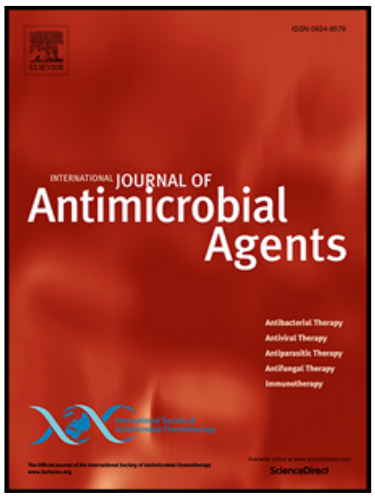

Vertical transmission and kidney damage in newborns from coronavirus disease 2019 infection pregnant mother

Zheng He , Yinian Fang , Qin Zuo , Xiaoxing Huang , Yongfang Lei , Xiuhua Ren , Dong Liu

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Highlights

COVID-19 caused by the SARS-CoV-2 has become the global pandemic;

The clinical characteristics of 22 neonates that born to mothers with COVID-19 infection firstly indicated its disease could yield to neonates' vertical transmission and kidney injury.

This study provides a theoretical basis for early diagnosis of developmental toxicity in neonates whose mother was infected with COVID-19.

Vertical transmission and kidney damage in newborns from coronavirus disease 2019 infection pregnant mother

Running Head: Vertical transmission and renal injury of COVID-19.

Zheng He [a], Yinian Fang [a], Qin Zuo [a], Xiaoxing Huang [b],Yongfang Lei [a], Xiuhua Ren [a], Dong Liu [a*]

[a] Department of Pharmacy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

[b] Department of Blood Transfusion, Zhongnan Hospital of Wuhan University, Wuhan, China

***Corresponding author:**

Prof. Dong Liu.

Department of Pharmacy, Tongji Hospital,

Tongji Medical College, Huazhong University of Science and Technology

Wuhan, 430030, Hubei Province, China

E-mail: l_d2069@163.com

What are the novel findings of this work?

The clinical characteristics of 22 neonates that born to mothers with COVID-19 infection firstly indicated its disease could yield to neonates' vertical transmission and kidney injury.

What are the clinical implications of this work?

This study provides a theoretical basis for early diagnosis of developmental toxicity in neonates whose mother was infected with COVID-19.

Abstract

Objectives: Coronavirus disease 2019 has now become a pandemic worldwide. However, the hazard to the newborn in pregnancy is still controversial. This study aims to investigate the vertical transmission of the virus from mother to child and its developmental toxicity in fetal.

Methods: All clinical information was recorded on 22 neonates born to the mother that was confirmed with coronavirus disease 2019 pneumonia in Tongji Hospital.

Results: The average birth weight of the 22 newborns (including 16 males and 6 females) was 2980 g, and the mean gestational week was 37W+3. Three babies' birth weight was lower than 2500g, the gestational week of all three low birth weight neonates was less than 36 W. Three newborns had minor lesions of infection in the lungs by Computed tomography scans. Furthermore, three newborns had elevated severe acute respiratory syndrome-related coronavirus-2 Ig (immunoglobin) M antibodies, and 11 newborns (52.4%) had positive IgG antibodies. Notably, both cystatin C and β2-microglobulin were increased in all newborns. Meanwhile, five of the 21 newborns had leukocytosis, and eleven newborns demonstrated increased neutrophil. Besides, the aspartate aminotransferase of 18 newborns and the γ-glutamyl transpeptidase of 19 newborns were increased. All the total bilirubin was elevated, and serum albumin in 90.9% of neonatal was reduced.

Conclusions: This study first discovered the coronavirus disease 2019 infection in the third trimester could cause fetal kidney development injury, specific performance as

increased cystatin C and β2-microglobulin in all neonates. Meanwhile, there is the possibility of the maternal-fetal transmission of the virus.

