

# Swineflu in reproductive age group female. Risk factors for high mortality in pregnant women

Ripal Gevariya<sup>1</sup>, Rohit Jain<sup>1</sup>, Haresh Doshi<sup>1</sup>, Pathik Parikh<sup>2</sup>

<sup>1</sup>Department of OBGY, Civil Hospital, Ahmedabad, India

<sup>2</sup>Department of Medicine, Civil Hospital, Ahmedabad, India

## ABSTRACT

**OBJECTIVES:** To study the risk factors for mortality in novel H1N1 positive women of reproductive age group admitted to our tertiary care centre.

**DESIGN & METHODS:** In this descriptive study we included all H1N1 positive young women of reproductive age group admitted in our hospital. These women were managed as per standard protocol including detailed history, general, systemic and obstetrics examination, laboratory investigations and standard treatment was started. All parameters were analysed in details for relevance of clinical and laboratory parameters in terms of survival.

**RESULTS:** Out of 70 patients 28 (40%) were pregnant and 42(60%) were non pregnant. Most commonly, women presented with fever, cough and breathlessness.

The average duration of symptoms at the time of admission was 4.9 days. Out of 70 patients 37 expired, among them 23 were pregnant and 14 were non pregnant. Two patients were unconscious at the time of admission and both expired. Cyanosis was present in 4(5.7%) at the time of admission and all 4 patients expired (p=0.528). 31(44.2%) patients had SpO<sub>2</sub> less than 90% on admission. In pregnant patients 20 (71.4%) had SpO<sub>2</sub> <90% and among them 19 (95%) expired. While in non-pregnant patient 11 (26%) had SpO<sub>2</sub> <90% out of which 6(54.5%) expired. Tachypnoea, anaemia, Pregnancy induced hypertension, consolidation on chest x-ray were other factors which were positively correlated with fatal outcome.

**CONCLUSION:** H1N1 present as an acute onset respiratory illness presenting within 3 to 4 days with mainly fever, cough and breathlessness. H1N1 in pregnancy is associated with high maternal mortality as compared to non pregnant patients. Unconsciousness, cyanosis, low SpO<sub>2</sub>, anaemia, tachycardia, tachypnea and consolidation are the markers suggestive of high mortality.

**Keywords:** Swineflu, H1N1 Influenza Virus, Pregnant Women

## INTRODUCTION

Influenza virus belongs to Family Orthomyxoviridae. It is sub classified into three main types, Type A (Multiple species), Type B (Humans), Type C (Humans and swine). Out of the three types A is the most virulent group<sup>(1)</sup>. The virus is sub classified on the basis of surface antigens, Hemagglutinin (H or HA) and Neuraminidase (N or NA). There are 15 HA and 9 NA for influenza A. Within influenza A,

Correspondence to: ripal179@gmail.com

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## SOMMARIO

**OBIETTIVI:** Studiare I fattori di rischio di mortalità in un inusuale gruppo di donne in età fertile H1N1 positive ricoverate nel nostro centro di cura terziario.

**DISEGNO DELLO STUDIO:** In questo studio di natura descrittiva abbiamo incluso tutte le giovani donne, H1N1 positive, in età fertile, ricoverate nel nostro ospedale. Queste donne sono state gestite seguendo un protocollo standard che includeva una anamnesi dettagliata, generale e sistemica; un esame ostetrico e analisi di laboratorio. E' stato, inoltre, avviato il trattamento standard. Tutti i parametri sono stati analizzati in dettaglio seguendo il criterio di rilevanza dei parametri clinici e di laboratorio in termini di sopravvivenza.

