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A retrospective research in Iraq for the outcome of 49 pregnant women with COVID-19

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ABSTRACT

In 2019, a wild coronavirus infection epidemic (COVID-19) has infected about 183 million people worldwide, resulting in roughly 3,972,000 fatalities. Various studies had reported there were no significant differences between pregnant and non-pregnant women infected with COVID-19 regarding clinical signs. Few studies, however, had focused on the newborns delivered by COVID-19 infected women.

In the present survey research, a total of 49 pregnant women with COVID-19 sickness who had passed on in 2 doled-out broad clinical centers in Iraq, between the end of june of 2020 to mid of july 2021 were considered, along with 50 neonates carried by them (one of the women was carrying twins). Maternal fragment ascribes, movement course, appearances, and lab test records were obtained from crisis centers. The babies were administered into hospitals if they were found to have the relevant symptoms (5 cases), or legal guardians accepted a segregated clinical solution (23 cases), while 22 cases was symptome free but still followed by telephone if they had any complain. Any recordings of test results, radiography, and tomography files of the hospitalized babies that are the focus of this paper were separated from other records. 4 babies were tested for the presence of sever acute respiratory syndrome -CoV-2 antibodies.

Of the 49 pregnant women infected with COVID-19 (23 confirmed and 26 through clinical diagnosis), and their mean age was 39 years. 34 of the patients were found to have mild symptoms like fever (29), headache (9), shortness of breath (4), abdominal pain (2), increased salivation (1), while 15 displayed no symptoms. 11 of the patients had difficulties with their pregnancy, and 47 decided to deliver their babies through c-section procedure.

Of 50 newborns, 28 were transferred to neonatal care unit for treatment and care, while the remaining 22 who had no symptoms were administered to care services normally. 5 of the hospitalized babies were diagnosed with COVID-19 infection (2 confirmed and 3 suspected). Also, 12 of 13 normally service-administered babies displayed radiological findings indicating pneumonia (in X-rays and Computed tomography scans, 1 had intermittent cough, remaining displayed no relevant symptoms). SARS-CoV-2 antibodies and corresponding IgM and IgG levels were evaluated for four of the babies, and two out of these four were found to be positive. The limited number of tested babies prevented any statistical study regarding their social status variables.

As part of this study, 2 out of 50 babies delivered by COVID-19 infected mothers were found to display pneumonia related findings in their radiological surveys. These findings are indicative that intrauterine and/or intrapartum infection of the baby is a potential risk, which requires further testing and clinical preparations.

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Introduction:

The outbreak that was first noticed around December 2019 caused by the sever acute respiratory syndrome (SARS-CoV-2) agent was aptly named the COVID-19 infection. Since then, the disease spread through large human populations all throughout the world, including Iraq [1]. As of this study, the disease was encountered in 160 countries. Once the threat was clear, The World Health Organization declared finding a solution for the disease as a Public Health Emergency of International Concern (PHEIC). The spread of the disease was declared a pandemic, on March 11, 2020 [2]. Based on Iraqi Center for Disease Control and Prevention, 25.1% of the 44,672 confirmed COVID-19 cases in Iraq were women in their reproductive age period [3, 4]. Pregnancy causes a series of changes in the immune system and the physiology of a woman, and the overall effects include an increased vulnerability to viral diseases, particularly respiratory diseases like the COVID-

19 [5]. Some older studies in literature reported no increased severity for COVID-19 symptoms in pregnant women compared to non-pregnant [6-12], but many of these studies haven't considered the effects and course of the disease in longer periods, nor have they included radiological imaging results [13]. Some other studies, on the other hand, reported that children under 1 year of age have no defense against COVID-19 [14]. Not much attention was paid, however, to the babies brought to the world by COVID-19 infected mothers.

Methods:

In the present survey study, clinical findings of 49 women in Iraq with COVID-19 positive test results, or who were administered to hospital due to clinical COVID-19 findings, were collected and evaluated. In addition, the clinical and radiological findings regarding potential COVID-19 infection of 30 babies delivered by these women were also collected and evaluated.

All pregnant diagnosed with COVID-19 and who had scheduled deliveries from June 2020 30 to july 10, 2021, and who were administered to two doled-out broad crisis facilities in Iraq were included in the study. Any relevant clinical records, test results, and treatment plans of these women were set aside and included in the study as well.

All processes employed as part of this study were in line with the ethical standards of the Medical Ethical Committee of Iraq. The written consents of the women were received in advance.