Keywords: COVID-19 infection mother; Vertical transmission; Newborns; Kidney developmental toxicity; Cystatin C

Introduction

Back in December 2019, the coronavirus disease 2019 (COVID-19) broke out in Wuhan, and it was contagion caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Within a few months, the epidemic had spread around the world. As of November 10th, more than 50 million people worldwide had been diagnosed with COVID-19, which caused over 1.26 million deaths. More seriously, there is no validated treatment of the SARS-CoV-2 at present, and only symptomatic supportive therapy is available for the patient. The disease is a devastating blow to all humanity. Therefore, there is an urgent need for the clinical studies of COVID-19 to understand the disease course, which would promote better control and cure of the disease.

To the outbreak of the COVID-19, more and more clinical and basic researches were reported. Back in February 2020, a study [1] published in Lancet reported the epidemiological, clinical, laboratory, and radiological characteristics of 41 COVID-19 patients as well as the clinical outcomes of these patients. With the global outbreak of disease, more researches conducted in other countries, such as Spain [2], the Indian [3], the American [4]. Correspondingly, the characteristics of the COVID-19 pneumonia disease are gradually recognized. However, the studies about COVID-19 pneumonia in pregnant women and the corresponding pregnancy outcome are still minimal, and the conclusion is controversial. A study in *Lancet* found no evidence for vertical transmission in the nine pregnant women with COVID-19 infection [5]. Wu and

colleagues [6] reported that the clinical characteristics in pregnant women with COVID-19 were similar to those of non-pregnant women.

Some studies are currently exploring the issue of vertical mother-to-child transmission of the SARS-CoV-2, but no consistent conclusions have been reached. For example, a case report published in JAMA [7] proposed the vertical transmission possibility from the view of antibodies. Baud D reported the second-trimester miscarriage in a pregnant woman with COVID-19 infection, which was related to the placental infection with SARS-CoV-2 [8]. Although the case report found no virus in the fetus, the authors suggest that vertical transmission of SARS-CoV-2 warrants further investigation. A study has reported that COVID-19 placentas show an increased prevalence of maternal vascular malperfusion, which is a pattern of placental injury and associated with adverse perinatal outcomes [9]. Penfield CA demonstrated the presence of SARS-CoV-2 RNA in placental or membrane samples of COVID-19 pregnant women and raised the possibility of intrapartum viral exposure [10]. The study suggested more research is needed to confirm the possibility of vertical transmission. Comment in *JAMA* proposed that the vertical transmission of the SARS-CoV-2 needs more definitive evidence [11]. The study suggests more research is required to confirm the possibility of vertical transmission. However, Zeng et al [12] found that 3 of 33 neonates (9%) born to mothers with COVID-19 were identified with positive SARS-CoV2 PCR, and the sources of SARS-CoV-2 in the neonates were likely maternal in origin. Hence, whether pregnant women confirmed COVID-19 could pass

the virus to the offspring remains controversial, which needs more definitive evidence.

Therefore, to facilitate the containment of COVID-19 pneumonia, we retrospectively collected the data from 22 newborns of COVID-19 pregnant women.

Methods

Study design and participants

All the newborns (including 16 males and six females) from pregnant women with COVID-19 pneumonia patients, admitted to Tongji Hospital affiliated to Huazhong University of Science & Technology (Wuhan, China) from January 1 to April 1, 2020, were recruited in this retrospective study and the relevant medical indicators were recorded. Pregnant women provided verbal consent to participate in this study. All the pregnant women with COVID-19 pneumonia diagnoses were based on the New Coronavirus Pneumonia Prevention and Control Program (the 7th edition) published by the National Health Commission of China. The studies involving human participants were reviewed and approved by the Ethics Committees of Tongji Hospital of Tongji Medical College, Huazhong University of Science & Technology (approval number TJ-IRB20200338).

