Investigation on Common Influenza Viruses Affecting Chickens and Ducks in Egypt

Ahmed A. H. Ali[1], Shimaa M.G. Mansour[1], Sozun M. Hefny[1], Serageldeen Sultan[2] [*]

[1]*Department of Virology, Faculty of Veterinary Medicine, 44511, Zagazig University, Zagazig, Egypt*

[2]*Department of Microbiology, Virology Division, Faculty of South Valley University, Qena 83523, Egypt*

[*]**Corresponding author:** Tel./fax: þ20 96 321 1223.

E-mail: sultanseragеldeen@gmail.com s.sultan@vet.svu.edu.eg

Abstract

Influenza viruses (IVs) consist of *Alphainfluenzavirus* (Influenzavirus A), *Betainfluenzavirus* (Influenzavirus B), *Gammainfluenzavirus* (Influenzavirus C), *Deltainfluenzavirus* (Influenzavirus D), Isavirus, Mykissvirus, Sardinovirus, Quarajavirus and Thogotovirus genera in the family *Orthomyxoviridae*. Owing to their surface glycoproteins, hemagglutinin (HA), and neuraminidase (NA), diversity in poultry influenza A virus is further categorized into 16 HA (H1–H16) and 9 NA (N1–N9) subtypes. However, these glycoprotein subtypes are 20 HA and 11 NA in mammals. The pathogenicity of avian IVs (AIVs) in birds exhibits a high pathogenic (HP) form of AIV which causes severe deaths among birds or a low pathogenic (LP) form of AIV where birds look normal. The H5 subtype is a considerable risk to the human population even if it is a low pathogenic one. The co-circulation of HPAIV and LPAIV subtypes among different avian species in Egypt detrimental effect on the national economy. H5N1, H5N2, H5N8, and H9N2 viruses will be addressed in this review as the predominant subtypes in Egypt. The contribution of migratory wild birds in maintaining the endemicity of AIV LPAIV or HPAIV among domesticated poultry will also be clarified.

Keywords: Avian influenza, Egypt, HPAI, LPAI, common subtypes.

Introduction

Avian Influenza virus (AIV) nucleic acid is a single-stranded and negative-sense RNA that has eight segments encoding 10 viral proteins (***King et al., 2011***). The *Orthomyxoviridae* family is categorized into 4 main genera of *Alphainfluenzavirus*, *Betainfluenzavirus*, *Gammainfluenzavirus*, and *Deltainfluenzavirus* as well as *Isavirus*, *Mykissvirus*, *Quarajavirus*, *Sardinovirus* and

Thogotovirus genera (***ICTV, 2022***). AIVs are widespread and can infect both birds and mammals (***Capua et al., 2004***). Pandemic outbreaks because of influenza viruses have been reported during 1924–1925, 1929, 1953, and 1971 in the USA. However, the severest pandemic outbreak has been reported in Hong Kong in 1997 after that it disseminated to Asia, Europe, and Africa associated with crossing species barriers and fatality among humans **(*Capua and Alexander, 2004*)**. The neuraminidase (NA) and haemagglutinin (HA) envelope proteins' genetic diversity is used to differentiate Influenza A virus subtypes. NA has nine subtypes (N1-N9) while HA has sixteen subtypes (H1 - H16) in avian species **(*Capua and Alexander, 2004*),** while these are 20 HA ***(Luo, 2012)*** and 11 NA ***(Tong et al., 2013)*** subtypes. Chickens, turkeys, and ducks are the most susceptible avian species to AIVs although other domesticated poultry are infected. Orders *Anseriformes* (ducks and geese) and *Charadriformes* (shorebirds, gulls, terns, and auks) consider the mixing vessel and reservoir for possible emerging HA (16 HA) and NA (9 NA) subtypes. Several geographical, environmental, host and seasonal factors are contributing to the spreading and prevalence of AIV **(*Capua and Alexander, 2004*)**. The antigenic shifts and antigenic drifts cause alternations in AIV surface glycoproteins (HA and NA) antigenicity **(*King et al., 2011***). The HA glycoprotein is created as a precursor, HA0, which must be post-translational cleaved by cellular proteases before it becomes active and virus particles are infectious (***Lu et al., 2013***). The HA precursor proteins of low virulence AIVs for chicken contain an arginine at their cleavage sites and one at position 4. These viruses are restricted to activation by cellular-specific proteases such as trypsin-like enzymes, so it replicates in the respiratory and intestinal tracts where these enzymes are available. The highly pathogenic avian influenza (HPAI) viruses have several basic amino acids (arginine and lysine) at their HA cleavage sites because of the insertion or substitution which are cleavable by a ubiquitous protease(s), several proprotein-processing subtilisin-related endo-proteases of which furin is the leading candidate (***Lu et al., 2012***). HPAIVAIVs must induce an intravenous pathogenicity index (IVPI) greater than 1.2 in 6-week-old chickens. The presence of multi-basic amino acids at the HA cleavage site is a reliable indicator of pathogenicity for H5 and H7 influenza viruses, regardless of their virulence for chickens (***Hoffmann et al., 2007***). These viruses can propagate inside the bird's body destroying its key organs and tissues and leading to illness and mortality (***Lu et al., 2013***). Because of this, molecular characterization

of the cleavage site using sequencing (***Londt et al., 2007***) is considered the best method for determining the virus pathogenicity. However, expensive tools and supplies, as well as skilled and experienced staff are necessary for this method. Other molecular approaches such as restriction enzyme digestion analysis using RT-PCR amplicons facilitate pathotyping by reducing the handling risk of infectious agents and analysis cost (***Höper et al., 2009***).

Avian Influenza Pathogenicity

According to EU regulations, AIVs could be classified as HPAIV-inducing infection in poultry if they have IVPI of more than 1.2 in 6-week-old chickens. Also, H5 and H7 influenza A subtypes amino acid motifs have many basic amino acids in the HA cleavage site that are notifiable as HPAIV (***Lu et al., 2012***). HPAIV causes generalized infection with widespread hemorrhages, edema, and cutaneous ischemia as characteristic symptoms of the disease in poultry. Virus isolation could be achieved from internal organs. In contrast, LPAIV produces localized infections related to the intestinal tract where the virus is excreted in the feces and spread via contaminated water (***Klenk et al., 2013***).

Viral pathogenesis is owing to the complex interactions that the virus undergoes when it utilizes the cell biosynthetic machinery for replication and exposes it to the host's defense mechanisms. All viral proteins take part in this process especially viral polymerases (PB2, PB1, and PA), non-structural (NS1), and HA proteins (***Klenk et al., 2013***).

