



RESEARCH ARTICLE

The Impact of the COVID-19 Infection During Pregnancy on the Placenta and Its Function, A Meta-Analysis Study

R. J. Al-Dahwi ^{1*}, D. Kostadinova², M. Angelova³, E. D. Georgieva ⁴, G. D. Nikolova ⁵ and Y. D. Karamalakova ⁶

^{1,2,2} Obstetrics and Gynaecology Clinic, UMHAT "Prof. St. Kirkovich", Stara Zagora, Bulgaria;

^{4,5,6} Chemistry and Biochemistry, Medical Faculty, Trakia University, Stara Zagora, Bulgaria;

ARTICLE INFO	ABSTRACT
Received: May 28, 2024 Accepted: Jun 16, 2024	<p>In this study, a meta-analysis was conducted on a number of studies aimed at “the effect of CoV-19 infection during pregnancy on the placenta and its function” where this study presents and compares five studies to identify their strengths and weaknesses, as well as their differences and similarities with the studies were supposed to cover an unspecified date range from December 2020 through August 2023. This research concludes that the discovery of damage to the placenta in pregnant women infected with the novel coronavirus, some of whom do not show symptoms, may be related to the results. Damage to the placenta can interrupt the transfer of oxygen and nutrients to the fetus, with the potential for adverse effects on fetal health. In addition to the damage to the placental blood flow, which ensures the fetus receives adequate nutrition and oxygen, there is also evidence of the presence of blood clots in the placenta, as well as a reduction in the size of the placenta. In light of these findings, it is crucial to closely monitor the function of the placenta in pregnant women infected with the SARS-CoV-2 virus. Additionally, it is vital to study the health of newborns to ascertain whether the observed placental damage is associated with any long-term health issues in the child.</p>
Keywords	
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*Corresponding Author:	
rafa.dzhasim@trakia-uni.bg	

INTRODUCTION

The first documented cases of infection with the Coronavirus (COVID-19) were recorded in the Chinese city of Wuhan in December 2019. [1] The virus causing this disease, designated SARS-CoV-2, was isolated and identified. SARS-CoV-2 belongs to the genus of beta coronaviruses, which are viruses of animal origin. SARS-COV-2, the virus that causes acute respiratory syndrome, is a member of this genus. A survey conducted by the Society of Obstetrics and Gynecology (SOCHOG) has demonstrated that pregnant women are at risk of contracting the disease. The survey collected information from 7,638 births that took place between March 1 and March 15, 2021. In this group,

30% of patients (115) were admitted to the intensive care unit, of whom 58% (66) required assisted ventilation. [2,3,4,5]

During pregnancy, a variety of environmental conditions can affect the health of the mother and child [6]. It is known that a pregnant woman's environment can create a permanent imprint on the fetus's physiology, which will continue throughout her life [7]. Accordingly, as posited by epidemiologist David Parker in his theory of the developmental origin of health and disease, fetal programming occurs during prenatal development, thereby determining the health and disease of the individual throughout its life outside the womb. Among the prenatal events that can affect the health of the developing fetus are exposure to viruses. [8,9,10].

With regard to perinatal outcomes in pregnant women with symptomatic SARS-CoV-2 infection, an increased risk of preterm birth, preeclampsia, termination of pregnancy by caesarean section, and perinatal death, in addition to intrauterine growth restriction, has been described in the literature. With regard to the fetal and perinatal outcomes in cases of mild or moderate infection, a few studies have been published. However, the results obtained thus far have not demonstrated any differences in newborn weight. [11,12,13]

Although the pathogenesis of coronavirus disease 2019 is still far from fully understood, it has now been demonstrated that in some cases, the course of COVID-19 can be accompanied by a severe systemic inflammatory reaction [6-9] and lead to a hypercoagulability state with microemboli. Publications dedicated to this aspect of pathogenesis continue to be produced, presenting clinical, laboratory, and structural manifestations using the example of different organs and systems [14,15]

MATERIAL AND METHOD

In this study, a meta-analysis was conducted on a number of studies aimed at “the effect of CoV-19 infection during pregnancy on the placenta and its function.”

The inclusion criteria were studies examining the effect of coronavirus infection on pregnant women and placental function, and the exclusion criteria were studies with incomplete data or irrelevant results.

In this study, five studies were identified, and a comparison was made between them to find out the positives and negatives that we will extract from this study and to extract the differences and similarities between these studies.

The meta-analysis inclusion criteria are publications that have more than ten COVID-19-related pregnancies with placental histologic evaluation being done in them. Additionally, the studies were supposed to cover an unspecified date range from December 2020 through August 2023 so as not to introduce any bias related to only including pathological findings practically explained cases.

A search was conducted on the MEDLINE database (PubMed®) using the following search terms: "covid placenta*," "sars-cov-2 placenta*," and "covid-19 placenta*". All search results were reviewed by the authors in a separate capacity, with any discrepancies being resolved through consensus.

