ISSN: 2349-2678

Contents lists available at www.ijpba.in

International Journal of Pharmaceutical and Biological Science Archive

Volume 3 Issue 2; May-June-2015; Page No.01-08

A review on Influenza a H1N1 virus

Mumal Shekhawat[1*], Manoj Sharma[2], Anil K. Gupta[3]

[1,3] Faculty of Pharmaceutical Science, Jayoti Vidyapeeth Women's University, Jaipur, Rajasthan-302122, India.

[2] School of Studies, in Pharmaceutical Sciences, Jiwaji University, Gwalior (MP)-474011, India

ARTICLE INFO

Short Review

Received 30 March. 2015
Accepted 31 April. 2015

Corresponding Author:

Mumal Shekhawat

Faculty of Pharmaceutical Science, Jayoti Vidyapeeth Women's University, Jaipur, Rajasthan-302122, India.

Email: mumalshekhawat.93@gmail.com

ABSTRACT

Influenza A H1N1 virus emerged as pandemic worldwide in 2009 and its re-emergence has taken place in India in 2013. The WHO has placed the pandemic threat alert to level 6. Swine flu refers to swine influenza or the viral infection caused by any of the several types of swine influenza virus. Only people who used to have direct contact with pigs were observed to get swine flu in the past. But, H1N1virus is a new swine flu virus and it contains the genetic material of swine, bird and human influenza virus. H1N1is an Influenza A virus. Symptoms include fever, cough, sore throat, body aches, headache and chill sand fatigue. Prevention of swine influenza has three components namely prevention in swine, prevention of transmission to humans, and prevention of its spread among humans Effective personal preventive measures include shielding one's mouth and nose while coughing and sneezing, frequent washing of hands with soap, avoiding mass gatherings and voluntary isolation by symptomatic individuals .The diagnosis may include Influenza Rapid Antigen Test; Influenza Type A and B Antigen Detection; Influenza A and B Culture; Influenza Type A H1N1; PCR for Influenza Virus. Tamiflu (Oseltamivir) and Ralenza (Zanamivir) can treat the H1N1swine flu strain. India developed and launched its own vaccines (killed and live attenuated) against Influenza A H1N1 in 2010 after establishing its safety and efficacy and with approval from Drug Controller General of India (DCGI). Ayurvedic remedies comprise pure natural herbs which are effective in preventing swine flu. Moreover, the herbs are used to relieve swine flu symptoms, and boost the immune system against the H1N1virus. Swine flu can produce a number of symptoms in both adults and children. In India day by day the graph of infected person has been climbed up so, it is important to take into consideration about this disease as it may prove deadly one.

INTRODUCTION

EPIDEMIOLOGY:

During the spring of 2009, a novel influenza A (H1N1) virus of swine origin caused human infection and acute respiratory illness in Mexico and has rapidly spread over the world, being reported in 214 countries 1 year after its first identification.[1,2] After initially spreading among persons in the United States and Canada.[3,4]the virus spread globally, resulting in the first influenza pandemic since 1968 with circulation outside the usual influenza season in the Northern Hemisphere. As of March 2010, almost all countries had reported cases, and more than 17,700 deaths among laboratory-confirmed cases had been reported to the World Health Organization (WHO).[5]The number of laboratory-confirmed cases significantly underestimates the pandemic's impact. In the United States, an estimated 59 million illnesses, 265,000 hospitalizations, and 12,000 deaths had been caused by the 2009 H1N1 virus as of mid-February 2010.[6]This article reviews virologic, epidemiologic, and clinical data on 2009 H1N1 virus infections and summarizes key issues for clinicians worldwide

H1N1 flu is also known as swine flu. It's called swine flu because in the past, the people who caught it had direct contact with pigs. That changed several years ago, when a new virus emerged that spread among people who hadn't been near pigs. In 2009, H1N1 was spreading fast around the world, so the World Health Organization called it a pandemic. Since then, people have continued to get sick from swine flu

The influenza pandemic caused by the new H1N1 virus has by now affected all the continents of the world. However, the extent and likely impact are still uncertain. Like seasonal flu, the illness is mild and self-limiting in a great majority of cases, with only 1%–2% of

patients requiring hospitalization. In a few cases, the clinical course can deteriorate in a matter of hours, leading to severe complications and eventually death. The risk of complications is higher among those who have pre-existing diseases, such as asthma, heart disease and kidney disease, and among pregnant women. In such cases, antiviral treatment should not be delayed pending laboratory confirmation.[7]

In the guidance document 'Global surveillance during an influenza pandemic' released by the World Health Organization, three parameters were highlighted that should be documented quickly in this respect: the incubation period (time between infection and symptoms), the serial interval (time between symptoms onset in primary case and secondary case), and the reproduction ratio/number (average number of secondary cases per primary case).[8] These parameters are instrumental to assessing the feasibility and efficacy of intervention strategies against pandemic influenza.[9]

