International Journal of Scientific Trends- (IJST)
ISSN: 2980-4299
Volume 3, Issue 12, December - 2024
Website: https://scientifictrends.org/index.php/ijst
Open Access, Peer Reviewed, Scientific Journal

Epidemiological Status and Pathogenetic Features of Renal Complications Associated with Post-Covid Syndrome

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Abstract

The aim of the study is to evaluate the condition and risk of renal complications associated with flat-sided syndrome within the framework of a review of existing scientific data. Materials and methods. The literature search carried out in the Internet resources: Cochrane databases Library, PubMed.gov, Elsevier.com, and Google Scholar. Analysis of the obtained data focused on the works published between 2020 and 2023. Results. After manuscript revision procedures, 20 scientific works selected that most fully reflect epidemiological status and pathogenetic features of renal complications associated with post-COVID syndrome. Conclusion. Post-COVID syndrome has a direct and indirect effect on renal function, leading to the development of acute and chronic renal complications. An important role in pathogenesis of these complications played by factors such as inflammatory response, endothelial dysfunction, hypoxia and hypercoagulation, including those characteristics of COVID-19.

Keywords: Post-covid syndrome; renal complications; epidemiology; COVID-19.

Introduction

Over the 3 years of the COVID-19 pandemic, the mortality rate among people infected with SARS-CoV-2 worldwide has decreased from 100 thousand/week of deaths as of 01.2021 to 6.5 thousand/week of deaths as of 03.2023. It was the decrease in mortality, morbidity and, apparently, the virulence of SARS-CoV-2 virus strains that prompted the World Health Organization (WHO) to decide to lift the level of restrictions associated with the COVID-19 pandemic [1, 2]. In part, these circumstances are due to the availability of effective and systematic vaccination of the world's population, which caused a significant decrease in the number of hospitalizations of patients in moderate and severe clinical conditions. In addition, the timely use of emergency treatments such as hormone therapy, anti-inflammatory cytokine therapy, and modern antiviral

therapy have made it possible to most effectively implement measures to prevent and contain the spread of the new coronavirus infection [3]. As with other similar respiratory viral infections (SARS-CoV and MERS-CoV viruses), which cause acute lung tissue damage followed by respiratory disorders, long-term post-infectious conditions have been described after the onset of the pandemic. On the one hand, this indicates a potential increase in patient survival, and on the other hand, it poses the medical community with the question of treating these complications [4, 5]. Post-infectious consequences of COVID-19, or post-covid syndrome (PCS), affect several organ systems, including the kidneys. This poses the medical community with the question of solving problems related to the treatment and diagnostic tactics of renal complications.

The aim of the study is to assess status and risk of renal complications associated with squamous cell syndrome within the framework of a review existing scientific data.

Materials and methods

A search for manuscripts devoted to issue of the epidemiological and pathogenetic status of renal complications associated with PCS was performed in the Cochrane electronic databases Library, PubMed.gov, Elsevier.com, Google Scholar. Data analysis period was set from 2020 to 2023. A total of 104 scientific articles were potential sources of literature; after the revision procedure for topic matching and the absence of duplicates, 20 manuscripts were included in the study. To simplify data processing, two blinded reviewers were provided with access to the Litmaps Internet resource (Litmaps Ltd., Wellington, New Zealand), [https://www.litmaps.com/] as an auxiliary tool.

Results

A diverse spectrum of symptoms persists among patients who have had acute respiratory novel coronavirus infection COVID-19 caused by the SARS-CoV-2 virus strain [6, 7]. This spectrum of various complications is usually referred to in the paradigm of PCS or long-term course of this viral infection (Long-COVID-19) [8]. At the same time, international epidemiological reports have shown that at least 65.0 million people suffer from PCS, and the number of newly diagnosed cases increases daily [9, 10]. The SARS-CoV-2 virus penetrates human cells through angiotensin-converting enzyme 2 (ACE-2) and damages several organs [6]. Typical and most common symptoms of PCS include fatigue/malaise, joint pain, muscle pain, cough, sputum, shortness of breath, chest pain, hair loss, memory impairment, decreased concentration, headache, depression, olfactory disturbance, taste disturbance, palpitations, diarrhea, abdominal pain, sleep disturbances, and muscle weakness [11, 12]. However, the most likely causes of PCS are still largely unknown. This is because PCS symptoms are directly observed in all organs and systems of the human body, therefore, disorders in blood vessels distributed throughout the body, subject to short-term vascular endothelial dysfunction, may be a strong candidate for the main cause of PCS. In turn, this supported by ACE-2, as it is an entry receptor for SARS-CoV-2 [13]. And the phenomenon of ubiquitous expression of ACE-2 in endothelial cells is just a probable prerequisite and contribution of endothelial dysfunction to the development of PCS [14]. H. Yanai et al. (2020) also put forward a hypothesis about a close relationship between risk factors for the development of atherosclerotic cardiosclerosis (AC), cardiovascular failure (CVF), as well as diabetes mellitus

(DM) and hypertension (HTN), with PCS. Thus, the authors of the study suggested that pre-existing endothelial dysfunction, which includes the initial damage to the walls of blood vessels, may be associated with previously suffered COVID-19 [15].

