

Morphological Changes in the Liver of Pregnant Women with Coronavirus Disease

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ABSTRACT

Macroscopically, the liver is greenish-red in color, enlarged in size, the gallbladder is sharply enlarged and filled with bile. Microscopically, hepatocytes contain microvesicular fat drops, focal necrosis of hepatocytes, the number of neutrophils predominates in the portal tracts, microthrombi are detected in the sinusoids. The autopsy results of mothers who died from COVID-19 have received important insights from a comprehensive liver study. Macroscopically, it is determined that the liver is enlarged, softened, its outer surface has a variegated color, that is, small foci of hemorrhages and foci of yellow-brown color appear under the shell, and its parenchyma also has a false nutmeg color when cut out.

Relevance of the topic: assessment of specific pathomorphological features of the liver in cases of maternal death with liver pathologies not related to acute and chronic hepatitis, assessment of specific pathomorphological features of the liver in cases of maternal death related to COVID-19, and the diagnostic value of quantitative indicators of morphological data in the differential diagnosis of primary and direct causes of maternal death conducting scientific research aimed at proving it is of particular importance. During the epidemic period of the COVID-19 pandemic, pregnant women infected with the virus are considered relevant in strengthening the measures taken to prevent them, taking into account the possibility of severe and life-threatening pathological processes in the liver.

Purpose: to clarify the degree of infection of pregnant women with COVID-19, the morphogenesis and pathomorphological changes of organ and tissue damage.

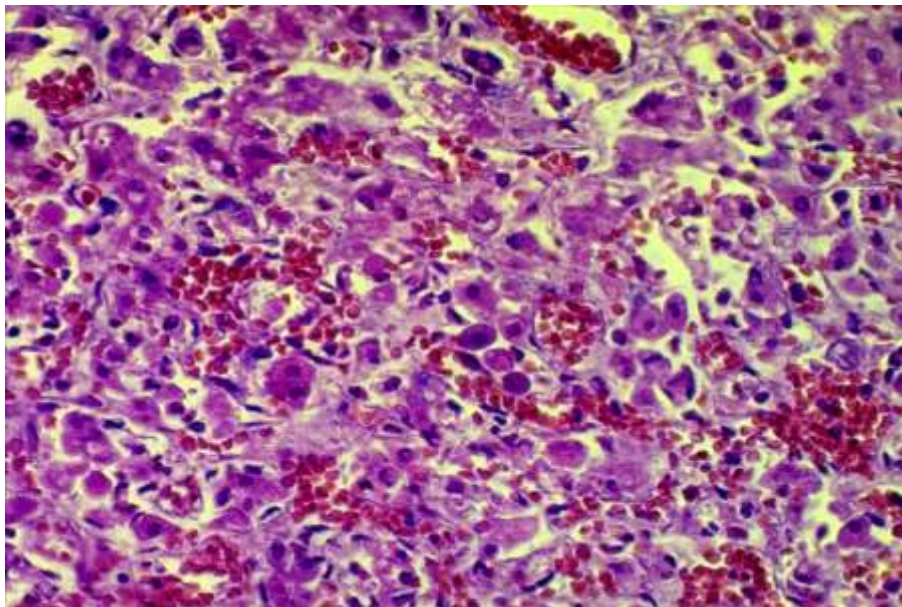
Materials and methods: clinical and anamnestic data of a total of 57 cases of maternal death autopsy, disease history and confirmed diagnosis of Kovid-19 during pregnancy, and autopsy materials of the liver of women who died with somatic diseases in 29 cases were

obtained.

Findings and Discussion: A comprehensive study of the liver in autopsies of maternal deaths from COVID-19 yielded important information. Macroscopically, the liver is enlarged, softened, its outer surface has a variegated color, that is, it is determined that small foci of hemorrhages and yellow-brown foci appear under the membrane, and when the tissue is cut, the parenchyma also has a false nutmeg color.

