

# Outcomes of COVID-19 in Cancer Patients who Developed Acute Kidney Injury During Hospitalization in a Tertiary Care Hospital in India

*Ram Singh*

Department of Onco-Anaesthesia and Palliative Medicine, Dr. B.R.A.I.R.C.H. & N.C.I., All India Institute of Medical Sciences, New Delhi, India.

*Hari Krishna Raju Sagiraju*

Department of Preventive Oncology, N.C.I., Jhajjar, All India Institute of Medical Sciences, New Delhi, India.

*Sudarsan Krishnasamy*

3 Department of Pediatric Nephrology, All India Institute of Medical Sciences, New Delhi, India.

*Prashant Sirohiya*

Department of Onco-Anaesthesia and Palliative Medicine, Dr. B.R.A.I.R.C.H. & N.C.I., All India Institute of Medical Sciences, New Delhi, India.

*Balbir Kumar*

Department of Onco-Anaesthesia and Palliative Medicine, Dr. B.R.A.I.R.C.H. & N.C.I., All India Institute of Medical Sciences, New Delhi, India.

*Brajesh Kumar Ratre*

Department of Onco-Anaesthesia and Palliative Medicine, Dr. B.R.A.I.R.C.H. & N.C.I., All India Institute of Medical Sciences, New Delhi, India.

*Sushma Bhatnagar*

Department of Onco-Anaesthesia and Palliative Medicine, Dr. B.R.A.I.R.C.H. & N.C.I., All India Institute of Medical Sciences, New Delhi, India.

**Background:** The development of acute kidney injury (AKI) in patients infected with COVID-19 has been observed to be associated with poor outcomes. Our study aimed to measure the outcomes of COVID-19 in cancer patients who developed AKI during hospitalization and the predictive baseline clinical and laboratory factors associated with the development of AKI.

**Materials and Methods:** This retrospective cohort study was conducted at a COVID hospital that included only cancer patients with COVID-19 infection. Acute kidney injury (AKI) was defined according to KDIGO (Kidney Disease: Improving Global Outcomes) criteria. The demographic, clinical, laboratory and outcomes data were collected from the hospital electronic database and abstracted from the case files.

**Results:** Thirteen (12.8%) of the total 102 cancer patients developed AKI during hospitalization. Out of 13, 11 (84.6%) patients presented with hypoxemia during admission and required oxygen support. Breathlessness [Odds Ratio (OR) (95% CI): 5.8 (1.1-31.3)] or hypoxemia [OR 22.6 (2.6-194.5)] at the time of presentation and requirement of oxygen support [OR 7.5 (1.4-40.5)] were significantly associated with AKI after adjusting for age, gender, vaccination status and comorbidities. Median baseline values of inflammatory markers were significantly higher among those who developed AKI. Out of 102, 27 (26.5%) patients had in-hospital mortality. Mortality was high among those who developed AKI compared to those who didn't develop AKI (92.3% vs 16.1%, p-value: <0.001).

**Conclusions:** The cancer patients infected by COVID-19 and who developed AKI were more vulnerable to poor outcomes in terms of in-hospital mortality. The patients with severe disease at presentation and higher levels of baseline inflammatory markers CRP, ferritin, and D-Dimer were more susceptible to the development of AKI and in turn, led to a higher risk of in-hospital mortality in these patients.

## Introduction

The immunocompromised state associated with malignancy and malignancy directed therapy makes patients with cancer more susceptible to COVID-19 infection as well as vulnerable to poor outcomes [1-4]. Renal involvement in patients with COVID-19 infection is quite common with an overall incidence rate of 35% to 46% [5-7]. Incidence of acute kidney injury (AKI) in cancer patients with COVID-19 infection ranged from 20% to 45% across different studies.[6-8] Clinical characteristics such as older age, hypertension and diabetes, were risk factors for the development of AKI as well as poor prognosis [1-3,8]. In our study we aimed to measure the outcomes of COVID-19 in cancer patients who developed AKI during hospitalization and the predictive baseline clinical and laboratory factors associated with the development of AKI.

## Materials and Methods

It was a retrospective cohort study conducted at the National Cancer Institute (NCI) of the All India Institute of Medical Sciences (AIIMS), New Delhi, India. The cancer institute was designated as a COVID-19 hospital during the pandemic. The protocol for this study was drafted using the relevant checklist and it was approved by the institute's ethics committee. The hospital's electronic database and case files were used to extract demographic and clinical data. The study period ranged from 1st April 2021 to 30th June 2021.

