RENAL REPLACEMENT THERAPY IN INTENSIVE CARE UNIT AT A TERTIARY CARE CENTER IN NEPAL

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ABSTRACT

Acute kidney injury is a major complication in intensive care unit patients. It is associated with increased in-hospital mortality and length of stay. The provision of renal replacement therapy in intensive care is not widely available in resource poor countries like Nepal. The study aims to look into clinical profile and outcome of patients who received renal replacement therapy in intensive care unit. It was an observational study done from 1st October 2016 till 30th September 2017. Patient's demographic data, indications, biochemical tests, outcomes, modality of renal replacement therapy were recorded. Statistical package for the social sciences version 17 was used for statistical analysis. There were total of 649 admissions in intensive care, among which 148 had kidney related complications. Of 148 patients, 69 (47%) received renal replacement therapy. Mean age, urea and creatinine on admission were 50.17 ± 18.42 years, 174.54 ± 63.46 mg/dl and 8.05 ± 3.49 mg/dl respectively. They underwent 4.32 ± 3.09 sessions and 14.94 ± 10.88 hours of renal replacement therapy. Total 42 (61%) had septic shock on admission and underwent sustained low efficiency dialysis as the modality of renal replacement therapy. In-hospital mortality was 19 (28%). Presence of septic shock on admission and mean number of ionotropes required 2.05 ± 1.12 was statistically significant for in-hospital mortality (p=0.01). About half of the patients were on mechanical ventilation which was statistically significant for in-hospital mortality (p<0.001). Sustained low efficiency dialysis can be done in patients on ionotropes and patients can be switched over to intermittent hemodialysis.

KEYWORDS

Intensive care unit, Nepal, renal replacement therapy; sustained low efficiency dialysis

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INTRODUCTION

Acute Kidney Injury (AKI) has a significant implication in hospital related morbidity and mortality including prolonged hospital stay and mechanical ventilation.[1] The burden of Chronic kidney disease (CKD) is also escalating and so is end stage renal disease (ESRD).[2] Patients with CKD have high rates of AKI and vice versa.[3] Thus, AKI and CKD are two interconnected renal syndromes.[4] Both these group of patients may land up in intensive care unit (ICU) due to sepsis, pulmonary edema, oliguria, multi organ dysfunction syndrome and may require renal replacement therapy (RRT) which is challenging in them. There are different modalities of RRT available for patients in ICU viz. intermittent peritoneal dialysis (IPD), hemodialysis (HD), hybrid therapy, continuous renal replacement therapy (CRRT).[5] IPD is less preferred in adults due to its procedural challenge whereas most patients cannot tolerate HD. CRRT has issues with cost and/or availability. A hybrid therapy called sustained low efficiency dialysis (SLED) can be performed in resource poor setting. Nephrology services were started in Nepal about 30 years ago with the first Nephrology outpatient department in 1984, first HD service in 1988 and first Nephrology unit in 1990 whereas the ICU services were started before Nephrology services in 1973.[6] There has been significant technological advances in the delivery of RRT, particularly to the critically ill patient population. Despite these advances, critically ill patients continue to carry a poor prognosis.[7] In a article published by Acharya[8] on status of ICU services in Nepal, found that RRT was available in the form of HD in only one ICU in Nepal. However, though there were risks involved with transferring patients, HD was done outside ICUs in 14 other hospitals within Kathmandu. Peritoneal dialysis was still the most common form of RRT therapy in ICUs in Kathmandu. There is no update to this data. Hence, this novel beginning of ICU dialysis in the form of SLED was started since January 2012 at Nepal Medical College Teaching Hospital (NMCTH). This study was designed to look into clinical profile, biochemical profile and outcomes of the patients during hospital stay receiving RRT in general ICU at NMCTH.

MATERIALS AND METHODS

We have followed strengthening the reporting of observational studies in epidemiology (STROBE) guidelines for reporting this hospital based observational study conducted at NMCTH from 1st October 2016 till 30th September 2017. Ethical approval was taken from institutional review committee (NMC-IRC). All the consecutive patients undergoing RRT (SLED or HD) were enrolled in the study after taking informed consent from the patient/patient's relatives. The primary outcome for the study was all cause in-hospital mortality. The data included demographic of the patients (such as age, sex, address, date of admission), clinical information (relevant brief history, physical examination), biochemical laboratory parameters (serum urea and creatinine), modality of RRT and the outcome of the course. Patients were classified as AKI or AKI on CKD or CKD. The cases were defined based on the definition given by kidney disease improving global outcomes (KDIGO) for AKI and CKD.[9,10] For statistical analysis SPSS software version 17 was used. Descriptive data and outcomes identified were analyzed using the $\chi 2$ test and independent t test was applied for comparison between mortality

