Zoonotic Potential of Avian Influenza Virus: Knowns and Unknowns

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ABSTRACT

Avian influenza viruses (AIVs) are one of the leading causes of economic losses to the poultry industry around the globe, and owing to their zoonotic and pandemic potential, AIVs present a considerable threat to animal and human health. Waterfowl are the natural reservoirs of the AIVs. Different species of birds vary considerably in their susceptibility to AIV infection. Genetic changes such as mutation, antigenic drifting, and reassortments in the different AIVs can develop new strains with increased transmission and pathogenicity. Due to the interrelation of the AIV and previous pandemics in humans, there is a dire need to perform molecular epidemiology studies. In humans, AIVs can cause eye irritation, flu-like symptoms, respiratory disease and even death, but its severity varies with the strain of the virus, age, dietary habits, and health status. For the prevention and control of AIV infection, definitive diagnosis, strict biosecurity, and vaccination are recommended. Many antiviral drugs, such as Dextran sulfate, DSA181, arbidol, etc., are effective against influenza viruses.

Keyword: Avian influenza virus, transmission, human health implication, biosecurity, vaccination

CITATION

Rehman S, Khan MA, Manzoor Z, Zafar MA and Rehman M, 2023. Zoonotic potential of avian influenza virus: knowns and unknowns. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 29-41. https://doi.org/10.47278/book.zoon/2023.83

CHAPTER HISTORY Received: 21-March-2023 Revised: 27-June-2023 Accepted: 20-July-2023

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1. INTRODUCTION

Avian influenza viruses pose significant risks to human and animal health and global food security due to their zoonotic and pandemic nature. Avian influenza viruses (AIV) cause avian influenza, commonly known as bird flu, and can infect Wild waterfowl, including ducks, geese, turkeys, chickens, and other avian species. These viruses belong to the influenza A virus category and are divided based on their surface proteins.

Frequent outbreaks of avian influenza and domestic poultry can lead to profound economic repercussions for the global poultry industry. Culling of the infected birds, market restrictions, and imposition of trade limitations can lead to considerable financial losses to poultry farmers and economies. Being the major source of animal protein, influenza outbreaks within poultry can lead to a decrease in poultry meat and egg production, significantly impacting nutritional well-being and food security. Waterfowl is a major source of influenza viruses that can transmit these viruses to migratory birds. These migratory birds can carry these viruses to longer distances and transmit them to animals and humans.

Avian influenza viruses can carry significant health ramifications due to human infections. Specific strains of AIVs having zoonotic potential can result in severe respiratory disorders and have caused outbreaks, even pandemics.

The genetic architecture of the avian influenza viruses makes them vulnerable to mutations and recombination, which facilitates them to leap the species barrier. The possibility of zoonotic transmission raises concerns regarding the emergence of novel strains that can cause widespread illness in humans. Previous outbreaks of the different influenza viruses like H5N1 and H7N9 have provided different basis for the virus evolution, transmission, and global response strategies. Dealing with the challenges posed by these zoonotic viruses necessitates collaborative efforts in the different sectors.

Future studies should be based on understanding the viral genomes that can lead to the transmission of viruses from animal hosts to humans and developing novel vaccines. These insights will be beneficial for pandemic preparedness and response.

2. HISTORICAL PERSPECTIVE

Many non-bacterial outbreaks in household birds causing high mortality were recorded during the nineteenth century and those outbreaks were named ‘‘fowl plague’’ (Alexander and Brown 2009). In 1955, Schafer concluded that the ‘fowl plague virus’ was in fact a type of Avian Influenza virus, having internal antigens similar to influenza viruses of humans & swine (Schäfer 1955). Several sequencing studies confirmed that the H7 subtype of the influenza A virus was responsible for those outbreaks (Röhm et al. 1995).

