

Characteristics of pregnant Women admitted with 2009 H1N1 Influenza in a referral maternity hospital at Al-Madinah, Saudi Arabia.

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ABSTRACT

Background: To date there has been no study done in Saudi Arabia to identify the risk factors for poor outcome of H1N1 infection in pregnancy.

Objectives: we aimed to evaluate the epidemiological data, clinical course, treatment modalities, and maternal and fetal outcomes of 33 pregnant women diagnosed with H1N1 Influenza A in a referral maternity and children hospital at Al- Madinah Saudi Arabia on the period from June 2009 till February 2010.

Methods: This retrospective cohort study reported 33 pregnant women (9.1% primigravida) aged 27.7 ± 5.6 years who were laboratory-confirmed cases diagnosed with H1N1 Influenza A in a referral maternity and children hospital at Al- Madinah Saudi Arabia on the period from June 2009 till February 2010. Their mean gestation age was 23.5 ± 10.9 weeks with history of bronchial asthma in 45.5%.

Results: The mean duration between symptoms' onset and hospital presentation was 5.0 ± 2.2 days with late presentation in 10 cases (30.3%). Large number of cases presented with fever more than 39 (24 (72.7%), sore-throat (24 (72.7%) and cough (29 (87.9%) while 19 patients presented with dyspnea (57.6%). Pregnant patients with H1N1 received Tamiflu (oseltamivir) from 2 to 7 days with a mean of 4.7 ± 1.3 days. They stayed at hospital for variable periods from 2 to 28 days with a mean of 7.9 ± 6.6 days (Table 4). Most patients (31(93.9%)) received antibiotics. Maternal poor outcome included hypoxia in 6 patients (18.2%), ICU admission for 2-3 days with mechanical ventilation in 4(12.1%). The main fetal poor outcome was intrauterine fetal death in 2 (6.1%) babies .

Conclusion:

The main presentation of H1N1 among pregnant women was typical influenza-like illness. Considerable percentage of patients presented late (30.3%). The duration of hospital admission is variable up to 28 days. Bronchial asthma was prevalent (45.5%) among pregnant women with H1N1 infection. The main poor outcomes were maternal respiratory failure (18.2%) and intrauterine fetal death (6.1%). There is increased risk of intrauterine fetal mortality (6.1%) rather than maternal mortality (0%) .

Keywords ; H1N1 , Pregnancy .

INTRODUCTION

The 2009 pandemic H1N1, a novel subtype of the influenza A virus, has been reported to cause broad spectrum of clinical syndromes, ranging from afebrile upper respiratory illness to fulminant viral pneumonia (WHO) (1). The rates of illness (7.5%-11%) and hospitalizations varied according to country (2). The overall case fatality rate has been less than 0.5% and occurred mainly among children and nonelderly adults (3).

Apart from patients with immune-suppression and neurologic diseases, studies showed that the risk groups for severe 2009 H1N1 virus infection include pregnant women especially in their second or third trimester and women who are less than 2 weeks post partum (3-8). Among patients with 2009 H1N1 virus infection, 7 to 10% of hospitalized patients (3-5), 6 to 9% of ICU patients (6,7), and 6 to 10% of mortal patients (4,8) were pregnant women. It was

found that the risk of death among infected pregnant women increased during the third trimester (9), and with human immunodeficiency virus (HIV) coinfection (10). Pregnant women are at increased risk for afebrile or atypical presentations, severe illness, spontaneous abortion, preterm labor and birth, and fetal distress (8,9,19,20). The risk of spread of the 2009 H1N1 virus to the fetus has been reported from both possible transplacental transmission (11) as well as respiratory transmission from a symptomatic mother during the postpartum period. Infected newborn infants were found to experience apnea, tachypnea, cyanosis, and lethargy (8,9).

The importance of the potentially pandemic H1N1 viral infection in public health in Saudi Arabia is unquestionable because of the possible transmission from and to the travelers for Omra and Pilgrimage performance. This necessitates proper characterization of clinical syndromes for improved public health consequences. Many Saudi researchers published data about communicability of influenza in households (12), characteristics of adults and children hospitalized with 2009 H1N1 Influenza (13-16), low prevalence of the virus among healthcare workers (17), very low pandemic prevalence among arriving pilgrims, and low amplification of transmission among departing pilgrim (18). However, available data on disease characteristics and outcome among Saudi pregnant women are limited. One Saudi study (21) found that Influenza A H1N1 was more common in the younger age group and in female dependents, and it was more severe among pregnant women. Therefore, this study aimed to report the epidemiological data, clinical course, treatment modalities, and maternal and fetal outcomes of 33 pregnant women diagnosed with H1N1 Influenza A in a referral maternity and children hospital at Al-Madinah Saudi Arabia on the period from June 2009 till February 2010.

