Original Article

Maternal and Neonatal Outcomes of Pregnant Women With Seasonal Influenza, A Single-Center Study

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Abstract

Objective: Influenza causes significant mortality and morbidity in pregnant women and neonates especially in developing countries. This study aimed to investigate the maternal and neonatal outcomes in pregnant women with influenza and compare them with non-infected mothers.

Materials and methods: This case-control single-center cohort study was conducted during the influenza season in 2022 and included all pregnant women with influenza during pregnancy. Baseline characteristics including age, body mass index, job, vaccination, and ethnicity were documented and outcomes including premature rupture of membranes (PROM), preterm labor, cesarean section, neonatal distress, and neonatal hospitalization were evaluated and compared with the control group.

Results: In this study 39 pregnant women in each case and control group were evaluated. There was no significant difference in demographic data between the two groups. None of the participants in the case group received the influenza vaccine during pregnancy. The rate of cesarean section (63.2% vs 43.5%), neonatal distress (38.5% vs 12.8%), and neonatal hospitalization (43.5% vs 15.3%) was significantly higher in the case group than in healthy women (P-value=0.022, 0.010, 0.006 respectively). Although, the rate of PROM was not significantly different between the two groups (P=0.556). Preterm labor was higher in the case group than in the control group, but the difference was insignificant (P=0.135).

Conclusion: The study findings suggest that pregnant women infected with influenza are at higher risk of neonatal complications and vaccination is helpful in these mothers as preventive measures to reduce complications.

Keywords: Influenza; Pregnancy; Neonatal Outcomes; Prenatal Care; Flu Season

Introduction

Influenza causes significant mortality worldwide with its epidemics annually (1) and nearly 3 million people are diagnosed with serious diseases yearly, and hundreds of thousands of deaths have been reported from this population (2). Severe influenza and pulmonary complications are reasons for

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justifying the higher risk of Pregnant wome (3). Physiological changes and changes in the mother's immunity are among the reasons for increasing the risk of pregnant mothers against influenza infection (4, 5). Moreover, a mortality rate of up to 45% during the pandemic has been reported in the literature (6).

The World Health Organization has announced that during the influenza season, pregnant women should be immunized with a vaccine (7). Despite strategies such as avoiding infected people and frequent hand washing for high-risk individuals, the effectiveness of these strategies is still under investigation (8). Also, vaccinating mothers during pregnancy is an appropriate deed to protect infants against influenza infection (9, 10).

Passive protection through the placental transfer of antibodies from mother to fetus provides this immune mechanism (11, 12); also, breast milk contains immunoglobulin A, making the infants immune (10). In addition, the Immunization of mothers might cause the birth of babies whose disease symptoms onset later and the duration of the disease is shorter (13). Infants are extremely vulnerable to getting infected with Influenza; Also, like mothers, infants have a higher mortality and hospitalization rate from influenza (12, 14); especially Infants under 6 months are considered high-risk groups (15). Vaccine administration is not strictly implemented in all countries. Also, vaccine uptake is questionable (12). Moreover, the vaccine's effectiveness depends on the host's characteristics and the compatibility of circulating influenza viruses with the viruses in the vaccine (16).

Studies showed that flu vaccination coverage is not appropriate in Iran (17, 18). This study aims to investigate the infants' outcome born to infected mothers during the flu season compared to mothers without infection. So, the results can better demonstrate the importance of this situation on the health outcome of the fetus and clarify the decision-making for the plans and national guidelines based on limitations and needs.

Materials and methods

Study design and population: This case-control study was conducted during the flu season (1st of December to the end of February) in 2022 at an academic hospital. All admitted primigravid pregnant mothers with influenza infection (RT-PCR positive from nasopharyngeal swabs) 7 days before delivery and birth to a singleton infant were included in the study as a case group. A control group included primigravid pregnant women with a singleton live infant without any infection. They were chosen randomly and the number of the control group was equal to the number collected in the case group. Mothers under 18 years of age and those who didn't give birth after 24 weeks, mothers with underlying diseases, and a history of infertility, were excluded from the study. Adolescents are still in their developmental stages, both physically and emotionally. Including them in studies involving maternal and fetal health could introduce variables related to their unique developmental needs and risks, which might not be representative of the general adult population so we exclude them to minimize confounding. Also, the 24-week mark is often considered the threshold of fetal viability, meaning the fetus has a reasonable chance of survival outside the womb with medical intervention. Births before this period are typically classified as miscarriages or extremely preterm births, which come with significantly different medical and developmental outcomes compared to births after 24 weeks. Excluding births before 24 weeks ensures that the study focuses on outcomes relevant to viable pregnancies and births, providing more consistent and applicable data for understanding maternal and fetal health in the context of viable pregnancies.it is added the manuscript (19, 20).