Common Subtypes of AIV in Egypt

The HA surface glycoprotein of the influenza virus encourages viral entry into the host cell by attaching sialic acid receptors on the host cell surface (***Lu et al., 2013***). Although HA polybasic cleavage site is a good predictor of H5 virus pathogenicity, the insertion of polybasic amino acid motifs into an HA LPAIV does not always convert into HPAIV in an experiment on chickens **(*Bogs et al., 2010*)**. Over 30,000 nucleotide sequences of different HA subtypes have been sequenced and analyzed by X-ray crystallography for three-dimensional structures such as H1 (***Russell et al., 2004***), H2 (***Liu et al., 2009***), H3(***Stevens et al., 2006***) H5 ***(Stevens et al., 2006)***, H7 (***Russell et al., 2004***), H13 (***Lu et al., 2013***), H16 (***Lu et al., 2012***), H17 **(*Zhu et al., 2013*)** and H18 **(*Tong et al., 2013*).**

Egypt experienced several outbreaks of AIV that detrimentally affect the poultry industry owing to the co-circulation of several subtypes among chickens in the same farm. Since its detection in 2006 in Egypt, HPAIVH5N1 (clade 2.2.1) has long been an endemic infection. In addition to that, LPAI H9N2 infection in quails was

confirmed in 2010. Since that time both viruses have been spreading among chicken farms (***Peyre et al., 2009*; *Bogs et al., 2010*; *El-Zoghby et al., 2012*).** The emergence of the pandemic HPAIH5N1 in Egypt posed a public health concern with 41.8% fatality of recorded human cases worldwide. In Egypt HPAIVH5N8 (clade 2.3.4.4b) was firstly isolated from common-coot in Egypt in December 2016 **(*Selim et al., 2017*)** after that it was identified in duck samples collected from backyard and commercial farms early in 2017 proposing repeated virus incursions by migratory wild birds **(*Salaheldinet al., 2018*; *Yehia et al., 2018*)**. Interestingly, HPAIVH5N8 spreading among domestic poultry flocks received genes from LPAIVH7N3 has been isolated in Egypt from wild birds **(*Naguib et al., 2019*)**. Egypt has been plagued with endemic AIV during last decades causing significant economic losses and public health risks **(*Aly et al., 2008*).** In 2017, H6N2 AIV subtype has been reported in wild birds in Egypt. In addition to these, a novel H5N2 reassortant has been detected in a poultry farm in 2019 which genetically composed of HA gene from HPAIVH5N2 and other 7 genes (PB2, PB1, NP, NA, M and NS) from H9N2 viruses ***(WOAH, 2021)***.

HPAIV H5N1

Aquatic birds including waterfowl are considered HPAIVH5N1 reservoirs. HPAIVH5N1 infected wild geese in the south of China has been claimed for spreading the virus to poultry in 1996. Since 2003, HPAIVH5N1 (A/goose/Guangdong/1996 **[**Gs/GD] lineage) has been recorded in 84 countries across Asia, Africa, Europe, and North America **(*Criadoet al., 2020*)**, associated with destructive economic losses and increasing human cases of H5N1 infection ***(Zhang et al., 2020)***. Also, the virus maintains its pathogenicity in poultry and human, in 2002 it has evolved to cause disease in domestic ducks and outbreaks among wild waterfowl in Qinghai Lake in 2005 **(*Liu et al., 2005*)**.

HPAIVH5N1 infected 486 human cases from them 287 deaths, in addition to reported deaths in China, Indonesia, Vietnam, and Egypt over 370 case fatalities in human have been recorded in 2003. Also, hundreds of millions of poultry have been contaminated because of HPAIVH5N1 infections leading to severe agricultural and economic problems **(*WHO, 2013*)**. Continuous spreading of the virus among vaccinated and non-vaccinated commercial chicken farms, backyard and live bird markets poultry has been proved through surveillance studies **(*Abdelwhab et al., 2010*)**. Furthermore, the virus can evolute and produce several variants that can complicate the epidemic situation of the virus. The circulated

H5N1 isolates in Egypt which has been evolved from Qinghai Lake H5N1 viruses have several genetic markers such as mutating glycosylation site at 154-156 in HA and missing 627K amino acid in PB2 ***(Herfst et al., 2016*)**. As the results of these remarkable changes the virus transmissibility in mammals and viral replication in human may be increased, indicating the public health concern of the Egyptian HPAIVH5N1 variant (***Neumann et al., 2012*)**. The Egyptian HPAIVH5N1 viruses have been reported in Egypt since 2006 inducing high mortality among chickens and can be fatal to waterfowls **(*Aly et al., 2008*)**. The intensive vaccination of chickens to control spreading of HPAIVH5N1 epidemics from farm to farm by H5 vaccines can contribute to virus mutation and evolution ***(Abdelwhab et al., 2010*)**. The viral transmission and pathobiology of the present Egyptian HPAIH5N1 viruses, the main source of epidemics among poultry in the country, are poorly understood. The pathological features of HPAIVH5N1 which caused epizootic outbreak in UK during 2020 – 2021 and considered the largest outbreak from HPAIVH5N1 among different avian taxa Owing to enormous number of examined birds has been reported in UK include pancreatic and splenic necrosis. However, many gross lesions characteristic to HPAIV were absent during post-mortem examination. In comparison to this outbreaks gross features HPAIVH5N1 infected birds shows variable lesions with little similarity to UK outbreak in 2020–2021 **(*Lean et al., 2022*)** .

LPAI- H9N2

The H9N2 endemicity among avian species in Asia and Middle East and its transmissibility from birds to mammals are impacting it as health hazards ***(Butt et al,2005*)**. The co-infection of LPAIVH9N2, HPAIVH5N1 and HPAIVH5N8 and their predominancy among chicken farms have detrimental effect on the poultry industry as well as public health concerns **(*Ahmed et al., 2012*)**. The occurrence of these subtypes together in the same host enhances the genetic evolution and leads to emergent of new variants may be able to induce uncontrolled pandemics as that one occurred in Bangladesh in 2013 **(*Monne et al., 2013*)**. In 1998 LPAIVH9N2 outbreaks among commercial chicken farms have been reported in Iran, since that time it is distributing in the Middle East **(*Adel et al,, 2021*)**. Also, LPAIVH9N2 is worldwide spreading between domesticated and wild birds ***(Banks et al., 2000*)**. LPAIVH9N2 has been isolated from human case sharing close relationship that isolated from quails in 1999 in Hong Kong **(*Peiris et al., 1999*)**. In addition to that, LPAIH9N2 viruses have demonstrated as genes donor for different reassortants ***(Peacock et***

