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A Single - Centred Prospective Cohort Study on Post – COVID - 19 Complications in Kidney

[1]Dr. Nusrat Aziz, [2]Dr. J.N. Ambika Bai, [3]Dr. Shobha Mohammed, [4]Dr Mujahid Mohammed, [5]Dr. Ponnala Harish Reddy

[1]Associate Professor of Physiology, Dr. VRK Women's Medical College Teaching Hospital and Research Center, Hyderabad, Telangana, India

[2]Assistant Professor of Physiology, Kamineni Institute of Medical Sciences, Narkatpally, Telangana, India

[3]Professor of Biochemistry, Mamata Academy of Medical Sciences, Bachupally, Hyderabad, Telangana, India

[4]Professor of Physiology, Mamata Academy of Medical Sciences, Bachupally, Hyderabad, Telangana, India

[5] Dr. Ponnala Harish Reddy, UG Scholar, Mamata Academy of Medical Sciences, Bachupally, Hyderabad, Telangana, India

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Corresponding Author: Dr Mujahid Mohammed, Professor of Physiology, Mamata Academy of Medical Sciences, Bachupally, Hyderabad, Telangana, India

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Abstract

Emerging data on Post COVID-19 suggests extrapulmonary manifestations its renal manifestations are not clearly defined as a post-COVID-19 complications. It has caused substantial morbidity and mortality worldwide and poses the most significant modern-day public health challenge. In this context, we designed a single-centred prospective cohort study to evaluate both conventional and novel renal biomarkers to detect kidney injury early in post-COVID-19 infected and cured patients. Both males and females participated in the study. Out of 104 individuals enrolled 71 were males from the age group 7-87 years, and 33 were females from the age group 13-85 years. The current research estimated the creatinine and cystatin C levels during COVID-19 and post-infection cured and discharged with a negative PCR result. Research results showed statistical significance between the variables.

Creatinine estimation during the COVID-19 infection was 0.95±0.45, SEM 0.04, 95% CI 0.86-1.0 and post-infection was 1.7±0.57, SEM 0.05, 95% CI 1.5 -1.8, paired t-test (two-tailed) p<0.0001, significant, t value 26.67 with df-103. Correlation coefficient (r) 0.88, p<0.0001 significantly effective. The estimated Cystatin C during the COVID-19 infection was 0.08±0.09, SEM 0.001, 95% CI 0.75-0.79 and post-infection was 0.12±0.02, SEM 0.002, 95% CI 0.12-0.13, paired t-test (two-tailed) p<0.0001, significant t value 30 with df-103. Correlation coefficient (r) 0.78, p<0.0001 significantly effective (Figure 3). eGFR was calculated by using the standard formulae and MDRD methods the eGFR during COVID-19 was 91±29, SEM 2.8, 95% CI 86-97, MDRD calculated eGFR was 94±43, SEM 4.2, 95% CI 85-102 and eGFR during post-COVID-19 was 50±21, SEM 2.1, 95% CI 46-54, MDRD calculated eGFR was 46±19, SEM 1.9, 95% CI 43-50, ANOVA (one way) p<0.0001, F 307, (Geiser-Greenhouse epsilon- 0.4938), multiple comparisons between fixed effects type III between the column's p<0.0001, F 574, Geiser-Greenhouse epsilon-0.1871. Conventional biomarkers like Creatinine, novel Cystatin C and estimated eGFR in post COVID- 19 infected and cured individuals may helpidentify the kidney's functional status so that early interventional methods can be adopted to prevent the further loss of kidney functions. Our study had some limitations being a one-centred study, and only 104 infected individuals showed their willingness to participate in the study out of 250 infected and hospitalized individuals.

