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Outcome of continuous renal replacement therapy in critically ill children.

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ABSTRACT… Objective: To determine the outcome of critically ill children undergoing CRRT. **Study Design:** Prospective Observational Study. **Setting:** Pediatric Intensive Care Unit at Aga Khan University Hospital. **Period:** Jan 2021 to Dec 2022. **Material & Methods:** The study comprised of collection of data of critically ill children from the age 1-18 years who were subjected to CRRT from Jan 2021 to December 2022. We reported primary diagnosis, demographics, indications, modality, and outcomes of CRRT. Statistical analyses were utilized to relate risk factors correlating with mortality among patients who underwent CRRT. Our main outcome measures were mortality among critically ill pediatric patients who were subjected to CRRT and its associated risk factors. **Results:** 42 patients underwent CRRT from Jan 2021 to December 2022. Mean age was 11.97 ± 4.3 years, with 64% male population. Most common primary diagnosis was infectious etiology (36%) followed by genitourinary system (27%). 83% patients were in failure according to pRIFLE criteria. 81% patients had multiorgan dysfunction (MODS) with renal, cardiovascular, and respiratory dysfunction sequentially being most common. The mean ionotropic score before & after CRRT was 38.57 & 49.71 respectively. Mean ICU duration of admission was 11.6 days. The most common indication for CRRT was fluid overload (85.71%). Median length of CRRT was 62 hours with a mean circuit life of 47.87 hours. Most common CRRT catheter site was the femoral vein (83%) followed by the internal jugular vein (14%). CVVHDF was the most used modality (64%) followed by CVVH (19%). We report an overall mortality of 71.4%, with a positive correlation with use of norepinephrine post CRRT, presence of multiorgan dysfunction, presence of cardiovascular dysfunction, respiratory dysfunction, and low platelet count (<150,000 per microliter) on univariate analysis. Only respiratory dysfunction was statistically significantly associated with mortality on multivariate analysis. **Conclusion:** The gross mortality in patients who underwent CRRT was high (71.4%). Norepinephrine use post-CRRT, multi-organ dysfunction, cardiovascular system, respiratory system dysfunction and low platelet counts were associated with high mortality while association of respiratory dysfunction with mortality was independently statistically significant.

Key words: Acute Kidney Injury (AKI), Acute Renal Failure (ARF), Continuous Renal Replacement Therapy (CRRT), Critically Ill Children, Pediatric Intensive Care Unit (PICU).

INTRODUCTION

Acute kidney injury (AKI) is often a complication of sepsis with multiple organ dysfunction (MODs), hemolytic uremic syndrome (HUS), or other severe diseases.[1] AKI can be defined using pediatric-modified RIFLE (pRIFLE), which categorizes AKI from a spectrum of mild to severe AKI.[1] Over the past many years, the epidemiology of AKI has been changing, specifically in developed countries.[2] The primary etiology of AKI is found to be nephrotoxic medications and sepsis. Other common etiologies of AKI have been found to be congenital cardiac pathologies, and acute renal failure.[3,4] However in less-developed nations, primary kidney pathologies are still the commonest causes of AKI.[2,5] Adults requiring renal replacement therapy for severe AKI have been found to have a 50-80% mortality rate and children have a 35-64% mortality rate.[6-11] Whereas, the mortality rate in patients with severe AKI can be 8-89% depending on etiology and 42% in patient that required CRRT.[5] Critically ill children also have an increased frequency for developing AKI due to treatments for acute disease process; greater than 25% of patients in the pediatric intensive care unit (PICU) develop

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AKI.[1,9] Treatment along the spectrum varies, but in a study it was seen that undergoing renal replacement therapy early in a disease, including AKI, has been shown to improve the prognosis of children with life-threatening illnesses.[2]

