A REVIEW ON BIRD FLU

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ABSTRACT

Avian flu has been creating a panic situation all round the world and has been confirmed epidemic in major part of the world. The common most among the bird flu influenza virus is H5N1. Most cases of H5N1 infection to humans are thought to have occurred as a result of direct or close contact with sick or infected poultry. Ongoing circulation of A(H5N1) and A(H7N9) viruses in poultry, especially where endemic, continues to pose threats to public health, as these viruses have both the potential to cause serious disease in people and may have the potential to change into a form that is more transmissible among humans. Continued surveillance for A (H7N9) will be necessary to detect and control the spread of the virus. The health care sector should work in an efficient way to get rid of this pandemic virus by encouraging the pharmaceutical companies to develop novel antiviral lead moieties which work efficiently than the prevailing drugs , the present antiviral drug used for treatment are oseltamivir and zanamivir as an alternative drug. The government also has to take necessary proactive measures to prevent the spread of this dreadful virus by public awareness with the help of electronic and print media. Hence, clinical management of this virus has to be taken prior importance. Mostly children and pregnant women are affected and people suffering from respiratory tract diseases like asthma, pneumonia, bronchitis are mostly prone to this dreadful virus.

KEYWORDS: Avian flu, H5N1 Virus, H7N9, Pandemic, Oseltamivir, Zanamavir.
INTRODUCTION

"Bird flu" is a phrase similar to "swine flu," "dog flu," "horse flu," "human flu" or the viral infection caused by any of the several types of bird influenza virus.\[1\] Avian influenza also known informally as avian flu or bird flu, refers to "influenza caused by viruses adapted to birds. Other influenza virus subtypes also circulate in poultry and other animals, and may also pose potential threats to public health.\[2\],[3],[4]\ Containment measures, including the closure of live bird markets for several months, have impacted the agriculture sectors of affected countries and international trade.

Proper sanitation facilities, vaccination, different diagnostic procedures to quarantine the infected people, preventing the mass gatherings, providing masks to cover mouth and nose has to be taken care off to protect from spread of the virus. Bird flu is mostly affected by influenza A virus. The flu subtype virus are adapted to different types of birds so mostly avian flu virus is also called as influenza A virus. The alphabet A does not stand for “Avain”. Among the different strains of bird flu virus (H5N1) (figure 1) is the most virulent and prevailing virus in most parts of Asia since 2003.\[5\][6][7]

In the past (1957-1958) flu caused a major disaster killed around 70,000 Americans. Avian influenza reached Europe in 2005, and the Middle East, as well as Africa, in 2006.\[8\] In the year 2012 (January 22) two death cases are been reported in china with the affect of bird flu.\[9\] Among the birds most of the cases are reported in chicken and ducks (around 85%) and around 15% in wild birds. The first deadly Canadian case was confirmed on January 3, 2014.\[9][10\] On December 2, 2014, two turkey farms in British Columbia, Canada, had been placed under quarantine after the Canadian Food Inspection Agency confirmed an avian flu outbreak.\[11\]

Every year in winter/spring the mortality rate gets increased due to the favorable conditions for the existence of the virus. People mostly with respiratory disorders like asthma, bronchitis, pneumonia and low immunity are affected by this influenza virus. As this is new virus for our immune system there are no antibodies developed in the body which will lead a person seriously ill and also may lead to death.
What is avian or bird flu?
The H5N1 strain of bird or avian flu is believed to be the source of infection across the globe and become the next flu pandemic, sickening and killing tons of people. The H5N1 bird flu virus from the infected bird passes it among the birds such as chickens or ducks that are being raised for human consumption. The infected wild birds may not show the symptoms of the bird flu but the tamed birds which are raised for human economical dependence will be seriously affected and also may lead to death. The bird flu is believed that it does not pass to human beings, but in the past there are several cases of bird flu in humans are reported and this also caused a major hazard in many of the regions in the world. Mostly the virus was believed to be transferred from birds to humans as a result of direct or intimate contact with the poultry. Mostly the poultry farmers are affected. As this is new virus for our immune system there are no antibodies developed in the body which will lead a person seriously ill and also may lead to death. Influenza infection cause major problem to nose throat and lungs. It is most likely to be prevailing in fall and winter. It spreads to humans either by handling dead infected birds or from contact of infected fluids. when the infected domestic fowl dies the flu virus get transferred to humans which is virulent. Spread of flu in Asia and Europe is due to illegal poultry trade.

