Arch Clin Infect Dis. 2019 June; 14(3):e96403. doi: 10.5812/archcid.96403.

Published online 2019 July 30. **Research Article**

Risk Factors Associated with Outcomes of Seasonal Influenza in Pregnant Women Referring to Healthcare Centers in Iran in 2015 - 2016

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Received 2019 July 16; **Accepted** 2019 July 16.

Abstract

Background: Influenza causes high mortality rate among pregnant women, while morbidity and mortality cases of this disease and its side effects among pregnant women can be simply prevented by vaccination and reducing risk factors such as cardiovascular diseases, diabetes, hypertension, etc.
Objectives: Hence, this study was conducted to investigate the risk factors and mortality rate of seasonal influenza among pregnant women referring to healthcare centers in Iran during 2015 - 2016.
Methods: This case-control study was conducted to examine the odds ratio of seasonal influenza among pregnant women with seasonal influenza who had referred to all healthcare centers in Iran with severe respiratory disease symptoms during 2015-2016. The statistical population consisted of 2,080 pregnant women of whom, 24 dead women constituted the case group and 100 randomly selected living women constituted the control group. A researcher-made checklist was used for data collection. The collected data were analyzed using the statistical test of the odds ratio with SPSS-22 software.
Results: Mean (standard deviation) of age was 31 (2.3) and 34 (3.8) in living and dead pregnant women, respectively. The most frequent type of conflicting influenza virus was H1N1 in both case and control groups (83% and 71%, respectively). There was a significant difference between case and control groups in the risk factors including diabetes (P = 0.003), blood pressure (P = 0.001), obesity (P = 0.026), cardiovascular diseases (P = 0.001), renal diseases (P = 0.013), and respiratory diseases (P = 0.012). Among these risk factors, the highest odds ratio (OR) was related to cardiovascular diseases (OR = 24), blood pressure (OR = 16.3), and diabetes (OR = 12.9), in sequence. Oseltamivir prescribed to all patients in the control group and 92% of patients in the case group. Seven patients in the control group and none in the case group had a history of influenza vaccination.
Conclusions: It is necessary to take steps and underpin training programs to reduce the risk factors of seasonal influenza among pregnant women based on the national vaccination guidelines.

Keywords: Pregnancy, Seasonal Influenza, SARI

1. Background

Influenza is one of the most frequent infections that poses unique risks to pregnant women due to physiologic and immune function changes in pregnancy, including increased heart rate, stroke volume, oxygen consumption, decreased lung capacity, and alterations in cell-mediated immunity (1-3). The mortality rate of influenza and pneumonia was 2 - 3 times higher in pregnant women than in non-pregnant women in 2009 (4-6). Moreover, it is estimated that women are up to five times more likely to be admitted for respiratory disease during their pregnancy than during one year before pregnancy (3). Besides, although available evidence suggests that viremia is infrequent and thus, the transplacental transmission is rare, influenza virus, especially H1N1, can increase perinatal mortality rate, stillbirth rate, preterm birth, low birth weight, admission to neonatal ICU, and low 5-minutes Apgar scores (7-12). About 5% of all deaths related to H1N1 were observed in pregnant women in the United States in 2009, putting pregnant women at high risks of complications, including hospitalization and death (13). Several studies have investigated the risk factors associated with morbidity, mortality, and complications of influenza for mother and fetus during pregnancy. Increasing knowledge is extremely cru-

cial to prevent complications in the future. Moreover, having sufficient information about risk factors can lead to the implementation of appropriate strategies for the management of pregnant women with influenza (3, 6, 11, 14).

2. Objectives

The aim of the present study was to examine the risk factors of mortality due to seasonal influenza among pregnant women referring to healthcare centers in Iran during 2015 - 2016 to find evidence for pregnancy as a risk factor for severe influenza disease.

3. Methods

In this routine database study, we surveyed pregnant women with severe acute respiratory illness (SARI) who had referred to healthcare centers of Iran during 2015 - 2016. Accordingly, based on Iran syndromic surveillance system, the statistical population consisted of 2,080 pregnant women of whom, 24 dead women constituted the case group and 100 living pregnant women were randomly selected to form a control group. Our research retrospectively collected the patients' clinical information without the involvement of the patients' personal information and samples; thus, there was no need for informed consent. Statistical tests were conducted using SPSS 22 software. Means and standard deviation (SD) were calculated for continuous variables and frequencies and percentages for categorical variables. Associations between categorical variables were assessed using the chi-square test or Fischer's exact test, as appropriate. Logistic regression and Mann-Whitney test were used for other analyses. P values of < 0.05 were considered significant. The original study was conducted upon approval by the Research Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.325).

