DISSERTATION ON

CASE SERIES STUDY ON CLINICAL PROFILE OF H1N1 SWINE INFLUENZA

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CERTIFICATE

This is to certify that the dissertation entitled **"CASE SERIES STUDY ON CLINICAL PROFILE OF H1N1 SWINE INFLUENZA"** is a bonafide work done by **DR.A.PUVANALINGAM, M.B.B.S.,** Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai-3, in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I Internal Medicine, under our guidance and supervision, during the academic year 2009 - 2012.

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I solemnly declare that this dissertation entitled **"CASE SERIES STUDY ON CLINICAL PROFILE OF H1N1 SWINE INFLUENZA"** was done by me at Madras Medical College and Government General Hospital during 2009-2012 under the guidance and supervision of **Prof. K. SIVASUBRAMANIAN,M.D.** This dissertation is submitted to **"THE TAMILNADU DR.MGR MEDICAL UNIVERSITY"** towards the partial fulfillment of requirement for the award of M.D Degree, in General Medicine Branch-I.

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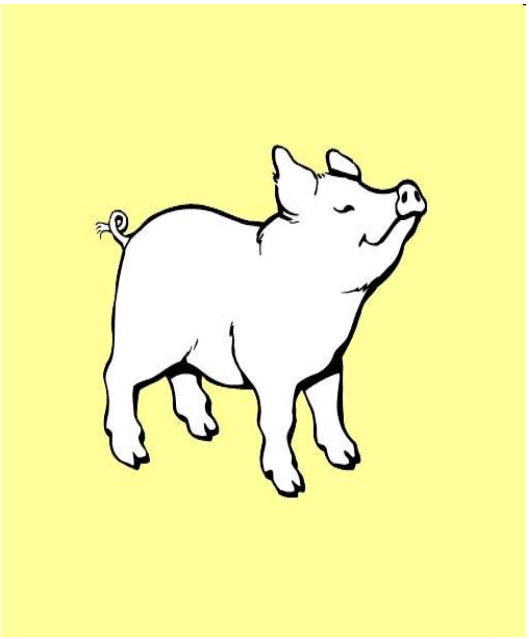
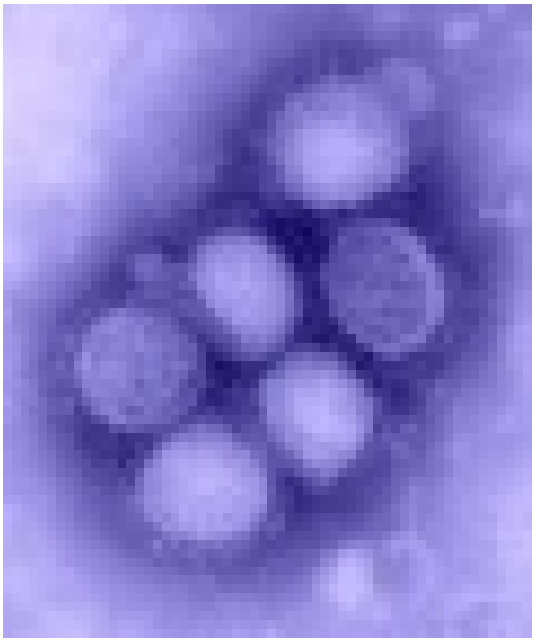
CASE SERIES STUDY ON CLINICAL PROFILE

OF H1N1 SWINE INFLUENZA





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ABBREVIATIONS

1)	ANOVA	:	One-way Analysis of Variance
2)	ATT	:	Anti tuberculous therapy
3)	CDC	:	Centre For Disease Control And Prevention
4)	COPD	:	Chronic obstructive pulmonary disease
5)	CT	:	Computed tomography.
6)	CXR	:	Chest X ray.
7)	DCM	:	Dilated cardiomyopathy
8)	ECG	:	Electrocardiogram
9)	H	:	Haemagglutinin
10)	HDL	:	High density lipoprotein
11)	N	:	Neuramidinase
12)	PCR	:	Polymerase chain reaction
13)	RHD	:	Rheumatic heart disease
14)	RT	:	Room temperature
15)	RT-PCR	:	Real-time reverse transcriptase –PCR
16)	WHO	:	World Health Organisation

INTRODUCTION

In late March and early April 2009, an outbreak of H1N1 influenza A virus infection was detected in Mexico, with subsequent cases observed in many other countries (1) (2).The pandemic that began in March 2009 was caused by an H1N1 influenza A virus that represents a quadruple reassortment of two swine strains, one human strain, and one avian strain of influenza. On June 11, 2009, the World Health Organisation (WHO) signaled that a global pandemic of novel influenza A (H1N1) was underway by raising the worldwide pandemic alert level to Phase 6. This was the first of the kind declared by WHO in the past 70 years. This action was a reflection of the spread of the new H1N1 virus. At the same time, more than 70 countries have reported cases of novel influenza A (H1N1) infection and there were ongoing community level outbreaks of novel H1N1 in different parts of the world (3). The pandemic started in India in the month of August 2009 and the index cases were reported from Pune and soon the epidemic spread itself to other parts of the country. With the fresh cases, as on 10th March 2010 the total number of H1N1 positive cases confirmed by both government and private laboratories in India had risen to

29,880 and the total number of swine flu deaths had risen to 1401. This epidemic was notoriously seen to affect the younger population in the age group of 15-40 years thereby affecting the workhouse of the country. Present analysis is our experience from a tertiary care referral institute admitting H1N1 positive cases. This is a prospective study of reported cases admitted from August 2009 to January 2010.

WHO ALERT LEVEL'S FOR INFLUENZA PANDEMICS

Inter-pandemic phase	Low risk of human cases	1
New virus in animals, no human cases	Higher risk of human cases	2
Pandemic alert	No or very limited human-to-human transmission	3
New virus causes human cases	Evidence of increased human-to-human transmission	4
	Evidence of significant human-to-human transmission	5
Pandemic	Efficient and sustained human-to-human transmission	6

AIMS AND OBJECTIVES

1) To study the clinical profile of the H1N1 influenza cases attending Madras Medical College & Government General Hospital, Chennai and Institute of child health, Egmore , Chennai .

2) To study the impact of H1N1 infection on pregnancy outcome.

3) To evaluate the mortality rates among hospitalized patients with H1N1 influenza.

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

Illness with influenza in pigs was first recognized during the influenza pandemic of 1918 to 1919, and a swine influenza virus was first isolated from a human in 1974 (4) (5) (6). In 1976, swine influenza virus caused a respiratory illness with one fatality among 13 soldiers in Fort Dix, New Jersey (7) . No exposure to pigs was found. A subsequent epidemiologic study showed that up to 230 soldiers had been infected with the virus (4), (8).

Between 1958 and 2005, 37 cases of swine influenza among civilians were reported (4). Six cases (17 percent) resulted in death. Forty-four percent of infected individuals had known exposure to pigs. Cases were reported in the United States, former Czechoslovakia, the Netherlands, Russia, Switzerland, and Hong Kong.

CASE DEFINITIONS

The following case definitions have been provided by the United States Centers for Disease Control and Prevention (4):

1) Influenza-like illness (ILI) is defined as fever (temperature of 100ºF [37.8ºC] or greater) with cough or sore throat in the absence of a known cause other than influenza.

2) A confirmed case of pandemic H1N1 influenza A is defined as an individual with an ILI with laboratory-confirmed H1N1 influenza A virus detected by real-time reverse transcriptase (rRT)-PCR or culture.

3) Pandemic H1N1 influenza A may be suspected in an individual who does not meet the definition of confirmed pandemic H1N1 influenza A, but has an ILI and an epidemiologic link.

VIROLOGY

Influenza subtypes:

Clinical influenza can be caused by several different influenza subtypes, although H1N1 is the most common subtype implicated in both swine and human infections (9). Human cases of swine H3N2 influenza A virus infection has been reported rarely(4). Other subtypes that have circulated in pigs include H1N2, H3N1, and H3N2.

Genetic and antigenic characterization

- The pandemic that began in March 2009 was caused by an H1N1 influenza A virus that had not been recognized previously in pigs or humans, although six of its eight gene segments were similar to ones previously detected in triple reassortant swine influenza viruses in pigs in North America (10). This strain represents a quadruple reassortment of two swine strains, one human strain, and one avian strain of influenza (11) (12) (13). The largest proportion of genes comes from swine influenza viruses (30.6 percent from North American swine influenza strains, 17.5 percent from Eurasian swine influenza strains), followed by North American avian influenza strains (34.4 percent) and human influenza strains (17.5 percent) (14).

- Analysis of the antigenic and genetic characteristics of the pandemic H1N1 influenza A virus demonstrated that its gene segments have been circulating for many years, suggesting that lack of surveillance in swine is the reason that this strain had not been recognized previously (15). One of the swine influenza viruses that contributed gene

segments to the strain causing the 2009 pandemic is thought to have derived from the strain that caused the 1918 influenza pandemic (16).

- Among the 2009 pandemic H1N1 influenza A viruses sequenced, each gene segment had high sequence identity (99.9 percent), suggesting that introduction into humans was either a single event or multiple events of genetically similar viruses (11). Furthermore, the H1N1 influenza A viruses causing the 2009 pandemic were found to be antigenically homogeneous. . Phylogenetic analysis has suggested that initial transmission to humans occurred several months before the outbreak was recognized (15).

- Sequence analysis of isolates from the United States and Mexico did not identify molecular features known to confer increased transmissibility or virulence (11).

ANTIGENIC DRIFT AND SHIFT

S.NO	ANTIGENIC DRIFT	ANTIGENIC SHIFT
1.	Gradual change over a period	Sudden complete change
2.	Involves point mutations	Genetic recombination of human with animal/avian virus
3.	Responsible for frequent epidemics,	Leads to novel subtype different from both parent viruses

INFLUENZA VIRUS – 3 TYPES

Type A	Type B	Type C
Causes significant disease: epidemics, pandemics	Causes significant disease: milder epidemics	Does not cause significant disease
Infects both humans and other species	Limited to humans	Limited to humans
Frequent antigenic variations	Infrequent antigenic variations	Antigenically stable

TRANSMISSION

PERSON-TO-PERSON TRANSMISSION

- Influenza virus is present in respiratory secretions of infected persons. As a result, influenza virus can be transmitted through sneezing and coughing via large-particle droplets (17,18). Transmission via contact with surfaces that have been contaminated with respiratory droplets or by aerosolized small-particle droplets may also occur, although these modes of transmission have not been proven . In addition to respiratory secretions, certain other bodily fluids (eg, diarrheal stool) should also be considered potentially infectious.
- In contrast to previous outbreaks of swine influenza viruses described above, the pandemic of H1N1 influenza A infection that began in March 2009 appears to involve sustained human-to-human transmission, as suggested by the large numbers of patients with respiratory illnesses identified within a short period of time at various locations around the world (19). Several of the isolates causing disease in the United States have been found to be nearly genetically identical to isolates in Mexico, supportive of person-to-person transmission (20).

- Based on analysis by the World Health Organization using early data from the outbreak in Mexico and other countries, transmissibility appears substantially higher compared with seasonal influenza (21). In one study, the secondary attack rate of the strain causing this pandemic was estimated to be 22 to 33 percent, compared with 5 to 15 percent for seasonal influenza (22). In another study, the secondary attack rate in households was estimated to be 27 percent, and an infected school child was estimated to infect 2.4 other children within the school (23). In contrast to the two studies cited above (22, 23), the United States Centers for Disease Control and Prevention has reported that the attack rate observed in the US is similar to that in seasonal influenza (24).
- Infection control and social distancing measures are important in the prevention of swine transmission .

INCUBATION PERIOD

Although the precise incubation period has not been established for pandemic H1N1 influenza A infection, it could range from one to seven days, and most likely from one to four days (18).

SHEDDING

Since the duration of shedding of pandemic H1N1 influenza A virus is currently unclear, the estimated duration of shedding is based upon what is known for seasonal influenza virus (25). Immunocompetent patients with pandemic H1N1 influenza A virus infection are likely to be contagious from one day prior to the development of signs and symptoms until resolution of fever (25). Longer periods of shedding may occur in children (especially young infants), elderly adults, patients with chronic illnesses, and immunocompromised hosts.

ROLE OF PIGS

- Pigs play an important role in interspecies transmission of influenza virus. Susceptible pig cells possess receptors for both avian (alpha 2-3-linked sialic acids) and human influenza strains (alpha 2-6-linked sialic acids), which allow for the reassortment of influenza virus genes from different species if a pig cell is infected with more than one strain (26-28).
- Since the late 1990s, triple reassortment swine influenza A viruses containing genes from swine, human, and avian strains of influenza have been detected among swine herds in North America (29-31). Eleven sporadic cases of triple

reassortment swine influenza A viruses were detected in the United States between December 2005 and February 2009(29). Nine patients had exposure to pigs.

- It is not clear yet how this virus arose or was initially transmitted to humans. On May 2, 2009, the Canadian government reported the identification of pandemic H1N1 influenza A from a swine herd in Alberta, Canada . It is suspected that the pigs became infected following exposure to a farm worker who had recently visited Mexico and had developed an influenza-like illness.