Data collection

We reviewed all the related indicators of pregnant women and the newborn with COVID-19 pneumonia, including the epidemiological history, clinical records,

gestational age on infection and admission, Apgar scores, laboratory index, chest CT scans, antibody information, and medical information. The amniotic fluid, cord blood, and neonatal throat swab samples were collected immediately as soon as a newborn was born. The neonatal blood was received within 24 h after birth for the standard biochemical and blood parameters detections, including antibody detection, blood routine examination, and blood biochemistry test. All the medical data were analyzed and interpreted by the authors ZH, FY. We record the data in a particular form and check the data accuracy against each other. If there is a discrepancy in the data, we will ask a third author to correct it. All the COVID‐19 pregnant women types were identified according to the New Coronavirus Pneumonia Prevention and Control Program (the 7th edition). All samples (including the feces, urine, blood, gastric juices, and throat swab of the neonatal once they are born) were tested for SARS-CoV-2 by use of qRT-PCR with the Chinese Center for Disease Control and Prevention (CDC) recommended Kit (BioGerm, Shanghai, China), following WHO guidelines for qRT-PCR [13, 14].

Sampling measurements

The Latex-enhanced Turbidimetric Immunoassay kit (Leadman CY7600, Beijing, China) was used to test the serum Cystatin C concentration on a Roche Cobas c 701 (Roche, C8000-701) chemistry analyzer, and it is used for clinical diagnosis (Medical Machinery Registration Certificate: 20172400748). And the quantitative range of the kit was 0.2 - 8 mg/L. All intra-assay coefficients of variation were < 5 %, and the

inter-assay coefficients of variation were < 10%. The recommended normal range of Cystatin C in the newborn is 0.63-1.25 mg/L. The Latex-enhanced Turbidimetric Immunoassay kit (Roche 05950783, Indianapolis, USA) was used to test the serum β2-microglobulin concentration on a Roche Cobas c 701 (Roche, C8000-701) chemistry analyzer, which is used for clinical diagnosis (Medical Machinery Registration Certificate: 20182402206). Meanwhile, the quantitative range of the kit was 0.1 - 8 mg/L; the intra-assay and inter-assay coefficients of variation were 0.8 % and 1.5 %, respectively. The recommended limit of β2-microglobulin is 0.2 mg/L. The Chemiluminescent immunoassay iFlash SARS-CoV-2 IgG (C86095G, YHLO, Shenzhen, China) and iFlash SARS-CoV-2 IgM (C86095M, YHLO, Shenzhen, China) kits were used to test the serum IgM and IgG concentration on the YHLO iFlash 3000 chemistry analyzer. Meanwhile, the intra-assay and inter-assay coefficients of variation were 10 % and 12 %, respectively. The recommended limit of IgM and IgG is both less than 10 AU/mL.

Statistical analysis

SPSS 23.0 (SPSS Science Inc., Chicago, Illinois) was used for data analysis. The continuous variables were expressed as mean ±S.D (standard deviations [SD]) or medians (min - max), or as the number and percentage, as appropriate. The categorical variables were summarized as counts and percentages.

Results

Clinical characteristics in newborns of the SARS-CoV-2 pregnant women

The clinical features and the relevant detection indicators of the 22 newborns (including 16 males and 6 females) were summarized in Table 1. The average birth weight of the newborn was 2980 g. Only three babies' birth weight were lower than 2500g (the proportion is 13.6%). Statistically, we found that only one of the fetuses (Fetus 7) was IUGR. All three low birth weight neonates had the gestational weeks less than 36 W (35W+2, 31W, 28W+5, respectively), and the mean gestational week was 37W+3. The mean gestational age on infection of the pregnant mother was 35W+5, which meant the pregnant women gave birth within two weeks of COVID-19 diagnosis. All the 22 neonates had a 1-min Apgar score of 8–9 (Except Fetus 7, Apgar score of 7) and a 5-min Apgar score of 9–10 (Except Fetus 7, Apgar score of 8), and there is no fetal death, neonatal death, or neonatal asphyxia observed in these patients. The mean inpatient day (min-max) of the newborns was 20.05 days (2-55). Because these neonates are at high risk to the SARS-CoV-2 infection, so the SARS-CoV-2 nucleic acid assay was tested in the feces, urine, blood, gastric juices, and throat swab of the neonatal once they are born. Happily, there were no SARS-CoV-2 nucleic acids in the newborns tested. Three of the newborns had minor lesions of infection in the lungs by CT scans. However, the minor lesions in the lungs by CT scan could be the result of COVID-19, and yet it could also be an aspecific lesion of other causes, like amniotic fluid resorption delay, etc.