There are many discrete modes for renal replacement therapy. However, continuous renal replacement therapy (CRRT) is a well-known and preferred modality for the treatment of hemodynamically unstable critically ill patients who require renal support in critical care settings.[1,12-15] It has superseded peritoneal dialysis as the chief modality of renal replacement.[1, 10,16] CRRT allows for a more controlled regulation of fluid and electrolyte balance, making it ideal for hemodynamically unstable children.[1,11] During early stages of development and introduction of CRRT, blood circulated through the extracorporeal circuit and filter and was mainly driven via the patient's circulatory pressure through an arterial-venous circuit.[1,16] However, the invent of pump operated CRRT devices with small extravascular volumes has resulted in more common use of veno-venous modes of CRRT.[3,12,13] CRRT is conducted under multiple different modalities. These include, continuous veno-venous hemofiltration (CVVH), continuous veno-venous hemodialysis (CVVHD), and continuous veno-venous hemodiafiltration (CVVHDF).[17]
Fluid overload and electrolyte abnormalities constituted 90% of indications for use of CRRT with CVVHD being the most frequently-used modality followed by CVVHDF, and CVVH.[12,13,17]
As many of the patients receive aggressive fluid resuscitation, therefore fluid overload has been commonly found in PICU, which has led to significant morbidity, including organ dysfunction.[18]
Many case reports have delineated the employment of CRRT in pediatric patients.[12,19] However, the literature on the usage of CRRT, its safety, and its impact on final outcome of the patient in critical care settings is still scarce, with no study from Pakistan thus far. Therefore, we aim to find out the outcomes among these critically ill patients who had undergone CRRT.

MATERIAL & METHODS

Study Design and Setting

This was a prospective observational study conducted at the Aga Khan University Hospital (AKUH), a multidisciplinary tertiary care university-affiliated center. Our ICU is a state of the art 12 bedded PICU, of which 4 beds are designated for post-cardiac surgery patients, whereas the remaining 8 beds are designated for all other critical medical and surgical patients. CRRT was performed as per the local hospital protocol. The machine we used was a Fresenius CRRT machine, Multifiltrate Ci-Ca. Only systemic anticoagulation in the form of heparin was used. The modality of CRRT as well as filtration rate was as per discretion of attending pediatric intensivist.

Study Duration

This study was conducted from January 2021 to December 2022 over a period of 02 years in the PICU AKUH after approval from ethical committee (20202-7235-21617).

Sample Size

In total, 51 critically ill children underwent CRRT from Jan 2021 to December 2022 and were registered into this study.

Inclusion Criteria

All critically ill children with age ranging from 1 year till 18 years who underwent CRRT were included in this study.

Exclusion Criteria

Out of 51 patients, 09 patients were ruled out due to incomplete data. Children who underwent other form of dialysis like peritoneal dialysis or intermittent hemodialysis were also exempted from the study.

Data Collection

Data collected included demographic information, including weight, height, age, gender, and baseline diagnosis. Data also incorporated CRRT indications, duration of admission in PICU in total, duration of CRRT in hours, number of circuits of CRRT, use of heparin in the circuit and use of vasoactive inotropes during CRRT. Clinical data collected included presence of organ failures, glomerular filtration rate (GFR) at the start of CRRT, urine output in mL/kg/h at the start of CRRT, platelet count and international normalized ratio (INR), CRRT site, CRRT modality and final outcome in terms of survival and mortality. We gathered the data on a structured proforma and then moved that to STATA for statistical analysis. We ensured the privacy of data by keeping the completed proformas in a locker and later in a password-protected file in the computer desktop system of the hospital.

Data Analysis

All the statistical analysis was conducted using statistical software STATA version 17.0. Mean and standard deviation (SD), and median and interquartile range were reported for continuous variables whether normally distributed or not, while frequency with percentages were reported for categorical variables. T-test, and nonparametric test was performed for continuous variables to assess their association with mortality, while chi-square or Fisher's exact test was used for categorical variables to assess their association with as applicable. A p-value less than 0.05 was considered as statistically significant.

RESULTS

The mean age of patients was 11.97 ± 4.3 years. Most of the patients had age greater than 10 years with a male majority; 64% of the sample.

The most common primary diagnosis was infectious etiology (36%), of which septic shock was the most common (82.5%), followed by genitourinary system (27%) with primary kidney disease being the most common (90%) (Table-II). Based on pRIFLE criteria, majority patients were in the Failure criteria (83%) (Table-I).