Background of Avian Influenza Virus (H5N1, H7N9 and Different strains)\(^{[12]}\)
In 1997 the first infected human case has been found out in Hong Kong and China, the virulent strain H5N1 was found to be the culprit. But this avian flu became wide spread and virulent in the year 2003 and 2004 it has affected in most parts of Asia, Africa and Europe. This outbreak of bird flu has lead to lot of changes in the livelihood, economy and international trade in the affected parts of the world.
H7N9 virus subtype is a low pathogenic virus which has been detected in Shanghai and Anhui in 2013. This has showed a great effect on the agricultural and poultry farming sectors to close the live chicken markets for several months and this has affected the international trade.

Fig 2: Genetic evolution of bird flu virion

There are several strains\(^{13}\) which have affected domestic fowls and the details are well illustrated in the Table1.

**Table 1: Showing different flu strains and fowl affected and places reported**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Flu Strain</th>
<th>Fowl Affected</th>
<th>Place Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H1N1</td>
<td>Duck</td>
<td>Alberta</td>
</tr>
<tr>
<td>2</td>
<td>H1N8</td>
<td>Duck</td>
<td>Alberta</td>
</tr>
<tr>
<td>3</td>
<td>H2N9</td>
<td>Duck</td>
<td>Germany</td>
</tr>
<tr>
<td>4</td>
<td>H3N8</td>
<td>Duck</td>
<td>Ukraine</td>
</tr>
<tr>
<td>5</td>
<td>H3N2</td>
<td>Turkey</td>
<td>England</td>
</tr>
<tr>
<td>6</td>
<td>H4N6</td>
<td>Duck</td>
<td>Czechoslovakia</td>
</tr>
<tr>
<td>7</td>
<td>H4N3</td>
<td>Duck</td>
<td>Alberta</td>
</tr>
<tr>
<td>8</td>
<td>H5N3</td>
<td>Tern</td>
<td>South Africa</td>
</tr>
<tr>
<td>9</td>
<td>H5N4</td>
<td>Duck</td>
<td>Ethiopia</td>
</tr>
<tr>
<td>10</td>
<td>H5N9</td>
<td>Chicken</td>
<td>Scotland</td>
</tr>
<tr>
<td>11</td>
<td>H6N2</td>
<td>Turkey</td>
<td>Massachusetts</td>
</tr>
<tr>
<td>12</td>
<td>H6N8</td>
<td>Turkey</td>
<td>Canada</td>
</tr>
<tr>
<td>13</td>
<td>H6N5</td>
<td>Shearwater</td>
<td>Australia</td>
</tr>
<tr>
<td>14</td>
<td>H6N1</td>
<td>Duck</td>
<td>Germany</td>
</tr>
<tr>
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<td>H7N1</td>
<td>Chicken</td>
<td>Brescia</td>
</tr>
<tr>
<td>16</td>
<td>H7N3</td>
<td>Turkey</td>
<td>England</td>
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<td>Turkey</td>
<td>Ontario</td>
</tr>
<tr>
<td>18</td>
<td>H9N6</td>
<td>Duck</td>
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<td>Turkey</td>
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</tr>
<tr>
<td>20</td>
<td>H11N6</td>
<td>Duck</td>
<td>England</td>
</tr>
</tbody>
</table>
KEY POINTS

- Avian influenza (AI), commonly called bird flu, is an infectious viral disease of birds.
- Most avian influenza viruses do not infect humans; however some, such as A (H5N1) and A(H7N9), have caused serious infections in people.
- Outbreaks of AI in poultry may raise global public health concerns due to their effect on poultry populations, their potential to cause serious disease in people, and their pandemic potential.
- Reports of highly pathogenic AI epidemics in poultry, such as A (H5N1), can seriously impact local and global economies and international trade.
- The majority of human cases of A (H5N1) and A (H7N9) infection have been associated with direct or indirect contact with infected live or dead poultry. There is no evidence that the disease can be spread to people through properly cooked food.
- Controlling the disease in animals is the first step in decreasing risks to humans.
- Avian influenza (AI) is an infectious viral disease of birds (especially wild water fowl such as ducks and geese), often causing no apparent signs of illness. AI viruses can sometimes spread to domestic poultry and cause large-scale outbreaks of serious disease. Some of these AI viruses have also been reported to cross the species barrier and cause disease or subclinical infections in humans and other mammals.

