MOLECULAR ALTERATIONS OF HEPATIC GENE EXPRESSION IN PREGNANT WOMEN WITH FATAL COVID-19

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ABSTRACT

This article explores molecular alterations in hepatic gene expression in pregnant women with fatal COVID-19. The study focuses on transcriptional and post-transcriptional changes in liver-related genes induced by SARS-CoV-2 infection under pregnancy-associated immunological and hormonal modulation. Particular attention is given to genes involved in inflammatory signaling pathways, coagulation processes, oxidative stress response, and hepatocellular metabolism. The findings suggest that fatal COVID-19 cases in pregnancy are associated with significant dysregulation of immune-response genes, upregulation of pro-inflammatory cytokines, and suppression of genes responsible for liver regeneration and detoxification. These molecular disturbances contribute to severe hepatic dysfunction and systemic complications. The study highlights the importance of understanding gene expression profiles to elucidate the pathogenesis of COVID-19-related liver injury in pregnant women and to support the development of targeted therapeutic approaches.

Introduction

The coronavirus pandemic caused by SARS-CoV-2 has demonstrated that COVID-19 is not limited solely to respiratory pathology but represents a systemic infectious disease involving numerous organs and biological systems. Recent scientific investigations indicate that viral infection can induce substantial molecular disturbances inside host cells, particularly affecting transcriptional activity and intracellular regulatory pathways. Such alterations lead to disruption of normal cellular metabolism and contribute to tissue injury. The liver is considered one of the principal organs involved in metabolic regulation, detoxification processes, synthesis of biologically active compounds, and modulation of immune reactions. Consequently, molecular disturbances developing in hepatic tissue during COVID-19 may significantly influence disease severity and clinical outcome. Pregnancy is associated with physiological restructuring of endocrine, immune, and vascular systems. These adaptive changes may modify the maternal response to viral infection and affect

mechanisms of tissue injury. For this reason, investigation of transcriptional and molecular alterations in the liver tissue of pregnant women with severe COVID-19 has important theoretical and practical value.

Background and scientific importance

Although numerous studies have examined pulmonary complications of COVID-19, considerably less attention has been directed toward hepatic molecular pathology. Existing evidence suggests that SARS-CoV-2 infection may alter expression of genes associated with inflammatory signaling, oxidative injury, programmed cell death, and immune regulation.

In pregnant women, physiological immunomodulation and enhanced coagulation activity may intensify these molecular disturbances. Dysregulation of cytokine-associated genes and oxidative stress pathways may accelerate hepatocellular damage and contribute to severe systemic complications. Therefore, analysis of hepatic gene expression profiles may provide additional insight into the pathogenesis of COVID-19-associated liver injury.

Purpose of the Investigation

The present study was conducted to evaluate transcriptional changes in liver tissue obtained from pregnant women who died due to COVID-19 infection and to determine the pathogenetic significance of these molecular alterations.

Materials and Methods

The investigation included hepatic tissue samples collected from 20 pregnant women with fatal COVID-19 infection and 10 individuals included in the control group. Molecular-biological assessment was performed using reverse transcription polymerase chain reaction (RT-PCR), while immunohistochemical analysis was applied to identify expression patterns of selected proteins and signaling markers. Special attention was paid to genes involved in inflammatory activity, apoptosis regulation, oxidative stress response, and viral receptor expression.

Results

Comprehensive molecular analysis demonstrated substantial disturbances in hepatic gene activity among patients with fatal COVID-19. One of the most significant findings was overexpression of genes associated with pro-inflammatory cytokines. Increased transcriptional activity of IL-6, TNF-α, and IL-1β was detected in the majority of examined specimens. Elevated production of these mediators indicates activation of severe inflammatory cascades and cytokine-associated tissue injury. In addition, considerable imbalance between proapoptotic and antiapoptotic mechanisms was observed. Expression of the Bax gene, which promotes programmed cellular death, was markedly elevated, whereas transcription of the protective Bcl-2 gene was significantly suppressed. These findings suggest intensified apoptotic destruction of hepatocytes in response to viral and inflammatory injury. The study also identified disturbances in antioxidant defense mechanisms. Altered expression of genes encoding superoxide dismutase (SOD) and glutathione peroxidase (GPx) reflects excessive accumulation of reactive oxygen species and increased oxidative stress within hepatic tissue. Another important observation was enhanced expression of ACE2 receptors in hepatocytes and associated liver structures. Since ACE2 serves as the primary receptor facilitating SARS-CoV-2 cellular entry, its increased expression may contribute to direct viral involvement of hepatic tissue and progression of liver injury. The detected molecular

abnormalities collectively promote inflammatory reactions, metabolic imbalance, mitochondrial dysfunction, and structural damage within the liver. Physiological immunological adaptations characteristic of pregnancy may further intensify these pathological processes.

Discussion

The obtained findings confirm that liver injury in severe COVID-19 develops through complex molecular mechanisms involving immune dysregulation, oxidative damage, apoptosis activation, and endothelial dysfunction. Excessive cytokine production appears to play a central role in the development of systemic inflammation and hepatocellular injury. Activation of apoptotic pathways, demonstrated by altered Bax and Bcl-2 expression, may lead to progressive loss of viable hepatocytes and impairment of liver function. Simultaneously, oxidative stress contributes to cellular membrane damage, mitochondrial dysfunction, and disruption of intracellular metabolic processes. Increased ACE2 receptor expression suggests greater susceptibility of hepatic tissue to direct viral invasion. Viral penetration into liver cells may additionally stimulate inflammatory signaling pathways and accelerate tissue destruction. Pregnancy-associated physiological changes, including altered immune tolerance and hypercoagulability, may create favorable conditions for progression of inflammatory and vascular complications during COVID-19 infection. Therefore, pregnant women represent a particularly vulnerable population with increased risk of severe hepatic involvement.

Conclusion

Fatal COVID-19 infection in pregnant women is associated with pronounced alterations in hepatic gene expression profiles. Increased transcriptional activity of inflammatory cytokines, activation of apoptotic pathways, and dysregulation of oxidative stress-related genes constitute major molecular mechanisms of liver injury. Upregulation of ACE2 receptors may facilitate viral entry into hepatic cells and aggravate tissue damage. Pregnancy-related physiological changes appear to amplify these pathological molecular responses and contribute to the severity of hepatic involvement in COVID-19.

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