LUMEN ET VIRTUS

Epidemiological profile of pediatric patients with acute kidney injury: A literature review

https://doi.org/10.56238/levv15n38-019

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ABSTRACT

Objective: To identify the epidemiological profile of hospitalized pediatric patients who progressed to Acute Kidney Injury. Method: A bibliographic survey was carried out through publications in indexed journals (MEDLINE, LILACS, SciELO, and PubMed), from 2007 to 2022, focusing on the topic in question. Results: In practically all studies, about 30% to 40% of AKI cases were due to sepsis and infection. Pediatric patients with sepsis and systemic multiorgan dysfunction had lower survival rates than those associated with other cases. Septic shock was associated with death in 62% of patients with AKI and was a risk factor for mortality. Conclusion: AKI is a severe disease, with a multifactorial etiology in many cases, and with variable mortality, which can reach more than 60% in dialysis patients. From an epidemiological point of view, there is still a significant lack of robust studies on the incidence, prevalence, and outcomes of AKI in the pediatric population.

Keywords: Acute Kidney Injury, Pediatrics, Epidemiology.

INTRODUCTION

Acute kidney injury (AKI), or Acute Kidney Injury, is a frequent complication in pediatric patients with severe conditions. It is characterized by an abrupt and, in most cases, reversible reduction of renal function, with loss of the body's ability to maintain homeostasis, which may or may not be accompanied by a decrease in diuresis, in addition to the instability of body homeostasis and, consequently, hemodynamic impairment[1,2].

Ryella (2018) describes Acute Kidney Injury (AKI) as the acute reduction of renal function in hours or days and refers mainly to the decrease in the glomerular filtration rate and/or urinary volume, also occurring disturbances of the hydroelectrolyte and acid-base balance[2].

The division of Acute Kidney Injury is then made into three subtypes. The first is called pre-renal, where there is a decrease in renal blood flow (RSF) due to inadequate cardiac output or intravascular volume; intrinsic kidney disease (Renal), where there is damage to the structures that make up the renal parenchyma, including ischemic, vascular, tubular, and glomerular disorders; and the so-called postrenal AKI, resulting from some degree of urinary tract obstruction in a single kidney or in both kidneys[2,3].

In the pediatric public, the main causes of AKI are sepsis, use of nephrotoxic drugs, and renal ischemia in critically ill patients. Children hospitalized in Intensive Care Units (ICU) with severe conditions are exposed to numerous conditions that can result in renal impairment, significantly increasing the morbidity and mortality rate. The incidence related to AKI in childhood has been associated with a higher mortality rate, longer length of stay in pediatric intensive care units and higher hospitalization costs[5,6].

For the identification and recognition of AKI, it is necessary to use the serum creatinine marker. Despite its wide dissemination, some researchers have indicated that slight elevations in serum creatinine can result in severe outcomes, which suggests that this parameter is not efficient as an early marker, but rather constitutes a late marker for renal dysfunction. There are other more precise markers, which can identify AKI earlier, but they are expensive and have low availability of laboratory detection[7].

Regarding the classification of AKI, the first standard definition was the RIFLE classification, published in 2004, with the initials of the five phases proposed for the classification of AKI: risk, injury, failure, loss of function, and end-stage renal disease. However, this classification did not fit the pediatric parameters, where the P-RIFLE was created. Another classification emerged soon after (AKIN), which classified AKI into three stages, according to its severity. Currently, since 2012, the KDIGO classification, unified and universal, has been instituted, which serves both adult and pediatric patients.

This definition, the most current available in the literature, takes into account two easily verifiable characteristics: serum creatinine (or estimated PCD for patients under 18 years of age) and urine output. Although it is the most current and appropriate classification for the pediatric age group, there was still a need to adapt to the neonatal period, a phase in which renal physiology presents particularities.

Thus, the KDIGO classification for AKI in the neonatal period was published in 2015, in which stage 2 AKI occurs when there is a reduction in urine output for a shorter period; and the absolute value of serum creatinine greater than or equal to 2.5 mg/dL is considered stage 3, as it represents a DCP less than 10 mL/min/1.73 m2 in neonates. Another peculiarity is that the baseline value of creatinine is defined as the lowest previous value, since creatinine at birth reflects maternal creatinine and evolves physiologically with falls in the first days of life[7,9].

In the pediatric age group, approximately 6% of critically ill patients may require renal replacement therapy (RRT) and these patients have an increase in mortality of 50 to 80%, especially if associated with sepsis, septic shock and multiple organ and system dysfunction[8].

Therefore, this study aimed to search the Brazilian and international literature to identify the epidemiological profile for the development of acute kidney injury in hospitalized children.

METHOD

An integrative literature review was adopted, as it contributes to the process of systematization and analysis of results, aiming at understanding a given theme, based on other independent studies. The integrative literature review proposes the establishment of well-defined criteria for data collection, analysis and presentation of results.