The Spanish flu pandemic caused by the influenza virus (H1N1) has been guessed to cause around 50 million deaths in humans in 1918 (Johnson and Mueller 2002). Three other major human pandemics have occurred since then: Asian flu caused by H2N2 (1957), Hong Kong flu caused by H3N2 (1968), and swine flu caused by H1N1 (2009). In all cases, Influenza A virus strains having RNA segments coding for novel HA or NA proteins quickly disseminated through a human population. In 1967 Pereira et al. outlined the connection between human influenza, avian influenza, and fowl plague and suggested the human H2N2 and H3N2 pandemic viruses could have had an avian origin on the basis of antigenic cross-reactivity (Pereira et al. 1967). Several other studies unequivocally established the avian virus origin of the human 1957 and 1969 pandemics (Fang et al. 1981). The pandemic of swine flu in 2009 occurred as a result of reassortment between diverse influenza A virus strains that had been circulating in pigs for the last few years but these pig-origin strains exhibited evidence of genomic segments that could be traced back to avian origins (Smith et al. 2009). There have been reports that many sporadic infections of humans

occurred directly from avian sources with a number of avian virus subtypes like H5, H6, H7, H9 & H10, but without leading to sustained human-to-human transmission as yet (Yuen et al. 1998).

3. AN OVERVIEW OF AVIAN INFLUENZA VIRUS

Avian influenza viruses belong to class *Insthoviricetes,* order *Articulavirales, family Orthomyxoviridae, Genus Alphainfluenzavirus* (ICTV 2022), previously known as influenzavirus A. These have a single standard, negative sense, and segmented RNA genomes (Wille and Holmes 2020). There are eight gene segments in their genomes and encodes ten different proteins (Perez et al. 2019). The surface proteins of the virus include membrane channel (M2) neuraminidase (NA) and hemagglutinin (HA). The viral RNAs encode proteins, including polymerase basic protein 1(PB1), polymerase basic protein (PB2), polymerase acidic protein, matrix proteins (M1, M2), and nucleoprotein (Shaw and Palese 2007). The influenza viruses produce two other non-structural proteins namely non-structural protein one (NS1) and non-structural protein two (NS2), also known as nuclear export proteins (Lee and Suarez 2005). The transcription of the alternative open reading frames can produce several accessory proteins, and most of these proteins' functions are unclear (Vasin et al. 2014). The HA plays a major role in the pathogenicity and initiation of the infection process by attaching to the host cells. There are 18 different HA subtypes of avian influenza viruses. The NA protein's basic function is to release the newly formed viruses from the infected cells, and there are 11 different subtypes of avian influenza viruses based on the NA gene. Different strains with distinct pathogenicity and characteristics are formed, such as H5N1 and H7N9, based on the various combinations of the HA and NA proteins.

The AIVs are categorized into highly pathogenic (HPAIV) and low pathogenic avian influenza viruses (LPAIV) based on their pathogenicity in chickens (Swayne and Suarez 2000). For the classification of the HPAI and LPAI and pathogenicity in poultry, the arrangement of multiple basic amino acids at the cleavage site of the HA serves as a pivotal factor (Medina and Garcia-Sastre 2011). HPAIV causes significant mortality in chickens, whereas LPAI causes a decrease in reproductive performance, depression, and respiratory signs.

4. UNDERSTANDING VIRAL GENETICS AND VARIABILITY

Genetically reassortments can occur in avian influenza viruses due to their segmented genome. It can lead to the shifting or exchange of the different genes, leading to the differences in the pathogenicity and immunogenicity of the newly formed viruses. This antigenic shift due to reassortments can lead to antigenic change known as antigenic shift. This antigenic shift may result in pandemics. Another way the antigenic drift alters the antigenicities of the receptor-binding HA and NA is the selection pressure of immune responses. It may be due to the non-proofreading ability of polymerase in influenza A viruses (Boivin et al. 2010), due to which there is a higher chance of base mutations leading to antigenic drift.

5. NATURAL RESERVOIRS, HOSTS RANGE, AND TRANSMISSION DYNAMICS

Influenza A viruses predominantly reside within wild waterfowl, particularly those belonging to the orders Anseriformes (ducks, geese, and swans) and, to a lesser degree, Charadriiformes (gulls, terns, sandpipers, and plovers), serve as their natural reservoirs (Caron et al. 2017; Neumann et al. 2010; Nishiura et al. 2009). Migratory species within these orders play a crucial role in expanding the geographical spread and perpetuation of these viruses (Verhagen et al. 2015; Viruses 2016). Conversely, influenza A prevalence remains low in other bird orders, like passerine songbirds, implying their status as spillover hosts, often

infected via contact with poultry or waterfowl (Fuller et al. 2010). It's worth noting that certain peri-domestic species including house sparrows (*Passer domesticus*) might still contribute to viral movement between poultry farms or even between wild birds and farms (Bahl et al. 2016; Hassan et al. 2017; Prosser et al. 2013).