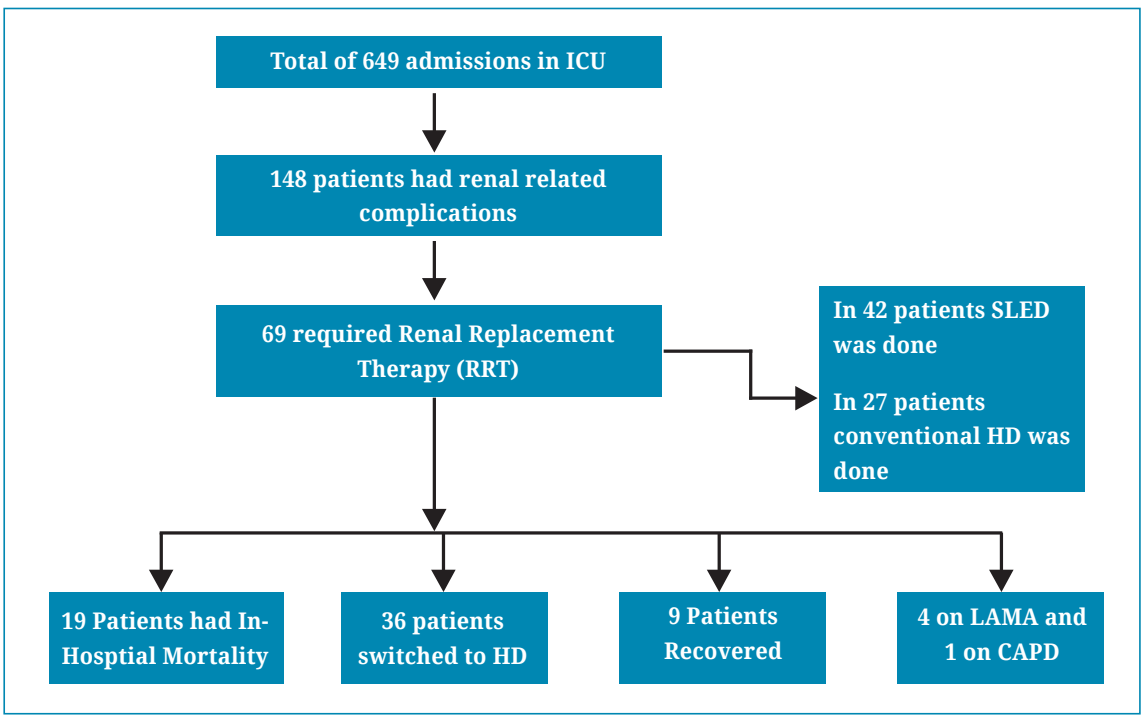

Fig. 1: Flow diagram of study population

and no mortality groups. The data was presented as percentage or mean ± standard deviation (SD) or median with inter quartile range (IQR). The confidence interval was 95% and p<0.05 was used for statistical significance.

RESULTS

There were 69 patients who underwent RRT in general ICU at NMCTH (Fig. 1) with a male: female ratio of 1:1.09. The baseline characteristic of study population is shown in Table-1. Diabetes mellitus and hypertension were present in 32 (47.0%) and 42 (61.0%) patients, respectively.

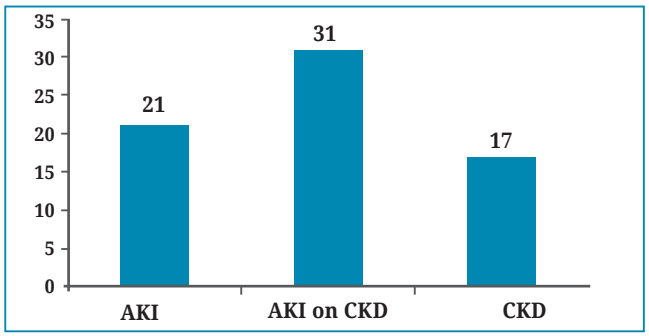

Fig. 2: Number of patients with different diagnosis (n=69)

