Evaluation of Synaptopodin, Nephrin Levels and Number of Biochemical Variables in COVID-19 patients

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Abstract
The study aimed to determination Synaptopodin and Nephrin levels and Number of Biochemical variable in Men with COVID-19. The The study groups included 30 patient men infected with COVID-19, 30 men who recovered and 30 healthy men as a control group. Protein and biochemical assays include: Synaptopodin, Nephrin, blood urea nitrogen, creatinine, calcium.**The results** was a significant increase at (P ≥ 0.05) in levels of Synaptopodin, blood nitrogen urea, creatinine in infected patients compare with control group and recovery group, while Nephrin showed significant decrease at (P≥ 0.05) **in infected men group** compare with control group and recovery group, calcium levels didn't show any significant differences between groups
Keywords: COVID-19, Synaptopodin, Nephrin.

1. Introduction

In a seafood market in Wuhan, China, a cluster of pneumonia cases brought on by an unidentified virus first surfaced in December 2019 (Huang and Wang, 2020). These cases exhibit symptoms of viral infection, such as fever and fatigue. Muscle aches and shortness of breath, as well as a dry cough (Wang et al, 2020) The World Health Organization has formally designated this new coronavirus as the seventh coronavirus and designated it as severe acute respiratory syndrome virus 2 (SARS-CoV-2). Around the globe. in the order Nidovirales. Coronaviridae family of (viruses). Alpha, beta, gamma, and delta are the four genera used to classify coronaviruses. The NL63, 229Ea-CoVs, HKU1, and other human coronaviruses are
(OC43 β-CoVs). That causes mild respiratory illness in addition to MERS-CoVs and SARS-CoV-1 (Azhar et al, 2019).
Corona virus kidney infection is widespread due to the SARS-Cov-2 virus's ability to infect renal tubular epithelium and podocyte cells via an ACEII-dependent pathway, according to a study by Ronco et al. (2020). After the viral protein connects to the receptor in the proximal tubular cells, it interacts to the angiotensin-converting enzyme receptor ACE-2, which is abundantly expressed in podocytes (specialized epithelial cells lining the outer borders of glomerular capillaries). In renal cells, the particular protein (TMPRSS2) Transmembrane Serine Protease 2 works in conjunction with ACE-2 to facilitate the fusion of the viral envelope with the cell membrane (Su et al, 2020). The cell is where viral proteins are created. the process of viral replication and spread in kidney cells gets under way (Chen et al, 2020). These occurrences involve podocyte deformation of the glomerular basement membrane, necrosis of proximal tubular cells, infiltration of macrophages and scattered lymphocytes in specific regions, such as the sub capsular space of kidney tissues, and edematous expansion of both interstitial space in distal convoluted tubules in the context of a cytokine storm.
As the virus enters the podocyte cells of the renal glomerulus, where it maintains the integrity of the cytoskeleton, and where these proteins enter into the formation of what is known as the slit diaphragm (which is known as the glomerular filtration barrier), measuring the concentration of synaptopodin and Nephrin is crucial for determining the extent of virus damage to podocyte cells. Nephrin is a crucial component of the podocyte, which together with endothelial cells and the basement form what is known as the glomerular filtration barrier. This barrier picks up proteins from the blood so that they remain in the body while allowing small molecules to cross and blocking the passage of larger proteins (Brinkkoetter *et al*, 2013).
Urea is a waste product that leaves the body, whether it comes from inside the body or from the outside. It either results from the breakdown of proteins during the processes of human tissue regeneration or from the demineralization of amino acids that are ingested through food. The major metabolite of dietary protein and tissue protein turnover is urea, and elevated blood urea levels are a sign of health issues (Ossman et al, 2014)
The breakdown of creatine phosphate in muscle produces creatinine, which is typically produced at a fairly constant pace (Farshidfar et al, 2017). As creatine is entirely filtered through the glomerular membranes and is not reabsorbed by the renal tubules, creatinine concentration is the most often used measure in determining the glomerular filtration rate (GFR). The renal tubules do not absorb it; it is likewise discharged. Kashani et al.(2020).

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The most prevalent mineral in the body is calcium, which is found in the teeth and bones 99% of the time. The remaining 1% of calcium is found in the blood or serum, and studies by Torres et al. (2021) have shown that calcium ions are crucial for cellular functions, metabolic pathways, and signaling pathways that are crucial for the survival and virulence factors of viruses.

2. Materials and Methods

Samples

In this study, (90) blood samples were collected for the period from 1/11/2021 to 1/2/2022, where the study samples were divided into three groups. The first group included healthy people as a (control group), and their number was 30 samples, all of them males who had no medical history, while the second group included Corona virus Covid-19-infected patients. This group consisted of 30 samples, all of whom were male, and they were all present in the isolation ward of Balad General Hospital as well as a few outpatient clinics in the cities of Al-Dholuiya and Samarra. As for the third group, it included similar patients, and their number was also 30 samples, all of them males, their ages ranged between (70-20) years in all group, after careful diagnosis by specialist doctors, and based on clinical symptoms

Collect blood samples

Blood samples weighing around 5 ml were taken from the cuboidal vein. The samples were kept at room temperature for 15 minutes. The serum was then transferred to test tubes and centrifuged for 10 minutes at 5000 rpm.