al., 2019) such as H5N1 variants in Hong Kong in 1997 and t H7N9 variants in China in 2013 which received internal gene segments from LPAIVH9N2 (***Gao et al., 2013***). Genetically and phylogeographically, Two main categories for LPAIH9N2 viruses the American lineage, which are spreading among wild birds, and the Eurasian lineages, which are consist of the G1 lineage (A/quail/Hong Kong/G1/1997), the Y280 lineage (A/chicken/ Beijing/1/94 and A/duck/HK-Y280–1997), and The Korean lineage (A/chicken/Hong Kong/Y439/1997) based on the nucleotides diversity and phylogenetic analysis ***(Guo et al., 2000)***. The G1 lineage viruses are worldwide distributing, and they are divided into A, B, C, and D groups **(*Fusaro et al., 2011*)** within two sub-lineages; western sub-lineage (G1-W) and eastern sub-lineage (G1-E) **(*Peacock et al., 2019)***. Although chickens are the most vulnerable avian species to H9N2 infection where young broiler chickens are more susceptible to infection than old layers, and breeders chickens ***(Fusaro et al., 2011*)**, LPAIVH9N2 has been reported in other species as ducks with lower infection rate than chickens which proposed their acting as virus carriers **(*Kayali et al., 2014*)**. The occurrence of LPAIH9N2 among chickens in Egypt adversely affects poultry sector, particularly when occurred as co-circulation with endemic HPAIVH5N1 ***(Arafa, et al., 2012*)**. In addition to that, the leakage in biosecurity system specially in mass production chicken farms enhances the virus transmission and applies more risk on the poultry **(*Capua and Cattoli, 2013*)**. So, the continuous investigation of H9N2 viruses among poultry is necessary to understand the virus ecology and epidemiology and its public health hazards. H9N2 viruses not only harm the national economy but also the population's health. Since 2011, LPAIH9N2 has become endemic among poultry flocks and the necessity to follow up its genetic evolution has been established. The continuous genetic sequencing of HA genes revealed that 9 amino acid substitutions especially amino acids at positions 180 and 216 which indicated positive selection pressure, have been reported in 44 isolates of H9N2 during 2017 – 2020 with 95 – 96% similarity in comparison to the original H9N2 isolate in 2011 (A/quail/Egypt/113413v/2011).

Also, these isolates have clustered phylogenetically in a new clade closely related to H9N2 viruses isolated in 2015 indicating the H9N2 virus evolution over years in Egypt **(*Adel et al., 2021*)**.

AIV H5N2

Owing to several outbreaks have been reported all over the world as H5N1 in Hong Kong, H5N2 in Italy, Mexico and USA, H7Nl in Italy, H7N4 in Australia, H7N3 in Canada and Pakistan, and H7N7 in

the Netherlands, HPAIV is considered a devastating agent for poultry industry **(*Fouchier et al., 2005*)**. Also, LPAIV and HPAIV H5N2 outbreaks have recorded in China, Taiwan, Thailand, Singapore, Australia, Italy, Ireland, Belgium, Russia, Ukraine, Germany, France, and UK. HPAIVH5/H7 viruses characterized by variety clinical signs in avian species, especially chickens with morbidity and mortality up to 100% **(*Capua and Alexander, 2004*)**. LPAIVH5 and H7 viruses are the precursors of HPAIV, therefore it is imperative for animal health organizations to investigate LPAIV H5 and H7 foci among poultry **(*Capua and Alexander, 2004*)**. ***Osman et al.*, (2015)** assessed the epidemiology of AIVs and the prevalence of H5 and H9 subtypes among poultry flocks in Qena and Luxor governorates in the South Egypt during 2009–2011. The correlation between the Goose/Guangdong lineage like Eurasian H5 viruses distribution among domestic flocks and wild birds mobility has been confirmed in East Asia, Western Europe and North America in 2014 ***(Verhagen et al., 2015*)**. Therefore, it is necessary to investigate AIVs H5 genetic features to recognize any mutations that enhance virus virulence and transmission especially in Asia owing to close contact between wild and domestic poultry. LPAIVH5N2 has been claimed as the progenitor for HPAIVH5N2 that causes outbreaks among poultry in the northern Europe (***Fouchier et al., 2005*)**. ***Sultan et al.*, (2016)** have reported multiple reassortant H5N2 viruses among migratory birds in Obihiro, Japan during 2009 and 2011 and provided a hypothesis for their genetic evolution. Where their evolutionary process in relation to other H5N2 isolates from wild birds and chickens has been investigated to draw a clear picture and to understand H5 virus genesis, which are considered of veterinary and public-health concern. The ministry of agriculture in Egypt has been confirmed the identification of HPAIVH5N2 as a new AIV from apparent health ducks in Dakahlia governorate in 2019 (***Hagag et al., 2019***). Also, an emergent H5N2 has been detected from broiler chicken flocks in Beheira and Fayoum in the same year. This emergent H5N2 viruses gained gene segments from pigeon H9N2 (PB1, PB2, PA, and NS) isolated in 2014, H5N8 clade 2.3.3.4b (HA segment) isolated from ducks in 2017 and chicken H9N2 (NP) isolated in 2010 (***Hassan et al., 2020***).

AIV H5N8

In South Korea during AIV outbreaks in 2014, a new reaasortant HPAIH5N8 clade 2.3.3.4 virus was reported (***Jeong et al., 2014***). Gochang-like and Buan2-like H5N8 types have been found during these outbreaks. The Buan2-like is the common type which segregated into three

subgroups is spreading by migratory birds through North America, Europe, and East Asia spread to Europe, East Asia, and North America (***Verhagen et al., 2021***). In mid-2016, HPAIH5N8 virus clade 2.3.4.4 was distributed into different regions worldwide with continuous waves predominate in Africa, Europe, and the Middle East (***Li et al., 2017***). HAPIH5N8 virus clade 2.3.4.4b has been recorded among poultry in many countries such as Iraq, Kazakhstan, and Russia (***Lewis et al., 2021***) also, human cases of H5N8 have been reported among chicken farm employees in 2020 in Russia (***Pyankova et al., 2021***) indicating its adverse effect on poultry production and public health threatens.

Since 2016, HPAIVH5N8 clade 2.3.4.4b has become predominate with multiple introductions among poultry in the Middle East indicating the area is an endemic hotspot for the virus. The phylogenetic analysis of H5N8 viruses revealed three genetic groups (Egypt I – III) circulating among Egyptian poultry. HPAIH5N8 viruses have been found in 45.1% of H5-vaccinated poultry flocks in Egypt during 2019 - 2021(***Salaheldin et al., 2017***; ***Selim et al., 2017***; ***Yehia et al., 2018***; ***Hassan et al., 2021***) revealed that the current vaccination efficacy should be assessed, and biosecurity measures should be strengthened.

