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2009 INFLUENZA A (H1N1) VIRUS PANDEMIC WITH RESPECT TO INDIAN SCENARIO: AN UPDATE

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ABSTRACT
The emergence of influenza A (H1N1) in 91 years ago led to a catastrophic universal pandemic. In the present scenario, the swine-origin influenza A (H1N1) virus (S-OIV) infections were reviewed. A reassorted influenza virus was first reported from Mexico on March 18, 2009. This virus rapidly gets circulated to neighboring United States and Canada, and from there on to the rest of the world. April 15 and April 17, 2009, the Centers for Disease Control and Prevention (CDC) identified two cases of human infection with S-OIV characterized by a unique combination of gene segments that had not been identified among human or swine influenza A viruses. In India Influenza A (H1N1) was first identified in April 2009. This review systematically focuses on an update of the Influenza A (H1N1) and its contribution to morbidity and mortality with respect to Indian Scenario.

KEYWORDS: Orthomyxoviridae, Swine influenza, genetic reassortment, Real-Time PCR, Mortality.

INTRODUCTION

Swine Influenza (SI) or 'Swine Flu' is an infectious respiratory disease caused by type A influenza virus of the family Orthomyxoviridae. Swine influenza is a highly contagious acute respiratory disease of pigs caused by one of the several strains of swine influenza A (Ajlan et al., 2009). The virus is spread among pigs by aerosols, through direct and indirect contact, and also by asymptomatic carrier *i.e.*, pigs. Swine influenza saw predominantly in the mid-western United States (and occasionally in other states), Mexico, Canada, South America, Europe (including UK, Sweden, and Italy), Kenya, Mainland China, Taiwan, Japan, and other parts of eastern Asia and in various parts of India. Influenza viruses are typed based on antigenically related nucleocapsid and matrix proteins into type A, B, C, and D viruses. Type B influenza virus is seen in human beings alone while type C is reported in humans and occasionally in swine and seals. Type A influenza viruses have been responsible for epidemics and pandemics, type B strains cause sporadic human cases and small-scale outbreaks, while type C causes only mild infections. Of the four influenza virus types, only IAV are of significant concern for the health of pigs and cause swine flu. IAV is a highly infectious respiratory pathogen in the respective natural hosts, which include birds, pigs, horses, other lower mammals, and humans (Alexander DJ 2000) and Webster et al., 1992). It is an enveloped RNA virus containing eight segments of negative-sense RNA (Figure 1), which encode 11 proteins, including haemagglutinin (HA), Neuraminidase (NA), matrix protein (M1, M2), nucleoprotein (NP), nonstructural proteins (NS1 and NS2), and a polymerase complex (PA, PB1, PB2, and PB1F2). The major proteins are HA and NA, seen as spikes on the viral surface. Among the viral proteins, the HA protein is responsible for attachment of the virus to the host cell, while NA protein plays a significant role in the release of progeny viruses from infected cells (Easterday et al., 1999). Of influenza A, B, C, and D viruses, influenza A virus mutate more rapidly thus showing more antigenic flexibility and hence are more virulent than the other three types (Eccles 2005). Each of the haemagglutinin sub-type can combine with all the sub- types of the neuraminidase, resulting in a huge and highly flexible pool of genetic diversity. The emergence of any novel HA sub- type to which a population does not have any immunity could lead to a pandemic. Recently proposed of all four influenza viruses is IDV. The genomics segments of Influenza D encode proteins: a glycoprotein hemagglutinin-esterase fusion (HF); polymerases PB1, PB2, and PB3; matrix protein (M1 and M2); and a non-structural protein (NSI and NEP). The genetically closet member of the Influenza family to IDV is ICV, former sharing less than 50% protein sequence identity with the latter (Nadkar et al., 2009). There is no cross-reactivity between IDV and human ICV generated serum (Nadkar et al., 2009, Hause et al., 2013, 2014). Influenza D virus was first identified in 2011 from swine having respiratory disease and was subsequently found in both healthy and sick cattle from multiple geographic areas across the United States, France,

and China (Haue et al., 2013, 2014, Collin et al., 2015 and Ferguson et al., 2015). The virus was recently detected in sheep and goat. Serological studies suggested that IDV has been presented in beef cattle at least since 2004 (Collin et al., 2015). The proposed reservoir for Influenza D virus is cattle's and young, weaned, comingled and immunologically naïve calves are most susceptible to infection due to dwindling maternal antibody levels after 6 months of age (Collin et al., 2015).

