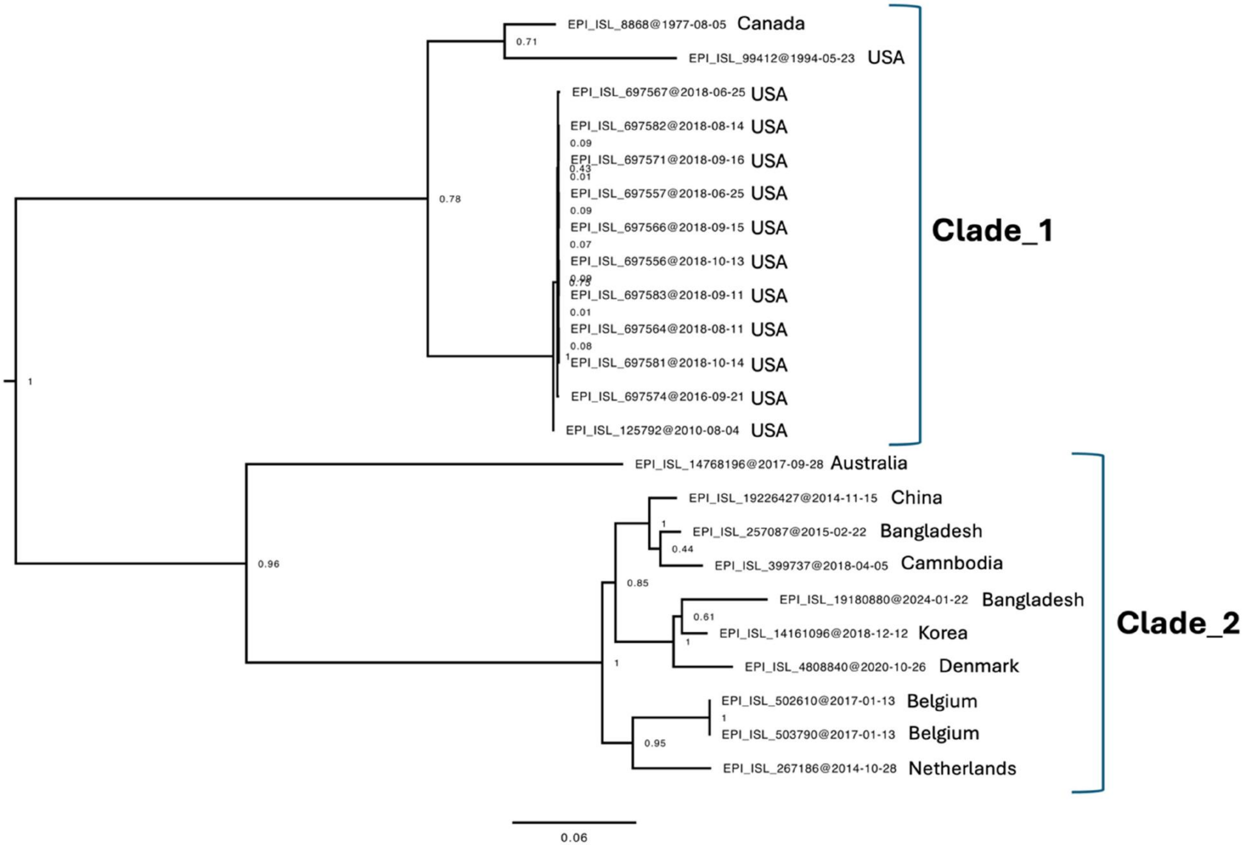

Figure 1. Phylogenetic tree obtained by using Bayesian inference implemented in the software MrBayes [6]. nodes values are expressed in PP (posterior probabilities). Figure has been edited using the software GIMP 2.8 (https://www.gimp.org/downloads/oldstable/).

reveals that there is not enough information to reconstruct an evolutionary path. This dataset is too flawed to provide a comprehensive understanding of the relationships between major strains and their origins, and it cannot depict evolutionary rate increases or local speciation events. The information provided by the current dataset indicates that the H7N5 lineage is represented by two main clades, but these two groups appear to have no epidemiological significance. From a genetic point of view, the tree shows a strong genetic structure based on geographic information. Clade I is composed of sequences from the Americas, while Clade II is more heterogeneous. It includes a sequence from Australia in a basal position, with the main group consisting of sequences from Asia and Europe.

The genetic distance between clades amount to 0.23 while the distance within clades amounts ranges from 0.001 to 0.04. The evolutionary rate of the gene HA amount to 2.2×10^{-3} subs/site/years, and NA to 3.1×10^{-3}. This condition suggests the occurrence of a great potential that may promote important changes. For this reason, the constant and uninterrupted genetic monitoring is the only way to develop an appropriate management plan.

In fact, the genetic potential allows the virus to evolve, making it more likely to adapt to different environments, host species, and immune responses, thereby increasing its potential to cause widespread disease. Such viruses can lead to epidemics, overwhelming healthcare systems and causing high morbidity and mortality rates. As the COVID-19 pandemic taught us, economically, they can disrupt trade, travel and everyday activities, leading to significant financial losses and economic downturns. Additionally, the rapid spread of a genetically versatile virus can strain international relations and necessitate coordinated global responses to effectively manage and contain outbreaks. Overall, the presence of a virus with high genetic potential underscores the importance of robust surveillance, research, and preparedness strategies to mitigate its impact.

In general, to avoid being caught off guard as with the COVID-19 pandemic, the establishment of an epidemiological monitoring group is necessary.

To the best of our knowledge the HA gene of the H7 subtype has been identified in combination with all nine NA subtype genes [2]; however, the possibility of a new reassortment, especially one that becomes highly pathogenic, cannot be excluded. Indeed, spillover happens when a pathogen with high prevalence in a reservoir population meets individuals of different species, leading to the pathogen jumping species and spreading within the new host population.

The only way to be prepared for potential new outbreaks is to continue monitoring, even of low pathogenic strains that may not seem concerning. The H7N5 outbreak occurred in Germany in early July demonstrates this necessity. To maintain constant updates, an epidemiological monitoring centre should be established to collect and promptly process data from all involved laboratories, providing tools for effective management.

Author's contributions

Conception and design: F.B., M.C., F.S.; Investigations: F.B., M.C., F.S.; Validation: M.C.; Supervision: M.C.; Writing – Original: F.B., M.C., F.S.; Writing – Revision: F.B., MC., F.S.

Disclosure statement

No potential conflict of interest was reported by the authors.

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