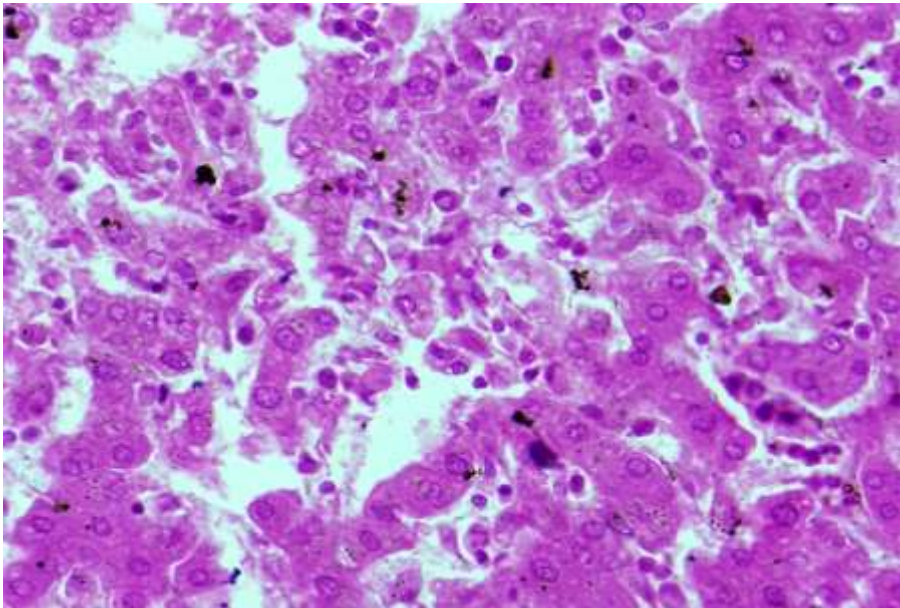
Different histological changes were detected in the microscopic study of the liver depending on the periods of the coronavirus disease. During the exudative period of the coronavirus, miscalculation processes predominate in the liver tissue of women who died, that is, sinusoids are sharply expanded, blood is poured around them, and hepatocytes are irregularly located (see Fig. 1).

Changes specific to the effect of the virus were manifested by the structure of the walls of the sinusoids, that is, by the enlargement of the Kupffer cells, the cytoplasmic protein and hydropic dystrophy, and the appearance of lymphoid cells. In this case, the columnar arrangement of hepatocytes was disturbed, the interstitial tissue expanded due to swelling, and a large accumulation of macrophages and lymphocytes was observed in its composition. It was found that the nucleus of Kupffer cells increased due to hypertrophy and vacuolization of the cytoplasm (see Fig. 2).

