

Current Understanding on Avian Influenza and its Public Health Impact: A Comprehensive Review

Review Article

Volume 4 Issue 2- 2023

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Article History

Received: September 23, 2023 Accepted: September 26, 2023 Published: September 27, 2023

Abstract

The threat posed by avian influenza viruses to agricultural biosecurity, public health, and the possible origin of pandemic human influenza viruses is now well acknowledged. Human infections with an avian influenza A virus (subtype H5N1) have been reported from Asia (H5N1, H5N2, H9N2), Africa (H5N1, H10N7), Europe (H7N7, H7N3, H7N2), and North America (H7N3, H7N2, H11N9). The objective of this paper is to review the current knowledge of avian Influenza and its public health implications. Public health impact from avian influenza includes low pathogenic as well as high pathogenic strains of various avian influenza virus subtypes, such as H1N1, H7N2, H7N3, H7N7, and H9N2. These risks are not limited to the highly pathogenic H5N1 "bird flu" virus. The disease's incidences and outbreaks predominantly affect poultry. Economic losses due to avian influenza include depopulation and disposal costs, high morbidity and mortality losses, quarantine and surveillance costs and compensation paid for elimination of birds. Avian influenza has raised public health concerns around the world as it threatens poultry, especially chickens.

Also, it has shown the potential to pass from poultry to humans and caused severe infection, and death. Numerous serological and molecular techniques have greatly facilitated the detection of avian flu in people. It is essential to adhere to WHO recommendations for surveillance, public awareness, and pandemic preparedness in order to stop bird flu epidemics. Controlling the spread of avian influenza viruses can be accomplished by implementing management practices that include biosecurity principles, personal hygiene, cleaning and disinfection measures, as well as cooking and processing standards. A description of the recent zoonotic spread of the avian H5 and H7 viruses into humans and the advent of highly dangerous avian influenza viruses is also provided. Although prevention in domestic avian populations can lessen the risk to human health, the threat of a novel avian influenza virus creating a human pandemic persists today.

Keywords: Avian Influenza virus; Bird flu; Outbreak; Poultry; Public health; Review

Introduction

Avian Influenza (AI) is a disease or asymptomatic infection caused by viruses in the family Orthomyxoviridae genus Influenza virus A, which contains a genome composed of eight segments of sin-

gle-stranded negative-sense RNA [1]. There are four main influenza virus species, namely A, B, C and D. Type A viruses are known to infect a wide range of birds and mammals while the other species have more constrained host ranges. Influenza A viruses (IAV), including all avian influenza viruses, possess eight separate genomic segments



ranging in size between 890 and 2341 nucleotides [2]. Influenza A viruses (IAVs) are among the most challenging viruses that threaten both human and animal health [3]. From a one health perspective, their capability to transmit from one species to another, causing multiple viral genome reassortments to occur is of major concern. At the end, the four most well-studied pandemic IVs in 1918, 1957, 1968, and 2009 acquired some or all of their gene segments from the avian IAV gene pool with genes of swine origin in a second order [4]. The last two decades have witnessed a growing list of Avian influenza viruses (AIVs) that could infect humans with severe consequences while the role of swine in interspecies transmission of Avian Influenza Viruses (IAVs) continues to be of concern [5].

Avian influenza virus are characterized by their subtypes, pathotypes, genetic lineages, and clades. Avian influenza viruses are subtyped by their surface hemagglutinin (HA) and neuraminidase (NA) glycoproteins, which are major determinants of the pathogenicity, transmission, and adaptation of the AI virus to other species, but these three traits plus infectivity are multigenic. However, the major determinant of pathogenicity is the HA. The HA is important for attachment and entrance into cells to replicate, whereas the function of neuraminidase is to release newly formed viruses [1]. There are 16 different hemagglutinin (H1-16) and 9 different neuraminidase (N1-9) subtypes. More than 100 species of wild birds have been shown to harbor these viruses, especially from orders Anseriformes (ducks, geese, and swans) and Charadriiformes (gulls, terns), however, they typically do not cause clinical symptoms and thus of low pathogenicity (LP) [6].

Mammals, such as humans, pigs, horses, seals, whales, and cats have been sporadically infected with avian influenza viruses [7,1]. The avian influenza is also known as fowl pest [7]. Some species of birds and in particular some ducks, are often asymptomatic carriers. Endemics have been shown to be active throughout the world, and the H5N1 avian virus seems to be adapted to temperate and cold areas (Siberia), as well as to hot zones, especially in Southeast Asia and Indonesia, with some foci in Africa, in the tropical zone [8]. Avian influenza has captured the attention of the international community over the years, with outbreaks in poultry having serious consequences on both livelihoods and international trade in many countries of the world [9]. Avian influenza viruses are known to produce two different types of diseases in poultry birds on the bases of their virulence and pathogenicity. Due to this unique characteristic, the viruses are further classified into two types known as a highly pathogenic avian influenza virus (HPAIV) and a low pathogenic avian influenza Virus (LPAIV) [10]. HPAIV are responsible for rapid and fatal systemic infection inducing mortality up to 100% in broilers, layers and breeders while LPAIV produce asymptomatic infection. All HPAI viruses belong to H5 and H7 subtypes, even though not all H5 or H7 viruses are truly pathogenic but most of them are non- pathogenic also [11].

