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Neonatal and Maternal Outcomes in Pregnant Women with Cardiac Disease in Iranian Population

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Abstract

Background: Maternal cardiac disease has a significant impact on fetal health; and increases the risk of neonatal complications. This case-control study was conducted to determine the prevalence and risk factors of fetal and neonatal morbidities among mothers with cardiac disorders.

Methods: In this retrospective case-control study, all pregnant mothers with underlying cardiac diseases, from March 2012 to September 2017, referred to Imam Khomeini Hospital were enrolled in the study through convenience and sequential sampling. The case group included 100 pregnant mothers with cardiac diseases and the control group comprised of 200 expectant mothers without any cardiac disease. Neonatal and maternal complications were investigated respectively.

Results: The mean age of mothers was 35.44 ± 4.52 years in the case group and 32.04 ± 4.92 years in the control group. Type of delivery, place of delivery, hospitalization ward, maternal age, gravidity, and gestational age were significantly different between the two groups (P = 0.001), as were neonatal weight, gestational age, 5-min Apgar score (P = 0.001), and 1-min Apgar score (P = 0.005). Needs for resuscitation and respiratory distress were significantly higher in cases (P = 0.001).

Conclusion: It was found that the investigated complications were more frequent in neonates of mothers with heart diseases. Detection of these complications can improve the outcomes in these neonates.

Key Words: Heart disease, Mothers, Neonatal outcomes, Severity of disease.

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1- INTRODUCTION

Maternal cardiac disease has a marked impact on fetal health, which affects the fetus in a variety of ways. Although cardiac complications usually are not severe, in some conditions serious complications can occur; and these forms of complications have important long-term effects on the health of the mother and child (1-4). The majority of cardiac complications occurred in the antepartum period, are followed by the postpartum period, with the lowest frequency at the time of labor and delivery (2). Moreover, cardiac arrhythmias is more likely to be presented in the second trimester, whereas heart failure is more likely to be presented in the third trimester or postpartum (5).

The risk of abortion is higher in mothers with heart diseases (6). Children of mothers with congenital cardiovascular disease are also more likely to inherit congenital heart disease (7). For example, the overall risk of polygenic congenital heart disease is 3-5% in infants of mothers with congenital heart disease, which is significantly than the reported percentage, i.e. 1% in the normal population (8). Moreover, the risk doubles if congenital heart disease is present in siblings (9). Several studies have investigated pregnancy outcomes in women with heart diseases and found the high prevalence of neonatal complications (1, 2, 10). However, limited access to care is significantly associated with adverse maternal outcomes (11).

It has been suggested that the risk of neonatal diseases and complications increases in mothers with underlying heart disease; however, the prevalence of these complications and their association with the related underlying risk factors in different societies are unclear (5,6,7).

Lack of information about the risks of pregnancy in these women, along with social and cultural drawbacks precludes any appropriate prevention strategy. Therefore, management of pregnancy in such patients is essential. Study on the neonatal outcomes of mothers with cardiac diseases helps to draw appropriate measures to prevent following complications and manage them. Therefore, this study was conducted to determine the prevalence and risk factors of neonatal and fetal complications of mothers with heart disease by considering cultural, social, and health-related factors involved in the diagnosis of complications.

2- MATERIAL AND METHODS

2-1. Study design and population

In this case-control study, assuming a coefficient of 0.05 and a study power of 80%, P1 = 0.18 and P2 = 0.07, the minimum number of participants needed for the study was 100 cases and 200 controls.

2-2. Methods

From March 2012 to September 2017, all pregnant mothers with underlying cardiac diseases, including congenital -ischemic-vascular problems, referred to Imam Khomeini Hospital, a national referral center for high-risk pregnancies were enrolled in the study through convenience and sequential sampling. For each mother with a heart disease, two mothers without any cardiac diseases, placental vascular disorders, pregnancy complications (such as preeclampsia and diabetes), or congenital fetal malformations other than congenital heart disease (CHD) were selected within the same timeframe and enrolled in the study.