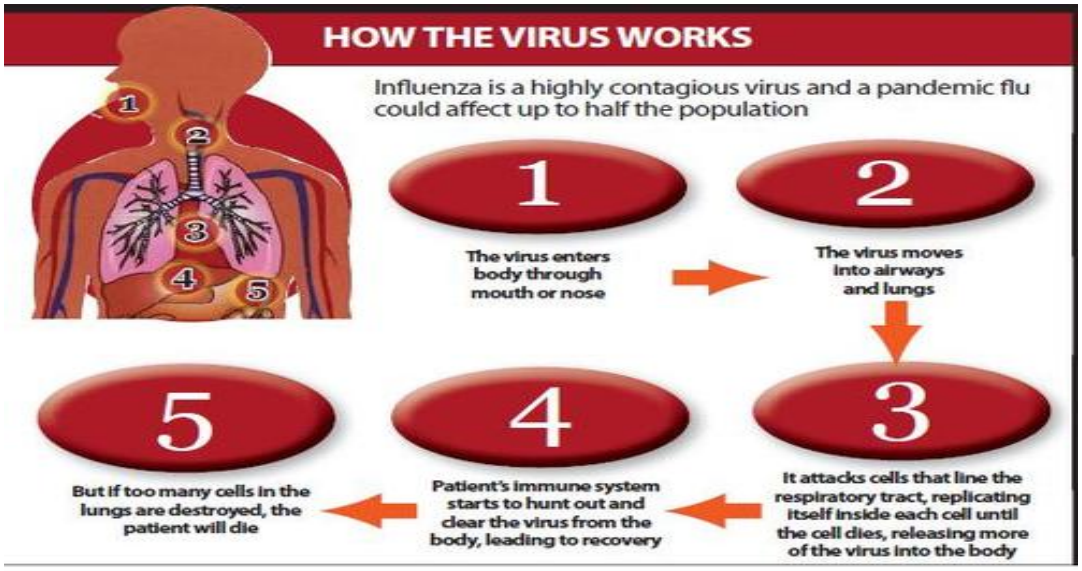

Figure 1: How the virus works

VIRAL CHARACTERISTICS:

Pandemic 2009 H1N1 virus derives six genes from triple-reassortant North American swine virus lineages and two genes (encoding neuraminidase and matrix proteins) from Eurasian swine virus lineages.[4]Although the 2009 H1N1 virus is antigenically distinct from other human and swine influenza A (H1N1) viruses,[4]strains of this virus have been antigenically homogeneous, and the A/California/7/2009 strain that was selected for pandemic influenza vaccines worldwide is antigenically similar to nearly all isolates that have been examined to date.[10]Multiple genetic groups have been recognized, including one recently predominant lineage,[11]but any possible clinical importance of different lineages remains uncertain Reassortment has not occurred with human influenza viruses to date. The level of pulmonary replication of the 2009 H1N1 virus has been higher than that of seasonal influenza A (H1N1) viruses in experimentally infected animals,[12,13] but the 2009 pandemic strain generally lacks mutations that are associated with increased pathogenicity in other influenza viruses .

Most influenza A viruses circulate naturally as constantly evolving RNA based avian influenza viruses among flocks of wild birds-especially ducks and waders. Some of these viruses have crossed species barriers and have become established in mammals, notably in humans (human influenza viruses) and pigs (swine influenza viruses)[14].They are usually classified by the type of haemagglutinin and neuraminidase proteins present on the virus surface. Each strain may have any one of 16 known haemagglutinins (HA or H), and any one of nine neuraminidase (NA or N) varieties of protein. In any inter pandemic period there is usually one, but sometimes two, predominant strains of influenza A viruses circulating in humans. It is infection with these plus the influenza B viruses (which have a less pathogenic human profile than the A viruses), that constitutes the inter pandemic (seasonal) human influenza. The number of possible 'H' and 'N' combinations are quite large but since the 1918 influenza pandemic, humans have been infected by viruses with only seven of the 16 possible haemagglutinins (H1, H2, H3, H5,H7, H9and H10), and four of the 9 possible neuraminidases (N1,N2, N3 and N7).Only three of the H types have successfully become human influenza (H1, H2 and H3), the others really being zoonoses .[1]