Lowly pathogenic avian influenza (LPAI) are all viruses of H5 and H7 subtype that are not highly pathogenic avian influenza (HPAI) viruses. Highly pathogenic avian influenza (notifiable Avian Influenza (AI) viruses have an intravenous pathogenicity index in 6-week-old chicken greater than 1.2 or, as an alternative cause at least 75% mortality in 4 to 8-week-old chickens infected intravenously [12]. The virus then re-emerged in 2003 and 2004 and spread from Asia to Europe and Africa causing several hundred human cases and deaths, as well as destruction of hundreds of millions of poultry [13]. In Ethiopia there has not been an outbreak of the AI disease, either in wild or domestic bird populations, however, considered at risk of being infected because millions of migratory bird's flocks into these countries during the European winter [14]. The primary objective of this communication is to critically review the current understanding of avian influenza and its public health impact.

Literature Review

Etiology

The pandemic influenza virus has its origins in avian influenza [15]. Its genomic material is composed of eight-segmented negative strand RNAs. The influenza A virus shows external spikes when examined with an electron microscope. There are roughly 5 times as many hemagglutinin (HA) spikes as neuraminidase (NA) spikes [16]. The 18 different subtypes of hemagglutinin (HA) and 11 different subtypes of neuraminidase (NA) exist allowing for 198 potential different viral strains. As of 2019, only 131 subtypes have been detected in nature [1]. Influenza type A viruses infect multiple species. Influenza type B and C both infect humans, but type C is also known to infect swine. Several human influenza strains are type B while all avian strains are type A. They are considered the most virulent group, although not all strains can use clinical disease. Type A influenza viruses are classified into subtypes based on two surface proteins, the HA and NA.

There is ordinarily little or no cross-protection between different HA or NA types. Two important proteins present on the surface of the virus type A: HA: Sticks the virus to cell receptors. NA: Frees the virus to infect other cells. These proteins serve as the basis for the classification of influenza viruses (e.g. Influenza A Beijing H1N1 or Panama H3N2). These proteins are always evolving. Type A influenza virus is defined as highly pathogenic avian influenza (HPAI) or lowly pathogenic avian influenza (LPAI) by its ability to cause severe disease in intravenously inoculated young chickens in the laboratory or by its possession of certain genetic features associated with HPAI viruses. Avian influenza is caused by the avian influenza virus type A and essentially two subtypes of H5 and H7 viruses among which there exist different strains more or less pathogenic. The strains differ from each other by the two types of glycoproteic spicules [17].

Epidemiology

In Guangdong Province, China, in 1994 and 1996, respectively, the first H9N2 (LPAIV) and H5N1 (HPAIV) viruses in Asia were discovered [18]. The outbreak of avian flu was first documented in 1878 in Italy. Later on, in 1924 and 1929 two massive outbreaks in poultry were recorded in the United States [19]. Since the first reported human case and death by the influenza virus in 1997 in Hong Kong, the eruption of the disease has been documented from wild and domestic birds including humans. HPAI H5N1 alone has been reported from over 77 countries [20]. Till date, a total of 860 human cases have been reported since 2003 with more than 50% deaths by H5N1 [21]. Since 2013, 1,568 human cases and 616 deaths were reported worldwide attributed to the novel H7N9. Geographically, the disease is globally prevalent dominating the Asia continent showing the higher outbreaks in China, Vietnam, India, Taiwan, Israel, Japan, and South Korea [22].

Geographical Distribution: Avian influenza virus (AIVs) were first reported in 1878 [23]. In Italy AI were subsequently isolated from chickens in 1934 [24]. An integrated analysis using phylogenetic data and global data on exotic bird trade, poultry imports, and bird migrations was conducted to determine the potential route of introduction for 36 of the 52 virus strains. Spread in Asia and Africa entailed both the commerce in poultry and migratory birds, but in Europe, migratory birds predominated (20 out of 23 countries). The entry of infected poultry into North America was seen as having a correlation with the spread of birds between North and South America [25].