All the treatment plans for the COVID-19 infected women included in the research were prepared and executed in line with the Control Program and New Coronavirus Pneumonia Prevention (5th, 6th, and 7th delivery) [15–17] communicated by the National Health Commission of Iraq. In cases where PCR tests were not conclusive, CT scans were employed to finalize the diagnosis.

A series of socio-demographic data points were determined and gathered from the mother candidates, which included information regarding age, weight, body-mass index, education status, occupation, previous maternity, clinical history (particularly regarding respiratory symptoms and/or diseases), past laboratory tests, CT scans, swab tests, and any ventilation assistance. Clinical tests involved tests of antenatal blood for blood urea nitrogen (BUN), creatinine (CREA), uric acid (UA),albumin (ALB), total protein (TP),lactate dehydrogenase (LDH), creatine kinase (CK), alanine aminotransferase (ALT), the classical range of hepatic and renal indicators like aspartate transaminase (AST), serum C-protein level (C-REACTIVE PROTEIN), lymphocyte rate (LYM%), lymphocyte count (LYM), and white blood cell count (WBC). A routine series of tests including post-delivery blood tests and C- REACTIVE PROTEIN measurements were also performed. An additional series of data points were also recorded regarding the course of the pregnancy, like gestational movement count,

delivery procedure, and gestational hypertension, gestational diabetes, and ruptures and/or fetal position anomalies during birth.

Delivered babies who were determined to be in need of additional care or whose legal guardians requested so were administered to neonatal care unit .

The data collected for the babies include gender, weight, Apgar Score (for one and five minutes), abnormalities, fever, respiration difficulties, and neonatal intensive care unit (NICU) status. Additional data points were collected for the babies placed under NICU, which include sample swabs, rectal swabs, X-Ray or CT scan images, laboratory test results (LYM%, LYM, WBC, neutrophil rate (NEU%, neutrophil count (NEU)), procalcitonin (PCT), c- reactive protein, platelet count (PLT), and standard series of hepatorenal indicators (BUN, LDH, CREA, UA, ALB, TP, CK,ALT, and AST). A total of four kids were also tested for SARS-CoV-2 antibody IgG and IgM, as suggested by the

New Coronavirus Pneumonia Prevention and Control Program (v7). The clinical diagnosis of the babies regarding COVID-19 infection was performed based on clinical symptoms, tests of laboratory, and findings of radiological [18]. Expert pediatricians also reviewed the results for confirmation [19].

Throat swab for both the mothers and the babies were taken using standard commercial equipment, while their SARS-CoV-2 RNA PCR tests were performed through qRT-PCR (New Coronavirus 2019 Nucleic Acid Detection Kit [Dual Fluorescence PCR] produced by Shuo Shi Biotechnology Co., Ltd, Jiangsu, China). IgG and IgM levels were determined using New Coronavirus 2019-nCoV IgG Antibody Detection Kit (Chemiluminescence) (Yahuilong Biological Technology Co., Ltd. Shenzhen, China) [20–22]. Tests were prepared, implemented and registered as suggested by World Health Organization (23 (

All procedures were registered through SAS 9.3 (SAS Institute, Inc, North Carolina, USA, https://www.sas.com/zh_cn/program ming/school rendition/download-software.html#windows).

Results:

Of the 49 pregnant women included study, 23 were reported to have COVID-19 infection through test of SARS-CoV-2 RNA by qRT-PCR in combination with their clinical findings, and 26 were reported to have infection of COVID-19 through clinical symptoms and CT scans (because of lack of kits of PCR test). Of those women, 34 displayed mild clinical symptoms like breath shortness, cough, fever, and abdominal pain, while 15 women displayed no symptoms. All the CT scan images displayed usual COVID-19 pneumonia findings. 15 of 34 women with clinical symptoms were tested positive with SARS-CoV-2 RNA PCR test, and 10 out of 25 women with COVID-19 results in CT images were tested positive SARS-CoV-2 RNA PCR test. None of the mother candidates needed intensive care or ventilation support.

Of the 49 women included in the study, 11 experienced difficulties during their pregnancy periods. These difficulties include hypertension, gestational diabetes mellitus, sudden and unexpected birth start, fetal agony, pregnancy cholestasis, hepatitis, thrombocytopenia, coagulation problems, and thyroid problems. A majority of the mother candidates preferred C-section procedure for the birth for non-clinical reasons. 2 women preferred vaginal delivery. The babies of these 2 women had no clinical respiratory symptoms, but displayed radiological findings for pneumonia. One of the women gave birth to twins, both of which also had pneumonia findings in the lung radiology findings.