Total number of patients with AKI and AKI on CKD was 52 (75.4%) and among them 49/52 (94.2%) had sepsis as a cause of AKI as shown in Fig. 2. The most common cause of sepsis was pneumonia followed by urosepsis as shown in Fig. 3. The most common pre-existing renal disease in patients requiring RRT was Diabetes (Fig. 4). The most common indication for RRT was refractory metabolic acidosis with oliguria (n=38, 55%) followed by pulmonary edema (n=15, 28%). SLED was done in 42 (61%) of total RRT patients among which 31 (74%) were on two or more ionotropes. Among the patients on SLED, 19/42 (45%) had in-hospital mortality. Among these 19 patients, 10 (53%) had AKI and nine (47%) had AKI on CKD. Septic shock was present in 42 (61%). A total of 28 (40%) were on HD prior to admission and 32 (46%) were on mechanical ventilation. The overall in-hospital mortality was seen in 19 (28%), 36 (52%) were switched to HD and 9 (13%) recovered. Septic shock on admission and need for mechanical ventilation was statistically significant for in-hospital mortality (p value <0.001). Bivariate analysis done among mortality and with no mortality is shown in Table-2 and -3.

Table-1: Baseline characteristics of study population (n=69)

Characteristics	Minimum	Maximum	Mean ± SD	Median (IQR)
Age in years	15	89	50.17 ± 18.42	52 (34-63)
Duration of hospital stay in days	1	64	12.86 ± 12.06	8 (5-16)
Serum urea (mg/dl)	53	308	174.54 ± 63.46	175 (123-196)
Serum creatinine (mg/dl)	3.1	18.30	8.05 ± 3.49	7.4 (5.4-9.8)
No. of sessions of RRT	1	16	4.32 ± 3.09	3 (2-5)
Duration of RRT in hours	2	52	14.94 ± 10.88	12 (8-18)
No. of ionotropes	0	4	1.23 ± 1.13	1 (0-2)

Table-2: Comparison of mean parameters with in-hospital mortality (n=69)

Characteristics	Mean ± SD in patients with mortality (n=19)	Mean ± SD in patients with no mortality (n=50)	P value
Age	52.84 ± 18.59	49.16 ± 18.44	0.46
Serum creatinine (mg/dl) on admission	6.90 ± 3.05	8.49 ± 3.58	0.09
Serum urea (mg/dl) on admission	183.00 ± 58.60	171.32 ± 65.48	0.49
No. of ionotropes on admission	2.05 ± 1.12	0.9 ± 0.99	<0.01
No. of sessions of RRT on admission	3.11 ± 1.85	4.78 ± 3.35	0.04
Duration of RRT in hours	11.16 ± 6.20	16.38 ± 11.94	0.07

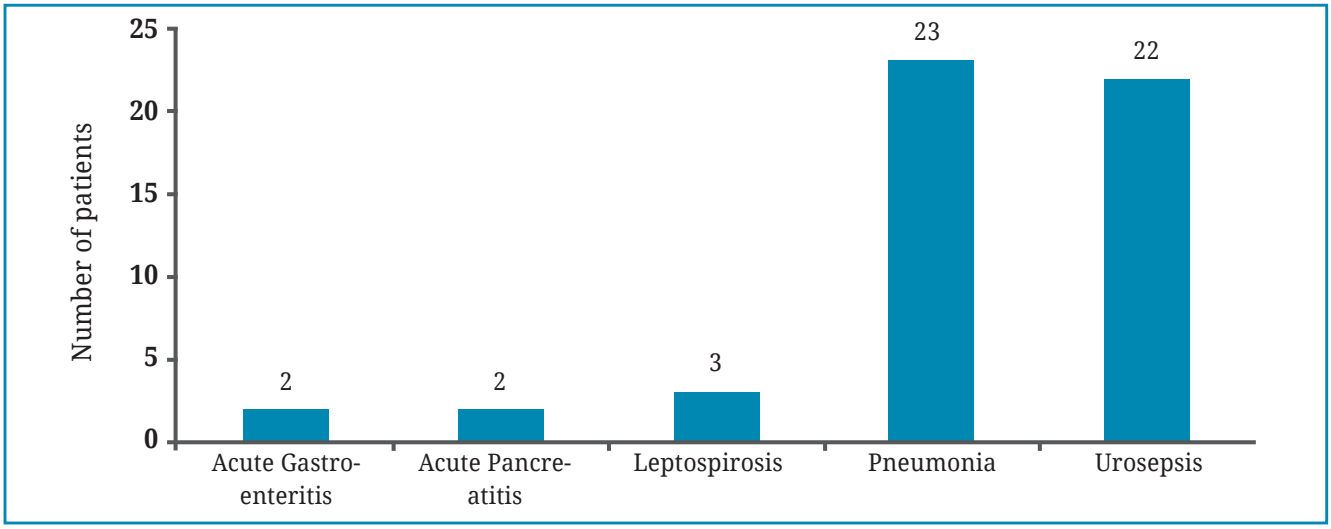

Fig. 3: Number of patients with sepsis and their etiologies (n=52)

