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Histopathological Changes in the Placenta of Women with COVID-19 Infection: A Review Article

Hameda Abd Al-Mahdi Ghazi*[1], Mariam Mohammed Burhan[2], Asmaa M. Mekkey[2], Hadeer Waleed Kazem[3]

Corresponding Author: Hameda Abd Al-Mahdi Ghazi

[1]Dep. of Anatomy & Histology, Hammurabi Medical Collage, Babylon University, Iraq
[2]Dep. of Anatomy & Histology, College of Medicine, University of Babylon, Iraq
[3]Hammurabi Medical College, Babylon University, Iraq.

Abstract

Background: The systemic nature of SARS-CoV-2 and the involvement of various organs by pathological changes have been reported by a lot of authors recently. The placenta plays a major role in providing the growing embryo with nutrients and oxygen in addition to its efficient role in protecting against toxins and infectious agents. However, viral transmission from mother to fetus has been documented.

Aim of the study: In the current review we were aiming at summarizing the main histopathological changes seen in placental tissues of women with COVID-19.

Results: Several authors documented histopathological changes in the placental tissues either in all cases examined or in some cases. These changes mainly involved chronic villi and their supporting structures and their vasculature. Necrosis, edema, thrombosis, vascular obliterations and inflammatory cell infiltrates were the main histopathological changes in various reports and various proportions. Some authors denied the specific nature of these changes while others blamed COVID-19 to be the causative agent of these changes.

Conclusion: The main histopathological changes reported in the placentas of pregnant women with SARS-CoV-2 infection can be summarized as follows: Chorangiosis, thrombus formation in the subchorionic spaces and the intervillous spaces, villous agglutination, debris accumulation in the intervillous space, trophoblast necrosis, focal avascular villi, decidual arteriopathy, accelerated villous maturation, fibrinoid necrosis, retroplacental hematoma, edematous villi, lymphocytic infiltration and macrophage infiltration of the deciduas, fibrotic villi, syncytial knots, microcalcifications, karyorrhexis in stromal cells, acute funisitis and acute chorioamnionitis; however, some opinions favor non-specificity of these findings.

Keywords: SARS-CoV-2, Histopathological changes, Placenta

Introduction

In the late months of 2019, a novel coronavirus strain appeared in China in Wuhan city and caused a rapid spread of serious infectious disease characterized by lower respiratory tract infection and a relatively high rate of morbidity and mortality (1-3). The virus was able to travel outside China and caused rapid spread all over the world and became a pandemic (4). The virus was named severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) and the disease resulting from it was named coronavirus disease (5).

The entry of the virus to respiratory tissue cells, as well as, other cells of the body is facilitated by angiotensin-converting enzyme receptors-2 and these receptors are also expressed in placenta cells (6). Several studies have documented the existence of virus particles in placental tissues (7). In mammals, the placenta plays the vital role of transmitting oxygen and nutrients to the growing embryo and takes away the waste products in addition to being a protective barrier against toxic materials (8). Moreover, the placenta participates effectively in protecting the growing embryo against infectious agents (9).

However, it has been shown recently that the SARS-CoV-2 virus can cross the placenta and establish infection in the growing fetus (10). The entry of the virus is via the previously mentioned receptors which are present on cell membranes and this provides a connection site to the viral spike protein (11). The maternal genital tract has been shown to widely express these receptors facilitating therefore the viral entry (11).

Some authors favor the theory of vertical transmission of the virus to the fetus bypassing the placenta (12), others stated that the virus may reach the baby during delivery (13).

In the current review, we were aiming at summarizing the main histopathological changes seen in the placental tissues of women with COVID-19.

Materials and methods

An extensive search was made by the authors participating in the current study in the available published articles involving the period between December 2019 and April 2022. The following search engines were included: BioMedical, Medrxiv, Google Scholar, Scopus, Science Direct, the Cochrane Library, Medlin, and PubMed. The principal keywords used in the current study were, pathological, placenta, histopathological, SARS-CoV-2, and COVID-19. The articles written in the English language were selected, while articles written in other languages were excluded from the study.

