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Research article

CRP and kidney function tests in patients with Covid-19

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Abstract

Purpose of study: Coronavirus disease 2019 (COVID-19) is a newly discovered respiratory disorder caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and recently declared as pandemic. Mild to moderate symptoms are the initial presentation of most of COVID-19 patients. Kidney damage is a frequent side effect of COVID-19. Acute phase reactants (APRs), are inflammation biomarkers that exhibit marked changes in blood concentrations at the time of inflammation. Important APRs include serum ferritin, C-reactive protein (CRP) and D-dimer. **This study aimed to** assess the role CRP and kidney function tests in Covid-19 and their impact on disease severity. **Basic procedures:** This study was conducted on 80 subjects including 20 apparently healthy individuals (group II) as a control group matched for age and sex and 60 Covid-19 patients diagnosed by PCR (group I) and was subdivided into 2 subgroups, G Ia: 30 (Non- ICU) Covid-19 patients and G Ib: ICU (intensive care unit) admitted COVID-19 patients with respiratory complications. This study was conducted at clinical pathology department, faculty of medicine, Minia University during the period from November 2021 to June 2022. **Main findings:** results of this study revealed a significant difference regarding CRP and kidney function tests (serum creatinine and urea) as covid-19 patients showed higher levels than control group, but there was no significant difference between both patient groups. **Principle conclusion:** Overall, this study revealed that elevation of both CRP and kidney function tests indicate a poor prognosis in individuals with covid-19, therefore, they may be involved in prediction of clinical course of the infection.

Key words: Covid-19, CRP, PCR, inflammation, creatinine, urea.

Introduction

In 2019, millions of people were affected by the worldwide pandemic resulted from Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection. COVID-19 causes numerous symptoms, many of which are complicated, primarily involving the respiratory system, but also multiple organs were affected in many cases leading to major health problems or even death [1].

The new (SARS-CoV-2) resulted in COVID-19 outbreak, which had developed into an emerging worldwide health disaster. Recently, numerous risk factors, such as advanced age, male gender, presence of comorbid conditions, and differences in racial and ethnic groups have been recognized as potentially having an effect on rising the morbidity of COVID-19 in adults. Additionally, the progress of COVID-19 to more severe and difficult form may be indicated by variations in laboratory parameters and pro-inflammatory cytokines and also potential consequences. Early in SARS-CoV-2 infection, patients may be present without symptoms, until development of dyspnea, severe pneumonia, organ damage, and eventually death[2].

Severe COVID-19 is marked by massive inflammatory reaction, involving excessive release of cytokines, that may be recognized in both the lungs and the bloodstream. Multiple immune cells are involved in the response, such

as inflammatory mediators are induced by neutrophils and macrophages when they detect pathogens and damaged self-structures [3].
Cardiac arrhythmias, rhabdomyolysis, shock, coagulopathy and acute organ damage like liver, cardiac and kidney damage, all may be consequences of severe COVID-19 [4].

Clinical and laboratory signs of inflammation, such as high fevers, thrombocytopenia, increased serum ferritin, and elevation of CRP and interleukin-6 (IL-6), may be accompanied with these organ failures [5].

CRP is known as a non-specific acute phase reactant which is increased during inflammation or infection. Elevated values point to a more serious infection. Elevated levels of CRP have been utilized to predict the of severity in COVID-19 disease, despite the lack of data supporting its use as a predictive marker [6].

When hepatocytes are activated during inflammation, they quickly produce CRP. It binds to numerous prokaryotic and eukaryotic pathogens, enabling activation of complement by classical pathway suggesting immunological activation, lymphocyte invasion, consumption of immune molecules and marked inflammatory response [7].

Individuals having serious form of Covid-19 with multiple organs affection and dead people were observed to have elevated values of CRP. CRP causes complement activation resulting in induction of apoptosis and the expression of pro-inflammatory cytokines that, when combined with the inflammatory condition of the disease, may result in worse prognosis [8].
Kidney affection in COVID-19 is common, although hypoxaemia and respiratory failure are the characteristic symptoms. Despite significantly decreased kidney function acute tubular damage commonly occurs, although it is frequently mild. Tubular damage is most likely a result of systemic hemodynamic instability. [9] .

COVID-19 infection directly results in acute kidney injury (AKI) which is frequent in markedly diseased patients and is among the worst clinical outcomes with a poor prognosis for survival. Between 10 and 40 percent of COVID-19 patients who are hospitalized continue to get AKI. From the beginning of the COVID-19 pandemic, AKI has killed a majority of older people with severe comorbidities [10].