Keywords

AKI (Acute Kidney Injury) COVID-19, Creatinine, Cystatin C and eGFR

Introduction

Emerging data on Post COVID-19 suggests extrapulmonary manifestations its renal manifestations are not clearly defined as post-COVID-19 complications. COVID-19 is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and was declared a global public health problem on 30 January 2020. It has caused substantial morbidity and mortality worldwide [1] and poses the most significant modern-day public health challenge. COVID-19 predominantly affects the respiratory system, typically manifesting as acute respiratory distress syndrome (ARDS) and severe pneumonia in a few patients, whereas the majority of patients are asymptomatic or present with mild symptoms such as common symptoms of COVID-19 fever, cough, myalgia or fatigue [2,3]. Aged male patients, with pre-existing comorbidities such as diabetes, hypertension, chronic kidney disease (CKD), and chronic liver disease are reported to be more likely to be infected with SARS CoV-2 [4] and they are at a higher risk of severe illness or death [5,6]. Previous data suggested that COVID-19 also affected multiple organs, leading to organ failure and eventually death [7]. The common cardiovascular complications reported to be associated with COVID-19 include myocardial injury and heart failure [8], which have been shown to correlate with the severity of or mortality with COVID-19 [9]. The emerging data also suggests that COVID-19 contributes to adverse renal manifestations such as acute kidney injury (AKI), and is also associated with the severity of COVID-19 or mortality [10]. Despiterapidly growing knowledge based on the clinical outcome of the disease; no effective therapeutic agents have been identified, so preventive methods need to be

developed to stop the progression of AKI in post-COVID-19 infected individuals. Further data on the extrapulmonary complications in the disease's clinical course could help reduce morbidity in post-COVID-19 individuals if detected earlier. Screening of available biomarkers may serve the purpose to developeffective treatment strategies. Understanding the aetiology of COVID-19 and its renal manifestations could assist in the management of individuals. In this context, wedesigned a prospective cohort study to evaluate both conventional and novel renal biomarkers to detect kidney injury early in post-COVID-19 infected and cured patients.

Materials and methods

The study was conducted from June to September 2022 based on the predefined protocol which was registered under the institutional ethical committee (IEC) approval no IEC/MAMS/2022/014.104 COVID-19-infected patients were admitted to the hospital of Mamata Academy of Medical Sciences, during the COVID-19 pandemic and were enrolled for the study after accessing their records from the medical record (MRD) section of the hospital. Patients were contacted through their contact mobile numbers given during hospitalization, out of 250 COVID-19-infected patients 104 individuals agreed to participate in the current study. Individuals were asked to visit pulmonology and nephrology OPD for their routine examination, and blood samples were collected to estimate the parameters of creatinine and cystatin C. Samples were collected and serum was separated by using a centrifuge with 3200 rotations (REMI-R-8C) on the same day as they visited the hospital and stored at -40^{0}c (LG Freezer, China) till the assessment was done. Once the sample of 104 COVID-19-infected individuals was accumulated the stored serum was brought to room temperature and processed for the evaluation of Creatinine on Mindray-240 fully automated analyser by the method of Sarcosine Oxidase method (CREA-SOX) and Cystatin C was estimated by using semi-autoanalyser make of Meril by methodparticle enhanced immunoturbidimetric test, DiaSys Diagnostic System, Germany.

Inclusion and exclusion criteria

Individuals infected with COVID-19 and cured and discharged from the hospital with negative PCR and willing to give informed consent were included in the study, and individuals suffering from diabetes hypertension and chronic kidney alignments were excluded from the study to avoid bias in the study.

Statistical analysis

The obtained data were calculated by using GraphPad Prism version 9.4.1 (USA) licenced version. Discrete variables, Mean ±SD, SEMand Student t-test (paired), Correlation coefficient (r), and one-way ordinary ANOVA were performed to prove the statistical significance of obtained dataat $p<0.05$, with Confidence Interval (CI) of 95% with an 80% of Power of the study.