Table-3: Comparison of risk factors with in-hospital mortality (n=69)

Characteristics	Categories	No Mortality	In-hospital mortality	P value
Diabetes mellitus	No	25	12	0.24
	Yes	25	7	
Hypertension	No	18	9	0.27
	Yes	32	10	
Septic shock on admission	No	24	3	0.01
	Yes	26	16	
On hemodialysis before admission	No	28	13	0.25
	Yes	22	6	
On mechanical ventilation	No	33	4	<0.01
	Yes	17	15	

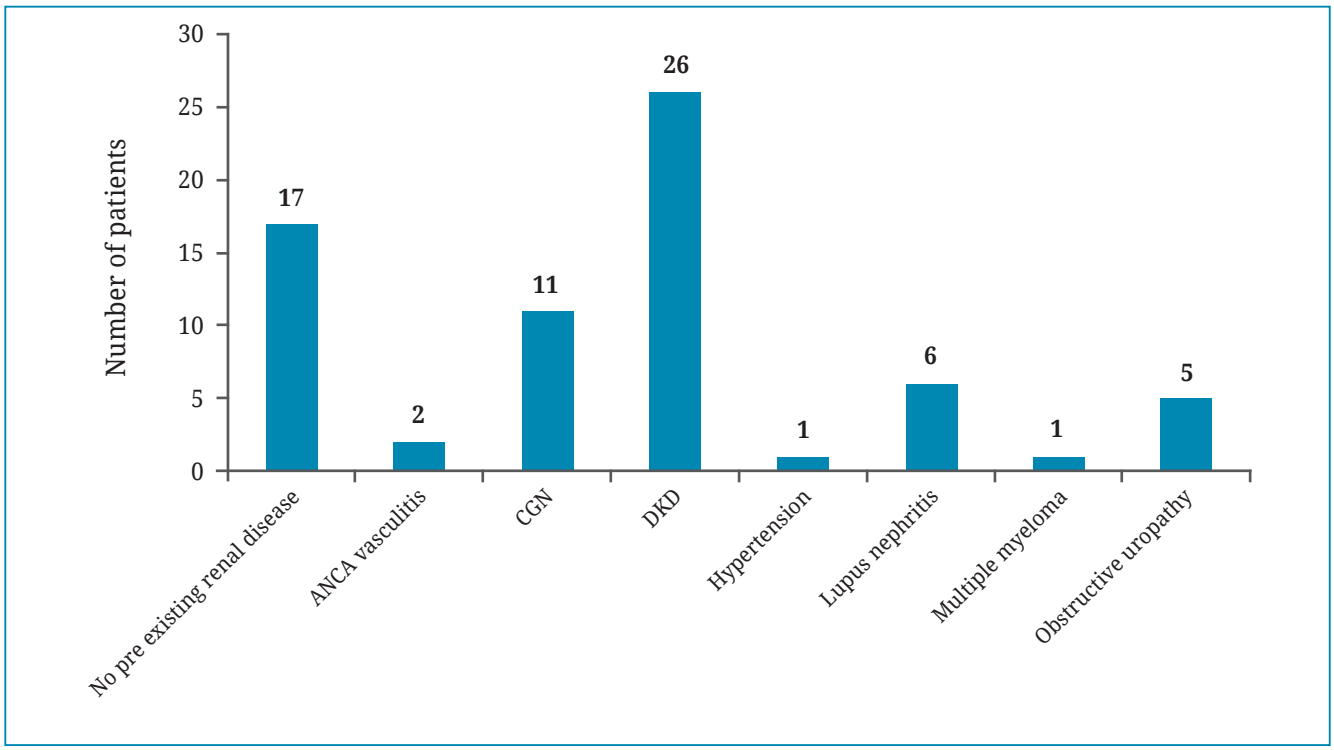

Fig. 4: Pre-existing renal disease (n=69)

