

Case Report

Pregnant with COVID-19 and Rubella: Impact in the Maternal and Newborn Health

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Introduction

COVID-19 is an infection disease caused by SARS-CoV-2 [1]. The clinical manifestations may include fever, difficulty in breathing, cough, coryza, sore throat, loss of smell and taste and even death from multiple organ failure. The first case was reported in December 2019 in Wuhan, China and has spread around the world at an accelerated rate, included Brazil. At present, scarce information is still available on the clinical and epidemiological outcomes of COVID-19 in pregnancy. Additionally, the COVID-19 pandemic has raised concerns about the possibility of mother-fetal vertical intrauterine transmission [2,3], coinfection with others microorganisms and the impact in the maternal and newborn health. This report case describes a Brazilian pregnant with COVID-19 (tested positive at the 28th week of pregnancy) and also positive for rubella (detected in 31st week). SARS-CoV-2 nucleic acid was not detected in the neonate nasopharyngeal swab, suggesting no vertical transmission. However, further laboratory analysis revealed anti-SARS-CoV-2 IgG antibody and anti-rubella IgG antibody in the newborn serum. This case may suggest transplacental transmission of protective antibodies against SARS-CoV-2 and rubella virus ensuring immediate immunity against these pathogens to newborn.

Case Presentation

A 33-year-old Brazilian 28-week pregnant woman with loss of smell and taste was diagnosed with COVID-19 by Reverse Transcription-quantitative Polymerase Chain Reaction (RT-qPCR). At this time, the patient did not present respiratory symptoms (runny nose, cough, fever or respiratory distress), diarrhea and myalgia. Additionally, anti-Rubella Virus IgM and IgG antibodies were detected in the pregnant woman's serum, indicating recent viral infection. Laboratory screening for HIV, hepatitis B, hepatitis C, toxoplasmosis, cytomegalovirus, and syphilis tested negative in the same sample. During the pregnancy, hematological tests

Abstract

Since December 2019, COVID-19 has become major global public health problem. The understanding of SARS-CoV-2, especially the effect on pregnant women and neonates, is still not fully elucidated. This report case describes a pregnant with COVID-19 and rubella. SARS-CoV-2 nucleic acid was not detected in the neonate just after birth, indicating that there was not vertical transmission. Although anti-SARS-CoV-2 Immunoglobulin G (IgG) antibody and anti-Rubella Virus IgG antibody were detected in the newborn serum, anti-SARS-CoV-2 (Immunoglobulin M) IgM and anti-Rubella Virus IgM were not detected. The observations may suggest transplacental transmission of coronavirus and rubella antibodies, ensuring immediate immunity against these pathogens to newborn.

Keywords: SARS-CoV-2; Rubella; Pregnant; Coinfection

(platelets, leukocytes, erythrocytes, hemoglobin, hematocrit), glucose, vitamins (B12 and D), ferritin, lactic dehydrogenase, d-dimer, C-reactive protein, thromboplastin time, prothrombin time, Thyroid-Stimulating Hormone (TSH) and Thyroxine (T4) showed results within the reference values indicated for their age and gender (Table 1A). After 14 days of COVID-19 positive test, the patient presented increased fibrinogen (acute phase protein), suggesting an increase in the inflammatory process (Table 1A). On the day of delivery, a nasopharyngeal swab was collected from the newborn and nucleic acid was not detected by RT-qPCR, indicating that there was no vertical transmission of SARS-CoV-2. Anti-SARS-CoV-2 IgG and anti-Rubella Virus IgG antibody were detected in the newborn serum. However, Anti-SARS-CoV-2 IgM and anti-Rubella Virus IgM antibody were not detected. These observations may suggest transplacental transmission of coronavirus and rubella antibodies, ensuring immediate immunity against these pathogens to newborn. Laboratory screening for HIV and syphilis of the newborn showed negative results. Bilirubin dosage showed to be elevated. Phenylalanine, neonatal hemoglobinopathy, TSH, 17 alpha hydroxyprogesterone, trypsin, t4, biotinidase, glucose-6-phosphate dehydrogenase (G6PD) deficiency, amino acid chromatography, galactose, toxoplasmosis were negative or within the expected range for the age group (Table 1B).

This pregnant woman is not a healthcare professional, non-alcoholic and non-smoking. She does not have diabetes, upper respiratory tract disease, autoimmune disease and high blood pressure. She used polyvitamins and did not use anticoagulant. After COVID-19 diagnostic, she did not use any medication, such as chloroquine or hydroxychloroquine. According to the anthropometric measurements she may be categorized as eutrophic (weight 63 kg/height 167 cm). At term, she gave birth by vaginal delivery. The newborn did not present clinical alterations, except jaundice.