Results

Both males and females participated in the study. Out of 104 individuals enrolled 71 were males from the age group7-87 years, and 33 were females from the age group 13-85 years (Figure 1). The current research estimated the creatinine and cystatin C levels during COVID-19 and post-infection cured and discharged with a negative PCR result. Research results showed statistical significance between the variables. Creatinine estimation during the COVID-19 infection was 0.95±0.45, SEM 0.04, 95% CI 0.86-1.0and post-infection was 1.7±0.57, SEM 0.05, 95% CI 1.5 -1.8, paired t-test (two-tailed) $p<0.0001$,

significant, t value 26.67 with df-103. Correlation coefficient (r) 0.88, p<0.0001 significantly effective (Figure 2). The estimated Cystatin C during the COVID-19 infection was 0.08±0.09, SEM 0.001, 95% CI 0.75-0.79 and post-infection was 0.12±0.02, SEM 0.002, 95% CI 0.12-0.13, paired t-test (two-tailed) p<0.0001, significant t value 30 with df-103. Correlation coefficient (r) 0.78, p<0.0001 significantly effective (Figure 3).eGFR was calculated by using the standard formulae and MDRD methods the eGFR during COVID-19 was 91±29, SEM 2.8, 95% CI 86-97, MDRD calculated eGFR was 94±43, SEM 4.2, 95% CI 85-102 and eGFR during post-COVID-19 was 50±21, SEM 2.1, 95% CI 46-54, MDRD calculated eGFR was 46±19, SEM 1.9, 95% CI 43-50, ANOVA (one way) p<0.0001, F 307, (Geiser-Greenhouse epsilon- 0.4938). multiple comparisons between fixed effects type III between the column's p<0.0001, F 574, Geiser-Greenhouse epsilon- 0.1871 (Figure 4).

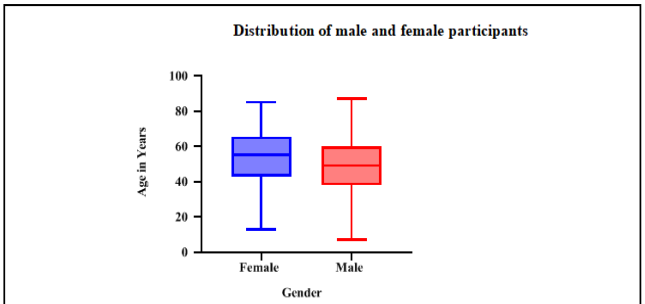

Figure 1- Distribution of male and female participants. Data presented as Mean ±SD, Males 50±15 and females 54±16. n (104), males (71) and females (33).

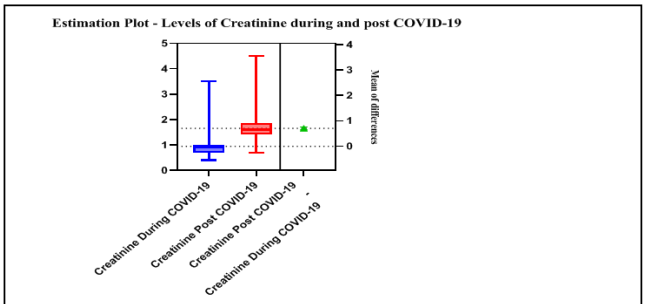

Figure 2 – Levels of Creatinine during and cured post-COVID-19. Data presented Mean±SD, SEM, n (104). Paired t-test p<0.0001, t value 27, r- 0.88.

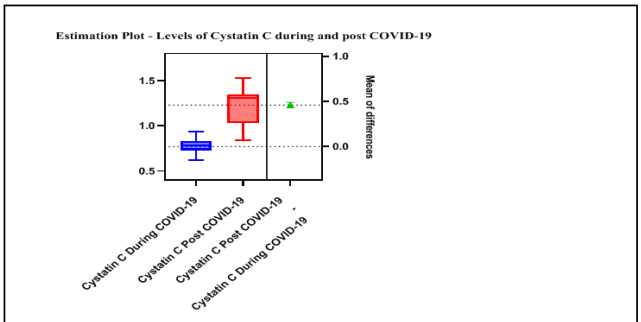

Figure 3 – Levels of Cystatin C during and post-COVID-19. Data presented as Mean±SD, SEM, n (104), paired t-test p<0.0001, t value 30.87, r- 0.77.