DISCUSSION

The present study is our experience with SLED at NMCTH. The prevalence of AKI, AKI on CKD ranges from 20% to 50% in ICU depending on the definition used. Among this around 30%-50% may require some form of RRT.[11] The current study used the KDIGO definition for AKI and observed that 75% of patients requiring RRT in ICU were due to AKI alone or AKI on CKD. In 2008 study done by Chhetri *et al*,[12] which was designed to look into the prevalence of AKI at the same center found that around 20% of patients with AKI required dialysis in ICU whereas the current study was designed to look into the RRT in ICU and not the prevalence of AKI.Sepsis was the leading cause of AKI in our study. In a systematic review by Case *et al*,[13] the major cause for AKI requiring RRT in medical ICU was sepsis. In the review, authors defined AKI by AKIN and RIFLE classification, however they did not define sepsis and classified the etiology of sepsis.13 In the current study, pneumonia followed by urosepsis contributed to more than two third of the cases of sepsis. In our study SLED was the modality of RRT in patients on ionotropes which was in difference with study done by Overberger *et al*, where CRRT were the most common used modality of RRT, with SLED and other "hybrid" treatments used in fewer than 10% of patients.[14] This difference of practice may be due to unavailability of CRRT at our center and also CRRT is not a feasible option in resource poor countries like Nepal and moreover SLED could be performed with lower cost, with no anti coagulation and nearly equal solute clearance.[15] The mean duration of SLED was 14.94 ± 10.88 hours in our study which was similar to a Canadian cohort study which compared SLED with CRRT, where the mean SLED and CRRT durations were 14.9 ± 4.4 and 15.9 ± 4.2 hours/session respectively.[16] In a major review on RRT in ICU by Ronco *et al*, the role of RRT was established not only for renal indications but also for other organ-supportive strategies.[17] In present study, most common indication of RRT in ICU was metabolic acidosis with oliguria which was comparable with a similarly designed study done by Mishra *et al*. Here the authors defined AKI by the KDIGO classification and used 6 hours session of SLED which was similar to our study. In comparing the serum creatinine among patients who had in hospital mortality versus having no mortality there was no significant difference in our study (p=0.09) whereas in the study conducted by Mishra *et al*, the serum creatinine was significantly higher in the group of non survivors (p<0.01). This observed difference between the two studies may be due to the mean difference in serum creatinine values in study population and difference in dialysis machinery and protocol.[18] In a systematic review by Nash *et al*,[19] studies on critically ill adults receiving CRRT, HD or SLED to treat AKI were taken. They did not find any definitive advantage for any RRT modality on short-term patient or kidney survival. SLED was suggested as an alternative treatment but still the evidence requires more studies to support this statement. The current study will add on to existing literature in support of SLED.

In the present study, mortality was statistically associated with increasing number of ionotropes (mean 2.05±1.12) and mechanical ventilation implying the severity of disease which was similar to study by Shin *et al*.[20] Overall in hospital mortality in patients who received RRT in ICU was less (28%) as compared to other studies where it ranged from 46% to 62%.[21,22] This difference is due to the difference of inclusion criteria in other studies where they considered only patients who underwent SLED or CRRT. However, our study included all patients who underwent RRT in ICU but the sub group analysis showed statistical significance in mortality when patients had septic shock and/or mechanical ventilation.

There are different names for SLED in the current literature. It is also known as extended daily dialysis (EDD) and prolonged intermittent renal replacement therapy (PIRRT). In SLED, dialysis therapy is extended to 8 to 12 hours with an idea of achieving the hemodynamic benefits of continuous dialysis. In the present study we extended the dialysis therapy upto 6 hours per session which was in accordance with study by Kitchlu *et al*. However, in their study, blood flow rate and dialysate flow rate was 200ml/min and 350ml/min respectively whereas in our study it was 150ml/min and 300ml/min respectively. Further studies are required to answer regarding the optimum duration of therapy in SLED. Currently, SLED is gaining over CRRT due to absence of mortality benefit and higher costs associated with the application of CRRT. Further practical advantages of SLED included the delivery of therapy without anticoagulation (when indicated).[16,23]

The outcome data of our study showed that nearly half of study population could be switched to conventional HD. In a study by Kovacs *et al*, where they compared the outcome data between SLED and CRRT found no significant differences in terms of renal recovery, days to renal recovery, number of treatments required for each dialysis modality and hemodynamic instability.[24]

Among all the uncertainties regarding the RRT in ICU setting, a recent review published by Bellomo *et al*. in December 2018 also led to the conclusion that RRT in ICU setting can be provided continuously or intermittently (CRRT or SLED). To date, no modality of RRT has shown superiority over others in terms of mortality and renal recovery. However, multiple observational studies from Canada, France, and Sweden (also disussed above) have identified a link between initial or exclusive use of IHD and decreased likelihood of renal recovery in short term compared with initial or exclusive use of CRRT. Additional studies are required to affirm these observations.[25] This study has opened up the field of critical care nephrology in Nepal.

Thus in conclusion, SLED can be done in critically ill patients on ionotropes as a hybrid therapy in resource poor setting where CRRT is not available and/or affordable. Moreover, SLED can be performed by conventional dialysis machine with simple adjustments in dialysis parameters and along with existing manpower.

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