Tubular damage and noticeable urine analysis abnormalities are characteristic features of typical kidney affection resulting from COVID-19. Also, impairment of glomerular filtration presents, that is typically recognized by high concentration of serum creatinine and blood urea nitrogen. individuals with kidney affection due to COVID-19 may experience mild form of proteinuria [11].

A negative impact on the maintenance of the acid-base balance and electrolyte in the human body results from impairment of renal function that may prevent the body from excreting metabolites and toxins. Additionally, uremia will develop when kidney function is markedly affected, and threatening life. Early identification of signs of renal affection and prompt, efficient therapies are of significant value for minimizing worse consequences and improving outcome [12].

Aim of the work:
The aim of this study is to assess the role of CRP and kidney function tests in Covid-19 and their impact on the disease severity.

Subjects and methods

This study was done on eighty subjects including 20 apparently healthy individuals (group II) as a control group matched for age and sex and 60 patients diagnosed Covid-19 patients by PCR (group I) and was subdivided into 2 subgroups: group Ia: 30 (Non – ICU) Covid-19 patients and group Ib: 30 ICU (intensive care unit) admitted COVID-19 patients with respiratory complications. This study was conducted at the department of clinical pathology, faculty of medicine, Minia University during the period from November 2021 to June 2022. The diseased subjects were diagnosed as Covid-19 patients by PCR. Molecular methods based on the real-time (quantitative) reverse transcriptase-polymerase chain reaction (RT-PCR) are recently considered as the gold standard method used in COVID-19 diagnosis [13]. This study was approved by the hospital ethical committee and a written consent was obtained from each subject (Approval number: 134:11/2021, Date of approval: 29 November 2021).

Inclusion Criteria:

- PCR positive RNA of Covid-19

Exclusion Criteria:

- Vaccinated patients against Covid-19

All subjects involved in the study were subjected to careful history taking, complete clinical examination and laboratory investigations. C-Reactive Protein (CRP) was measured using **GENRUI, biotech Inc, kinetic assay,China.** Kidney function tests (blood urea & serum creatinine) were measured using **auto-analyzer SELECTRA PRO XL, ELITech Group, clinical chemistry automation systems, Netherlands**, using the commercially available kits according to the manufaturer's instructions.

Results

All selected subjects in this study were divided into two groups: Group I: which included 60 Covid-19 patients diagnosed by PCR and was subdivided into 2 subgroups, group Ia: 30 (Non-ICU) Covid-19 patients and group Ib: 30 ICU (intensive care unit) admitted COVID-19 patients with respiratory complications. Group II: 20 apparently healthy individuals as a control group matched for age and sex.

Table (I): Comparison of the different studied groups as regarding to CRP:

	Group Ia (n = 30)	**Group Ib (n = 30)**	**Group II (Control) (n = 20)**	**p value Among all groups**	**p value G Ia vs G Ib**	**p value G Ia vs G II**	**p value G Ib vs G II**
CRP (mg/l)							
Median	24	48	2				
IQR	(12.78-48.5)	(24 - 96)	(1.63 - 3)	**<0.001***	0.065	**<0.001***	**<0.001***
Range	10 – 96	11 – 96	1 - 4				
CRP (mg/l):							
• Positive N (%)	30 (100%)	30 (100%)	0 (0%)				
• Negative N (%)	0 (0%)	0 (0%)	20(100%)				

A high statistically significant difference in CRP was found when comparing it among all groups, between control group and both group Ia and group Ib (P value = **< 0.001***) but no statistically significant difference was found when comparing it in group Ia Vs group Ib (P value = **0.065).** (Fig.1)

Table (II): Comparison of the different studied groups as regarding to serum creatinine:

	Group Ia ***(n = 30)***	**Group Ib (n = 30)**	**Group II (Control) (n = 20)**	**p value Among all groups**	**p value G Ia vs G Ib**	**p value G Ia vs G II**	**p value G Ib vs G II**
Creatinine (mg/dl)							
Mean ± SD	1.63 ± 1.17	1.60 ± 1.4	0.844 ±0.23	**0.007***	>0.99	**0.016***	**<0.001***
Range	0.5 - 5.2	0.5 - 7.2	0.5 - 1.3				

There was statistically high significant difference in creatinine level when comparing group Ib to control group (P value = **< 0.001***) and statistically significant difference when comparing it among all groups and in group Ia Vs control group (P value = **0.007***, P value = **0.016***) respectively, but there was no statistically significant difference when comparing it in group Ia Vs group Ib (P value = **>0.99**). (Fig.2)

Table (III): Comparison of the different studied groups as regarding to serum urea:

	Group Ia *(n = 30)*	**Group Ib** **(n = 30)**	**Group II (Control) (n = 20)**	**p value Among all groups**	**p value G Ia vs G Ib**	**p value G Ia vs G II**	**p value G Ib vs G II**
Urea (mg/dl) Mean ± SD	73.6 ±51.32	68.7 ± 46	30.5 ± 3.45	**<0.001***	>0.896	**<0.001***	**0.001***
Range	24 – 215	15 - 256	20 – 35				

There was statistically high significant difference in serum urea level when comparing it among all groups and between group Ia & control group (P value = < **0.001***), also there was significant difference between group Ib and control group (P value = **0.001***) but there was no statistically significant difference when comparing it in group Ia Vs group Ib (P value = **>0.896**). (Fig.3)

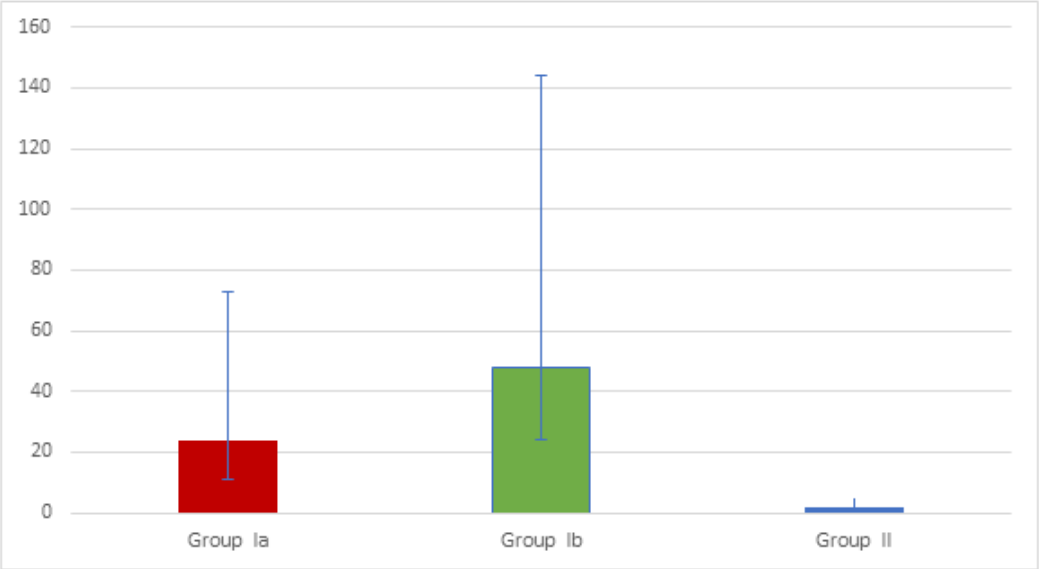

Figure (1): Comparison of the different studied groups as regarding to CRP.