The cohort was defined as the population of patients having the following 3 criteria: (1.) All adult cancer patients (aged  $\geq 18$  years); (2.) COVID-19 infection confirmed by the real-time polymerase chain reaction (RT-PCR) test from the nasopharyngeal swab sample; (3) Patients with evidence of acute kidney injury (AKI), defined as per KDIGO (Kidney Disease: Improving Global Outcomes) criteria based on serum creatinine (SCr) measurements. Cancer patients  $\leq 18$  years of age, or having chronic kidney disease or renal transplantation, or baseline creatinine value  $\geq 1.2$  mg/dL (a value  $\leq 1.2$  mg/dL is considered the normal value of creatinine in the absence of any previously available SCr value), inadequate SCr measurements (less than two measurements), or incomplete clinical or laboratory data, and patients transferred out of the hospital, were excluded.

The primary objective was to compare in-hospital mortality among cancer patients who developed AKI and those who did not. The secondary objective was to examine the clinical or laboratory markers associated with the development of AKI in these patients.

Demographic details, comorbidities, symptoms at presentation, the severity of the disease at admission, oxygen support, mechanical ventilatory support, length of hospital stay, resolution of AKI at discharge, persistent requirement of hemodialysis at discharge, and in-hospital mortality were recorded. The laboratory data included baseline routine and inflammatory parameters at admission (within 24 hours of admission).

## Definitions of terms

Based on KDIGO (Kidney Disease: Improving Global Outcomes) criteria, AKI is defined as either: (i) an increase in SCr by  $\geq 0.3$  mg/dl within 48 hours from the baseline (the value of SCr obtained within 24 hours of admission); or (ii) an increase in SCr to  $\geq 1.5$  times baseline within 7 days of admission to the hospital. The maximum SCr gain from baseline or the most severe stage of AKI attained during the hospital stay was used to further categorise AKI stages, 1 to 3. Stage 1 comprised an increase in SCr level by 0.3 mg/dL within 48 hours or 1.5 to 1.9 times increase in SCr level from baseline within 7 days. Stage 2 was defined as an increase of 2 to 2.9 times in SCr level within 7 days of hospitalization. Stage 3 of AKI was, a 3 or more times increase in S. cr. level within 7 days or a requirement or initiation of dialysis. AKI stage 3D was defined as a patient with stage 3 AKI on dialysis. Suffix "D" was added to the stage of AKI to denote ongoing dialysis. Due to unreliable documentation and missing bodyweight and height data, the urine output and estimated

glomerular filtration rate (eGFR) criteria could not be applied to define AKI.

## Results

Out of 102 cancer patients, the number of haematological & solid malignancies were 40 and 62 respectively. Thirteen (12.8%) of the total 102 cancer patients developed AKI during hospitalization (10.5% among haematological tumours & 16.1% among solid tumours, p-value: 0.445). Out of 13, 11 (84.6%) patients presented with hypoxemia during admission and required oxygen support. Breathlessness [Odds Ratio (OR) (95% CI): 5.8 (1.1-31.3)] or hypoxemia [OR 22.6 (2.6-194.5)] at the time of presentation and requiring oxygen support [OR 7.5 (1.4-40.5)] were significantly associated with AKI after adjusting for age, gender, vaccination status and comorbidities. Median baseline values of inflammatory markers such as CRP, Ferritin and D-Dimer were significantly higher among those who developed AKI compared to those who did not. Out of 102, 27 (26.5%) patients had in-hospital mortality. Mortality was high among those who developed AKI, compared to those who didn't develop AKI (92.3% vs 16.1%, p-value: <0.001).

## Discussion

The incidence rate of AKI observed among the cohort of cancer patients at our institution was quite low (i.e.13%) as compared with previous studies that have reported an incidence of 20%, in a cancer centre,[8] while it was 36 to 45% in other studies [6-7]. A small sample size of our study and different criteria used to define AKI among studies could be a reason for that. Among other clinical characteristics older age and comorbidities like hypertension and diabetes were associated with the development of AKI and worse outcomes, a similar findings were observed in patients with no malignancy [1-3,8-10]. In our observation, among presenting symptoms, patients with breathlessness on admission or requiring oxygen supplementation and higher baseline level of inflammatory markers CRP, ferritin, and D-Dimer had a higher incidence of AKI, a similar finding in previous studies in patients with or without malignancy [1,3,6-7,9- 10]. In a similar study, cancer patients with COVID-19 demonstrated elevated D-dimer levels in more than 88% of the patients who developed AKI during hospitalization [11].