AI viruses are divided into 2 groups based on their ability to cause disease in poultry. High pathogenicity or low pathogenicity. Highly pathogenic viruses result in high death rates (up to 100% mortality within 48 hours) in some poultry species. Low pathogenicity viruses also cause outbreaks in poultry but are not generally associated with severe disease.
Geographical Distribution\[13\]

Bird flu has conquered most of the continents and affected many of the people all over the world. It is well illustrated in figure 2.

![Geographical Distribution of flu around the world.](image)

**OUTBREAK OF BIRD FLU IN INDIA**

Bird flu also made a mark in India. It has swiped out many of the fowls in the poultry and many of the cases are reported in different parts of India. In view of the outbreak of bird flu in India Indian Council for Agricultural Research (ICAR) here, the Imphal West district magistrate has banned the transportation of fowls and eggs from the infected area.\[14\] In Ranga Reddy district (Hayathnagar) the poultry are infected by H5N1 virus which have affected five poultry farms. In Andhra Pradesh and Telangana states around 20,000 crore turnover poultry is under scared condition due to adverse condition of bird flu.\[15\] Some of the Universities in both the states have banned consumption of chicken and egg in the student mess. The Telangana government ordered the immediate culling of 1.45 lakh chicken in poultry farms located in a one kilometre radius of the infected farm in Thorrur.\[16\] Death of as many as 40 chickens over the past three days in Valsad-Paardi village near Valsad city has created a scare among people who suspected the resurgence of bird flu in the area. A close watch on migratory birds are also been initiated near the wetlands and water bodies in some of the district of telangana. In the month of April 2015 chicken consumption in Hyderabad has gone down to 80% due to fear of bird flu outbreak in Hyderabad.\[17\] On april 15\textsuperscript{th} pathogenic avain flu virus (H5N1) has been confirmed in the state of telangana. In March 2015 Uttar Pradesh has witnessed the death of 4000 poultry in the capital city Agra which are
under investigation. Many of the places in west Bengal also witnessed the mark of this dreadful virus.\cite{18}

**FRAMEWORK OF INFLUENZA VIRION\cite{19}\**

Influenza virion is spherical in shape. The outer layer is a lipid membrane which is taken from the host cell in which the virus multiplies. Inserted into the lipid membrane are "spikes", which are proteins, actually glycoproteins, because they consist of protein linked to sugars known as HA (hemagglutinin) which is a antigenic trimer and NA (neuraminidase) which is a tetramer. These are the proteins that determine the subtype of influenza virus (A/H5N1, for example). The HA and NA are important in the immune response against the virus; antibodies (proteins made to combat infection) against these spikes may protect against infection. The virion contains genetic material RNA, these are encapsulated by M1 (matrix protein) and M2 which is a ion channel.

![Fig 4 Structure of influenza virion](..)

**PREVALENCE AND DISSEMINATION OF VIRUS\cite{20}\**

Bird flu is mostly affected by direct contact with the infected fowl or by close contact with that of the infected persons, it is a air borne disease, like other viruses through different routes it enters from the cavities of our body (like nose, mouth, mucous membranes), bird flu is mostly affected in spring/winter season. The infected person are mostly infants and pregnant women and people suffering from asthma the droplets which carry the influenza virus spreads through direct contact from human to human or indirect contact. Mostly this infection spread
before the appearance of the symptoms and after one week of illness. Bird flu effected personals should be properly screened and they have to be attended for medical supervision mostly the young adults and children the bird flu virus persists for a long period of time. It was wrongly believed that eating chicken will infect personnel with bird flu but properly cooked meat at 72°C for one hour will probably kill the virus and they are safe and can consume the meet.