Host Factors: The host range of a virus can be limited due to receptor specificity, which determines attachment to the receptor or release of progeny virions, or at other steps in viral replication. Binding of the HA to its sialic acid receptor is the initial event in influenza infection. There are differences between the receptor specificities of avian and



human influenza viruses, which are proposed to determine the host range of avian and human influenza A viruses [26]. All domestic and wild avian species (especially migratory birds of the family Anatidae and water birds are sensitive to avian influenza. It is mentioned that chicken, turkeys, peacocks, quails, and guinea fowl are most sensitive species [7]. Domestic ducks appear to be resistant to AI viruses or less susceptible. Some of the viruses isolated from birds can infect horses, humans, rats, mice, mink, ferrets, pigs, cats, tigers and dogs. In aquatic birds, domestic ducks or wild ducks, infection may be with or without clinical signs [22].

Although infections in these birds are typically asymptomatic, several species of wild birds, especially ducks and seabirds, are also susceptible. Avian influenza viruses were isolated from domestic and wild avian species, such as guinea fowl, domestic geese, quail, pheasant, parrots, gulls, shore birds, sea birds, etc. Pigs, ferrets, cats, mink, monkeys and humans can be affected also by AI viruses. Migratory waterfowl have yielded more viruses than any other group, while domestic turkeys and chickens have experienced the most substantial diseases problems due to influenza. Mostly from hens and turkeys, highly virulent avian influenza isolates have been discovered. It is reasonable to assume that all avian species are susceptible to infection [21].

Transmission

Human influenza is spread through inhaling viral droplets and droplet nuclei, direct touch, and may be indirect (fomite) contact, as well as self-inoculation onto the upper respiratory tract or conjunctival mucosa [27]. Human-to-human transmission has been described for H5N1 and H7N7 avian influenza viruses. Human-to-human transmission of an H5N1 HPAI virus was first documented during the 1997 outbreak in Hong Kong, and subsequent instances of probable human-to-human transmission of H5N1 viruses have been reported from Thailand, Vietnam, Indonesia, and Pakistan. In conjunction with a widespread series of outbreaks of a highly pathogenic H7N7 virus among poultry farms in the Netherlands between March and May 2003, where at least one human fatality from this virus was among the 89 cases diagnosed at the time of the outbreak, human-to-human transmission of the H7N7 virus was documented [28]. Avian influenza virus is found distributed in a wide variety of hosts. Predominantly free-flying water birds, like geese, ducks, shorebirds, and gulls, are major reservoirs of AIVs. Besides this, AIV can infect both wild and domestic birds like chicken, turkeys, partridges, pheasants, quails, pigeons, and ostriches [29]. However, avian influenza virus (AIVs) primarily associated with transmission in chickens but not in ducks were found to be adapted to ducks by acquiring genes from duck influenza viruses [30].

Avian influenza virus (AIV) is essentially a disease of birds, but evidence has shown that the infection can be transmitted in cats, dogs, eagles, ferrets, hamsters, horses, humans, macaques, marine mammals, mice, minks, pigs, and tigers; but the zoonotic infection had been only reported in China [21]. The transmission and spread of disease were primarily related to poultry contact, yet human-to human transmission is also possible [31]. Moreover, the outbreak of avian flu is also associated with the vicinity of water source [7], and 97.5% of reported cases showed the proximity of water source [22]. In some countries, the cultural preference for the consumption of freshly slaughtered poultry meat supports village production systems, which increases the risk of transmission of avian influenza virus [32]. The spread of infection between premises is mostly by the movement of the workers, contaminated utensils, and mechanical carriers etc. [7]. Birds can acquire the infection by contact with fecal material and infected air borne secretion [7]. It is stated that a migratory infected bird can carry infection miles away to other flocks of wild or domesticated birds [7].

Clinical Signs

The virulence of the viruses involved, the species affected, age, any

concurrent viral or bacterial disease, and the environment all have a significant impact on the clinical indications of AI. In poultry, especially domestic ducks, the infections may be asymptomatic, and only a serological examination will reveal them. With HPAI viruses, there are pronounced depression and decreased activity, decreased feed consumption, excessively watery eyes and sinusitis, cyanosis of the combs, wattle and shanks, emaciation, increased broodiness of hens and decreased egg production, oedema of head and face, diarrhoea, ruffled feathers, mild to severe respiratory signs, such as coughing, sneezing, rales and excessive lacrimation, nervous disorder, cyanosis of unfathered skin. Some birds are discovered deceased before any clinical symptoms are noticed. There may be neurological signs and reduction in normal vocalizations [33]. The mortality rate may be reach from 50 to 100 % in the severely affected birds [7].

The kind of avian influenza may affect the signs and symptoms. A virus brought on the illness. Human infections with LPAI A virus have been linked to mostly mild, non-fatal disease. Conjunctivitis, influenza-like illnesses (fever, cough, sore throat, muscle aches), and lower respiratory diseases (pneumonia) requiring hospitalization have all been reported as signs and symptoms LPAI A virus infections in humans. In contrast, HPAI A virus infections in humans have been linked to a wide range of illnesses. Illness has ranged from conjunctivitis only, to influenza like illness, to severe respiratory illness [28].

