SARS-Cov-2 Infection Impact on Maternal-Fetal Immunity

The ongoing coronavirus disease 2019 (COVID-19) pandemic, which is brought about by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), poses a serious threat to human health worldwide. Previous research has indicated higher rates of adverse outcomes in pregnant women who are infected with SARS-CoV-2.

The effect that maternal asymptomatic COVID-19 had on decidual and peripheral immune cells during the later stage of pregnancy.

Pregnancy and COVID-19

Pregnant women with severe COVID-19 infection have a 62% higher chance of getting admitted to the intensive care unit (ICU) as compared to non-pregnant women of the same reproductive age.

Although pregnant women are a higher risk group for COVID-19, most remain asymptomatic or have mild symptoms after being exposed to the virus.

"These differences are primarily driven by peripheral immune adaptations during pregnancy that balance fetal tolerance and growth with host defense," says the team of researchers from the University of California Irvine and Oregon Health and Sciences University.

Recent studies show that the peripheral immune system of pregnant women with asymptomatic disease has increased low-density neutrophils (LDN) without causing any significant changes in leukocyte frequencies, activation, and function. Additionally, cytokine storms characteristic of severe COVID-19 in the general population are rare among pregnant women. Results support the hypothesis that pregnancy limits exuberant peripheral inflammatory responses to SARS-CoV-2, which are more common in non-pregnant individuals.

In addition to the changes in blood, the maternal-fetal interface (placenta) also undergoes significant changes. The decidual compartments of the placenta harbor maternal immune cells, including macrophages, natural killer (NK) cells, and T-cells, all of which exhibit mixed phenotypic signatures

that correlate with gestation and can respond to foreign particles at the maternal-fetal interface. Nevertheless, details about decidual adaptations to respiratory infections such as COVID-19 are slowly emerging.

Data strongly suggest that there is no vertical transmission of COVID-19, although rare detection of viral ribonucleic acid (RNA) in the placenta has been observed. Still, severe COVID-19 infection has been shown to trigger maternal inflammation at maternal-fetal interfaces.

Researchers report increased markers associated with preeclampsia, activation of placental NK cells and T-cells, as well as a rise in the expression of heat shock proteins and interferon-related genes related to stress.

However, there is still little understanding of how placental immune rewiring relates to peripheral immune adaptations due to mild infections.

About

The current study involved the collection of blood samples from participants and their separation into peripheral immune blood cells (PMBC) and plasma samples. The PMBC then undergoes phenotyping. First, the serological assay was performed using an enzyme-linked immunosorbent assay (ELISA), followed by placenta processing and decidua immunophenotyping.

Subsequently, 3' multiplexed single-cell RNA sequencing using decidual immune cells was followed by 5' multiplexed single-cell RNA sequencing with feature barcoding. Finally, single-cell RNA-seq data analysis and single-cell T-cell receptor (scTCR) sequencing analysis were carried out.

Study Findings

The results of the current study show that the number of monocytes, granulocytes, and platelets increased during asymptomatic and mild COVID-19 cases, whereas no changes were observed in the level of lymphocytes. In addition, infection was associated with a decrease in the abundance of CD4 naïve T-cells that was accompanied by an increase in memory cells. These observations indicate a less severe inflammatory immune response in pregnant women with mild/moderate COVID-19.

No difference was observed concerning total B-cells and NK cells frequencies upon infection. Also, no differences were found in the expression of activation marker CD86 and major histocompatibility complex (MHC)-Class II molecule HLA-DR on infection.

The study also showed differential outcomes with two decidual macrophages. These included dMac1, which is a tissue-resident decidual macrophage, and dMac2, which is a blood monocyte-derived decidual macrophage.

In patients with asymptomatic COVID-19, a selective loss of dMac1 macrophages was observed. This reduction in the frequencies of dMac1 was accompanied by an increased expression in cytokines IL1B, CCL3, and CCL20.

Both types of macrophages brought about cytokine and chemokine signaling, as well as higher TCR expression, while the expression of heat shock proteins was brought about by only dMac1. Additionally, dMac1 macrophages were associated with increased induction of genes involves in viral sensing, antiviral response, and the signaling of nuclear factor – B (NF-B).

Interferon signaling pathways were also attenuated by dMac2 in the decidua. The dMac2 subset was also associated with differences in immune activation, as well as the upregulation of chemotaxis, cell death, and interleukin 17 (IL-17) signaling genes.

Additionally, activated CD4 and CD8 T-cells were observed in both the blood and decidua of pregnant mothers who were asymptomatic or experienced mild symptoms of COVID-19. High levels of cytotoxic T-cells were observed in the blood, while upregulation of only CD8 T-cells was observed in the decidua.

The study had certain limitations; firstly, the sample size of the study was small. Secondly, it is unclear whether virus-specific T-cells in the placenta are derived from the blood. Thirdly, further research needs to be done to determine whether maternal infections have any long-term consequences on the offspring's immunity.

Source:

Messaoudi, I. et al. (2021). Deep immune profiling of the maternal-fetal interface with mild SARS-CoV-2 infection.