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ORIGINAL ARTICLE

Can Fetal Heart Lie? Intrapartum CTG Changes in COVID-19 Mothers

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Abstract

Background COVID-19 infection has raised multiple concerns in pregnant mothers; many questioned the risk of vertical transmission and the implication on the feto-maternal outcome. Cardiotocogrm (CTG) is the principal method to observe intrapartum fetal well-being. This paper aims to verify intrapartum CTG changes seen in seropositive COVID-19 mothers versus healthy controls and looks into their relation to subsequent delivery mode and neonatal outcome.

Methods A case–control study recruited 90 pregnant women at the labor word of AL Yarmouk Teaching Hospital. All were term pregnancy admitted for delivery. They were grouped into 2: seropositive COVID-19 confirmed by real-time RT-PCR test (30/90) and healthy controls (60/90). We recorded their demographic criteria, laboratory results, CTG changes, delivery mode, and indication.

Results COVID-19 cases showed significantly higher pulse rate, temperature, and leukocyte counts. Cesarian deliveries (CS) were higher in cases versus healthy controls (70 % vs. 53.3 %) and P = 0.45. Analysis of the CS indications showed that abnormal fetal heart tracing accounts for 33.3 % versus 15.6 % (P-value = 0.015) for cases versus healthy controls. 60 % of COVID-19 cases exhibited abnormal CTG changes versus 19.4 % in healthy controls. These changes were primarily fetal tachycardia and reduced variabilities.

Conclusions The higher incidence of abnormal CTG in COVID-19 cases, alongside infection signs and symptoms, underlies the exaggerated inflammatory reactions inside the pregnant mother. These inflammatory reactions are the main causes of CTG changes and higher CS rates. Therefore, obstetricians are advised to optimize the maternal condition to rectify reactive CTG changes rather than proceeding into urgent CS.

Keywords COVID-19 · Cesarian section · CTG changes · Seropositive mothers

Introduction

There is a lot of conflicting scientific information out there about the COVID-19 pandemic, including its cause, how it spreads, and how drugs are used to fight it. The transplacental transfer has generated contradictory evidence. Uncertainty about vertical transmission has led to an unexpected rise in cesarian section (CS) deliveries among seropositive cases to protect their unborn babies [1, 2]. Lessons from the current pandemic showed higher rates of adverse pregnancy outcomes, like abortion, preterm labor, and preeclampsia [3, 4]. Interestingly incidence of admission to intensive care was (3 percent) with no documented fatalities. Breslin et al. declared that most mothers, including those with intensive care units(ICU) admissions, had been discharged well [5].

The immaturity of unborn babies' innate and adaptive immune systems makes them more susceptible to infections. Dysregulation of cytokines and an overactive inflammatory response may harm the brain's development and cognitive function in women who have confirmed infection [6]. However, most authors have reported no adverse newborn effects [7–9].

On the other hand, Zhu et al.recorded one neonatal death and six admissions to ICU. Six out of 10 neonates were premature babies, and eight out of 10 neonates were delivered via CS, two reasons that may have led to increased morbidity. The higher maternal morbidity and prenatal mortality rates raised by COVID-19 infection warranted close monitoring [10]. Intrapartum cardiotocography (CTG) is by far

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the most prevalent medical intervention in obstetrics wards that have been widely researched. Nonetheless, interpreting fetal heart rate (FHR) changes is a disputed and challenging topic in obstetrics [11]. Obstetricians should be able to comprehend the physiologic processes of FHR change that underpin these changes for accurate interpretation and sound clinical judgment [12]. Earlier in the COVID-19 pandemic, higher maternal death rates were attributed to the rise in CS rates and anesthesia complications in an already compromised maternal inflammatory status [13, 14]. Reviewing literature reveals a shift in practice to vaginal birth rather than CS delivery, which is now indicated for obstetrical indications in seropositive mothers [15]. It was confirmed that fetal distress was widely documented as the indication of CS 92 % of all deliveries[10, 16].

Therefore, this study aimed to compare intrapartum CTG alterations in seropositive COVID-19 mothers to healthy controls and investigate how they relate to delivery mode and newborn prognosis.