Epidemiology of AIV among poultry in Egypt

The leakage in biosecurity barriers in poultry farms and continuous circulation of multi-infections such as HPAIH5N1, HPAIH5N8 and LPAIH9N2 viruses diminished the possibility for controlling the endemic diseases such as AIV using vaccination process **(*Kayali et al., 2016*)**. Viruses infecting the respiratory system of broiler chickens are considered the crucial factor for the investment in poultry production. These viruses can infect birds as co-infection as H5N1, H5N2, H5N8, and H9N2 or act as predisposing factor for flaring up the commensal or other concurrent pathogens and enhancing its pathogenicity to the host **(*Samy and Naguib, 2018*).**

HPAIV H5N1 has become endemic among different poultry species in Egypt since 2006 with the highest fatality among humans in the world. Also, LPAIV H9N2 and HPAIV H5N8 are continuously circulating among domesticated birds after their first detection in Egypt in 2010 and 2016, respectively, **(*Naguib et al., 2018*)**. The persistency of HPAIV H5N1 and LPAIV H9N2 con-infection among poultry and genetic evolutions of LPAI viruses are considered potential risk factors for the emergence of unique variants of AIV forebode the future occurrence of poultry flocks' devastation. Among the probable causes of AIV endemicity in Egypt is migratory wild birds which play a

vital role in introducing H5N1 and H5N8 HP strains as well as their harboring several combinations of AIVs (H1-16 and N1-9). The mechanism of genesis and emergent of new AIV strains from wild and domestic birds is unclear because of lacking full genome sequences data of several AIV isolates (H5N1 and H9N2) in Egypt and doing only sequence analysis of the surface glycoprotein (AH and NA) rather than other internal gene segments (PB2, PB1, PA, NP, M, and NS). Therefore, research works on the full gene segment analysis of LP and HP AIV strains are necessary to clarify the role of birds, especially wild birds, in genetic donations for the prevalent AIVs in Egypt. In addition to this, AIV genotyping and sub-genotyping data for H5N1, H9N2 and other subtypes persistent among birds will clarify the virus endemicity and choosing suitable measures such as strict biosecurity in poultry farms to prevent virus dissemination and evolution among birds due to leakage barriers between wild and domesticated birds **(*Abdelwhab and Abdel-Moneim, 2015*)**. In 1970, AIV H3N1, H4N1, and H11N6 subtypes were identified from samples collected from wild birds in Egypt **(*Amin et al., 1980*)**. HPAI H5N1 was detected in crows, cattle egrets, and great egrets **(*Soliman et al., 2012*),** HPAI H5N1 and H5N8 viruses were identified in Eurasian green-winged teal samples **(*Sheta et al., 2014*)**. Wild birds on Egypt have been investigated for HPAIV H5N1 (***Njabo et al., 2016*)** as control measurement since its identification in 2003 in China. AIV H7 and H10 were the most predominate subtypes detected from wild birds **(*Gerloff et al., 2013*)**. AIV subtypes such as H1N1, H1N2, H2N8, H4N6, H5N1, H5N2, H6N2, H7N7, H7N1, H7N3, H7N7, H7N9, H10N1, H10N4, H10N7, H10N9 H11N9, and H13N9 were isolated from northern shoveler and Eurasian green-winged teal sampled in Egypt **(*Soliman et al., 2012*; *El-Zoghby et al., 2013*)**. Although AIV surveillance in wild birds mainly identified H5 **(*Sheta et al., 2014*)**, as well as H7 and H9 subtypes ***Saad et al.*, (2007); *Soliman et al.*, (2012) and *Gerloff et al.*, (2013)** reported that 201/1304, 732/7894, and 703/7678 sampled birds, respectively, were AIV positive H5 negative without further investigations. These non H5 AIV infected birds contributed to distribution, pathogenesis, and evolution of the virus among domestic poultry through introduction of new subtypes or strains genetic reassortments.

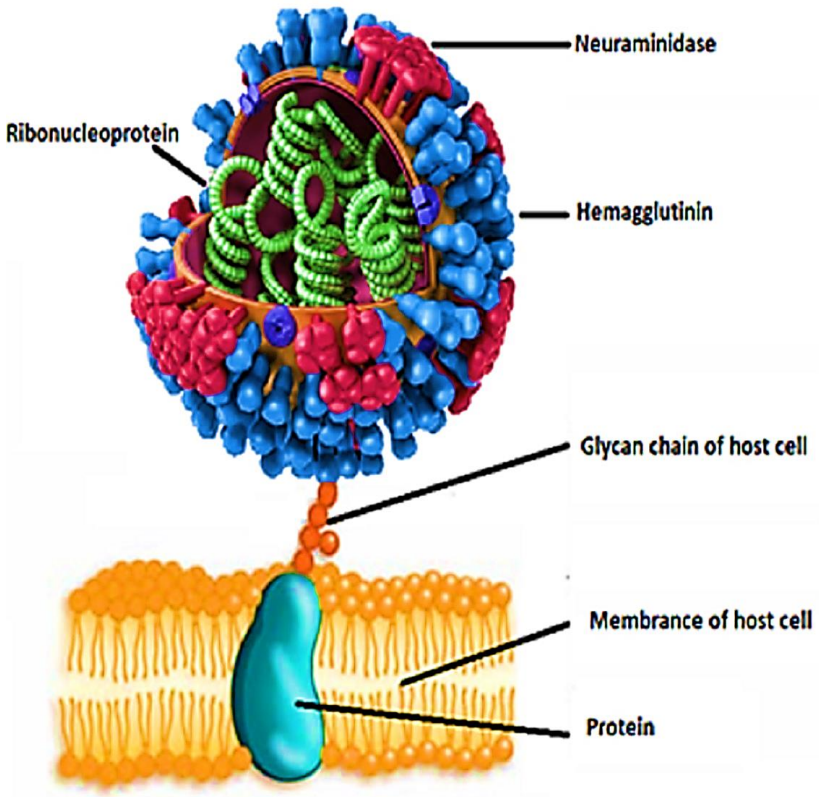
Economic Impact of AIV on poultry industry

Several respiratory viral diseases including AIV detrimental effected the national income and devastated the poultry industry in Egypt which consider the main source of animal protein in form of meat and eggs ***(Hassan et al., 2021*)**. HPAIV H5 multiple introductions have

adversely affected poultry flocks and humans since its first detection in 2006, with the highest high fatality cases of 114 out of 336 (34%) confirmed HPAIV H5N1in human (***WHO, 2010***). Poultry industry in Egypt experienced severe economic losses estimated as 1 billion US dollar and 30 million culled birds because of HPAIVH5N1 waves which negatively influenced wages of 1.5 million people work in poultry industry (***Meleigy, 2007***). ***Cui et al.,* (2022)** reported that 2,782 outbreaks of H5N8 have occurred in over 25 countries destroying about 38 million birds in Jun 2021.