Domestic poultry, including chickens, ducks, and turkeys, exhibit varying degrees of susceptibility to infection, each displaying a range of clinical signs and severity levels. Additionally, avian influenza strains can infect various avian species, encompassing both captive and wild birds, resulting in sporadic outbreaks. Recently sporadic cases or outbreaks of H5 HPAIV have been reported in different mammals like foxes, otters, minks, and sea lions (Aguero et al. 2023; Huang et al. 2023; Kupferschmidt 2023; Sidik 2023) which raise a lot of concerns for human. There are several factors that influence the distribution of Avian Influenza viruses like wild bird populations, migratory patterns, climatic conditions, human interaction, and live bird trading. The outbreaks of AIV are reported in the Middle East, Africa, Bangladesh, India, Pakistan, Europe, and America indicating its global distribution.

Influenza virus can be transmitted from the natural host that is aquatic birds to domestic poultry or pigs (Long et al. 2019). The AIV spread is influenced by the complex combination of factors among birds, human and other species. Primarily AIV is transmitted through direct contact between infected and susceptible birds. This can occur in various ways, such as through close interactions, sharing of feeding and drinking sources, or mating behaviors. Indirect transmission can occur from the contaminated environment, equipment, feed, water, etc. In the areas with higher population of commercial or domestic poultry airborne transmission is possible for short distances. The direct or indirect contact of the infected birds, their dropping or contaminated environment can lead to zoonotic transmission and it is observed in the outbreaks in Egypt and Asia (Li et al. 2019).

Novel strains with higher pathogenicity and transmissibility can arise from genetic changes such as mutation and reassortments in the different AIVs. Migratory birds can shed these viruses in the environment and waterbodies leading to their contamination and transmit the viruses to the longer distances due to their ability to carry in their digestive and/or respiratory system. Across continental migration of birds can transmit viruses to those continents. Rearing of the ducks at the interface of domestic poultry and migratory birds in different countries like China, Indonesia, Vietnam and Bangladesh provide a significant role in the spread and ecology of AIVs (Cappelle et al. 2014). Many environmental factors such as water bodies, temperature, and humidity influence the movement of migratory birds and viral survivability (Bozó et al. 2018; Brown et al. 2009; Brown et al. 2007). In the similar way live poultry transportation and live bird markets can transmit the AIVs to the domestic poultry (Gilbert et al. 2014).

6. FACTORS INFLUENCING ZOONOTIC POTENTIAL OF AIV

The zoonotic potential of the AIV is influenced by the different factors like viral genetics, antigenic drifting, reassortments, and virus evolution. The glycoprotein HA binds to the sialic acid receptors and enables virus attachment to host cells. The human influenza viruses primarily replicate in the upper respiratory tract (URT) glycans, which are rich in terminal α2,6-linked sialic acid (SA). On the other hand, AIVs preferably binds to the α2,3-linked SAs which are commonly present in the gastrointestinal and respiratory tracts of birds (Pillai and Lee 2010). Selected mutations in the HA gene of the AIVs can lead to their ability to bind to α2,6-linked SA effectively which is necessary for successful infection and transmission in humans (Peacock et al. 2021). Reassortments occur when viruses of two different strains/lineages infect the same host. During replication, these viruses can exchange/mix their RNAs leading to the formation of new viruses which may have the characteristics of both the parents. This type of formation of new viruses increases the cross-species transmission

of AIV and may result in zoonotic transmission (Hoye et al. 2021) or potential pandemics. During replication and transmission within the birds, AIV can mutate resulting in the emergence of new strains with altered genetic and pathogenic characteristics, increasing their genetic potential (Lee et al. 2010).