- There is no risk of becoming infected with influenza virus from eating pork.

CLINICAL MANIFESTATIONS

The signs and symptoms of influenza caused by pandemic H1N1 influenza A virus are similar to those of seasonal influenza, although gastrointestinal manifestations appear to be more common with pandemic H1N1 influenza A(18,19 ,22). The severity appears to be less than what was observed during the influenza pandemic of 1918 to 1919 (21).

Signs and symptoms:

The most common clinical findings of the 2009 H1N1 influenza A pandemic have been fever, cough, sore throat, malaise, and headache; vomiting and diarrhea have also been common, both of which are unusual features of seasonal influenza (32). Other frequent findings have included chills, myalgias, and arthralgias(18).In New York City, 95 percent of patients with pandemic H1N1 influenza A have met the case definition for influenza-like illness (subjective fever plus cough and/or sore throat) (18). In contrast, approximately one third of patients seen at two hospitals in Mexico had no fever at presentation (33). Certain groups, such as infants, elderly individuals, and immuno-compromised hosts, may have atypical presentations. Among 268 patients in the United States requiring hospitalization for pandemic H1N1 influenza A infection, clinical findings included fever (93 percent), cough (83 percent), shortness of breath (54 percent), fatigue or weakness (40 percent), chills (37 percent), myalgias (36 percent), rhinorrhea (36 percent), sore throat (31 percent), headache (31 percent), vomiting (29 percent), wheezing (24 percent), and diarrhea (24 percent) .

Children:

Young children are less likely to have the usual influenza signs and symptoms, such as fever and cough (34). Infants may present with fever and lethargy, and may not have cough or other respiratory symptoms. Symptoms of severe disease in infants and young children may include apnea, tachypnea, dyspnea, cyanosis, dehydration, altered mental status, and extreme irritability.Young children (eg, <5 years of age) are at increased risk for influenza complications (34, 35).

High Risk Adults:

Among 553 patients with confirmed or probable pandemic H1N1 influenza A in California, the most common risk factors for influenza complications were chronic lung disease (asthma or chronic obstructive pulmonary disease, 37 percent), immunosuppressive conditions (17 percent), cardiac disease (17 percent), pregnancy (17 percent), diabetes mellitus (13 percent), and obesity (13 percent) (36).

Although elderly patients are considered to be at an increased risk for complications of influenza, pandemic H1N1 influenza A infections in such individuals have been uncommon to date possibly as a result of preexisting immunity against antigenically similar

influenza viruses that circulated prior to 1957(24) . In one study, 39 of 115 (34 percent) of individuals born before 1950 had preexisting microneutralization titers ≥80 against pandemic H1N1 influenza, whereas only 4 of 107 (4 percent) of individuals born after 1980 had titers ≥40 (27). Microneutralization titers ≥80 to 160 in adults and ≥40 in children often correlate with at least a 50 percent decrease in risk for influenza infection or disease, but whether these titers offer partial protection against pandemic H1N1 influenza A virus infection or disease is unclear (28).

DIAGNOSIS

Guidelines for the diagnosis of pandemic H1N1 influenza A virus have been released by the United States Centers for Disease Control and Prevention (CDC) (35).

Whom to test ?

Most patients with an uncomplicated influenza-like illness who reside in areas where influenza viruses are known to be circulating do not need to be tested for influenza infection. Recommendations regarding whom to test may differ by state or community.

Patients in whom influenza testing should be considered

- Hospitalized patients with suspected influenza infection

- Patients for whom a diagnosis of influenza will affect decisions regarding clinical care, infection control, or management of close contacts.
- Individuals who died of acute illness in whom influenza was suspected.

Specimens:

To establish the diagnosis of pandemic H1N1 influenza A, an upper or lower respiratory sample should be collected . Appropriate specimens include:

- Nasopharyngeal swab
- Nasal aspirate, wash, or swab
- Endotracheal aspirate (in intubated patients)
- Bronchoalveolar lavage (BAL) fluid
- Combined nasopharyngeal or nasal swab with oropharyngeal swab

In patients with severe pneumonia who are suspected of being infected with influenza and who are intubated or undergoing bronchoscopy, lower respiratory samples (endotracheal aspirate or BAL fluid) should be obtained and tested for influenza infection.

For proper specimen collection, instructions in the test's package insert should be followed. Furthermore, specimens should be obtained as soon as possible following the onset of symptoms.

Swabs with a synthetic tip (eg, polyester or Dacron) and an aluminum or plastic shaft should be used. Swabs with cotton tips and wooden shafts are not recommended. Swabs made of calcium alginate are not acceptable. The collection vial in which the swab is placed should contain 1 to 3 mL of viral transport media.

Specimens should be placed in viral transport media and placed on ice (4ºC) or refrigerated immediately for transportation to the laboratory. Once the samples arrive in the laboratory, they should be stored either in a refrigerator at 4ºC or in a -70ºC freezer. If a -70ºC freezer is not available, they should be kept refrigerated. Refrigerated samples should ideally be processed within 24 hours, and should not be stored for >72 hours.

Diagnostic tests:

- Real-time reverse transcriptase (RT)-PCR is the most sensitive and specific test for the diagnosis of pandemic H1N1 influenza A virus infection (35).

- Isolation of pandemic H1N1 influenza A virus using culture is also diagnostic, but culture is usually too slow to help

guide clinical management. A negative viral culture does not exclude pandemic H1N1 influenza A infection.

- Several rapid antigen and immunofluorescent antibody tests are available for the diagnosis of influenza virus infection. However, the sensitivity of these tests varies widely, and although some assays are able to distinguish between influenza A and B viruses, they are not able to distinguish between pandemic and seasonal strains of H1N1 influenza A.

Polymerase chain reaction:

- Nucleic acid amplification tests, such as real-time reverse transcriptase (rRT)-PCR, are the most sensitive and specific tests for the diagnosis of influenza virus infection (35).

- However, they may not be readily available and/or may require several days for processing since many hospitals and clinics must send samples to be processed at public health or commercial laboratories. Test performance depends on the individual rRT-PCR assay used.

- The United States Food and Drug Administration has authorized several rRT-PCR assays for the diagnosis of

pandemic H1N1 influenza A infection under an Emergency Use Authorization (36).

Rapid antigen tests:

- Clinicians may consider using rapid influenza antigen tests as part of their evaluation of patients suspected of having pandemic H1N1 influenza A, but results should be interpreted with caution (38), (39).
- Certain rapid influenza antigen tests that are commercially available can distinguish between influenza A and B viruses, but cannot distinguish among different subtypes of influenza A (eg, pandemic H1N1 influenza A versus seasonal H1N1 or H3N2 influenza A).
- Confirmation of pandemic H1N1 influenza A infection can only be made by real-time reverse-transcriptase (rRT)-PCR or culture.
- The sensitivity of rapid antigen testing for pandemic H1N1 influenza A virus infection has ranged from 10 to 70 percent compared with rRT-PCR (37-42). Thus, a negative result does not rule out infection.

- The specificity of rapid antigen testing has generally been >95 percent (35), although in one study it was only 86 percent (41).

- Among 39 patients with pandemic H1N1 influenza A confirmed by rRT-PCR, 20 had a positive rapid antigen test using the QuickVue Influenza A+B (Quidel) assay (sensitivity 51 percent)(38).

- Twelve of 19 patients who had seasonal H1N1 influenza confirmed by rRT-PCR had a positive rapid antigen test (sensitivity 63 percent).

- In the same study, the specificity of rapid antigen testing was 99 percent for patients with either the pandemic strain or a seasonal strain of H1N1 influenza A.

Immunofluorescent antibody testing:

- Direct or indirect immunofluorescent antibody testing (DFA or IFA) can distinguish between influenza A and B, but does not distinguish among different influenza A subtypes (35).

- In one study, among 42 samples that were positive for pandemic H1N1 influenza A by real-time reverse-

transcriptase polymerase chain reaction, 39 were positive by direct fluorescent antibody testing (43).

- However, a negative DFA or IFA does not exclude pandemic H1N1 influenza A infection since larger studies are required to define the sensitivity to detect this virus.

Choice of test:

- Most patients with an uncomplicated influenza-like illness who reside in areas where influenza viruses are known to be circulating do not need to be tested for influenza infection .

- However, among patients for whom a diagnosis of influenza will affect decisions regarding clinical care, infection control, or management of close contacts, it is reasonable to use a rapid antigen or immunofluorescence antibody test.

- In regions where the majority of circulating influenza viruses are known to be pandemic H1N1 influenza A, a positive result using one of these assays can be presumed to indicate infection with pandemic H1N1 influenza A.

- If identification of pandemic H1N1 influenza A is required, such as in pregnant patients and those with severe immunosuppression, then real-time reverse transcriptase

polymerase chain reaction (rRT-PCR) testing should be performed.

- In addition, rRT-PCR testing should be performed in hospitalized patients with suspected influenza infection who have a negative rapid antigen or immunofluorescence antibody test.
- Influenza subtype testing with rRT-PCR or viral culture should also be prioritized for use in individuals who have died from suspected or confirmed influenza infection.

COMPLICATIONS OF H1N1 VIRUS INFECTION:

- Pneumonia
- Acute respiratory distress syndrome (ARDS)
- Multi-organ failure
- Cardiac and renal dysfunction
- Gastrointestinal involvement
- Sepsis-like syndrome, shock
- Reye's syndrome

TREATMENT

High risk groups

High risk groups for the development of complications of pandemic H1N1 influenza A are thought to be similar to those defined for seasonal influenza. They are (43)- (49):

- Children younger than 5 years of age, but especially those younger than 2. (48)
- Individuals of 65 years of age or older:- Although individuals ≥65 years of age who become infected with H1N1 influenza virus are thought to be at increased risk for complications,

this age group appears to be at lower risk of becoming infected with pandemic H1N1 influenza virus compared with younger persons, presumably because of immunity (antibodies) related to previous exposure to related virus strains. Thus, the US Centers for Disease Control and Prevention recommends that members of this age group who do not have other high-risk conditions have a low priority for vaccination with the pandemic H1N1 influenza virus vaccine.

- Pregnant women
- Individuals younger than 19 years of age who are receiving long-term aspirin therapy and who therefore might be at risk for Reye syndrome after influenza virus infection.
- Individuals of any age with chronic medical conditions requiring ongoing medical care. They include
  - Cardiovascular disease, except isolated hypertension
  - Active malignancy
  - Chronic renal insufficiency
  - Chronic liver disease

- Diabetes mellitus
- Hemoglobinopathies such as sickle cell disease
- Immunosuppressive states.
- Individuals who have any condition that can compromise handling of respiratory secretions (eg, cognitive dysfunction, spinal cord injuries, seizure disorders, neuromuscular disorders, cerebral palsy, metabolic conditions)
- Children with an underlying metabolic disorder, such as medium-chain acyl-CoA dehydrogenase deficiency, who are unable to tolerate prolonged fasting

Obesity and H1N1 influenza:

- Obesity has not been recognized as a risk factor for severe seasonal influenza.
- But cases of severe pandemic H1N1 influenza A, including pneumonia and acute respiratory distress syndrome, have been reported in obese individuals without known underlying conditions (50) (51).

Antiviral therapy:

- Therapy should be started as soon as possible, since evidence of benefit is strongest for seasonal influenza when treatment is started within 48 hours of illness onset (47), (48) .
- Furthermore, in a study of 272 patients requiring hospitalization for pandemic H1N1 influenza A in the United States between April and mid-June 2009, the receipt of antiviral drugs within two days after the onset of illness was significantly associated with a positive outcome in a multivariable model (53).
- Some studies of hospitalized patients have demonstrated benefit even when therapy for seasonal influenza is started >48 hours after onset of illness.
- In patients who are more than mildly ill, initiate therapy even past 48 hours of symptoms (48).

Resistance Patterns:

- The vast majority of strains of pandemic H1N1 influenza A virus circulating in 2009 appear sensitive in vitro to the neuraminidase inhibitors, oseltamivir and zanamivir, but all strains tested have been resistant to amantadine and rimantadine (54)- (56).

- However, there are no reported studies yet on the clinical benefits of antiviral therapy.
- As of September 2009, 99 percent of influenza isolates circulating in the United States were pandemic H1N1 influenza A, the vast majority of which are sensitive to oseltamivir (48).
- A notable difference between pandemic and seasonal strains of H1N1 influenza A is the resistance pattern to oseltamivir.
- The low rate of oseltamivir resistance among pandemic H1N1 influenza A strains to date contrasts with the extremely high rate among seasonal H1N1 influenza A strains.
- A small minority of isolates of pandemic H1N1 influenza virus with resistance to oseltamivir have been detected from patients in Japan, the United States, China, Hong Kong, Singapore, Denmark, and Canada (61).
- Several patients had been taking oseltamivir prophylaxis before becoming ill.
- No tested isolates have been resistant to zanamivir, and most of the patients whose clinical courses have been reported

recovered without complications (56),(58). One severely immunocompromised patient remained hospitalized at the time her case was reported (59).