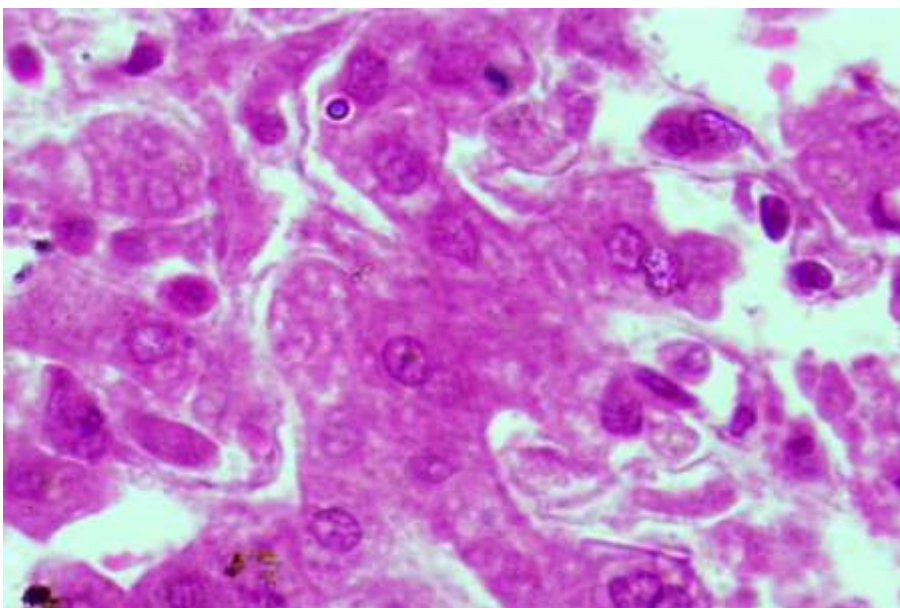


Picture 1. L. who died in the 36th week of pregnancy infected with coronavirus. a woman with the name Fullness of sinusoids in the liver, hemorrhages around it, irregular location of hepatocytes, enlargement of Kupffer cells, appearance of lymphocytes. Paint: G-E. Floor: 10x40.

Eosinophilic and hematoxylin inclusions appeared in the cytoplasm and nucleus of some Kupffer cells, which was characteristic of viral injury. When studied under a microscope, it is clear that the Kupffer cells are separated from the liver cells and the sinusoid wall, and the cytoplasm is darkly stained with eosin and contains hematoxylin (see Fig. 3). This situation is evident from the analysis of literature data, that is, it confirms the damage of endothelium and Kupffer cells by SARS-CoV-2.



Picture 2. K. who died in the 33rd week of pregnancy infected with coronavirus. a woman named Hepatocytes were shriveled and arranged irregularly, lymphocytes appeared among them, eosinophilic inclusions appeared in the cytoplasm of Kupffer cells. Paint: G-E. Floor: 10x40

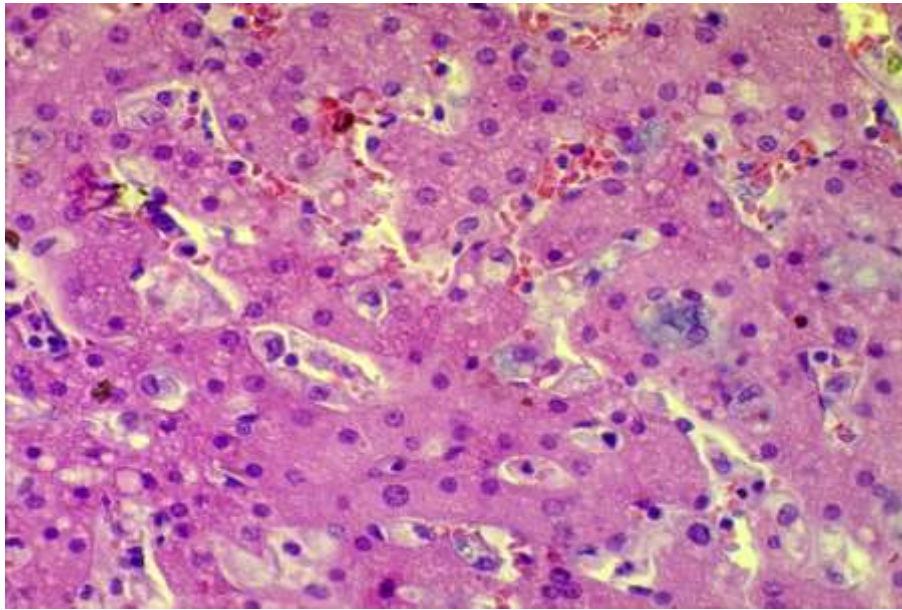


Picture 3. K. who died in the 33rd week of pregnancy infected with coronavirus. Kupffer's cells were enlarged, and inclusions with hematoxylin appeared in the cytoplasm. Paint: G-E. Floor: 10x100.

Under the influence of SARS-CoV-2, damage to the endothelium of liver sinusoids as well as Kupffer cells, accumulation of lymphocytes around them, i.e., they become larger, dystrophy in their cytoplasm increases, metachromasia develops, and blue coloration indicates that the exchange of proteins and carbohydrates is also disturbed.