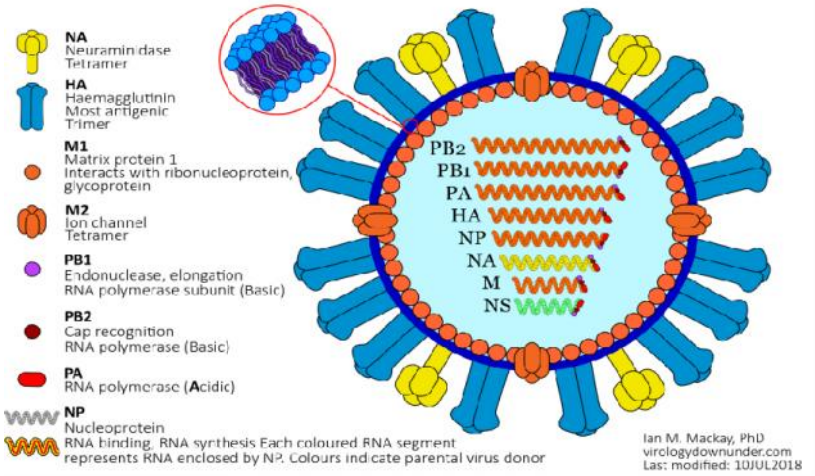

FIGURE 1. The flu virus haemagglutinin (HA) gene segment codes for the HA glycoprotein. Along with M2 protein and neuraminidase (NA) glycoprotein, HA is embedded in a double layer of lipid, derived from the host cell. https:// figshare.com/ articles/Influenza_virus/6817112

TABLE 1. Comparison of the structure, virulence and efficacy of treatment of influenza virus A, B and C (Rewar , 2015).

Severity of illness	Type A	Type B	Type C
	++++ (sever)	++ (moderate)	+ (mild)
Animal reservoir	Yes	No	No
Human pandemics	Yes	No	No
Human epidemics	Yes	Yes	No (sporadic)
Antigenic changes	Shift ,drift	Drift	Drift
Segmented genome	Yes	Yes	Yes
Amantadine, rimantadine	Sensitive	No effect	No effect
Zanamivir (Relenza)	Sensitive	Sensitive	Not known
Surface glycoproteins	2	2	1

Epidemiology

As influenza is caused by a variety of species and strains of viruses, in any given year some strains can die out while others create epidemics with a potential to cause a pandemic. The incubation period of this virus is generally 1-4 days, with an average of two days (Khanna and Kumar, 2002). The adults transmit influenza one day prior to the onset of symptoms and up to 5 days after the symptoms begin. The children usually transmit it for 10 or more days (Elveback et al., 1976). The groups of people, that is at a high risk for contracting influenza and influenza related complications include (Mathew, 2006), all individuals 50 years and older, children 6–23 months of age, women who are pregnant during influenza season, residents of long-term care facilities, children 6 months to 18 years of age and who are receiving aspirin therapy for extended period, persons 6 months and older with any chronic illness. The most outstanding characteristic of influenza viruses is their rapid evolution which leads to great variability, especially in influenza A virus. Being an RNA virus with segmented genome (eight separate single-stranded segments), genetic reassortment or recombination can occur during mixed infections with other influenza viruses, resulting in the generation of novel reassortment influenza A viruses (Kothalawala et al., 2006 and Mathew et al., 2006). This phenomenon is also called genetic or antigen shift, a salient feature of all influenza A viruses. Here, exchange of whole genome segments occurs while concurrent infection of a cell by two different influenzas A viruses, thereby creating viruses with thoroughly new combinations of genes resulting in a variety of different hybrid viruses possessing selective advantage compared with their parent viruses. By this mechanism, there is a possibility of production of 256X108 genetically different progeny viruses (Dhama et al. 2005 & 2009). The assemblage of point mutations could also lead to a step-by-step modification of the virus proteins by a mechanism described as 'antigen drift', seen predominantly in HA and NA glycoproteins, which favour the emergence of more pathogenic biovars and allows the viruses to escape the immunity acquired through infection or vaccination and to cause further outbreaks and epidemics. Mutations resulting from the error-prone replication of the ss-RNA and an ability to produce reassortment viruses both contribute to

