ARTICLE

# Short term outcomes of children with acute kidney injury treated with hemodialysis in a tertiary pediatric hospital: a six-year review

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**OBJECTIVE:** This paper aimed to describe the clinical profile and short-term clinical outcomes of children with Acute Kidney Injury (AKI) requiring hemodialysis in a tertiary pediatric hospital.

**MATERIALS AND METHODS:** A retrospective cohort on in-patients who received hemodialysis treatments at our institution was performed. Medical charts of patients admitted between July 2018 and July 2023 were retrieved. Demographic data, clinical profiles and subsequent outcomes in terms of mortality and recovery or non-recovery from AKI were recorded.

**RESULTS:** After meeting the inclusion and exclusion criteria, 129 patients were included in the study's statistical analysis. There was an even distribution between males and females. The average age of treated patients was 10 years old (SD ± 4.3). The average weight of patients was 35kg (SD ± 16.9). The most common diagnosis of patients was severe dengue (21.7%), followed by severe sepsis (14.7%). More than half of patients (51.9%) had an existing co-morbidity, of which Systemic Lupus Erythematosus (22.4%) and solid tumors (22.4%) were most common. The most common indication for hemodialysis was uremia (52.7%). In terms of short-term outcome, majority of patients died during the same admission (56.5%), while 31 patients (24.0%) recovered.

**CONCLUSION:** The clinical profile of patients who underwent hemodialysis treatments for AKI were comparable to international data. The study did not differentiate deaths from AKI or underlying illness, but demonstrated a higher mortality rate compared to other existing studies. This study is the first known local paper to describe the profile and outcomes of children who received hemodialysis for AKI.

**KEYWORDS:** *Pediatric AKI. Hemodialysis. Outcomes. Severe sepsis. Severe dengue.*

## Introduction

Acute Kidney Injury (AKI) is a well-recognized complication in hospitalized children and has been observed in patients both critically-ill and non-critically ill. Its clinical implications include a wide range of short-term to long-term complications of varying degrees of severity. It may result in immediate consequences such as death or may extend well beyond the initial inciting event, and eventually be a risk factor for the development of Chronic Kidney Disease (CKD) in adulthood. To date, there are no known published studies profiling patients who develop pediatric AKI in the country and their subsequent outcomes. Consequently, there is also a lack of robust data on the most common etiologies of pediatric AKI in the country, as well as the most common indications for Renal Support Therapy (RST), and outcomes of RST in these patients. Such information is important in guiding physicians and policy-making bodies make important and informed decisions with regards to managing these cases on the clinical and public health level.

In the latest local report of Renal Disease Registry by the Pediatric Nephrology Society of the Philippines (1), there was a total of 408 reported cases of AKI in 2022, with 10.8% requiring any form of RST. No data are available outlining the etiologies and outcomes of the cases above. A review of studies in other countries showed a predominance of infectious etiologies of AKI. Clinical outcomes of these cases varied widely depending on the etiology of the disease, existing co-morbidities, and other factors such as availability of different modalities of RST.

This study was conducted in a referral institution receiving cases from secondary and provincial hospitals around the country. The unit is manned by pediatric-trained nursing and physician staff. The aim of this study was to describe the clinical profile and outcomes of children who required hemodialysis treatments in the management of AKI in a tertiary pediatric hospital in the Philippines. Further, it aims to provide a picture of the most commonly encountered cases of pediatric AKI in the country.

## Materials and Methods

The study was a single-center retrospective cohort of patients admitted at a tertiary children's hospital who underwent hemodialysis treatment for AKI between July 2018 and July 2023. All records of admitted patients who underwent hemodialysis treatments for AKI between the said study period were retrieved and reviewed for completion of data.

Following approval from the Institutional Research Ethics Committee, a list of all patients who received hemodialysis treatments for AKI was submitted to the

medical records section for chart retrieval. Records of patients who fulfilled the inclusion and exclusion criteria were included in the study. Patients who underwent treatment for reasons other than acute kidney injury (hemoperfusion only, drug intoxication, etc.) were excluded.