METHODOLOGY

This retrospective cohort study was conducted according to the Declaration of Helsinki and approved by the local ethical committee.

A case was defined as a pregnant woman of any age, of any nationality, and of any parity who was hospitalized for at least 24 hours or died with laboratory results indicative of confirmed pandemic 2009 influenza A(H1N1) virus infection. A confirmed case was defined as an acute respiratory illness with laboratory-confirmed pandemic H1N1 virus infection by real-time reverse-transcriptase PCR. According to the hospital palsy, nasopharyngeal and oropharyngeal aspirates or swabs were sent to the Ministry of Health (MOH) Regional Laboratory in Madinah, KSA to confirm the diagnosis using conventional or real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay for Viral RNA detection (22)

For all H1N1 confirmed hospitalized pregnant women, data including age, gestational age, gravity, medical history, clinical presentation and course, comorbid conditions, and laboratory and radiographic findings, hospitalization data, treatment modalities and maternal and fetal outcomes were abstracted from medical records after verbal consent from all included women.

RESULTS

This study reported 33 pregnant women diagnosed with H1N1 Influenza A in a referral maternity and children hospital at Al-Madinah Saudi Arabia on the period from June 2009 till February 2010. The mean age of the patients was 27.7 ± 5.6 years with 48.5% of them between 20-29 years old. They included primigravida (9.1%) as well as multipravid (90.9%). Their mean gestation age was 23.5 ± 10.9 weeks (24.2% in the first trimester, 36.4% in the second trimester and 39.4% in the third trimester) (Table 1).

Two cases of the included patients were having diabetes (6.1%), 1 was obese (3%) and a substantial number was having bronchial asthma (15 (45.5%)) (Table 2).

The mean duration between symptoms' onset and hospital presentation was 5.0 ± 2.2 days. The majority (14 (42.4%)) presented after 4 days, however 10 cases (30.3%) presented late (7 cases (21.2%) presented after 6 days and 3 cases (9.1%) presented after 8 days) (Table 3). Large number of cases presented with fever more than 39 (24 (72.7%)), sorethroat (24 (72.7%)) and cough (29 (87.9%)) while 19 patients presented with dyspnea (57.6%)(Table 3).

Pregnant patients with H1N1 received antiviral medication (Tamiflu (oseltamivir)) from 2 to 7 days with a mean of 4.7 ± 1.3 days. They stayed at hospital for variable periods from 2 to 28 days with a mean of 7.9 ± 6.6 days (Table 4).

Most patients (31(93.9%)) received antibiotics. Maternal complications included hypoxia in 6 patients (18.2%), ICU admission for 2-3 days in 4 (12.1%) and need for mechanical ventilation in all of them (4(12.1%)). The main fetal poor outcome was intrauterine fetal death in 2 (6.1%) babies (table 5).

STATISTICAL ANALYSIS

The data were analyzed using SPSS software version 17. Data were expressed as mean \pm SD for quantitative parametric measures and both number and percentage for categorized data. All tests were 2-tailed and considered significant when $p < 0.05$.

DISCUSSION

This study reported the epidemiological data, clinical course, treatment modalities, and maternal and fetal outcomes of 33 pregnant women, aged 27.7 ± 5.6 years and diagnosed with H1N1 Influenza A in a referral maternity and children hospital at Al- Madinah Saudi Arabia on the period from June 2009 till February 2010.

This number of confirmed cases from one Saudi hospital is extremely high compared to the 34 confirmed or probable cases of pandemic H1N1 in pregnant women that were reported to CDC from 13 states over the period from April 15 to May 18, 2009 (23). This is true even if we compare this reported number to what was reported in 2

other Saudi studies who reported 52 cases (37 females) (13) and 47 (24) hospitalized non pregnant adults with H1N1 infection.

Most patients presented with typical influenza-like illness with fever (72.7%), sorethroat (72.7%) and cough (87.9%) but a considerable percentage of cases (57.6%) presented with and dyspnea. Systemic symptoms and gastrointestinal symptoms were absent in this series of cases in contrast to other studies in non pregnant adults (26,27).