The following parameters were collected and analyzed: the number of cases of the placenta, the age of the mother, the gestation period, the child's sex, pre-term deliveries, stillbirths, and the in-situ hybridization and/or polymerase chain reaction detection of SARS-CoV-2 positive/negative placenta samples.

The pathologies of the placenta were classified into the following categories: placenta too small for gestational age (below the 10th percentile) or too large for gestational age (above the 90th percentile), maturation disorders, Chorangiomas, MA perfusion, infarctions, fetal thrombosis-related diseases (FTV), acute inflammation, villitis of unknown etiology (VUE), plasma cell-rich villitis, cytomegalovirus.

RESULTS

Table 1- Characteristics of 5 study according to object, Year, Method, Maternal age (yr)

	Name of article	Object	Year	Method	Maternal age (yr)
<u>M</u> <u>V</u> <u>Surekha</u> ¹ , <u>N</u> <u>Suneetha</u> ² , <u>N</u> <u>Balakrishna</u> ³	Impact of COVID-19 during pregnancy on placental pathology, maternal and neonatal outcome – A cross-sectional study on anemic-term pregnant women from a tertiary care hospital in southern India	Pregnant women who are anaemic are more likely to become infected with SARS-CoV-2 and suffer a placental hypoxia-related injury;	2023	The study, conducted in India during the second wave of COVID-19, involved 212 term pregnant women.	24.11 (3.65) Positive, 23.58 (3.19) Negative
Giovanna Giordano, corresponding author ¹ Chiara Petrolini, ² Emilia Corradini, ¹ Nicoletta Campanini, ¹	COVID-19 in pregnancy: placental pathological patterns and effect on perinatal outcome in five cases		2021	five cases, Case reports	From 26- to 36 years
Shoichi Magawa ¹ , Masafumi Nii ¹ , Naosuke Enomoto ¹	COVID-19 during pregnancy could potentially affect placental function	The study utilized BOLD-MRI to assess the lasting impact of COVID-19 on placental oxygenation during pregnancy.	2023	The researchers studied eight one-off pregnancies with mothers who had coronavirus in case-control research involving eight patients to assess placental oxygenation through BOLD-MRI after 32 weeks of pregnancy.	From 22- to 27 years

Fangqi Zhao 1, Ann-Christin Tallarek 1, Yiru Wang 1	A unique maternal and placental galectin signature upon SARS-CoV-2 infection suggests galectin-1 as a key alarmin at the maternal-fetal interface.	Upon infection with SARS-CoV-2, it turns out that the only maternal and placental galectin signature may indicate galectin-1 is a key maternal-fetal interface alarmin.	2023	prospective cohort of pregnant women and their children, located at the University Medical Center Hamburg-Eppendorf	31.6 (22-40) Pregnant COVID-19 patients (n=20)
Chiara Tasca 1, Roberta Simona Rossi 2	Placental pathology in COVID-19 affected pregnant women: A prospective case-control study	compares placental morphology and histology of pregnant women affected by SARS-CoV-2 to non-infected controls.	2021	64 pregnant women	31.9 ± 5.5

Table 2- Results of the study according to Placental weight (g)

Placental weight (g)	Value	P-value
1	Positive 122 (410.84 ± 84.31), Negative 90 (420.60 ± 78.49)	0.39
2	440±33.8	0.65
3	551.5 (506.0, 623.75) COVID-19, Normal 531.0 (465.5, 573.8)	.397
4	---	---
5	Asymptomatic =487.3 ± 88.2 , Symptomatic=487.3 ± 81.1	0.418

Table 3- Gestational Age at delivery (wks) and Apgar of 5 studies

v	Gestational Age at delivery	Apgar
1	Positive =102 (38.22 ± 1.05), Negative= 78 (38.73 ± 5.82)	APGAR score 1 min=122 (6.20 ± 3.01) , APGAR score 5 min=100 (9.43 ± 0.68)
2	38.7 ± 3.7	Apgar score 1'-5' 9; 10
3	19.38±4.8	8.3±1.9
4	39 + 5 (37-41) Pregnant COVID-19	Neonatal Apgar, 5 min:10 (7-10) 10 (9-10) 10 (9-10) Pregnant healthy controls (n=20) Pregnant COVID-19 patients (n=20) Pregnant vaccinated women (n=30)
5	Asymptomatic =39.0 ± 1.1, Symptomatic=38.8 ± 1.4	APGAR score at 5 minutes <7 =0%

Table 4- The final summary of the cases studied in this research

Author	Outcomes
M V Surekha 1, N Suneetha 2, N Balakrishna 3	A seropositive woman, which may signify that the placenta lacks in oxygen, had exhibit villus hypervascularity, dilated capillaries, and syncytiotrophoblasts as observed through placental examinations for normality. There is a strong relationship between adverse placental histology outcomes and being SARS-CoV-2 positive.
author1 Chiara Petrolini,2 Emilia Corradini,1 Nicoletta Campanini,1 Susanna Esposito,3 and Serafina Perrone2	The placental tissue studies show poor signals of maternal vascular ischemia (MVUs) or fetal vascular ischemia (FVUs) and mildlings. In all situations, CD 15 immune reactivity in placental tissue remained low, suggesting the absence of neonatal hypoxia/asphyxia associated with this condition.
Shoichi Magawa with 10 authors	There were no significant differences in maternal background, gestational age, birth weight, or placenta weight between the two groups.
Fangqi Zhao 1, Ann-Christin Tallarek 1,	Upon analysis of the placenta transcriptome, it was observed that several PSGs were upregulated, as well as the expression of gal-1, gal-3 and