Pathogenesis

Highly pathogenic avian Influenza virus strains may cause high morbidity and mortality in most domestic avian species, but may present different pathobiologies, depending on the strain and host species. The emerging H5- and -H7 (HPAIV) have shown to be highly virulent to chickens and to have a short incubation period in inoculated embryos. The signs brought on by the Eurasian strains in ducks have evolved from mild respiratory signs to viremia, visceral and CNS infection, severe respiratory signs, and minimal fecal transmission. High lethality was demonstrated in young ducks, with cardiac and CNS infection. However, infected ducks excrete only 1% of the titer excreted by infected chickens [34]. The phylogenetic analysis of the duck pathogenic strains did not reveal alterations in the genes linked to pathogenicity but rather in other genes [35].

The sequential subtypes infections in natural reservoir species were analyzed, showing that the homo sub typic immunity protected birds from clinical expression and greatly reduced virus excretion. However, the hetero sub typic immunity only partially reduced both. The hetero sub typic immunity in reservoir birds ensures clinical protection despite enabling transmission [36]. The incubation period in chickens and turkeys can last between three and seven days, after which there may be sudden death, severe depression, ruffled feathers, lack of appetite, severe drop in egg production, edema and cyanosis of the head, neck, comb, and wattle, petechial hemorrhages in serosa membranes, excessive thirst, watery diarrhea with a greenish to whitish color, edema and congestion of the Mortality in chickens and turkeys may reach 100%, and death frequently occurs 48h after the clinical signs appear illness [30].

Diagnosis

Influenza virus can be identified in clinical specimens via virus culture, antigen detection, viral nucleic acid detection by RT-PCR, and measurement of growing antibody titers [7]. Further subtyping is not required for routine diagnostics when there are no epidemiological connections to regions where the H5N1 influenza virus is active. However, in countries where avian influenza H5N1 virus is known to be active, patients with severe pneumonia of unexplained etiology should be investigated virologically for influenza virus and, if positive, the case should be further looked into utilizing H5-subtype-specific assays in order to start the proper treatment, infection control procedures, and epidemiological investigations at the right time [21].

Therefore, there is a need for rapid diagnostic assays which distin-



guish influenza virus subtypes. Since the virus has been identified and viral RNA has been found in respiratory samples taken from H5N1-infected patients for as long as 16 days after the commencement of illness, it is clear that the virus may be found in the body and is shed over an extended period of time. Nasopharyngeal aspirates (NPA) and nasopharyngeal, throat, and nose swabs have all been used for the detection of H5N1 virus, but it remains unclear which is the diagnostic specimen of choice, because parallel studies comparing different diagnostic specimens are limited [37]. National Influenza Centre at National Public Health Laboratory (NPHL) is currently recognized by WHO and so is a member of the WHO Global Influenza Surveillance Network. Initially, influenza viruses were detected in suspected cases by rapid diagnostic test (RDT), but now qPCR is employed. The center is primarily focused on collecting appropriate clinical specimens from patients, storing, transporting, and processing. Initial identification of virus type and subtype is done, and isolates are forwarded to the WHO Collaborating Centre for Reference and Research on Influenza and alert the WHO Global Influenza Programme [21].

Prevention and Control

The United States of America Food and Agriculture Administration (FDA) authorized the first (HPAIV) H5N1 vaccine to humans for the protection of groups at high risk [38]. The list of vaccine producers for chicken influenza was released by the Food and Agriculture Organization of the United Nations. With birds posing a smaller hygienic risk than humans do, vaccinations may minimize the risk of infection and lower virus output, and they may be utilized for poultry outside outbreak zones [39].

The three categories of vaccination strategies suggested by FAO are:

A. Response to an outbreak, using perifocal vaccination (ring vaccination) or vaccination only of domestic poultry at high risk, in conjunction with the destruction of infected domestic poultry.

B. Vaccination in response to a “trigger,” upon the detection of the disease by surveillance studies, in areas where biosecurity is difficult to implement (e.g., high density of poultry farms).

C. Response to a “trigger” in areas where biosecurity is difficult to implement. Improvements in biosecurity and the use of inactivated vaccines are the two primary alternatives for controlling the disease after influenza outbreaks in poultry and the possible pandemic danger produced by (HPAIV) of the H5N1 subtype.

The goal of avian influenza vaccines is to protect flocks and stop outbreaks. They can also be employed as a tool in perifocal vaccinations to combat the disease's isolated outbreaks. Although eradication initiatives were used in the United States to control the (HPAIV), measures were also used to combat the velogenic and mesogenic strains of Newcastle disease virus [40].