Table 1A: Laboratory data of the pregnant.

Parameter	Stantard Value	Day						
		10-08-2019	01-16-2020	02-27-2020	03-23-2020	04-06-2020	04-17-2020	04-24-2020
White bloodcells (x 10 ⁹ /l)	4-10	71	86	78	-	66	64	-
Hematocrit (%)	36-46	374	349	-	-	387	375	-
Neutrophils (x 10 ⁹ /l)	2-7	48	76	73	-	69	43	-
Lymphocytes (x 10 ⁹ /l)	0,8-4	19	18	19	-	25	17	-
Eosinophils (x 10 ⁹ /l)	0,04-0,6	04	05	09	-	00	04	-
Hemoglobin (g/dl)	11-17	129	116	118	-	130	124	-
Platelets (x 10 ⁹ /l)	140-450	270	278	231	-	215	175	-
Prothrombin time (s)	131	-	-	-	-	137	-	-
Lactate dehydrogenase (U/l)	200-480	-	-	-	-	218	-	-
C-reaction protein	Negative	-	-	-	-	negative	-	-
Fibrinogen (mg/dL)	175-400	-	-	-	-	532	-	-
SARS-CoV-2 nucleic acids	-	-	-	-	Detected	-	No detected	-
TSH (mcUI/mL)	0,4-5,0	16	27	-	-	-	34	-
T4 (ng/dL)	0,7-1,8	085	076	-	-	-	084	-
Glucose (mg/dL)	60-99	85	83	-	-	-	73	-
B12 vitamin (pg/mL)	187-883	200	808	-	-	-	322	-
D vitamin (ng/mL)	>20	284	307	-	-	-	430	-
Ferritin (ng/mL)	10-204	522	182	126	-	88	-	-
Anti-HIV antibodies	NR	NR	NR	NR	-	-	NR	-
IgG Toxoplasmosis	NR	NR	NR	NR	-	-	NR	-
IgM Toxoplasmosis	NR	NR	NR	NR	-	-	NR	-
Anti-HCV antibody	NR	NR	NR	NR	-	-	NR	-
HBsAg	NR	NR	NR	NR	-	-	NR	-
IgG Citomegalovirus	-	-	-	-	-	-	NR	-
IgM Citomegalovirus	-	-	-	-	-	-	NR	-
Syphilis test	-	-	-	-	-	-	NR	-
IgG Rubella	-	-	-	-	-	-	Reactive	Reactive
IgM Rubella	-	-	-	-	-	-	Reactive	Reactive

Discussion

With the world widespread of COVID-19, concerns have been raised on the impact of pandemics on pregnant women and mother-fetal vertical intrauterine transmission [2,3]. It should be noted that the physiologic and immunologic changes that occur as a normal component of pregnancy may have systemic effects which may increase the risk for complications of respiratory infections [4]. Limited data is available about COVID-19 during pregnancy [5], however information about the disease should be reported in order to understand the impact on pregnant women and newborns.

Coronaviruses are single-stranded RNA, nonsegmented, enveloped viruses, that measure about 50–200 nm in diameter, which cause illness ranging in severity from the common cold to severe and fatal illness. The virus viewed by electron microscopy display a crown-like fringe typically referred to as spikes. The new coronavirus SARS-CoV-2 is transmitted through respiratory droplets, physical contact, and aerosols [3,4].

The rapid diagnosis of COVID-19 is an important strategy for preventing the spread of viruses. RT-qPCR is widely deployed in diagnostic virology and represents the gold standard method for confirmation of COVID-19 [1,6]. The RT-qPCR test performed on the mother's nasopharyngeal swab during pregnancy was positive for new coronavirus. In relation to clinical manifestations, the common symptoms of these pregnant women at the onset of COVID-19 were fever and cough, and the less common symptoms were diarrhea and shortness of breath. Laboratory tests showed that absolute lymphocyte counts were reduced, C-reactive protein, erythrocyte sedimentation rate and D-dimer were increased, and leucocytes were normal in most of the seven pregnant patients. It is reported that SARS-CoV-2 may cause a decrease in peripheral white blood cell and lymphocyte counts in the early stages of the disease [7], however some patients did not showed laboratorial alterations. Comorbidities such as diabetes, obesity and high blood pressure have been identified as a risk factor in the pathogenesis of COVID-19 [8]. The pregnant woman in this study did not present hyperglycemia, did not report

Table 1B: Laboratory data of the newborn.