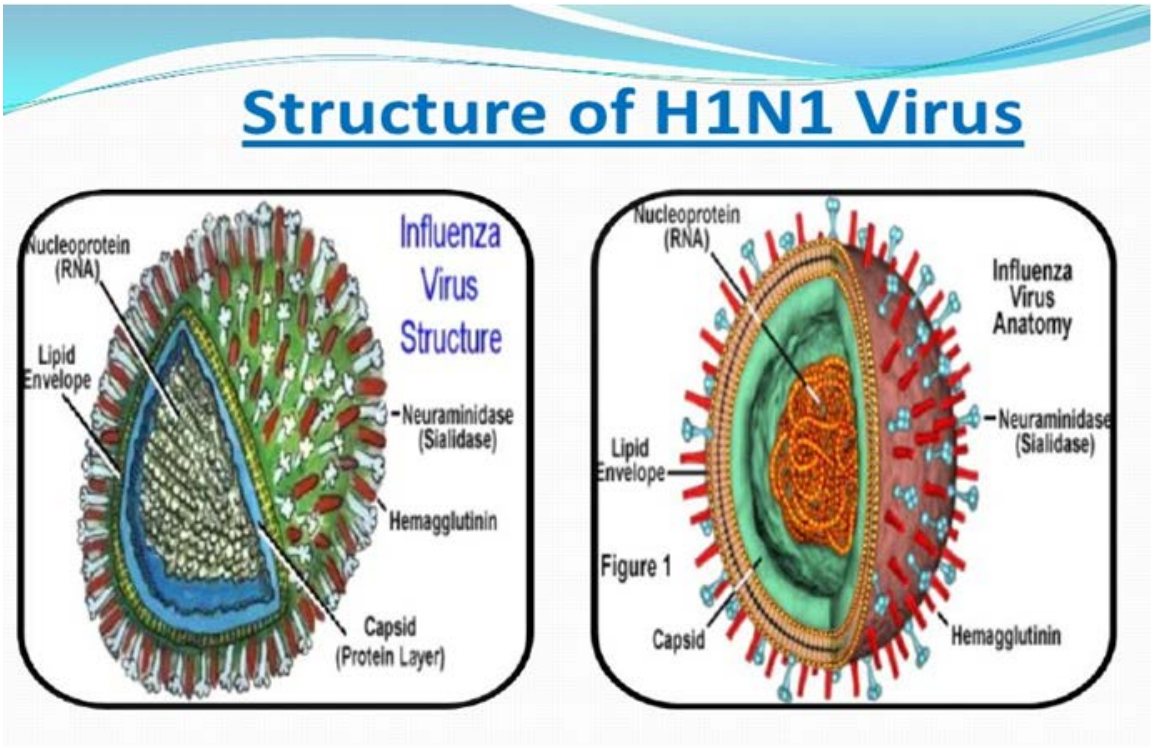

Figure 2: Structure of H1N1 virus

CLASSIFICATION:

The three genera of influenza viruses that cause human flu, two also cause influenza in pigs, with influenza-A being common in pigs and influenza-C being rare. Influenza-B has not been reported in pigs. Within influenza-A and influenza-C, the strains found in pigs and humans are largely distinct, although due to ressortment there have been transfers of genes among strains crossing swine, avian and human species boundaries.[16]

SIGNS AND SYMPTOMS:

In Swine:

In pigs influenza infection produces fever, lethargy, sneezing, coughing, difficulty breathing and decreased appetite.[17]

In Humans:

Symptoms include fever, cough, sore throat, body aches, headache and chill sand fatigue. The 2009 outbreak has shown an increased percentage of patients reporting diarrhea and vomiting. The 2009 H1N1virus is not zoonotic swine flu, as it is not transmitted from pigs to humans, but from person to person.[18]

Typical Symptoms-

- A sudden fever-100 degrees F or above
- A sudden cough

Other Symptoms-

- Tiredness
- Chills
- Malaise
- Myalgias
- Cough and sneezing
- Headache
- Weakness and fatigue
- Aching muscles and joints
- Sore throat
- Runny nose
- Diarrhoea or stomach upset
- Loss of appetite

DIAGNOSIS:

For diagnosis of swine influenza A infection, respiratory specimen (nasopharyngeal swab, throat swab nasal aspirate, nasal washing) would generally need to be collected within the first 4 to 5 days of illness (when an infected person is most likely to be shedding virus). Most of the tests can distinguish between A and B types. The test can be negative (no H1N1infection) or positive for type A and B. If the test is positive for type B, the flu is not likely to be swine influenza (H1N1). If it is positive for type A, the person could have conventional influenza strain or swine influenza (H1N1)[19].

Sample Collection:

It should be labeled clearly and include patient's complete information and should be sent to NIV, Pune or NICD, Delhi within 24 hours for further investigations. Laboratory biosafety measures should be followed for collection, storage, packaging and shipping of influenza samples.

