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# Comparison the Echocardiographic Findings in Neonates Born to Mothers with COVID-19 and Neonates Born to Healthy Mothers

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## Abstract

**Objective:** The aim of this study was to compare echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers referred to Amir Al-Momenin Hospital of Semnan in 2021.

**Methods:** This case-control study was conducted on 60 neonates born to mothers with COVID-19 (case group; n=30) and neonates born to healthy mothers (control group; n=30) referred to Amir Al-Momenin Hospital of Semnan in 2021. The sampling method was random and the data collection tool was a checklist including sex, birth weight, gestational age, heart rate, mitral valve E wave, mitral valve A wave, TAPSE and LVEF. The evaluation of echocardiographic parameters performed using Philips Affinity 50 Ultrasound Machine. Finally, data analysis was applied by SPSS 24 at 5% significant level.

**Results:** There was no statistically significant difference between the two groups in terms of birth weight, gestational age, heart rate, mitral valve E wave, mitral valve a wave, left ventricular function, TAPSE and LVEF. In addition, the means TAPSE and LVEF according to sex were not significant in the two groups. We observed a significant Positive correlation between gestational age with TAPSE and LVEF in the two groups, however, the correlation between the left ventricular function and gestational age was negative in newborns of infected mothers. Also, a significant positive correlation between birth weight with TAPSE and LVEF in the two groups.

**Conclusion:** This study showed the echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers were not significantly different, however, cohort studies with higher sample size are recommended.

**Keywords:** Echocardiographic findings • Neonates • TAPSE • LVEF • COVID-19

## Introduction

Coronavirus disease 2019 (COVID-19) D is a disease that was first reported on December 30, 2019 in Wuhan, China, and quickly spread worldwide and took the form of a large pandemic [1]. Although COVID-19 affects all age groups, the symptoms are more severe in people with weakened immune systems, the elderly, and those with comorbidities. In addition, pregnant women, fetuses, and their infants are prone to pneumonia, pyelonephritis, and periodontal infections due to physiological changes, immune deficiencies, and dysregulation of cytokines [2-5]. There are few observations about the effect COVID-19 infection on the fetus during pregnancy. However, due to the possibility of vertical transmission from mother

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to fetus, there is concern that fetus may be exposed to the congenital consequences of COVID-19. ACE-2 receptor at the level of placental cells, contact of the mother's blood and body fluids with the fetus during labor and subsequent maternal contacts can facilitate the transmission of infection from mother to fetus [6]. In a number of infected mother transmission of the COVID-19 has been observed in the third trimester and there are reports of positive COVID-19 test in infants born to pregnant mothers [7-9].

COVID-19 infection can cause maternal viremia, placental infection and inflammation, and eventually neonatal viremia [10]. A number of studies have reported higher incidence of preeclampsia, eclampsia, HELLP syndrome, preterm labor, and low birth weight infants in mothers with COVID-19 compared with healthy mothers [11]. In addition, clinical manifestations such as fever, respiratory distress, gastrointestinal symptoms, vomiting, and increased heart rate have been observed in neonates of infected mothers. Placental inflammation may also cause fetal distress and cardiac abnormalities that require emergency cesarean section. Despite the negative results of most COVID-19 tests in infants born to infected mothers, however, these infants have inflammation in various organs, including coronary artery ectasia. In fact, placental infection by COVID-19 may lead to the deposition of fibrin filaments, impede gas exchange between mother and fetus, and ultimately cause respiratory distress in the fetus [6,12].

Little information is available about the effect of COVID-19 infection on the cardiovascular system of infants born to infected mothers. Also, the mechanism of action of COVID-19 infection on cardiovascular system involvement in infants born to infected mothers has not been precisely elucidated.

Given the limited studies conducted on the effects of COVID-19 on the cardiovascular system on the one hand and the importance of being aware of the adverse consequences of COVID-19 infection in fetuses and infants on the other hand, the present study was designed and conducted to compare echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers referred to Amir Al-Momenin Hospital of Semnan in 2021. Hopefully, the results of this study will help diagnose cardiovascular disorders in infants following maternal COVID-19 infection, complement epidemiological findings, develop maternal-child health policies, and implement early and effective treatments.