Indications for antiviral therapy:

- All hospitalized individuals with confirmed or suspected influenza virus infection (either pandemic or seasonal strains).
- Individuals with confirmed or suspected influenza virus infection who are severely ill, such as those with lower respiratory tract infection (eg. dyspnea, tachypnea, unexplained oxygen desaturation), and those who are showing signs of rapid clinical deterioration.
- Individuals with obesity (particularly those with morbid obesity) may be at increased risk of hospitalization and death due to pandemic H1N1 influenza infection; many obese persons have underlying conditions that increase the risk of influenza complications, such as diabetes mellitus, asthma, chronic respiratory illness, or liver disease. Thus, patients with morbid obesity (BMI >40) and possibly those with obesity (BMI 30 to 39) with suspected or confirmed influenza virus infection should be carefully evaluated for the presence

of conditions that confer an increased risk of influenza complications. If any such conditions are present, treatment should be given.

Antiviral therapy should be considered for:

- Outpatients with confirmed or suspected influenza virus infection who are at increased risk for complications.

- During the current pandemic, patients with mild illness do not need to be tested or treated unless they have risk factors for complications (48). Patients who are recovering from influenza generally do not require antiviral therapy. The decision of whether to initiate antiviral therapy for each patient should be based upon the clinician's judgment and on what is known about the benefits of therapy for seasonal influenza.

Timing of antiviral initiation:

- Treatment should be initiated as soon as possible since antiviral therapy is most likely to provide benefit when initiated within the first 48 hours of illness.

- Treatment should not be delayed while awaiting the results of diagnostic testing.

- Furthermore, patients who have a negative rapid antigen test for influenza but in whom the clinical suspicion for influenza infection is high should be treated with antivirals since the sensitivity of these tests is generally low.

Steps to reduce delays in treatment initiation:

- Informing patients at increased risk for complications of the signs and symptoms of infection and the importance of early initiation of therapy

- Ensuring rapid access to telephone consultation and clinical evaluation for patients at high risk for complications and those with severe influenza

- Considering empirical treatment of patients at high risk for complications based on telephone contact

- Considering certain patients at high risk for complications (eg, patients with neuromuscular disease) with prescriptions that could be filled following telephone consultation with a healthcare provider.

Choice of antiviral:

- For patients requiring treatment, zanamivir or oseltamivir is recomended (48). Zanamivir is contraindicated in patients with asthma or chronic obstructive pulmonary disease.

- During this pandemic, in patients suspected to have influenza, neuraminidase inhibitor (zanamivir or oseltamivir) is recommended (48).

- However, if surveillance data indicate that oseltamivir-resistant seasonal H1N1 influenza A virus is circulating zanamavir should be given instead of oseltamavir.

- In such a setting, for patients who are unable to take zanamivir, the addition of rimantadine (or, less preferably, amantadine) to oseltamivir (48) should be done .

- Of note, prior to the emergence of pandemic H1N1 influenza A, the majority of seasonal H1N1 influenza A isolates in the United States were resistant to oseltamivir.

Dosing:

- The dosing of antivirals for the treatment of pandemic H1N1 Influenza A infection in adults is the same as for seasonal Influenza. Zanamivir inhalation powder should not be reconstituted in any liquid formulation and is not recommended for use in nebulizers or mechanical ventilators (62).
- Antiviral therapy should be continued for five days, as with seasonal influenza.

- The US Centers for Disease Control and Prevention note that some experts have advocated increased (doubled) doses of oseltamivir and that hospitalized patients with severe infections might require longer treatment courses, although the possible benefit of these approaches has not been adequately studied.

Other Drugs Under Evaluation:

- Peramivir and other cyclopentane derivatives: A single injection in mice strongly suppreses influenza virus.
- Dimeric Neuraminidase Inhibitors: It is 100 times more potent than Zanamivir. It also opens possibility of once a week dose.
- Ribavarin and Interferon alpha.
- Sialidase fusion proteins & siRNAs.

VACCINATION

General consideration for vaccination:

- H1N1 influenza vaccine elicit less immune response than seasonal vaccine.
- Whole virus vaccine appear to be more immunogenic than split or subunit vaccine.

- Adjuvant may reduce the amount of antigen required.
- Vaccine produced from one clad may confer cross reactivity with other clads but this is likely to decrease with further evolution of virus.

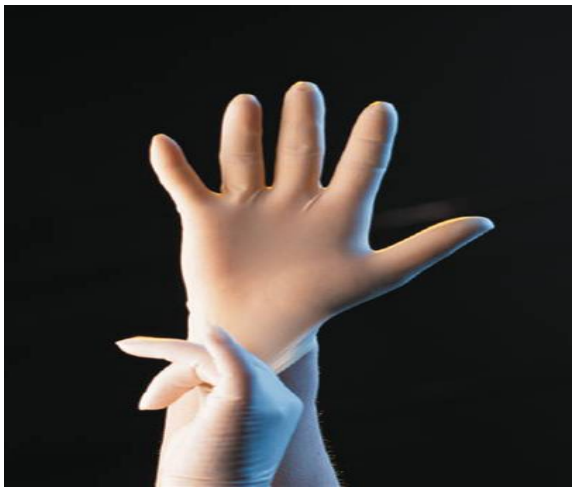
Problems with vaccines:

- Production facilities are limited.
- Mutations keep on occurring in Influenza - A viruses so we cannot be sure of viral strain for which vaccine is to be produced.
- It is very difficult to produce vaccine against H1N1.
- Vaccine is unlikely to be available during initial 4 to 6 weeks of a new pandemic.

PERSONAL PROTECTIVE EQUIPMENT

- Gloves
- Gowns
- Masks
- Boots
- Eye protection

GLOVES



Different kinds of gloves:

- ❖ Housekeeper gloves
- ❖ Clean gloves
- ❖ Sterile glove

Precautions while using gloves:

- ❖ Work from clean to dirty.
- ❖ Avoid touch contamination with eyes, mouth, nose and body surfaces.
- ❖ Change gloves between patients.

GOWNS

ADVANTAGES

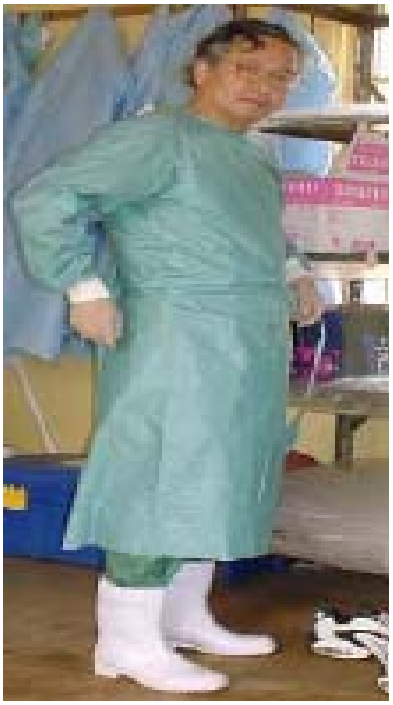
- Fully covers torso.
- Has long sleeves.
- Fits snuggly at the wrist.

MASKS AND RESPIRATORS

Particulate respirators (N95)

- Fit testing is essential
- Very effective in preventing H1N1 infection.

BOOTS



EYE PROTECTION

Advantages:

- ❖ Shields face
- ❖ Goggles protects eyes

PRECAUTION

Precaution Levels:

- Standard Precautions
- Contact Precautions
- Droplet Precautions
- Airborne Precautions

Standard Precautions:

- Prevent the transmission of common infectious agents
- Hand washing is important
- Assume infectious agent could be present in the patient's
  - Blood
  - Body fluids, secretions, excretions
  - Non-intact skin
  - Mucous membranes

Hand Washing:

- Wet hands with clean (not hot) water
- Apply soap
- Rub hands together for at least 20 seconds
- Rinse with clean water
- Dry with disposable towel or air dry
- Use towel to turn off faucet.

Contact Precautions:

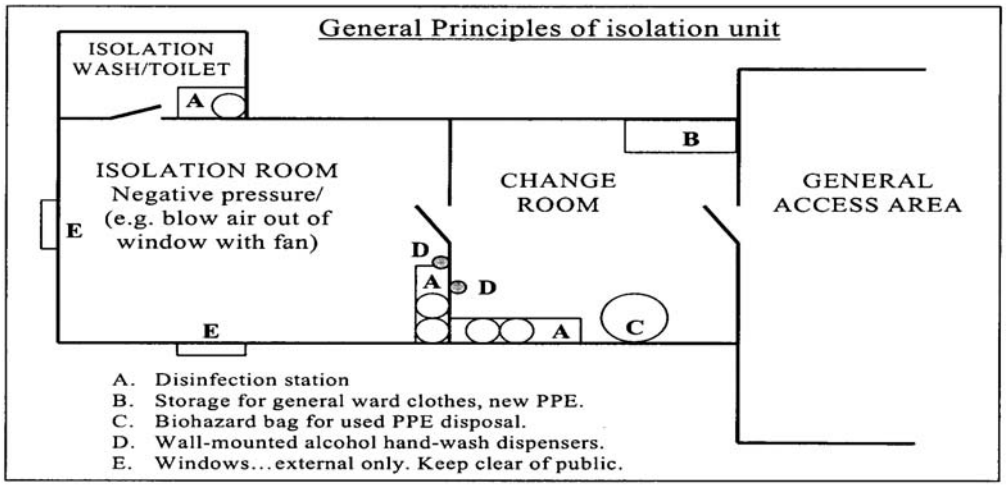
(Prevent infection through direct or indirect contact with patients or patient care environment)

- ❖ Limit patient movement
- ❖ Isolate or cohort patients
- ❖ Gown + gloves for patient / room contact
  - o Remove immediately after contact
  - o Do not touch eyes, nose, mouth with hands
  - o Avoid contaminating environmental surfaces

Droplet Precautions:

- ❖ Wear surgical mask within 1 meter of patient
- ❖ Wear face shield or goggles within 1 meter of patient
- ❖ Place patients in single rooms or cohort 1 meter apart
- ❖ Limit patient movement within facility
- ❖ Patient wears mask when outside of room

NEGATIVE PRESSURE ISOLATION ROOM



CONTAINMENT AND INFECTION CONTROL

- Timely recognition and high index of suspicion with continuous monitoring and surveillance
- Quarantine of the exposed persons
- Implementation of standard infection control precautions.
- Droplet precautions: Larger particle droplets (>5µm in size) - generated during coughing, sneezing, talking or the performance of procedures.
- Contact precautions
- For aerosol generating procedures – Airborne precautions

VIRUS INACTIVATION AND DISINFECTION

- Surfaces contaminated with secretions or fluids should be cleaned daily
- Damp dusting should be done rather than dry dusting
- Disinfectants that can be used:
  - Phenolic disinfectants
  - Quaternary ammonia compounds
  - Peroxygen compounds
  - Sodium hypochlorite (household bleach)
  - Alcohol (Ethyl alcohol)

Note:

- Do not spray (i.e. fog) with disinfectant
- Virus is killed by heat (56*c for 3 hrs or 70*c for 30 minutes)

OCCUPATIONAL HEALTH

- Prompt recognition of healthcare workers with influenza like illness and those who are symptomatic should be evaluated and excluded from duty
- Develop a system to monitor work absenteeism for health reason
- Those staff caring for influenza patients should not be posted elsewhere
- Availability of antiviral agents for treatment of exposure.

EDUCATION AND TRAINING

- Infection control procedures should be discussed.
- Modes of transmission of the pathogen should be explained.
- Attention to respiratory hygiene should be reinforced by displays of posters.
- Importance of reporting symptoms to authorities should be explained

MATERIALS AND METHODS

SETTING

Patients admitted with diagnosis of H1N1 influenza pneumonia in the Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai and Institute of child health, Chennai were evaluated in the study.

COLLABORATING DEPARTMENTS:

Institute of Internal Medicine , Madras Medical College

Institute of Child Health, Madras Medical College

Institute of Microbiology, Madras Medical College

ETHICAL COMMITTEE APPROVAL

Institute Ethical Committee approved the study.

STUDY DESIGN : Case series Study

DURATION OF THE STUDY : 6 Months

SELECTION OF PATIENTS : Sample Size - 442 Patients

INCLUSION CRITERIA:

1) Patients with suspected symptoms of influenza like illness admitted in Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai and Institute of child health.

2) Proven cases of H1N1 influenza admitted in Rajiv Gandhi Government General Hospital, Chennai and Institute of child health.

EXCLUSION CRITERIA

1) Patients who are negative for H1N1 influenza.

2) Patients who are not willing for the study

CONSENT

Informed Consent obtained from all the patients.

CONFIRMATION OF INFLUENZA

It was done by RT-PCR in King Institute, Guindy, Chennai.

STUDY PATTERN

Prospective study.

DATA ANALYSIS

Data analysis was done using SPSS and Epi-info software.