Patients and Method

We conducted a case–control study in the Obstetrics and Gynecology Division of AL Yarmouk Teaching hospital-Baghdad/ Iraq. A tertiary center that receives thousands of cases annually. Over four months from the 1st of June 2020 to the 1st of October 2020, a total of 90 pregnant women were recruited by this study. Inclusion criteria for participation in the study were:

1. Term pregnancies based on the early pregnancy dating and/or last menstrual period estimated date attending our labor ward.
2. Pregnant in labor confirmed by an abdominal and pelvic examination.
3. All participants had RT-PCR upon admission, and we enrolled seropositive cases as (study cases) while seronegative cases were taken as (healthy controls).

An exclusion was made to cases that did not have the required gestational age or were not in labor. Moreover, we exclude those with medical comorbidities like diabetes hypertension.

The study enrolled (30/90) seropositive pregnant women confirmed by PCR (polymerase chain reaction), and the remaining (60/90) were apparently healthy pregnant females. The Ethical Committee of Mustansiriyha University/Department of Obstetrics and Gynecology approved the study (MOG/167 on the 2nd March 2020). Verbal consent was taken from all participants involved in the study.

According to the local guidelines of the Ministry of Health during the COVID-19 pandemic, all patients attended to the hospital should be evaluated by history concentrated on the positive history of contact with COVID-19 patient or typical history of fever and malaise, cough and dyspnea, loss of taste and smell sensation, and diarrhea. Owning to the high infectivity of the disease, all patients examined by the medical team with complete personal protection equipment from the protective suit, mask, gloves, and face shield, starting from general examination including vital signs (pulse rate, blood pressure, temperature, respiratory rate, oxygen saturation by oximeter). Obstetric examination, including auscultation of fetal heart and fetal well-being assessment by cardiotocography, was well recorded and evaluated. Pelvic examination was performed when patients started labor, had a positive uterine contraction, or history of a leak. Any suspected cases were isolated in a special department prepared for COVID-19 cases, nasal and throat swabs, and tested for SARS-CoV-2 infection by real-time RT-PCR; blood samples were aspirated and sent for:

-Complete blood count.
-Renal function test.
-Liver function test.
-Coagulation profile.

The radiological testing, including chest X-ray and CT scan with abdominal shield, was limited to patients with cough, dyspnea, and high suspicion of pneumonia. All cases were followed up by a multidisciplinary team including obstetrician, neonatologist, respiratory specialist, anesthetics, and midwife from the time of admission till discharge home. The maternal and fetal outcomes were well recorded for all.

Statistical Analysis

Continuous variables were expressed as means and standard deviations with their respective *P*-values by SPSS version 24 analysis; Student's t test was used to compare means and standard deviation data. Categorical variables were analyzed using the Chi-square test. *P*-value < 0.05 was significant.

The sample size was calculated according to the formulae for case–control studies [17]:

$$\text{Sample size} = r + 1(p*)(1 - p*)\left(Z_{\beta} + Z_{\alpha/2}\right)^2 \Big/ r\left(p_1 - p_2\right)$$

where r = ratio of control to cases, P^* = average proportion exposed, P_1-P_2 = different in proportion expected based on previous studies. Z_{β} is a standard normal variant for 80 % power of the study.

$Z_{\alpha/2}$ is the standard normal variant at 0.05 P-value significance. The sample size is 70; we collect 90 participants.