**INCUBATION AND LIFE CYCLE OF BIRD FLU**[^21]

The incubation period for H5N1 is more than the normal seasonal influenza virus infection which is around 2 to 3 days. After entering into the body the influenza virus incubates for two days. In most of the cases the influenza virus was believed to incubate from two days to one week. Current data for H5N1 infection indicate an incubation period ranging from 2 to 8 days and possibly as long as 17 days. Current data for H7N9 infection indicate an incubation period ranging from 2 to 8 days, with an average of five days. WHO currently recommends that an incubation period of 7 days be used for field investigations and the monitoring of patient contact, hence, as a suggestion it would be wise to keep an eye out for approximately 10 days to be sure of the infection. Most US cases have shown the incubation period to be between two to seven days. In these cases, the course of medication should begin as soon as possible after exposure to the virus and continue for 7 to 10 days after the last known exposure.

![Life cycle of the virion in the host cell](image-url)

**Fig 5: Life cycle of the virion in the host cell**
Can I Eat Meat?
The most popular myth is that bird flu will be affected to the people who consume chicken. But the fact is Bird flu is not transmitted through cooked food. The food should be thoroughly cooked and it is completely safe to eat poultry and eggs during the pandemic conditions also. Small measures will make the meet safe and free from flu are.

- Use different utensils for cooked and raw meat.
- Careful monitoring should be done while handling the meat.
- Wash your hands thoroughly with soap and warm water before and after handling meat.
- Ensure that meat is thoroughly cooked and sparkling hot before serving.

You may be infected by

- Having direct contact with infected birds that are dead or alive
- inhaling or being in contact with dried dust from the droppings or bedding of infected birds
- inhaling droplets sneezed by infected birds
- slaughtering, butchering or preparing infected poultry for cooking
- Live markets, where birds are sold in crowded and unsanitary conditions.

SIGNS AND SYMPTOMS
Symptoms seen in the persons who are infected with avian influenza virus have

- High fever, usually with a temperature higher than 38°C
- Persistent coughing with sore throat
- Diarrhea
- Vomiting
- Abdominal pain
- Chest pain
- Bleeding from nose and gums
- Respiratory distress
- Hoarse voice
- Crackling sound when inhaling are commonly seen
- Sputum bloody
- Redness of eyes
- Increase in the body temperature
• Headaches,
• Muscle ache
• Dizziness
• In children this may affect the diet by making reluctance towards the food
• It also causes for discoloration of lips and skin

Complications of A (H5N1) and A(H7N9) infection include\textsuperscript{[27,28]}
• Hypoxemia
• Multiple organ dysfunction
• Secondary bacterial and
• Fungal infections

Fig 6: Symptoms of bird flu strain (H1N1 and H5N1) infected persons

GENERAL PRECAUTIONS\textsuperscript{[29]}
• Good hygiene conditions to be followed while cooking meat.
• Washing hands should be a regular practice, mostly after going to the toilet and before taking food.
• Be isolated from the people when you are infected with flu and cover your mouth with the help of a handkerchief/ tissue during cough or sneeze.
• Dispose the handkerchief/ tissue immediately after use or bin it and incinerate it and wash your hands with soap and warm water.
• When you are affected with flu avoid mass gatherings.
• Immediately consult the doctor as soon as you find out the symptoms of flu and take necessary medication.
• Don’t hesitate to take vaccination during the pandemic outbreak and make sure that you are vaccinated with the usual pneumococcal or seasonal flu vaccine.

Diagnostic tests for avian flu
If you think that you are infected with bird flu, the following tests should be carried
• Nose and throat swab
• Chest X-ray
• Blood Tests
• Gram Stain (a process that detects different bacteria).