## Materials and Methods

### Study design and subjects

The present study was a case-control study which designed to compare echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers referred to Amir Al-Momenin Hospital of Semnan in 2021. A total of 60 infants were examined into 2 groups: The first group consisted of neonates born to mothers with COVID-19 (case group; n=30) and the second group of neonates born to healthy mothers (control group; n=30). The sampling method was random and the samples were selected among the infants of mothers who had referred to Amir Al-Momenin Hospital of Semnan city for delivery during 2021. Inclusion criteria in the case group include a history of COVID-19 during pregnancy (based on positive Real Time PCR test of nasopharyngeal and oropharyngeal samples), lack of underlying disease, no history of heart disease. Inclusion criteria in the control group also included no history of COVID-19 during pregnancy, lack of underlying disease, no history of heart disease. Exclusion criteria also included underlying diseases and unwillingness to participate in the study.

### Data collection

In the present study, the data collection tool was a checklist including baseline and clinical variables such as sex, birth weight, gestational age, heart rate, mitral valve E wave, mitral valve A wave, left ventricular function, Tricuspid Annular Plane Systolic Excursion (TAPSE) and Left Ventricular Ejection Fraction (LVEF) (by mode). In the present study, infants of affected mothers and infants of healthy mothers underwent echocardiography after examination by a neonatal specialist, up to the first ten days of birth. It should also be noted the evaluation of echocardiographic parameters performed using Philips affinity 50 ultrasound machines.

### Statistical analysis

The relevant data were entered into the SPSS24 for analysis. In descriptive analyzes, mean and standard deviation were used for quantitative variables, and number and relative frequency were used for qualitative variables. Then, *Chi-square* test, independent sample t-test and Pearson correlation coefficient were used to examine the relationship between baseline and clinical variables in two groups of neonates born to infected and healthy mothers and P-value<0.05 was considered as a significant level.

## Results

The aim of this study was to compare echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers referred to Amir Al-Momenin Hospital of Semnan in 2021. A total of 60 infants were examined into 2 groups: The first group consisted of neonates born to mothers with COVID-19 (n=30) and the second group of neonates born to healthy mothers (n=30). The numbers (%) of boys in two groups of infants born to infected and healthy mothers were 13 (43.33) and 14 (46.66%), respectively (P-value=0.795). Table 1 shows baseline and clinical characteristics of two groups of infants born to infected and healthy mothers. As is clear, there was no statistically significant difference between the two groups in terms of birth weight, gestational age, heart rate, mitral valve E wave, mitral valve A wave, left ventricular function, Tricuspid Annular Plane Systolic Excursion (TAPSE) and Left Ventricular Ejection Fraction (LVEF) (P-value>0.05).

| Variables | Groups | N | Min | Max | Mean | S.D** | P-Value* |
|---|---|---|---|---|---|---|---|
| Birth weight (gr) | Newborns of infected mothers | 30 | 914 | 3523 | 2128.67 | 791.27 | 0.71 |
| | Newborns of healthy mothers | 30 | 1216 | 3302 | 2199.67 | 675.62 | |
| Gestational age (week) | Newborns of infected mothers | 30 | 28.23 | 40.12 | 34.7 | 3.84 | 0.41 |
| | Newborns of healthy mothers | 30 | 30.35 | 40.74 | 35.4 | 2.94 | |
| Heart rate (per minute) | Newborns of infected mothers | 30 | 138 | 177 | 156 | 10 | 0.78 |
| | Newborns of Healthy mothers | 30 | 134 | 177 | 156 | 11 | |
| Mitral valve E wave (cm/s) | Newborns of infected mothers | 30 | 44.3 | 85 | 61.12 | 10.02 | 0.42 |
| | Newborns of healthy mothers | 30 | 44.3 | 88.2 | 63.47 | 12.35 | |
| Mitral valve A wave (cm/s) | Newborns of infected mothers | 30 | 52.9 | 87 | 71.07 | 7.57 | 0.36 |
| | Newborns of healthy mothers | 30 | 54.9 | 87.3 | 72.94 | 8.41 | |
| LVEF (%) | Newborns of infected mothers | 30 | 63.61 | 72 | 4.09 | 55 | 0.01 |
| | Newborns of healthy mothers | 30 | 91.3 | 67.26 | 6.48 | 56 | |
| TAPSE (mm) | Newborns of infected mothers | 30 | 0.65 | 1.2 | 0.92 | 0.3 | 0.58 |
| | Newborns of healthy mothers | 30 | 0.61 | 1.2 | 0.9 | 0.3 | |

**Note:** *: Indepent sample t-test; **S.D: Standard Deviation

**Table 1.** Comparison of baseline and clinical characteristics of two groups of infants born to infected and healthy mothers.