2-3. Measuring tools: Laboratory measurements

Information was recorded by filling out a questionnaire by a neonatologist. The place of delivery (labor room, cesarean section operating room, and cardiac surgery room), postpartum maternal hospitalization ward (postpartum room,

ICU and CCU) as well as the peripartum, postpartum, and neonatal complications were recorded. Maternal demographics including age, gravidity, parity, and gestational age were collected. Neonatal birth complications including low Apgar score, neonatal death, respiratory distress, sepsis with a positive blood culture, hospitalization or neonatal intensive care unit (NICU) admission, cerebral hemorrhage, and congenital cardiac abnormalities as well as laboratory test abnormalities such as leukopenia, thrombocytopenia, and neonatal hypoglycemia were also recorded. For laboratorial parameters, the recorded values corresponded to the first 24 hours of birth. In the neonatal control group, if they had any risk factors other than egress criteria, the CBC and 4 turns of blood glucose were also recorded.

2.4. Ethical consideration

This study was approved by the Research Ethics Committee of Tehran University of Medical Sciences (No. IR.TUMS.VCR.REC.1396.2657) Ethical considerations were observed.

2-5. Inclusion and exclusion criteria

Mothers with mitral valve prolapse, patent foramen oval (PFO), and bicuspid aortic valve were excluded from both of the case and control groups.

2-6. Data Analyses

SPSS software version 22 was used for data analysis. Qualitative variables are described as percentages, and quantitative variables are presented as mean and standard deviation (for parameters with a normal distribution) or median and first and third quartiles (for parameters without a normal distribution). Chi-square and Fisher's exact tests were used to compare the qualitative variables. Independent t-test (for comparison of parameters with a normal distribution) or Mann-Whitney test (for comparison of parameters without a normal distribution) was applied to compare quantitative variables. P-values less than 0.05 were considered significant.

3- RESULTS

A total of 17291 deliveries were performed; and a total of 300 pregnant mothers and 292 neonates were enrolled in the study. Nine fetuses were aborted in the case group and there was a twin pregnancy in the control group.

According to **Table 1**, the mothers in the case group had lower gravidity (p=0.001), and higher mean age (p=0.001); moreover, the majority of them underwent C-section (p=0.001). **Table 2** present neonatal outcomes. According to **Table 2**, birth weight, 1-minute Apgar score, 5-minute Apgar score, and blood glucose level were significantly lower in the case group compared to the control group ($p<0.05$). **Table 3** shows that needs for resuscitation at birth, resuscitation during hospitalization, and respiratory distress syndrome were more common in the case group ($p<0.05$).

4- DISCUSSION

This study was conducted to compare the outcomes of neonates born to mothers with and without cardiac disease. In this study, 100 pregnant mothers with heart diseases and their neonates were investigated at Imam Khomeini Hospital, a national referral center for high-risk pregnancies, for the first time in Iran. We found that case group had lower gravidity and higher age; moreover, the majority of them underwent C-section, and birth weight, 1-minute Apgar score, 5-minute Apgar score, and blood glucose level were significantly lower in the case group compared to the control group. Need for resuscitation at birth, resuscitation during hospitalization, and respiratory distress syndrome were more common in the case group.

Table-1: Comparison of the variables between mothers with and without cardiac disease

Variables		Groups		P value**
		Case N=100	Control N=200	
Pregnancy termination type	NVD	2 (2%)	148 (74%)	0.001
	Cesarean section	89 (89%)	50 (25%)	
	Abortion	9 (9%)	2 (1%)	
	Total	100	200	
Place of delivery	Heart surgery room	74 (81.3%)	0 (0%)	0.001
	Cesarean section operating room	15 (16.4%)	50 (26%)	
	Labor room	2 (2.1%)	148 (74%)	
	Total	91	198	
Maternal outcome after delivery	Hospitalization in postpartum ward	12 (12%)	188 (94%)	0.001
	Hospitalization in ICU	80(80%)	7 (3.5%)	
	Hospitalization in CCU	80 (80%)	5 (2.5%)	
	Total	100	200	
Maternal age (year)	Mean	35.44	32.04	0.001
	Standard deviation	4.52	4.92	
Gravidity*	Mean	1.86	2.74	0.001
	Standard deviation	0.70	0.79	
Gestational age (week)	Mean	34.16	38.01	0.001
	Standard deviation	8.25	1.22	
Maternal death	Mean	0	0	---
	Standard deviation	0	0	