Laboratory characteristics in newborns of the SARS-CoV-2 pregnant women

Furthermore, we collated the laboratory indicators of the 22 neonates. As shown in table 2, the mean cardiac troponin I (cTnI) of the newborn was 21.85 pg/ml, fluctuating from 3.1 to 115 pg/ml. Meanwhile, the mean NT-pro brain natriuretic peptide (NT-pro BNP) of the newborns (min-max) was 4833.6 (611-22119) pg/ml. The blood cells count results showed that five of the 21 newborns had leukocytosis, and 57.1% of the newborns demonstrated increased neutrophil. Six fetal had reduced lymphocytes, and seven neonates had increased platelet counts. Besides, the aspartate aminotransferase (AST) of 18 newborns and the γ-glutamyl transpeptidase (GGT) of 19 newborns were increased. All the total bilirubin increased, and the serum albumin in 90.9 of neonatal reduced. 63.6% of patients had elevated concentrations of C-reactive protein (CRP). It was worth noting that both cystatin C and β2-microglobulin increased in all the newborns.

About the SARS-CoV-2 antibodies in the neonates, we found only three newborns had elevated IgM antibodies, but 52.4% of the newborns were SARS-CoV-2 IgG positive. Fetus 1 was delivered by cesarean section and was hospitalized for 16 days. The fetus had no other abnormal symptoms and was not treated with any drugs. The IgM antibodies in the umbilical cord blood and fetal blood were 184.32 and 48.93 AU/ml, respectively. Meanwhile, the delay between maternal infection and delivery for fetus 1 was 41 days. The maternal symptoms were fever with cough and fatigue (the highest body temperature was 39°C), nausea, and vomiting with diarrhea. The mother

was admitted to the hospital 32 days before the delivery, and she was given symptomatic support treatment, such as oxygen inhalation therapy, prevention of infection, and promotion of fetal lung maturation. By 14 days before delivery, all symptoms of the pregnant woman had improved significantly. Fetus 2 was delivered by cesarean section and was hospitalized for 18 days. The fetus had no other abnormal symptoms and was not treated with any drugs. The IgM antibody in the fetal blood was 15.75 AU/ml. The mother was diagnosed with COVID-19 infection just before the delivery by CT examination, and she did not have any symptoms. Fetus 16 was delivered by cesarean section and was hospitalized for 16 days. The fetus had no other abnormal symptoms and was not treated with any drugs. The IgM antibody in the fetal blood was 22.8 AU/ml. Furthermore, the delay between maternal infection and delivery for fetus 16 was 14 days, and she did not have any symptoms.

Discussion

Clinical features in newborns of the SARS-CoV-2 pregnant women

In this study, we report the clinical data from 22 neonates born between January and April 2020, whose mother was diagnosed with COVID-19 pneumonia. Recent literature suggests that [15] the infection of SARS-CoV-2 in late pregnant women does not show adverse outcomes in the newborns, including no asphyxia and positive result of SARS-CoV-2 nucleic acid in the pharyngeal swab, amniotic fluid, and umbilical cord blood. Similar in this study, we found all the 22 newborns without fetal death or

neonatal asphyxia, and all the SARS-CoV-2 nucleic acids were observed negative. However, 17 newborns showed hyperbilirubinemia, which may be physiological. The average birth weight of the newborn was 2980 g. Only three babies had a low birth weight, and it may be related to the gestational weeks less than 36 W. Besides, only three newborns had a CT scan. They were all found to have minor lesions of infection in the lungs, which indicates newborns of SARS-CoV-2 pregnant women are at risk of COVID-19 at birth. The above results suggest that SARS-CoV-2 disease in the late pregnant stage does not affect the weight and SARS-CoV-2 infection of the neonates.