Table 2 shows changes of ventricular function in two groups of infants born to infected and healthy mothers according to sex. As can be seen, the results of independent t-test showed in the two groups, the mean variables of left ventricular function, Tricuspid Annular Plane Systolic Excursion (TAPSE) and Left Ventricular Ejection Fraction (LVEF) in girls and boys are not statistically significant (P-value>0.05).

| Variables | Groups | Sex | N | Mean | S.D | P-Value* |
|---|---|---|---|---|---|---|
| LVEF | Newborns of infected mothers | Boy | 13 | 63.64 | 4.28 | 0.97 |
| | | Girl | 17 | 63.59 | 4.07 | |
| | Newborns of healthy mothers | Boy | 14 | 68.21 | 7.99 | 0.46 |
| | | Girl | 16 | 66.43 | 4.91 | |
| TAPSE | Newborns of infected mothers | Boy | 13 | 0.57 | 0.19 | 0.11 |
| | | Girl | 17 | 0.71 | 0.29 | |
| | Newborns of healthy mothers | Boy | 14 | 0.59 | 0.24 | 0.73 |
| | | Girl | 16 | 0.63 | 0.27 | |

**Note:** *: Indepent sample t-test

**Table 2.** Comparison of changes of ventricular function in two groups of infants born to infected and healthy mothers according to sex.

Table 3 shows relationship between gestational age and COVID-19 infection in pregnant women (by week) with changes of ventricular function in two groups of infants born to infected and healthy mothers. The results of Pearson correlation coefficient showed that there is a statistically significant positive correlation between gestational age with Tricuspid Annular Plane Systolic Excursion (TAPSE) and Left Ventricular Ejection Fraction (LVEF) in the two groups, so that with increasing birth age, TAPSE and LVEF values increase (P-Value<0.05). However, the correlation between the left ventricular function and gestational age was inverse and negative in newborns of infected mothers (P-value<0.05). In addition, there was a significant positive correlation between COVID-19 infection according week and Tricuspid Annular Plane Systolic Excursion (TAPSE) (P-value<0.05) (Table 3).

| Variables | Gestational age | | | |
|---|---|---|---|---|
| | Groups | N | r-coefficients* | P-Value |
| LVEF | Newborns of infected mothers | 30 | -0.372 | 0.04 |
| | Newborns of healthy mothers | 30 | -0.106 | 0.59 |
| TAPSE | Newborns of infected mothers | 30 | 0.804 | >0.01 |
| | Newborns of healthy mothers | 30 | 0.725 | >0.01 |
| **COVID-19 infection in pregnant women (by week)** | | | | |
| **Variables** | **Group** | **N** | **r-coefficients*** | **P-Value** |
| LVEF | Newborns of infected mothers | 30 | -0.317 | 0.09 |
| TAPSE | Newborns of infected mothers | 30 | 0.396 | 0.03 |

**Note:** *r: Pearson correlation coefficient

**Table 3.** Relationship between gestational age and COVID-19 infection in pregnant women (by week) with changes of ventricular function in two groups of infants born to infected and healthy mothers. ex.

Table 4 shows relationship between birth weight and changes of ventricular function in two groups of infants born to infected and healthy mothers. The results of Pearson correlation coefficient showed that there is a statistically significant positive correlation between birth weight with Tricuspid Annular Plane Systolic Excursion (TAPSE) and Left Ventricular Ejection Fraction (LVEF) in the two groups, so that with increasing birth weight, TAPSE and LVEF values increase (P-value<0.05). However, there was no significant correlation between left ventricular function and birth weight in the two groups (P-value>0.05).

| Variables | Groups | N | r-coefficients* | P-Value |
|---|---|---|---|---|
| LVEF | Newborns of infected mothers | 30 | -0.336 | 0.07 |
| | Newborns of healthy mothers | 30 | -0.131 | 0.49 |
| TAPSE | Newborns of infected mothers | 30 | 0.836 | <0.01 |
| | Newborns of healthy mothers | 30 | 0.716 | <0.01 |

**Note:** *r : Pearson correlation coefficient

**Table 4.** Relationship between birth weight and changes of ventricular function in two groups of infants born to infected and healthy mothers.