In one Saudi study (13) of total of 52 adult patients with 2009 H1N1 influenza, similar presentation was recorded apart from less frequent dyspnea (34.5%).

This could be explained by relatively high prevalence of bronchial asthma among our pregnant patients (45.5%). Among hospitalized patients with 2009 H1N1 infection, a history of asthma has been reported in 24 to 50% of children and adults, and COPD in 36% of adults (4, 28).

In this study, 18.2% of pregnant patients developed severe infection with hypoxia and 12.1% was on mechanical ventilation to manage their respiratory failure with no reported mortality. These complications were less frequent than that reported in non pregnant Saudis with the same disease (13) who reported hypoxia in 55.6%, pneumonia in 40.2 %, ICU admission in 19.2% and death (16.7%). For the 2009 H1N1 viral infection, diffuse viral pneumonitis may complicate the course of the illness leading to hospitalization and intensive care and is associated with severe hypoxemia, ARDS, and sometimes shock and renal failure (7, 28). Pregnant women with H1N1 virus infection are considered high risk group particularly in their second or third trimesters (3-8,9) and may present with afebrile or atypical presentations (8, 9, 19, 20). In one Saudi study conducted in Aramco Medical Services Organization in the Eastern province (21) a total of 587 cases were diagnosed with H1N1. Their study showed that H1N1 was more common in the younger age group and in female dependents, and it was more severe among pregnant women (21). On study in US

reported six deaths in pregnant women with H1N1, all were in women who had developed pneumonia and subsequent acute respiratory distress syndrome requiring mechanical ventilation (23). However, in the current study no maternal mortality was reported despite respiratory complications, ICU admission with mechanical ventilation in 12.1 % of cases. This low mortality among Saudi pregnant women could not be explained by early hospitalizations as 30.3% presented late or early treatment as some received treatment as late as 7 days. Other environmental factors may be responsible as different countries have reported different rates of death (3). Low mortality rate among Saudi adults was also reported by other Saudi study (14) who studied 47 hospitalized cases with confirmed novel H1N1 virus infection.

On the other hand, the main fetal poor outcome was intrauterine fetal death in 2 (6.1%) cases. There was no reported increased risk for spontaneous abortion, preterm labor and birth as seen in other studies (8,9,19,20). Transplacental transmission of the 2009 H1N1 virus (11) could explain the reported 2 cases of intrauterine fetal death that were reported.

All pregnant patients in our study received neuraminidase inhibitor antiviral medication (Tamiflu (oseltamivir)) from 2 to 7 days with a mean of 4.7 ± 1.3 days. Early treatment with oseltamivir is especially important for patients with severe or progressive clinical illness and pregnancy (28), unless viral resistance has been documented or is suspected. and most patients (31(93.9%)) received antibiotics for suspected coexistent bacterial pneumonia however, bacterial infection has been reported by other researchers in only 20 to 24% of ICU patients and in 26 to 38% of patients who died (7,27). This may reflect over use of antibiotics among our patients.

The main strength point in this study was the recorded number of pregnant women with 2009 H1N1 viral infection while the main limitations include the study design and the absence of proper assessment of risk factors for severity of cases.

Conclusion:

The majority of pregnant women with 2009 H1N1 influenza A-associated hospitalization in this study presented with typical influenza-like illness and had an uncomplicated course. Some patients presented late (30.3%). The duration of admission is variable up to 28 days. Bronchial asthma was prevalent (45.5%) among pregnant women with H1N1 infection. The main poor outcomes were fetal ((6.1%)) rather than maternal mortality with respiratory failure (18.2%) as the main complication among women. We can recommend that early detection, admission and specific treatment should be given to pregnant women with any influenza outbreak. Special care should be given to pregnant women prior to each influenza season and immunizing with H1N1 influenza A vaccination to women in the child bearing period should be encouraged. Further work are recommended to better identify the risk factors for severity of the disease and the poor outcome among pregnant women.