7. HUMAN HEALTH IMPLICATIONS

The AIVs can cause illness in humans, spanning from mild flu-like symptoms or eye irritation to critical, sudden respiratory disease and even potential fatality. The severity of the condition hinges on the specific strain of the virus and the particularities of the infected individual such as age, genetics, dietary habits, health status, variation in the immune system, etc. Influenza symptoms typically manifest approximately 2 days following exposure to the virus. These symptoms encompass an abrupt onset of fever, a typically dry cough, headaches, muscle and joint discomfort, pink eye, a profound feeling of unwellness, a sore throat, and a runny nose (Wong and Yuen 2006; Yuen et al. 1998). The cough can persist intensely for a span of 2 weeks or more. For the majority, recovery from the fever and other associated symptoms generally occurs within a week, necessitating no medical intervention. However, influenza has the potential to provoke severe illness or even fatalities, particularly in individuals classified as high-risk. Additionally, it can exacerbate symptoms of pre-existing chronic ailments. In more critical instances, influenza can lead to complications such as pneumonia, acute respiratory distress, respiratory failure, or sepsis. Individuals with underlying medical conditions or experiencing severe symptoms should promptly seek medical attention. On rare occasions, instances of gastrointestinal and neurological symptoms have been documented.

8. PREVENTION AND CONTROL

8.1. ANTIVIRALS

Monoclonal antibodies against specific AIVs have shown promising results in clinical treatment and post-exposure prophylaxis. In addition, polypeptide drugs have also been developed (Saito et al. 2021; Zhao et al. 2020), but their efficacy is challenged by the continual mutation of AIVs (Baz et al. 2010), necessitating the exploration of new antiviral strategies (Huang et al. 2023).

Various small compounds have been created to combat influenza viruses by targeting different stages of their life cycle (Figure 1). These include inhibitors of the HA protein, which can hinder virus adsorption or fusion. HA1 inhibitors like Dextran sulfate and DSA181 (Belser et al. 2007) obstruct the binding of HA1 to cell surface receptors, while HA2 inhibitors such as BMY-27709 (Luo et al. 1997) and arbidol (Boonma et al. 2022) prevent virus entry by impeding HA2-mediated membrane fusion. The viral fusion process relies on host enzymes like proteases and endosomal acidification indicating the role of the enzyme inhibitors like aprotinin (Zhirnov et al. 2011) and bafilomycin A1 (Ochiai et al. 1995) can be used as antiviral drugs. Inhibitors like rimantadine and amantadine block the release of the viral RNA in the cytoplasm of the host cell by targeting the M2 ion channel (Bright et al. 2006). Similarly, NA inhibitors such as zanamivir, peramivir, and oseltamivir can prevent the release of newly formed viruses from infected cells (De Clercq 2006; De Clercq and Neyts 2007). But resistance to NA inhibitors can be seen due to the mutations in the NA protein (Burnham et al. 2014). Antiviral agents include a variety of substances that target different stages of viral replication, such as NP inhibitors (Correa-Padilla et al. 2023), PB2 inhibitors (Li et al. 2023), PA inhibitors (Govorkova et al. 2022), and RNA-dependent RNA polymerase inhibitors (Shiraki and Daikoku 2020) can be used as antiviral agents (Huang et al. 2023).

8.2. BIOSECURITY

Strict biosecurity measures are the most significant means of preventing avian influenza outbreaks in poultry, preserving the food supply chain, and reducing the probability of outbreaks in human. Thus, controlling and preventing the spread of AI expects strict biosecurity protocols and excellent hygiene standards. These procedures have a direct effect on reducing the risks of contamination related to workers and equipment. Direct of contact of the wild birds from the domestic poultry should be prevented because wild birds are the primary source of infection to the domestic poultry (Peiris et al. 2016). Poultry production facilities and flocks need to strictly regulate vehicles, employee, and equipment access, as well as ensure thorough cleaning and disinfection. It is crucial to put in place the proper educational initiatives to guarantee that people who interact with poultry species are aware of the risks associated with avian influenza (AI), know how to prevent it, and know how to report, monitor, and handle possible outbreaks. This level of knowledge is crucial to enable the farmers and employees to identify the disease's clinical symptoms and mortality patterns, and report to Veterinary Services and the appropriate authorities right away. If disease is revealed within a flock, the OIE Terrestrial Animal Health Code prescribe that affected animals be culled together with any animals that are in touch with them (or within a specified radius of affected premises), and that carcasses and animal products be disposed of appropriately. It is also advised to impose movement limitations and implement quarantine procedures to mitigate the spread of the disease. There are several ways to successfully reduce the environmental contamination of the virus in live bird markets. These include forbidding the sale of live aquatic birds (Figure 1), separation of water fowl and poultry species, and introduction of monthly rest days when markets are cleared and thoroughly disinfected before introduction of the new birds (Peiris et al. 2016). Poultry workers involved in the culling and disposal of the infected or dead birds must use protective wears and receive antiviral drugs as preventive measures. Moreover, high risk individuals such as the staff of poultry live markets, poultry farm workers, and poultry veterinarians should get the seasonal vaccinations to lessen the chances of the infection and co-infection of the different AIVs leading to the reduction in the risk of genetic reassortments.