The maternal-fetal transmission of SARS-CoV-2 infection

At present, there are few reports on the influence of SARS-CoV-2 infection on newborn babies, so our understanding of this aspect is still lacking. The question of whether the SARS-CoV-2 transmission can occur through mother-baby vertically has not been established yet. A few reports confirm that this spread does not exist. For example, Chen *et al*. found no evidence for vertical transmission in the nine pregnant women with COVID-19 infection [5]. A handful of other studies have supported mother-to-child transmission is unlikely for this virus, which mostly based on evidence that the SARS-CoV-2 has not been detected in fetuses [16-18]. However, these studies had small sample sizes and only focused on the SARS-CoV-2 nucleic acid results, which is inadequate. In our cohort study, SARS-CoV-2 nucleic acids in all the newborns were negative, which is similar to the above studies. However, we found three newborns

had elevated SARS-CoV-2 IgM antibody, and 52.4% of the newborns were IgG positive as they were born. As we all know, the antibodies detection of IgG has no reliable value as it could be one of the mothers that have been transferred. Although the IgM could reflect a fetal immune reaction, some cross-reactions have been described between the antibodies of COVID-19 and others. Recent studies showed that there were cross-reactions between rheumatoid factor and the IgM of SARS-CoV-2, leading to false-positive results [19]. And the intra-assay and inter-assay coefficients of variation were 10 % and 12 % for the IgM detection. So there's a possibility of cross-reaction. Meanwhile, the placental alterations may allow the passage of IgM. The study suggests that IgM was transported from the maternal tissues to embryos via a unique pathway in the viviparous teleost [20]. Meanwhile, none of the newborns had SARS-CoV2 nucleic acids positive, so the elevated SARS-Cov2 IgM level in the three newborns at born would suggest that there was very probable an intrauterine infection of the SARS-CoV-2. And interestingly enough, the umbilical cord blood IgM of fetus one was detected and showed positive (184.32 AU/ml). Unfortunately, antibodies in the umbilical cord blood of the remaining 21 fetuses were not detected. So we speculate the possibility of the maternal-fetal transmission of the virus, which is similar to the study published by Zeng et al [12].

The kidney damage in the newborn of SARS-CoV-2 pregnant women

Most research reports no symptomatic neonates born to mothers with confirmed

COVID-19 [5, 16]. Li *et al.* found COVID-19 infection mothers could not develop severe neonatal complications [21]. However, in this study, we found the mean cTnI of the newborn was 21.85 pg/ml, and the mean NT-pro BNP was 4833.6 pg/ml. Besides, the blood cells count results showed that five of the 21 newborns had leukocytosis, and 57.1% of the newborns demonstrated neutrophil was increased. Furthermore, about the liver function, the AST of 18 newborns was raised, all the total bilirubin elevated, and the serum albumin in 90.9 of neonatal reduced. Some studies indicated that COVID-19 patients showed elevated GGT levels [22, 23]. A meta-analysis analyzed 128 COVID-19 studies and found that the most frequent abnormality in liver functions was hypoalbuminemia, followed by disorders in GGT [24]. In this study, we found that the GGT of 19 newborns was increased. These results indicate the possibility of neonatal liver damage. Of course, as part of the neonates has hyperbilirubinemia, which does not rule out physiological jaundice.