**RISULTATI:** 28 pazienti su 70 (40%) erano incinte e 42 (60%) non erano incinte. Solitamente, le donne presentavano febbre, tosse e stato di apnea. La durata media dei sintomi al momento del ricovero è stata di 4,9 giorni. Su 70 pazienti, 37 sono decedute, tra di loro 23 erano incinte e 14 no. Due pazienti, al momento del ricovero, erano in stato di incoscienza, entrambe sono poi decedute. 4 pazienti (5,7%) al momento del ricovero erano cianotiche e tutte e 4 sono decedute (p=0,528). 31pazienti (44,2%), presentavano SpO<sub>2</sub> a meno del 90%, al momento del ricovero. Tra le pazienti incinte, 20 (71,4%) di loro presentavano SpO<sub>2</sub><90% e tra queste 19 (95%) sono decedute; mentre nelle pazienti non incinte, 11 (26%) avevano SpO<sub>2</sub><90%, 6 (54,4%) delle quali sono decedute. Tachipnea, anemia, ipertensione indotta dalla gravidanza e addensamento alla radiografia toracica sono altri fattori correlati con l'esito fatale.

**CONCLUSIONI:** L'H1N1 si presenta inizialmente con acuti problemi respiratori, nei primi 3-4 giorni si rileva principalmente febbre, tosse e stato di apnea. Nelle pazienti incinte causa un alto tassi di mortalità in confronto a le pazienti non incinte. Lo stato di incoscienza, la cianosi, la SpO<sub>2</sub> bassa, l'anemia, la tachicardia, la tachipnea, e l'addensamento polmonare sono marker che suggeriscono un'alta probabilità di esito fatale.

because of reassortment, there have been transfers of genes among strains crossing swine, avian, and human species boundaries leading to epidemics<sup>(2)</sup>. Annual influenza epidemics are estimated to affect 5–15% of the global population. Although most cases are mild, this still causes severe illness in 3–5 million people and around 250,000–500,000 deaths worldwide<sup>(3)</sup>. In addition to these annual epidemics, Influenza A virus strains caused three major global epidemics during the 20th century: the Spanish flu in 1918, Asian flu in 1957 and Hong Kong flu in 1968–69. The influenza virus

has also caused several pandemic threats over the past century, all caused by the H1N1 strains. However swine influenza is also known to be caused by influenza A subtypes sH1N2, H2N3, H3N1, and H3N2<sup>(4-5)</sup>. Influenza A, H1N1 swine flu is a strain of the flu that has moved from pigs to humans and can be transmitted from human to human. This strain contains genes from four different flu viruses, namely, North American swine influenza, North American avian influenza, Human influenza and two swine influenza viruses typically found in Asia and Europe<sup>(6-7)</sup>. This 2009 flu pandemic is a global outbreak of a new strain of H1N1 influenza virus, commonly referred to as "swine flu"<sup>(8)</sup>. But some authorities object to calling the flu outbreak "swine flu" and so various names have been suggested such as, H1N1 influenza virus, "Novel influenza A (H1N1), Pig Flu, Mexican flu, Mexican virus, SI-"swine influenza", H1N1 Flu, New Flu, North American influenza, In July 2009 WHO gave the name - pandemic H1N1/09 virus to distinguish it from the current seasonal H1N1 viruses<sup>(9-10)</sup>. "The virus kills about 0.01-0.03% of those infected and spreads in the same way sneezing<sup>(11)</sup>. The disease is communicable from 1 day before to 7 days after the onset of symptoms with majority of cases being in healthy young.

Ever since the detection of this virus, the virus has been spreading and the cases rising throughout the world. The first cases were seen in Mexico, but within no time the virus spread to rest of America and now has become a pandemic affecting most of the countries of the world (213 countries). It is known that this virus affects young people more as compared to the extremes of age unlike the seasonal flu which affects the later. Besides, pregnancy alters the state of immunity and also Centre for Disease Control stated in July 2009 that, "while pregnant woman have always had a higher risk of severe disease from influenza in general, the new H1N1 virus is taking an exceptionally heavy toll". Even if previously healthy, pregnant women on getting H1N1 had poor outcome<sup>1</sup>. As swine flu carries exceptionally high mortality risks in pregnant females and there are limited studies reported addressing this issue, we carried out this study to see the outcome of such young, pregnant as well as non pregnant females admitted to tertiary care centre with H1N1 virus infection and epidemiological, clinical, biochemical, radiological and obstetric parameters were analysed in relation to mortality.