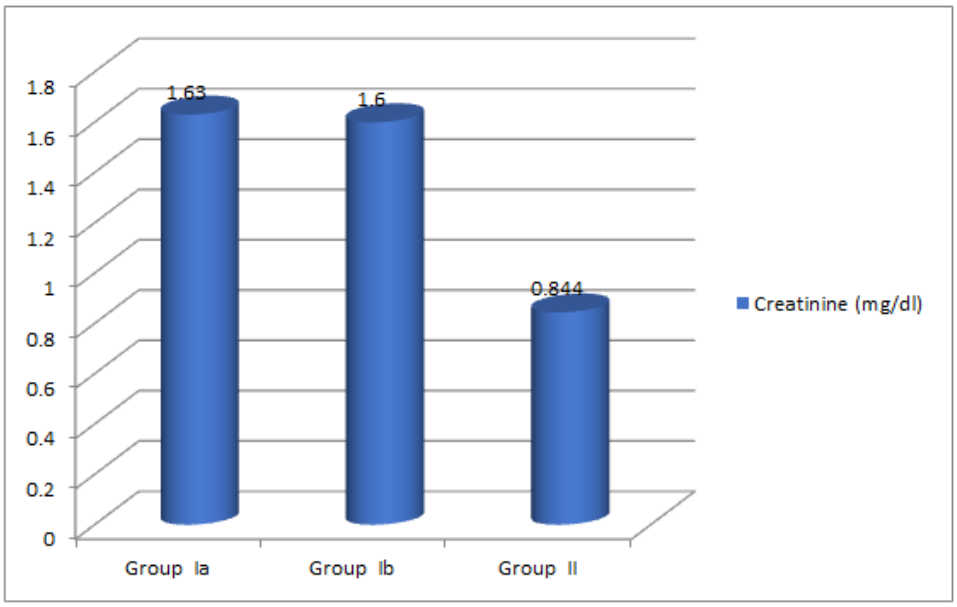

Figure (2): Comparison of the creatinine (mg/dl) in different studied groups

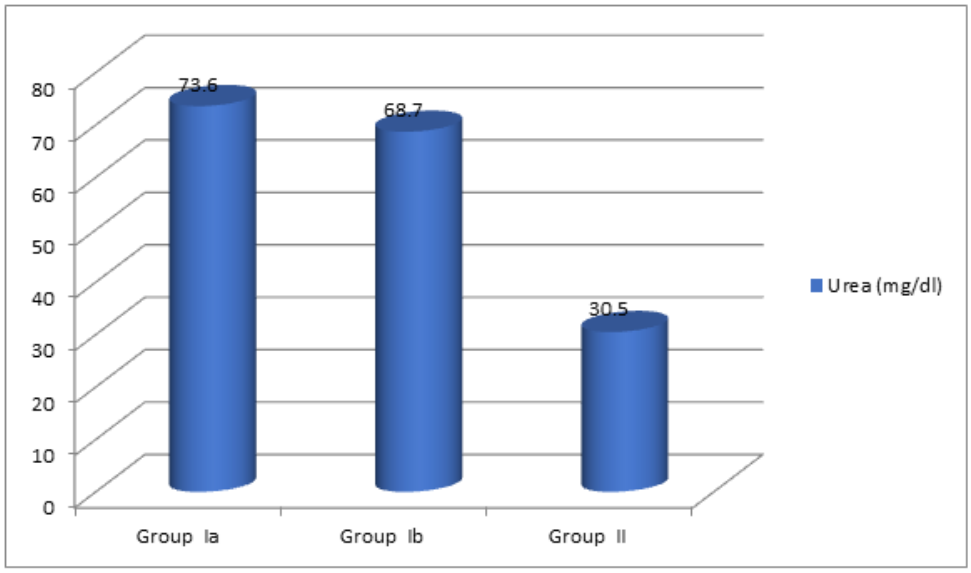

Figure (3): Comparison of the Urea (mg/dl) in different studied groups

Discussion

Most of individuals with severe Covid-19 develop lymphopenia, and some of them also have thromboembolic complications and problems of either peripheral or central nervous system [14]. A long with rhabdomyolysis, coagulopathy, cardiac arrhythmias and shock, additionally severe Covid-19 may lead to acute kidney, cardiac, and liver damage [15]. Clinical and laboratory indicators of inflammation, such as high fevers, thrombocytopenia, increased serum ferritin, and elevations in CRP and IL-6, can be linked to these organ failures [16].

In this study there was statistically significant elevation in CRP level in patient groups than control group and this was in agreement with **stringer and his colleague** who showed that increased levels of CRP have been recognized in COVID-19 patients which is used to assist in diagnosis, triage and prognosis. CRP is defined as a non-specific acute phase protein that is

synthesized by liver cells and is raised during acute inflammation or infection [6].
High levels of CRP have been linked to death due to SARS-CoV-2 infection, regarding to elevation in CRP level during this infection. CRP has been demonstrated as a chemical that can cause damage during infection with SARS-CoV-2 [8].

Clinically, elevated CRP levels may serve as early warning signs of hospital-acquired infections in patients with COVID-19 that make slow progress, also it may help physicians to begin empirical antibiotics therapy as early as possible to avoid worsened outcome [17].

There was statistically significant difference in renal function tests between the patient groups and control group as both (urea & creatinine) were significantly increased in patient group than control group and this was in agreement with **Liakopoulos and his colleague** who showed that acute kidney injury (AKI) is among the popular outcomes of COVID-19, making kidney among the target organs of SARS-COV-2 disease. Multiple pathogenic pathways have been recognized, including critical hypoxia, hemodynamic changes, inflammation and sepsis, rhabdomyolysis, mitochondrial injury, acute cardiorenal syndrome, endothelial dysfunction, microembolism, renal infarction and use of nephrotoxic medications [18].

Symptoms of the kidneys affection in COVID-19 frequently range from mild proteinuria to advanced AKI that need renal replacement treatment, increased blood urea nitrogen (BUN), serum creatinine (SCr), hematuria, proteinuria are characteristics of this renal impairment [19].
Due to immune system suppression, individuals with CKD show higher risk of infection with COVID-19 that could result in worse COVID-19 outcomes. CKD appears to be linked to elevated risk of severe form of COVID-19. As a result, CKD Patients must be warned to do additional precautions for reducing possibility of viral exposure [20].

Conclusion

Overall, results of the present study revealed that elevation of both CRP and kidney function tests indicate a poor prognosis in patients with covid-19, therefore, they may be involved in prediction of clinical course of the infection.

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