METHODOLOGY

A hospital based case series study was conducted in government general hospital, Chennai and in Institute of child health, Egmore, Chennai, India prospectively from August 09 upto January 2010. The study had ethical clearance from the Institutional ethical committee. All suspected cases were confirmed by RT-PCR performed at the King institute laboratory, Guindy, Chennai. A total number of 442 H1N1 positive patients (198 inpatients and 244 outpatients) from two government hospitals in Chennai ,Madras Medical College & Government General Hospital and Institute Of Child Health, Egmore were studied prospectively during a period of 6 months from August 2009 to January 2010.A confirmed case of pandemic H1N1 influenza A is defined as an individual with an ILI with laboratory-confirmed H1N1 influenza A virus detected by real-time reverse transcriptase (RT)-PCR or culture. During this period the clinical profile of H1N1 cases was analysed with reference to age distribution, sex distribution, time distribution, clinical manifestations, risk factors, complications etc. Detailed physical examination and other investigations like complete blood count, renal function test, liver function test, ECG, chest X ray was done for all persons. Data was analyzed using statistical SPSS software and using chi square test.

Statistical analysis:

Following statistical methods have been employed in the present study.

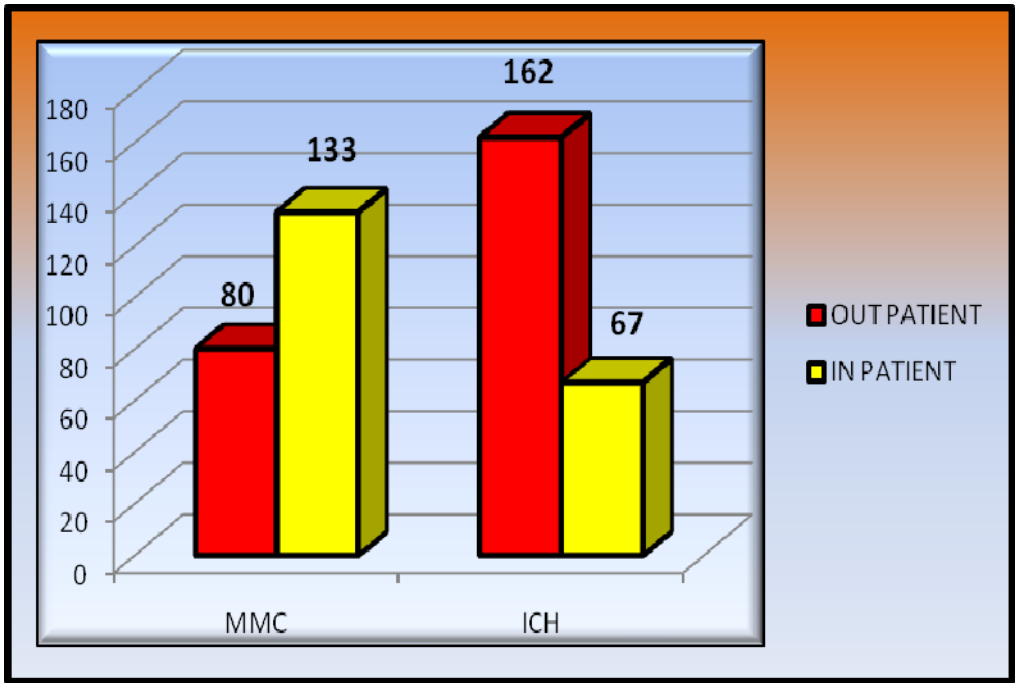
- Independent samples ‘t’ test-Unpaired.
- Independent samples ‘t’ test-Paired.
- One-way Analysis of Variance (ANOVA).
- Pearson correlation coefficient.
- Relative risk.

OBSERVATION AND RESULTS

CASES DISTRIBUTION
TABLE-1

S.NO	CASES	MMC	ICH
1.	OUT PATIENT	80	162
2.	IN PATIENT	133	67
TOTAL CASES		**213**	**229**

CASES DISTRIBUTION
CHART-1



ICH – Institute of Child Health (Paediatric Cases)

MMC – Madras Medical College (Adult Cases)

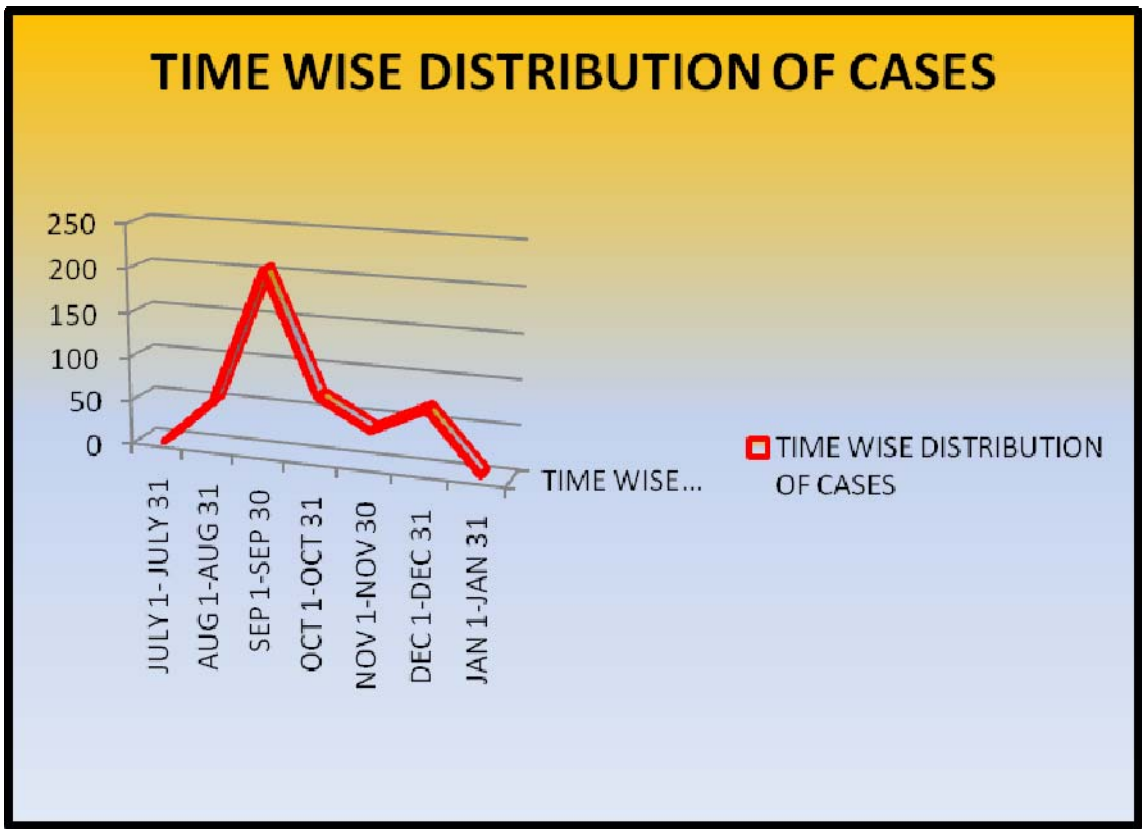
TIME WISE DISTRIBUTION OF CASES

The epidemic peaks in September and December correlated with the rains and chill climate that prevailed at that time in Chennai city.

TIME WISE DISTRIBUTION OF CASES
TABLE -2

S.NO	TIME PERIOD	CASES
1.	JULY 1-JULY 31	0
2.	AUGUST 1-AUGUST15	1
3.	AUG 16 –AUG 31	53
4.	SEP 1-SEP15	116
5.	SEP16 –SEP30	90
6.	OCT1 –OCT 15	51
7.	OCT 16 –OCT31	20
8.	NOV 1-NOV 15	12
9.	NOV 16-NOV 30	27
10.	DEC1 –DEC 15	50
11.	DEC 16– DEC 31	19
12.	JAN 1 –JAN 15	1
13.	JAN 16- JAN 31	2
	TOTAL CASES	442

TIME WISE DISTRIBUTION OF CASES
CHART -2

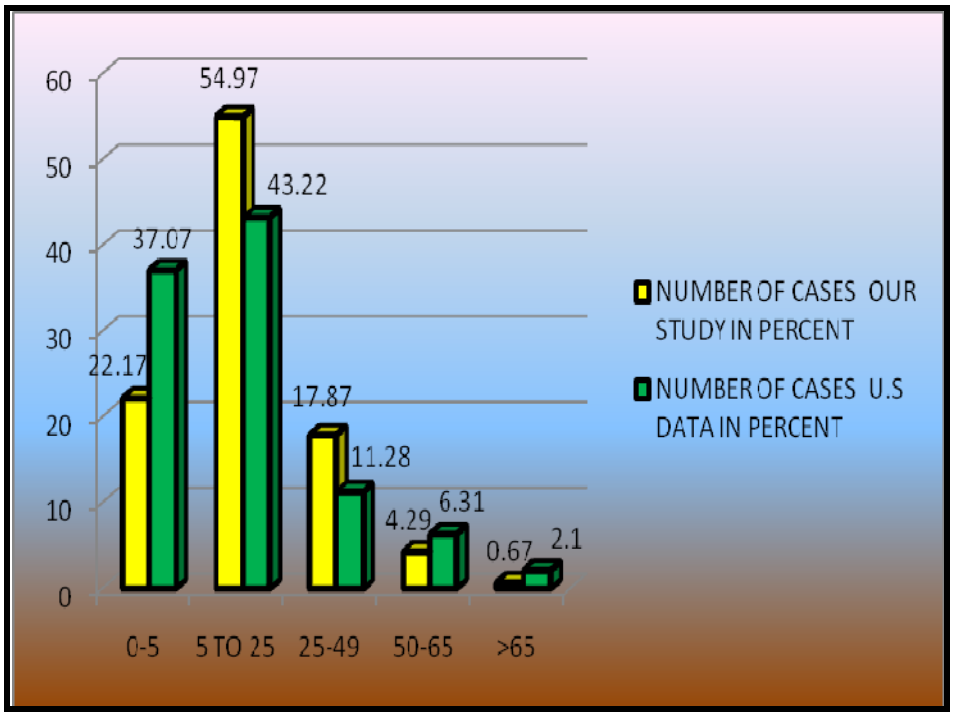


A characteristic M pattern was observed in the time distribution of swine flu cases. This is similar to the pattern observed in the 1918 spanish flu pandemic.

AGE WISE DISTRIBUTION OF TOTAL CASES
TABLE - 3

S.NO	AGE GROUP	NUMBER OF CASES	PERCENT-CASES
1.	0-5	98	22.17%
2.	5-25	243	54.97%
3.	25-49	79	17.87%
4.	50-65	19	4.29%
5.	>65	3	0.67%
	TOTAL	442	

COMPARATIVE ANALYSIS OF OUR AGE DISTRIBUTION OF TOTAL CASES WITH U.S DATA
CHART -3

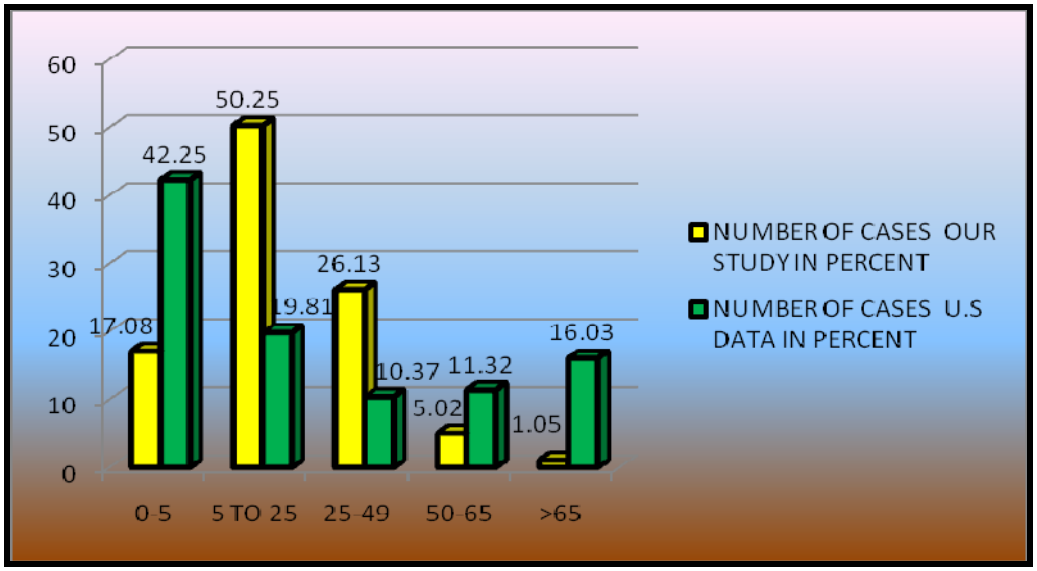


Maximum cases were reported in the age group of 5-25 years in our study as well as in the United States study

AGE DISTRIBUTION OF TOTAL CASES – U.S DATA
TABLE-4

S.NO	AGE DISTRIBUTION	PERCENT OF CASES
1.	0-5	37.07%
2.	5-25	43.22%
3.	25-49	11.28%
`4.	50-65	6.31%
5.	>65	2.10%

COMPARATIVE ANALYSIS OF OUR AGE DISTRIBUTION OF HOSPITALISED CASES WITH U.S DATA
CHART-4



In US population, maximum no.of H1N1 swine flu influenza cases requiring hospitalisation were reported in the age group of (0-5 years) where as in our study, maximum hospitalised cases were documented in the age group of 5-25 years.