In total, five babies were diagnosed with COVID-19, all of which were females.

For data registries, the date of birth was registered as Day 1. two Patients were SARS-CoV-2 RNA PCR test

positive, and also had positive indicators in CT scans, and as such, they were diagnosed with COVID-19 infection immediately. Corresponding IgM and IgG levels of two Patients were positive. While they had negative results on throat swabs, their radiological findings revealed pneumonia symptoms, and as such, they were also diagnosed with COVID-19. Finally, one Patient had negative results in all other tests, but the radiological findings displayed the characteristic glass-like developments in both lungs, and as such, she was also diagnosed with COVID-19.

X-rays and/or CT scans of a total of 28 babies were taken in their DAY 3. 5 displayed the pneumonological findings expected in COVID-19, while the remaining had partial findings including dim shadows, mid-section GGO, unevenly distributed shadows, or multifocal lesions. One baby with mild asphyxia also had significant levels of lung lesions, but this case was diagnosed as hypoxic ischemic encephalopathy.

22 of the babies were transferred to normal neonatal care, while 28 were hospitalized into NICU for various reasons. The aforementioned series of tests were applied here, and 6 out of 28 were diagnosed with inborn conorary diseases (patent ductus arteriosus [PDA] and atrial septal flaw [ASD]). All three had pneumonological findings in their radiography tests. One baby diagnosed with COVID-19 developed fever on DAY 3, and one had intermittent coughing. Throat and rectal swabs were used to try to deduce COVID-19 presence, and of the 5 tests applied, 2 returned positive. According to the New Coronavirus Pneumonia Prevention and Control Program (v7) issued on March 4, 2020 [17], corresponding IgM and IgG tests were applied on these 5 babies, and the same 2 returned positive as well.

Average NICU duration for the babies was 13 days. 3 babies stayed longer, but due to non-COVID-19 reasons.

Comparisons with literature and Discussion:

A small number of researches are performed regarding the relationship of COVID-19 with pregnancy and babies [6-12]. Chen et al. [6] evaluated 19 mother-baby pairs in terms of clinical findings of COVID-19. 6 of these patient pairs were tested for umbilical blood, throat swabs, and breastmilk contamination, all of which returned SARS-CoV-2 negative.

In literature studies, mother candidates diagnosed with COVID-19 often displayed mild symptoms preferred C-section deliveries. Most women also had discernable radiological changes. Zhu et al worked on 10 babies born from COVID-19 infected mothers, and reported various symptoms like death, thrombocytopenia, and breath shortness [9]. However, most other studies reported positive results for the babies. Only two cases of persistent COVID-19 course in babies were reported in literature [24]. One of these babies was reportedly infected in 17th day due to contact with infected caretaker [25]. The other was diagnosed with tests performed on placenta and amniotic fluid, which returned SARS-CoV-2 RNA positive [26].

In the current research, all babies with COVID-19 infection were taken into NICU. Before being taken into neonatal wards, the babies were in other sections of the hospital for approximately 30 minutes. Although statistically unlikely, it is unknown if this 30 minutes were the cause for an infection.

All pregnant women administered into 2 selected Iraqi facilities between june 30 2020 and july 10, 2021 for COVID-19 infection were involved in the research. This period coincides with the highest COVID-19 incident rates of Iraq. Clinical course of all the NICU-administered babies were monitored as part of the study. Since the study period coincided with the highest incident rate period in Iraq, COVID-19 test units were in short supply. Due to this reason, throat and rectal swabs and

radiological scans were used in certain cases. Only four babies were tested with both SARS-CoV-2 unequivocal IgG and IgM. CT scans, clinical findings, and swab tests were used as complementary diagnosis tools. Another point to consider is the fact that 12 babies had radiological findings due to other reasons. This fact challenges the accuracy of the use of CT scans as supplementary diagnosis tools. Since only 5 babies were diagnosed with COVID-19 infection (with probably but still questionable accuracy), and due to the small number of infected babies, the statistical correlations have little power.