Conclusion

This review highlights the co-circulation of HPAIV and LPAIV subtypes among different avian species in Egypt and their harms on the national economy. Also, the urgent need for future studies focuses on the investigation of other AIV subtypes than those reported here to avoid emergent of new AIV pandemic variants.



Fig, 1. Structure and interaction of influenza virus surface glycoprotein with a host cell.

References

Abdelwhab, E. M., and Abdel-Moneim, A. S. (2015). Epidemiology, ecology and gene pool of influenza a virus in Egypt: Will Egypt be the epicentre of the next influenza pandemic? Virulence, 6 (1), 6–18.

Abdelwhab, E. M., Selim, A. A., Arafa, A., Galal, S., Kilany, W. H., Hassan, M. K., Aly, M. M., & Hafez, M. H. (2010). Circulation of avian influenza H5N1 in live bird markets in Egypt. Avian Diseases, 54(2), 911–914.

Abdelwhab, E. S. M., Veits, J., & Mettenleiter, T. C. (2013). Genetic changes that accompanied shifts of low pathogenic avian influenza viruses toward higher pathogenicity in poultry. Virulence, 4(6), 441–452.

Adel, A., Mady, W., Mosad, Z., Amer, F., Shaaban, A., Said, D., Maged, M. A. A., Arafa, A.-S., Morsi, M. K., & Hassan, M. K. (2019). Molecular and Epidemiological overview on Low Pathogenic Avian Influenza H9N2 in Egypt between 2015 and 2016. Hosts and Viruses, 6 (2).

Adel, A., Mosaad, Z., Shalaby, A. G., Selim, K., Samy, M., Abdelmagid, M. A., Hagag, N. M., Arafa, A. S., Hassan, W. M., & Shahien, M. A. (2021). Molecular evolution of the hemagglutinin gene and epidemiological insight into low-pathogenic avian influenza H9N2 viruses in Egypt. Research in Veterinary Science, 136, 540–549.

Ahmed, S. S. U., Themudo, G. E., Christensen, J. P., Biswas, P. K., Giasuddin, M., Samad, M. A., Toft, N., & Ersbøll, A. K. (2012). Molecular epidemiology of circulating highly pathogenic avian influenza (H5N1) virus in chickens, in Bangladesh, 2007-2010. Vaccine, 30(51), 7381–7390.

Alexander, D. J. (2000). A review of avian influenza in different bird species. Veterinary Microbiology, 74(1–2), 3–13.

Aly, M. M., Arafa, A., & Hassan, M. K. (2008). Epidemiological findings of outbreaks of disease caused by highly pathogenic H5N1 avian influenza virus in poultry in Egypt during 2006. Avian Diseases, 52(2), 269–277.

Amin A, Shalaby MA, Imam IZ (1980). Studies on influenza virus isolated from migrating birds in Egypt. Comp Immunol Microbiol Infect Dis., 3:241–246.

Arafa, A. S., Hagag, N. M., Yehia, N., Zanaty, A. M., Naguib, M. M., & Nasef, S. A. (2012). Effect of cocirculation of highly pathogenic avian influenza H5N1 subtype with low pathogenic H9N2 subtype on the spread of infections. Avian Diseases, 56(4 SUPPL.1), 849–857.

Banks, J., Speidel, E. C., Harris, P. A., & Alexander, D. J. (2000). Phylogenetic analysis of influenza A viruses of H9 haemagglutinin subtype. Avian Pathology, 29(4), 353–359.

Bogs, J., Veits, J., Gohrbandt, S., Hundt, J., Stech, O., Breithaupt, A., & Jens, P. (2010). Highly Pathogenic H5N1 Influenza Viruses Carry Virulence Determinants

beyond the Polybasic Hemagglutinin Cleavage Site. 5(7), 1–8.

Butt, K. M., Smith, G. J. D., Chen, H., Zhang, L. J., Leung, Y. H. C., Xu, K. M., Lim, W., Webster, R. G., Yuen, K. Y., Peiris, J. S. M., & Guan, Y. (2005). Human infection with an avian H9N2 influenza A virus in Hong Kong in 2003. Journal of Clinical Microbiology, 43(11), 5760–5767.

Capua, I., and Alexander, D. J. (2006). The challenge of avian influenza to the veterinary community. In Avian Pathology (Vol. 35, Issue 3, pp.189–205.

Capua, I., and Cattoli, G. (2013). Prevention and control of highly pathogenic avian influenza with particular reference to H5N1. Virus Research, 178(1), 114–120.

Capua, I., and Alexander, D. J. (2004). Avian influenza: recent developments. Avian Pathol. 33:393-404. doi: 10.1080/03079450410001724085

Criado, M. F., Sa e Silva, M., Lee, D.-H., Salge, C. A. de L., Spackman, E., Donis, R., Wan, X.-F., & Swayne, D. E. (2020). Cross-Protection by Inactivated H5 Prepandemic Vaccine Seed Strains against Diverse Goose/Guangdong Lineage H5N1 Highly Pathogenic Avian Influenza Viruses. Journal of Virology, 94(24), e00720-20.

Cui, P., Zeng, X., Li, X., Li, Y., Shi, J., Zhao, C., Qu, Z., Wang, Y., Guo, J., Gu, W., Ma, Q., Zhang, Y., Lin, W., Li, M., Tian, J., Wang, D., Xing, X., Liu, Y., Pan, S., Zhang, Y., Bao, H., Liu, L., Tian, G., Li, C., Deng, G., Chen, H. (2022). Genetic and biological characteristics of the globally circulating H5N8 avian influenza viruses and the protective efficacy offered by the poultry vaccine currently used in China. Sci China Life Sci., 65(4):795-808. doi: 10.1007/s11427-021-2025-y.

El-Zoghby, E. F., Aly, M. M., Nasef, S. A., Hassan, M. K., Arafa, A. S., Selim, A. A., Kholousy, S. G., Kilany, W. H., Safwat, M., Abdelwhab, E. M., Hafez, H. M. (2013). Surveillance on A/H5N1 virus in domestic poultry and wild birds in Egypt. Virol J., 10:203.

El-Zoghby, E. F., Arafa, A. S., Kilany, W. H., Aly, M. M., Abdelwhab, E. M., & Hafez, H. M. (2012). Isolation of avian influenza H5N1 virus from vaccinated commercial layer flock in Egypt. Virology Journal, 9, 1–8.

Fouchier, R. A. M., Munster, V., Wallensten, A., Bestebroer, T. M., Herfst, S., Smith, D., Rimmelzwaan, G. F., Olsen, B., & Osterhaus, A. D. M. E. (2005). Characterization of a novel influenza A virus hemagglutinin subtype (H16) obtained from black-headed gulls. Journal of Virology, 79(5), 2814–2822.