For this review, we searched the MEDLINE database, through the PUBMED portal, using the term Mesh (Medical SubjectHeadings) "Acute Kidney Injury", selecting the subtopic "Pediatric". Then, filters were applied for age (0 to 18 years) and year of publication (last 20 years). This search was conducted in July 2023, and resulted in 112 articles. The terms "acute renal failure" and "epidemiology", "acute tubular necrosis" and "epidemiology" were also searched in the "title" and "abstract" fields with the same filters (age and year of publication). The researcher evaluated all abstracts and the articles considered most relevant were examined in full.

A search was also performed in the LILACS database (Latin American and Caribbean Literature on Health Sciences) through the Virtual Health Library portal, using a series of articles on AKI in Brazil and Latin America, using the following search terms: "acute kidney injury" or "acute kidney failure" or "acute kidney injury" and the age filter (0 to 18 years). This second search selected 59 articles, whose abstracts were examined by the authors. The most relevant articles were evaluated in full, and those selected were included in this review.

The following inclusion criteria were adopted for the selection of articles: all article categories (original, literature review, reflection, update, experience report, etc.); articles with abstracts and full texts available for analysis; those published in Portuguese, English or Spanish, between the years 2004 and 2022.

The criteria for the exclusion of the articles were used based on the reading of the abstract and the discussion, in order to highlight the studies that escaped or did not present data relevant to the research.

Of the material obtained, 25 articles were read in detail (abstract/article), and those that contemplated the theme of the research were highlighted, in order to organize and tabulate the data. Following the inclusion and exclusion criteria mentioned above, a total of 13 studies were selected for analysis and included in this integrative review. Table 1 presents the specifications for each article.

Table 1. Articles collected in the MEDLINE and LILACS databases on AKI in pediatrics.

Origin	Article Title	Authors	Newspaper
1. LILACS	Outcomes of critically ill children requiring continuous renal replacement therapy.	Hayes LW, Oster RA, Tofil NM, Tolwani AJ.	J CritCare
2. MEDLINE	AssociationbetweenpediatricRisk, Injury, Failure, LossandEndStage Renal Disease score andmortality in a pediatricintensivecareunit: a retrospectivestudy.	Almeida JP, Valente IF, Lordelo MR.	Rev. bras. have. Intensive Vol.30 No.4
3. LILACS	Predictivefactorsofmortality in pediatricpatientswithacute renal injuryassociatedwithsepsis.	Riyuzo MC, Silveira LVA, Macedo CS, Fioretto JR.	J. Pediatr. (Rio J.) vol.93 nº.1
4. MEDLINE	Sepsis-associatedacutekidneyinjury: is it possibleto move theneedleagainstthissyndrome?	Devarajan P, Basu RK.	J Pediatr (Rio J). 93:1-3
5. MEDLINE	Acutekidneyinjury in children: incidenceandprognosticfactors in criticallyillpatients.	Freire KMS, Bresolin NL, Farah ACF, Carvalho FLCC, Góes JEC.	Rev. bras. have. Intensive Vol.22 Nº2
6. MEDLINE	AcuteKidneyInjuryEpidemiology in pediatrics.	Gomes CLR, Suassuna JHR, Nogueira PK.	J. bras. nefrol ; 41(2): 275-283
7. LILACS		Olowu WA.	ClinNephrol

8. LILACS	Acute kidney injury in children in Nigeria.	Sutherland SM, Ji J, Sheikhi FH, Widen E, Tian L, Alexander SR, et to the.	Clin J AmSocNephrol
9. LILACS	AKI in hospitalized children: epidemiology and clinical associations in a national cohort.	Kaddourah A, Basu RK, Bagshaw SM, Goldstein SL;	N Engl J Med
10. LILACS	Epidemiology of Acute Kidney Injury in Children and Young Adults in Severe.	Rustagi RS, Arora K, Das RR, Puni PA, Singh D.	PaediatrIntChild Health 2017.
11. LILACS	Incidence, risk factors, and outcome of acute kidney injury in critically ill children – a developing country perspective.	Bresolin N, Silva C, Halllal A, Toporovski J, Fernandes V, Góes J, et to the.	PediatrNephrol.
12. LILACS	Prognosis for children with acute kidney injury in an intensive care unit.		PediatricCritCareMed 2017.
13. LILACS	Epidemiology and outcome of acute kidney injury according to risk Pediatric, injury, failure, loss, end-stage renal disease, and renal disease: criteria for improving global outcomes in a prospective study of critically ill children.	Volpon LC, Sugo EK, Consulin JC, Tavares TL, Aragon DC, Carlotti.	Pediatric Adolescent Med.
	Acute renal failure: a pediatric experience over 20 years.	Williams DM, Sreedhar SS, Mickell JJ, Chan JC.	

RESULTS AND DISCUSSION

AKI is known for its great impact on the prognosis of patients in serious and very serious condition, most of whom are hospitalized in ICUs. In these patients, it is a common clinical condition and its etiology can be multifactorial. AKI can progress to renal failure, making it impossible to perform its primary function, which is the maintenance of the body's homeostasis[10].