Yiru Wang 1, Yiran Xie 1, Anke Diemert 1,	enzymes driving the synthesis of gal-1-associated glycoproteins in pregnant women. This phenomenon was observed in pregnant women who were positive for the SARS-CoV-2 virus.
Chiara Tasca 1 , Roberta Simona Rossi2	The placenta was found to be heavier than the untreated control, yet the fetal-to-placenta ratio was not found to be different. Furthermore, delayed villous maturation was more prevalent among treated women, although this was not statistically significant. The umbilical cord of babies born to mothers who received oxygen therapy exhibited higher oxygen levels.

DISCUSSION

According to research, the Coronavirus disease contracts when a woman is pregnant, which leads to the placenta changes significantly. Many researchers have recorded different types of lesions in the placentas from women with COVID-19, like thrombus formation, fibrin deposition, avascular villi, infarction, and villous edema. Moreover, COVID-19 can stimulate maternal vascular MA perfusion, early villous maturation, central villous infarcts, villous agglutination and fetal vascular MA perfusion resembling avascular hyalinized villi as well as fetal vascular thrombi [16,17,18] Such modifications may cause adverse gestational outcomes like preterm labor, abortion, intrauterine death, and newborn diseases including respiratory distress syndrome (RDS) as well as pneumonia [19]. Placentas of infected women were found to have inflammation, which indicates that COVID-19 is also affecting the health of placentas.” as follows: [20,21] The presence of inflammatory pathology in the placentas of infected women further highlights the impact of COVID-19 on placental health. Similarly, most importantly is the finding that pregnant individuals who test positive for SARS-CoV-2 typically suffer adverse effects as far as placental development processes are concerned, such as formation and function. Most importantly and importantly are the words used in sentence [22,23,24] construction, the latter emphasizing the aspect being discussed. The study PLAXAVID, along with other research works, has demonstrated that maternal COVID-19 infection contributes to various placental lesions, including maternal/fetal vascular MA perfusion, inflammatory pathology as well as accelerated villous maturation [25]. In SARS-CoV-2-positive gestating females, the placentas contain fibrin deposition, thrombus formation, avascular villi, infarcts, and villous edema that could result in preterm births, miscarriages, or stillborn fetuses [26].

Furthermore, COVID-19 infection has the potential to result in biochemical alteration of the placenta marked with heightened levels of TNF- α and ADAMTS-8, indicative of acute and chronic harm to the placental tissues [27].

A recent study has demonstrated that even mild symptoms of the coronavirus during pregnancy can have a detrimental impact on the placenta, exhausting it and compromising its immune response [28].

According to a report in The Independent, the study included 164 pregnant women, 140 of whom were infected with the virus at some stage of their pregnancy, while the other 24 women were not infected. [29]

further noted, "At the outset of the pandemic, numerous scientists posited that infection with the Coronavirus did not harm fetuses, given that very few children were born with the infection [30]. However, the current evidence suggests that the virus may infect the placenta and alter its function, which in turn may affect fetal development. [31]

It is crucial to acknowledge that the risk of infection with SARS-CoV-2 in pregnant women is 70% higher than in the general population of the same age. Previous studies have indicated that the risk of a serious development or admission to intensive care for pregnant women with an underlying illness is 5-10%. "The risk of premature birth is elevated by a factor of 2 to 3." Furthermore, it is known that the risk of fetal death (intrauterine fetal demise IUD) also increases by a factor of 2 to 3.

This risk is threefold when a pregnant woman is infected. Consequently, pregnant women and their fetuses are considered to be particularly susceptible to infection with the SARS-CoV-2 virus.

CONCLUSION

It is possible for the placenta to become infected with SARS-CoV-2 (16–20), although this appears to be a rare occurrence. However, the viral receptor is expressed throughout pregnancy, which could potentially increase the risk of infection. The placentas of pregnant women infected with SARS-CoV-2 appear to exhibit a greater number of signs of maternal vascular MA perfusion (20-22), which may have implications for fetal development. It is possible that the virus can be transmitted from mother to infant during pregnancy. Some infants may exhibit symptoms of the disease. Nevertheless, the majority of newborns who test positive shortly after birth have positive results.

A study conducted revealed an increase in the number of stillbirths during the peak of the epidemic, yet the causal relationship between the virus and this phenomenon remains uncertain. Finally, the risk of premature birth in pregnant women with severe COVID-19 infection appears to be higher (25-30%), mainly due to the deterioration of the mother's condition. Studies are currently being conducted at the national and international levels to better determine the risks to the fetus and mother.

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