Fusaro, A., Monne, I., Salviato, A., Valastro, V., Schivo, A., Amarin, N. M., Gonzalez, C., Ismail, M. M., Al-Ankari, A.-R., Al-Blowi, M. H., Khan, O. A., Maken Ali, A. S., Hedayati, A., Garcia Garcia, J., Ziay, G. M., Shoushtari, A., Al Qahtani, K. N., Capua, I., Holmes,

E. C., & Cattoli, G. (2011). Phylogeography and Evolutionary History of Reassortant H9N2 Viruses with Potential Human Health Implications. Journal of Virology, 85(16), 8413–8421.

Gao, R., Cao, B., Hu, Y., Feng, Z., Wang, D., Hu, W., Chen, J., Jie, Z., Qiu, H., Xu, K., Xu, X., Lu, H., Zhu, W., Gao, Z., Xiang, N., Shen, Y., He, Z., Gu, Y., Zhang, Z., Shu, Y. (2013). Human Infection with a Novel Avian-Origin Influenza A (H7N9) Virus. New England Journal of Medicine, 368(20), 1888–1897.

Gerloff NA, Jones J, Simpson N, et al. A high diversity of Eurasian lineage low pathogenicity avian influenza A viruses circulate among wild birds sampled in Egypt. PLoS One. 2013;8:e68522.

Guo, Y. J., Krauss, S., Senne, D. A., Mo, I. P., Lo, K. S., Xiong, X. P., Norwood, M., Shortridge, K. F., Webster, R. G., & Guan, Y. (2000). Characterization of the pathogenicity of members of the newly established H9N2 influenza virus lineages in Asia. Virology, 267(2), 279–288.

Hagag, N. M., Erfan, A. M., El-Husseiny, M., Shalaby, A. G., Saif, M. A., Tawakol, M. M., Nour, A. A., Selim, A. A., Arafa, A. S., Hassan, M. K., Hassan, W. M. M., Fahmy, H. A., Ibraheem, E., Attia, M., Abdelhakim, A. M. M., Shahein, M. A., Naguib, M. M. (2019). Isolation of a novel reassortant highly pathogenic avian influenza (H5N2) virus in Egypt. Viruses., 11:565. 10.3390/v11060565

Hassan, K. E., El-Kady, M. F., EL-Sawah, A. A. A., Luttermann, C., Parvin, R., Shany, S., Beer, M., & Harder, T. (2021). Respiratory disease due to mixed viral infections in poultry flocks in Egypt between 2017 and 2018: Upsurge of highly pathogenic avian influenza virus subtype H5N8 since 2018. Transboundary and Emerging Diseases, 68(1), 21–36.

Hassan, K. E., King, J., El-Kady, M., Afifi, M., Abozeid, H.H., Pohlmann, A., Beer, M., Harder, T. (2020). Novel Reassortant Highly Pathogenic Avian Influenza A(H5N2) Virus in Broiler Chickens, Egypt. Emerg Infect Dis., 26(1):129-133. doi: 10.3201/eid2601.190570.

Herfst, S., Schrauwen, E. J. A., Linster, M., Chutinimitkul, S., De, E., Munster, V. J., Sorrell, E. M., Bestebroer, T. M., Burke, D. F., Derek, J., Rimmelzwaan, G. F., Osterhaus, A. D. M. E., & Fouchier, R. A. M. (2016). HHS Public Access. 336(6088), 1534–1541.

Hoffmann, B., Harder, T., Starick, E., Depner, K., Werner, O., & Beer, M. (2007). Rapid and highly sensitive pathotyping of avian influenza A H5N1 virus by using real-time reverse transcription-PCR. Journal of Clinical Microbiology, 45(2), 600–603.

Höper, D., Hoffmann, B., & Beer, M. (2009). Simple, sensitive, and swift sequencing of complete H5N1 avian influenza virus genomes. Journal of Clinical Microbiology,

47(3), 674–679.

ICTV (International commettee for virus toxonomy) (2022). Virus Taxonomy: 2022 Release. https://ictv.global/taxonomy.

Jeong, J., Kang, H. M., Lee. E. K., Song, B. M., Kwon, Y. K., Kim, H. R., Choi, K. S., Kim, J. Y., Lee, H. J., Moon, O.K., Jeong, W. , Choi. J., Baek, J. H., Joo, Y. S., Park, Y. H., Lee, H. S., Lee, Y. J. (2014). Highly pathogenic avian influenza virus (H5N8) in domestic poultry and its relationship with migratory birds in South Korea during 2014. Vet Microbiol., 10;173(3-4):249-57. doi: 10.1016/j.vetmic.2014.08.002.

Kayali, G., Kandeil, A., El-Shesheny, R., Kayed, A. S., Gomaa, M. M., Maatouq, A. M., Shehata, M. M., Moatasim, Y., Bagato, O., Cai, Z., Rubrum, A., Kutkat, M. A., McKenzie, P. P., Webster, R. G., Webby, R. J., & Ali, M. A. (2014). Active surveillance for avian influenza virus, Egypt, 2010-2012. Emerging Infectious Diseases, 20(4), 542–551.

Kayali, G., Kandeil, A., El-Shesheny, R., Kayed, A. S., Maatouq, A. M., Cai, Z., McKenzie, P. P., Webby, R. J., El Refaey, S., & Kandeel, A. (2016). Avian influenza A (H5N1) virus in Egypt. Emerging Infectious Diseases, 22(3), 379

King, A. M. Q., Lefkowitz, E., Adams, M. J., & Carstens, E. B. (2011). Virus taxonomy: ninth report of the International Committee on Taxonomy of Viruses (Vol. 9). Elsevier.

Klenk, H. D., Garten, W., & Matrosovich, M. (2013). Pathogenesis. Textbook of Influenza, 157–172.

Lean, F. Z. X., Núñez, A., Banyard, A. C., Reid, S. M., Brown, I. H., & Hansen, R. D. E. (2022). Gross pathology associated with highly pathogenic avian influenza H5N8 and H5N1 in naturally infected birds in the UK (2020–2021). Veterinary Record, 190(1).

Lewis, N. S., Banyard, A. C., Whittard, E., Karibayev, T., Al Kafagi, T., Chvala, I., Byrne, A., Meruyert, Akberovna, S., King, J., Harder, T., Grund, C., Essen, S., Reid, S. M., Brouwer, A., Zinyakov, N. G., Tegzhanov, A., Irza, V., Pohlmann, A., Beer, M., Fouchier, R. A. M., Akhmetzhan Akievich, S., Brown, I. H. (2021). Emergence and spread of novel H5N8, H5N5 and H5N1 clade 2.3.4.4 highly pathogenic avian influenza in 2020. Emerg Microbes Infect. 2021 Dec;10(1):148-151. doi: 10.1080/22221751.2021.1872355.