Some of the pregnant women who died from the coronavirus have other unique pathomorphological changes in their livers, i.e., it is found that the Kupffer cells are swollen and enlarged due to the effect of the coronavirus. In this case, it is observed that the cytoplasm of

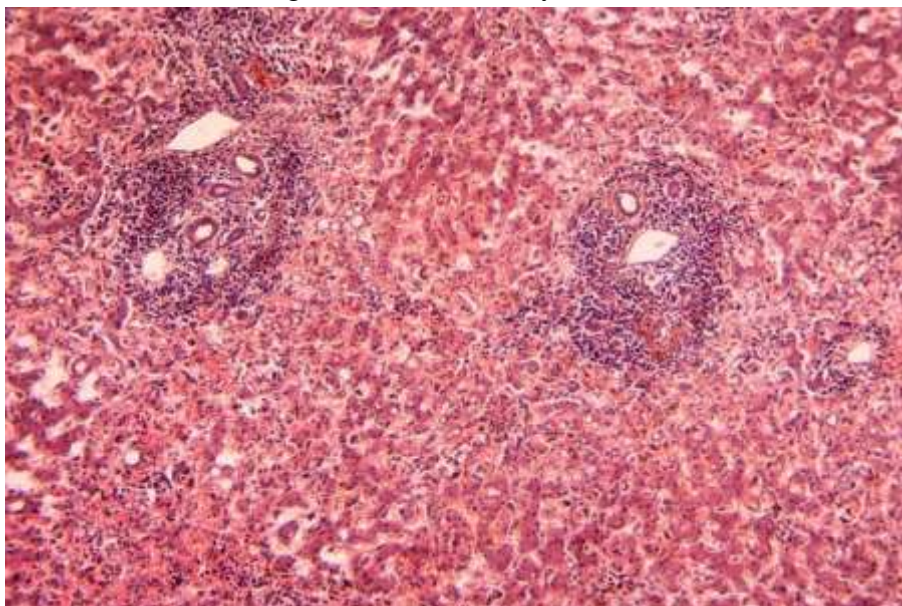
Kupffer cells becomes vacuolated and stained with blue color, myxomatosis is caused by the violation of carbohydrate metabolism along with protein (see **Fig. 4**).



Picture 4. A. who died in the 38th week of pregnancy infected with coronavirus. Cytoplasm of female Kupffer cells is vacuolated and stained blue. Paint: G-E. Floor: 10x40.

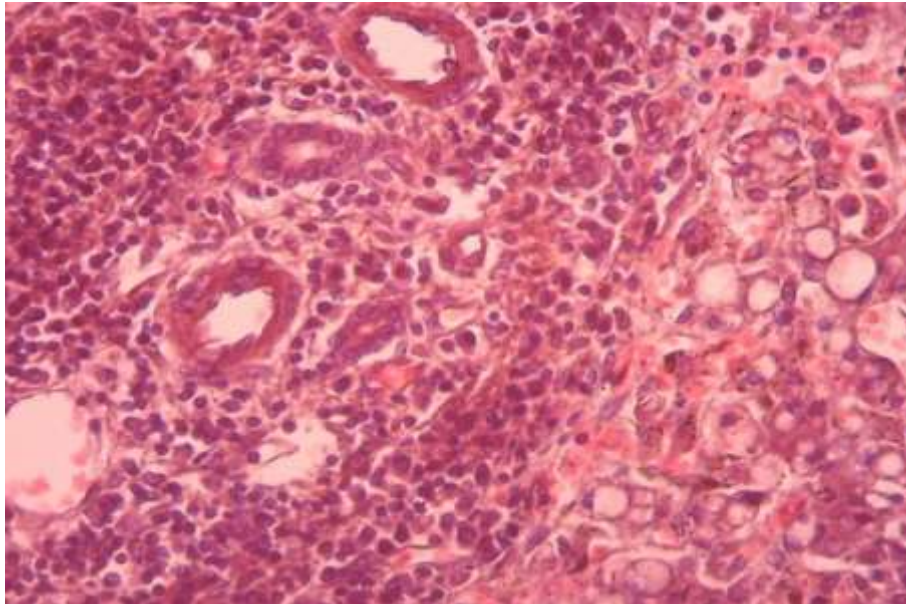
Lymphocytes appear next to these cells and adhere to the Kupffer cell, which means that an immunopathological process has developed against the autoantigen caused by the virus. It is observed that some areas of the liver parenchyma are filled with blood, and the cytoplasm of hepatocytes is affected by small vesicular dystrophy due to protein and hydropic dystrophy.