*Number of pregnancies; NVD: Natural vaginal delivery; ICU: Intensive care unit
**Chi square for categorical variables and t-test for continuous variables

Table-2: Comparison of clinical and laboratory parameters of neonates born to mothers with and without heart disease

Variables	Groups	Number	Mean	Standard deviation	P value***
Neonatal weight	Case	91	2024.75	510.37	0.001
	Control	200	3276.58	466.47	
1-minute Apgar	Case	91	8.12	0.81	0.005
	Control	200	8.47	1.31	
5-minute Apgar	Case	91	7.89	0.61	0.001
	Control	200	9.75	0.51	
Hb*(gr/dl)	Case	91	13.04	1.86	0.837
	Control	200	13.09	2.17	
BS** (mg/dl)	Case	91	53.01	26.05	0.001
	Control	200	81.32	23.78	

*Hemoglobin, **Blood sugar, *** t-test

Table-3: Frequency of variables in neonates born to mothers with and without heart disease

Variables		Groups		Total	P value***
		Case N=100	Control N=200		
Need for resuscitation in infants (at birth)	Yes	35 (38.46%)	26 (13%)	61 (20.33%)	0.001
	No	56 (61.53%)	174 (87%)	230 (76.66%)	
	Total	91	200	191	
Resuscitation (in the ward)	PPV*	19 (54.28%)	18 (69.23%)	37 (60.65%)	0.001
	PPV+ Cardiac massage	4 (11.42%)	3 (11.53%)	15 (24.59%)	
	CPAP**	12 (34.28%)	5 (19.23%)	9 (14.75%)	
	Total	35	26	61	
Intrauterine growth retardation	Yes	12 (13.18%)	4 (2%)	16 (5.49%)	0.334
	No	79 (86.81%)	196 (98%)	275 (94.50%)	
	Total	91	200	291	
Respiratory distress syndrome	Yes	21 (23.07%)	8 (4%)	29 (9.96%)	0.001
	No	70 (76.92%)	192 (6%)	262 (90.03%)	
	Total	91	200	291	
Confirmed Septicemia (positive blood culture)	Yes	8 (8.79%)	2 (1%)	10 (3.43%)	0.065
	No	83 (91.20%)	198 (99%)	281 (96.56%)	
	Total	91	200	291	
Cerebral hemorrhage	Yes	3 (3.29%)	0 (0%)	3 (1.03%)	0.058
	No	88 (96.70%)	200 (100%)	288 (98.96%)	
	Total	91	200	291	
Congenital heart defect	Yes	1 (1.09%)	0 (0%)	1 (0.34%)	-
	No	90 (98.90%)	200 (100%)	290 (99.65%)	
	Total	91	200	291	
Leukopenia	Yes	2 (2.19%)	0 (0%)	2 (0.68%)	-
	No	89 (97.80%)	200 (100%)	289 (99.31%)	
	Total	91	200	291	
Thrombocytopenia	Yes	4 (4.39%)	0 (0%)	4 (1.37%)	-
	No	89 (97.80%)	200 (100%)	289 (99.31%)	
	Total	91	200	291	

* Positive pressure ventilation
** Continues positive air way pressure
***Chi square

In a study by Siu in 1997, 14 of 221 (6%) pregnant mothers with cardiac disease had IUGR (12). Moreover in the studies by Albalawi in 2017 (14), and Hayward et al. in 2017 (13), CHD was associated with three fold higher risk of IUGR. In the present study, 12 IUGR cases were detected among 91 pregnancies in the case group (13%), which was about two times higher than the percentage reported in the above study. However, this rate was not significant in comparison to the case group. This could be due to the fact that the rate of IUGR births varies in different societies and different case groups. Patients with complex diseases are at particular risk for intrauterine growth restriction, and monitoring for such complications requires vigilance by obstetricians. According to several studies, the rate of IUGR in LBW neonates is higher in developing countries. Thus, it may be the reason why IUGR was not significant in the present study. Another possible reason could be the small sample size of the present study.