the evolutionary success of these viruses. Extreme genetic variations exhibited by the influenza viruses are the hallmark, which makes the disease difficult to be controlled. Influenza A virus sub-types are distinguished by differences in their genetic sequences, which translate into differences in their antigenic structure. Influenza A viruses are classified into sub types on the basis of their HA and NA antigens. Till date, 16 H sub types (H1-H16) and 9 N sub types (N1-N9) have been recognized, giving rise to 144 possible combinations (Easterday et al., 1999, Hampson et al., 2006 & Olsen et al., 2006). All of which are maintained in aquatic birds (Fouchier et al. 2005 & Ro¨hm et al., 1996). The combination of HA and NA sub types are designated such as H1N1, H1N2, and so on up to H16N9. However, certain sub types are specific to certain species, except for birds, which are hosts to all known sub types of influenza A. The binding affinity of haemagglutinin to the Sialic acid residues partly account for the host specificity of various sub types. Relatively few HA and NA combinations have over and over again generally circulated among pigs or people (predominantly H1N1, H1N2 and H3N2 in pigs causing swine flu; H1N1, H1N2, H2N2 and H3N2 in humans causing human flu) (Olsen, 2004). Other sub types are found most commonly in other animal species. In poultry, H5N1, H5N2, H5N3, H5N9, H7N1, H7N2, H7N3, H7N4, H7N7, H9N2, H10N7 and also H1N2, H2N2, H6N1 and H3 sub types; and in equines, H3N8 and H7N7 sub types have been reported.

Pandemic 2009 H1N1 strain

Infections with the human influenza viruses have a worldwide distribution. Epidemics of seasonal influenza occur regularly in the northern and southern hemispheres each winter. It is estimated that influenza epidemics cause around 500,000 deaths per year worldwide (Olsen, 2004). There is very little information about influenza epidemiology in tropical countries, but it is believed that influenza may occur throughout the year. The genetic redirection in the influenza virus causes rapid and unpredictable antigenic changes in important immune targets that lead to recurrent outbreaks of febrile respiratory diseases every 1 or 3 years and constantly require the development of new vaccines. Every century there has been some pandemics that are progressing rapidly in all parts of the world due to the appearance of a new virus for which the general population has no immunity. In addition to previous epidemics and pandemics, special attention has been given to the public for deaths in humans from the H5N1 sub type of highly pathogenic avian influenza (HPAI) and the current swine flu pandemic caused by the new influenza virus, influenza A H1N1 (Dhama et al., 2005 & 2009, De Wit and Fouchier, 2008). These cases have shown that a completely new influenza A virus can cause life-threatening infections in humans. Seroepidemiological and virological studies since 1889 suggest that human influenza pandemics were caused by the influenza A virus sub types H1, H2, and H3. The history of human influenza pandemics could offer significant indications for upcoming events. A human flu pandemic in 1580 that struck Europe, Asia and Africa, the main regional epidemics in the seventeenth century and more epidemics and pandemics in the eighteenth century (1729-30, 1732-33 and 1781-82), 19 (1830-31, 1833 and 1889-90) and the twentieth century (1918, 1957, 1968) (Crosby, 1993; Lina, 2008 and Quinn, 2008). In humans, the appearance of different influenza strains occurred antigenically four times in the twentieth century: 1918 (H1N1), 1957 (H2N2), 1968 (H3N2), and 1977 (H1N1), each of which produced severe pandemics. During 1957 ("Asian" influenza) and 1968 (the “Hong Kong” influenza), bird flu viruses were grouped with previously circulating human influenza viruses to create viruses with different sub types of hemagglutinin (from H1 to H2 in 1957 and H2 to H3 in 1968 (Kothalawala et al., 2006; Mathew et al., 2006 and Myers et al., 2006). Pandemic influenza occurs at irregular and unpredictable intervals and is the result of an important antigenic change is known as “antigenic shift”, which occurs translates into a new HA sub type against which the population has no immunity Currently, influenza viruses of the sub types H1, H2 and H3 have been successfully established in humans (Myers et al., 2007) . The current influenza A (H1N1) virus of swine origin was first detected in April 2009, especially in North and South America. As tabulated in table 2, it began with the report of influenza-like illnesses on March 17, 2009, by the Mexican government which was subsequently confirmed as swine flu. Shortly after the reports of the Mexican government, the United States government, UK also began to report confirmed laboratory cases of H1N1 swine flu. The virus after infecting humans is spreading more from person to person, with an increasing number of cases reported all over the world. Sporadic human infections with swine flu have been reported before April 2009. In these cases, swine flu occurred in people with direct exposure to pigs. However, in the current swine flu epidemic, the virus is spreading from man to man, not through contact with infected pigs, which favours the possibility of sustained transmission in human communities around the world. To date, the infection has involved around 140 countries around the world and continues to spread further thanks to a faster communication and transport system.

