

Predictors of maternal mortality during H1N1 pandemic

Mamatha, Umadevi K, Sujani BK, Urvashi T, Shruti R

ABSTRACT

Background: Pandemic influenza A(H1N1) 2009 is a benign disease when infecting healthy adults, but it can lead to severe consequences in pregnant women and the fetus. There is also an increased mortality in pregnant women compared to the general population. The 2009 influenza A(H1N1) pandemic was the first ever to occur in the era of modern obstetric and intensive care management.

Aim: To study the maternal and fetal outcome in patients with H1N1 infection and to establish its influence on gestational age, mode of delivery and nutritional status as well as to look into the effect of early initiation of antiviral drug (oseltamivir).

Method: Study design- retrospective study (2009-2011). Study population-obstetrics patients (20) admitted to MSR hospital, Bangalore with flu like symptoms and tested positive with H1N1. All the patients were treated with oseltamivir and outcome measured in terms of maternal and perinatal mortality.

Result: Out of 20 patients who were tested positive, 14(70%) required ICU admission, 6(30%) women died. There was one intrauterine death and 01(5%) had termination of pregnancy at 18 weeks of gestation.

Conclusion: In developing countries like India, H1N1 infection in pregnant women is associated with significant maternal mortality. Delayed presentation to tertiary care centre, lack of awareness, restricted access to treatment might have contributed to high mortality.

Key words: H1N1 influenza, pregnancy, oseltamivir

INTRODUCTION

March 2009 witnessed a series of cases of influenza-like illness in Mexico caused by a novel H1N1 virus containing genes from swine, avian, and human influenza strains.¹ In early April 2009, an outbreak of A(H1N1) influenza spread worldwide.^{2,3} On June 11, 2009, the World Health Organization declared that criteria for influenza Pandemic had been met. Concern that this pandemic would rival the 1918 pandemic was high. Fortunately, that was not the case. Influenza-related disease activity peaked in late October to November 2009. By August 2010, the H1N1 influenza virus had moved into the post pandemic period. In contrast to previous seasonal influenza strains, the novel 2009 H1N1 strain preferentially affected young adults, with a clustering of severe and fatal cases in adults between the ages of 30 and 50 years. Additionally, H1N1 displayed a heightened potential for severe lung injury as well as gastrointestinal symptoms. Risk factors for severe disease included morbid obesity, pregnancy, immunosuppression, asthma (in children), chronic obstructive pulmonary disease,

neurological disorders, HIV-infection, poverty, and lack of access to care.⁴

H1N1-infected pregnant women were shown to have increased frequency of complications and greater morbidity than the general population.^{5,6} All the lower respiratory infections have poor prognosis in pregnant women, because the growing uterus decreases the lung expansion. H1N1 infection causes rapid deterioration of the lung function mimicking adult respiratory disease leading to hypoxia requiring high ventilator setting revealing high resistance in the lungs.

We aim to analyze the maternal and fetal outcome in patients with H1N1 infection with respect to gestational age, mode of delivery and nutritional status, and to establish the influence of early initiation of antiviral drug (oseltamivir) on its overall outcome.

MATERIAL AND METHODS

Present study is a retrospective analysis of medical records of all women (20), pregnant or

post partum, admitted to MRS hospital, Bangalore (2009-2011) who were presented with flu like symptoms and tested positive for H1N1. We documented the information about their obstetric history, length of gestation, management of current pregnancy, any complication encountered during the current pregnancy, the time of onset of labour, and mode of delivery (spontaneous, induced or cesarean section) and any post partum hemorrhage (more than 1500 ml). The data were analyzed and tabulated as frequency tables. Descriptive statistics was calculated for all study variables. Continuous variables are expressed as medians (ranges) and categorical variables as percentages. P values were calculated by using Fischers Exact test.

RESULTS

Twenty women of childbearing age consisting 12 cases of antenatal and 08 cases of post partum were admitted with confirmed H1N1 infection. The age group most affected was 20-30 years (Table-1). None of them were immunocompromised or belonged to positive retroviral status.

Table 1: Distribution of cases as per demographic profile and obstetric history

Age	<20	01(5%)
	20-30	18(90%)
	>30	01(5%)
Gravidity	Primi	06(50%)
	Multi	06(50%)
Parity	<1	04(50%)
	<2	04(50%)
Gestational age	<37 weeks	08(66.6%)
	>37weeks	04(33.3%)
Other illness	Diabetes Mellitus	01(5%)
	Rheumatic Heart Disease	02(10%)
	Anemia	04(20%)
Obstetric problems	Preeclampsia	04(20%)
	Chorioamnionitis	01(5%)

Majority of the cases (58.3%) delivered during their stay in the hospital through LSCS (Table -2). It was necessitated for the reason of maternal hypoxia leading to fetal heart abnormalities and also to decrease the mechanical restriction of the diaphragmatic movements. MTP was done in one

patient at 18 weeks as she had septicemia and renal failure. Two (16.6%) women died due to Multi Organ Dysfunction (MODS). All babies delivered through LSCS survived. Out of 08 puerperal women delivered outside, 50% got treated and discharged, whereas 50% died during treatment.