Articles were first identified then duplicated reports were excluded. Screening of the abstracts for pathological and histopathological findings was performed; otherwise, articles devoid of such findings were excluded. Later on, full-text articles were reviewed and those articles with irrelevant data were excluded. Articles with histological findings and gross morphological changes were included, while data dealing with immunohistochemistry findings were not included. Any article with no proven viral infection (using polymerase chain reaction) was excluded as well as any article with no histopathological study.

Results and Discussion

Although the placenta is an efficient barrier against infectious agents, it has been documented that viruses such as Herpes simplex virus, Cytomegalovirus (CMV), and rubella virus can cross the placenta and infect the embryo leading to serious congenital malformations (14).

One of the main complications during pregnancy was the possibility of transmission of SARS-CoV-2 to growing embryos of pregnant women and one of the recent systemic reviews about pathological changes seen in placentas of women with COVID-19 has been done by Motwani *et al* (11). In their systemic review, they discussed gross, microscopical, ultrastructural, and immunohis-tochemical placental changes in pregnant women with COVID-19 (11), but in the current review, concentration has been made to include histopathological changes determined by Hematoxylin and Eosin stain.

Fetal, as well as maternal vascular malperfusion due to chorangiosis in association with thrombus formation in the subchorionic spaces and the intervillous spaces, were reported in a case-control

study and villous agglutination and thrombosis in fetal vessels were the principal reported findings (15) which were also observed by other authors (16) and debris accumulation in the intervillous space and trophoblast necrosis were observed by other authors (17-19).

Thrombin formation in the large blood vessels of all enrolled cases was the main finding in the study carried out by some researchers. Focal avascular villi and fibrin in blood vessels of villous stroma were also reported (20). Decidual arteriopathy and intervillous thrombi formation were the main findings in the study of Shanes *et al* in addition to accelerated villous maturation, villous agglutination, villous infarctions, and fibrinoid necrosis. A retroplacental hematoma and Edematous villi were also identified in their study (21).

Lymphocytic infiltration and macrophage infiltration of the decidua and fibrin deposition together with thrombosis and hemorrhage was the main finding in the study of Bertero *et al* (22). In one study which was designed to be a case-control study, villous agglutination, small fibrotic villi, syncytial knots, microcalcifications, and fibrin deposition were observed (23).

According to research carried out by Khong et al on 20 placental samples obtained from women infected with SARS-CoV-2, Hematoxylin, and Eosin (H&E) tissue sections evidence of intramural fibrin deposition and malperfusion of fetal vasculature have been reported. In some cases, karyorrhexis in stromal cells of villi has been also reported, in addition, to peri-villous fibrin deposition and were intramural non-occlusive thrombi. Acute funisitis and acute chorioamnionitis have been described and these changes were associated with severe pneumonia. Obliterative vasculopathy has been seen in one case and chronic villitis was seen in 4 cases (24). Chronic villitis was also confirmed by many authors (25-27).

Some authors failed to identify the virus particles in placental tissues (28-30); while others have documented the existence of virus particles in cell processes of fibroblasts and syncytiotrophoblast cells of chorionic villi and this was regarded as evidence of the risk of viral vertical transmission in pregnant women with COVID-19 (31-33).

Denial of gross or microscopic findings was reported by some authors (34). Acute chorioamnionitis was also documented by several authors (35-38). trophoblast necrosis and perivillous fibrin deposition were seen by some authors (39).

Conclusion

The main histopathological changes reported in the placentas of pregnant women with SARS-CoV-2 infection can be summarized as follows: Chorangiosis, thrombus formation in the subchorionic spaces and the intervillous spaces, villous agglutination, debris accumulation in the intervillous space, trophoblast necrosis, focal avascular villi, decidual arteriopathy, accelerated villous maturation, fibrinoid necrosis, retroplacental hematoma, edematous villi, lymphocytic infiltration and macrophage infiltration of the deciduas, fibrotic villi, syncytial knots, microcalcifications, karyorrhexis in stromal cells, acute funisitis and acute chorioamnionitis; however, some opinions favor non-specificity of these findings.

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