Ethical consideration: Written informed consent was obtained from all participants. This study has been approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (Ethics code IR.TUMS.MEDICINE.REC.1402.062). The main study was an Investigation of the clinical, laboratory, and radiological symptoms in patients with different influenza subtypes of infection, this study was performed through the data among pregnant women.

Measurements and data collection: Data such as demographic information, influenza vaccination in the last two years, treatment, and mother complications were collected through questionnaires. All infected women and non-infected women were followed up until delivery. Also, the birth weight of the infants and infant sex were recorded. According to WHO guidelines, a weight of fewer than 2500 grams is "underweight", a weight of fewer than 1500 grams is "very low underweight", and a weight of fewer than 1000 grams is classified as "extremely underweight" (21). Neonatal distress is diagnosed

based on clinical symptoms (increased work of breathing including; tachypnea, nasal flaring, expiratory grunting, sub, and intercostal retractions, reduced or absent breath sounds, cyanosis, and increased oxygen requirement), chest x-ray findings (a diffuse ground glass reticulogranular appearance with air bronchogram and low lung volume) (22) by an expert neonatologist.

The primary outcome was a comparison of birth outcomes between infected and non-infected mothers including premature rupture of membranes (PROM), preterm labor, cesarean section, neonatal distress, and neonatal hospitalization**.** Data including maternal demographic characteristics, risk factors for influenza infection, infant sex, and Job were compared between two groups. Gestational age was measured as a comparison variable considering length, last menstrual period (LMP), and delivery. An infant born before 30 weeks is classified as "extremely premature", before 35 weeks as "very premature" and before 37 weeks as "premature" (21) according to the Australian Immunization Guide (16), to determine whether there are differences between infected and non-infected groups of influenza was analyzed.

Data analysis: Data were analyzed using SPSS version 25 software. Analytical analysis and the mean of quantitative data were reported. The Kolmogorov-Smirnov test checked the normality of data distribution. All quantitative variables in this study had a normal distribution. The t-test and the chi-square test were calculated to determine the relationship between the vaccination status and the outcome variables the significance level in this study was calculated with an alpha error of 5% (P-value < 0.05).

Results

After the prospective evaluation of 102 pregnant women, 39 pregnant women with influenza in the case group and 39 women without influenza in the control group were included in this study. All infected women received Oseltamivir as a treatment for 5 days. The result indicated that none of the case and control group participants received influenza vaccine during pregnancy. Maternal and obstetrical information on pregnant women is shown in Table 1. There was no significant difference in age, body mass index (BMI), race, or job between the two groups. No women declared a history of smoking and alcohol consumption. In the case group, the common signs among infected women were fever (25.6%) and body pain (12.8%). Also, three (7.7%) of pregnant women were admitted to ICU and no maternal mortality was reported (Table 1).

Neonatal and pregnancy outcomes are summarized in Table 2.

Table 1: Demographic Characteristics of the Participants

Variables	Case (n=39)	Control (n=39)	P-value
Age (year)	30.90 ± 6.92	29.28 ± 4.28	0.219
Body Mass Index (kg/m2)	28.34 ± 5.01	27.96 ± 5.43	0.76
Gestational age at delivery (weeks)	31.39±7.019	33.3+6.19	0.167
Ethnicity			0.556
Iranian	37 (94.7)	38 (97.4)	
Non-Iranian	2 (5.1)	1 (2.6)	
Job			-
Employed	36 (92.3)	36 (92.3)	
Unemployed	3 (7.7)	3 (7.7)	
Maternal sign and symptoms			
Fever	10 (25.6)	--	--
Dyspnea	4 (10.3)	--	--
Body pain	5 (12.8)	--	--
Fever and Body pain	5 (12.8)	--	--
Lethargy and Body pain	1 (2.6)	--	--
Maternal outcomes			
ICU admission	3 (7.7)	--	--
Mechanical ventilation	0	--	--
Morbidity (Mechanical ventilation + ICU admission)	3 (7.7)	--	--
Mortality	0	--	--

Data are presented as Mean (+ SD, range) or n (%), or Median (range). ICU: Intensive care unit

