

21-Fold Higher COVID-19 Mortality Rate in Patients with Severe Renal Dysfunction on Admission

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Since December 2019, coronavirus disease (COVID-19) has quickly become a pandemic. The associated mortality rate is higher in patients with hypertension, diabetes, cardiovascular diseases, cancer, and acute kidney injury^(1,2). Chronic renal failure (CKD) is one of the comorbidities that can affect the disease severity, the treatment process, and the mortality rate; *Clark A et al.* reported that CKD, after age, is among the strongest risk factors for severe COVID-19 disease⁽³⁾. Previous studies showed an association between severity of renal function impairment (RFI) and disease aggravation, ICU admission, and mortality rate⁽⁴⁾. It seems that evaluation of renal function is important as one of the predictors of COVID-19 severity. To enhance patients' outcomes and decrease mortality, prompt risk stratification of disease severity is important; thus, we observed the potential relation of estimated Glomerular Filtration Rate (eGFR) and COVID-19 patients' outcomes.

We enrolled 186 patients of our COVID-19 center from March to April 2020. We included patients with confirmed COVID-19 (based on PCR or CT scan). Patients less than 18 years or those with a history of CKD or dialysis were excluded. We categorized patients into four groups according to their eGFR on admission: normal (≥ 90 mL/min), mild impairment (60–90 mL/min), moderate impairment (≥ 30 –60 mL/min), and severe impairment (< 30 mL/min)⁽⁵⁾. eGFR of patients was calculated using the Cockcroft-Gault formula.

The mean age of the participants was 60.74 ± 16.88 years. Of 186, 113 (60.8%) were female. According to eGFR, individuals were divided into four groups; 43 (23.1%) were normal, 67 (36%) were mild, 58 (31.2%) were moderate, and 18 (9.7%) had severe RFI. Subjects with severe renal dysfunction were older than normal subjects (43.11 ± 13.22 vs. 79.55 ± 10.99 ; $P < 0.001$). The most common comorbidity among patients was hypertension (86.5%). There was no significant difference between the four groups regarding sex and severity of pulmonary infection and admission to the intensive care unit (ICU). There was a significant difference between the four groups in length of hospital stay ($P = 0.011$) and death ($P = 0.01$). The demographic characteristics of patients are shown in Table 1. There was a significant difference between the four groups in heart rate ($P = 0.027$) and respiration rate ($P = 0.001$) on admission.

Comparison of eGFR levels with radiological and laboratory parameters showed that severe RFI was associated with higher plural effusion on CT scan (2.3% VS 22.2, $P=0.048$) and lower levels of red blood cells ($4.83 \times 10^9/L$ VS $4 \times 10^9/L$, $P=0.005$). Pearson correlation between renal function indicators including eGFR, Blood nitrogen urea (BUN), Serum Creatinine (SCr), and various laboratory parameters showed a significant negative correlation between eGFR and White Blood Cells (WBC) ($r = -0.158$, $P=0.032$), SCr ($r = -0.472$, $P<0.001$), BUN ($r = -0.507$, $P<0.001$), and potassium ($r = -0.282$, $p<0.001$). BUN was significantly and positively correlated with neutrophil percentage ($r = 0.106$, $P=0.025$), WBC ($r = 0.131$, $P=0.004$), as well as a significant negative correlation with hemoglobin ($r = -0.181$, $P<0.001$), and platelets ($r = -0.120$, $P=0.009$). We detected a significant negative correlation between SCr and hemoglobin ($r = -0.184$; $p < 0.001$), platelets ($r = -0.149$, $P=0.001$) and Erythrocyte sedimentation rate (ESR) ($r = -0.222$, $P=0.01$), but a significant positive correlation existed with potassium ($r = 0.373$; $p < 0.001$) and total bilirubin ($r = 0.378$ $p < 0.001$).

Similar to previous studies ⁽⁵⁾, 40.8% of our COVID-19 patients had moderate to severe kidney disease, and patients with severe RFI were older than those with normal eGFR levels. Our study indicated that Hypertension and Ischemic heart disease were the most common underlying comorbidities in patients with moderate-severe RFI among COVID-19 patients, like in previous studies ⁽⁶⁾. We found a significant association between length of hospital stay and mortality rate with severe RFI; this finding is expected as lower eGRF increases the risk of infection ⁽⁷⁾. We found that severe renal dysfunction is associated with a 21.2-fold excess risk of mortalities in patients with COVID-19 (OR, 21.2; 95% CI, 2.29-191.82, $P=0.007$); whereas adjustment for age and gender in this group was not statistically significant (OR, 10.35; 95% CI, 0.71-135.52, $P=0.075$). These findings suggest that renal failure may be an independent prognostic factor in hospitalized patients with COVID-19 infection.