Table 2: Distribution of cases as per mode of delivery and birth weight

Mode of delivery	Medical Termination of Pregnancy	01(5%)
	Pre term vaginal delivery	01(5%)
	Lower section cesarean section	07(58.3%)
Birth weight	<2.5kg	04(50%)
	>2.5kg	04(50%)

It was observed that all those who got admitted early to the hospital and treated within one day survived; whereas those who came late (after two days) and received treatment late stayed for a longer duration in ICU and required ventilation.

Table 3: Descriptive statistics of study variables

Study Variables	Expired = 06 & DAMA= 02	Survived = 12
Interval from onset of symptoms to admission to intensive care unit	3 to 6 days	1 to 2days
Interval from onset of symptoms to first positive test result for H1N1	2 to 6 days	1 to 3 days
Suffered secondary bacterial pneumonia	07	11
ARDS	03	0
Require invasive mechanical ventilation	08	0
Require Hemodialysis	01	0
Require Vasopressors	05	03
Initiated Antiviral drugs	06	11
Interval between onset of symptom to antiviral treatment	0 to 5days	0 to 1 day
Duration of stay in intensive care unit	3 days; 21 days (one patient)	Median stay-1 day 4 patients stayed for 7days
Duration of stay less than 5 days	02	04
Duration of stay ranging from 5 to10 days	05	06
Duration of stay more than 10days	01	02

Early initiation of treatment was instituted in 90% of patients who had survived. The recommended timing for starting antiviral treatment is within 48 hours from the onset of symptoms. None of them had received vaccination.

Table 4: Interval from onset of symptoms to admission to intensive care unit

Interval		Survival	Death
From onset of symptoms and hospitalization	Less than 2 days	09(90%)	01(10%), (P<0.02)
	More than 2 days	03(30%)	07(70%)
From onset of symptoms and Admission to ICU	Less than 2 days	10(100%)	00, (P<0.001)
	More than 2 days	02(20%)	02(20%)
Initiation of ARV treatment	Less than 2 days	08(72.7%)	03(27.3%), (P<0.36)
	More than 2 days	04(44.4%)	05(55.6%)

DISCUSSION

The data reported herein are consistent with previous studies which demonstrated that pregnant women with influenza are at increased risk of serious illness and death.^{7,8,9} In addition, delayed treatment with antiviral therapy was associated with more severe illness and increased mortality, as shown previously for both seasonal influenza and 2009 influenza A(H1N1). Whereas, early treatment initiation has been associated with reduced illness duration, symptom severity, mortality, secondary complications and hospitalizations.^{10,11}

Present study also showed that among the hospitalized patients, early initiation of treatment (within 1 to 2 days) was associated with much better outcome compared to late treatment. These data are not consistent with other studies which suggest that some benefit might be achieved even if treatment is delayed as many as 4 days after onset of symptoms.¹²

Puvanalingam et al., in a case series study of clinical profile of H1N1 influenza infection concluded that in those individuals with comorbid conditions, pregnancy were found to be severely affected and most common cause of death in

patients was due to pneumonia.¹³ Ventilator requirement was associated with poor prognosis in H1N1 patients. Their observations are very much consistent with the findings of our study.

We observed that while making right decision in regard to mode of delivery, one must consider the viability of fetus as well as the inherent risk of intractable maternal hypoxia. Although cesarean section allows more rapid delivery in the critically ill patients, the increased operative stress may be associated with higher mortality.¹⁴ Therefore, delivery should not be performed with the sole purpose of improving maternal oxygenation or ventilation. However, it is important that urgent delivery and neonatal resuscitation has to be available in the event of sudden maternal or fetal deterioration. Obstetric indications should always determine the mode of delivery.

CONCLUSION

Pregnant women especially in the second half of pregnancy had a disproportionately high risk of mortality due to 2009 influenza A (H1N1). Early institution of antiviral treatment with oseltamivir in pregnant women appeared to be associated with fewer admissions to an ICU and fewer deaths.

AUTHOR NOTE

Mamatha, Assistant Professor, Contact- 09900377955, E-mail: mamatha750@ymail.com

(Corresponding Author)

Umadevi K, Professor and Head of Department

Sujani BK, Professor

Urvashi Thukral, Lecturer

Shruti Rammohan, Junior resident

Department of OBG, MS Ramaiah Medical College, Bangalore- 560054, Karnataka, INDIA.

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