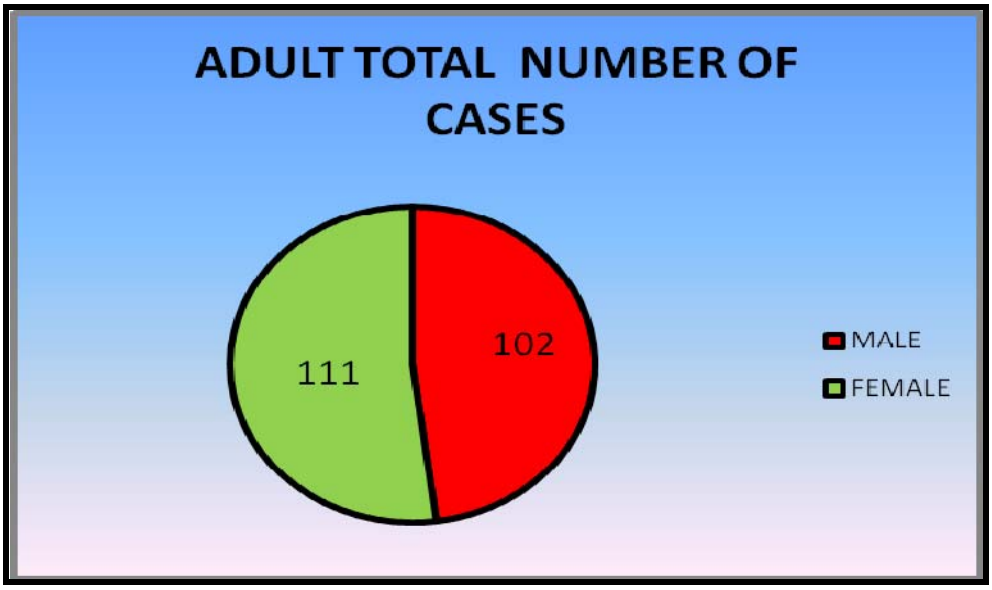
HOSPITALISED PATIENTS
TABLE-5

S.NO	AGE DISTRIBUTION	CASES NUMBER	PERCENTAGE OF Cases
1.	0-5	34	17.08%
2.	5-25	100	50.25%
3.	25-49	52	26.13%
4.	50-65	10	5.02%
5.	>65	3	1.05%
TOTAL NUMBER		**199**	

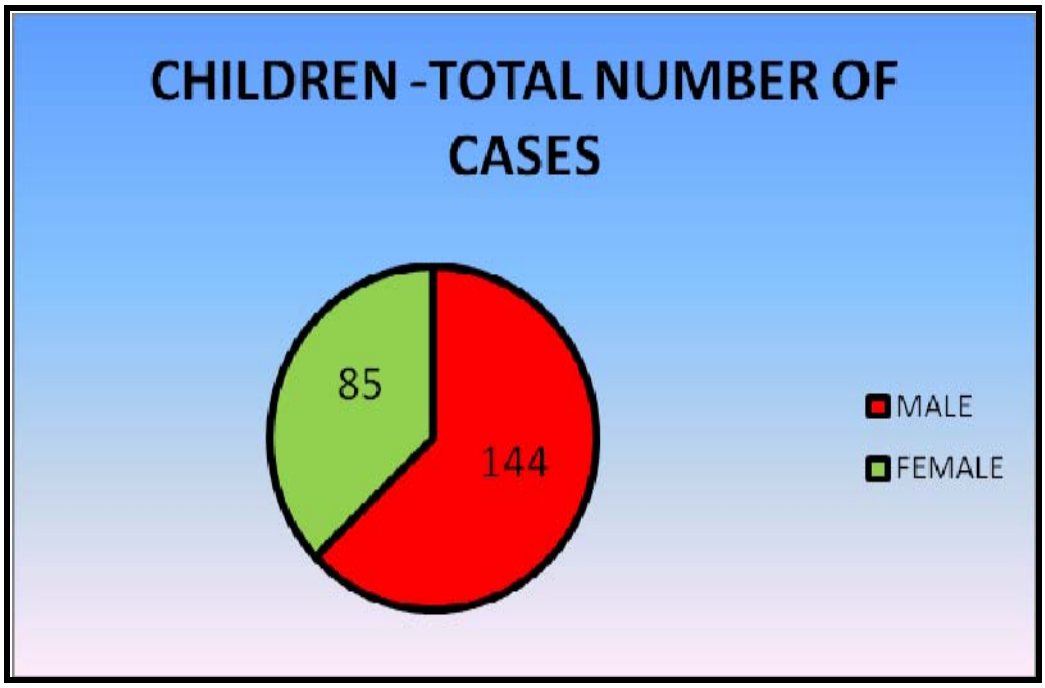
AGE WISE DISTRIBUTION OF HOSPITALISED PATIENTS-U.S DATA
TABLE -6

S.NO	AGE DISTRIBUTION	PERCENT OF PATIENTS
1.	0-5	42.45
2.	5-25	19.81
3.	25-49	10.37
4.	50-65	11.02
5.	>65	16.03

ADULT TOTAL NUMBER OF CASES
CHART -5



CHILDREN – TOTAL NUMBER OF CASES
CHART -6



SEX DISTRIBUTION
TABLE-7

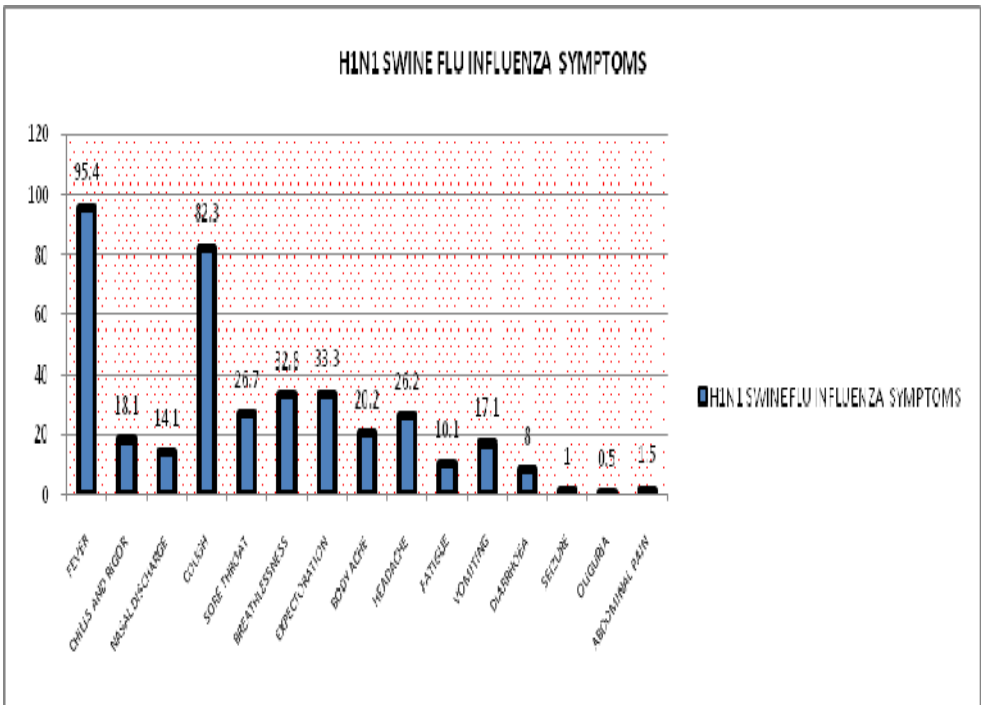
	CHILDREN	ADULT	TOTAL
MALES	144	102	246
FEMALES	85	111	196
TOTAL	**229**	**213**	**442**

H1N1 cases were equally distributed in both the sexes in the adult population (male -111, female-102). But in the paediatric population there was an apparent increase in male cases. This was due to increased rate of admissions of male children when compared to female children.

CLINICAL MANIFESTATIONS
TABLE 8

Symptoms	Percent	Symptoms	Percent	Symptoms	Percent
1.Fever	95.45%	7.Breathlessness	32.82%	13.Diarrhoea	8.08%
2.Chills and rigor	18.18%	8.Expectoration	33.33%	14.Seizure	1.01%
3.Nasal discharge	14.14%	9.Bodyache	20.20%	15.Oliguria	0.50%
4.Ear discharge	0	10.Headache	26.26%	16.Abdominal pain	1.51%
5. Cough	82.32%	11.Fatigue	10.1%		
6.Sore throat	26.76%	12.Vomitting	17.17%		

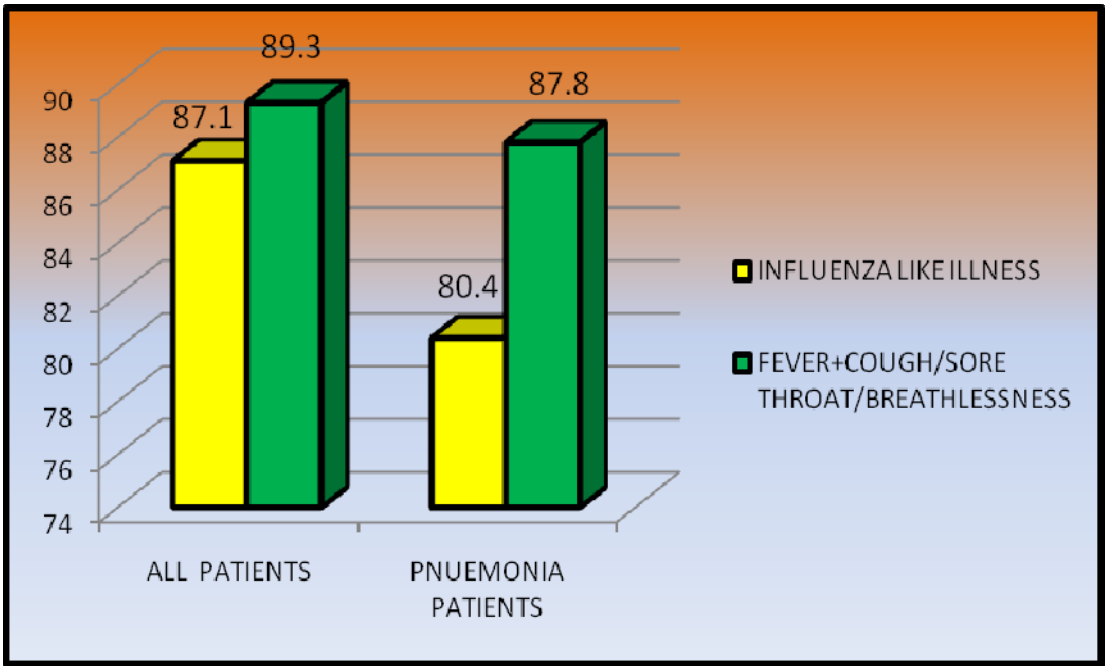
CLINICAL MANIFESTATIONS
CHART- 7



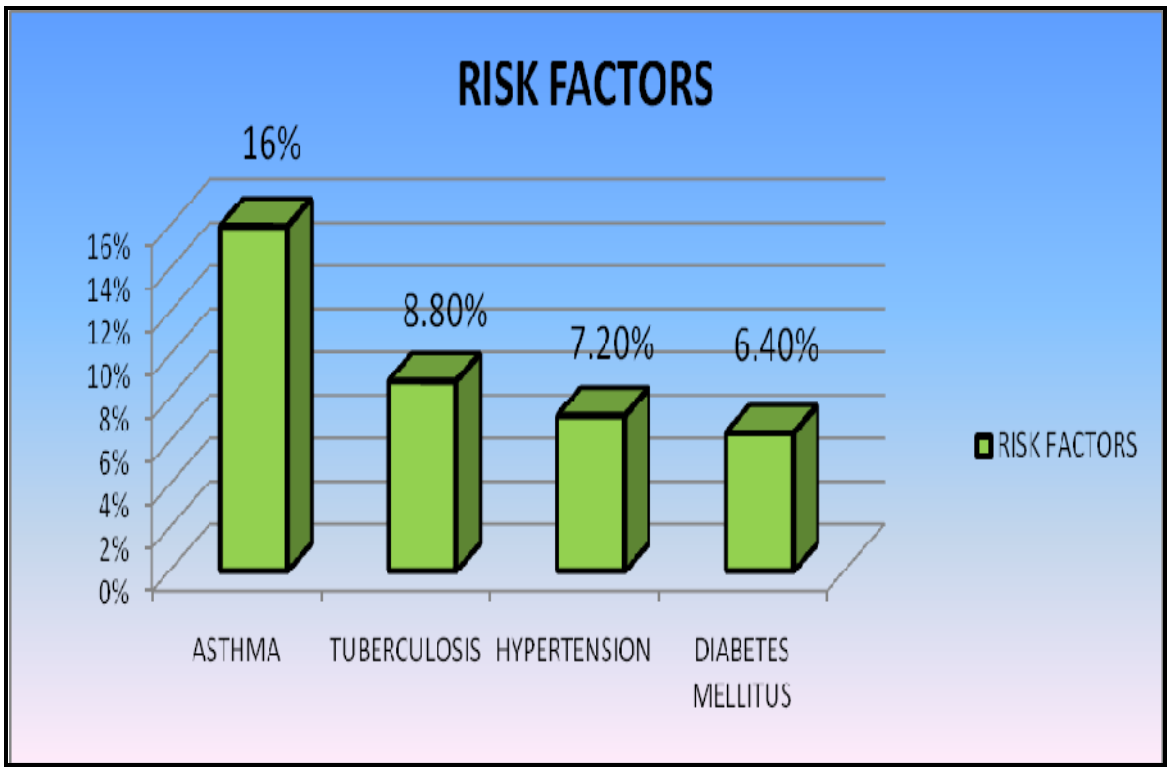
INFLUENZA LIKE ILLNESS
TABLE - 9

S. No	Clinical Picture	All patients	Pnuemonia patients
1.	INFLUENZA LIKE ILLNESS	87.12%	80.48%
2.	FEVER+ COUGH/ SORETHROAT/ BREATHLESSNESS	89.39%	87.80%