8.3. PROTECTIVE MEASURES AND OPTIONS FOR PUBLIC HEALTH RESPONSE

Most of the influenza viruses exhibit limited host range but in the last decades AIVs have caused zoonotic infections by the direct transmission from birds to humans. Certain strains of HPAIV and LPAIV commonly isolated from the poultry have shown their abilities to initiate zoonotic outbreaks. These occurrences of zoonotic transmission are of substantial concern for public health due to the seriousness and mortality associated with the diseases they cause. There is also a significant apprehension that a novel virus with competent human-to-human transmission might prime to a pandemic. It's essential to recognize that all influenza pandemics over the past century resulted from viruses with genetic components originating from animals, with avian species being the main source (Taubenberger and Morens 2009). Terrestrial birds, such as quail, chickens, turkeys, and similar species, have been known as the hosts capable of amplifying avian/human reassortant influenza viruses (Makarova et al. 2003; Perez et al. 2005; Perez et al. 2003; Pillai et al. 2010). Hence, biosafety is a paramount concern for individuals who come into contact with the virus. Those at risk of virus exposure can be categorized into two groups. The first group comprises those engaged in controlling outbreaks and AI eradication, with responsibilities such as culling infected birds, disposing of carcasses, and sanitizing premises. The second risk group involves laboratory personnel working with contaminated specimens and samples containing the virus (Capua and Alexander 2009). Following are the different recommendation for the individual involved in the handling of birds and field outbreaks of AIVs.