Available Laboratory Tests:

- Rapid Antigen Test /Rapid influenza diagnostic test (RIDT) : not as sensitive as other available tests, used to detect the virus in nasal secretions and one of the most common methods used to diagnose this infection. Depending on the method, it may be completed in the doctor's office in less than 15 minutes or be sent to a

laboratory, with the results available the same day. It can help differentiate influenza from other viral and bacterial infections with similar symptoms that may be serious and must be treated differently. The main disadvantage of the rapid influenza antigen test is the high rate of false-negative results. RIDTs will occasionally be positive when someone does not actually have the flu.

- RT–PCR: In this detection and quantification of mRNA is done. This test detects the viral load in an individual. molecular tests detect viral genetic material in respiratory samples like a nasal or throat swab and are the most sensitive for influenza virus. These tests may be ordered to diagnose influenza A infection, especially in those who are seriously ill (hospitalized), and to help track influenza outbreaks. Some false negatives can occur with this method. Some molecular tests can distinguish between A and B virus and between different types of influenza A virus.
- Virus isolation: The throat swab is generally taken to culture virus from the suspected cases. Though if it is not detected doesn't rule out the disease.
- Viral culture: has been considered the "gold standard" for diagnosing influenza, but it can take up to 3-10 days for results. It can be used for confirmation of a positive rapid test result, to check a negative test result, or when someone is suspected to have flu. In this test, the influenza virus is actually grown and further identified in the laboratory. It has the advantage of identifying which viruses (A, B, or another respiratory virus) and which strains of virus are present
- Virus Genome Sequencing.[2]

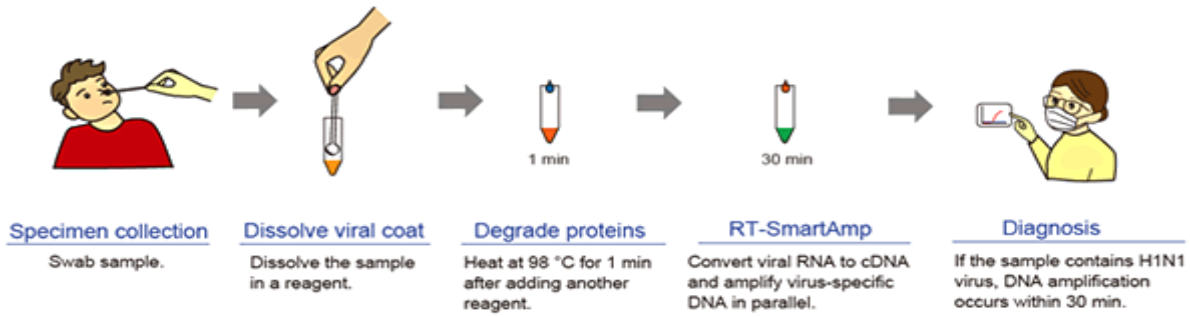

Figure 3: diagnosis steps of H1N1 virus

PRECAUTIONS:

According to World Health Organization, swine flu has been declared as a pandemic disease. The following are the WHO safety precautions to be taken against swine flu:[21]