The essentially of biosecurity is to minimize the risk of extraneous organisms from entering the premises where poultry are housed, and therefore it is the best strategy to reduce the risk of diseases in general, particularly when poultry are reared in confinement. Farms should ideally be built with biosecurity in mind from the start. Due to the need for adjustments to structures, equipment, and labor management, adaption costs could be substantial and ineffective. In view of the potential risk represented by free range chickens in regions where industrial broiler production is practiced, the confinement of the former is recommended [41].

The control of avian influenza in poultry, from village to commercial sectors, requires farm-to-table risk management. Implementing appropriate agricultural practices, such as training employees in good management and biosecurity procedures, especially poultry cullers, and creating a bio-secure environment to isolate chickens from potential pests, are some of the basic requirements. Avian influenza virus carriers, supplying a source of potable water, providing a feed supply

that is secure and free of contaminants, disinfection and decontamination of the area and machinery before the arrival of a new flock or after the culling of existing flocks of poultry, routine composting of litter and carcasses for all flocks, and secure disposal of carcasses from known infected farms are also recommended [7,18].

Culling: Culling is the method by which slaughtering all infected and potentially infected birds and dispose of the carcasses. All susceptible poultry species in infected and dangerous contact premises, or in a large area if this is deemed necessary, must be slaughtered, whether they are obviously diseased or apparently healthy [42].

Quarantine and movement controls: Ideally, quarantine should be implemented on all farms and towns where an infection is either known or suspected, and it should be strictly enforced to make sure that nobody including inhabitants, owners, staff members, and other visitors leaves without changing into new clothes and shoes. To prevent the disease from entering the farm from outside sources (such as feed suppliers, staff who maintain the equipment, or wild birds), strict on-farm biosecurity and cleanliness are required. A restricted area (RA) will be a relatively modest proclaimed area surrounding contaminated locations that is under rigorous movement controls and surveillance. Movement out of the RA will, in general, be prohibited, and movement into the area would be only through regulatory approval [43].

Public Health Impact

Influenza A viruses are significant diseases for both people and animals. While influenza in humans is a respiratory illness that is highly contagious and, for the most part, self-limiting, it nonetheless has a significant global morbidity and mortality rate. In the United States alone, there is an annual average of greater than 200,000 hospitalizations and 36,000 deaths due to complications from seasonal influenza [44]. World Organization for Animal Health (OIE) defines avian influenza virus (AIV) as “an infection of poultry by any influenza A virus, including by subtypes H5 and H7 [45]. OIE requires notification for all Low-Pathogenic Avian Influenza (LPAI) virus outbreaks, i.e. H7 and H5 subtypes as they can mutate into (HPAI) viruses as documented in some poultry outbreaks. Non-H5 and non-H7 LPAI are not deemed notifiable. Some HPAI viruses, such H5N1, have been demonstrated to not cause sickness in some birds, like ducks. AIV subtypes H5 and H7, including the viruses H5N1, H7N7, and H7N3, have been linked to HPAI. Human infections have varied from moderate (H7N3, H7N7) to severe and lethal (H5N1) infections [46].

Now days, due to ongoing circulation of various strains (H5N1, H5N2, H5N8, H7N8), outbreaks of avian influenza continue to be a global public health concern. The type A influenza viruses that cause poultry plague were proven to exist in 1955. High mortality was produced by a virus associated with the first isolates of the fowl plague (surface antigens H7N1 and H7N7) in chickens, turkeys, and other species. It has since been found that AI viruses cause a wide range of disease syndromes, ranging from severe to mild to high in domestic poultry [47]. Avian influenza viruses are considered species specific and rarely cross the species barrier [48]. The occurrence of the H5N1 (HPAI) virus throughout Asia, Africa and Europe has raised concerns about food safety issues for poultry products for human consumption and for the risk of transmission of infection to animals via will feeding, predation and scavenging. These worries have grown as a result of reports that the disease was brought into an undeveloped nation through the trade of poultry products [49].

Food-borne transmission of infection through poultry products may only occur if there is viable virus in the commodity and the concentration of the virus is sufficient to infect the given host(s) that are exposed to the source of infection. To date, there is no reported evidence of the transmission of H5N1 infections to mammals through feeding using carcasses of infected birds. Moreover, in some cases of human infection with H5N1 virus, viral transmission was suspected to have