REMEDIES FOR THE TREATMENT OF BIRD FLU VIRUS INFECTION[30]

Homeopathic Remedies
Homeopathy is a system of medicine based on a natural law. In France where homeopathy is well known, the largest selling flu treatment prescribed by doctors and practitioners alike is a homeopathic remedy. Those who have used it say it significantly reduces the severity and duration of symptoms. Homeopathy uses minute doses of naturally occurring substances to stimulate a self-healing reaction from the body. First, the body is helped to remove its own symptoms, and second, it is strengthened to be more resistant to the problem in the future. Philadelphian doctors, for instance, treated 26,795 flu cases with homeopathy, with a death rate of 1.05%. This was in stark contrast to a death rate of 30% for those using the other medicines of the day. In another account, Dr T. A. McCann of Ohio reported that of the one thousand patients he treated homeopathically, all survived. Likewise, the National Homeopathic Hospital had no fatalities among its patients. Gelsemium was the main homeopathic medicine prescribed during this pandemic because the weakness, trembling and collapse that victims experienced were symptoms well treated by it.

Conventional Drug Remedies
Antiviral drugs are prescription medicines (pills, liquid or an inhaler) with activity against influenza viruses, including other influenza viruses. Antiviral drugs can be used to treat bird flu or to prevent infection with bird flu mutated viruses. These medications must be prescribed by a health care professional. Influenza antiviral drugs only work against influenza viruses -- they will not help treat or prevent symptoms caused by infection from other viruses that can cause symptoms similar to the flu. There are four influenza antiviral drugs approved for use in the United States and UK they are Amantadine, Rimantadine, Zanamivir (Relenza), Oseltamivir (Tamiflu), Peramivir (Actrapid). The bird influenza A (H5N1) viruses that have been detected in humans in the UK and Mexico are resistant to amantadine and rimantadine so these drugs will not work against these bird influenza viruses. Laboratory testing on these bird influenza A(H5N1) viruses so far indicate that they are susceptible (sensitive) to oseltamivir, zanamivir and Peramivir.

Peramivir

Peramivir is an antiviral drug developed by BioCryst Pharmaceuticals. It is sold under the trade name of Rapivab used for the treatment of influenza. Peramivir is a neuraminidase inhibitor, acting as a transition-state analogue inhibitor of influenza neuraminidase and thereby preventing new viruses from emerging from infected cells. It is approved for intravenous administration.

Oseltamivir
Oseltamivir is developed by US based Gilead Sciences which licensed exclusive rights to Roche in 1996. It is a potential drug moiety for the treatment of Influenza A and Influenza B. It is generally marketed in the trade name of Tamiflu. It is administered orally. It is a neuraminidase inhibitor the main side effects of this drug is vomiting, headache.

Zanamivir.

Zanamivir is developed by Australian biotech firm Biota holding. It is a potential drug moiety for the treatment of Influenza A and Influenza B. It is generally marketed in the trade name of Relenza. It is currently marketed by Glaxo Smithkline. It is administered as oral inhalation. It is a neuraminidase inhibitor. The main side effects of this drug is broncho spasm, headache.

Acetaminophen

Acetaminophen is a non-opiate, analgesic and antipyretic, prescribed for headache, pain (muscle ache, backache) and fever either alone or combined with other medications.

Amantadine
It is developed by Endo Pharmaceuticals is a drug that has USFDA approval for the use as an Antiviral drug. This also show CNS side effects, nervousness, anxiety, agitation, insomnia. According to US CDC seasonal H3N2 2009 pandemic flu samples are tested resistance to adamantanes and it is now not recommended for the treatment of influenza virus.

**Rimantidine**

![Rimantidine molecule](image)

It is used in the treatment of influenza A in rare cases, it will shorten the duration and moderate sensitivity of influenza. It is marketed in the trade name of Flumadine. It is an USFDA approved drug in 1994. But it is no longer used in the treatment of influenza. According to US CDC seasonal H3N2 2009 pandemic flu samples are tested resistance to adamantanes and it is now not recommended for the treatment of influenza virus.

**Ibuprofen**

![Ibuprofen molecule](image)

Ibuprofen is a non steroidal anti-inflammatory drug (NSAID), prescribed for mild to moderate pain, inflammation and fever. This medication decreases the hormones that cause pain and inflammation in the body.

**NATURAL REMEDIES**[^31]

The bird flu virus is more susceptible to the people who have low immune system. The natural system of medicine is mainly based upon the upgrading the body defense mechanism and decreased side effects.