The diagnosis of AKI was made with the fulfillment of the KDIGO criteria and staging system for AKI based on the presence of an increase in serum creatinine and decrease in urine output. A review of charts was done to collect data on demographics, clinical impression on referral, existing co-morbidities, if present, and indications for dialysis. Short-term outcomes were defined as any one of the following outcomes upon discharge from the present admission, or death:

a) mortality

b) AKI – recovered

c) Acute Kidney Disease or

d) Chronic Kidney disease

All patients and corresponding medical records were assigned a case number during data collection. Identifying information including name and addresses were not recorded and a non-disclosure and confidentiality agreement with the Medical Records was also completed prior to data collection.

All data were encoded in Microsoft Excel. SPSS 24 was used for data processing and analysis. Patient characteristics were summarized as means with standard deviation for continuous variables and frequency with proportions for categorical variables. The rates mortality, AKI recovery, AKD and CKD were summarized using incidence rates with 95% confidence interval.

## RESULTS

A total of 174 acute hemodialysis (HD) treatments were identified from the Hemodialysis Unit master list of patients. Thirty-nine patients who were treated with hemoperfusion only (no diagnosis of AKI), and six patients who had a diagnosis of AKI on top of CKD were excluded from data analysis. A total of 129 patients were analyzed.

Baseline clinical profile showed a comparable distribution between males and females. Most patients who received HD treatments belonged to the 11-15 year-old age group. The average weight of patients was 35kg and ranged between 9-78kg. Average body surface area (BSA) was 1.1.

*Table 1. Demographic profile, underlying disease and comorbidities of children with AKI who underwent hemodialysis treatments between July 2018 – July 2023*

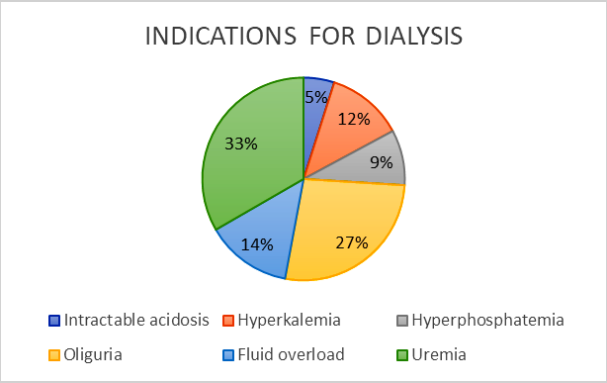
| **DEMOGRAPHICS** | | **N=129** |
|---|---|---|
| **Age, years (mean ± SD)** | | *10.4±4.3* |
| **Gender** | | |
| | *Male* | *62 (42.1%)* |
| | *Female* | *67 (51.9%)* |
| **Weight, kg (mean ± SD)** | | *35.4±16.9* |
| **Height, cm (mean ± SD)** | | *134.8±25.9* |
| **Body surface area, m2 (mean ± SD)** | | *1.1±0.4* |
| **UNDERLYING DISEASE** | | **N=129** |
| ***AKI/MODS sec to Severe Dengue*** | | *28 (21.7%)* |
| ***AKI/MODS sec to Severe sepsis*** | | *19 (14.7%)* |
| ***RPGN sec to Glomerulonephritis (excluding SLE)*** | | *15 (11.6%)* |
| ***Tumor Lysis Syndrome*** | | *13 (10.1%)* |
| ***AKI/MODS sec to Leptospirosis*** | | *12 (9.3%)* |
| ***AKI/RPGN sec to Lupus nephritis*** | | *11 (8.5%)* |
| ***Others*** | | *10 (7.8%)* |
| ***AKI sec to obstructive uropathy*** | | *7 (5.4%)* |
| ***AKI sec to diabetic ketoacidosis*** | | *3 (2.3%)* |
| ***AKI sec to autoimmune vasculitis*** | | *3 (2.3%)* |
| ***AKI sec to Vancomycin toxicity*** | | *2 (1.6%)* |
| ***AKI sec to MIS-C*** | | *2 (1.6%)* |
| ***AKI sec to atypical HUS*** | | *2 (1.6%)* |
| ***AKI sec to cardiorenal syndrome*** | | *1 (0.8%)* |
| ***AKI sec to hepatorenal syndrome*** | | *1 (0.8%)* |
| **CO-MORBID CONDITIONS** | | **N=67** |
| ***Solid tumor*** | | *15 (22.4%)* |
| ***Systemic Lupus Erythematosus*** | | *15 (22.4%)* |
| ***Leukemia*** | | *7 (10.4%)* |
| ***Tuberculosis infection*** | | *5 (7.5%)* |
| ***Cardiac condition*** | | *3 (4.5%)* |
| ***Diabetes mellitus type 1*** | | *3 (4.5%)* |
| ***Autoimmune vasculitis*** | | *3 (4.5%)* |
| ***Nephrotic Syndrome*** | | *2 (3.0%)* |
| ***Renal tubular acidosis*** | | *2 (3.0%)* |
| ***Cerebral palsy*** | | *2 (3.0%)* |
| ***COVID infection*** | | *2 (3.0%)* |
| ***Portal hypertension*** | | *1 (1.5%)* |
| ***Hereditary Spherocytosis*** | | *1 (1.5%)* |
| ***Henoch Schonlein Purpura nephritis*** | | *1 (1.5%)* |
| ***Neurogenic bladder*** | | *1 (1.5%)* |
| ***Anti-NMDAR encephalitis*** | | *1 (1.5%)* |