Li, M., Liu, H., Bi, Y., Sun, J., Wong, G., Liu, D., Li, L., Liu, J., Chen, Q., Wang, H., He, Y., Shi, W., Gao, G. F., Chen, J. (2017). Highly Pathogenic Avian Influenza A(H5N8) Virus in Wild Migratory Birds, Qinghai Lake, China. Emerg Infect Dis., 23(4):637-641. doi: 10.3201/eid2304.161866.

Liu, J., Stevens, D. J., Haire, L. F., Walker, P. A., Coombs, P. J., Russell, R. J., Gamblin, S. J., & Skehel, J. J. (2009). Structures of

receptor complexes formed by hemagglutinins from the Asian Influenza pandemic of 1957. Proceedings of the National Academy of Sciences, 106(40), 17175–17180.

Liu, J., Xiao, H., Lei, F., Zhu, Q., Qin, K., Zhang, X. W., Zhang, X. L., Zhao, D., Wang, G., Feng, Y., Ma, J., Liu, W., Wang, J., & Gao, G. F. (2005). Epidemiology: Highly pathogenic H5N1 influenza virus infection in migratory birds. Science, 309(5738), 1206.

Londt, B. Z., Banks, J., & Alexander, D. J. (2007). Highly pathogenic avian influenza viruses with low virulence for chickens in in vivo tests. In Avian Pathology (Vol. 36, Issue 5, pp. 347–350).

Lu, X., Qi, J., Shi, Y., Wang, M., Smith, D. F., Heimburg-Molinaro, J., Zhang, Y., Paulson, J. C., Xiao, H., & Gao, G. F. (2013). Structure and receptor binding specificity of hemagglutinin H13 from avian influenza A virus H13N6. Journal of Virology, 87(16), 9077–9085.

Lu, X., Shi, Y., Gao, F., Xiao, H., Wang, M., Qi, J., & Gao, G. F. (2012). Insights into avian influenza virus pathogenicity: the hemagglutinin precursor HA0 of subtype H16 has an alpha-helix structure in its cleavage site with inefficient HA1/HA2 cleavage. Journal of Virology, 86(23), 12861–12870.

Luo, M. (2012). Influenza virus entry. Adv Exp Med Biol. 726:201-21. doi: 10.1007/978-1-4614-0980-9_9.

Meleigy, M. (2007). Egypt battles with avian influenza. The Lancet, 370(9587), 553–55.

Monne, I., Yamage, M., Dauphin, G., Claes, F., Ahmed, G., Giasuddin, M., Salviato, A., Ormelli, S., Bonfante, F., Schivo, A., & Cattoli, G. (2013). Reassortant avian influenza A(H5N1) viruses with H9N2-PB1 gene in poultry, Bangladesh. Emerging Infectious Diseases, 19(10), 1630–1634.

Naguib, M. M., Harder, T. (2018). Endemic situation of multiple avian influenza strains in poultry in Egypt: A continuing nightmare. Zoonoses and Public Health, 65:908-910

Naguib, M.M., Verhagen, J.H., Samy, A., Eriksson, P., Fife, M., Lundkvist, A., Ellstrom, P., and Jarhult, J.D. (2019). Avian influenza viruses at the wild–domestic bird interface in Egypt. Infect. Ecol. Epidemiol., 9(1): 1575687.

Neumann, G., Macken, C. A., Karasin, A. I., Fouchier, R. A. M., & Kawaoka, Y. (2012). Egyptian H5N1 Influenza Viruses-Cause for Concern? PLoS Pathogens, 8(11).

Nili, H., & Asasi, K. (2003). Avian influenza (H9N2) outbreak in Iran. Avian Diseases, 47(SPEC. ISS.), 828–831. https://doi.org/10.1637/0005-2086-47.s3.828

Njabo, K. Y., Zanontian, L., Sheta, B. N., Samy, A., Galal, S., Schoenberg, F. P., Smith, T. B (2016). living with avian FLU–persistence of the H5N1 highly

pathogenic avian influenza virus in Egypt. Vet Microbiol., 187:82–92.

Osman, N., Sultan, S., Ahmed, A. I., Ibrahim, R. S., Abd El-Wanes, S. A., & Ibrahim, E. M. (2015). Molecular epidemiology of avian influenza virus and incidence of H5 and H9 virus subtypes among poultry in Egypt in 2009-2011. Acta Virologica, 59(1), 27–32.

Peacock, T. H. P., James, J., Sealy, J. E., Iqbal, M. (2019). A Global Perspective on H9N2 Avian Influenza Virus. Viruses,11(7):620. doi: 10.3390/v11070620.

Peiris, M., Yuen, K. Y., Leung, C. W., Chan, K. H., Ip, P. L. S., Lai, R. W. M., Orr, W. K., & Shortridge, K. F. (1999). Human infection with influenza H9N2. The Lancet, 354(9182), 916–917.

Peyre, M., Samaha, H., Makonnen, Y. J., Saad, A., Abd-Elnabi, A., Galal, S., Ettel, T., Dauphin, G., Lubroth, J., Roger, F., & Domenech, J. (2009). Avian influenza vaccination in Egypt: Limitations... In J Mol Genet Med (Vol. 3, Issue 2).

Pyankova, O. G., Susloparov, I. M., Moiseeva, A. A., Kolosova, N. P., Onkhonova, G. S., Danilenko, A. V., Vakalova, E. V., Shendo, G. L., Nekeshina, N. N., Noskova, L. N., Demina, J. V., Frolova, N. V., Gavrilova, E. V., Maksyutov, R. A., Ryzhikov, A. B. (2021). Isolation of clade 2.3.4.4b A(H5N8), a highly pathogenic avian influenza virus, from a worker during an outbreak on a poultry farm, Russia, December 2020. Euro Surveill., 26(24):2100439. doi: 10.2807/1560-7917.ES.2021.26.24.2100439.

Russell, R. J., Gamblin, S. J., Haire, L. F., Stevens, D. J., Xiao, B., Ha, Y., & Skehel, J. J. (2004). H1 and H7 influenza haemagglutinin structures extend a structural classification of haemagglutinin subtypes. Virology, 325(2), 287–296.

Saad, M. D., Ahmed, L. S., Gamal-Eldein, M. A., Fouda, M. K., Khalil, F., Yingst, S. L., Parker, M. A., Montevillel, M. R. (2007). Possible avian influenza (H5N1) from Migratory Bird, Egypt. Emerg Infect Dis. 2007;13:1120–1121.

Salaheldin, A. H., Abd El-Hamid, H. S., Elbestawy, A. R., Veits, J., Hafez, H. M., Mettenleiter, T. C., & , E. M. (2018). Multiple introductions of influenza A (H5N8) virus into poultry, Egypt, 2017. Emerging Infectious Diseases, 24(5), 943.