INFLUENZA LIKE ILLNESS
CHART -8



RISK FACTORS
CHART -9

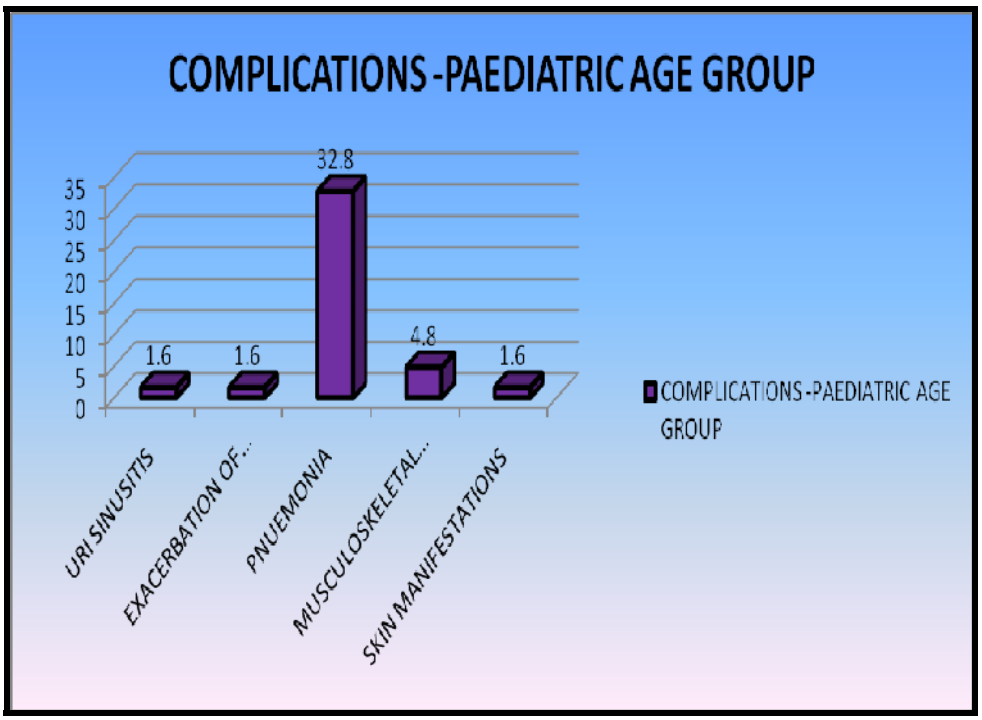


RISK FACTORS
TABLE 10

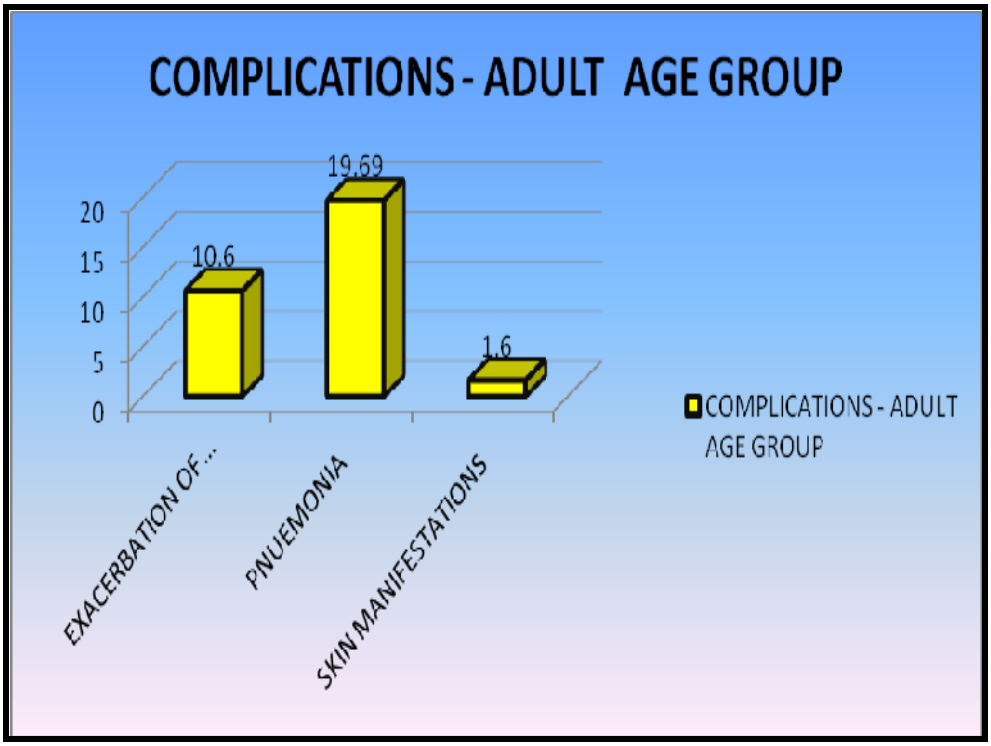
RISK FACTOR	PERCENTAGE OF CASES	POPULATION PREVALENCE	P value
ASTHMA	16%	2.38% . ref(5)	<0.01
TUBERCULOSIS	8.8%	0.4%	<0.01
HYPERTENSION	7.2%	8.4%	
DIABETES	6.4%	4%	

Note: Asthma and TB were found to be risk factors for the occurrence of H1N1 swine flu influenza.

COMPLICATIONS PAEDIATRIC AGE GROUP
CHART 10



COMPLICATIONS ADULT
CHART 11



Note: Exacerbation – Exacerbation of Asthma

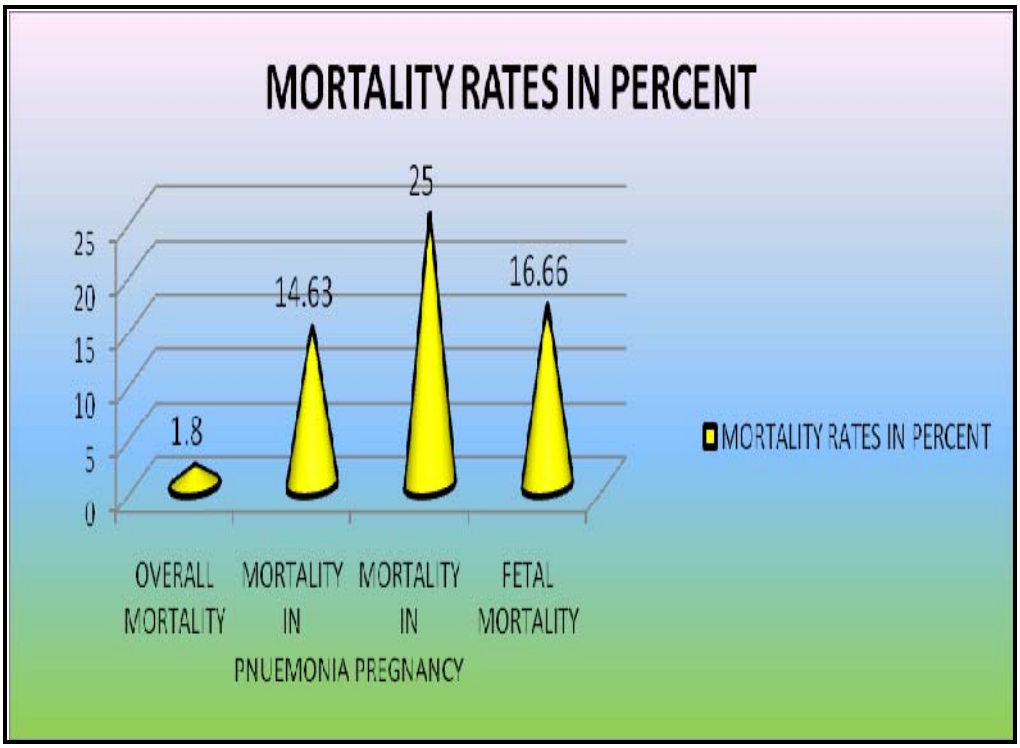
COMPLICATIONS ADULT
TABLE-11

S. No	Complications (Adult)	Percent (n=199)
1.	URI-SINUSITIS	1.6%
	EXACERBATION OF BRONCHITIS, BRONCHIAL ASTHMA	1.6%
2.	PNUEMONIA	32.8%
3.	MUSCULOSKELETAL-MYALGIA,ARTHRITIS	4.8%
4.	SKIN MANIFESTATIONS	1.6%

COMPLICATIONS-PAEDIATRIC AGE GROUP
TABLE -12

S. No	Complications	Percent (n=66)
1.	EXACERBATION OF BRONCHITIS, BRONCHIAL ASTHMA	10.60%
2.	PNUEMONIA	19.69%
3.	SKIN MANIFESTATIONS	1.6%

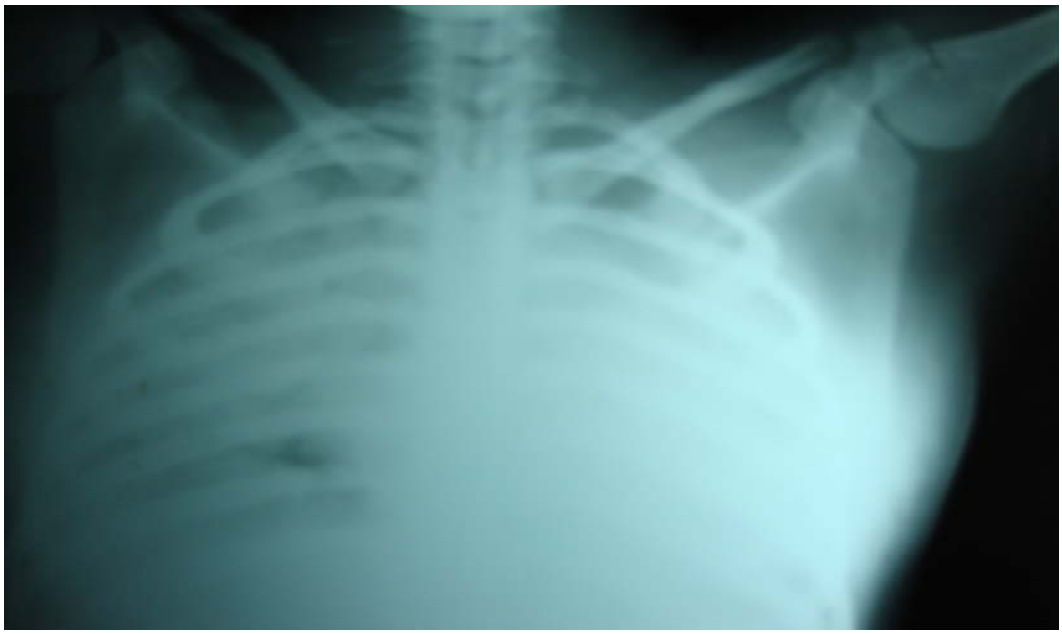
MORTALITY RATES
CHART 12



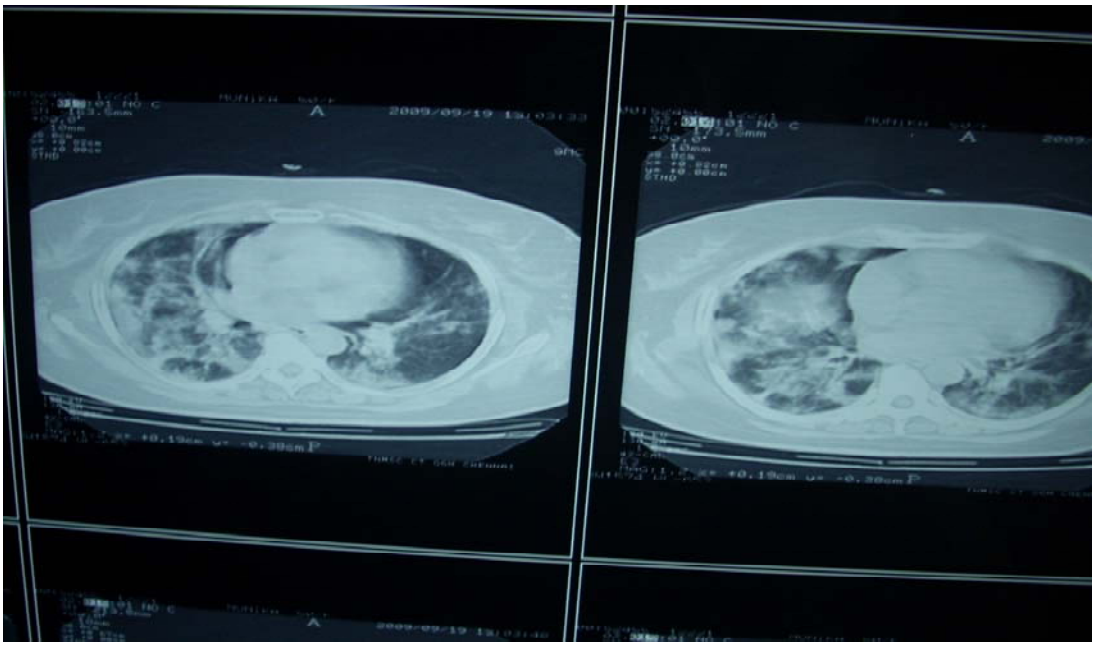
MORTALITY RATES
TABLE- 13

CONDITION	MORTALITY RATES
1.OVERALL MORTALITY	1.8% (8 out of 442)
2.MORTALITY IN PNUEMONIA	14.63% (8 out of 54)
3.MORTALITY IN PREGNANCY	25% (3 out of 12)
4.MORTALITY IN FETUS	16.66% (2 out of 12)

