Original Article

Obstetric Outcomes of Influenza A H1N1 (2009) Infection in Pregnancy – Experience of a Singapore Tertiary Hospital

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Abstract

Introduction: Influenza A H1N1 (2009) pandemic has affected countries worldwide including Singapore. Data on obstetric outcomes of women with H1N1 (2009) in pregnancy are lacking. Materials and Methods: This was an observational study analysing the obstetric outcomes of pregnant women with influenza A H1N1 (2009) infection who had delivered at a viable gestation (24 weeks or more) in our centre. Results: Between 23 June 2009 and 30 September 2009, 235 pregnant women were diagnosed with influenza A H1N1 (2009) at our centre, with 42 having delivered and comprising the study cohort. Median age was 27.5 years (range, 16 to 42). Multiparous women comprised 59.5% (25/42) whilst 40.5% (17/42) were primiparous. In terms of ethnicity, 61.9% were Malays, 26.2% Chinese, 4.8% Indians and 7.1% Others. All women received oseltamivir. All had shown recovery from the acute influenza infection. There were no respiratory complications. Twenty-nine women (69.0%) delivered at term. Twenty-five women (59.5%) had spontaneous labour whilst 15 (35.7%) had labour induction. Two women (4.8%) did not labour. Thirty-six women (85.7%) had vaginal delivery, of whom 3 were instrumental deliveries. Apgar scores of greater than 8 at 1 min and 5 min were documented in babies of 95.2% (40/42) women, respectively. Thirty-two women (76.2%) delivered babies with birthweights greater than 2500 g. Compared with historical data from 2008, the H1N1 cohort had comparable mean birthweight and average gestational age at delivery of 38 weeks. Conclusion: Our study suggested that obstetric outcomes were not adversely affected by influenza A H1N1 (2009) infection.

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Key words: Apgar score, Babies, Birthweight, Gestational age

Introduction

Influenza A H1N1 (2009) is a new viral strain containing gene segments from human, swine and avian lineages.[1] Soon after reports of human cases of the infection in April 2009,[2] the World Health Organization declared the situation a public health emergency of international concern.[3] In previous influenza pandemics and epidemics, pregnancy was noted to be a high risk group associated with increased maternal mortality and morbidity.[4-7] The current H1N1 pandemic has appeared to be no less severe, with reports of maternal death and pneumonia in the early stage of the outbreak.[8] Data relating to the effects of H1N1 (2009) on pregnancy outcomes are limited. The scarce data on influenza and obstetric outcomes, however, present conflicting findings in terms of risk of congenital malformation, abortion, stillbirth, premature delivery and low birthweight.[9-11]

With this in mind, we set out to determine the obstetric outcomes of women with influenza A H1N1 (2009) infection in pregnancy.

Materials and Methods

KK Women's & Children's Hospital, a tertiary referral centre, is responsible for over 12,000 deliveries per annum which accounts for 30% of births in Singapore. We identified all pregnant women with influenza A H1N1 (2009) diagnosis made between 23 June 2009 (date of diagnosis of first

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case in pregnancy at our centre) and 30 September 2009. All women who had delivered in our centre at the time of writing were included for analysis.

"Cases" were defined as pregnant women who presented with flu-like illness and/or fever and were confirmed to be positive for influenza A H1N1 (2009) infection on nasopharyngeal swab. A real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay was set up on the Rotor-Gene Q (Qiagen, Germany) using primers and probe that target the haemagglutinin gene of influenza A H1N1 (2009). The assay was adapted from primers and probe used by the National Public Health Laboratory Singapore.

Patients confirmed to have influenza A H1N1 (2009) were offered treatment with oseltamivir (75 mg twice daily for 5 days). Inhaled zanamivir was offered as a second-line drug. In cases presenting with severe symptoms, empirical treatment was offered pending the result of the nasopharyngeal swab.

Using Stata 9.2, statistical analysis was performed on variables such as age, parity, ethnicity, gestation when H1N1 infection was diagnosed, contact history [contact with a confirmed influenza A (H1N1) 2009 case], travel history, presence of comorbidity, interval between symptom onset and commencement of antiviral therapy, whether labour was spontaneous or induced, gestation at delivery ("term" defined as 38+0 weeks), mode of delivery, 1 min and 5 min Apgar scores and birthweight. Distributions of sample characteristics were examined using proportions in percentages or central tendencies. Using one sample *t*-test, gestational age at delivery, birthweight and mode of delivery were compared with our institutional average based on year 2008 delivery data.