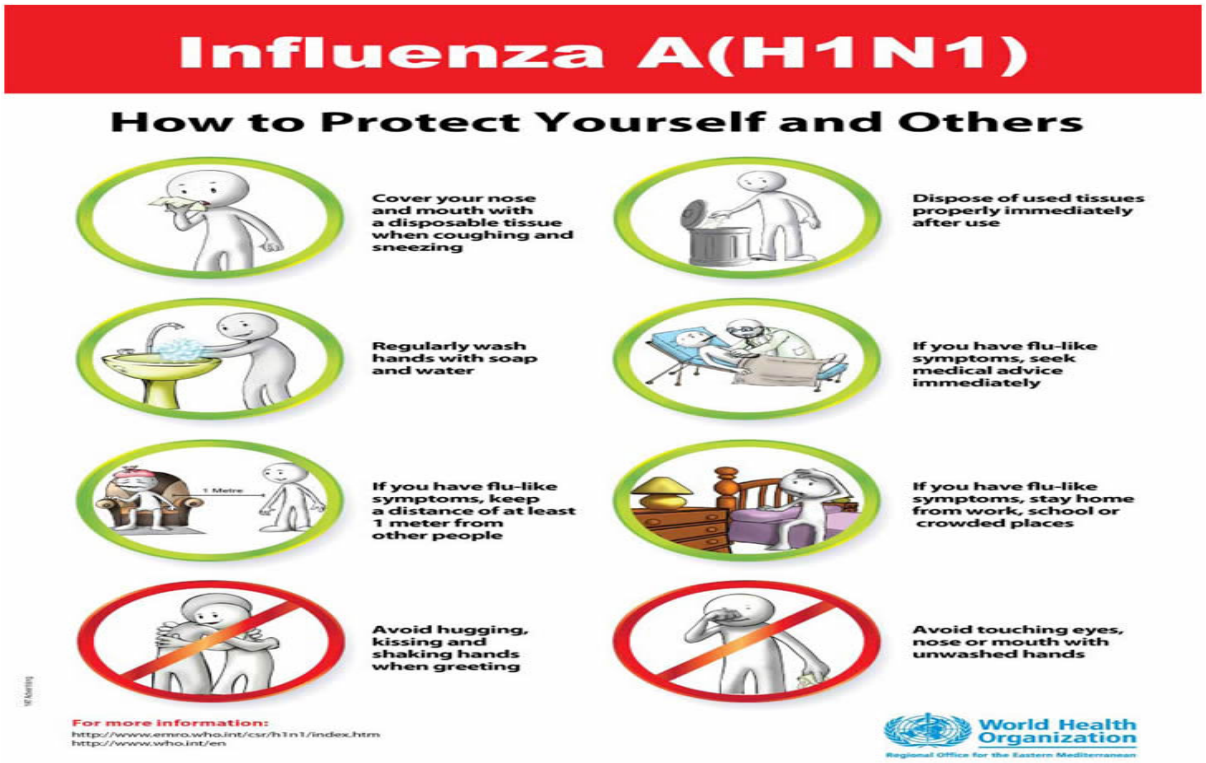

Figure 4: how to protect yourself and others

- The nose and mouth must be covered with disposable tissues while coughing or sneezing.
- The used tissues must be disposed off immediately after using them.
- Hygiene and cleanliness must be maintained by washing hands frequently with soap and water.
- Touching the eyes, nose or mouth without washing hands must be totally avoided.
- A doctor must be consulted immediately, in case flu-like symptoms are observed.
- In case of flu-like symptoms, the patient must be quarantined.
- One should stay at home from work, school and crowed places in case flu-like symptoms are observed.
- Face masks and gloves must be used when moving out in crowded places or nursing any ill patient. If a person is ill, then he or she should avoid contact with other people and stay isolated. Visit an authorized swine flu treatment hospital or doctor for further treatment. One should keep their surroundings clean and maintain hygiene.
- Avoid unnecessary travelling and crowded areas.

PREVENTION:

Prevention of swine influenza has three components namely prevention in swine, prevention of transmission to humans, and prevention of its spread among humans.

In Swine:

Methods of preventing the spread of influenza among swine include facility management, herd management, and vaccination. Because much of the illness and death associated with swine flu involves secondary infection by other pathogens, control strategies that rely on vaccination may be insufficient. Control of swine influenza by vaccination has become more difficult in recent decades, as the evolution of the virus has resulted in inconsistent responses to traditional vaccines. Standard commercial swine flu vaccines are effective in controlling the infection when the virus strains match enough to have significant cross-protection, and custom (autogenous) vaccines made from the specific viruses isolated are created and used in the more difficult cases. Facility management includes using disinfectants and ambient temperature to control virus in the environment. The virus is unlikely to survive outside living cells for more than two weeks, except in cold (but above freezing) conditions and it is readily inactivated by disinfectants. Herd management includes not adding pigs carrying influenza to herds that have not been exposed to the virus. The virus survives in healthy carrier pigs for up to 3 months and can be recovered from them between outbreaks.

In Humans:

Prevention of pig to human transmission:

Swine can be infected by both avian and human flu strains of influenza, and therefore are hosts where the antigenic shift scan occurs that create new influenza strains. The transmission from swine to human is believed to occur mainly in swine farms where farmers are in close contact with live pigs. Although strains of swine influenza are usually not able to infect humans this may occasionally happen, so farmers and veterinarians are encouraged to use a face mask when dealing with infected animals. The use of vaccines on swine to prevent their infection is a major method of limiting swine to human transmission. Risk factors that may contribute to swine-to-human transmission include smoking and, especially, not wearing gloves when working with sick animals thereby increasing the likelihood of subsequent hand-to-eye, hand-to-nose or hand-to-mouth transmission[22].

Prevention of human to human transmission:

Influenza spreads between humans when infected people cough or sneeze, then other people breathe in the virus or touch something with the virus on it and then touch their own face. Recommendations to prevent spread of the virus among humans include using standard infection control against influenza. This includes frequent washing of hands with soap and water or with alcohol-based hand sanitizers, especially after being out in public. Chance of transmission is also reduced by disinfecting household surfaces, which can be done effectively with a diluted chlorine bleach solution. Experts agree that hand-washing can help prevent viral infections, including ordinary influenza and the swine flu virus and also not touching eyes, nose or mouth with hands helps to prevent the flu. Alcohol-based gel or foam hand sanitizers work well to destroy viruses and bacteria.[23]

AT - RISK GROUPS:

Individuals that have been identified as “at-risk” of more complicated or severe illness associated with infection by influenza virus include:

- Pregnant women (particularly in the later stages of pregnancy);
- Infants and children (<age 5);
- Patients with chronic health conditions such as cardiovascular, respiratory or liver disease, or diabetes;
- Patients with immune suppression related to treatment for transplant surgery, cancer or due to other diseases.