Table 1 The demographic and clinical data of the study groups

Parameter	COVID-19 no = 30 mean ± SD	Control no = 60 mean ± SD	*P*-value
Maternal age (years)	27.5 ± 6.38	31.84 ± 6.98	0.053
Weeks of gestation	36.73 ± 2.47	38.38 ± 1.6	0.03*
PR/min	96.23 ± 9.91	85.84 ± 5.19	0.001*
SBP mmHg	116.3 ± 12.9	113.84 ± 11.9	0.56
DBP mmHg	74.16 ± 9.38	70.38 ± 5.18	0.18
SPO2 %	96.53 ± 1.38	97.38 ± 0.86	0.047*
Temperature C^0	37.51 ± 0.32	37.03 ± 0.16	0.001*
Hemoglobin (gm/dl)	10.62 ± 0.69	10.81 ± 0.56	0.39
WBC $*10^9/mm^3$	10.27 ± 1.37	6.61 ± 1.5	0.001*

* Refers for significant values

PR: pulse rate, SBP: systolic blood pressure, DBP:diastolic blood pressure,SPO2 % partial oxygen pressure, WBC: white blood cell count

Table 2 Cardiotocography findings and mode of delivery of both groups

Parameter	COVID -19 no = 30 frequency(%)	Control no = 60 frequency(%)	*P*- value
Cardiotocography			
Normal trace	12 (40 %)	49 (81.67 %)	
Variable deceleration	2 (6.67 %)	5 (8.3 %)	
Tachycardia	8 (26.67 %)	0	0.01*
Reduced variability	7 (23.33 %)	6 (10 %)	
Dead fetus	3 (10 %)	0	
Combined	2 (6.67 %)	0	
Mode of delivery			
Vaginal delivery	9 (30 %)	28 (46.67 %)	0.46
Cesarian section	21 (7o %)	32 (53.3 %)	

Results

A descriptive case–control study enrolled 90 pregnant women, 30 seropositive for COVID-19, and 60 matched healthy controls. The demographic criteria are shown in Table 1. seropositive women showed significantly lower gestational age and partial oxygen concentration (SPO2 %). Furthermore, they exhibit substantially higher temperatures, pulse rates, and total WBC counts than healthy controls. Maternal age, blood pressure, and hemoglobin concentration were all nonsignificant. Table 2 shows that 40 % of seropositive cases showed normal fetal heart tracing, while 60 % showed significantly higher CTG abnormalities manifested as tachycardia, reducing variability by 26.67 % and 23.33 %, respectively, highlighted in Figs. 1, 2, and 3. In addition, 10 % were already dead, and 6.7 % showed variable and combined variabilities.

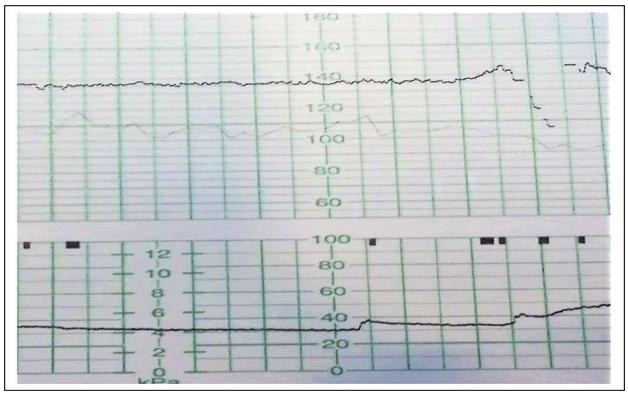

Fig. 1 Reduced variability and variable deceleration in CTG tracings among seropositive cases