4. Results

According to the findings of the study, the mean ± SD age was 31 ± 2.3 in living pregnant women and 34 ± 3.8 in dead women. The mean ± SD age of pregnancy was 28 ± 4.5 weeks among living women and 31 ± 3.6 weeks in dead women. About 66% of the living women had their first pregnancy while 70% of dead women had their second and more pregnancy. The mean ± SD of delay in referral to healthcare centers was 1 ± 1.64 day among living pregnant women due to respiratory disease and 6 ± 1.3 days among dead pregnant women. The mean ± SD duration of hospitalization was 5 ± 2.3 and 7 ± 4.5 days for living and dead pregnant women, respectively (Table 1). As can be seen in Table 1, the mean of all variables was higher in the dead group than in the group of living patients. The distribution of living and dead patients according to the risk factors was also studied. Accordingly, pregnant women in the dead group (case group) had risk factors more frequently than pregnant women in the living group (control group). It was also found that multiparity was associated with a higher mortality rate than primiparity so that pregnancy of more than twice increased the risk of death due to influenza up to 21.35. The history of influenza vaccination was positive in none of the case group women while 7 (7%) women in the control group were positive in this regard. The influenza virus type included H1N1 (71; 71%), untyped (10; 10%), and H3N2 (3; 3%) in the control group and H1N1 (10; 83%), untyped (2; 8%), and H3N2 (0; 0%) in the case group.

Table 1. Mean Age, Gestational Age, Delay in Referral, and Hospitalization Duration in Pregnant Women Referring to Healthcare Centers in the Case and Control Groups[a]

Groups	Variables		P Value
	Living	Dead	
Age, y	31 ± 2.3	34 ± 3.8	0.000
Gestational age, wk	28 ± 4.5	31 ± 3.6	0.002
Delay in referral to health centers, days	1 ± 1.64	6 ± 1.3	0.000
Hospitalization, days	5 ± 2.3	7 ± 4.5	0.003

[a]Values are expressed as mean ± SD.

Overall, the differences between dead and living pregnant women in all the measured parameters were significant ($P < 0.05$), except for neurological disease, preeclampsia, gestational diabetes, smoking, and drug abuse. The highest OR belonged to diabetes (OR = 12.9) and the lowest OR belonged to multiparity (OR = 0.000) (Table 2).

5. Discussion

In the present study, we estimated the probable risk factors of death among pregnant women afflicted with influenza in the Iranian population. Maternal age, gestational age, delay in referral to health centers (days), duration of hospitalization (days), diabetes, obesity, cardiovascular diseases, renal diseases, respiratory diseases, and multiparity were found as major risk factors of death among Iranian pregnant women with influenza. In a cross-sectional study of 266 women by Koul et al. in two tertiary care referral centers in India, 82% of the infections were caused by influenza A/H1N1pdm09, 16% by A/H3N2, and 2% by influenza B virus (15). In another prospective national cohort study by Yates et al. in the UK, maternal obesity

Table 2. Odds Ratios of Risk Factors for Seasonal Influenza in Pregnant Women[a]

	Living Group, N = 24	Dead Group, N = 100	P Value	OR	P Value, Logistic Regression
Diabetes	5 (20.8)	2 (2)	0.003	12.9	0.003
Hypertension	6 (25)	2 (2)	0.001	16.3	0.001
Obesity	4 (16.7)	3 (3)	0.026	6.5	0.02
Cardiovascular disease	12 (50)	4 (4)	0.001	24	0.001
Renal disease	4 (16.7)	2 (2)	0.013	9.8	0.011
Respiratory disease	6 (25)	6 (6)	0.012	5.2	0.009
Neurological disease	2 (8.3)	1 (1)	0.09	9	0.08
Gestational diabetes	3 (12.5)	4 (4)	0.13	3.4	0.12
Preeclampsia	3 (12.5)	3 (3)	0.08	4.6	0.07
Drug abuse	2 (8.3)	1 (1)	0.09	9	0.08
Smoking	1 (4.2)	1 (1)	0.35	4.3	0.3
Multiparity	22 (91.6)	34 (34)	0.000	21.35	0.000

[a]Values are expressed as frequency (%).

and smoking during pregnancy were associated with hospital admission due to AH1N1v infection and these women were more likely to have asthma requiring inhaled or oral steroids (16). In our study, we did not find any significant difference in smoking between the two study groups. It seems that this finding may be related to Iranian culture regarding no smoking habit in women, especially during pregnancy.