TABLE 2. An overview of the 2009 pandemic Influenza A (H1N1) outbreaks.

2009	Novel Influenza A (H1N1) Outbreak and Pandemic Milestones
17 March	First case (Mexico) in the world which was later identified as swine flu
28 March	First case in the US, which was later identified as swine flu
12 April	First known death in Mexico due to swine flu
24 April	First Diseases’ outbreak of the swine flu notified by the WHO
27 April	First case confirmed in Canada, United Kingdom & Spain
28 April	First death confirmed in the USA; First case confirmed in New Zealand
30 April	First case confirmed in Hong Kong, China
7 May	First death confirmed in Canada

8 May	First case confirmed in Japan
9 May	First case confirmed in Australia
10 May	First case confirmed in China
16 May	First case confirmed in India
22 May	First case confirmed in Russia
26 May	First case confirmed in Singapore
3 June	First case confirmed in Saudi Arabia
11 June	The WHO raises its Pandemic Alert to Phase 6 • 135 countries have officially reported 94,512 human cases of influenza A (H1N1) infection, resulting in 429 deaths in 19 countries (Fig. 3). • The USA has reported the largest number of laboratory-confirmed human cases (33,902) with the death of 170 persons, the highest reported mortality among countries • Mexico has reported 10,262 human cases with a casualty amounting up to 119.
Current WHO83 Update* as of 6th July 2009	• Other countries experiencing size able number of human cases but with fewer deaths are Canada (7983 – 25 deaths/), UK (7447 – 3 deaths), Chile (7376 – 14 deaths), Australia (5298 – 10 deaths), Argentina (2485 – 60 deaths), Thailand (2076 – 7 death), New Zealand (1059 – 3 deaths), Uruguay (195 – 4 deaths), Costa Rica (277 – 3 deaths); and China (2040) and Japan (1790) but with no human casualty. • Countries reporting 1-2 human casualties of swine flu include Philippines (1 death/ 1709 cases), Spain (1 death/ 776 cases), Brazil (1 death/ 737 cases), Guatemala (2 deaths/ 286 cases), Paraguay (1 death/ 106 cases), Dominican Republic (2 deaths/108 cases), Colombia (2 deaths/118 cases), and Honduras (1 death/123 cases).

Courtesy: As per CDC Atlanta 436 deaths and 99,222 human cases.(http://en.wikipedia.org/ wiki/ 2009_ flu_ pandemic_ by_ country as on 08 July 2009).

Swine flu outbreak; Indian Scenario

In India the first case of swine flu was reported on 16 May 2009. The second case was reported on 1 June 2009 at the National Institute of Virology (NIV), Pune in a mother and son duo from Chennai (Khanna et al., 2009).during the 2009 pandemic of swine flu the Government of India initiated a series of preventive actions approved by the inter menstrual task force (IMTF) on influenza at it's meeting held on 28 April 2009 to carry out sevilance activities at all health care facilities (WHO 2009).

TABLE 3. Number of swine flu (H1N1) positive deaths in India (Rewar and Suresh 2015).