As a potential biomarker for neonatal renal function, cystatin C and β2-microglobulin significantly improved the risk classification for death and renal disease across diverse populations [25, 26]. Elevation of cystatin C occurs before the increase of serum creatinine. Some pediatric studies showed that cystatin C was more accurate for estimating renal function in newborns compared with the serum creatinine [27, 28]. Cystatin C was a better marker for glomerular filtration estimation in preterm infants [29]. Bokenkamp, A et al. found that the cystatin C and β2-microglobulin concentrations in fetal serum would be useful predictors for the postnatal kidney

function [30]. It was worth noting that both cystatin C and β2-microglobulin increased in all the newborns, which was not reported in previous studies. The above results suggest that mothers with confirmed COVID-19 may lead to fetal kidney damage.

Strengths and Limitations

Although this paper found the possibility of vertical transmission between mother and child, due to the small sample size, more researches are needed to confirm this conclusion. In this study, only one fetus umbilical blood was detected the antibody, and the remaining 21 fetuses umbilical cord did not perform the antibody tests. All the 22 fetal serum was tested for SARS-CoV-2 antibodies; only three newborns' IgM was positive. So far, only Zeng et al [12] found that 3 of 33 neonates (9%) born to COVID-19 mothers were identified with positive SARS-CoV2 PCR, and the sources of SARS-CoV-2 in the neonates were likely maternal in origin. That is why vertical propagation can only be suggested, and more studies will follow to confirm this conclusion. Most researchers are focusing on the presence of COVID-19 nucleic acids in the neonates. When the results were negative, they concluded that there was no mother-to-child transmission. That is not reliable because infectious diseases are inherently self-healing. Therefore, follow-up studies should verify this conclusion in more samples and more different time points. COVID-19 caused kidney damage in the neonates is not reported before, which needs more follow-up studies to explore whether the impact is long term.

Conclusions

In conclusion, the clinical characteristics in the newborns show that the SARS-CoV-2 pregnant women have a favorable pregnancy outcome, and the SARS-CoV-2 infection in the late pregnant stage does not affect the fetus's weight and its SARS-CoV-2 infection. Moreover, there is the possibility of the maternal-fetal transmission of the SARS-CoV-2 virus, due to the presence of COVID-19 IgM antibody in umbilical cord blood and fetal blood. Meanwhile, we found early kidney damage in the neonates of the SARS-CoV-2 pregnant women, due to the increased cystatin C and β2-microglobulin in all the newborns. This study proposes the vertical mother-to-child transmission of the SARS-CoV-2 virus and the resulting renal damage, which is vital for understanding the clinical characteristics of newborns of COVID-19 infection pregnant women. Although our result should be evaluated with caution due to the small number of newborns, it can also increase the awareness of the SARS-CoV-2 virus effects on the newborns. This study provides some clinical supports for the early warning of the SARS-CoV-2 virus damage on the neonates.

Declarations

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Competing Interests: No conflicts of interest are declared by the authors.

Ethical Approval: The studies involving human participants were reviewed and approved by the Ethics Committees of Tongji Hospital of Tongji Medical College, Huazhong University of Science & Technology (approval number TJ-IRB20200338).

Author contributions:

ZH, YF, and QZ contributed to the acquisition of patients data. ZH and XH performed the study design, interpretation and manuscript writing. ZH and YL assisted with data analysis and statistical methods. YL, XR and DL provided critical revision of the manuscript for important intellectual content.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table 1: The clinical characteristics in newborns of the SARS-CoV-2 pregnant women