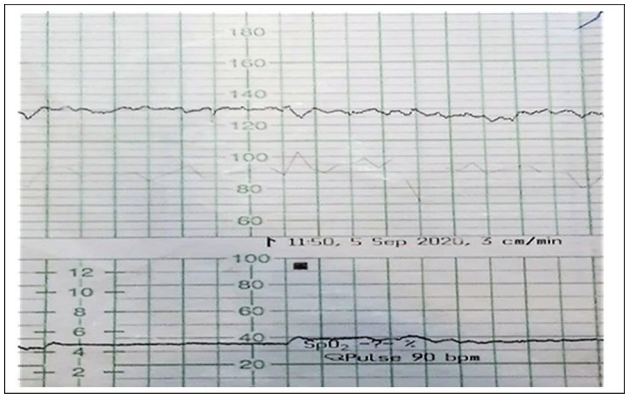

Fig. 2 Minimal and reduced variability in COVID-19 seropositive case

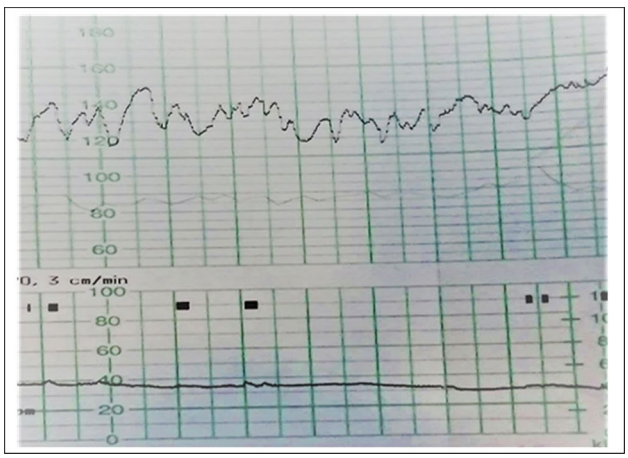

Fig. 3 Marked variability in CTG tracing of a seropositive mother

A trend of cesarian sections among seropositive COVID-19 cases was illustrated in Table 2, although it fails to gain

meaningful values. The frequencies and percentages of C sections based on their indications are clarified in Table 3.

Among 30 neonates delivered to seropositive mothers, 19 (63.3 %) neonates were delivered with 5-min Apgar scores > 7; the rest are shown in Table 4.

Table 4 The neonatal outcome in 30 seropositive cases:

5- minute Apgar score	Numbers (frequencies)	Neonatal care units admission
> 7	19(63.33 %)	–
5–7	6 (20 %)	1–3 days
< 5	2 (6.66 %)	7–10 days
Dead neonate	3 (10 %)	–

Discussion

Although the impacts of COVID-19 illness on pregnant pathophysiology have become understood, the probable maternal and newborn outcome of gestation with COVID-19 is still disputed. The result of this study showed that 60 % of seropositive COVID-19 cases suffered from abnormal fetal heart tracings. These abnormalities were significantly higher among seropositive mothers versus healthy controls.

The most frequent irregularities were fetal tachycardia and reduced variabilities. Nevertheless, 40 % of the seropositive women showed normal fetal heart tracing, which could be attributed to the placenta's defensive role that protected the growing fetus from invading viruses, or linked to the severity of maternal infection since most enrolled cases were mild-moderate cases [18].

Another likely cause is the role of innate immunity, which showed a wide diversity range affecting the severity of the maternal infection and consequently on fetal heart tracing. The pandemic has spread around the globe, yet many parts of the world have suffered from exceptionally severe infections alongside higher mortality rates. Different explanations were made related to racial and genetic differences, and many are still to be determined [19].

Fetal tachycardia could be explained in more than one way: First, it could be reactionary to maternal tachycardia; second, it could respond to maternal pyrexia. Third, it could be a reaction to the inflammatory and cytokine release that has been observed in many COVID-19 cases [20, 21].

Maternal tachycardia and pyrexia were significantly higher among seropositive women than healthy controls. Maternal tachycardia can be attributed to increased core body temperature by fever, which is markedly higher among seropositive cases than healthy women. It established that 70 % of maternal body temperature is transferred to the baby [22]. Mental health and stress-related tachycardia were also reported in many SARS-CoV-2 patients [23]. Moreover, the increase in total WBC noticed in seropositive cases points to an underlying inflammatory process where leukocytosis is triggered as part of the primary immune response to inflammation [14].

Pregnancy is a unique state of immunological tolerance to accommodate the growing in-utero fetus; thus, the immune response to inflammation may be modified. Pregnancy by itself does not increase the risk of acquiring COVID-19 [24]. However, if the pregnant woman suffers from COVID-19infection, she is more liable to get a more severe illness [25]. It is not unusual to have fetal signs of disease in mothers who suffer no clinical symptoms. In fact, 90–85 % of chorioamnionitis cases showed fetal tachycardia in asymptomatic mothers [26].

