УДК 616.634

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СВЯЗЬ ВНЕКЛЕТОЧНЫХ ВЕЗИКУЛ МОЧИ И ИММУННЫХ МЕДИАТОРОВ С ТЯЖЕСТЬЮ ОСТРОГО ТЕЧЕНИЯ COVID-19 В ПОСТКОВИДНЫЙ ПЕРИОД

Резюме: В постковидный период (после COVID-19) проводился анализ внеклеточных везикул (ВКВ), а также циркулирующих и выделяемых с мочой воспалительных медиаторов в связи с клиническими и лабораторными исходами. Методы: В рамках поперечного исследования лица с анамнезом COVID-19 были разделены на категории в зависимости от наличия постковидного состояния (ПКС) и госпитализации в острой фазе заболевания. Уровни воспалительных медиаторов в крови и моче оценивались с помощью мультиплексных анализов.

Ключевые слова: внеклеточные везикулы, воспалительные медиаторы, COVID-19, интерлейкин (ИЛ), моноцит, лимфоцит, протромбиновое время, лактатдегидрогеназа, плазменные внеклеточные везикулы.

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ASSOCIATION OF URINARY EXTRACELLULAR VESICLES AND IMMUNE MEDIATORS WITH ACUTE COVID-19 SEVERITY IN THE POST-COVID PERIOD

Resume: During the post-COVID-19 (coronavirus illness 2019) phase, extracellular vesicles (EVs) and circulating and urine inflammatory mediators were analyzed in connection with clinical and laboratory outcomes. Methods: In a cross-sectional study, individuals with a history of COVID-19 were categorized according to the presence of a post-COVID condition (PCC) and hospitalization

during the acute phase. The levels of inflammatory mediators in the blood and urine were assessed using multiplex assays.

Keywords: Extracellular vesicles, inflammatory mediators, COVID-19, interleukin (IL), monocyte, lymphocyte, prothrombin time, lactate dehydrogenase, plasma EVs.

Abstract: Extracellular vesicles (EVs) and circulating and urine inflammatory mediators were examined in relation to clinical and laboratory results during the post-COVID-19 (coronavirus illness 2019) phase. Methods: People with a history of COVID-19 were classified based on the occurrence of a post-COVID condition (PCC) and hospitalization during the acute phase in a cross-sectional research. Using multiplex assays, the amounts of inflammatory mediators in the blood and urine were measured. Hospitalized PCC patients showed lower levels of circulant interleukin (IL)-9 ($p = 0.03$), higher monocyte-to-lymphocyte ratio ($p = 0.03$), prothrombin time ($p = 0.02$), and lactate dehydrogenase ($p = 0.01$), but there were no variations in plasma EVs between the groups. The same group also showed increased levels of granulocyte-macrophage colony-stimulating factor ($p = 0.04$), chemokine (Csingle bondC motif) ligand (CCL)-2 ($p = 0.02$), CCL-11 ($p = 0.002$), and total urine EVs (uEVs, $p = 0.006$) and uIL-4 ($p = 0.01$).

Introduction

Following the coronavirus disease-2019 (COVID-19), the post-COVID condition (PCC) is defined by the emergence or persistence of symptoms (such as fatigue, shortness of breath, brain fog, cardiovascular, gastrointestinal, and renal symptoms) and/or changes in laboratory tests (Ayoubkhani et al., 2021; Adli et al., 2024; Crook et al., 2021). According to studies (Crook et al., 2021), people with mild, moderate, or severe forms of COVID-19 are affected by PCC. According to numerous studies (Groß et al., 2020), COVID-19 causes an intensified proinflammatory response known as "cytokine storm," which contributes to the development of multi-organ dysfunction and severe acute respiratory syndrome. In cases of severe acute COVID-19, the virus's direct renal damage and heightened immune response can cause renal cellular stress and acute kidney injury (AKI), with some patients going on to develop chronic kidney disease (CKD) (de Faria et al., 2025). According to Mainous et al. (2021), PCC symptoms are thought to be linked to persistent inflammation, long-lasting cell activation, and cytokine production. Despite these results, there are still few studies that concentrate on EV identification and quantification in the post-COVID era, particularly in urine. Therefore, the purpose of this study was to determine whether changes in immune mediators and EVs, both in blood and urine, months after the infection may cause the proinflammatory state observed in acute COVID-19 to remain systemically or

locally in people who developed PCC. Additionally, we sought to determine whether these changes were related to the severity of acute COVID-19 as well as clinical and standard laboratory results.

Materials and methods

We included adults who, between 2020 and 2022, had an RT-qPCR diagnosis of SARS-CoV-2 infection. Pregnancy, CKD at stages 4 and 5, long-term illnesses such viral hepatitis and HIV, and a lack of information for PCC classification were the exclusion criteria. Medical records and a questionnaire completed during recruiting were used to collect demographic and clinical data. According to the WHO definition, two groups were identified based on PCC classification (Adli et al., 2024). The PCC group was categorized for additional analysis based on the necessity of hospitalization during acute COVID-19, which was thought to be a sign of the severity of the illness.

Discussion

SARS-CoV-2 infection is known to cause an inflammatory state that can be either transient or permanent and may serve as a risk factor for the emergence of various systemic consequences that might result in PCC, particularly following severe COVID-19 instances (Andrade et al., 2021). In this case, the study's objective was to assess urinary and systemic inflammation in the post-COVID era. In order to do this, we evaluated circulant platelet- and leukocyte-derived EVs, urinary total and podocyte-derived EVs in PCC, and inflammatory markers in blood and urine in relation to the acute phase illness severity.

In conclusion

When combined, our findings demonstrate that urinary EVs and immune mediators are significantly altered in PCC patients who needed hospitalization during the acute phase of COVID-19, but not in circulant EVs or cytokines. These findings may indicate an organ-specific indication of ongoing cellular stress and inflammation, potentially involving a Th2 response, but they do not support the theory that a robust systemic inflammatory process causes PCC. Since these changes were only seen in patients who had previously been hospitalized and are unrelated to PCC symptoms, it is crucial to note that they are not directly linked to PCC.

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