The elderly (>65) appear less susceptible to infection by pandemic H1N1 influenza virus, but are assumed to be at higher risk of more severe or complicated illness if infected.

TREATMENT:

Treatment of swine flu can be done by 3 ways –

- Vaccination: Vaccines have been developed to protect against the virus that causes swine flu. There

are two different brands of vaccine Pandemrix and Celvapan. Many people given the Pandemrix vaccine will only need one dose. People who have the Celvapan vaccine will need two doses three weeks apart. The swine flu vaccine is different from the seasonal flu vaccination that's offered every year. The seasonal flu vaccine does not protect against swine flu. 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 swine flu. There are only a few people who cannot have the swine flu vaccine. The vaccines should not be given to anyone who has had a severe allergic reaction to a previous dose of the vaccine or any component of the Vaccine.[24]

- Antiviral Therapy: Two classes of antiviral drugs are available for the prevention and treatment of influenza: neuraminidase inhibitors and adamantanes, which inhibit a viral protein called M2. Influenza A H1N1, formerly known as swine flu, has been found to be resistant to adamantanes (Amantadine and Rimantadine). Oseltamivir (Tamiflu) and Zanamivir (Relenza) are the two neuraminidase inhibitors currently availble by prescription.These drugs reduce the median duration of symptoms by approximately one day and reduce the chance of contracting influenza by 70 to 90 % when used for known influenza exposure. Zanamivir and Oseltamivi rare structurally related drugs that have been approved by the United States Food and Drug Administration (FDA) for the prophylaxis and treatment of influenza. In addition to their activity against current influenza A and influenza B strains, they are also active against the strain that caused the 1918 pandemic and against avian influenza a strains.[25,26]-

✓ **OSELTAMIVIR :**

- Generic name: oseltamivir, brand name: Tamiflu.
- Drug class and mechanism: Oseltamivir is an oral medication used for treating and preventing the "flu." It is similar to zanamivir (Relenza). Oseltamivir suppresses and decreases the spread of influenza A and B viruses, the viruses responsible for the flu. It does this by blocking the action of neuraminidase, an enzyme produced by the viruses that enables the viruses to spread from infected cells to healthy cells. By preventing the spread of virus from cell to cell, the symptoms and duration of influenza infection are reduced. On average, oseltamivir reduces the duration of symptoms by one and a half days if treatment is started within forty-eight hours of the beginning of symptoms. The FDA approved oseltamivir in October 1999.
- Swine Flu and Ayurveda: Ayurveda promotes the concept that if one's immune system is strong, then even if the body is exposed to viruses, one will not be affected. During a pandemic or an epidemic, Ayurveda emphasizes on the immunity of people living in regions affected by viruses. This branch of medicine promotes the intake of special herbs or decoctions to increase the immunity level of the people. Ayurvedic remedies comprise pure natural herbs which are effective in preventing swine flu. Moreover, the herbs are used to relieve swine flu symptoms, and boost the immune system against the H1N1virus. Ayurvedic treatment for swine flu involves the use of following herbs -

✓ Basil: Basil, Ocimum basilicumis a great Ayurvedic treatment option for swine flu. Ayurvedic practitioners claim that basil not only keeps the nasty swine flu virus at bay, but it also assists in the fast recovery of an affected person. They claim that basil improves the body's overall defense mechanism, thereby increasing its ability to fight viral diseases. It is also believed to strengthen the immune system of the afflicted person. For the control and prevention of swine flu, basil must be consumed in the fresh form. The paste or juice of a minimum of 25 leaves (medium size) should be consumed twice a day. Moreover, it should be had on an empty stomach. Basil is safe, with no side effects and is great to prevent swine flu from spreading like wildfire.

✓ Ginger: Ginger, Zingiber officinalisis one of the natural remedies for swine flu prevention. It boosts the body's immunity level and helps protect the body. Ginger has been known to fight cold, fever and flu conditions, and is also good to reduce inflammation.

✓ Garlic: Garlic, Allium sativumon the other hand is a powerful natural antibiotic, which features an unusual property of repelling bacteria and viruses.

✓ Gooseberry: Gooseberry, Embelica officinalisis one of the best fruits known to boost the immune system of the body. Since gooseberry is rich in Vitamin C, it helps raise the body's resistance to flu viruses. If fresh gooseberry is not available in the market, then the form of jam or juice is also great.

✓ Aloe vera: Aloe vera is an easily available plant and is also beneficial to boost immunity. One should consume a teaspoon of gel with water on a daily basis.