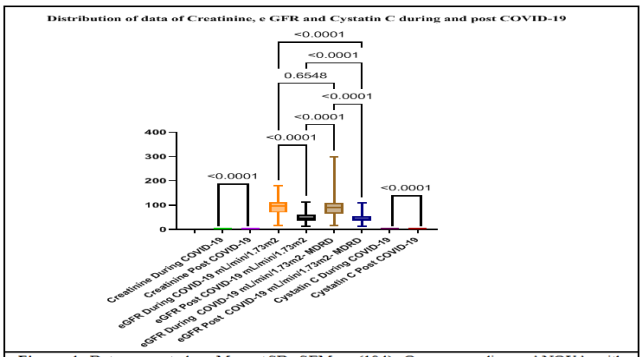

Figure 4- Data presented as Mean ±SD, SEM, n (104). One-way ordinary ANOVA with Tukey's multiple comparisons, p<0.0001 Significant, F value 307.

Discussion

Predominantly COVID-19 affects the respiratory system, it has affected other organs leading to multiorgan failures, such as the gastrointestinal system, the cardiovascular system, and the kidneys. Post-COVID-19 complications are not well established and studied as these multiple organ disturbances may then interact with each other, which correlates with the severity of the disease. SARS-CoV-2 is known to enter human lung cells by binding to angiotensin-converting enzyme 2 (ACE_2) [11]. The multiorgan involvement of SARS-CoV-2 has been linked to ACE_2 receptors which are widely distributed in the body; the highest expression of ACE_2 is found in the ileum and kidneys [12,13]. ACE_2receptors are expressed in several parts of the kidney including Bowman's capsule's parietal epithelium, mesangial cells, podocytes, and the collecting ducts [14]. Although the mechanism for the renal manifestations of COVID-19 is still elusive, a complex multifactorial pathway has been proposed and which includes (I) the direct viral involvement and replication in the kidneys leading to dysfunction; (II) local disruption in the renin-angiotensin-aldosterone system (RAAS) homeostasis; (III) lung protective fluid management strategy during treatment of ARDS and (IV) as a result of a systemic inflammatory response "cytokine storm" [15].COVID-19 infection represents a great medical challenge in the near future and appears to have multisystem effects, including renal manifestations. The available data based on up-to-date evidence suggests that AKI is commonly reported as a complication among patients with COVID-19 and also an independent risk factor for AKI [16]. Consistently, our study findings showed that males are more infected when compared to females. Emerging evidence also suggests that renal manifestations of COVID-19 are also associated with an increased risk of severe COVID-19 and fatal outcomes on post-COVID-19 complications [17]. Monitoring renal markers during and post-hospitalization for COVID-19 could help identify patients at a higher risk for worse outcomes. In a previous study by Pei G; et.al most of the patients infected with COVID-19 presented with haematuria and proteinuria in severely infected and ill patients[18]our study is in favour of this study. 35% of 1733 subjects recovered from COVID-19 and with a baseline eGFR > 90 ml/min/1.73 m^2 had a statistically significant decline in eGFR at the six-month follow-up, including 13% who did not demonstrate any signs of AKI during the initial hospitalization period[19]. Estimated eGFR in our study also showed a decline in post-COVID-19 infected and cured patients, studies

investigating renal function during the post-COVID-19 period are limited in number and in terms of follow-up duration. The current evidence from our research enables researchers to focus on biomarkers of creatinine, cystatin C and eGFR that may help COVID-19-infected and cured individuals to identify and treat them early to avoid further complications. However, more research is needed to help us better understand the pathophysiology underlying renal manifestations of COVID-19 and to help in the identification of effective management strategies.

Conclusion

Conventional biomarkers like Creatinine, novel Cystatin C and estimated eGFR in post COVID- 19 infected and cured individuals may help identify the kidney's functional status so that early interventional methods can be adopted to prevent the further loss of kidney functions. Our study had some limitations being aone-centred study, and only 104 infected individuals showed their willingness to participate in the study out of 250 infected and hospitalized individuals. More studies are warranted by using the cluster sampling method with a larger sample size.

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