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Augmented Renal Clearance in COVID-19

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Dear Editor,

The concept of augmented renal clearance (ARC) has been previously proposed in critically ill patients [1]. Vasodilatation and the hyperdynamic state in systemic inflammation result in high cardiac output, and renal perfusion may be enhanced with an increase in glomerular filtration rate (GFR). It is now very well known that the hyper-inflammation state in the context of cytokine release syndrome might be a component of the clinical picture of COVID-19. Aggressive fluid resuscitation and certain vasoactive drugs in the management of the systemic inflammatory response may also contribute to an increase in renal perfusion, which eventually increases GFR.

Cr levels tended to decrease in 13 of our patients with COVID-19. ARC could be defined in 5 patients who had their estimated GFR reaching more than 130 mL/min/1.73 m^2. Their mean age was 42.6 ± 21.8 years and there was a male predominance (80%). The patients had an average basal Cr of 0.81 ± 0.12 mg/dL, their Cr levels dropped as low as 0.33 ± 0.07 mg/dL, and their estimated GFR increased to 154.4 ± 19.8 mL/min/1.73 m^2. The median day to observe ARC was the 13th day of patients' hospital admission [range: 3–46 days]. Patients spent 5.0 ± 1.0 days with their ARC functions and the average length of hospital stay of the patients was 33.6 ± 25.6 days.

ARC was found to coincide with an increase in inflammatory markers. The day when ARC first observed was strongly correlated with the day of peak ferritin, the day of peak C-reactive protein and the day of peak D-dimer (Pearson's $r = 0.82$ [$p = 0.08$], 0.92 [$p = 0.03$], and 0.88 [$p = 0.04$], respectively). Such high correlations indicate the inflammatory response as the pathophysiologic background of ARC in patients with COVID-19. These patients also had high intensive care admission and mortality rates at 80 and 60%, respectively.

It was previously proposed that GFR might increase with certain stimuli and the capacity of kidneys to increase GFR was called the renal functional reserve [2]. This concept may explain the protection of a certain level of GFR after kidney injuries. However, as seen in our cohort, it may be a surrogate marker of a systemic inflammatory response.

In addition to being a marker to show the hyper-inflammatory state, ARC may also have therapeutic failure consequences with an increase in renal clearance of drugs [3]. Dosing of certain renally eliminated drugs should be evaluated in conjunction with GFR calculations. It should be noted that Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) formulas may underestimate GFR. Although 24-h urine studies would give the most accurate results, 8-h studies will also be adequate for frequent calculations [4].

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Similar to our cohort, who were younger than general inpatients with COVID-19, younger age was previously defined as a contributor in the development of ARC [5]. In addition to acute kidney injury, which has been shown as a poor prognostic factor in COVID-19, physicians should also take care about the tendency for a decrease in Cr levels of their patients with COVID-19 as the latter might indicate an inflammatory response.

Conflict of Interest Statement

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Author Contributions

Ahmet Murt conceptualized the idea, collected and analyzed the data, performed the literature search, and wrote the first draft of the text. Mevlut Tamer Dincer and Cebrail Karaca helped in the collection of the data. All authors commented on the previous versions of the manuscript and approved the final version.

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