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REFERENCES

1. **Pandemic (H1N1) 2009** — update 94. Geneva: World Health Organization, April 1, (2010). (Accessed April 9, 2010, at http://www.who.int/csr/don/2010_04_01/en/index.html.)
2. **Baker MG, Wilson N, Huang QS, et al.** (2009); Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill*;14:pii19319-pii19319

3. Transmission dynamics and impact of pandemic influenza A (H1N1) 2009 virus. *Wkly Epidemiol Rec* .,(2009);84:481-484.
1. **Louie JK, Acosta M, Winter K, et al.** (2009) ;Factors associated with death or hospitalization due to pandemic 2009 influenza A(H1N1) infection in California. *JAMA*;302:1896-1902. [CrossRef](#) | [Web of Science](#) | [Medline](#)
2. **Jain S, Kamimoto L, Bramley AM, et al.** (2009); Hospitalized patients with 2009 H1N1 influenza in the United States, April-June. *N Engl J Med* 2009;361:1935-1944. [Free Full Text](#) | [Web of Science](#) | [Medline](#)
3. **The ANZIC Influenza Investigators.** (2009) ;Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med*;361:1925-1934. [Free Full Text](#) | [Web of Science](#) | [Medline](#)
4. **Kumar A, Zarychanski R, Pinto R, et al.** (2009) ; Critically ill patients with 2009 influenza A(H1N1) infection in Canada. *JAMA*;302:1872-1879. [CrossRef](#) | [Web of Science](#) | [Medline](#)
5. **Louie JK, Acosta M, Jamieson DJ, Honein MA.** (2010) ; Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med* ;362:27-35. [Free Full Text](#) | [Web of Science](#) | [Medline](#)
6. **Jamieson DJ, Honein MA, Rasmussen SA, et al.** (2009) ; H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet*;374:451-458. [CrossRef](#) | [Web of Science](#) | [Medline](#)
7. **Archer B, Cohen C, Naidoo D, et al.** (2009) ; Interim report on pandemic H1N1 influenza virus infections in South Africa, April to October 2009: epidemiology and factors associated with fatal cases. *Euro Surveill* ;14:pii19639-pii19639.
8. **Dulyachai W, Makkoch J, Rianthavorn P, et al.** (2010);Perinatal pandemic (H1N1) 2009 infection.; Thailand. *Emerg Infect Dis* 16:343-344. [Web of Science](#) | [Medline](#)
9. **Mohamed AG, BinSaeed AA, Al-Habib H, Al-Saif H.** (2012) ; Communicability of H1N1 and seasonal influenza among household contacts of cases in large families. *Influenza Other Respi Viruses.* (3):25-9.
10. **Agha A, Alrawi A, Munayco CV, Alayed MS, Al-Hakami M, Korairi H, Bella A.**(2012); Characteristics of Patients Hospitalized with 2009 H1N1 Influenza in a Tertiary Care Hospital in Southern Saudi Arabia. *Ann Saudi Med.* 32(1):86-9.
11. **Al-Tawfiq JA, Abed M, Saadeh BM, Ghandour J, Shaltaf M, Babiker MM.** (2011) ; Pandemic influenza A (2009 H1N1) in hospitalized patients in a Saudi Arabian hospital: epidemiology and clinical comparison with H1N1-negative patients. *J Infect Public Health.* 4(5-6):228-34.
12. **Mansour MM, Al Hadidib KM.** (2012); 2009 H1N1 influenza A in children: a descriptive clinical study; *Ann Saudi Med.* 32(1):59-63.
13. **Al Subaie SS, Al Saadi MA.** (2012);Features associated with severe disease in hospitalized children with 2009 influenza A (H1N1) infection at a university hospital in Riyadh, Saudi Arabia ;*Ann Saudi Med.* 32(1):53-8.
14. **Memish ZA, Assiri AM, Alshehri M, Hussain R, Alomar I.** (2012) ; The prevalence of respiratory viruses among healthcare workers serving pilgrims in Makkah during the 2009 influenza A (H1N1) pandemic. *Travel Med Infect Dis.* 10(1):18-24.)
15. **Memish ZA, Assiri AM, Hussain R, Alomar I, Stephens G.** (2012) ; Detection of respiratory viruses among pilgrims in Saudi Arabia during the time of a declared influenza A(H1N1) pandemic. *J Travel Med.*;19(1):15-21.
16. Human infection with new influenza A (H1N1) virus: clinical observations from Mexico and other affected countries, May 2009. *Wkly Epidemiol Rec*(2009) ; 84:185-189 [Medline](#)
17. **Kidd IM, Down J, Nastouli E, et al.** (2009) ; H1N1 pneumonitis treated with intravenous zanamivir. *Lancet*; 374:1036-1036. [CrossRef](#) | [Web of Science](#) | [Medline](#)
18. **Herzallah HK, Bubshait SA, Antony AK, Al-Otaibi ST.** (2011); Incidence of influenza A H1N1 2009 infection in Eastern Saudi Arabian hospitals. *Saudi Med J.* 32(6):598-602.
19. Clinical management of human infection with pandemic (H1N1)(2009): revised guidance. Geneva: World Health Organization, (Accessed April 9, 2010,at : http://www.who.int/csr/resources/publication/s/swineflu/clinical_management/en/index.html.)
20. Mangtani P, Mak TK, Pfeifer d. (2009); Pandemic H1N1 infection in pregnant women in the USA. *The Lancet* 374, 9688,8–14, 429-430.
21. **Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team** (2009);

- Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med* 2009;360:2605-2615[Erratum, *N Engl J Med*;361:102.]
22. Human infection with new influenza A (H1N1) virus: clinical observations from Mexico and other affected countries, (2009). *Wkly Epidemiol Rec* 2009;84:185-189.[Medline](#)
23. **Jain S, Kamimoto L, Bramley AM, et al.** (2009); Hospitalized patients with 2009 H1N1 influenza in the United States, *N Engl J Med* 2009;361:1935-1944.[Free Full Text](#) | [Web of Science](#) | [Medline](#)
24. **The ANZIC Influenza Investigators** (2009);. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med* 361:1925-1934 [Free Full Text](#) | [Web of Science](#) | [Medline](#)
25. **Lim ML, Chong CY, Tee WS, Lim WY, Chee JJ.** (2010) ; Influenza A/H1N1 (2009) infection in pregnancy — an Asian perspective. *BJOG* (Epub ahead of print).

Table (1): Personal and obstetric characteristics of the studied pregnant females admitted with H1N1 Influenza

Personal and obstetric characteristics	Studied pregnant females (n=33)	
	No.	%
Patient age (years)		
Less than 20	3	9.1
20-<30	16	48.5
30-<40	14	42.4
Min-Max	17-40	
Mean±SD	27.7±5.6	
Gestational age (weeks)		
First trimester(1-12)	8	24.2
Second trimester (13-28)	12	36.4
Third trimester (29- 40)	13	39.4
Min-Max	6-38	
Mean±SD	23.5±10.9	
Parity		
G1	3	9.1
G2	6	18.2
G3	7	21.2
G4	6	18.2
G5	8	24.2
G6 or more	3	9.1

Table (2): Past medical history of the studied pregnant females admitted with H1N1 Influenza

Past medical history	Studied pregnant females (n=33)	
	No.	%
Diabetes Mellitus		
Absent	31	93.9
Present	2	6.1
Hypertension		
Absent	33	100.0
Present	0	0.0
Bronchial asthma		
Absent	18	54.5
Present	15	45.5
Obesity		
Absent	32	97.0
Present	1	3.0
Hypoxia		
Absent	27	81.8
Present	6	18.2

Table (3): Medical presentation and complications among the studied pregnant females admitted with H1N1 Influenza

Medical presentation and complications	Studied pregnant females (n=33)	
	No.	%
Duration between onset of symptoms till hospital presentation (days)		
2-	9	27.3
4-	14	42.4
6-	7	21.2
8 or more	3	9.1
Min-Max	2-11	
Mean±SD	5.0±2.2	
Fever more than 39		
Absent	9	27.3
Present	24	72.7
Sore throat		
Absent	9	27.3
Present	24	72.7
Cough		
Absent	4	12.1
Present	29	87.9
Dyspnea		
Absent	14	42.4
Present	19	57.6
Intrauterine fetal death		
No	31	93.9
Yes	2	6.1

Table (4): Treatment modalities used among the studied pregnant females admitted with H1N1 Influenza

Treatment modalities	Studied pregnant females (n=33)	
	No.	%
Duration of using Tamiflu (days)		
2-	9	27.3
4-	19	57.6
6-	5	15.1
Min-Max	2-7	
Mean±SD	4.7±1.3	
Duration of ICU stay		
None	29	87.9
Yes (2-3 days)	4	12.1
Duration of hospital stay (days)		
Less than 5	11	33.3
5-	14	42.5
10-	4	12.1
15 or more	4	12.1
Min-Max	2-28	
Mean±SD	7.9±6.6	
Need for mechanical ventilation		
No	29	87.9
Yes	4	12.1
Use of antibiotics other than Tamiflu		
No	2	6.1
Yes	31	93.9