## **METHODS AND MATERIALS**

In this descriptive study we had included all H1N1 positive young women of reproductive age group admitted in our hospital in isolation ward. All 70 women were detected novel H1N1 positive by virus isolation from their respiratory specimens. These tests were carried out by the WHO recognised Microbiology laboratory at our hospital via QIAGEN™, PCR method.

These women were then subjected to detailed history including their duration, type of symptoms, associated illness, menstrual history, obstetric history, details of delivery (if it occurred) in hospital, maternal and foetal outcome. General and systemic examinations including obstetrics examination were carried out.

Various investigations like Haemoglobin, Total count, Platelet Count, random blood sugar, Blood Urea, Serum Creatinine and electrolytes were carried out in these patients

Chest x-rays on admission (with shield in pregnant women) were taken. Antenatal Ultrasound was also carried out for foetal wellbeing, liquor, placenta and maturity of the foetus.

Oseltamivir was started in these patients as advised by the physician. The duration for which the Oseltamivir was given before discharge or death was also noted.

Based on these parameters at the time of admission the correlation of these parameters with the outcome was studied and calculated. The statistical significance was calculated on the basis of Chi square test.

## **RESULTS**

### **Epidemiology**

A total of 70 patients were studied. Out of these 70 patients, 28 (40%) were pregnant and 40 (57.1%) belonged to the age group between 21 and 30. The mean age was 28.7 years. Among pregnant women 10 patients (35.7%) belonged to second trimester while 18 patients (64.3%) belonged to the third trimester. Twenty seven (38.5%) women came from Ahmedabad and rest came from other places in Gujarat like Sabarkantha, Banaskantha, Nadiad, Kheda, Kutch, Porbandar, Baroda, Junagadh and neighbouring state like Rajasthan.

### **Clinical Features**

The average duration of symptoms at the time

of admission was 4.9 days. Twenty six (37.1%) women presented between the time periods of 3 to 4 days while 20 women (28.5%) presented between 5 to 7 days. Less commonly women also presented acutely (22.8%) in  $\leq 2$  days duration from onset of illness. Only 8 (11.4%) women presented after 7 days of onset. Most commonly, women presented with fever, cough and breathlessness. Out of 70 patients 63(90%) women had cough, 62(88%) had fever and 42(62%) had breathlessness. Other symptoms like chest pain, diarrhoea, sore throat and headache were less common. Sixteen of non pregnant patients had associated co morbid conditions, one being Rheumatic Heart Disease, 2 women had hypertension and 13 had anaemia. Among pregnant women 5 had pregnancy induced hypertension and 10 had anaemia.

At the time of admission, 2 patients presented with unconsciousness and four patients (pregnant = 3) had cyanosis. Overall, thirty seven patients (52.8%) had tachycardia (pulse > 100/min), being higher in pregnant patients [n=20(71.4%)] as compared to non pregnant women [n=17(40.4%)]. Fifty two (74.2%) had tachypnoea overall (respiratory rate greater than 20), again being higher in pregnant patients [n=22(78.5%)] as compared to non pregnant patients [30(71.4%)]. Out of 28 pregnant patients, 5 patients (17.8%) had PIH. 3 patients (4.2%) had hypotension (blood pressure <100).

### Investigations

Thirty one (44.2%) patients had SpO<sub>2</sub> less than

90% on admission of which 20 were pregnant. Twenty Three patients (32.8%) had haemoglobin levels of  $\leq 9$  g/dl. Four pregnant patients (14.2%) had Hb <7 g/dl and six (21.4%) pregnant patient had haemoglobin levels of 7- 9 g/dl. While in non-pregnant patients 3(7.1%) had haemoglobin <7g/dl and 9(21.4%) had haemoglobin levels of 7-9 g/dl. Twenty Eight (40%) patients had total count  $\geq 10000$  per cumm, among which 14(50%) were pregnant and 14(50%) were non pregnant.