occurred after the consumption of fresh duck blood or undercooked poultry products [50]. The HPAI H5N1 virus has raised concerns around the world as it threatens poultry, especially chickens; also it has shown the potential to pass from poultry to humans and caused severe infection and death [51]. The first reported human infection of H5N1 occurred in 1997 in Hong Kong [17]. The virus has been endemic in several countries after the re-emergence of H5N1 in Asia, Africa, the Pacific region, Europe, and the Middle East in 2003, and continues to cause poultry outbreaks [52]. One hundred years ago, in 1918, the 'Spanish flu' pandemic, caused by an H1N1 influenza virus is estimated to have contributed to the deaths of around 50 million people. Since then, three other human AIV pandemics have occurred: H2N2 in 1957 (Asian flu), H3N2 in 1968 (Hong Kong flu), and H1N1 again in 2009 (swine flu) [12]. Avian influenza A (H5N1) results in high death rate amongst infants and young children with case fatality rate at 89% among under 15 years of age [53]. As variable as the signs and morbidity and mortality are dependent upon the species and virus, as well as age, environment and concurrent infections. Morbidity rates generally are poorly defined, largely because of the very large size of flocks involved and the ill-defined signs of disease in many of the outbreaks. The most virulent viruses cause HPAI (H5 and H7), in which mortality may be high as 100%. Other viruses cause a much milder (primarily respiratory) disease designated LPAI [54].

Avian influenza virus infections in humans: In 1997, Hong Kong had the first human outbreak of the avian influenza A (H5N1) virus. Six people who had the infection were proven dead. Without the need of a middle host, infections were directly transferred from chickens to humans. The outbreak was stopped at the tail end of December 1997 when more than 1.5 million hens were slaughtered nationwide until February 2003, when H5N1 viruses were once again connected to human disease in a family group in Hong Kong, resulting in 2 confirmed H5N1 virus infections and 1 death, was prevented by the application of increasingly stricter control measures in the live bird markets [55]. The majority of infections in humans affect children and young adults. Most human infections are characterized by presentation with severe pneumonia and rapid progression to acute respiratory distress syndrome with complications including multiorgan failure [56]. The H5N1 viruses obtained from humans have genomes that are entirely avian in origin and closely linked to viruses isolated from avian species, showing that there has not yet been any significant reassortment with human viruses or adaptation to the human host. Although there has only been sporadic human-to-human H5N1 viral transmission reported [57]. Moreover 80 cases of H7N7 infection were found in people who had contact with the sick birds and a small number of their family members, demonstrating that the H7N7 virus is only occasionally transmitted from one person to another [58].

Outbreak of Avian influenza

In China, H5N1 illness seems to affect younger patients more often than H7N9 infection, and both seem to affect men more frequently than women [59]. A pandemic is a widespread outbreak that happens when a brand-new, highly pathogenic strain of influenza type A virus appears in the human population and spreads quickly and readily from person to person across the globe due to the absence of human immunity to the novel strain [60]. Although there have been isolated reports of infection from West Africa, H5N1 epidemics have primarily affected the Middle East and Southeast Asia [61]. Effective outbreak management or prevention, as well as reducing its effects when it does happen, can all be achieved with good preparedness planning. This planning should take into account the best ways to identify an outbreak quickly, validate the diagnosis, and establish a quick and efficient control campaign. It requires an assessment of veterinary service capabilities and capacity and the legal framework in which these services operate. The structure of national poultry industries should be examined to determine the potential for virus entry. Provision for good public awareness programmes should be made, as it is critical to have public support for disease control activities and good public

knowledge to minimize the risk of human infection [43].

Avian influenza surveillance: Active surveillance activities should be initiated as soon as a country considers itself at risk for an incursion of AI. In cases of suspected disease, representative samples from all domestic species of birds that die in the area should be investigated, and specimens should be submitted to approved veterinary diagnostic laboratories for diagnosis. Field surveillance examinations should seek to detect changes in flock health. Trained personnel should be aware of the potential risk to human health and wear protective gear (goggles or face shield, mask, gloves, disposable gowns or coveralls and rubber boots) that can be discarded on site or disinfected before leaving the investigation site [62].

Domestic poultry surveillance: The identification of poultry at risk should include flocks of poultry kept in high-risk agricultural and agro-ecological systems that attract migratory birds. Sentinel birds within flocks, notably domestic ducks, which are the most likely to be exposed, may benefit from active serological and virological surveillance during periods of particularly high perceived risk, such as the arrival of migrating birds. In order to determine the best surveillance method, it is advised that governments conduct risk assessment studies of the introduction of AI. In any case, each nation will have unique goals, and its surveillance systems should be adjusted to take these interests into account. For instance, nations free of HPAI or those with a lower risk of infection will look for access to thorough, current information on dangers and concentrate on finding incursions, making early warning and surveillance their top priorities. The gathering of thorough, current data on human health risks, ecological zones, and production systems that pose the greatest risk for the introduction and maintenance of HPAI infection will be one of the surveillance priorities for infected countries or those at high risk of infection introduction [45].