Based on organ dysfunction either primary or secondary, 81% of the patients had multi-organ dysfunction (MODS), with 81% patients had renal dysfunction, 57% patients had cardiovascular dysfunction, 45% patients had respiratory dysfunction, and 31% patients had central nervous system involvement (Table-I). The mean ionotropic score before CRRT was 38.57, with epinephrine being the most commonly used inotropic agent (88%) followed by norepinephrine (52%) and dopamine (33%), while mean ionotropic score after CRRT was 49.71 (Table-I). The mean admission duration of PICU was 11.6 days, while the admission duration of PICU before the start of CRRT was 4.1 days. Fluid overload was the most common reason for CRRT (85.71%) followed by cytokine storm (80.95%) and acidosis (71.43%) (Table-I). The median GFR value before the start for CRRT was 33.4 ml/min/1.73-meter square (Table-I).

The median duration of CRRT was 62 hours (IQR, 23.0-117.0) with a mean circuit life of 47.87 hours (SD 47.55) (Table-I). First circuit had the highest mean life of 55.99 hours (SD 55.07). 37.84% of circuits lasted for less than 24 hours while 62.16% of circuits lasted for more than 24 hours. Systemic heparin anticoagulation was used in 55% of the first circuits. The commonest CRRT catheter site was the femoral vein (83%) followed by the internal jugular vein (14%). CVVHDF was the most used modality (64%) followed by CVVH (19%) (Table-I).

LOS= length of stay, SD= standard deviation, UOP= urine output, ICU= intensive care unit, INR= international normalized ratio, MOD= multi-organ dysfunction, CVVH= continuous veno-venous hemofiltration, CVVHDF= continuous veno-venous hemodiafilteration, GFR= glomerular filtration rate, ESRD= end stage renal disease.

An overall mortality of 71.4% was reported among patients who were critical and admitted to the PICU requiring CRRT. The univariate analysis showed a positive correlation between use of norepinephrine post CRRT, presence of multi-organ dysfunction, presence of cardiovascular dysfunction, respiratory dysfunction, and low platelet count (<150,000 per microliter) with mortality. Multivariate analysis (using statistically significant variables in univariate analysis) identified presence of respiratory dysfunction to be independently associated with mortality in the critically ill children who had undergone CRRT (Table-III).

Age (Years), (mean ± SD)	(12.0±4.3)
< 1 Years	1 (2.3%)
1-10 Years	12 (28.5%)
>10 Years	29 (69%)
Gender	
Male	27 (64.2%)
Female	15 (35.7%)
Weight (kg), (mean ± SD)	(39.4±20.3)
Height (cms), (mean ± SD)	(141.8±27.3)
ICU LOS, (mean ± SD)	(11.6±11.3)
ICU before CRRT, (mean ± SD)	(4.1±3.9)
Ionotropic score before CRRT	(38.57± 39.47)
Epinephrine, (n=42)	37 (88.09%)
Norepinephrine, (n=42)	22 (52.3%)
Dopamine, (n=42)	14 (33.3%)
Milrinone, (n=42)	5 (11.9%)
Vasopressin, (n=42)	3 (7.1%)
Ionotropic score after CRRT, (mean ± SD)	(49.71+37.79)
Epinephrine, (n=42)	26 (81.25%)
Norepinephrine, (n=42)	22 (68.7%)
Dopamine, (n=42)	11 (34.3%)
Milrinone, (n=42)	2 (6.2%)
Vasopressin, (n=42)	6 (18.7%)
Total length of CRRT (hours) median (IQR)	62.0 (23.0-117.0)
Average circuit life (hours) (mean ± SD)	47.87(±47.55)
<24	17 (40%)
>=24	25 (60%)
Reason for CRRT	
Acidosis	30 (71.43%)
Electrolyte imbalance	8 (19.05%)
Intoxication	2 (4.76%)
Fluid overload	36 (85.71%)
Uremia	23 (54.76%)
Cytokine storm	34 (80.95%)
Metabolic	3 (7.14%)
CRRT catheter site	
Internal jugular	6 (14%)
Femoral	35 (83%)
Femoral, Intrajugular	1 (2%)
Heparin	
Heparin Used	23(55%)
Heparin Not Used	19(45%)
CRRT modality	
CVVHDF	27 (64%)
CVVH	8 (19%)
CVVHDF & CVVH	7 (17%)
RIFLE criteria	
ESRD	5 (12%)
Failure	34 (81%)
Risk	2 (5%)
loss	1 (2%)
UOP (ml/kg/hour), median (IQR)	0.3 (0.0-0.6)
GFR (ml/min/1.73m^2), median (IQR)	33.4 (19.7-46.4)
Organ failure	
No MOD	8 (19%)
MOD	34 (81%)
Central Nervous System	
NO	29 (69%)
Yes	13 (31%)
Cardiovascular System	
NO	18 (43%)
Yes	24 (57%)
Respiratory System	
NO	23 (55%)
Yes	19 (45%)
Gastrointestinal System	
NO	35 (83%)
Yes	7 (17%)
Hepatic System	
NO	35 (83%)
Yes	7 (17%)
Renal	
NO	8 (19%)
Yes	34 (81%)
INR	(2.4±2.6)
<1.3	10 (24%)
>=1.3	32 (76%)
Platelets	(102.1±110.1)
<150	29 (69%)
>=150	13 (31%)