Sixty three patients (90%) had some abnormality on chest x- ray. In pregnant patient 12(44.4%) had unilateral consolidation and 13(48%) had bilateral consolidation. In non-pregnant patients 18(50%) had unilateral consolidation and 10(27.7%) had bilateral consolidation.

### Management

All admitted patients received Oseltamivir, Antibiotics, Intravenous fluid as per Central Venous Pressure. Forty Two patient required ventilatory support. Four patients required only non invasive support in the form of BIPAP, while 38 patients require intubation and volume or pressure controlled ventilation with low PEEP.

### Overall Outcome

The mortality rate was 52.8%, being higher in pregnant women, 82.1%. Both unconscious patients and all four cyanosed patients at presentation expired. Of patients presenting with tachycardia, 19 of 20 pregnant women

Parameters	Total patients (n=70)	Pregnant (n=28)	Non-Pregnant (n=42)	P value
Unconscious	2	2	-	0.30
Cyanosis	4	1	3	0.528
Tachycardia (pulse $\geq 100$ )	37	20	17	0.01
Tachypnoea (RR $\geq 20$ )	52	22	30	0.503
High BP ( $\geq 140$ )	6	5	1	0.02
Low BP (<100)	3	1	2	0.810
Low SpO <sub>2</sub> (< 90%)	31	20	11	<0.0001
Hb < 7	7	4	3	0.329
Hb 7-9	16	6	10	0.816
Total Count ( $\geq 10,000$ )	28	14	14	0.163
Unilateral consolidation on CXR	30	12	18	1
Bilateral Consolidation on CXR	23	13	10	<0.0001
Expired	37	23	14	<0.0001

**Table I:**

Table showing comparison of all parameters in swine flu patients in the two groups, pregnant and non pregnant.

Student's t test is utilized for continuous variable while chi square test is used for discrete variables. P value < 0.05 is considered significant

(95%) expired, while in non-pregnant patients, 7 patients (41.1%) had expired. 21(95.4%) pregnant patients with tachypnoea expired, while in non-pregnant patient 10(33.3%) expired. Sixty Seven percent of patients with hypotension expired. 95% of pregnant patients with hypoxia at presentation expired (19 out of 20) as compared to 54.5% (6 out of 11) mortality in non pregnant women. All ten pregnant women with anemia expired as compared to 46.1% mortality in non pregnant women. 85.7% pregnant and 42.8% non pregnant women with leucocytosis (TC >10000 per cumm) expired. 70% of pregnant women with unilateral consolidation and 100% with bilateral consolidation expired as compared to 16.6% with unilateral consolidation and 27.7% with bilateral consolidation in non pregnant women respectively. All four patients who required just non invasive ventilator support survived as compared to only one of 38 patient requiring invasive ventilation survived.

### Outcome of Pregnant Women

Twenty Eight pregnant patients had been admitted overall. Out of total 70 patients, 37(52.8%) patients expired. Of these 37 expired patients, 23 (62.16%) were pregnant, implying that the mortality in pregnant women was 82.1% (23 of 28 expired). Among 23 expired pregnant patients, 7 belonged to second trimester and 16 belonged to third trimester. None of the women in first trimester expired. All patients who developed PIH, expired.

### Outcome of Foetus

Three (10.7%) pregnant patients developed intra uterine death of the foetus during the course of admission. Seven patients of all these 28 women delivered. Five (71.4%) babies were alive while the rest two (28.5%) were still birth. The foetal survival rate was 17.8% (5/28).