This is done by prescribing various digestive enhancers strengthening herbs such as...
Fig 7 Natural remedies for the treatment of Bird flu

Digestive Enhancers

Fig 8 Natural drugs used to increase the digestion power

More commonly available household natural remedies for treatment of bird flu involves

Fig 9 Commonly available natural household remedies
VACCINATION\textsuperscript{[32]}

Vaccines which are used in the treatment of H5N1 bird flu influenza virus are

\textbf{Pandemrix}

Pandemrix is an influenza vaccine, H5N12003 flu pandemic colloquially called the .bird flu. The vaccine was developed by Glaxo SmithKline and patented in September 2006. The vaccine is one of the H1N1 vaccines approved for use by the European Commission in September 2009 upon the recommendations of the European Medicines Agency (EMEA). The vaccine is only approved for use when an H1N1 influenza pandemic has been officially declared by the World Health Organization (WHO) or European Union (EU). This vaccine was initially developed as a pandemic mock-up vaccine using an H5N1 strain.

\textbf{Celvapan}

The 2003 flu pandemic vaccines are the set of influenza vaccines that have been developed to protect against the pandemic H5N1 virus. These vaccines either contain inactivated (killed) influenza virus, or weakened live virus that cannot cause influenza. The killed vaccine is injected, while the live vaccine is given as a nasal spray. Both these types of vaccine are usually produced by growing the virus in chicken eggs. Around three billion doses will be produced annually with delivery from November 2009. Pandemrix vaccine will only need one dose. People who have the Celvapan vaccine will need two doses three weeks apart. The .bird flu vaccine is different from the seasonal flu vaccination that’s offered every year.
The vaccine is being offered first to pregnant women at any stage of pregnancy, child and people who are most likely to become seriously ill if they catch bird flu. The vaccines contraindicated in those who had a severe allergic reaction to a previous dose of the vaccine or any component of the Vaccine.

These medications work by stopping the virus from multiplying in your body. They help reduce the severity of the condition, prevent complications and help improve the chances of survival. In regular flu, these medications are most effective if given within 48 hours of symptoms developing, but it is not clear if this is the case for bird flu. Nevertheless, they should be given as soon as possible to people suspected or proven to be infected, even if it's more than 48 hours after the onset of symptoms.

These medications may also be given as a preventative measure to people who could have been exposed to bird flu viruses – for example other household members, healthcare workers or people who have had close contact with infected birds.

In these cases, the course of medication should begin as soon as possible after exposure to the virus and continue for 7 to 10 days after the last known exposure.

**MASK PROTECTION**

People should avoid mass gathering and also should protect themselves from dreadful influenza virus by covering Mouth, Ear and Nose with the help of N-95 masks. Mostly people with less immunity are more prone to this influenza. Mostly children, pregnant women should take care as they are more susceptible.

![Image of mask](image_url)

*Figure 13: Usage of mask as a preventive measure.*
BIRDS BEING TREATED BY THE EXPERTS\textsuperscript{[34]}

STEPS BEING TAKEN TO STOP THE SPREAD OF THE FLU BY THE LOCALS AS WELL AS THE EXPERTS.\textsuperscript{[35]}

CONCLUSION

Bird flu is a new virus, lethal within a brief span of time. Proper medical attention has to be paid to those people who are infected with this dreadful virus. Bird flu is new to the human race and so the body does not develop any antibodies against the virus so it is a panic situation and the medics should become alert in scrutinizing and treating the infected personals. If a person infected with flu and if it continues more than 4 days he has to be immediately attended and should be given medical attention.

In this review overall points about the bird flu are been discussed about the prevalence of bird flu in various continents and especially in India. Birds flu laid its death hands on India and caused a lot of damage to the international trade and also the livelihood of the people. It also
changed the lifestyle of the people especially on those who depend on the poultry farming. So the government has to take necessary steps to overcome this dreadful situation. We have also discussed about the signs and symptoms, and also different system of medicines used in the treatment of influenza virus such as Homeopathy, ayurvedic and conventional system of medicine. The people should not forget that “Prevention is better than Cure” and maintain proper sanitation and personal hygiene and also avoid mass gathering and should also have proper information about bird flu virus to lead a healthy and prosperous life ahead and should follow the instruction provided by the government through print and social media and protect the fowl and the people from the death hands of this dreadful virus.

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