

# Outcomes of Patients Undergoing Renal Replacement Therapy in ICU in a Tertiary Level Teaching Hospital in Nepal: A Registry Based Retrospective Study.

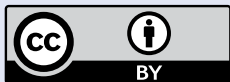
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## ABSTRACT

**Background and aims:** Requirement of renal replacement therapy (RRT) is associated with adverse clinical outcomes in intensive care unit (ICU). However, most of the studies have not included data from low- and middle-income countries (LMICs). This study aims to compare the characteristic and outcomes of patients undergoing RRT with those not requiring RRT (NRRT) in ICU.

**Methods:** This is a registry based retrospective cohort study of patients requiring RRT in a tertiary level university hospital in Nepal. We compared patients requiring RRT with those not requiring RRT for outcomes including ICU mortality, Length of stay in ICU (LOS-ICU) and duration of mechanical ventilation (MV). Odds ratio (OR) was calculated for between group comparison.

**Results:** Of the 3,733 patients admitted during the period of 3 years (January 1, 2020 to December 31, 2022), 516 (13.82%) underwent RRT. When compared with NRRT group, acute physiology and chronic health evaluation (APACHE) II scores, requirement of MV and non-invasive ventilation (NIV) were higher in RRT group. Also, RRT group had higher ICU mortality (OR 3.00, 95% CI 2.42-3.70,  $p < 0.05$ ), more prolonged LOS-ICU and a longer duration of MV (both with median of 5 days compared to 3 days;  $p < 0.05$ ). Directives for treatment limitations were more likely in the RRT group (OR 1.55, 95% CI 1.21-1.99,  $p < 0.05$ ) when compared with NRRT group.

**Conclusion:** Patients who require RRT in ICU have poor outcomes in terms of duration of MV, LOS-ICU and ICU mortality.

**Key words:** Critically ill patients; Intensive Care Unit; low- and middle-income countries; renal replacement therapy.

## INTRODUCTION

Acute kidney injury (AKI) and renal replacement therapy (RRT) are frequent occurrences in any intensive care unit (ICU). Depending on the definition used, incidence of AKI can be as high as 57%.<sup>1</sup> Its cause and grade have been found to vary among different ICUs and regions of the world with many patients requiring renal replacement therapy (RRT).<sup>2-4</sup> For example in Tanzania, a retrospective single centered study found that among the 233 patients included from 2009-2012, renal dysfunction was prevalent in 57.9%. The mortality rate was found to be very high (94.1%) among these patients. The risk factors found to be significantly associated included sepsis and septic shock, mechanical ventilation and need for vasopressors.<sup>3</sup> This increase in mortality associated is extremely high as compared to other studies.<sup>5,6</sup> A prospective database analysis done by Jiang et al in 2021 which included more than 1,000 patients from seven ICUs in China reported the incidence of new onset renal dysfunction to be 30%. This study had found development and non-resolution of AKI to be the independent risk factors for 28-day mortality.<sup>7</sup>

Multiple studies have indicated requirement of RRT to be adversely associated with outcomes including mortality.<sup>3,5,8,9</sup> However, the risk factors and degree of the effect on the outcomes varies in different areas among different population. In addition, there is limited data from low and middle income countries (LMICs).<sup>4,10-12</sup>

This study aims to determine the outcomes in patients requiring RRT and admitted to the ICUs of a tertiary center of a lower middle income country (LMIC). We conducted this study to compare important clinical outcomes in terms of mortality, length of stay in ICU (LOS-ICU) and need for mechanical ventilation (MV) between two cohorts of patients requiring new RRTs in ICU to the ones not requiring them.

## METHODS

Tribhuvan University Teaching Hospital (TUTH) is a tertiary level public university hospital situated in Kathmandu, the capital of Nepal. This is one of the largest medical centers of the country and receives referrals from all the nearby and remote areas of the country. The department of critical care medicine runs doctorate level academic training program in critical care medicine. The department has 4 mixed medical surgical ICUs (including a transplant ICU) and a high dependency unit including a total of 35 level III beds and 5 level II beds which are run in a closed ICU model. Cardiology, cardiac, thoracic and vascular surgical patients requiring ICU services are catered in a separate facility within the university premises, the data of which was not included in this study.