When the livers of pregnant women who died during the second period of the coronavirus, i.e. during the proliferative inflammatory period, were studied, it was observed that changes typical of the proliferative inflammatory process also appeared in this organ. In this case, it is determined that a strong lymphoid and macrophage infiltration has appeared around the portal tracts of the liver. The peculiarity of this process is that the lymphoid infiltration developed around the biliary tract (see **Figure 5**), the accuracy presented in the scientific literature shows, that is, it confirms the damage of more choanocytes with coronavirus.



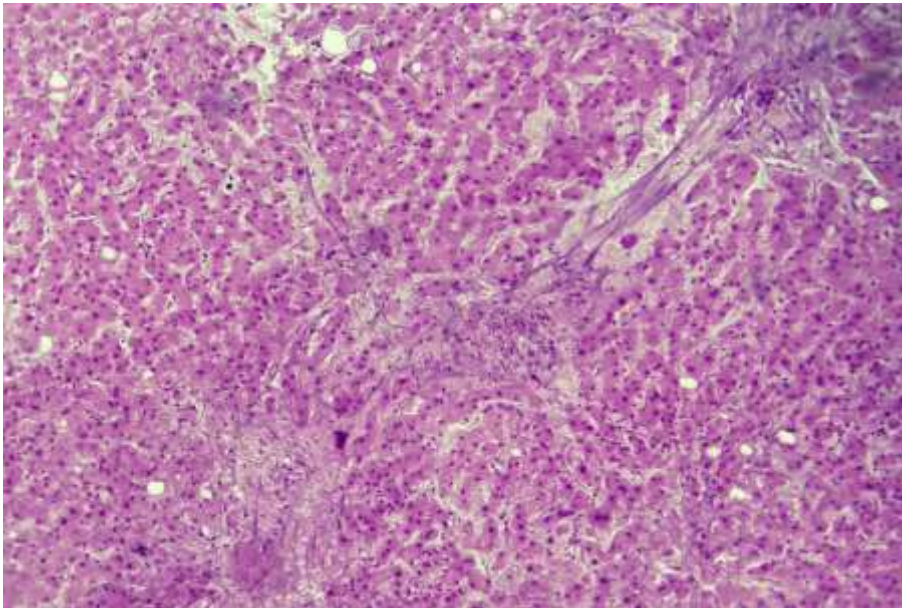
Picture 5. M. who died in the 35th week of pregnancy infected with coronavirus. strong lymphoid infiltration in female portal tracts, bile duct proliferation. Paint: G-E. Floor: 10x10.

It should be noted that T-lymphocyte infiltration occurs against any viral infection. When studied under a microscope lens, it is determined that the epithelium of the bile ducts in the portal tracts is swollen and enlarged, as a result, the bile ducts are proliferated. In this case, it is determined that the surrounding lymphoid infiltration is mainly located near the bile ducts, and lymphocytes form a symbiosis with cholangiectasis (see Fig. 6).