Wild bird surveillance: It is known that wild birds are a reservoir for numerous avian influenza viruses (particularly waterfowl and waders). If surveillance sampling of healthy wild birds is not possible to test for the presence of AI viruses, it is important to at least set up wild bird monitoring programmes to check for wild bird mortalities, both near farms where outbreaks are occurring [63]. Although HPAI virus outbreaks in domestic and wild birds are uncommon, when they do happen, the consequences for veterinary, medical, and public health can be severe. Since the H5N1 HPAI epidemic in Hong Kong in 1997 and the H7N7 HPAI outbreak in the Netherlands in 2003, there have been worries that AI viruses could persist in select chicken populations and eventually mutate or reassort to become a pandemic virus for humans. During the twentieth century, the emerged viruses had been new hemagglutinin subtypes for which the human population has no exposure and thus no immunity [46].

Risk Factors for Avian Influenza Outbreak

Risk of introduction by migrating bird: Water bird migration poses a significant concern for the long-distance transmission of AI viruses, with a complex network of interconnecting flyways allowing for the possibility of widespread virus dispersion but in-depth field research has not been able to establish if migratory wild birds are dispersing the H5N1 HPAI virus over great distances. Current information suggests that infected birds may move short distances carrying H5N1, but long migratory movements with this strain of virus have not been confirmed [64]. AI virus-infected wild birds typically continue to discharge the virus for up to one month. However, research on various species of ducks and H5N1 suggests that viral shedding lasts only 3-4 days. Wild birds from various locations congregate in wetlands or other habitats during breeding season, during moult, and at overwintering places, where virus transmission may take place. As a result, during the course of a year, birds from various regions and flyways have the potential to interchange viruses and other infections, which could lead to the fast spread of infectious agents across continents. Numerous wild bird species have perished from the H5N1 HPAI virus



during the present pandemic, but the role wild birds play in the spread of this disease remains undetermined because no reservoir species have been identified [17].

Risk of importation of poultry: Currently, several nations prohibit the importing of chicken and poultry products from nations where notifiable AI has been detected. Given the possibility for disease transmission across borders, it would be prudent to handle all poultry products very carefully, especially those that may be infected. The risk from live birds is by far the largest, but other potential sources of infection include dressed corpses of diseased birds, eggs from infected hens, poultry waste, and feces-contaminated fomites. Fighting cocks and other birds used for recreational purposes travel from place to place and across borders; as a result, they pose a risk that needs to be closely monitored through regulation and inspection rather than bans, which are more likely to encourage such birds to move clandestinely. Likewise, the illegal movement of live birds represents a risk that will not be mitigated by imposing bans on legal importation [65].

Risk of spread from infected poultry: Surveillance in poultry as well as in wild birds should be strengthened in countries at immediate risk to prevent further spread of avian influenza. Resources should be focused on the reduction of close contacts between humans, poultry and wildlife through better management practices and improved biosecurity practices in poultry production enterprises, especially small and “open-air” facilities where poultry and waterfowl mingle with wild birds or local resident bridge species. The influenza viruses are easily spread by fomites and generally survive well in water, especially in cold climates. Furthermore, certain species of ducks are able to carry influenza viruses without exhibiting any clinical signs of disease. All individuals working with poultry should significantly increase their level of hygiene practices once HPAI has been identified in a nation's marketing environment. This is done both to prevent the virus from entering an operation (bioexclusion) and from leaving if it has already entered a flock, village, or region (biocontainment) [43]. The sale of infected birds to markets, the departure of wild waterfowl that have mixed with infected backyard poultry units, the wearing of contaminated clothing or footwear by those handling or selling poultry, and the transfer of contaminated cages and egg crates to markets or poultry farms are the main ways that the virus spreads from one area to another. Poultry keepers and communities must therefore take practical measures to avoid introducing the virus and to reduce the risk of spread when disease has been detected [64].

Virus survival environment: In aerosols, low relative humidity and low temperature increase the time that influenza viruses survive, whereas in feces, low temperature and high moisture levels increase the time that they survive. Most studies on viral environmental persistence have been carried out in cool northern climates, with the following finding (Martin, 2006). The AI virus can survive in faeces for at least 35 days at 4°C; it can survive within the poultry house environment for up to 5 weeks. For up to 4 days at 22°C and for more than 30 days at 0°C, the virus can remain contagious in lake water. The influenza virus is stable over a pH range of 5.5-8 and is vulnerable to a variety of disinfectants, including detergents because it is an enveloped virus. Lake water with ducks can be used to isolate the AI virus. Acidification of potentially contaminated drinking water to pH 2.5 or chlorination should minimize spread of infection [66].