Results

Between 23 June 2009 and 30 September 2009, a total of 235 pregnant women were diagnosed with influenza A H1N1 (2009) infection at our centre. Of these, 101 were undelivered at the time of writing, 47 had delivered and 87 were booked for obstetric care elsewhere.

Of the 47 women who had delivered, 1 woman had spontaneous miscarriage at 19 weeks gestation (H1N1 diagnosis at 15 weeks gestation), 1 had social termination of pregnancy at 13 weeks gestation (H1N1 diagnosis at 6 weeks gestation), 1 had termination of pregnancy for multiple fetal anomalies at 20 weeks gestation (H1N1 diagnosis at 17 weeks gestation) and 2 had spontaneous miscarriage in the first trimester (H1N1 diagnosis at the time of admission for miscarriage). Forty-two women had delivered at viable gestations (24 weeks or greater). The final analysis was made on the 42 women.

The characteristics of this cohort of 42 women are detailed in Table 1. The median age was 27.5 years (range, 16 to

Table 1. Characteristics of 42 Women with Influenza A H1N1 (2009) Infection who had Delivered

	Frequency	%
Maternal age (y)		
<18	2	4.8
18-29	26	61.9
>29	14	33.3
Parity		
Primiparous	17	40.5
Multiparous	25	59.5
Gestation when H1N1 diagnosed (weeks)		
Second trimester	11	26.2
Third trimester	31	73.8
Race		
Chinese	11	26.2
Malay	26	61.9
Indian	2	4.8
Others	3	7.1
Travel history		
Yes	1	2.4
No	41	97.6
Contact history		
Yes	1	2.4
No	41	97.6
Comorbidity		
Yes	6	14.3
- Asthma	5	
- Hypertension	1	
No	36	85.7
Symptoms at presentation		
Fever	34	81.0
Cough	36	85.7
Rhinorrhoea	20	47.6
Sorethroat	27	64.3
Breathlessness	5	11.9
Headache	9	21.4
Myalgia	13	31.0
Interval between onset of symptoms and presentation (days)		
<=1	14	33.3
<=2	18	42.9
>=3	10	23.8
Interval between onset of symptoms and commencement of treatment (days)		
<=1	8	19.0
<=2	16	38.1
>=3	18	42.9

Table 2. Obstetric Outcomes of 42 Women with Influenza A H1N1 (2009) Infection who had Delivered

		Frequency	%
Gestation at delivery (weeks)			
37 weeks or less		13	31.0
38 weeks or above		29	69.0
Labour			
Spontaneous		25	59.5
Induction		15	35.7
No labour		2	4.8
Mode of delivery			
Normal vaginal delivery		33	78.6
Caesarean section		6	14.3
Instrumental delivery		3	7.1
Apgar score			
1 minute	<=7	2	
	>=8	41*	
5 minute	<=7	2	
	>=8	41*	
Birthweight			
2500 g or less		11*	
2501-3500 g		26	
3501-4000 g		6	

(*includes a set of twins)

42). Twenty-five women (59.5%) were multiparous and 17 (40.5%) were primiparous. The diagnosis of influenza A H1N1 (2009) was made in third trimester of pregnancy in 31 women (73.8%) and the remaining 11 women (26.2%) had the diagnosis made in the second trimester. Malays made up 61.9% (26/42), Chinese 26.2% (11/42), Indians 4.8% (2/42) whilst Others comprised 7.1% (3/42). Travel and contact histories were elicited in 2 women, respectively. Six women (14.3%) had comorbidities, notably asthma and hypertension. Symptoms reported at presentation included fever (n = 34), cough (n = 36), rhinorrhoea (n = 20), sorethroat (n = 27), breathlessness (n = 5), myalgia (n = 13) and headache (n = 9). The median time interval between onset of symptoms and presentation to hospital was 2.0 days (range, 1 to 7). The median time interval between onset of symptoms and commencement of treatment was 2.0 days (range, 1 to 8). All women received oseltamivir. All recovered from the acute influenza infection. None developed respiratory complications.