The most common clinical impression of patients who were referred for hemodialysis treatments was severe dengue, followed by severe sepsis, with rapidly progressing glomerulonephritis (excluding those secondary to lupus nephritis).

About half of all patients (51.9%, N=67) had preexisting co-morbidities, with systemic lupus erythematosus (SLE) and solid tumors as the most common conditions.

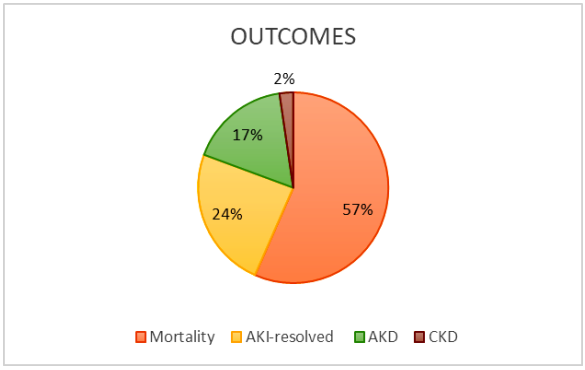
Fifty-six patients (43.4%) presented with a multiple indications for hemodialysis, with uremia as the most common indication, followed by oliguria (42.6%) and fluid overload (21.7%), and hyperkalemia (19.4%).

*Figure 1. Indications for initiation of hemodialysis in 129 children with AKI*




In terms of short-term outcomes, most patients who underwent hemodialysis died within their admission. Twenty-four (24%) percent had complete recovery from AKI. Twenty-two (22%) were discharged with stable, but elevated serum creatinine levels, while 3% were discharged as confirmed cases of chronic kidney disease.

*Figure 2. Outcomes of 129 children with acute kidney injury treated with hemodialysis*




## Discussion

Acute Kidney Injury or AKI is defined as a decrease in glomerular filtration rate (GFR), as manifested by an elevated or a rise in serum creatinine from baseline, and/or a reduction in urine output (2), that may result from renal ischemia, sepsis, or toxicant-induced renal cell injury (3). In pediatrics, the most commonly adopted criteria and staging system is the KDIGO criteria which takes into account either an increase in serum creatinine levels or a decrease in urine output for a certain time period. This criteria system was used in the identification of cases of pediatric AKI for this study.

Owing to the advancements in diagnosis and early detection of the condition, AKI has been increasingly recognized as a common complication in hospitalized patients in the

recent years. It has been best described in cases of critically-ill children but has also been found to play a significant role in non-critically ill patients. Some studies report that it can occur in 5% of hospitalized children, while it may be present in 20-30% of critically-ill children (3). AKI may result from a host of risk factors and inciting events and may as well, result in various short-term and long-term outcomes.