Year	Cases of swine flu (H1N1)	Deaths
2009 (May-Dec)	27,236	981
2010	20,604	1,763
2011	603	75
2012	5,044	405
2013	5,253	699
2014	937	218
2015	42592	2990

Source: Ministry Of Health and Family Welfare, Govt. of India

The ministry of health and family welfare records cases of swine flu and deaths caused by it annually. In India during the pandemic year 2009 27,234 cases of swine flu were recorded out of which 981 died. In 2010, 20,604 cases were recorded out of which 1,763 died. In the year 2011, 603 were reported of which 75 deaths occurred. In 2012 and 2013, 5,044 and 5,253 cases were reported out of which 405 and 699 patients died, respectively. In 2014, 937 were reported out of which 218 died. In 2015, out of 42592-recorded cases, 2990 deaths occurred (Table 3).

Diagnosis

For diagnosis of swine influenza A infection, the specimen is collected from the respiratory tract within the first 4-5 days of illness (when an infected person is not likely to be shedding virus). However, in children virus shedding occurs after 7 days or longer. Identification of swine flu influenza A virus is done at a referral laboratory. In medical terms, a suspected case of swine influenza A (H1N1) virus infection is a person with infection is a person with acute febrile respiratory illness (fever ≥38ºC) with onset within 7 days of close contact with a person who is a confirmed case or within & days of close contact with a person who is a confirmed case or within 7 days of travel to or resides in an area where there are one or more confirmed swine influenza A (H1N1) cases. WHO approved laboratories are set up for swine flu tested by one or more of the following tests: Real-time PCR, viral culture and a four-fold rise in swine influenza A (H1N1) virus specific neutralizing antibodies. RT-PCR based test is far more sensitive than rapid antigen test. TaqMan-based RT-PCR methods for the detection of influenza A (H1N1)virus target haemagglutinin (H) and neuraminidase (N) genes (Whiley et al., 2009) and study on influenza A (H1N1) by cellular and molecular profiling in Uttarakhand (Sharma et al., 2019). The respiratory samples preferred for swine influenza A (H1N1) testing are nasopharyngeal swab and throat swab. From incubated patients admitted in the ICU, the sample is bronchoalveolar lavage or tracheal aspirates. Samples are transported in viral transport medium (VTM) at 2-8ºC (provided by solidified ice pack) and can be stored at –70ºC. All sample collection tubes should be labelled clearly with the patient's name and ID, and must be transported to referral laboratory within 24hrs for clinical sample testing. The biosafety measures should be followed properly for sample collection, storage, transport, and testing (Machado, 2009 and Nadkar et al., 2009).

TABLE 4. Seasonal Influenza (H1N1) – State/UT- wise, Year- wise number of cases and death from 2010 to 2018 In India by NCDC