In a report published by CDC in 2011, asthma, obesity, and diabetes (gestational or pre-gestational) were considered as the risk factors of death due to influenza during pregnancy (11); the finding of CDC is in line with the finding of the present study.

In a review by Bhalerao-Gandhi et al. (17) in India, pandemic influenza was associated with high mortality among Indian pregnant women. In a study by Pramanick et al. (18) mortality among pregnant women with influenza was associated with a significant delay in presentation to hospitals, dyspnea, the need for ICU admission, the need for mechanical ventilation, and renal failure. The findings of these studies are in agreement with the finding of our study.

In another retrospective observational study conducted in pregnant women with suspected infection by influenza virus A/H1N1 in Japan, Calvo Aguilar et al. reported atypical pneumonia as the main complication in four pregnant women (19). In the present study, the incidence of respiratory disease was significantly different between the two study groups.

In a study by Yamada et al in Japan, multiparous women had a higher risk of influenza regardless of vaccination status than primiparous women (20). Likewise, in the present study, we found that parity was a significant factor affecting the consequence of influenza during pregnancy.

In a hospital-based surveillance study by Chacon et al. in the USA, most cases who died of influenza had suffered from obesity (15%), diabetes (13%), asthma (11%), metabolic disorders (8%), chronic obstructive pulmonary disease (5%), and neurological disorders (10%) (21).

In the current study, 7% of the control group women had a history of influenza vaccination and this group had a lower mortality rate and other related complications than the case group. These findings emphasize the important role of influenza vaccination in mother and infant protection against side effects and other risk factors of influenza during pregnancy. In a study by Getahun et al. 247,036 pregnant women were examined, 53% of whom were vaccinated during their pregnancy. It was also found that influenza vaccination in pregnant women was associated with the reduced risk of influenza, maternal fever, preeclampsia, placental abruption, stillbirth, and NICU admission. Influenza vaccination during pregnancy was not associated with adverse prenatal and neonatal outcomes and vaccinated pregnant women benefited from fewer adverse outcomes than unvaccinated women (22). Nunes et al. carried out a systematic review of observational studies to evaluate the effect of influenza vaccination during pregnancy and found that influenza vaccination could improve birth outcome during pregnancy. It was concluded that influenza vaccination could decrease the risk of PTB and LBW but no significant effect on SGA was observed (23). According to a commentary published in Lancet, influenza vaccination during pregnancy could significantly improve

maternal and fetal outcomes even compared to recommended interventions for premature birth, including progesterone treatment and smoking cessation. According to this paper, to improve outcomes for mother, fetus, and infant, we need to focus on influenza immunization during pregnancy and understand the pathogenic mechanisms of influenza infection in pregnancy. Moreover, further research is needed to investigate the pathophysiology of influenza to guide further development of vaccines and antiviral treatments targeting influenza in pregnancy (24).

5.1. Conclusions

Since Iran has a young population with a high fertility rate, it is suggested that epidemiologic studies be conducted on risk factors, maternal and fetal mortality rates, and the effect of vaccination on mortality and abortion reduction among pregnant women with influenza in different population groups. According to the recommendations of international organizations on influenza vaccination in pregnant women, it is proposed to promote vaccination among pregnant women and facilitate cost-effective vaccination for this population. Effective measures and training programs should be prioritized to reduce the risk factors such as diabetes, hypertension, etc. among pregnant women in every country and joint policies should be implemented to control contagious and non-contagious diseases in pregnant women.

Acknowledgments

Thanks Dr. Mohammd Mehdi Gouya from Ministry of Health of Iran for his great contribution.

Footnotes

Conflict of Interests: None declared by the authors.

Ethical Approval: The original study was conducted upon approval by the Research Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.325).

Funding/Support: There was no funding/support for this study.

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