The study was registered in [clinicaltrials.gov](https://clinicaltrials.gov) (NCT06897254). After ethical clearance from the Institutional Review Committee (IRC) [Ref: 518(6-11)E2- 079/080], de-identified data of patients admitted in the ICUs of the Department of Critical Care Medicine, TUTH, Kathmandu, Nepal was retrieved from ICU registry between January 1, 2020 and

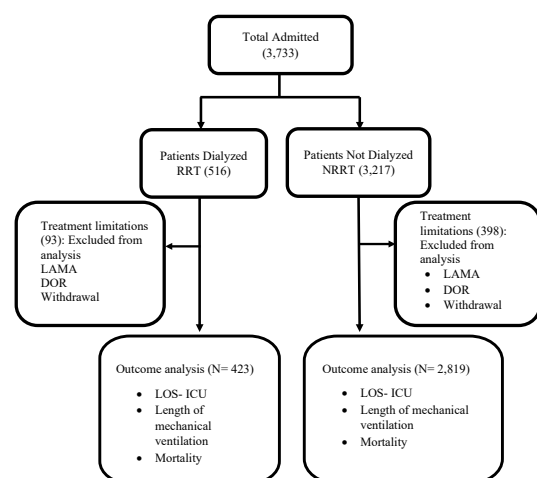
December 31, 2022. The registry is maintained by Nepal Intensive Care Research Foundation (NICRF) which collects data prospectively from TUTH and 19 other centers from Nepal at the time of writing this research.<sup>13</sup> All data were retrieved in Microsoft Excel. The study was conducted in accordance with the STROBE guidelines.

### Statistical analysis

Comparisons between the groups were done using Chi-square test or Fisher's exact test for categorical variables. A two-sample t-test or Mann Whitney U test was used to compare numeric variables. Outcomes were described in terms of ICU mortality, LOS-ICU and duration of mechanical ventilation (MV). We excluded patients whose outcomes were not known (patients with treatment withdrawal, left against medical advice (LAMA) or those discharge on request (DOR)). Odds ratio and corresponding 95% confidence interval was calculated to compare ICU mortality and treatment limitations between the groups. Level of statistical significance was set at a p value of <0.05 for all comparisons. All statistical analyses were done using Statistical Package for Social Sciences (SPSS, version 22.0).

## RESULTS

A total 3,733 patients were admitted during the period of 3 years (Figure 1). Of these, 516 (13.82%) underwent RRT. The baseline demographics with comparison between RRT and NRRT groups are presented in Table 1. All of these baseline characteristics were statistically significant. Of note, the median APACHE II score was 17 (IQR 12-24) in the RRT group compared to 12 (IQR 7-18) in the NRRT group ( $p < 0.05$ ). Similarly, requirement of respiratory support in the form of invasive intermittent positive pressure ventilation (IPPV) was higher in RRT group (42.0% vs 35.0%) and so was the requirement of non-invasive ventilation (NIV) (20.3% vs 15.0%) as compared to NRRT group. Higher proportion of patients in the NRRT group had no requirement or requirement of low flow oxygen, 44.4% vs 35.3%.



**Figure 1.** Flowchart showing the patient data management.

RRT: Renal Replacement Therapy; NRRT: No Renal Replacement Therapy; LOS-ICU: Length Of Stay-Intensive Care Unit; LAMA: Left Against Medical Advice; DOR: Discharge On Request.

**Table 1.** Baseline characteristics (n= 3,733)

Parameter	RRT group (n=516)	NRRT group (n= 3,217)
Median Age in years (IQR)	48 (31-62)	52 (36-65)
Sex (%) Female (Male)	37 (63)	44 (56)
Diagnosis- Number (%) • Operative • Non-operative	52 (10.1) 464 (89.9)	1085 (33.7) 2132 (66.3)
Median APACHE II on admission (IQR)	17 (12-24)	12 (7-18)
Ventilation support during ICU stay (%) • IPPV • NIV • HFNC • Tracheostomy • No support or low flow O <sub>2</sub> therapy	217 (42.1%) 105 (20.3%) 8 (1.6%) 4 (0.8%) 182 (35.3%)	1145 (35.6%) 481 (15.0%) 123 (3.8%) 40 (1.2%) 1428 (44.4%)
Inotrope requirement on admission (%)	134 (25.9%)	627 (19.5%)

APACHE II score: Acute Physiology And Chronic Health Evaluation II score; ICU: Intensive Care Unit; HFNC: High Flow Nasal Cannula; IPPV: Intermittent Positive Pressure Ventilation; IQR: Inter-Quartile Range; NIV: Non-Invasive Ventilation.