Parameters	Total expired patients (n=37)	Expired Pregnant (n=23)	Expired Non-Pregnant (n=14)	P value
Unconscious	2	2	-	0.700
Cyanosis	4	1	3	0.105
Tachycardia (pulse ≥100)	36	19	17	0.421
Tachypnoea (RR ≥20)	31	21	10	0.112
High BP (≥140)	5	5	0	0.061
Low BP (<100)	2	0	2	0.062
Low SpO2 (< 90%)	25	19	6	0.012
Hb < 7	6	4	2	0.804
Hb 7-9	10	6	4	0.859
Total Count (≥10,000)	18	12	6	0.582
Unilateral consolidation on CXR	12	9	3	0.265
Bilateral Consolidation on CXR	19	13	6	0.420

**Table II:**

Table shows comparison between pregnant and non pregnant females in terms of mortality.

Student's t test is utilized for continuous variable while chi square test is used for discrete variables. P value < 0.05 is considered significant

### Outcome of Postpartum females

Seven patients underwent labour and delivered the baby. Six of these were delivered vaginally, while one underwent LSCS. One patient had convulsion on 5th postpartum day and expired. Overall, five patients (71.4%) expired after delivery. Only two of these postpartum females were discharged after delivery and came healthy one month after discharge on followup.

### DISCUSSION

In our study the disease mainly affects the young women with majority being affected were between 20 and 30 unlike the seasonal flu which mainly affects the extreme of age. Anaemia, Hypertension and Rheumatic heart disease were comorbid diseases in our patients.

Like any other respiratory disease which spreads through aerosols and respiratory

	Total pregnant (n=28)	Survived (n=5)	Expired (n=23)	P value
Unconscious	2	-	2	0.493
Cyanosis	1	0	1	0.635
Tachycardia (pulse $\geq 100$ )	20	1	19	0.005
Tachypnoea (RR $\geq 20$ )	10	6	4	0.859
High BP ( $\geq 140$ )	22	1	21	<0.0001
Low BP (<100)	5	0	5	0.250
Low SpO <sub>2</sub> (< 90%)	0	0	0	
Hb < 7	20	1	19	0.005
Hb 7-9	4	0	4	0.314
Hb 7-9	6	0	6	0.198
Total Count ( $\geq 10,000$ )	14	2	12	0.622
Unilateral consolidation on CXR	12	3	9	0.393
Bilateral Consolidation on CXR	13	0	13	0.02
IUD on USG	3	0	3	0.393
Delivered	7	2	5	0.393
Post-partum Complication	1	1	-	
Maternal outcome of delivery	7	2	5	0.393
Fetal outcome of delivery	7	5	2	-

**Table III:**  
Table shows comparison between pregnant and non pregnant females in terms of mortality.

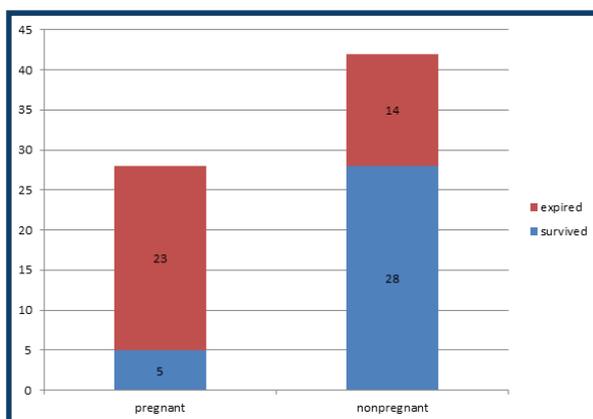
Student's t test is utilized for continuous variable while chi square test is used for discrete variables. P value < 0.05 is considered significant

secretions, the patients here had acute onset with most of them presenting between 3 and 4 days. The symptoms of the disease are similar to other respiratory viral diseases like cough, breathlessness, fever, sore throat, running nose. Clinical features indicating poor prognosis are altered sensorium, cyanosis, tachypnoea, hypotension, PIH and anaemia in pregnant patient, Spo<sub>2</sub><90% and bilateral consolidation. Unconsciousness is an indicator of hypoxia and hypercarbia, the patient presenting with it had