Protein analysis

Using commercial kits (ELIZA kit, MyBioSource, China), the protein concentrations (Synaptopodin and Nephrin) were determined using the enzyme-linked immune sorbent assay (ELIZA). The procedures were carried out in accordance with the instructions provided in the kit catalogs

Biochemical analysis

Blood urea nitrogen, creatinine, and calcium concentrations are measured using the kit's provided technique (Biolabo, France)

3. Statistical Analysis

All values expressed as mean± S.D data analyzed done by using analysis of variance (ANOVA).

4. Results

The results showed in Table (1) significant increase Synaptopodin levels, Urea levels and creatinine levels in patient group compare with control group, and recovery or Follow-up group, while significant decrease Nephrin levels in patient group compare with control group, and recovery or Follow-up group, while significant decrease Synaptopodin levels, Urea levels and creatinine levels in recovery group compare with control and patient groups, calcium levels didn't show any significant differences between groups

Groups	Synaptopodin	Nephrin	urea	creatinine	Calcium
Control group	24.794±5.15	14.07±3.93	34.61±7.89	1 ± 0.29	8.82± 0.67
Patient group	41.355±9.26	9.01±2.3	40. 761±6.2	1.09 ± 0.32	8.95 ±0.85
Follow-up group	21.909±5.65	13.96±2.60	35.73±5.37	0.70 ± 0.1	8.82 ±0. 52

5. Discussion

High levels of synaptopodin could be accompanied by elevated interleukins IL-6 and IL-17 in urine and serum as these pro-inflammatory cytokines are involved with biomarkers in the initiation and progression of the kidney (Emanuela et al. 2021), The study of Kwon et al (2016) suggested that an increased level of synaptopodin in urine could predict glomerular damage as a potential marker of Podocyte damage associated with elevated serum creatinine in patients with glomerulonephritis.

Decreased Nephrin levels and increased proteinuria due to Acute kidney injury (AKI) is a severe symptom of SARS-CoV-2 due to acute tubular necrosis of direct infection, sepsis, cytokine storm, rhabdomyolysis and hypoxia of cells podocyte by inducing autophagy, a functional decrease of ACE-2 Durvasula et al.(2020), The study by Nandula et al. (2021) indicated that urinary nephrin levels of diabetic patients with covid 19 were 10 times higher than that of non-diabetic patients with the virus. This increase leads to a loss of podocyte specific protein within 12 months after infection, leading to long-term renal failure and hypertension.

An rise in urea levels reveals COVID-19-induced kidney injury as tubular destruction with glaring urinalysis anomalies. 59 COVID-19 patients (including 28 severe patients) exhibited high urea nitrogen levels. Seventeen studies looked at blood urea in relation to chronic kidney disease (CKD) and acute kidney injury (AKI) in COVID-19. Impaired glomerular filtration also occurs. Hachim et al. (2020). reported that the combined data showed that blood urea nitrogen was considerably higher in the acutely injured group than in the seriously injured group Naicker et al. (2020). In their study, Dai et al. (2021) reported that while creatinine did not significantly alter after 6 months of recovery, the urea value increased. In prior six-month research, 479 (35%) of 1,378 COVID-19 patients exhibited declining eGFR at follow-up

As they discovered that renal dysfunction in COVID-19 patients was connected with increasing age, male sex, comorbidities, higher levels of infection indices, and poor coagulation, high creatinine levels were linked to a higher risk of mortality. Furthermore, Cheng et al (2020). found a positive correlation between the incidence of AKI, or acute renal

damage, and death.The link between COVID-19 severity and hypertension, increased creatinine, and kidney damage from hypovolemia, as well as failure of the renin-angiotensin system in response to SARS-CoV-2, has been noted by Kreutz et al (2020). AKI kidney damage (AKI) patients with COVID-19 also had lower mean blood creatinine levels at recovery, which may have been due to more severe muscle loss, a longer hospital stay, or other COVID-19-related variables.

As this increase appears to be a more specific predictive indicator for severe forms than is a diagnostic sign, new research reveals that COVID-19 is related with a greater 3-month mortality rate in fragile elderly individuals with normal or high calcium levels. The strong 19-covid effect and its function in the development of what is known as a "cytokine storm," in which IL-6 is produced by bronchial epithelial cells, are the causes of hypercalcemia in the inflammatory response with the production of cytokines and interleukins. The severity of the disease and poorer outcomes are linked to high levels of IL-6. According to Pamart et al, (2021) IL-6 triggers osteoclast activation, bone resorption, and hypercalcemia.According to certain research, after After recovering from the disease and one to three months after contracting the Covid-19 infection, calcium levels were normal to low, and this decline was accompanied by a decline in parathyroid hormone (PTH), suggesting that one of the potential reasons is a problem with the PTH axis. -Normal Ca as a result of the development of antithyroid antibodies or the release of inflammatory cytokines like interferon, which have been known to reduce serum calcium levels. Bentata et al. (2022).

6. Conclusion

COVID-19 may have relation with increase synaptopodin levels and urea, creatinine levels and decrease Nephrin levels in blood.

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