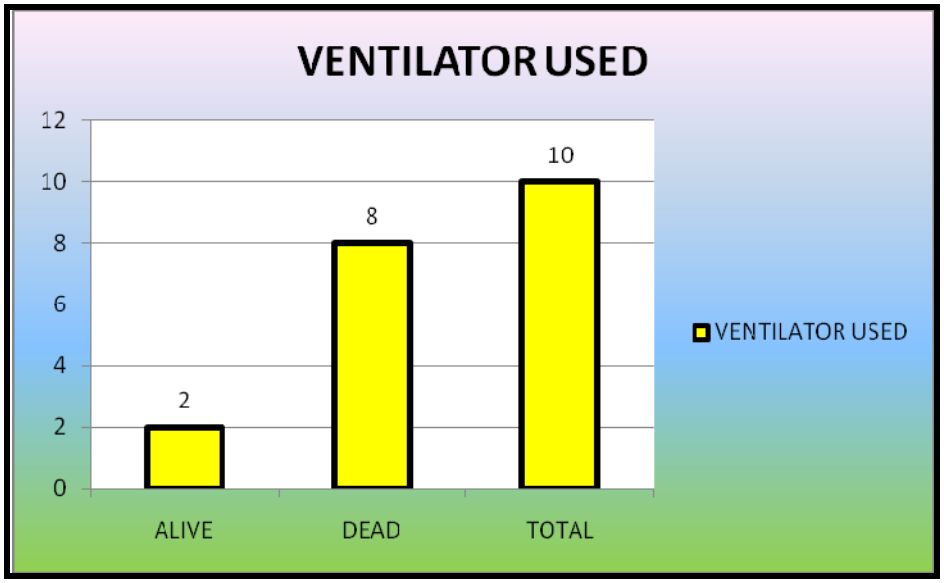
X RAY CHEST OF THE H1N1 SWINE FLU PATIENT WITH BILATERAL PNEUMONIA



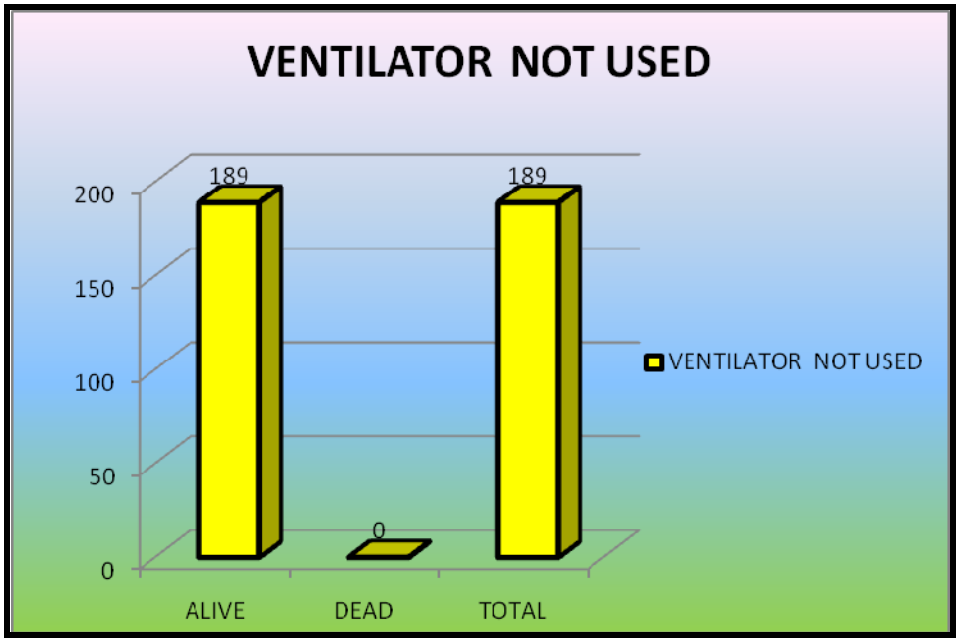
CT CHEST DEMONSTRATING BILATERAL PNEUMONIA IN H1N1 SWINE FLU PATIENT



VENTILATOR USED
CHART- 13



VENTILATOR NOT USED
CHART -14



VENTILATOR REQUIREMENT AND OUTCOME
TABLE-14

	ALIVE	DEAD	TOTAL
VENTILATOR USED	2	8	10
NOT USED	189	0	189
Total	**191**	**8**	**199**

Ventilator requirement was an independent risk factor correlating with higher mortality rate and poor prognosis in H1N1 patients. P value<0.01.

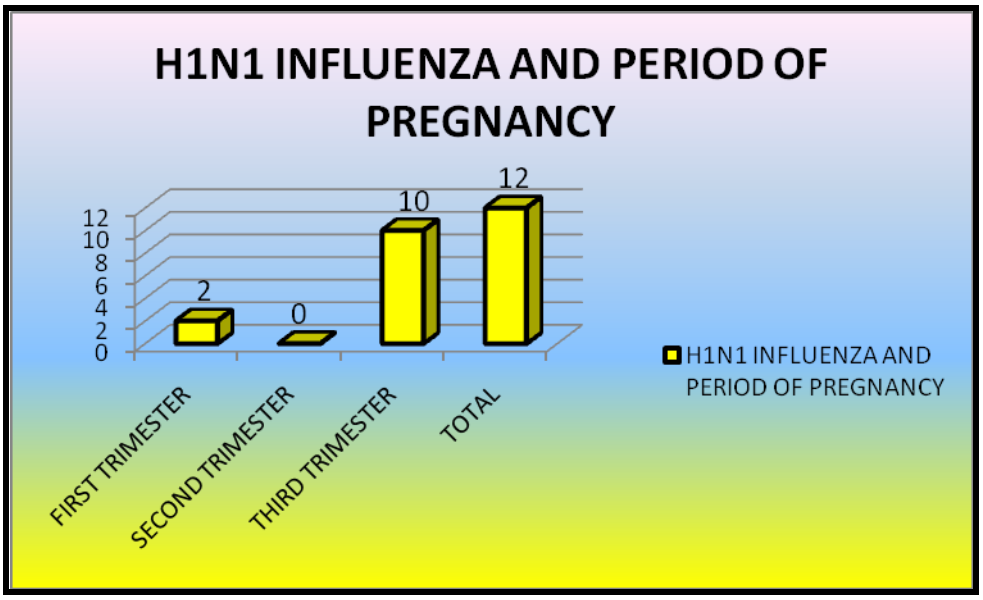
H1N1 INFECTION AND PNEUMONIA:

The x rays of the pneumonia patients that was analyzed showed that there was a predominance of lower lobe involvement (p value <0.01). 50% - lower lobe , 5.2% - upper lobe , 18% - middle lobe , bilaterality -100%. Similar findings have been observed in studies in brazil (73) . The predominance of lower lobe involvement was probably due to the gravitational bias in blood supply. Pneumonia as a complication was more common in the age group of 25-49 ie 53.4%, it was equally reported in both sexes (men 21,women 20).

X RAY FINDINGS IN PNEUMONIA
TABLE 15

S. No	X ray Findings	Number	Percent
1.	Predominant involvement of upper lobe only	2	5.2%
2.	Predominant involvement of middle lobe	2	5.2%
3.	Involvement of lower lobe only	14	36%
4.	Involvement of both middle lobe and lower lobe	5	13%
5.	All lobes involved diffusely (random involvement)	15	38.3%
TOTAL NUMBER OF CASES		38	

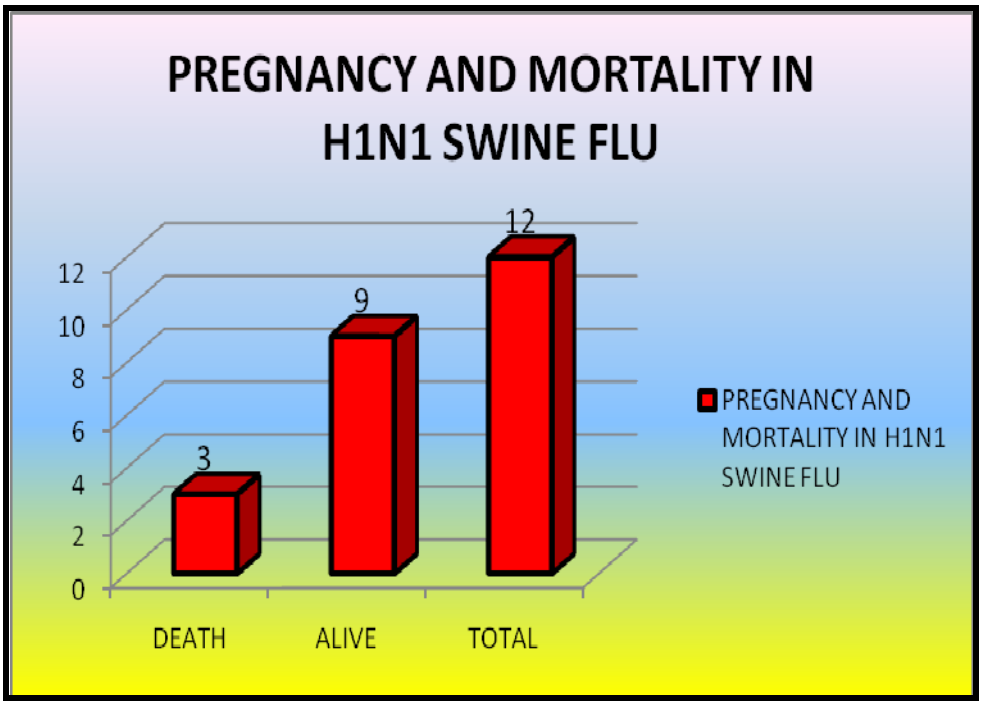
H1N1 INFLUENZA AND PERIOD OF PREGNANCY
CHART-15



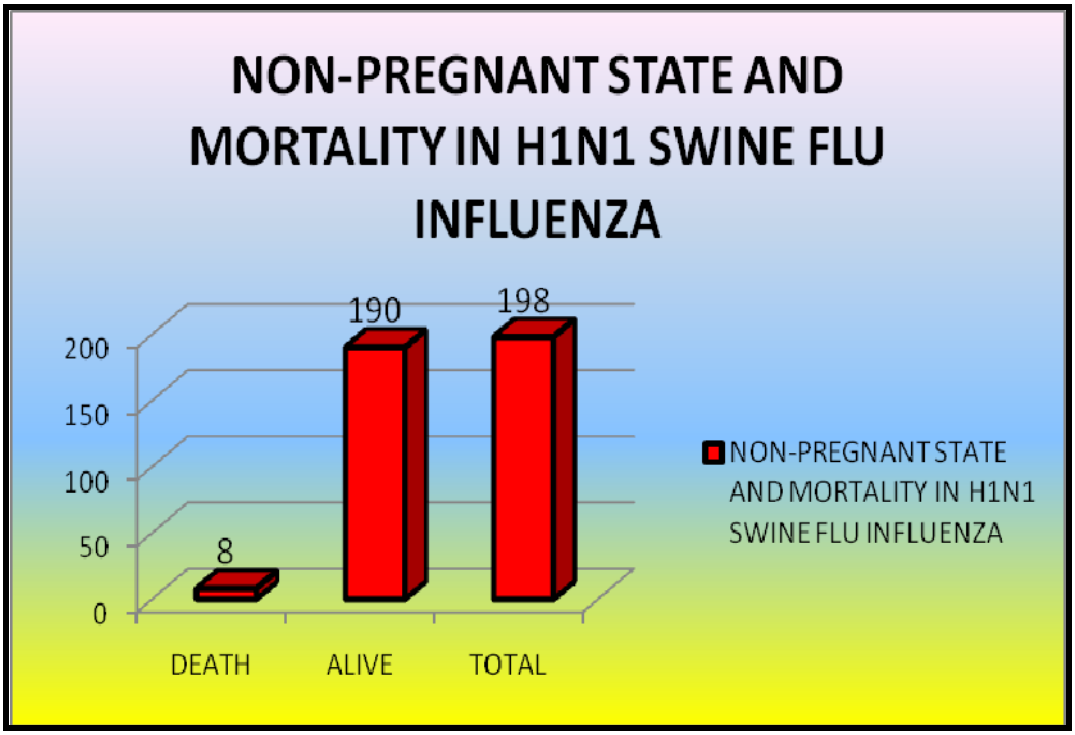
PREGNANCY AND H1N1 EPIDEMIC RELATION TO PERIOD OF PREGNANCY
TABLE-16

Period of pregnancy	No of cases(n=12)	Percent
First trimester	2	16.67%
Second trimester	0	0
Third trimester	10	83.33%
Total no. of cases	**12**	