Samy, A., & Naguib, M. M. (2018). Avian respiratory coinfection and impact on avian influenza pathogenicity in domestic poultry: Field and experimental findings. In Veterinary Sciences 5(1).

Selim, A. A., Erfan, A. M., Hagag, N., Zanaty, A., Samir, A. H., Samy, M., Abdelhalim, A., Arafa, A. A., Soliman, M. A., Shaheen, M., Ibraheem, E. M., Mahrous, I., Hassan, M. K., Naguib, M. M. (2017). Highly pathogenic avian influenza virus (H5N8) clade 2.3.4.4 infection in migratory birds, Egypt. Emerg Infect Dis., 23:1048–1051

Sheta, B. M., Fuller, T. L.,

Larison, B., Njabo, K. Y., Ahmed, A. S., Harrigan, R., Chasar, A., Abdel Aziz, S., Khidr, A. A., Elbokl, M. M., Habbak, L. Z., Smith, T. B. (2014). Putative human and avian risk factors for avian influenza virus infections in backyard poultry in Egypt. Vet Microbiol. 2014;168:208–213.

Soliman, A., Saad, M., Elassal, E., Amir, E., Plathonoff, C., Bahgat, V., El-Badry, M., Ahmed, L. S., Fouda, M., Gamaleldin, M., Mohamed, N. A., Salyer, S., Cornelius, C., Barthel R. (2012). Surveillance of avian influenza viruses in migratory birds in Egypt, 2003–09. J Wildl Dis., 48:669–675.

Stevens, J., Blixt, O., Tumpey, T. M., Taubenberger, J. K., Paulson, J. C., & Wilson, I. A. (2006). Structure and receptor specificity of the hemagglutinin from an H5N1 influenza virus. Science, 312(5772), 404–410.

Suarez, D. L., & Schultz-Cherry, S. (2000). Immunology of avian influenza virus: a review. Developmental & Comparative Immunology, 24(2–3), 269–283.

Sultan, S., Bui, V. N., Hill, N. J., Hussein, I. T. M., Trinh, D. Q., Inage, K., Hashizume, T., Runstadler, J. A., Ogawa, H., & Imai, K. (2016). Genetic characterization of H5N2 influenza viruses isolated from wild birds in Japan suggests multiple reassortment. Archives of Virology, 161(12), 3309–3322.

Tong, S., Zhu, X., Li, Y., Shi, M., Zhang, J., Bourgeois, M., Yang, H., Chen, X., Recuenco, S., & Gomez, J. (2013). New world bats harbor diverse influenza A viruses. PLoS Pathogens, 9(10), e1003657.

Verhagen, J. H., Fouchier, R. A. M., Lewis, N. (2021). Highly Pathogenic Avian Influenza Viruses at the Wild-Domestic Bird Interface in Europe: Future Directions for Research and Surveillance. Viruses. 30;13(2):212. doi: 10.3390/v13020212.

Verhagen, J. H., van der Jeugd, H. P., Nolet, B. A., Slaterus, R., Kharitonov, S. P., de Vries, P. P., Vuong, O., Majoor, F., Kuiken, T., & Fouchier, R. A. (2015). Wild bird surveillance around outbreaks of highly pathogenic avian influenza A(H5N8) virus in the Netherlands, 2014, within the context of global flyways. Eurosurveillance, 20(12), 21–32.

WHO, (2010). H5N1 avian influenza: timeline of major exents reported to WHO. World Health Organization, Geneva, Switzerland) Available at Www. Who. Int/Csr/Disease/Avian_influenza/Timeline_10_01_04. Pdf. Accessed April, 9, 2010.

WHO, (2013). Cumulative number of comfirmed human cases for avian influenza A (H5N1) reported to WHO 2003-2013. Http://Www. Who. Int/Influenza/Human_animal_interface/EN_GIP_20130705CumulativeNumberH5N1CASES_2. Pdf.

WOAH, (2021). Highly Pathogenic Avian Influenza IN EGYPT Summary experiences, challenges

faced and socio-economic impact on the livelihood (2006-2021).https://rr-middleeast.woah.org/wp-content/uploads/2021/11/4-highly-pathogenic-avian-influenza-2021-egypt.pdf

Yehia, N., Naguib, M. M., Li, R., Hagag, N., El-Husseiny, M., Mosaad, Z., Nour, A., Rabea, N., Hasan, W. M., & Hassan, M. K. (2018). Multiple introductions of reassorted highly pathogenic avian influenza viruses (H5N8) clade 2.3. 4.4 b causing outbreaks in wild birds and poultry in Egypt. Infection, Genetics and Evolution, 58, 56–65.

Zhang, J., Chen, Y., Shan, N., Wang, X., Lin, S., Ma, K., Li, B., Li, H., Liao, M., & Qi, W. (2020). Genetic diversity, phylogeography, and evolutionary dynamics of highly pathogenic avian influenza A (H5N6) viruses. Virus Evolution, 6(2), veaa079.

Zhu, X., Yu, W., McBride, R., Li, Y., Chen, L.-M., Donis, R. O., Tong, S., Paulson, J. C., & Wilson, I. A. (2013). Hemagglutinin homologue from H17N10 bat influenza virus exhibits divergent receptor-binding and pH-dependent fusion activities. Proceedings of the National Academy of Sciences, 110(4),1458–1463.

الملخص العربي

تضم فيروسات الانفلونزا اجناس انفلونزا فيروس الفا، بيتا، جاما، دالتا، ثوجوتا فيروس، كيورا فيروس وايسا فيروس ضمن عائلة ارثوميكسو. فيروسات انفلونزا الطيور تقسم حسب بروتينات الي 16 نوع من الهيمواجلوتنين و9 أنواع من النيورامينيدز. تحدث انفلونزا الطيور ضراوة شديدة تتسبب في نفوق عالي للطيور وضراوة ضعيفة تكون فيها الطيور طبيعية. تشكل انفلونزا الطيور من التوع اتش 5 خطر على الصحة العامة حتى إذا تواجدت في صورة ضعيفة الضراوة. يعد الانتشار المزدوج للفيروسات شديدة وضعيفة الضراوة بين الطيور في مصر ذو أثر هدام على الاقتصاد القومي. فيروسات اتش 5 ان 1، اتش 5 ان 2، اتش 5 ان 8 و اتش 9 ان 2 سوف يتم تناولها لأنها تعتبر الأنواع الأكثر انتشارا في مصر. الدور الذي تلعبه الطيور البرية المهاجرة في استمرار وبائية فيروس انفلونزا الطيور منخفضة او شديدة الضراوة بين الطيور الداجنة سيتم توضيحه في هذا المقال.