The low sample size limited our findings. Our study is also a retrospective, single-center study; thus, our laboratory data (such as proteinuria, another renal function index) was missing. Finally, we did not assess long-term renal function outcomes in survivors, and further research is needed to extend our results to a larger population.

Final point

The present survey of COVID-19 patients demonstrated that age and degree of RFI were associated with increased length of hospital stay and in-hospital mortality. Our findings highlight the importance of evaluating the renal function indicators as predictors of disease severity and outcomes.

Table1: Demographics characteristics, the laboratory features, and their association with eGFR of COVID-19 patients

| | Normal n=43(23.1%) | Mild n=67(36%) | Moderate n=58(31.2%) | Severe N=18(9.7%) | p-value |
|---|-------------------------------|---------------------------|---------------------------------|------------------------------|----------------|
| Mean Age | 43.11±13.22 | 59.86±12.34 | 68.96±12.95 | 79.55±10.99 | <0.001 |
| Male | 31(72.1) | 43(64.2) | 30(51.7) | 9(50) | 0.138 |
| Female | 12(27.9) | 46(15.5) | 25(84.5) | 9(50) | |
| ICU admission | 5(11.6) | 8(11.9) | 2(3.4) | 2(11.1) | 0.348 |
| Hospital stay: (Mean± SD) | 8.37±9.43 | 5.56±4.57 | 6.25±5.05 | 10.83±9.81 | 0.011* |
| Expired | 1(2.3) | 8(11.9) | 9(15.5) | 6(33.3) | 0.01* |
| Hemoglobin (g/L) | 14(12.8,15.1) | 13.4(12.6,14.2) | 13.8(12.6,14.2) | 12.35(10.77,15.37) | 0.095 |
| RBC | 4.83(4.55,5.2) | 4.6(4.28,4.9) | 4.3(4.58,4.89) | 4(3.69,4.83) | 0.005 |
| Lymphocyte % | 15(19,26.25) | 17(10.75,24.25) | 16(11,24) | 20(11.5,26.25) | 0.310 |
| WBC | 6.20(4.20,7.30) | 6.20(4.80,8.50) | 7.20(5.10,9.10) | 6.60(5.02,12.62) | 0.170 |
| Neutrophils % | 75.5(69,82) | 77(70,84.25) | 79(72,85) | 75(69.75,84.25) | 0.318 |
| Monocyte % | 2.2(2,3) | 3(2,3) | 3(2,3) | 3(2,3) | 0.982 |
| Platelet count (×10⁹) | 177(145,230) | 187(147,241) | 160(144,210) | 158.5(137.75,211) | 0.436 |
| Fasting Blood Sugar | 105(97,150) | 124.5(104,176.5) | 131(106,158) | 113(86.85,127) | 0.04* |
| Serum creatinine (µmol/L) | 1(0.8,1.1) | 1.1(1,1.3) | 1.4(1.17,1.6) | 2.2(1.67,3.62) | <0.001* |
| BUN | 12.7(10,15) | 16(11,20) | 24(18.75,36) | 41.8(31.2,63.5) | <0.001* |
| Na | 135(133,137) | 134(132,137) | 135(133,137) | 135.5(131.75,137) | 0.519 |
| K | 3.9(3.5,4.1) | 4(3.67,4.32) | 4.2(3.85,4.8) | 4.35(4.07,5) | <0.001* |
| CPR | 34(23,44.5) | 48(23.5,48) | 31(19.25,43.5) | 33.5(23.75,49) | 0.380 |
| ESR | 50(27,87) | 69(46,93) | 51(40.5,77.5) | 37.5(13.5,101.25) | 0.612 |

References

1. Sobhani S, Aryan R, Kalantari E, et al. Association between Clinical Characteristics and Laboratory Findings with Outcome of Hospitalized COVID-19 Patients: A Report from Northeast Iran. Interdisciplinary perspectives on infectious diseases. 2021;2021.
2. Sobhani S, Kazemi A, Kalantari F, et al. Hematological and Biochemical Parameters Associated with Mortality in COVID-19 Infection and Their Correlation with Smoking. Journal of Patient Safety & Quality Improvement. 2021;9:41-6.

3. Clark A, Jit M, Warren-Gash C, et al. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study. *The Lancet Global Health*. 2020;8:e1003-e17.
4. Flythe JE, Assimon MM, Tugman MJ, et al. Characteristics and outcomes of individuals with pre-existing kidney disease and COVID-19 admitted to intensive care units in the United States. *American Journal of Kidney Diseases*. 2021;77:190-203. e1.
5. Hachim IY, Hachim MY, Naeem KB, et al. Kidney dysfunction among COVID-19 patients in the United Arab Emirates. *Oman Medical Journal*. 2021;36:e221.
6. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama*. 2020;323:1239-42.
7. Ishigami J, Matsushita K. Clinical epidemiology of infectious disease among patients with chronic kidney disease. *Clinical and experimental nephrology*. 2019;23:437-47.

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