Economic Impact

Most countries affected with HPAIV H5N1 presented poultry losses of around 1% of GDP, reaching 0.6 in Vietnam and Thailand and up, gradually expanding its avian host range. In June 2007, it had an impact on 62 countries of the world, killing or butchering more than 250 million birds, with an estimated cost of more than US\$ 12 billion. Prior recommendations to lessen the effects of the condition came from research, educational, and industrial institutions [26]. More than 200 million birds have died as a result of H5N1 and related strains, costing the poultry industry more than US\$10 billion in research,

human lives, and financial losses. Costs to farmers in China rose to roughly \$1 billion in 2004 while business sales fell by up to US\$2.5 billion. International animal health regulations are adopted by nations that participate in international trade, together with national laws. It is possible to plan a timeline of events from the initial epidemic through the start of production in order to arrange the disease control activities [67]. In 2006, the consumer market for meat and eggs in the majority of nations experienced a decline of 15% in unaffected nations like Argentina and Brazil, and 30% in disease-affected nations [68].

Direct Impact: The amount of money lost due to avian influenza varies depending on the virus strain, kind of bird that was infected, number of affected farms, control approaches, and the speed at which control or eradication plans are put into action. Direct losses include depopulation and disposal costs, high morbidity and mortality losses, quarantine and surveillance costs and compensation paid for elimination of birds. LPAI outbreaks have caused significant economic losses. Growers lost a total of \$22 million U.S. As a result of suppressing seasonal outbreaks of LPAI in Minnesota between 1978 and 2003. The northeastern United States saw an HPAI (H5N2) outbreak in 1983, which led to losses of around \$65 million, the death of almost 17 million birds, and a 30% increase in egg prices. Italy experienced an HPAI (H7N1) outbreak in 1999–2000, and the government compensated farmers with \$100 million (U.S.). The 1997 outbreak of HPAI (H5N1) in Hong Kong live poultry market cost \$13 million (U.S.) for depopulation and compensation for 1.4 million birds. The 2001 outbreak, which also affected Hong Kong, cost \$3.8 million and resulted in the death of 1.2 million birds. Compensation for 18 million birds with total indirect losses was estimated at \$ 500 million [69].

Indirect Impact: Affected sectors will probably make several requests for compensation to the government. Those in the poultry industry will first demand reimbursement for their losses due to culling during the pre-pandemic era. But in the event of a full-blown pandemic, many other industries, including tourism, transportation, retail, and insurance, would probably suffer, and a number of other industries would go bankrupt. In general, many otherwise viable businesses may not survive the weeks or months of much lower demand, and unemployment may increase [70].

Socio-Economic Impact: Market shocks and negative consequences for livelihoods as a result of the disease and control processes applied to control it; and changes to the structure of poultry market chains, induced either by heightened biosecurity regulations created through government policy. This includes reduction of global trade in poultry (bans) by 80%; Increase of poultry products by 20% socio-economic impact.

Conclusion and Recommendations

In populations of wild birds, avian influenza virus strains have been spreading and evolving. Avian influenza viruses rarely cross the species barrier since they are species-specific. However, subtypes H5, H7, and H9 have brought on occasional infections in humans, typically because of close contact with sick birds. The poultry industry, trade, and public health could be severely impacted by AI outbreaks on an economic and social level. The cost of culling and replacing birds, customer dissatisfaction, losses in domestic and international trade, the cost of biosecurity, and the expense of veterinary and infrastructure improvements all contribute to the severe economic impact of HPAI epidemics. All segments of the poultry industry within a country lose as a result of international trade embargoes. Controlling the transmission of the AI viruses can be accomplished by implementing management practices that combine biosecurity concepts, personal hygiene, cleaning and disinfection processes, vaccination, as well as cooking and processing standards. The most concern for public health from the H5N1 HPAI viruses because of human infections and fatalities resulted from direct exposure to live or dead infected poultry. Humans have occasionally become infected with H5N1 HPAI viruses, mostly



through close contact with diseased birds, with a high case fatality rate (60%) for human infections.

Because of HPAI does not necessarily kill its anseriform hosts, re-assortment with co-circulating LPAI viruses can occur, furthering evolution of the virus, while the low severity symptoms allow the long-range and intercontinental transport of the disease. Therefore, enhancing biosecurity and immunizing domestic poultry are probably crucial methods to limit outbreaks in these populations.

Based on the above conclusion, the following recommendations are forwarded.

- a) Good risk communication with workers, veterinarians, and suppliers is important to manage risk.
- b) Practicing good hygiene is imperative to prevent cross contamination.
- c) Movement restrictions of poultry and poultry product should be reinforced from infected area to market and other area.
- d) Effective vaccination is essential to prevent systemic infection of poultry.
- e) There is a need to have better coordination with officials and technocrats of various departments.
- f) It is emphasized that government must ensure easily access to diagnostics, and vaccines particularly to the poor resource nations of the world.

Acknowledgements

We are very thankful to Prof. Dr. R.K. Narayan for going through the manuscript and giving his valuable suggestions. This paper is dedicated to all the scientists who made significant contribution in the field of Influenza viruses.

Contribution of Authors

Each author contributed equally. We read the final version and approved it for final submission to the Editor for its publication.

Conflict of interest

No conflict of interest.

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