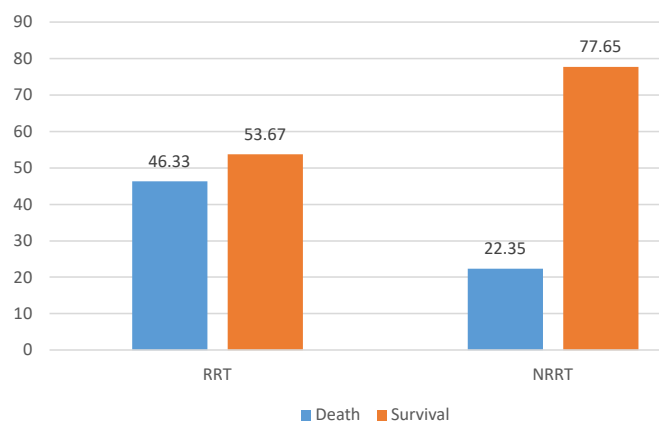
**Table 2.** Mortality and treatment limitations

Group	RRT (%)	NRRT (%)	Total (%)	OR (95% CI)	p value
<b>Mortality*</b>					
Death	196 (46.33)	630 (22.35)	826 (25.48)	3.00 (2.42- 3.70)	<0.05
Survival	227 (53.67)	2189 (77.65)	2416 (74.52)		
<b>Treatment limitation orders (LAMA, DOR and withdrawal of treatment)</b>					
Treatment limited	93 (18.02)	398 (12.37)	491 (15.14)	1.55 (1.21-1.99)	<0.05
Full treatment	423 (81.98)	2819 (87.63)	3242 (84.86)		

\*Note: Excludes patients with LAMA , DOR, or withdrawal of treatment. Odds ratio are unadjusted.

All the baseline characteristics were significantly different between the two groups with p-value of <0.05.

Higher proportion of patients in the RRT group had ICU mortality (46.3%) compared to those not requiring RRT (22.3%) (Figure 2). Patients requiring RRT were at 3 times higher odds of dying as compared to NRRT group (OR 3.00, 95% CI 2.42-3.70, p<0.05) (Table 2).



**Figure 2.** Bar graph of mortality in RRT and NRRT groups (the numbers are in %)

RRT: Renal Replacement Therapy; NRRT: No Renal Replacement Therapy

The median length of MV was longer for patients in RRT group by 2 days. It was found to be 5 days in patients who received RRT (IQR 2-9) vs 3 days in patients who didn't receive RRT (IQR 1-7), which was statistically significant (p<0.05) (Table 3). Similarly, the median duration of ICU stay was also higher in those who underwent RRT as compared to those not receiving RRT; (5 days, IQR 2-9 compared to 3 days IQR 2-7). This too was statistically significant with a p value of <0.05 (Table 2). Proportion of patients having treatment limitation orders (LAMA, DOR, withdrawal of active treatment) were also calculated. It was found that the rates of having orders

for limitation of medical treatment in the ICU (Table 2) was higher in patients who underwent RRT as compared to those who did not receive RRT (18.0% vs 12.3%, OR 1.55, 95% CI 1.21-1.99,  $p < 0.05$ ).

**Table 3.** Duration of mechanical ventilation and length of ICU stay

Group	RRT	NRRT	P value
Median length of MV in days (IQR)	5 (2-9)	3 (1-7)	<0.05
Median length of ICU stay (IQR)	5 (2-9)	3 (2-7)	<0.05

## DISCUSSION

This registry-based study includes data of more than three thousand patients. This is probably the largest study from the country to date in terms of the number of participants enrolled. The mortality rate of the ICU in this study was 25.48% (826 out of 3,242). The odds of mortality among patients requiring RRT was 3 times higher than those not requiring RRT. The higher odds of mortality can be partly explained by the higher median APACHE II scores in the patients requiring RRT. Other studies too have found such results. The factors found to be associated with development of AKI in critically ill patients were coronary artery disease, hypertension, chronic liver disease, use of nephrotoxic drugs, sepsis, sequential organ failure score (SOFA), APACHE II scores and use of vasopressors. Furthermore, development and nonresolution of AKI within 48 hours was found to be an independent risk factor for 28-day mortality.<sup>7</sup> The results of our study show that patients requiring RRT were sicker in terms of requirement of MV and inotropic support. These factors may be one reason for higher mortality rates. However, we did not explore the risk factors for development of AKI in our study.