PREGNANCY AND MORTALITY IN H1N1 SWINE FLU
CHART 16



NON PREGNANT STATE AND MORTALITY IN SWINE FLU
CHART 17



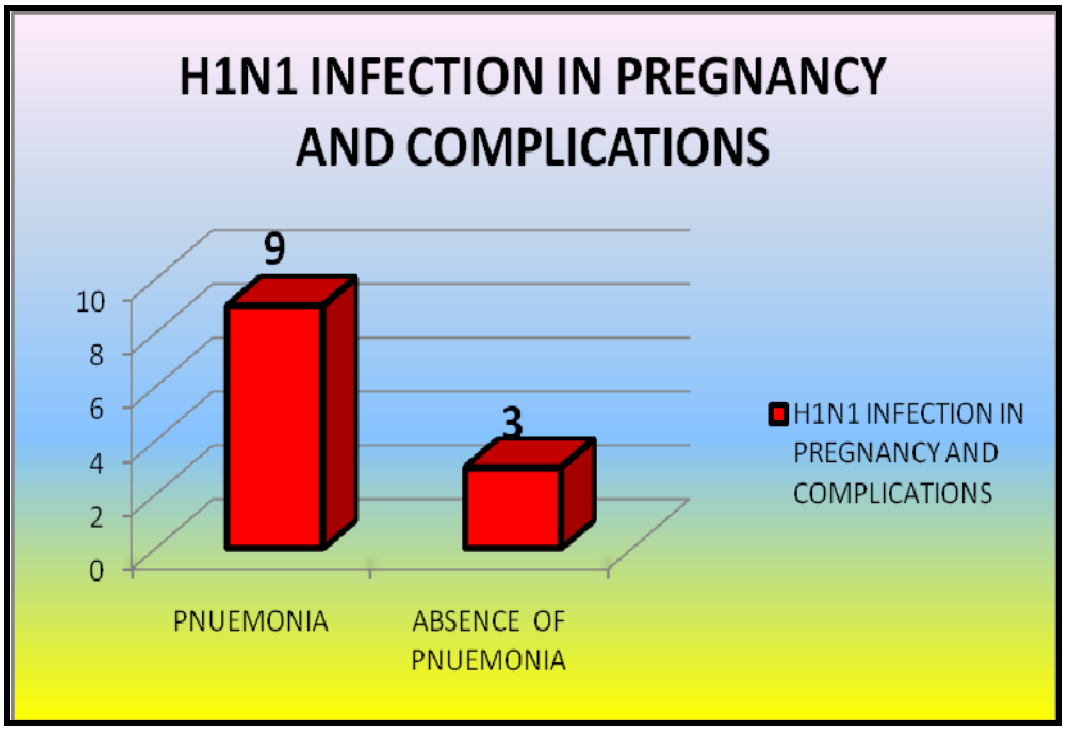
PREGNANCY AND MORTALITY
TABLE 17.

H1N1 INFECTION	DEATH	ALIVE	
PREGNANT	3	9	12
NON-PREGNANT	5	181	186
TOTAL	**8**	**190**	**198**

PREGNANCY AND COMPLICATIONS
TABLE 18

H1N1 INFECTION	PNEUMONIA	NO PNEUMONIA	
PREGNANT	9	3	12
NONPREGNANT	45	141	186
TOTAL	**54**	**144**	**198**

H1N1 INFECTION IN PREGNANCY AND COMPLICATIONS
CHART 18



H1N1 influenza occuring in pregnancy is associated with a higher mortality and more complications. P value--<0.001**

DISCUSSION

The current H1N1 pandemic had witnessed more number of cases in the age group of 5-25 years which is unusual in the conventional seasonal flu. Hospitalisation rates were more common in our study in the age group of 5-25 years but in U.S it is more common in the extremes of age group (72, 64, 67). In our study 86.92% percent of patients with pandemic H1N1 influenza A have met the case definition for influenza like illness (subjective fever plus cough and/or sore throat) whereas it was 95% in New York City. (65). Fever ,cough, sorethroat ,breathlessness were the most common symptoms observed in our population with H1N1 infection which is similar to that of the U.S studies. [64].In contrast, approximately one third of patients seen at two hospitals in Mexico had no fever at presentation.

The prevalence of certain underlying conditions was significantly higher among 198 patients requiring hospitalization for pandemic H1N1 Influenza A in our study than in the general population. Bronchial asthma and tuberculosis were found to be risk factors. Seizure disorder was reported in 3% of persons, cardiac lesion was seen in 2% of persons and persons with

immunosuppressive conditions accounted for 1% of the total cases .Smoking was reported in 8% of cases and alchoholism reported in 10.4% of cases. Similar picture was observed in the United states where 32 percent of these patients had asthma compared with only 8 percent of the US population. Out of the 133 patients requiring hospitalization, 80 percent of the persons had the underlying condition that increased the risk of influenza complications. Of 272 patients requiring hospitalization in the United States, 73 percent had at least one underlying condition that increases the risk of influenza complications (68).

Few elderly individuals have been infected ie (0.67% in persons>65 years), which may be due to some degree of preexisting immunity in older individuals against antigenically similar influenza viruses. However, elderly individuals who are infected are still thought to be at increased risk for complications. In our study, approximately 25% (2 out of 8) of deaths caused by pandemic H1N1 influenza A virus in the study have occurred in pregnant women, although only 2.1 percent of the population is pregnant at any given time (63). During prior influenza epidemics and pandemics, as well as during the current pandemic, pregnant women have had increased morbidity and mortality (69). The

mortality rate among pregnant women in the U.S among H1N1 influenza cases has been around 28% (71).Similarly in our study mortality rate in H1N1 influenza in pregnancy was found to be 25%. (3 out of the 12) . During previous influenza pandemics, increased rates of spontaneous abortion and preterm birth have been reported among pregnant women, especially in those with pneumonia (71). Out of the 12 pregnant women requiring hospitalization in our study two had spontaneous abortion following intrauterine death in the third trimester. The fetal loss rate was 16.67% (2 out of 12). Similar to our analysis, studies in other countries have also reported an increased risk of influenza among pregnant women , particularly during the third trimester (70).

CONCLUSION

- The rate of reported cases and hospitalization rates were highest among individuals aged 5 to 24 years.
- H1N1 cases were equally distributed in both the sexes in the adult population
- In our study **86.92%** of patients with pandemic H1N1 influenza A met the case definition for influenza like illness (subjective fever plus cough and/or sorethroat).
- Similar to the western data **bronchial asthma ,pulmonary tuberculosis were found to risk factors for complications in H1N1 infection**. The overall mortality rate was 1.8% and the most common cause of death in patients was due to pneumonia.
- Ventilator requirement was associated with poor prognosis in H1N1 patients. P value <0.01.
- **The percentage of persons > 65 years who were affected was far less ie 0.67% which is quite unusual in the case of seasonal flu .**

- H1N1 pnuemonia was found to **involve predominantly the lower lobe of lung.**(p value <0.01).

- The mortality rate among pregnant women with H1N1 infection was 25% and the fetal loss rate was 16.67%.

- There was an **increased risk** of H1N1 influenza infection during **the third trimester of pregnancy.** (p value-0.027)

- The clinical profile of H1N1 influenza that was observed in our study was similar to that of the western data with some differences.

- Individuals with comorbid conditions, pregnancy were found to be severely affected. Hence individuals with risk factors need to be protected by vaccination..

LIMITATION OF THE STUDY

This study was basically conducted as a prospective study in a tertiary care institute. Hence the milder forms of the infection as well as the index case which occurred at the community level could have been missed out. Hence this analysis may not reflect the actual distribution of the cases at the population level. Further community based studies are required to analyse the actual impact of H1N1 infection in the community.

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CASE RECORD FORM

NAME OF THE PATIENT

AGE

SEX

ADDRESS

SOCIOECONOMIC STATUS

EDUCATIONAL STATUS

MONTHLY INCOME

CLINICAL MANIFESTATIONS

DATE OF ILLNESS ONSET

DATE OF FEVER ONSET

MAIN PRESENTING COMPLAINTS:

SYMPTOMS	YES	NO	DURATION	COMMENT
1.Sudden onset of symptoms<12hours				
2.fever				
3.chills and rigor				
4.nasal discharge				
5.ear discharge				
6. cough				
7.sore throat				
8.breathlessness				
9.expectoration				
10.headache				
11.bodyache				
12.fatigue				
13.ARI in family in last 2 weeks				
14.concomitant illness				
15.vomitting				
16.diarrhoea				
17.seizure				
18.other symptoms				

Anyone at home having similar illness Yes/no

Any recent history of foreign travel yes/no

How many days of work or school have you missed

Have you visited someone else to treat your illness prior to this visit

PAST HISTORY:

Any history of tuberculosis ,bronchial asthma, systemic hypertension, diabetes or other comorbid condition in the patient.

PERSONAL HISTORY:

H/O smoking, alchoholism, in the patient.

Is the occupation of the patient related to poultry or with people working with poultry in the last 2 weeks.

FAMILY HISTORY:

Any history of similar episodes in the family members.

GENERAL EXAMINATION:

VITALS

EXAMINATION OF RESPIRATORY SYSTEM

EXAMINATION OF UPPER RESPIRATORY SYSTEM:

NASAL MUCOSA ,TONSILS ,PHARYNX

EXAMINATION OF THE CARDIOVASCULAR SYSTEM

EXAMINATION OF THE CNS

EXAMINATION OF THE ABDOMEN

COMPLICATIONS

S.No	COMPLICATIONS	Present/not
1.	URI -sinusitis, otitis media, croup	
2.	LRI-pneumonia, bronchiolitis, status asthmaticus	
3.	Cardiac-myocarditis, pericarditis	
4.	Musculoskeletal -myositis, rhabdomyolysis	
5.	Neurologic acute and post-infectious encephalopathy, encephalitis, febrile seizures,	
6.	Toxic shock syndrome	
7.	Secondary bacterial pneumonia with or without sepsis.	
8.	Other complications	

TREATMENT DETAILS

*Was tamiflu given or not ? yes/no

*How many days was tamiflu given ?

*Did you feel any improvement of symptoms?

Some improvement / no improvement /complete improvement

*after how long you felt the improvement of symptoms?

* any additional side effect patient felt due to that drug?

PATIENT CONSENT FORM

STUDY DETAIL.: "CASE SERIES STUDY ON THE ,

CLINICAL PROFILE OF H1N1 INFLUENZA EPIDEMIC".

STUDY CENTRE : INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

PATIENTS NAME :

PATIENTS AGE :

IDENTIFICATION NUMBER :

✓

Patient may check ( ) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records both in respect of current study and any further research that may be conduction in relation to it,even I withdraw from the study I agree to this access.However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological .biochemical, radiological tests. ☐

Signature/thumb impression: place date

Patients Name and Address:

Signature of investigator : place date

Study investigator's Name:

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-600 003

Telephone 25363970
Fax 044 2535115
Dated : 12.05.2010

L.Dis.No.14597/ME5/Ethics Dean/MMC/2010

Title of the work : "CASE SERIES STUDY ON CLINICAL PROFILE OF H1N1 SWINE INFLUENZA"

Principal Investigator : Dr. A. Puvanalingam.
Designation : PG in MD Internal Medicine.
Department : Institute of Internal Medicine MMC & GGH, Ch-3

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 12th May 2010 at 2.p.m in Pharmacology Seminar Hall, Madras Medical College, Chennai -3

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
4. You should not deviate form the area of the work for which you applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulation of the institution(s).
7. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, MMC, CHENNAI

CHAIRMAN
IEC, MMC, CHENNAI

DEAN
MADRAS MEDICAL COLLEGE,
CHENNAI -3.