## Discussion

Infection during pregnancy can have dangerous consequences for the pregnant mother and the developing fetus. Vertical transmission, which is defined as the transmission of infection from mother to fetus, can be caused by bacterial, viral, and parasitic infections and has irreversible consequences for the fetus. Congenital malformations, growth retardation, stillbirth, miscarriage, neonatal death, premature birth and maternal complications can be the consequences of infections during pregnancy [13,14]. With the onset of the COVID-19 epidemic, concerns were heightened about the behavior of the virus and its possible effects and consequences during pregnancy on the fetus and mother, hence, the present study was designed and carried out to compare echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers referred to Amir Al-Momenin Hospital of Semnan in 2021.

The results of this study showed that there was no statistically significant difference between the two groups in terms of birth weight, gestational age, heart rate, mitral valve E wave, mitral valve A wave, left ventricular function, TAPSE and LVEF (P-Value>0.05). In addition, the means of left ventricular function, TAPSE and LVEF according to sex were not significant in the two groups (P-Value>0.05). We observed a significant positive correlation between gestational age with TAPSE and LVEF in the two groups, however, the correlation between the left ventricular function and gestational age was inverse and negative in newborns of infected mothers (P-Value<0.05). Also, a significant positive correlation between birth weight with TAPSE and LVEF in the two groups (P-Value<0.05).

These results were consistent with some studies in this field. For example, in a case series study by Goldshtrom et al. on seven neonates with congenital heart and lung malformations born to mothers with a positive COVID-19 test, no COVID-19-related symptoms were observed. Also, nasopharyngeal test for COVID-19 was not positive in any of them. Finally, the authors of this study concluded that maternal infection with COVID-19 during pregnancy does not cause adverse cardiopulmonary effects in neonates born to these mothers [12]. Sukhikh et al. have shown that SARS-CoV-2 during pregnancy can lead to decreased blood flow in the umbilical artery of the fetus, fetal growth restriction, right ventricular hypertrophy, hydropericardia with features of hypoxic-ischemic brain injury and intraventricular hemorrhage. Also, laboratory findings in this study confirmed the transmission of placental virus to the fetus [15]. Electrocardiographic findings in a study by Wardell et al. on a 19-day-old infant with COVID-19 showed an increase in troponin levels, poor left ventricular function, and an EF of 49% [16]. Echocardiographic results of a newborn born by cesarean section at 36 weeks of gestation from a mother with COVID-19 showed a 40% EF in the first 12 hours after birth, mild Pulmonary Hypertension (PH), and left and right ventricular dilatation [17]. To our knowledge, most of the studies conducted in this field are case report and case series, so one of the important reasons for the difference between the results of our study and these studies may be due to differences in design.

This study has some limitations, perhaps the most important limitation of the present study is the low sample size of neonates in the study groups. Second, in neonates born to healthy mothers (control group), the basis for the mother not being infected with COVID-19 was a question from her (through an interview) about the lack of a history of COVID-19 during pregnancy, who she may have had an asymptomatic infection or has not referred to a health center for diagnosis despite the symptoms, this phenomenon is a type of recall bias which occurs in case-control studies and can lead to differential classification bias [18-21]. Third, our study is a case-control study, whereas detailed studies such as cohort studies are needed to accurately investigate the effect of COVID-19 on the neonatal cardiovascular system.

## Conclusion

This study showed the echocardiographic findings in neonates born to mothers with COVID-19 and neonates born to healthy mothers were not significantly different, however, cohort studies with higher sample size are recommended.

## Competing Interests

The authors declare no conflict of interest regarding publication of this article.

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## Ethical Consideration

First, the objectives of the study were explained to the mothers, and then, if they wished to participate, informed consent was obtained from them. In addition, this study was conducted according to the principles expressed in the Declaration of Helsinki and was approved by the Deputy of Research and Ethics review board identification.

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