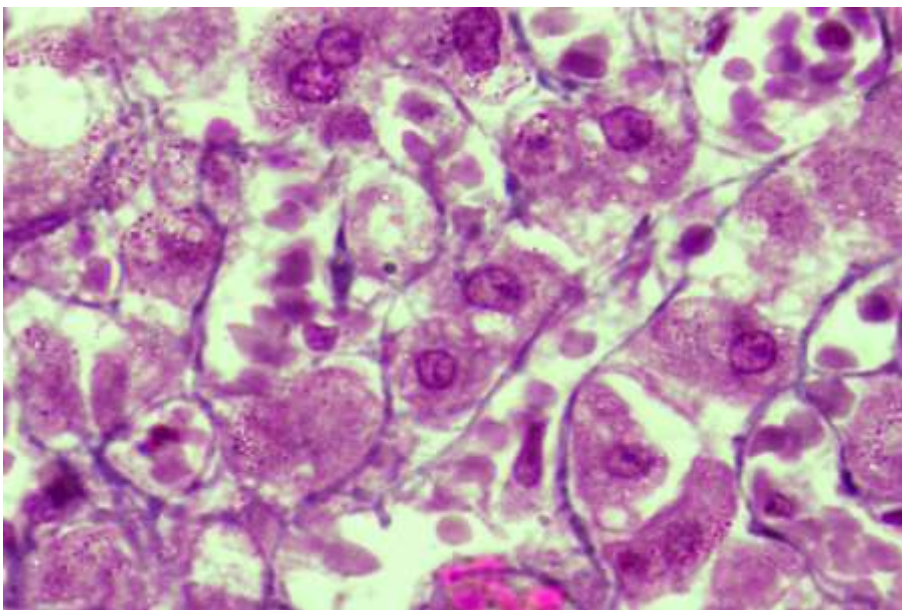


Picture 6. M. who died in the 35th week of pregnancy infected with coronavirus. female bile duct proliferation, enlargement of choanocyte's. Paint: G-E. Floor: 10x40.

During the prolonged proliferative inflammatory period of the coronavirus, when fibroblasts were found to proliferate and multiply in the lungs, a strong proliferation of fibroblasts and fibrous structures was observed in the liver around the portal tracts. In this case, it was found that connective tissue rich in fibrous structures grew around the portal tracts and liver lobes (see Fig. 7).



Picture 7. T. died in the 37th week of pregnancy infected with coronavirus. named female liver portal tracts, fibrous structure connective tissue grew and increased around the lobes. Paint: G-E. Floor: 10x10.



Picture 8. T. died in the 37th week of pregnancy infected with coronavirus. the increase of fibrous structures in the wall of female liver tissue sinusoids. Paint: G-E. Floor: 10x100.

When the histochemical method for the determination of connective tissue fibers was used, fibrous structures stained red with profusion were identified along the portal tracts, around the liver lobes, and in the wall of the sinusoids.

According to the results of the scientific research conducted by the scientists of the world, although SARS-CoV-2 and MERS-CoV can cause damage to the liver. However, the mechanism of liver damage is hardly understood. Virus-induced effect, systemic inflammation,

hypoxia, hypovolemia, hypotonia also damage the liver in case of coronavirus infection. ACE-2 is expressed more in cholangiocellular epithelium and less in hepatocytes, therefore it damages cholangiectasis more than hepatocytes. As a result of molecular genetic examination, SARS-CoV-2 was detected not only in lung epithelium, but also in hepatocytes.

SARS-CoV-2 directly affects the liver, depends on the replication of the virus in liver cells and its direct cytotoxic effect. Studies have shown that high-level RNA-seq detection of SARS-CoV-2 results in strong expression of AAF2 in the liver, mainly in cholangiocytes, Kupffer cells, and endothelium. SARS-CoV increased the apoptosis of hepatocytes with the help of its special protein. These data confirm that there is a direct effect of the coronavirus on the liver.

Conclusions

Morphological examinations of the liver tissue showed that depending on the periods of coronavirus infection, various pathomorphological changes were observed in the liver. During the exudative period of the coronavirus, a strong miscalculation process in the liver, swelling, disruption and hemorrhage of the interstitial tissue, development of proteinaceous and hydropic dystrophy in the liver parenchyma, that is, in hepatocytes, is observed.

In the second proliferative inflammatory period of the disease, the increase of lymphoid infiltration along the portal tracts of the liver, the myxomatous metaplasia of Kupffer cells, the proliferation and increase of fibroblasts, the growth of connective tissue, the appearance of fibrous structures in the portal tracts, around the lobes, and even in the walls of the sinusoids are determined.

Therefore, taking into account the main functions of the liver, the pathologic-anatomical analysis of liver tissue damage in different strains of coronavirus infection was evaluated as one of our main tasks, and this is the basis of our scientific innovation.

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