Table-I. Characteristic of patients who underwent continuous renal replacement therapy

Primary Diagnosis (n=42)	n (%)
Central Nervous System (CNS)	**9 (21.4%)**
Status epilepticus	1
Intracranial hypertension	1
Meningoencephalitis	1
Uremic encephalopathy	2
Hepatic encephalopathy	4
Cardiovascular System (CVS)	**3 (7.1%)**
Myocarditis	1
Arrhythmia	1
Cardio-renal syndrome	1
Respiratory System (RESP)	**6 (14.2%)**
Acute respiratory	2
Pneumoniae	4
Abdominal System (ABD)	**10 (23.8%)**
Pancreatitis	2
Hepatic dysfunction or failure	1
Appendectomy	2
Intestinal perforation	1
Acute liver failure	3
Hepatitis A	1
Genito Urinary System (GU)	**30 (71.4%)**
Hemolytic uremic syndrome	2
Acute kidney injury	27
Acute tubular necrosis	1
Endocrine System	**3 (7.1%)**
Diabetic ketoacidosis	3
Haem-oncology System	**3 (7.1%)**
Veno-occlusive disease	1
Tumor lysis syndrome	2
Infectious Etiologies	**40 (95.2%)**
Septic shock	33
Dengue shock	3
Sepsis	4
Autoimmune Etiologies	**1 (2.3%)**
Immune thrombocytopenic purpura	1
Miscellaneous Etiologies	**6 (14.2%)**
Metabolic disorder	1
Trauma	2
COVID multisystem	3
Poisoning	1

Table-II. Primary diagnosis of patients who underwent continuous renal replacement therapy

DISCUSSION

Acute Kidney Injury (AKI) is frequently seen in patients admitted to the critical care with increasing frequency with increase in severity of disease.[11] The etiologies for acute renal failure are changing during recent times with a shift from primary renal diseases towards secondary renal involvement as a part of any systemic disease. CRRT is being widely used nowadays in critical care settings in most developed countries for renal, as well as extra renal causes. It provides a controlled, yet efficient way to filter the blood, correct acid-base balance and electrolyte imbalance, that is more suitable for any unstable critical patient as compared to peritoneal or intermittent dialysis.[1,2] The outcome of the patient depends primarily on the underlying disease process.[3] Other factors that might contribute to the survival chances are the time of presentation, number of organ systems involved as well as time of initiation of CRRT. Despite being used frequently over the last two decades, data from pediatric critical care on CRRT is still limited.[17]