	Clinical characteristics									
	Birthday	Bodyweight（kg）	Apgar score (1 min, 5 min)	Inpatient days	Gestational age on infection	Gestational age on admission	Complications	SARS-CoV-2 nucleic acid assay	CT detection	
Fetus 1	Mar, 5	2.70	8, 9	16	32W	38W	Anemia,Hyperbilirubinemia	Negative	Infection on	lungs
Fetus 2	Mar, 4	3.10	8, 9	18	38W	38W	NA	Negative	Infection on	lungs
Fetus 3	Feb, 16	1.58	8, 9	30	30W+5	31W	Anemia,Hyperbilirubinemia	Negative	—	
Fetus 4	Feb, 15	2.92	8, 9	25	37W+5	38W+3	Hyperbilirubinemia	Negative	—	
Fetus 5	Feb, 13	2.84	8, 9	32	34w	36w+3	Hyperbilirubinemia	Negative	—	
Fetus 6	Feb, 16	3.29	8, 9	36	36W+1	39W+1	NA	Negative	—	
Fetus 7	Mar, 4	1.06	7, 8	55	26W+6	28W+5	Hyperbilirubinemia	Negative	Infection on	lungs
Fetus 8	Feb, 20	4.12	8, 9	16	41W+1	41W+2	Hyperbilirubinemia	Negative	—	
Fetus 9	Mar, 17	3.10	8, 9	45	30W	38W+2	Hyperbilirubinemia	Negative	—	
Fetus 10	Feb, 14	2.58	8, 9	34	35W+1	35W+2	NA	Negative	—	
Fetus 11	Feb, 27	3.86	8, 10	13	34W+3	38W	Hyperbilirubinemia	Negative	—	
Fetus 12	Feb, 29	3.93	8, 9	14	34W+6	39W	Hyperbilirubinemia	Negative	—	
Fetus 13	Feb, 21	3.17	8, 9	15	38W+2	39W	Hyperbilirubinemia	Negative	—	
Fetus 14	Mar, 19	2.58	8, 9	9	35W+3	35W+6	Hyperbilirubinemia	Negative	—	
Fetus 15	Mar, 19	2.29	8, 10	6	35W+3	35W+6	Hyperbilirubinemia	Negative	—	
Fetus 16	Mar, 18	3.14	8, 9	16	31W+3	38W	Hyperbilirubinemia	Negative	—	
Fetus 17	Feb, 17	2.64	8, 9	14	37W+4	37W+5	Hyperbilirubinemia	Negative	—	
Fetus 18	Feb, 20	3.71	9, 10	10	38W+3	38W+6	NA	Negative	—	
Fetus 19	Apr, 17	3.05	8, 9	5	38W+2	38W+3	Hyperbilirubinemia	Negative	—	
Fetus 20	Apr, 6	2.75	9, 10	16	39W+4	39W+5	Hyperbilirubinemia	Negative	—	
Fetus 21	Apr, 3	3.60	9, 10	2	39W+6	40W	Hyperbilirubinemia	Negative	—	
Fetus 22	Apr, 18	3.55	8, 10	14	38W+2	38W+3	NA	Negative	—	

NA: represent no complications; —: represent not tested

Table 2:

The laboratory characteristics in newborns of the SARS-CoV-2 pregnant women

			Routine blood test					Liver function test						Renal function test		SARS-CoV-2 Antibodies	
	cTnI	NT-por BNP	White blood cell count *10^9/L	Neutrophils count *10^9/L	Lymphocyte count *10^9/L	Hemoglobin g/L	Platelet count *10^9/L	ALT (U/L)	AST (U/L)	GGT (U/L)	Albumin (g/L)	Total bilirubin (umol/L)	CRP (mg/L)	Cystatin C (mg/l)	β2-micro globulin（mg/L）	IgM (AU/ml)	IgG (AU/ml)
Fetus 1	11.8	1464	13.77	7.72	4.52	123↓	258	13	91↑	200↑	33.5↓	61.3↑	0.9	1.86↑	0.38↑	48.39↑	181.12↑
Fetus 2	13	1828	18.73	11.93↑	4.75	161	295	7	38↑	58↑	33.9↓	75.2↑	3.7↑	1.75↑	2.56↑	15.75↑	222.11↑
Fetus 3	20.9	8354	8.91	5.49	1.9↓	200↑	299	8	61↑	291↑	35.2↓	88.1↑	2.2↑	1.97↑	12.06↑	2.6	113.00↑
Fetus 4	32.1	4633	16.53	11.41↑	3.68	189	260	29	87↑	614↑	34.6↓	94.5↑	4.2↑	1.76↑	3.09↑	5.29	120.77↑
Fetus 5	7.1	857	11.09	6.91	2.41↓	218↑	301↑	7	31	136↑	40.2	43.8↑	0.1	1.82↑	0.34↑	1.33	1.61
Fetus 6	65.8	6197	12.44	7.93	3.33	165	295	54↑	340↑	146↑	34.4↓	67.3↑	1.4↑	1.49↑	3.67↑	0.6	1.28
Fetus 7	12.2	16357	13	7.13	4.25	141	233	6	44↑	98↑	27.2↓	62.0↑	0.3	—	—	0.25	0.36
Fetus 8	10	3029	16.14	10.84↑	4.34	119↓	242	7	35↑	56↑	36.5↓	59.6↑	2.8↑	1.77↑	13.02↑	1.55	2.68
Fetus 9	21.2	4146	31.75↑	23.15	4.79	185	420↑	12	40	95↑	32.7↓	113.8↑	0.4	—	—	2.98	145.75↑
Fetus 10	6.4	2293	15.46	8.23	4.29	164	154	10	40↑	250↑	36.1↓	109.7↑	2.2↑	2.1↑	0.67↑	0.35	3.45
Fetus 11	26.8	1342	16.48	11.15↑	3.43	140↓	369↑	6	26	58	35.3↓	76.4↑	0.5	1.87↑	1.55↑	3.52	134.13↑
Fetus 12	20.2	6362	30.43↑	21.52↑	5.43	180	307↑	15	89↑	50	53.8	84.9↑	1.1↑	1.52↑	5.34↑	2.2	78.41↑
Fetus 13	12.7	22119	20.9↑	16.21↑	2.67↓	179	300	11	70↑	254↑	37.9↓	100.7↑	10.8↑	1.38↑	5.83↑	0.49	1.77
Fetus 14	12.5	2678	10.57	6.37	2.55↓	179	318↑	15	90↑	270↑	34.1↓	67.5↑	1.3↑	—	—	0.19	3.37
Fetus 15	17.4	2615	13.32	7.98	3.73	161	287	22	120↑	133↑	35.8↓	62.6↑	1.7↑	—	—	0.25	3.26
Fetus 16	6.2	4746	15.16	7.85	4.65	170	333↑	14	46↑	153↑	34.6↓	176.3↑	3.8↑	—	—	22.8↑	116.48↑
Fetus 17	115	611	20.66↑	14.91↑	3.03	211↑	266	5	25	247↑	33.9↓	36.6↑	<0.1	2.47↑	5.45↑	2.73	0.59
Fetus 18	22.5	3460	16.88	13.51↑	2.22↓	130↓	362↑	9	54↑	60	33.8↓	58.3↑	9.2↑	1.65↑	1.95↑	—	—
Fetus 19	10.1	—	31.36↑	23.94↑	4.13	194↑	276	12	81↑	92↑	37↓	102.0↑	—	1.42↑	—	0.71	100.99↑
Fetus 20	7.6	1935	15.96	11.28↑	3.27	153	298	13	66↑	67↑	37↓	93.4↑	1.7↑	1.65↑	—	6.62	96.17↑
Fetus 21	3.1	2959	17.92	12.73↑	2.66↓	175	282	9	63↑	81↑	33↓	88.6↑	4.6↑	—	—	0.18	0.46
Fetus 22	26.2	3521	—	—	—	—	—	9	65↑	193↑	35.4↓	62.7↑	0.6	—	—	1.15	110.38↑

cTnI: cardiac troponin I; NT-porBNP: NT-pro brain natriuretic peptide; ALT: Alanine transaminase; AST: aspartate aminotransferase; GGT: γ-glutamyl transpeptidase; CRP: C-reactive protein;

↑: represent that the test value higher than normal; ↓: represent that the test value lower than normal; —: represent not tested