✓ Camphor and Eucalyptus Oil: Camphor has great ability to keep different air borne diseases under control. It is available in the form of camphor oil, which can be burnt in the room or office all the time. Inhaling the steam of Eucalyptus oil is also good. Just add a few drops of Eucalyptus oil into lukewarm water and inhale the steam. This helps to clear the nasal track and promotes the health of the respiratory tract.

Thus, it can be seen that while swine flu and Ayurveda both target the immune system, swine flu destroys it and Ayurved a focuses on keeping it.

CURRENT AFFAIRS:

Union Government issued guidelines to tackle increasing number of H1N1 cases on 12TH Feb, 2015.[JAGRAN JOSH]

Four people test positive for H1N1 in Maharashtra in the last few days. Femina Believe conducts workshops

for individuals and corporate in soft skills. Since January, Pune city has reported a total of 813 cases of swine flu and 87 deaths. As many as 1,71,561 people with influenza like symptoms have undergone swine flu screening in Pune city so far this year.

The total number of swine flu cases has gone up to 5,140 while the number of casualties has increased to 499 in Maharashtra so far this year. The state health officials confirmed 10 fresh cases and 4 deaths due to swine flu on Thursday.

With the soaring temperatures, watermelon and sugarcane stands make a killing while the number of H1N1 cases has been seeing a downward spiral. On Tuesday 19th may 2015, the government

hospital saw 2 admissions while six people were treated for the flu compared to the 23 admissions a fortnight ago .On Sunday, 44 people tested positive for the virus in the city, while 75 cases were detected across Maharashtra.[THE TIMES OF INDIA]

The number of deaths across India due to swine flu reached 774 on Saturday, with 31 more people succumbing to the disease. States like Gujarat, Rajasthan, Delhi, Maharashtra and Telangana witnessed a rise in number of swine flu cases and the figure of those infected with H1N1 virus stands at 12,963 till February 21, according to Union health ministry.

In Rajasthan "Four deaths and 288 positive cases were reported today 20th feb 2015 (Friday)," B R Meena, director for public health, said. The highest number of deaths at 34 was reported from Jaipur, followed by Ajmer at 27. Delhi recorded 2,060 cases of swine flu till 20th feb 2015.[HINDUSTAN TIMES]

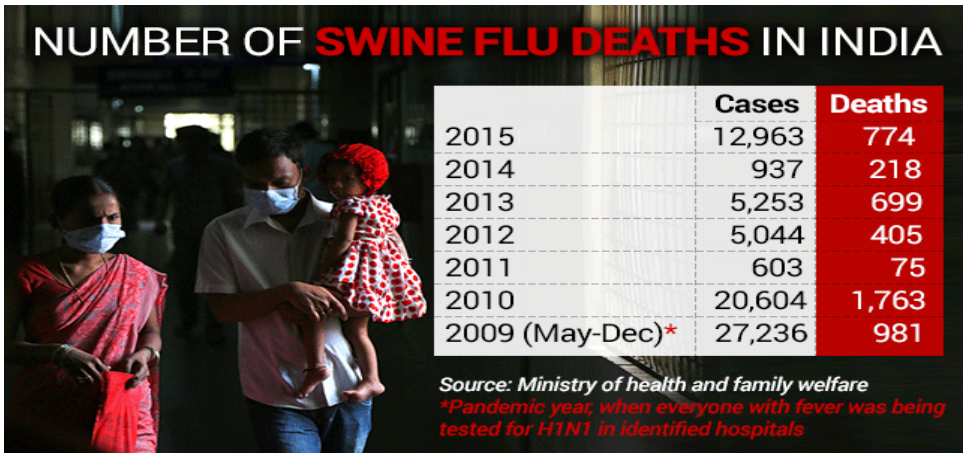

Figure 5: number of swine flu deaths in india

CONCLUSION:

From the above survey of information it can be well known that the Swine flu is a dangerous disorder which is spreading worldwide and this is a casual thing to be considered that more and more people in India are affected by it and the cases may increase. So, it is important to take into Consideration about this disease as it may prove deadly one. And thus the intensity of this disorder can be lowered by diagnosing and taking proper treatments. Swine flu is a new virus that the world has never seen before, it has many similarities to the past pandemics and could ultimately turn into another 1918, however unlikely that sounds at this moment in time. Since its discovery in April it has spread around the globe and has caused infections in 74 countries, but the real number will be much closer to 500000. With the vaccine development, it is now possible to control the transmission of Influenza A H1N1. Studies conducted by Serum Institute of India have shown that live attenuated vaccine is able to provide herd immunity apart from individual immunity so as to prevent the spread of virus across the barriers in a population. Therefore close contacts of patients and vulnerable age groups must get themselves vaccinated and boosters to be given every year. The benefit risk ratio is more than 1 and vaccines (inactivated and LAIV) have been of proven safety and efficacy. Oseltamivir (Tamiflu) or Zanamivir (Relenza) can be used for prophylaxis and treatment as per the CDC Advisory Committee Guidelines.