Our case, as well as others, reported male gender predominance; however, in contrast to other studies our cohort had majority of patients over 10 years of age.[11,12,17] The possible explanation for the dominance of the adolescent age group could be due to the comfort level of the treating intensivist in doing CRRT in this age group along with the non-availability of smaller size dialysis catheters throughout the year. We reported a mortality of 71.4% in our data which is higher than that reported in other pediatric data (i.e. 46.3%, 36%, 43% and 50%).[9,11,12,17] A possible explanation for higher mortality rate could a later presentation to the hospital leading to delay in initiating the therapy or delay in the institution of CRRT early on day 1, as the mean PICU length of stay before institution of CRRT was 4.1 days as mentioned in Table-I. This is also supported by the higher percentage of patients in our cohort, though not statistically significant on multivariate analysis, having multi-organ dysfunction syndrome (MODS) (i.e. 81%). MODS is also reported to be higher among non-survivors and the association with mortality is statistically significant (i.e. 38% vs 93%) among survivors' vs non-survivors on univariate analysis. As described in another study, children with septic shock had significantly higher mortality (88.4% vs 18.9%).[9,11,17]

Characteristics	Total	Discharged	Expired	Unadjusted	
	N=42	N=12	N=30	OR (95% CI)	P-Value
Age (Years), (mean ± SD)	(12.0±4.3)	(12.0±3.4)	(12.0±4.6)	0.997(0.851-1.169)	0.98
< 1 Years	1 (2.3%)	0 (0%)	1 (3%)	-	-
1-10 Years	12 (28.5%)	3 (25%)	9 (30%)	1.35(0.293-6.204)	0.39
>10 Years	29 (69%)	9 (75%)	20 (67%)	Ref	-
Gender					
Male	27 (64%)	5 (42%)	22 (73%)	Ref	-
Female	15 (36%)	7 (58%)	8 (27%)	0.259(0.06-1.05)	0.06
Weight (kg), (mean ± SD)	(39.4±20.3)	(33.1±14.8)	(41.9±21.8)	1.024(0.986-1.065)	0.21
Height (cms), (mean ± SD)	(141.8±27.3)	(141.9±20.5)	141.7±29.9)	0.999(0.975-1.024)	0.98
ICU LOS, (mean ± SD)	(11.6±11.3)	(16.9±17.6)	9.4±6.7)	0.943(0.880-1.010)	0.09
ICU before CRRT, (mean ± SD)	(4.1±3.9)	(1.3±0.7)	(5.2±4.1)	2.894(0.882-9.498)	0.08
Ionotropic score before CRRT	(38.57± 39.47)	(39.25±55.13)	(38.29±32.40)	0.99(0.98-1.01)	0.94
Epinephrine, (n=42)	37 (88.09%)	12 (100%)	25 (83%)	-	
Norepinephrine, (n=42)	22 (52.3%)	5 (42%)	17 (57%)	1.830(0.471-7.104)	0.328
Dopamine, (n=42)	14 (33.3%)	5 (42%)	9 (30%)	0.6(0.149-2.404)	0.47
Milrinone, (n=42)	5 (11.9%)	2 (17%)	3 (10%)	0.55(0.080-3.830)	0.551
Vasopressin, (n=42)	3 (7.1%)	0 (0%)	3 (10%)	-	-
Ionotropic score after CRRT, (mean ± SD)	(49.71+37.79)	(32.59±25.86)	(52.88±39.16)	1.01(0.98-1.05)	0.27
Epinephrine, (n=42)	26 (81.25%)	4 (80%)	22 (81%)	1.1(0.100-12.086)	0.938
Norepinephrine, (n=42)	22 (68.7%)	1 (20%)	21 (78%)	14(1.306-150.019)	0.029
Dopamine, (n=42)	11 (34.3%)	3 (60%)	8 (30%)	0.280(0.039-2.014)	0.206
Milrinone, (n=42)	2 (6.2%)	2 (40%)	0 (0%)	-	-
Vasopressin, (n=42)	6 (18.7%)	0 (0%)	6 (22%)	-	-
Total length of CRRT (hours), median (IQR)	62.0 (23.0-117.0)	57.5 (27.0-110.5)	62.0 (17.0-141.0)	1.001(0.991-1.010)	0.82
Average circuit life (hours), (mean ± SD)	(56.0±55.1)	(58.7±66.5)	(54.9±51.1)	0.99(0.98-1.01)	0.84
<24	17 (40%)	5 (42%)	12 (40%)	0.93(0.23-3.63)	0.92
>24	25 (60%)	7 (58%)	18 (60%)	Ref	-
Reason for CRRT					
Acidosis, (n=42)	30 (71.43%)	9 (75%)	21 (70%)	0.77(0.16-3.56)	0.74
Electrolyte imbalance, (n=42)	8 (19.05%)	1 (8%)	7 (23%)	3.34(0.36-30.67)	0.28
Intoxication, (n=42)	2 (4.76%)	2 (17%)	0 (0%)	-	-
Fluid overload, (n=42)	36 (85.71%)	11 (92%)	25 (83%)	0.45(0.04-4.36)	0.49
Uremia, (n=42)	23 (54.76%)	8 (67%)	15 (50%)	0.5(0.12-2.02)	0.33
Cytokine storm, (n=42)	34 (80.95%)	8 (67%)	26 (87%)	3.25(0.65-16.04)	0.14
Metabolic, (n=42)	3 (7.14%)	0 (0%)	3 (10%)	-	-
CRRT catheter site					
Internal jugular	6 (14%)	3 (25%)	3 (10%)	0.296(0.049-1.764)	0.18
Femoral	35 (83%)	8 (67%)	27 (90%)	Ref	-
Femoral, Intrajugular	1 (2%)	1 (8%)	0 (0%)	-	-
Heparin					
Heparin Used	23(55%)	8(67%)	15(50%)	0.5(0.12-2.02)	0.33
Heparin Not Used	19(45%)	4(33%)	15(50%)	Ref	-