Interestingly, it has to be noted that APACHE II scores undermine the actual mortality rates in our study. The expected mortality from APACHE II scores would be around 25% for a score of 17 in RRT group which is far lower than the observed rate of 46%. Some papers have found APACHE II to accurately represent the mortality rates.<sup>14,15</sup> Other papers however, have found it to highly underestimate the observed mortality rates.<sup>16-18</sup> Presence of these mixed evidences can be used to conclude that various other factors may be at play which are not captured adequately by these scoring systems. These factors may be uniquely inherent to patients of renal failure requiring RRT. Furthermore, mortality is not adequately predicted even in patients not requiring RRT. This may lead us to think that patient from LMICs may have factors different than those of higher income countries from which these scoring systems were derived.<sup>2,3</sup> Other scoring systems may have to be explored in this regard or may be these scoring

systems have to be specifically re-calibrated for the patients of LMICs.

Patients requiring RRT were found to have higher need of other organ system support as well, which included mechanical ventilation, use of NIV, and inotropes. These patients also had longer length of stay as well as longer days of mechanical ventilation. This could be because of the effects of renal failure in other organ systems. Pathways of cross talk between the failing kidneys and other organs have been explored. This cross talk can affect multiple organ systems including heart, lungs, fluid homeostasis, hormonal balance, immunity to name a few.<sup>19</sup> The increase in mechanical ventilation may be due to various reasons like fluid overload, oxidative stress, secondary infections etc.<sup>20,21</sup> Interestingly however, lower proportion of patients undergoing RRT has tracheostomy and use of HFNC as compared to NRRT group. Lower tracheostomy rates could be explained by higher treatment limitation orders being placed in the RRT group since tracheostomy in a mixed medical surgical ICU is often performed in patients who have prolonged mechanical ventilation.<sup>22</sup> The reason of lower use of HFNC in RRT group however is not very obvious. This could just be because of chance. The requirement of vasopressors may similarly be secondary to the effects of AKI and RRT on the cardiovascular system. Evidences have been found that link cardiac injury biomarkers with AKI which are associated with worsened outcomes.<sup>23,24</sup> In addition, hormonal alterations may also be present in patients with AKI. This may be one of the causes for increased vasopressor requirement in these patients.

Our study had excluded 491 patients from the outcome analysis in whom the full treatment was limited due to DOR, LAMA and withdrawal. This represents 15.14% of the total patients admitted during the time of the study. This is quite a large proportion and has been a consistent finding in studies in this region.<sup>25</sup> This could be because of the poor coverage of health insurance and the resultant large out of pocket expenses that the family has to bear for ICU admission and treatment.<sup>26,27</sup> Further since this represents a significant proportion of the sample size, this may have included bias to the study since we did not explore the reasons for treatment limitations.

This study includes a large dataset from a prospectively collected online registry system. Data collected in this registry has been found to be of a high quality and comparable to those from high income countries.<sup>13</sup> This ensures that the findings obtained from this dataset are valid. Another strength of this study is that the site of the study being a referral tertiary university hospital, receives patients from all over the country. This makes the data collected to be representative of a broader patient population despite being obtained from a single center. Furthermore, the large cohort of patient makes the findings more generalizable and representative of the status of LMICs from which significant data are often missing.

However, this research has several limitations. First, the data is from a single center, limiting generalizability of the findings. A multicenter study in future will be helpful. Secondly, though the registry data is prospectively collected, this was a retrospective study. This would limit the variables collected and analyzed. The registry data is primarily intended for benchmarking and quality improvement projects. As the study is observational in nature, a causal relation cannot be established.

## CONCLUSION

Patients who require RRT in ICU have poor outcomes in terms of duration of mechanical ventilation, ICU length of stay and ICU mortality. They also have higher odds of getting treatment limitations.

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## DISCLOSURE

The abstract of this study was presented in the Indian Society of Critical Care Medicine Conference, Kochi 2025, as a poster and is published as an abstract in Indian Journal of Critical Care Medicine. (Volume 29, (S1):S81-S82. DOI:10.5005/jaypee-journals-10071-24933.56). The authors declare some use of AI to improve on the language and flow of the content. The author reviewed, revised and approved the final content, verified the intellectual accuracy of the manuscript, and takes full responsibility for all statements, interpretations, references and conclusions.

## CONFLICT OF INTEREST

None

## FUNDING

None

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