Sr. No.	States/UTs	2010		2011		2012		2013		2014		2015		2016		2017		2018	
		C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D	C	D
1	Andaman and Nicobar	2	0	0	0	0	0	0	0	0	0	4	0	0	0	2	1	0	0
2	Andhra Pradesh	733	49	11	1	326	34	71	8	10	5	258	36	12	5	476	14	402	17
3	Arunachal Pradesh	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	1	0	0
4	Assam	5	1	0	0	0	0	0	0	0	0	31	4	0	0	199	5	0	0
5	Bihar	0	0	1	0	0	0	0	0	0	0	352	6	0	0	26	0	1	0
6	Chandigarh	75	0	0	0	1	0	37	5	0	0	23	7	6	0	63	6	4	2
7	Chhattisgarh	50	12	0	0	10	3	1	1	0	0	239	53	6	4	305	64	12	4
8	Dadra and Nagar Haveli	2	0	0	0	0	0	0	0	0	0	26	6	1	0	15	4	4	2
9	Daman and Diu	0	0	0	0	0	0	0	0	0	0	5	1	0	0	6	2		0
10	Delhi	2725	77	25	2	78	1	1511	16	38	1	4307	12	193	7	2837	16	205	2
11	Goa	68	1	7	0	9	0	0	0	1	1	193	19	6	0	260	12	55	4
12	Gujrat	1682	363	7	4	101	30	989	196	157	55	7180	517	411	55	7709	431	2164	97
13	Haryana	216	16	6	4	18	5	450	41	5	0	433	58	68	5	252	9	61	7
14	Himachal Pradesh	10	3	14	3	2	2	0	0	0	0	123	27	14	5	77	15	7	2
15	Jammu and Kashmir	20	2	13	1	0	0	76	2	0	0	495	20	2	0	140	26	77	14
16	Jharkhand	1	0	0	0	0	0	0	0	0	0	16	6	1	1	35	2	4	1
17	Karnataka	2575	116	100	12	878	48	122	19	303	33	3565	94	110	0	3260	15	1733	72
18	Kerala	1533	89	210	10	623	14	10	1	62	15	928	76	23	1	1414	76	879	53
19	Lakshadweep	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	Madhya Pradesh	395	110	9	4	151	26	113	32	17	9	2445	367	38	12	802	146	100	34
21	Maharashtra	6814	669	26	5	1551	135	643	149	115	43	8583	905	82	26	6144	778	2593	461
22	Manipur	1	0	0	0	0	0	0	0	0	0	5	2	0	0	8	1	0	0
23	Meghalaya	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2	1
24	Mizoram	0	0	0	0	0	0	20	1	0	0	4	0	0	0	0	0	0	0
25	Nagaland	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0
26	Odisha	92	29	0	0	2	0	0	0	0	0	76	13	1	0	414	54	33	7
27	Pondicherry	50	6	1	0	63	2	0	0	0	0	57	4	1	0	168	9	319	10
28	Punjab	139	14	46	14	13	4	183	42	27	6	300	61	177	64	295	86	47	11
29	Rajasthan	1710	153	36	11	343	60	865	165	64	34	6858	472	157	45	3619	279	2375	221
30	Sikkim	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	Tamil Nadu	1184	13	34	4	750	40	37	6	58	0	898	29	122	2	3315	17	2812	43
32	Telangana	-	-	-	-	-	-	-	-	78	8	2956	100	166	12	2165	21	1007	28
33	Tripura	0	0	0	0	0	0	0	0	0	0	0	0	0	0	44	0	1	0
34	Uttarakhand	25	7	0	0	1	1	24	7	0	0	105	15	20	5	184	22	9	2
35	Uttar Pradesh	376	29	57	0	124	0	98	8	2	0	1578	50	122	16	3858	132	65	8
36	West Bengal	121	4	0	0	0	0	3	0	0	0	544	30	7	2	716	26	21*	0*
Cumulative Total		20604	1763	603	603	5044	405	5253	699	937	218	42592	2990	1786	265	38811	2270	14992	1103

Abbreviations used in table 4.: C-Cases, D- Deaths;

*The reports on cases and deaths of influenza A (H1N1) are based on the reports received from States/UTs to Central Surveillance Unit, Integrated Disease Surveillance Programme, NCDC, Delhi. Revised on Dated 06.05.2018, Time: 02.20 PM

An overview of swine flu cases and deaths from 2010 to 2018 is tabulated above. the table gives the year wise and state wise description of seasonal Influenza cases and deaths that occurs in the past years. Maximum number of cases and deaths were reported in 2015. Minimum number of cases and deaths were reported in 2011.

Prevention

Highly recommended measures to prevent viral infection consist of the standard personal precautions against influenza (Lynch and Walsh, 2007). These include (a) Hand Washing – Single most important measure to reduce the risk of transmission from one person to another, washing hands frequently with soap and water especially with alcohol-based hand sanitizers (b) Covering the nose and mouth during coughing and sneezing (c) Limit your contact with other people if you are Sick (c) Avoidance of crowded areas (d) Use N95 mask – reduces the risk of swine influenza virus transmission by aerosols by 80%.