CRRT modality					
CVVHDF	27 (64%)	7 (58%)	20 (67%)	Ref	
CVVH	8 (19%)	4 (33%)	4 (13%)	0.35(0.06-1.78)	0.2
CVVHDF & CVVH	7 (17%)	1 (8%)	6 (20%)	2.1(0.21-20.63)	0.52
RIFLE criteria					
ESRD	5 (12%)	2 (17%)	3 (10%)	0.461(0.652-3.266)	0.43
Failure	34 (81%)	8 (67%)	26 (87%)	Ref	-
Risk	2 (5%)	1 (8%)	1 (3%)	0.307(0.017-5.496)	0.42
loss	1 (2%)	1 (8%)	0 (0%)	-	-
UOP (ml/kg/hour), median (IQR)	0.3 (0.0-0.6)	0.2 (0.0-0.7)	0.3 (0.0-0.6)	1.39(0.53-3.66)	0.49
GFR (ml/min/1.73m^2), median (IQR)	33.4 (19.7-46.4)	24.9 (17.2-40.8)	33.4 (24.7-55.0)	1.01(0.98-1.05)	0.23
Organ failure					
No MOD	8 (19%)	5 (42%)	3 (10%)	Ref	-
MOD	34 (81%)	7 (58%)	27 (90%)	6.42(1.22-33.64)	0.02
Central Nervous System					
NO	29 (69%)	8 (67%)	21 (70%)	Ref	-
Yes	13 (31%)	4 (33%)	9 (30%)	0.85(0.20-3.58)	0.83
Cardiovascular System					
NO	18 (43%)	8 (67%)	10 (33%)	Ref	-
Yes	24 (57%)	4 (33%)	20 (67%)	4(0.96-16.55)	0.05
Respiratory System					
NO	23 (55%)	10 (83%)	13 (43%)	Ref	-
Yes	19 (45%)	2 (17%)	17 (57%)	6.53(1.21-35.12)	0.02
Gastrointestinal System					
NO	35 (83%)	11 (92%)	24 (80%)	Ref	-
Yes	7 (17%)	1 (8%)	6 (20%)	2.75(0.29-25.76)	0.37
Hepatic System					
NO	35 (83%)	11 (92%)	24 (80%)	Ref	-
Yes	7 (17%)	1 (8%)	6 (20%)	2.75(0.29-25.76)	0.37
Renal					
NO	8 (19%)	4 (33%)	4 (13%)	Ref	-
Yes	34 (81%)	8 (67%)	26 (87%)	3.25(0.65-16.04)	0.14
INR	(2.4±2.6)	(1.7±0.7)	2.6±3.0)	1.49(0.66-3.37)	0.97
<1.3	10 (24%)	2 (17%)	8 (27%)	1.81(0.32-10.15)	0.49
>=1.3	32 (76%)	10 (83%)	22 (73%)	Ref	-
Platelets	(102.1±110.1)	(142.9±132.0)	(88.0±100.3)	0.99(0.98-1.00)	0.19
<150	29 (69%)	5 (42%)	24 (80%)	Ref	
>=150	13 (31%)	7 (58%)	6 (20%)	0.17(0.04-0.76)	0.02