Parameter	Stantard Value	Day	
		05-08-2020	05-13-2020
Bilirubin (mg/dL)	< 0,8	-	125
Phenylalanine (mg/dL)	< 2,2	-	08
Neonatal hemoglobinplasty	Normal	-	Normal
TSH (mcU/mL)	< 15	-	141
17 alpha hydroxyprogesterone (ng/mL)	< 15	-	13
Trypsin (mg/mL)	< 90	-	152
T4 (mcg/dL)	6-22,1	-	69
Biotinidase	Normal	-	Normal
G6PD deficiency (U/g Hb)	> 2,4	-	45
SARS-CoV-2 nucleic acids	No Detected	No Detected	-
Amino acid chromatography	Normal	-	Normal
Galactose (mg/dL)	< 9,0	-	12
Anti-HIV antibodies	NR	NR	-
IgM Toxoplasmosis	NR	-	NR
IgG COVID-19	NR	Reactive	-
IgM COVID-19	NR	NR	-
Syphilis test	-	-	-
IgG Rubella	NR	Reactive	-
IgM Rubella	NR	NR	-

hypertension and is not obese.

The RT-qPCR test performed on the neonatal's nasopharyngeal swab was negative in the first hours of life, suggesting no vertical transmission of coronavirus. Along with molecular RT-qPCR testing, IgM and IgG screening are relevant and figure out as alternative diagnostic methods [9]. In this report, virus-specific antibodies (IgG) were detected in neonatal serum, suggesting transplacental transmission of coronavirus antibodies, ensuring immediate immunity to newborn, once questions are being raised on the length of COVID-19 immunity. IgG is passively transferred across the placenta, beginning at the end of the second trimester [9]. Anti-coronavirus IgM was not detected, what is expected once IgM is not transferrable between mother and fetus due to its large macromolecular structure [9]. Data from a case reports published earlier in this year described SARS-CoV-2 infected women with no laboratory evidence of vertical mother-fetal intrauterine transmission [4,5,10,11]. According to these reports, some newborn were symptomatic but throat swab testing of all retrieved negative results for SARS-CoV-2, suggesting that these neonatal complications could not be related to intrauterine transmission.

Rubella is a mild viral disease that typically occurs in childhood. Rubella infection during pregnancy causes congenital rubella syndrome, including the classic triad of ocular and cardiac abnormalities and sensorineural deafness. Highly effective vaccines have been developed since 1969, and vaccination campaigns have been established in many countries, including Brazil. Although there has been progress, the prevention and diagnosis of rubella remain problematic [12]. The consequences of rubella infection in the first

20 weeks of pregnancy, and the relationship between gestational week of exposure and likelihood of fetal loss or features of congenital rubella syndrome have been related [13]. The rubella virus belongs to the *Togaviridae* family and is an enveloped, positive single-stranded RNA virus, with a 9.8-kb nucleotide length.

Humans are the only known reservoir of infection, and the rubella virus is transmitted through direct inter-human contact through the aerosol route. After being inhaled, the virus replicates in the respiratory mucosa and cervical lymph nodes, before reaching the target organs *via* systemic circulation. The infectious period extends approximately 8 days before to 8 days after the rash onset. Viremia is transient and is detected during the week before the rash. Rubella is less contagious than measles or influenza; because many rubella cases are asymptomatic, the true attack rate is uncertain [12]. In this case report, Anti-rubellaVirus IgG antibody was detected in the neonatal serum, indicating transplacental transmission of antibodies, ensuring immunity to neonatal. Anti-rubella Virus IgM antibody was not detected, indicating that there was not vertical transmission of virus.

In an epidemic situation, special care should be taken in pregnancy management and in making decisions on termination of pregnancy and handling of the neonate in order to minimize the risk of subsequent health consequences [14].

SARS-CoV-2 nucleic acid was not detected in the newborn nasopharyngeal swabs, which strongly suggest that there was not vertical transmission of virus. However, laboratory analysis revealed Anti-SARS-CoV-2 IgG antibody and Anti-rubella Virus IgG antibody in the newborn serum. This case reveals evidence of transplacental transmission of coronavirus and rubella antibodies, ensuring immunity against these pathogens to newborn.

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Ethical Conduct of Research Statement

The case report was carried out through consultation and consent of the participant, according to a project approved by the Research Ethics Committee of UFJF, with number 4.057.992, CAAE 31527720.3.0000.5147.

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