The limitations of our study include small sample size, so the findings of this study couldn't be extrapolated to the whole population of cancer patients infected with COVID-19. Our study, being a retrospective study is vulnerable to the inherent information and selection bias during data retrieval. The cancer patients infected by COVID-19 and who developed AKI were more vulnerable to poor outcomes in terms of high in-hospital mortality.

Like the general population, cancer patients with severe disease at presentation and higher levels of baseline inflammatory markers CRP, ferritin, and D-Dimer were more susceptible to the development of AKI and in turn, led to a higher risk of in-hospital mortality and poor outcomes.

## References

## References

1. Zhang H, Han H, He T, Labbe KE, Hernandez AV, Chen H, Velcheti V, Stebbing J, Wong K. Clinical Characteristics and Outcomes of COVID-19-Infected Cancer Patients: A Systematic Review and Meta-Analysis. *Journal of the National Cancer Institute*. 2021; 113(4)[DOI](#)
2. Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Desai Aakash, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet (London, England)*. 2020; 395(10241)[DOI](#)
3. Brar G, Pinheiro LC, Shusterman M, Swed B, Reshetnyak E, Soroka O, Chen F, Yamshon S,

- Vaughn J, Martin P, Paul D, Hidalgo M, Shah MA. COVID-19 Severity and Outcomes in Patients With Cancer: A Matched Cohort Study. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*. 2020; 38(33)[DOI](#)
4. Xie Z, Saliba AN, Abeykoon J, Majeed U, Almquist DR, Wiedmeier-Nutor JE, Bezerra E, Andrade-Gonzalez X, Hickman A, Sorenson K, Rakshit S, Wee C, Tella SH, Kommalapati A, Abdallah N, Pritchett J, De Andrade M, Uprety D, Badley A, Manochakian R, Ailawadhi S, Bryce AH, Hubbard JM, Gangat N, Thompson CA, Witzig TE, McWilliams RR, Leventakos K, Halfdanarson TR. Outcomes of COVID-19 in Patients With Cancer: A Closer Look at Pre-Emptive Routine Screening Strategies. *JCO Oncology Practice*. 2021; 17(9)[DOI](#)
5. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, Paranjpe I, Somani S, Richter F, Miotto R, Lala A, Kia A, Timsina P, Li L, Freeman R, Chen R, Narula J, Just AC, Horowitz C, Fayad Z, Cordon-Cardo C, Schadt E, Levin MA, Reich DL, David L., Fuster V, Murphy B, He JC, Charney AW, Böttinger EP, Glicksberg BS, Coca SG, Nadkarni GN. AKI in Hospitalized Patients with COVID-19. *Journal of the American Society of Nephrology: JASN*. 2021; 32(1)[DOI](#)
6. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, Barnett RL, Hazzan AD, Fishbane S, Jhaveri KD. Acute kidney injury in patients hospitalized with COVID-19. *Kidney International*. 2020; 98(1)[DOI](#)
7. Ng JH, Hirsch JS, Hazzan A, Wanchoo R, Shah HH, Malieckal DA, Ross DW, Sharma P, Sakhiya V, Fishbane S, Jhaveri KD. Outcomes Among Patients Hospitalized With COVID-19 and Acute Kidney Injury. *American Journal of Kidney Diseases: The Official Journal of the National Kidney Foundation*. 2021; 77(2)[DOI](#)
8. Simbaqueba C, Mamlouk O, Dickson K, Halm J, Mandayam S, Turin A, D'Achiardi D, Franco-Vega M. Acute kidney injury and major outcomes in cancer patients with no history of chronic kidney disease (CKD) with coronavirus 2019 (COVID-19) infection.. *Journal of Clinical Oncology*. 2021; 39(15\_suppl)[DOI](#)
9. Lin L, Wang X, Ren J, Sun Y, Yu R, Li K, Zheng L, Yang J. Risk factors and prognosis for COVID-19-induced acute kidney injury: a meta-analysis. *BMJ Open*. 2020; 10(11)[DOI](#)
10. Liu Y, Zhang Z, Pan X, Xing G, Zhang Y, Liu Z, Tu S. The chronic kidney disease and acute kidney injury involvement in COVID-19 pandemic: A systematic review and meta-analysis. *PLOS ONE*. 2021; 16(1)[DOI](#)
11. Gerardine S., Jaimes E. A., Derkach A., Sathick I. J., Gutgarts V., Latcha S., Glezerman I.. AKI in COVID-19 patients and history of cancer: Role of d-dimer as a potential risk factor. *Journal of the American Society of Nephrology*. 2021.