Table-III. Univariate analysis for increased mortality among patients undergoing continuous renal replacement therapy

LOS= length of stay, SD= standard deviation, UOP= urine output, ICU= intensive care unit, INR= international normalized ratio, MOD= multi-organ dysfunction, CVVH= continuous veno-venous hemofiltration, CVVHDF= continuous veno-venous hemodiafilteration, GFR= glomerular filtration rate, ESRD= end stage renal disease

One explanation could be late initiation of CRRT among non-survivors (i.e. mean 5.2 day of ICU admission) as compared to survivors (i.e. mean 1.3 day of ICU admission), although it was not statistically significant due to decrease in number of patients in each arm. CRRT initiation timing is linked significantly to higher mortality among patients with CRRT initiation after 24 hours of ICU admission.[9] Gerard Cortina and Rosemary McRae reported that survivors were subjected to CRRT earlier than non-survivors, although the difference was statistically insignificant (12.5 vs

25.5hr; p = 0.095).[11]

The most common primary diagnosis among our patients were infectious etiologies (95.2%) with 82.5% patients having septic shock. Our percentage of patients with sepsis is significantly higher as compared to other studies (i.e.16.9%, 19% and 30% of the patients).[9,11,12] This might be supported by the fact that primary infectious etiologies are still among the topmost causes of illness in the developing countries causing significant morbidity and mortality. Almost two-third (78.5%) of our patients had AKI with 83% in renal failure according to pRIFLE criteria. Failure was reported to be higher (55.2%) as in another study.[17] The most common indication for CRRT was fluid overload (85.71%) followed by cytokine storm (80.95%) and acidosis (71.43%), though none of these was statistically significant with mortality. Fluid overload was also reported to be the top indication for CRRT (67.2%) while removal of inflammatory mediators was the main indication in 40.2% and 22%.[9,11,17]

The most common modality of CRRT was CVVHDF (i.e. in 64% of patients), a result similarly in another study (i.e. 82.3%), while in contrast to what was reported by others.[12,16,17] This can possibly be explained by a high number of patients presenting with MODS, in which case it is desirable to remove all sized molecules through CRRT, including small-sized molecules like urea and creatinine and medium to large-sized molecules like interleukin-8 (IL-8), interleukin-10 (IL-10) and TNF-alpha (TNF-α). Selection of the catheter site for dialysis catheter placement varies based on hospital policies, comfort level of the intensivists, the clinical status and placement of other central accesses for that patient. The femoral vein was used in majority of our cohort for dialysis catheter placement, a site preferred in other studies but one data showed the internal jugular vein as being the most common site.[12,16,17]

Our study is first of its kind from Pakistan. Validation of the results needs further studies to be conducted. Our study had various limitations. First limitation is that this study is retrospective observational, that can lead to recall bias, interpretation bias and missing data, leading to limited collection and analysis of the data. Second important limitation is the low number of patients that underwent CRRT since the employment of the machine, that renders our data non-generalizable to other parts of the world. Third limitation is non-availability of ECMO that could have improved the survival among the patients. Fourth limitation is our inability to add further useful details of the CRRT into our data that includes circuit life, priming technique, anticoagulation used in detail, history of transfusion of blood products, and CRRT operation indices like blood flow, ultrafiltration volume and type of filters used.

CONCLUSION

The overall mortality in patients who underwent CRRT was high (71.4%). Norepinephrine use post-CRRT, multi-organ dysfunction, cardiovascular system, respiratory system dysfunction and low platelet counts were associated with high mortality while association of respiratory dysfunction with mortality was independently statistically significant. However, more studies are needed that can direct the nephrologists and pediatric intensivists towards the best practice guidelines on operations of CRRT.

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