This study included only patients who encompass AKI stage 3, who required hemodialysis during their hospitalization, and aimed to define the clinical profiles of these patients. Short-term clinical outcomes were defined as outcomes within the same admission as the initiation of hemodialysis treatments and were recorded upon discharge or occurrence of death.

***Patient Anthropometrics***

As in many other medical procedures, pediatric hemodialysis differs from that of the adult population in that many technical considerations are dependent on the patient's anthropometrics (weight, height and BSA). Calculated blood flow and dialysate flow rates for hemodialysis are based on a patient's weight and equivalent estimated blood volume, and are therefore much lower compared to adult prescriptions. Additionally, most of available equipment and consumables related to hemodialysis use in the country are adult-sized given that majority of hemodialysis centers cater mostly to adult patients. This may serve as a challenge for hemodialysis centers catering to small children who will need modifications to their HD prescriptions and setups in order to utilize adult blood lines, dialyzers, catheters and other supplies. Results of this study found that most patients who required hemodialysis treatments for AKI weighed an average of 35kg, translating to an estimated blood volume of 2,450mL. Dialyzer size was determined by the patient's corresponding BSA and available dialyzers in the institution ranged between BSA of 1.0 and 1.8. Subsequent extracorporeal blood volume was then determined by the dialyzer size appropriate for the patient's BSA. The rule that the volume of extracorporeal blood circuit should not exceed 10% of the patient's estimated blood volume is a generally accepted one (4). In cases where ECV exceeds 10% due to the inappropriately-large extracorporeal volumes associated with using adult lines and dialyzers, priming of dialysis circuits is employed in our center. Depending on the patient's hemodynamic stability and current hematocrit current practice in our center includes using either 5% albumin or blood products, such as packed red blood cells or reconstituted whole blood for priming, depending on the individual needs of patients. This consideration has important operational implications for pediatric hemodialysis units.

Because pediatric patients vary significantly in terms of anthropometrics, a dialysis unit catering to this population must be equipped not only with a range of differently-sized blood lines and dialyzers, but also with resources that will allow for accessible blood and other priming products to ensure that safe and efficient dialysis treatments are delivered to patients.

This becomes an important consideration in future pediatric centers in the country. In order to effectively cater to very small children, availability of pediatric blood lines and dialyzers in addition to availability of priming products such as albumin and blood are mandatory. \

***Illnesses and AKI***

Several factors have been known to incite kidney injury resulting in laboratory and clinical manifestations of AKI, and underlying illnesses may differ from population to population. Additionally, it has been suggested that that severity of AKI correlates with disease severity (5). Our study has found that the most common diagnosis of patients who received hemodialysis treatments for AKI was severe dengue (21.7%) followed by severe sepsis (14.7%), and then by various etiologies of glomerulonephritides (11.6%). This is similar to findings of international studies that identified infection and glomerular disease as leading causes of etiology of AKI in children, especially in lower-income countries where access to healthcare and health-seeking behavior are lacking, and where communicable diseases, including zoonotic diseases are still prevalent. This is in comparison to more developed countries where etiologies of AKI are commonly associated with complex surgical procedures as a consequence of volume depletion, prolonged ischemia from cardiac surgeries, or use of nephrotoxic medications. This highlights the fact that there remains to be much room for improvement in terms of early detection and prevention of communicable diseases that result in major health implications in the country.

This study also identified tumor lysis syndrome as one of the top etiologies of hemodialysis-requiring AKI. This may be due in part to the institution being a cancer and hematology referral center in the country, with a significant population of patients with hematologic and oncologic conditions, in whom tumor lysis syndrome may occur.

***Comorbidities and AKI***

Other than etiology of AKI, this study also to identified pre-existing co-comorbidities of children who underwent hemodialysis treatment for AKI. We found that 52% (N=67) of patients had pre-existing conditions prior to initiation of treatment. The most common comorbidities were found to be solid tumors and systemic lupus erythematosus, which are consistent with the most common primary diagnoses of patients mentioned above.