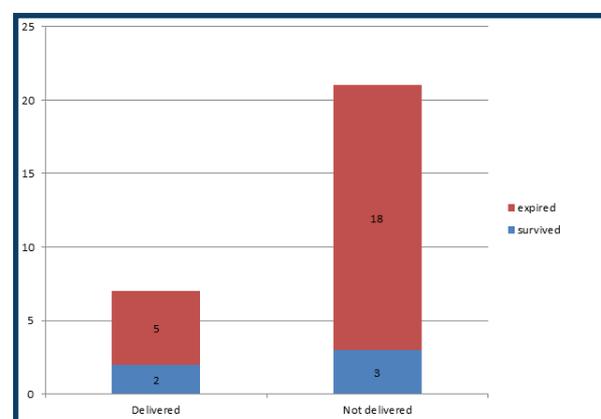
severe respiratory decompensation.

Pregnancy has poor outcome in swine flu especially those who associated with poor prognostic factors. The mother as well foetus is adversely affected. All the extrapulmonary manifestations of H1N1 are because of secondary bacterial infection or systemic inflammatory response syndrome (SIRS), which affect the mother as well as the child, making the prognosis grave not only for the mother but also for the foetus.

Twenty three (82.1%) out of 28 pregnant



**Figure 1:** Figure showing mortality in pregnant women as compared to non pregnant women ( $p < 0.05$ ).



**Figure 2:** Figure showing the difference in mortality among delivered and non delivered pregnant females.

patient had expired. The reason for poor outcome in pregnant women as compared to non pregnant women is as pregnancy is already a hyperventilated state with decrease functional residual capacity, residual volume and total lung capacity thereby, being more prone to respiratory insufficiency. Also it is an immunosuppressed state so as to act as a risk factor for secondary bacterial infection and worsening of course of the illness. Most of our patients had consolidation, which acted as a source for sepsis and septicemic shock explaining the significantly high mortality in pregnant women.

Regina Phelps in 2009 concluded that Pregnancy is a risk factor for critical illness related to 2009 H1N1 influenza, which causes maternal and neonatal morbidity and mortality. Compared with non-pregnant women of childbearing age, pregnant or postpartum women with 2009 H1N1 influenza were at increased risk of admission to an intensive care unit<sup>(11)</sup>.

The mortality appears to be higher in anaemic patient especially in pregnancy. Also the outcome in patients with chest x ray showing bilateral consolidation is less favourable than the patients with normal chest x ray. Outcome of patient on ventilator in our study was dismal, that could be explained by the fact that, only those with severe respiratory acidosis, in whom there was already onset of SIRS, were given ventilatory support.

The overall case fatality rate was 52.8% which is much higher. While in pregnancy it was 82%. Most of the patients had duration of illness less than 10 days suggesting the rapid course of the illness.

There a similar study carried out by Singhal et al.<sup>(12)</sup> which included 24 patients with pregnancy. Six patients (25%) had associated co-morbidities.

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Nine patients (37.5%) presented within 48 h of onset of symptoms and 15 (62.5%) reported after 48 h. In 17 (70.83%) patients treatment was delayed by >48 h. ICU admission was needed in 20.8 per cent patients and mortality rates was 8.3 per cent. The study states that the presenting symptoms of pregnant women with H1N1 were similar to that of general population. Acquiring infection in late trimester, late initiation of antiviral treatment and presence of co-morbid illness were high risk factors for developing critical illness. The findings resemble what we have observed in our own study.

## CONCLUSION

Novel H1N1 is a new strain of Influenza A virus that presents as an acute onset respiratory illness with the patients presenting within 3 to 5 days of onset of illness. It affects young people However, the presentation is similar to the seasonal flu virus, as the patients' presents with acute onset fever, cough and breathlessness. The mortality is much higher in pregnant women. Pregnant women also don't present with classical symptoms. Unconsciousness, cyanosis, lowspo2, anaemia, tachycardia, tachypnea, consolidation on chest-x ray are various markers associated with high mortality in pregnant women. These findings emphasize on early detection of the clinical features of swine flu and having a high degree of suspicion and low threshold for carrying out tests in pregnant women and also the treatment as the outcome in such patients is poor.

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