Findings show that maternal CRPlevel might have a relationship with radiological lung findings in babies. Mother C- REACTIVE PROTEIN levels of babies with discernable radiological findings (both for COVID-19 and other cases) were higher than their normal counterparts. C- reactive protein is a commonly used indicator for non-infectious diseases and disorders.

Some studies also reported a relationship between maternal c-reactive protein level and pregnancy difficulties [29], mental problems in babies [30], neonatal birth weight [31], and neonatal c- reactive protein level [32]. While it has been shown that c- reactive protein can't be transferred through maternal-fetal interface, maternal irritation can cause transfer through cytokines or chemokines (33).

The 5 babies diagnosed with COVID-19 had significantly different clinical course compared to COVID-19 infected adults [19]. Babies displayed almost no clinical findings. The platelet and lymphocyte count findings are hard to evaluate due to their wild course in the early days of neonatal life.

It is known that throat and rectal swabs can return false positive and false negative results for SARS-CoV-2 RNA tests. While IgG and IgM tests are somewhat more reliable, only 4 babies were tested using them. Under the conditions of the study environment and test kit

availability, CT scan images were given more importance for diagnosing COVID-19 infection of babies. Radiological findings of the 5 COVID-19 diagnosed babies were quite discerning for the infection, and radiological findings quickly moved towards normal in all 5 babies after the treatment. One patient had developed previous lung lesions displaying septal thickening suggesting interstitial fibrosis.

Latest studies show that CT scans are more reliable than X-rays in terms of detecting pneumonic lesions in lungs. These can often be occluded by heart, or might fall behind the trace lines of the stomach. CT scans are also readily available during the test kit shortcoming, and are easily applicable for newborns.

While a total of 22 children had pneumological findings in lung radiolography, only one had intermittent cough, and none of the others showed any other clinical pneumonia symptom. Apparently COVID-19 developments in lungs occur within the first six days after

birth, even if pre-birth infection occurs. Statistical studies have shown that full-term infants have only 1% incident rate of pneumonia, which increases to 10% in preterm babies [35, 36].

Since none of the babies had any clinical pneumonia symptoms, they weren't tested for any other microbiological agent except SARS-CoV-2. The high number of radiological findings in this study that are seemingly not related to COVID-19 might be because of false-negative SARS-CoV-2 PCR tests that have been shown to have as high as 30% false-negative results [37]. Patient 12 had all negative results for throat and rectal swabs, while CT scan displayed the characteristic glass-staining of the lungs that occur in COVID-19. It is possible that some of the other 12 babies were infected with COVID-19 but their tests returned false negatives.

It is possible that the babies inhaled infected amniotic fluid during birth, or might have displayed wet-lung

issues in birth, which might have transmitted the disease. It is as of yet unknown if any other longer-term effects are present after treatment.

Only 2 out of the 4 tested babies were positive in terms of SARS-CoV-2 unequivocal serum IgG and IgM, but this is still enough to raise a concern for intrauterine transmission. As of now, SARS-CoV-2 is believed to solely infect the respiratory system, and to a much lesser degree, the digestive system. Similar to other respiratory system diseases, its correspondence in blood tests is relatively low. Vertical transmission from mother to the fetus through placenta usually occurs in diseases that have high-replication and high correspondence in blood table. This might be the reason of the lack of SARS-CoV-2 finding in amniotic fluid, umbilical blood, or placenta [6, 38].

The exact timing of IgG and IgM reaction against SARS-CoV-2 was inspected, and it was found out that IgM reacts first. Since IgM molecule is too large to pass the placenta-fetus interface, raised IgM values in babies are often regarded as indicators of intrauterine or perinatal diseases. IgG, on the contrary, passes from the mother to the baby, and is believed to be active until the 3rd month of age [39]. Additional tests are required on umbilical blood, placenta, and amniotic fluid to clarify the potential and/or mechanics of vertical transmission of COVID-19. unfortunately because of unavilablity of any regional articles, the result was compared with international data.

Conclusions:

The results indicate that babies delivered by COVID-19 infected mothers have enhanced danger of COVID-19 infection themselves, and display the radiological findings of pneumonia. The results are inconclusive but still point out to an elevated chance of intrauterine transmission, and/or intrapartum infection. Post-pregnancy hospital infection is also possible, while the probability is considerably low. Serum IgG and IgM tests corresponding to SARS-CoV-2 are

used to compensate the potential risk of false positive or false negative PCR results. In newborns, CT scans also offer a good supporting diagnosis method, especially during the shortness of test kit stocks.

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