REFERENCE:

1. Echevarría-Zuno S, Mejía-Aranguré JM, Mar-Obeso AJ, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. Lancet 2009;374:2072-9.
2. Perez-Padilla R, delaRosa Zamboni D, Ponce de Leon S, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. N Engl J Med 2009; 361:680-9.
3. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med 2009; 360:2605-15. [Erratum, N Engl J Med 2009;361:102.]
4. Garten R J, Davis CT, Russell CA, et al. Antigenic and genetic characteristics of swine-origin 2009 A(H1N1) influenza viruses circulating in humans. Science 2009; 325:197-201.

5. Pandemic (H1N1) 2009 — update 94. Geneva: World Health Organization, April 1, 2010. (Accessed April 9, 2010, at http://www.who.int/ csr/don/2010_04_01/en/index.html.)
6. CDC estimates of 2009 H1N1 influenza cases, hospitalizations and deaths in the United States, April 2009–February 13, 2010. Atlanta: Centres for Disease Control and Prevention, 2010. (Accessed April 9, 2010, at http://f lu.gov/ individual family/about/h1n1/ estimates_ 2009_ h1n1.html.)
7. Narain Jai P., Kumar Rajesh, Bhatia Rajesh, et al. Pandemic (H1N1) 2009: Epidemiological clinical and prevention aspects, Natl Med J India 2009;22:e 1-e6
8. World Health Organization. Global surveillance during an influenza pandemic 2009
9. Halloran ME, Ferguson NM, Eubank S et al. Modeling targeted layered containment of an influenza pandemic in the United States. Proc Natl Acad Sci U S a 2008; 105:4639–4644.
10. 10. Recommended composition of influenza virus vaccines for use in the 2010 influenza season (southern hemisphere winter). Wkly Epidemiol Rec 2009; 84: 421-31.
11. 11.Valli MB, Meschi S, Selleri M, et al. Evolutionary pattern of pandemic influenza (H1N1) 2009 virus in the late phases of the 2009 pandemic. PLoS Curr Influenza 2010:March 3:RRN1149
12. Maines TR, Jayaraman A, Belser JA, et .al. Transmission and pathogenesis of swine-origin 2009 A(H1N1) influenza viruses in ferrets and mice. Science 2009; 325:4 8 4 -7.
13. Munster VJ, de Wit E, van den Brand JM, et al. Pathogenesis and transmission of swine-origin 2009 A(H1N1) influenza virus in ferrets. Science 2009; 325:481-3.
14. Webster RG, Bean WJ, Gorman OT, Chambers TM, Kawaoka Y. Evolution and ecology of influenza A viruses. Microbiol Rev. 1992;56:152–179.
15. Kilbourne ED. Influenza pandemics of the 20th century. Emerg Infect Dis 2006; 12:9–14.
16. Kothalawala, H., M.J. Toussaint and E. Gruys,. An Overview of Swine Influenza, 2006; 28; 46-53
17. "Q & A: Key facts about swine influenza (swine flu) –Spread of Swine Flu". Centers for Disease Control and Prevention. http://www.cdc.gov/
18. Myers KP, Olsen CW, Gray GC. Cases of swine influenza in humans: a review of the literature. Clinical Infectious Diseases, 2007; 44(8): 1084–8.
19. CDC H1N1 Flu | H1N1 Flu and You". Cdc.gov. http://www.cdc.gov/H1N1flu/qa.htm
20. FDA Approves Vaccines for 2009 H1N1Influenza Virus". FDA. http://www.fda.gov
21. Swine. Custom Vaccines. Novartis. http://www. livestock.novartis.com/cv_swine.html
22. Swine Flu: The predictable pandemic?".http:// www.newscientist.com/article
23. NIH studies on Swine flu vaccine". NIH. http:// www. nlm.nih.gov/medlineplus/ news/ fUllstory_ 89221.html
24. US Centers for Disease Control and Prevention. Interim guidance on the use of influenza antiviral agents during the 2010-2011 influenza season http://www.cdc.ov/flu/professionals/ Antivirals/guidance/summary.htm
25. Swine Flu Vaccination: What You Need to Know, http://www.direct.gov.uk /prod_consum_dg/groups/dg_digitalassets/@dg/ @en/documents/digitalasset/dg_181508.pdf
26. Tumpey TM, García-Sastre A, Mikulasova A.Existing Antivirals Are Effective Against Influenza Viruses With Genes from the 1918 Pandemic Virus. Proc Natl Acad Sci USA, 2002; 99:138-149.