Table 2: The Effect of Influenza on Maternal and Neonatal Outcomes

Variables	Case (n=39)	Control (n=39)	P-value
PROM	2 (5.1)	1 (2.56)	0.556
Preterm labor	6 (15.38)	2 (5.1)	0.135
Cesarean section	27 (69.20)	17 (43.59)	0.022
Neonatal Distress	15 (38.50)	5 (12.82)	0.010
Neonatal hospitalization	17 (43.59)	6 (15.38)	0.006
Neonatal PCR (positive)	2 (5.1)	0	--

Data are presented as n (%), PROM: Premature rupture of membranes, PCR: Polymerase Chain Reaction

The rate of PROM wasn't significantly different between the two groups (P=0.556). Moreover, preterm labor was reported in (15.38%) of patient women which was higher than in the control group (5.1%), but the difference wasn't significant (P=0.135). Furthermore, the rate of cesarean section, neonatal distress, and neonatal hospitalization was significantly higher in the case group than in healthy women (P=0.022, P=0.010, and P=0.006, respectively). Also, two (5.1%) of neonates in the case group had positive PCR results after delivery. These two neonates were discharged healthy without any additional treatment requirements.

Discussion

Influenza is a significant public health concern for pregnant women, as they are at a higher risk of severe illness and complications from the virus. However, influenza vaccination coverage has been reported as low as 5.5 to 6 percent in the region (18), but none of the pregnant women in this study received vaccination during the pandemic season. This low vaccination rate is concerning, as it leaves many pregnant women vulnerable to the virus. Furthermore, during the pandemic season, none of the pregnant women in the study received influenza vaccination. This is particularly worrying given the increased risk of severe illness and complications from COVID-19 for pregnant women. It is crucial for healthcare providers to educate pregnant women about the importance of influenza vaccination and to make it readily available to them. Vaccination not only protects pregnant women from the flu but also protects the newborn during the first few months of life. Therefore, increasing influenza vaccination coverage among pregnant women is an essential public health priority (23).

All of the infected women received Oseltamivir as a treatment. The Society for Maternal-Fetal Medicine (SMFM) declared that all suspected or confirmed cases of influenza among pregnant women should undergo antiviral therapy despite vaccination status. Also, the best treatment is oseltamivir for 5 days (24). However, the best choice of treatment advised by SMFM is the same choice in our study.

The mortality of infected women in our study was zero; just three required ICU admission. A multicentral study showed that the rate of influenza A mortality in Iran was 3.8% in 2009 while 10% of them were pregnant (25). Also, Mardani and his colleagues showed that some underlying factors like maternal and gestational age, multiparity, duration of hospitalization, diabetes, and obesity could be significant risk factors for the mortality of infected pregnant women to flue (26). In our study, we excluded patients with underlying diseases regardless of confounding effects.

This study showed that neonatal hospitalization, neonatal distress, and cesarean sections were significantly higher in infected women while preterm labor and PROM were not statistically different. A study in South Korea showed that influenza infection could cause increasing preterm birth (27), while a systematic review showed that influenza virus infection is not associated with preterm birth. The second study supports our results; however, more studies with huge participants are required to clarify the disparity (28). Moreover, He et al. illustrated that the cesarean section rate is not associated with influenza during pregnancy despite our study (29). Furthermore, our study shows that hospitalization among neonates is higher than in non-infected women. This result is supported by a population-based study in the USA between 2009 and 2010 that showed admission to a neonatal ICU is higher among neonates born out infected pregnant to influenza (30).

There are some limitations in this study. First, it is a single-center study and the population involved is limited. So multicentral studies with huge participants are required. Also, the outcomes among pregnant women and neonates should be followed up through the years to be able to demonstrate prognosis and outcomes better. Moreover, none of the participants had received an influenza vaccination. It did not let us investigate the different outcomes in pregnant women due to immunization. However, no significant differences between the case and control groups in aspects of characteristics factors, and treatments limited confounding effects.

Conclusion

In conclusion, neonatal hospitalization, distress, and cesarean sections are higher in pregnant women infected with influenza than in non-infected women. While preterm labor and PROM are not different between them. Also, all pregnant women (including infected and non-infected) did not receive Influenza vaccination. Policymakers and primary care providers should notice the challenges due to influenza infections among pregnant women and the role of vaccination in eliminating them.

Conflict of Interests

Authors declare no conflict of interests.

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