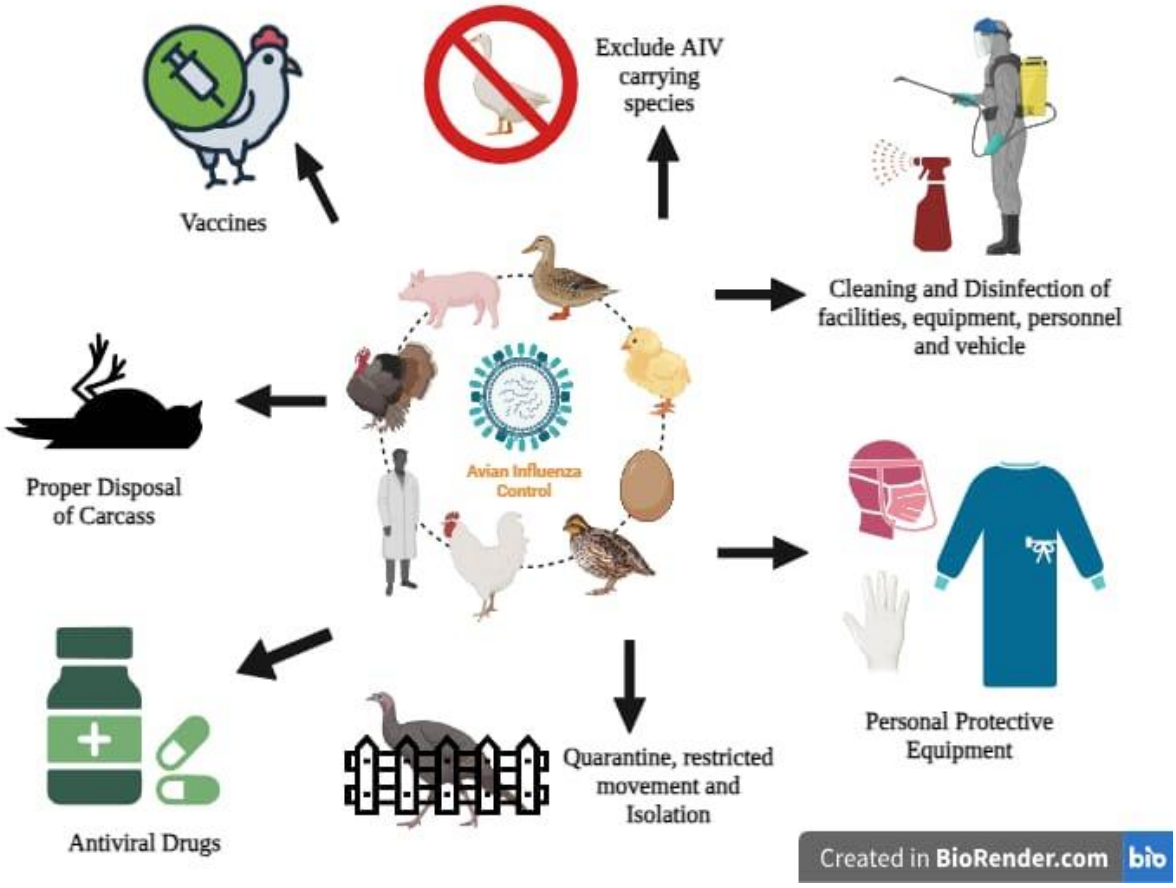

Fig. 1: Control strategies for Avian influenza. Avian influenza virus can infect chicken, turkey, waterfowl, pigs, human etc. For the prevention of the outbreaks of the Avian influenza, cleaning, disinfection and strict biosecurity measures should be adopted to prevent the movement of poultry, wild birds, and other potential carriers at the sites of poultry farming. Individuals should use protective measures to prevent contamination and proper disposal of the dead birds is important to spread the viruses. Poultry farmers should vaccinate their flocks against the avian influenza viruses and antivirals should be used in case of outbreaks.

- Decrease the number of personnel engaged in depopulation and stamping-out activities.
- Efficient management of AI outbreaks within affected flocks reduces the risk of virus transmission to personnel.
- Personnel should strictly follow effective biosafety protocols to prevent further virus dissemination and personal exposure.
- Eating and smoking are strictly forbidden in work areas, and any contact between potentially contaminated hands and the nose, mouth, and eyes should be prevented.
- Once depopulation and stamping-out operations are finished, all PPE needs to be disposed of properly or cleaned and disinfected completely.

Individuals who are in close proximity to potentially infected birds or who could be at risk of infection should wear the designated personal protective equipment including disposable head cover, facemask, protective goggles, waterproof apron, long sleeved overalls, rubber gloves and boots.

Whenever possible, individuals working in the poultry field should be vaccinated against the seasonal influenza viruses to decrease the risk of co-infection and genetic reassortment between avian and human

viruses. Individuals that come into close touch with diseased poultry or their secretions should take appropriate antiviral medication daily, continuing for 5–7 days after the potential exposure to the virus. All the personnels working with the infected poultry should observe their health closely and report any clinical symptoms such as fever, conjunctivitis, and respiratory issues for one week following any possible exposure.

Personnel protective equipment should be taken off after use, hands should be washed and disinfected in the subsequent order.

1. Start with the gloves.
2. Remove the overalls.
3. Wash and disinfect hands.
4. Take off the protective goggles.
5. Remove the visor and face mask.
6. Finish by washing and disinfecting hands.

8.4. TESTING AND DIAGNOSIS

The definitive diagnosis of avian influenza requires serological and virological techniques to distinguish it from other diseases that can manifest similar symptoms, such as avian pneumovirus, Newcastle disease virus, chlamydia, mycoplasma, infectious bronchitis virus, fowl cholera (*Pasteurella multocida*), infectious laryngotracheitis virus, E. coli, and various bacteria. Concurrent infections with avian influenza are common among poultry. Samples like cloacal, fecal, or tracheal swabs obtained from birds are employed to detect AIVs through conventional methods like virus isolation, or by identifying components of the viral particle such as nucleic acids or proteins. Post-exposure assessment is typically carried out by checking for antibodies against specific viral proteins. With advancing technologies, there is ongoing development of more specific, sensitive, and cost-effective diagnostic assays. The gold standard for the identification of avian-origin AIVs is still viral isolation (VI) in specific pathogen-free (SPF) embryonated chicken eggs (Hirst 1941).

The method involves the inoculation of the samples into the allantoic cavity of chicken embryonated eggs at the 9 to 11 days of incubation. Allantoic fluid will be harvested after 48 hours of incubation and hemagglutination inhibition assay (HAI) assay should be performed for subtyping AIVs isolates hyperimmune sera specifically prepared for different HA subtypes and NDV. Similarly, subtyping of the basis of the NA can be performed through the neuraminidase inhibition assay (NI) by using the sera specific for different NA subtypes.