There were 2 cases of obstetric complications. One woman had presented with preterm labour at 25 weeks gestation and progressed to delivery. One woman had presented with threatened preterm labour at 33 weeks gestation but settled and eventually delivered at 38 weeks. The obstetric outcomes for the cohort of 42 women are summarised in Table 2. Of those who delivered preterm (n = 13), 12 were at gestations between 35 weeks and 37 weeks and 1 was at 25 weeks as described. Assisted vaginal deliveries in 3 women were performed for indications of maternal exhaustion and non-reassuring fetal heart tracing. Indications for caesarean section included failure to progress (n = 2), maternal request (n = 1), previous caesarean section (n = 1), failed induction of labour (n = 1) and twin pregnancy (n = 1). Induction of labour was performed in 15 women for the following reasons: favourable cervix = 1, maternal request = 1, post-dates = 3, reduced fetal movements = 2, hypertension = 1, rupture of membranes = 4 and abnormal amniotic fluid index = 3.

When compared with the population delivering in our institution for the year 2008, we found that the caesarean section rate for the influenza A H1N1 (2009) cohort was significantly lower than the previous year's average, at a difference of 15.7% with 95% CI, -27% to -5%. The H1N1 cohort delivered at an average gestational age of approximately 38 weeks which was comparable with the institutional average. We also did not see any significant differences in birth weight; at a mean difference of 136.46 g at 95% CI, -318.66 to 45.73 (Table 3).

Discussion

In this paper, we report the clinical characteristics and obstetric outcomes of a delivered cohort of H1N1 (2009)-infected pregnant women. Of the women who delivered at viable gestation, almost 70% had delivered at term. Of the remaining, all (with the exception of 1 woman) had delivered between a gestation of 35 weeks and 37 weeks. Compared with our institutional mean gestational age at delivery for the period between 1 January 2008 and

Table 3. Comparison of Outcome Measures with Institutional Deliveries for Year 2008

Outcomes	Mean outcome measure (H1N1 cohort of 42 deliveries)	Mean outcome measure (2008 of 12,468 deliveries)	Difference in mean	95% confidence interval
Gestational age at delivery	37.71	37.93	-0.216	-0.96 to 0.53
Birthweight	2890.28	3026.74	-136.46	-318.66 to 45.73
Caesarean deliveries	14%	30%	-15.7%	-27% to -5%

31 December 2008, no significant difference was detected. Looking at the birthweight, the mean for the H1N1 (2009) cohort was comparable with the institutional mean. The novelty of H1N1 (2009) virus means there is limited knowledge about its pathogenicity and impact on pregnancy outcomes. Although there had been observations of a higher incidence of adverse outcomes from past influenza pandemics and epidemics, these reports faced limitations such as reliance on a clinical diagnosis of influenza (rather than laboratory confirmation) and retrospective historical data.[9,10]

Our preliminary observations suggest that the influenza A H1N1 (2009) infection is relatively benign and not associated with significant adverse obstetric outcomes. It is possible that this is true. For a fetus to be affected by an injurious agent, transplacental transmission must occur. The latter is thought not to occur with influenza infection. This assertion was made by authors of a case-control study which found an absence of influenza-specific IgM in the cord blood of infants born to mothers with influenza infection during pregnancy.[11] It is also plausible that the observed favourable outcomes were attributed to prompt institution of oseltamivir which has been shown to reduce the duration of fever, the severity of illness and the duration of illness.[12] By shortening the acute phase of the infection, the viraemic state is reduced and hence a lower chance of spread of infection beyond the respiratory tract. In our cohort, all confirmed cases received the recommended 5 days of oseltamivir 75 mg twice daily. The median interval between symptom onset and treatment was 2.0 days. The expeditious commencement of treatment was possible due to early presentation as evident in the median time interval between the onset of symptoms and presentation of 2.0 days.

Our study was however subject to limitations. Firstly, data presented were derived from a small sample size with follow-up limited to immediate post-delivery period. Secondly, a proportion of the women were lost to follow-up as they were booked for antenatal care in other hospitals. Thirdly, it is possible some H1N1-infected pregnant women may be asymptomatic and hence not captured in the study.

To date, there is little published data on obstetric outcomes in the context of influenza A H1N1 (2009) infection. Despite our limitations, this is the largest case series available at the time of writing.

Conclusion

Our observational study suggests that obstetric outcomes are not adversely influenced by the influenza A H1N1 (2009) infection. It is perhaps appropriate to regard this infection to be similar to seasonal influenza infection.

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