In these groups of patients, 86% of those with solid tumors and 46% of those with SLE were mortalities. This is consistent with a study published in 2015, where Asinobi et al. found that patients with irreversible comorbidities such as malignancies and glomerulonephritis were at higher risk of mortality compared to those who had a reversible cause of AKI (6). This information may prompt physicians to more closely monitor these patients in whom worse outcomes are associated, compared with patients who do not have pre-existing comorbidities.

***Indications for Hemodialysis***

Despite the numerous possible etiologies of AKI, there are only a number of indications for initiation of renal replacement therapy. Dialysis modalities are often employed when medical management is not sufficient nor effective, or when consequences of AKI have become life threatening and must be reversed immediately. In our institution two modalities of RST are available: hemodialysis and peritoneal dialysis. Each has its own advantages and disadvantages and the choice of modality ultimately depends on multiple factors determined by the patient's clinical status and availability of equipment and staff knowledgeable about each RST modality. Historically, peritoneal dialysis has performed satisfactorily in the management of pediatric AKI and has been the choice of pediatric nephrologists for RST due to its wide availability in settings of both high-income and low-income countries. In the advent of newer technologies however, such as CRRT and increasing availability of pediatric-specific supplies for conventional dialysis, there had been a decline in the choice of RRT for pediatric AKI (7). Our study showed that the most common indication for hemodialysis in patients with AKI was uremia (52.7%), which may present as uremic encephalopathies and uremic bleed, among other manifestations. This was followed by oliguria (42.6%), fluid overload (21.7%), and hyperkalemia (19.4%) which requires rapid correction to avoid potentially lethal cardiac arrhythmias. As earlier mentioned, all of these indications may be addressed effectively with peritoneal dialysis, albeit with slightly less room for modifications of prescriptions as compared to hemodialysis.

Fluid and ultrafiltration management in hemodialysis may also be slightly more advantageous as compared to peritoneal dialysis in patients presenting with severe fluid overload. This is due to the fact that hemodialysis machines can be modified to attain a more precise ultrafiltration over a specified time of treatment. Furthermore, rates of ultrafiltration may be adjusted in real time at any point during the treatment, which is particularly helpful in patients whose hemodynamics are labile.

Hyperkalemia as an indication for dialysis may correlate with one of the most common etiologies of AKI found in this study.

The institution, being a tertiary referral institution with multiple specialties including hematology and oncology, caters to a large population of children who may present with hematologic emergencies such as tumor lysis syndrome (TLS). Renal replacement modalities such as hemodialysis in particular, are an integral part of the management of these patients. Hyperkalemia remains the most dangerous component of TLS (8) due to the possibility of cardiac arrhythmias and therefore must be corrected promptly. Compared with the other available modality of RST in the institution, hemodialysis offers a much faster ability to correct hyperkalemia and other electrolyte derangements associated with TLS, addressing potentially fatal consequences in a timely manner.

***Outcomes of Children with AKI who Received Hemodialysis Treatments***

Compared to the adult population, studies exploring outcomes of pediatric cases of AKI requiring HD are limited. This may be due in part to the lack of a standard definition of AKI in the past, which precludes a timely and accurate diagnosis. There had also been several classification and criteria systems that are employed by different centers, resulting in some differences in statistical data of AKI in children. The recent iteration of the KDIGO criteria for diagnosis of AKI will hopefully usher in more standardized data and result in more studies exploring outcomes of HD-requiring AKI in children. Despite the relative paucity of well-documented outcomes of AKI following RST, it is now known that the diagnosis of AKI is a risk factor for the development of chronic kidney disease, hypertension, cardiovascular disease and death in adulthood (9). Short-term sequelae on the other hand include a greater risk for mortality among other complications. Existing studies vary greatly in the incidence of mortality in patients, depending on the geographical location of the centers and the population studied. We found that mortality rates in pediatric AKI ranged between 6.5 – 40% (6, 10, 11, 12). In contrast, our study revealed a higher incidence of mortality with the outcome occurring in 56.5% of patients. It is important however to note that mortalities recorded in our study were all-cause mortalities and did not discriminate between deaths attributable to AKI or deaths attributable to other causes which may have occurred after recovery from AKI but have occurred within the same admission. Further statistical analyses with this data set may help elucidate better a causal relationship between the study's exposures and outcomes.