Treatment

Adamantanes and neuraminidase inhibitor are the two groups of antiviral drugs that are effective against influenza infection. Adamantanes includes amantadine and rimantadine, and neuraminidase inhibitors include zanamivir, oseltamivir, peramivir and laninamivir. Peramivir and laninamivir are not licensed in all countries (Reynolds et al., 2014; Allerson et al., 2013; Uscher et al., 2011; Cho et al., 2014; Thorlund et al., 2011). Effectiveness of antiviral drugs is most when they are administered within first 48 hrs after the clinical symptoms begin, although they are used even after this time (Reynolds et al., 2014; Allerson et al., 2013; Uscher et al., 2011). Development of resistance against antivirals can be rapid or may emerge during treatment (Reynolds et al., 2014; Allerson et al., 2013; Isaacs, 2010; Orozovic et al., 2011). A recent study reported that the N2 neuraminidase containing, 9% of swine influenza viruses are resistant to neuraminidase inhibitor (Orozovic et al., 2011). Zanamivir and Oseltamivir are active against both influenza type A and type B. These antivirals are an additive supplement to the vaccine and not a replacement to the vaccine. Vaccination is the principal means for preventing morbidity and mortality related to influenza (Bucher et al., 2009).

TABLE 5. Dose for the treatment of swine flu (H1N1).

By Weight	For Infants
•For weight <15kg 30 mg BD for 5 days	• < 3 months 12 mg BD for 5 days
•15-23kg 45 mg BD for 5 days	• 3-5 months 20 mg BD for 5 days
• 24-<40kg 60 mg BD for 5 days	• 6-11 months 25 mg BD for 5 days
•>40kg 75 mg BD for 5 days	• It is also available as syrup (12mg per ml)

The S-OIV is resistant to amantadine and rimantadine (CDC, 2009). FDA has approved oseltamivir and zanamivir for treatment and prevention of S-OIV. Oseltamivir is administered to children aged ≥1 year and adults whereas zanamivir is given to those adults and children aged ≥7 years who have been symptomatic for <2 days. Oseltamivir can also be used to treat children aged <1 year and to prevent S-OIV in children aged 3 months-1 year (CDC, 2009). Mass dispense of this antiviral medication is only done in case of endemic or pandemic conditions. Unnecessary use of oseltamivir and zanamivir may induce resistance against the same in S-OIV. Use of respirators has been authorized by FDA, which help reduce exposure to pathogenic air borne particles during public health emergency including S-OIV. Respirators should be used by persons who cannot avoid close contact with an infectious person, this includes individuals who take care of the sick person (e.g., family member at home or nursing staff at hospital) (CDC, 2009).

Side effects of Oseltamivir: Generally Oseltamivir is well endured but increase in doses (above 300 mg/day) may causes gastrointestinal side effects such as nausea, vomiting, and sometimes bronchitis, insomnia and vertigo.

Supportive Theory: In humans' uncomplicated influenza, supportive care includes rest and fluid intake. Supportive treatment varies with the severity of the case and includes antibacterial to treat or prevent secondary bacterial pneumonia, ventilatory support, and vasopressors for shock (Kumar et al., 2009). Medication prescribed for fever, myalgia and headache are paracetamol or ibuprofen. It is advisory for the patient to intake plenty of fluids. Smoking must be avoiding by smokers. Oxygen therapy is provided to patients with complaint of respiratory distress, dyspnea, tachypnea, and oxygen saturation less than 90%.

Chemoprophylaxis: Chemoprophylaxis for health care's workers at high risk. The treating physicians and other paramedical personnel at the isolation facility would be put on chemoprophylaxis. Chemoprophylaxis for contacts, chemoprophylaxis is advised for those contacts with high risk (with underlying systemic diseases; extremes of age [< 5 years and 65> years] **.** In phase-5, if the clusters are reported for the first time, and given that those exposed are known and can be traced easily, then family, social and community contacts should be given chemoprophylaxis. Mass Chemo-prophylaxis, the strategy of containment by geographic approach by giving oseltamivir to every individual in a prescribed geographic limit of 5 km from the epicentre would be applied, If the virus is lethal and causing severe morbidity and high mortality. Though affecting humans, is not efficiently transmitting in our population. Condition the cluster is limited by natural geographic boundaries. All close contacts of suspected, probable and confirmed cases. Close contacts include household/social contacts, family members, workplace or school contacts, fellow travellers, etc. All health care personnel meeting suspected probable or confirmed case. Oseltamivir is the drug of choice. Prophylaxis should be provideduntil 10 daysafter last exposure (maximum period of 6 weeks) (CDC, 2009, Update).

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper

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