In the study by Siu, neonatal complications were found in 17 % of the neonates, including neonatal death (2 cases), respiratory distress syndrome (16 cases), intra-ventricular hemorrhage (2 cases), and premature birth (35 cases). However, because it was a descriptive study, it is not possible to compare its results with the present study. The gestational age of the neonates was different in the study by Siu compared to our study. In other words, the neonates were more premature in that study. And there were no neonatal deaths in the present study. Yet it should be considered that Siu's study was conducted in the early years of this century, and prenatal care advances have improved the maternal and neonatal outcomes since then. In the present study, neonatal complications occurred in 11% of the cases but there were no cases of maternal death.

Siu et al. performed another study on 302 mothers with cardiac disorders and 572 controls in 2002. The results showed that maternal pulmonary edema, arrhythmia, stroke, and death caused neonatal complications in 13% of the pregnancies. A history of cardiac events or arrhythmias, low functional capacity of mothers, cyanosis, or left ventricle disorders were all predictive factors, which could cause neonatal outcomes in these mothers (15).

In another study conducted by Hayward et al. in 2017, CHD was associated with incident CHF, atrial arrhythmias, and fetal growth restriction; and complex CHD was associated with ventricular arrhythmias and maternal in-hospital mortality (13). In addition, in the study by Silversides et al., pregnancy in women with heart disease was associated with significant morbidity, although mortality was rare (2).

One of the strong points of the present study was its greater focus on the neonatal outcomes, which were addressed less in previous studies. It was not clear whether the higher occurrence of the outcomes is related to prematurity and low birth weight or maternal heart disease. To answer this question, a regression analysis was conducted and the results showed that apart from prematurity and low birth weight, maternal cardiac disease independently caused an increase in neonatal complications, such as the need for resuscitation immediately after birth and hypoglycemia. A 3-fold increase was displayed in the needs for resuscitation immediately after birth; and the blood sugar of these neonates, independent of prematurity and low birth weight, was about 30 units (30 milligrams per deciliter) lower as compared to the neonates born in the control group. However, it was found that prematurity caused by respiratory distress and maternal heart disease was not an effective factor independently. Low birth weight was a determinant factor in low 5-minute Apgar score while it was not

significantly affected by heart disease alone.

The results of the study showed that the neonates of mothers with cardiac diseases were more susceptible to adverse outcomes such as prematurity, low birth weight, hypoglycemia, need for resuscitation immediately after birth due to maternal disease, and respiratory distress. Identification of these problems and the related factors can reduce their occurrence and improve the neonatal outcomes.

Another factor affecting neonatal outcomes in these mothers may be drugs used for the treatment of heart disease. For example, hypoglycemia and need for resuscitation may be side effects of these drugs. It is recommended to conduct further studies to clarify the effects of drugs.

5- CONCLUSION

The aim of this study was to identify the neonatal complications of mothers with heart disease. This study found that complications were more frequent in neonates of mothers with heart diseases. Detection of these complications can improve the outcomes in these neonates. In general, it was found that maternal heart disease is independently effective on lowering blood sugar and increasing the need for resuscitation among these neonates. But respiratory distress is only due to prematurity and is not affected by maternal heart disease.

6- STUDY LIMITATIONS

One of the limitations of this study was the existence of files with incomplete information that led to the removal of that file from the study; and the other was the low sample size in the case group.

7- ACKNOWLEDGEMENT

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8- CONFLICT OF INTEREST

None.

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