Other methods to detect the influenza antibodies involve the agar gel immunodiffusion (AGID) assay and the enzyme-linked immunosorbent assay (ELISA). According to OIE, AGID holds the "gold standard" status for anti-influenza antibody detection. It is cost effective and sensitive in detecting anti-influenza NP or M1 antibodies in the sera of chickens and turkeys but it is less consistent for other avian species (Spackman et al. 2009). Real-time reverse transcription polymerase chain reaction (RRT-PCR) is commonly utilized to diagnose AIVs due to its high sensitivity, specificity, and fast detection ability.

8.6. VACCINATION

Vaccination can be regarded as the third line of defense against avian influenza. However, there is often hesitancy surrounding poultry vaccination because these vaccines typically protect against clinical signs rather than infection. Consequently, they can mask outbreaks and facilitate the spread of HPAIV. Vaccination has proven effective in countries where standard stamping-out protocols are insufficient for controlling the spread (Figure 1), when an irrevocable impact on the poultry industry may occur, or when

there is a risk to the food supply (Naeem and Siddique 2006; Villarreal 2007). Routine vaccination is implemented in certain nations as a preventive strategy to limit the spread and protect susceptible populations when avian influenza viruses have become endemic. This approach is commonly used to target H5, H7, and H9 viruses (Domenech et al. 2009; Spackman and Pantin-Jackwood 2014). Most vaccine doses administered in real-world situations have been in Mexico (H5N2 and H7N3) and China, Egypt, Vietnam, and Indonesia (H5N1) in response to outbreaks. Nevertheless, avian influenza remains entrenched in these regions (Swayne et al. 2011). Most avian influenza vaccines used in practical applications comprise inactivated whole virus formulations, enhanced with powerful oil-based adjuvants, and administered through intramuscular injection in multiple doses (Swayne et al. 2011). Numerous inactivated avian influenza vaccines have obtained licenses in the USA and other nations, alongside live recombinant vectors, including fowl pox, Avian paramyxovirus type 1 - NDV, Duck enteritis virus, and Turkey Herpesvirus.(Halvorson 2002; Swayne et al. 2001; Swayne et al. 2000). Recombinant vector vaccines against avian influenza are less prevalent in poultry than inactivated vaccines. Nevertheless, this vaccine category holds the potential for automated mass immunization methods like spray or drinking water administration, offering a speedy, efficient, and cost-effective means of immunization.

Significantly, vaccines that use NDV as a vector for H5 and H7 have demonstrated their ability to induce significant levels of HI antibodies and provide protection to chickens when exposed to challenges from H7N9 or HPAI H5N1 viruses, respectively (Liu et al. 2015).

However, the practical use of these vectored vaccines may be hindered by pre-existing immunity to the NDV vector (Spackman et al. 2014). An alternative strategy involves a chimeric NDV vector in which the F and HN ectodomains are replaced with avian paramyxovirus serotype-2 viruses. This alternative vector is safe and does not cross-react with NDV. It partially protected chickens immunized at one day of age against challenges from the highly pathogenic avian influenza virus H5N1 (Kim et al. 2017).

Moreover, a recombinant vaccine employing a turkey herpesvirus vector to express the HA gene of the H5N1 HPAIV consistently demonstrated robust protection against the same strain. It conferred cross-protection against various clades of the H5N1 highly pathogenic avian influenza virus (Gardin et al. 2016). Unconventional strategies for developing avian influenza vaccines are HA proteins, DNA-based immunization, and live vaccines (Bright et al. 2003).

9. CONCLUSION

Avian influenza viruses pose a multifold threat for animal and human health, as well as global food security. The continuous outbreaks in domestic poultry along with the competence of these viruses to undergo genetic reassortment, pose a constant threat to the poultry industry and raise apprehensions about the emergence of novel strains with pandemic potential. Previous outbreaks of the AIVs highlight the interrelationship between the avian and human influenza viruses which emphasize the need for a thorough interpretation of their evolution and transmission dynamics. Furthermore, continuous surveillance is necessary to predict the future outbreak and viral characteristics circulating in the field.

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