In themselves, diabetes and hypertension are important health risk factors for patients who have previously had COVID-19 and cause endothelial dysfunction, which is an early sign of atherosclerosis. However, in the same study, H. Yanai et al. (2020), it was found that the prevalence of diabetes in patients who had suffered severe COVID-19 significantly higher than in non-severe patients (odds ratio (OR) at 95% CI: 2.65-4.67, and the prevalence of hypertension in patients who had suffered severe COVID-19 significantly higher than in non-severe patients OR 95% CI: 2.16-3.34 [15]. An identical picture observed when analyzing the incidence of CVF. Thus, among patients with severe COVID-19, the incidence of CVF was significantly higher than in patients without severe form OR 95% CI: 3.73-7.74, which indicates a significant relationship between vascular damage and the severity of COVID-19. In addition, in the study of L. Busetto et al. (2020), it found that the presence of obesity in patients who had COVID-19 is also an important aspect and predictor of CVF. At the same time, overweight and obese patients admitted to a medical facility due to acute respiratory infection COVID-19, regardless of age, more often required artificial ventilation and access to intensive care, compared to patients with normal body weight [16].

According to M. Hoffmann et al. (2020), ACE-2 is a cellular receptor for SARS-CoV-2 virus invasion. The study found a significant increase in ACE-2 expression in the bronchial epithelium of patients who had COVID-19 and obese compared to patients with normal body weight. The authors suggested that the SARS-CoV-2 virus is more likely to harm the body of people suffering from obesity compared to people without it [6]. This conclusion is confirmed in the study by A. Higham et al. (2020), [17].

However, much earlier, JSYudkin et al. (1999) suggested that increased secretion of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) in adipose tissue under conditions of obesity may underlie insulin resistance, endothelial dysfunction and coagulopathy [18]. Later, H.Yanai et al. (2023) established a close relationship between chronic increase in circulating insulin levels and the onset of endothelial dysfunction. Insulin resistance observed in metabolic syndrome, type 2 diabetes, hypertension and obesity determines important changes in circulatory homeostasis [19]. For example, the synthesis of endothelin-1 (ET-1), stimulating the sympathetic system and acting as a growth factor for vascular wall cells, activates a number of reactions that provoke the development of atherosclerosis [20]. Insulin resistance is associated with increased expression and secretion of plasminogen activator inhibitor-1 (PG-1) by endothelial cells, causing endothelial damage. Von Willebrand factor (VWF) also increases in insulin-resistant states, suggesting that insulin resistance causes endothelial dysfunction [18]. And in support of this, H. Yanai (2020) proved in their observational study that increased levels of inflammatory cytokines, endothelial dysfunction, and a procoagulant state are already present in obese people even before SARS-CoV-2 virus invasion [16]. Under the influence of the SARS-CoV-2 virus, the level of inflammatory cytokines can significantly increase, which leads to a cytokine storm and causes further damage to the vascular endothelium. In turn, the synthesis of PG-1 against the background of damage to the vascular wall reliably leads to thrombosis.

This mechanism of COVID-19 pathogenesis and the influence of the viral load on the body of SARS-CoV-2 has led and leads to a significant increase in the likelihood of in-hospital death - F. Zhou et al. (2020), [22]. In this regard, a group of authors led by M. Panigada et al. (2020) analyzed a number of thrombosis-related laboratory markers in large samples of patients with COVID-19. Thus, the analysis of the correlation of the thrombosis marker d-dimer demonstrated that an increase in the level of this indicator by more than 1.0 μg / ml (OR 95% CI: 2.64-128.55; p = 0.0033) with a high probability leads to a protracted course of COVID-19, and is also a predictor of PCS. And an elevated level of the endothelial damage marker VWF is significantly more common among patients with COVID-19 who receive intensive care in the intensive care unit. An increase in the level of fibrinogen and d-dimer among patients with COVID-19 significantly increased hypercoagulation, leading to severe systemic inflammatory phenomena such as systemic coagulopathic vasculitis [23]. Thus, an increase in endothelial dysfunction in cases of COVID-19 leads to a significant deterioration in the course of the disease and is highly likely to cause PCS phenomena.

Regarding nephrological complications associated with COVID-19, the most significant reflection of the impact of the new coronavirus infection on the renal system provided by the study by H. Yanai et al. (2020) and M. Atiquezzaman et al. (2024). Thus, in the first study, the authors were able to establish that among patients with COVID-19 and suffering from chronic renal failure (CRF), the mechanism of progression of the concomitant disease is also based on disorders of the endothelial function of the vascular wall. At the same time, endothelial dysfunction plays a leading role in the progression of CRF in PCS [19]. The authors of the second study, devoted to the analysis of renal complications in CRF, report the impact of CRF on the renal function of more than 2.0 thousand patients observed in COVID-19 recovery clinics in England, Columbia, and Canada. The epidermal growth factor receptor gene (eGFR) decreased by 2.96 ml/min/1.73 m2 within 1.0 year after COVID-19 infection, which is equivalent to a 3.39% decrease from the initial conventional standard indicator. Moreover, more than 40.0% of patients were at risk of CRF because of the course of PCS. Also, among patients with PCS, a significant decrease in eGFR was observed within 1 year from the date of registration of COVID-19 infection. In addition, the authors analyzed the prevalence of proteinuria, which as a result had high values compared to the normalized indicator [24].

Conclusions

Thus, the epidemiological status and impact of PCS on kidney function is an ongoing scientific study. However, it can already be reliably stated that PCS under certain circumstances has an adverse effect on the kidney.

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