Earlier reports have discussed the value of fetal heart tracing among in-utero infections. Although affected fetuses may show no bradycardia by CTG tracing nor acidosis upon fetal scalp blood sampling, they suffer a higher risk of encephalopathy and cerebral palsy. This implies that infection can exert direct neurological injury by decreasing the threshold of neonatal apoptosis induced by hypoxia or indirectly by a non-hypoxia pathway. Fetal inflammatory process and hypoxia seem to work synergistically, resulting in abnormal rapid fetal tracing [27, 28].

In line with our finding, a case of fetal tachycardia was reported in an apparently healthy pregnant mother; testing confirmed a + ve infection, suggesting that fetal tachycardia

Table 3 Indications of cesarian sections

Indications	COVID-19 CS no. = 21 frequency(%)	Healthy control CS no. = 32 frequency(%)	*P*- value
Previous 2 CS and more	5 (23.8 %)	11 (34.8 %)	0.015
Previous 1 CS	3 (14.3 %)	5 (15.6 %)	
Failure to progress	4 (19 %)	6 (18.8 %)	
Fetal distress	7 (33.3 %)	5 (15.6 %)	
Malpresentation	2 (9.5 %)	3 (9.4 %)	
Chorioamnionitis	0 (0 %)	2 (6.3 %)	

CS = csesarian section

was part of the systemic manifestation of the SARS-CoV-2 infection that implicated her baby.

The fetus suffered from reduced variability on the third day of admission, and an urgent C-section was performed; the newborn was admitted to NCU for respiratory distress syndrome [29]. 23 % of our cases showed reduced variabilities, which were accredited to maternal fever, cytokine release, and exaggerated maternal inflammatory state. The latter contributes to reduced fetal sleep patterns and indirectly inhibits the fetal autonomic system. In accordance with our results, Gracia-Perez-Bonfils. A study reported that 58.3 percent of their cases showed reduced variability, although their study included only 12 patients. They followed them postnatally, and the perinatal outcome was primarily good, which implies that CTG changes in the fetus were secondary to maternal illness rather than fetal infection [4, 25, 30].

3 % of seropositive cases had dead fetuses, which can be attributed to maternal hypercoagulability state induced by pregnancy, exaggerated by the viral pro-thrombotic effect, added to the fever, and released inflammatory mediators, all of which contribute to thrombosis of placental and umbilical veins, causing fetal death [4, 14, 25]. In a recently published meta-analysis study, the authors studied 1787 seropositive mothers and revealed that only 2.8 % of their neonates tested positive for SARS-CoV-2. Interestingly, even in the absence of positive testing, there were placental changes evident by histopathology, showing placental ischemia and thrombosis. These changes were more prominent in + ve tested neonates, and they mirrored the underlying inflammatory reaction rather than viral vertical transfer [1].

The rate of CS was significantly higher in seropositive cases compared to healthy controls; the *P*-value was 0.015. Interestingly, subgroup analysis revealed a higher incidence of abnormal CTG as an indication for CS in the COVID-19 cases versus controls (33.3 vs. 16.5), though the neonatal outcome proved good, which is in line with earlier studies [30].

Seropositive moms should be closely monitored in delivery, and anticoagulant medications should be considered [25]. Intrapartum fetal heart changes and adverse neonatal outcomes, like meconium aspiration and respiratory difficulties, are more likely to be expected. These are attributed to placental insufficiency and fetal hypoxia rather than fetal infection. Therefore, instead of proceeding to urgent CS, obstetricians are advised to improve the maternal conditions to correct reactive CTG alterations. Moreover, the presence of a pediatrician in the delivery suite during and after birth is strongly recommended.

The current study has its limitations, being a single-center study. As for the study strengths, all recruited patients were term pregnancies and were admitted to our labor ward, which allowed for careful and close monitoring of cases, adding validity to our results. Earlier studies took multiple gestational ages from various centers where the evaluation was made by more than one party.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13224-022-01663-6.

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Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical Approval Ethics committee of Mustansiriyha University issued the study approval.

Ethical standards Declaration of Helsinki were followed in all procedures.

Consent for Publication An informed consent was taken from all participants before enrolling in the study.

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