Less than half of patients included in the study were eventually discharged, with 24% having completely recovered from AKI prior to their discharge from the institution. The remaining patients (19.4%) were discharged with non-normal serum creatinine levels. Three of whom (2.3%) were discharged as cases confirmed of chronic kidney disease while 17% were found to have elevated serum creatinine levels on discharge. The latter group of patients are those in whom serum creatinine levels remained elevated but did not yet meet

the duration of three months to be managed as chronic kidney disease. These patients represent a condition in the spectrum of kidney injury now recognized as Acute Kidney Disease (AKD), who may carry the same risk of progression to chronic kidney disease and other renal complications in adulthood as AKI does. Close monitoring for these patients is imperative as they may exhibit sustained recovery or progressive decline in serum creatinine.

Data from this study demonstrated that the institution through its hemodialysis unit is able to deliver urgent renal support therapy in various cases of acute kidney injury even in very small children despite the lack of age-specific blood lines and pediatric-specific machines. The cases of AKI treated in our dialysis unit were similar to cases documented in international studies, in terms of etiology and indications. Treatments were made possible by the resources available in the institution such as a dedicated blood bank providing essential blood products for circuit priming, which allows hemodialysis treatments for children in whom the extracorporeal blood volume exceeds 10% of estimated blood volume. Such dialysis prescription modifications require special staff knowledge and training and are difficult to carry out in primarily adult-dedicated hemodialysis centers, where experience with pediatric patients are minimal. A study published in 2017 by Raina, et al. reported that pediatric dedicated HD units and trained staff were available only in 33.3% of hemodialysis centers in developing countries (13). This underscores the need for more hemodialysis units able to cater to the pediatric population. In fact, in the 2005 revision of the Hemodialysis General Practical Guidelines from the European Pediatric Dialysis Working Group in 1999, outlined as the first guideline the need for hemodialysis treatments to be "delivered in a pediatric dialysis center with a multidisciplinary support team which supports individualized and integrated therapy" for patients (14). The institution's unit, being an exclusive pediatric hemodialysis center has its staff training focused on pediatric cases and has been integral in the efficacy of delivery of care for these patients. In addition to this, the hospital is also home to several other subspecialties able to attend to patients with differing needs and are part of the multi-disciplinary approach to the management of acute kidney injury in children.

Compared to other existing studies, outcomes of patients treated at our institution were relatively less satisfactory, with more than half of patients succumbing to death. A limitation of the study is not being able to determine which deaths were due to immediate complications of AKI or as a result of other complications of the primary disease. Additionally, the study followed up patients up until their discharge, which meant that patients who may have recovered from their AKI and who died for other reasons after recovery from

AKI were still considered as mortalities in their final outcomes.

## Conclusions

Our study characterized pediatric patients who underwent acute hemodialysis treatments for AKI in a tertiary pediatric hospital, and showed similar clinical profiles including etiology of AKI, nature of comorbidity, and indications for hemodialysis, as existing studies, particularly in developing nations. In terms of outcomes, majority of our patients fell under mortalities, which, unfortunately, did not distinguish between mortalities directly due to AKI and mortalities not related to renal failure. Dialysis treatments of even very small children were made possible by the institution's pediatric-dedicated facilities such as the blood bank and other subspecialties available, as well as the hemodialysis unit's pediatric-trained nursing and physician staff. This emphasizes the urgent need for more hemodialysis units capable of catering to and effectively delivering pediatric-specific hemodialysis treatments.

To the author's best knowledge, this is the first local study to describe the clinical profiles and short-term outcomes of children who received hemodialysis treatments for AKI. Recommendations for future studies include establishing associations and correlations between etiologies of AKI and outcomes, and delineating mortalities that may directly be attributed to the initial kidney injury from mortalities that are unrelated to acute kidney injury. Thus, a prospective study on this topic is recommended. Additionally, future research may include identification of risk factors for development and incidence of long-term outcomes in patients who developed hemodialysis-requiring AKI in children including other markers of dialysis adequacy, and markers of disease severity such as hospital stay, inotropic support, mechanical ventilation, among others.

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