From the reading of the selected articles, it can be seen that acute kidney injury (AKI) is a frequent complication in pediatric patients with severe conditions. In all studies, most children with abnormal renal function were male, approximately in 60% of the cases, with ages ranging from 2 to 4 years. The study by Freire et al (2010) showed a prevalence of the infant age group [7].

The average length of hospital stay was around 8 days, and associated with mechanical ventilation (30%), oligoanuria (20%), patients with other pathologies that included cardiac, neurological, endocrine, and hematological diseases, and who developed AKI around 3 to 4 days of hospitalization. In the study by Riyuzo (2017), diuresis ranged from 0 to 11 mL/kg/h. Some children had hypertension, 98% required vasopressor drugs, and 92.2% received more than two vasoactive drugs, and 42.8% required acute renal replacement therapy. The therapy of choice in all cases was peritoneal dialysis. The use of PD in pediatrics began in 1960. In the following years, the indications and use of this modality increased. Generally, Peritoneal Dialysis is the treatment of choice for acute kidney injury, as it has low cost and requires basic technical and operational knowledge, in addition to presenting excellent results for pediatric patients, as they have an increased ratio between peritoneal surface and body weight [9,10,11,12,14].

Other studies relate AKI to postoperative patients, especially cardiac surgery, and also respiratory failure, associated with sepsis and septic shock[10,11,12].

There is a lack of publications on risk factors for mortality in pediatric patients with AKI and sepsis. The frequency of AKI associated with infection and sepsis has increased every year. Most studies have reported data in neonates and children with AKI after cardiac surgery. Several conditions may be involved in the etiology of AKI in children with sepsis. Approximately 10 to 30% of AKI cases were due to sepsis and infection. Pediatric patients with sepsis and systemic multiorgan dysfunction had lower survival rates than those associated with other cases. Septic shock was associated with death in 62% of patients with AKI and was a risk factor for mortality[6,10,12,15,16].

One of the risk factors for developing sepsis is malnutrition, which also involves multiple organ failure, associated with impaired kidney function. It is alarming that in all the articles studied, the difference between sepsis and other etiologies as causal factors of AKI was statistically significant.

It is important to remember that sepsis, or multiple organ dysfunction syndrome, constitutes an exaggerated immune response of the host to the presence of a microorganism or its toxic components. A wide variety of microorganisms can cause sepsis in pediatric patients, especially neonates, immunosuppressed and hospitalized patients exposed to nosocomial germs, and is included in the conditions most frequently found in pediatric hospitals[15,16].

Sepsis is one of the most important risk factors, as stated in the literature. It is important to understand that the mediation of kidney damage in patients with infections can be by agents such as bacteria, viruses, fungi, and parasites. Sepsis causes endotoxin-mediated effects, substances that stimulate the release of cytokines, which interact directly with the cells of the renal parenchyma or indirectly, activating polymorphonuclear cells, causing different degrees of ischemia at the renal

level. These cytokines induce vasodilation, with rapid production of platelet activating factors. This leads to the slowing of renal circulation, and can even reach cortical necrosis.

Thus, critically ill pediatric patients at risk of sepsis should be frequently analyzed for renal function, in view of the great association with morbidity and mortality. Sepsis is the leading cause of death not related to trauma in pediatric patients worldwide, both in developed and developing nations[10,12,17].

Studies report that acute glomerulonephritis as a cause of AKI occurred in few patients, approximately 8%[10].

The study by Almeida (2019) reported the influence of nephrotoxic drugs as the main causes of acute kidney injury, where about 25% of his sample used two or more drugs. The most commonly used nephrotoxic drug was iodinated contrast, present in 17.2% of the sample, followed by vancomycin in 15.1%, non-steroidal anti-inflammatory drugs in 10.9%, aminoglycosides in 10.4%, amphotericin B in 8.3%, and chemotherapy for the treatment of neoplasia in 6.3% of the patients. In the same study, among the patients who died, approximately 74% had AKI[4,6].

In the case of neonates (age up to 28 days of age), an epidemiological study conducted in 2014 in the United States showed that an incidence of AKI of 39.8% was reported in extremely low birth weight preterm infants, according to the modified KDIGO classification for the neonatal period, as well as higher mortality and length of hospital stay adjusted for the patient's severity[11].

Studies on the epidemiology of AKI in pediatric patients in Brazil are very limited. In a study conducted in 2008, an overall mortality rate of 53.3% was reported in children aged 0 to 12 years on dialysis due to ARI, who underwent peritoneal dialysis, being even higher (73.9%) in the neonatal period[8].

CONCLUSION

Several factors are associated with the high mortality rate of children with ARI. Among them, socioeconomic aspects, prolonged time in the evaluation of renal function, and inadequate management of AKI stand out.

In virtually all studies, about 30% to 40% of AKI cases were due to sepsis and infection. Pediatric patients with sepsis and systemic multiorgan dysfunction had lower survival rates than those associated with other cases.

Acute kidney injury associated with severe sepsis is common and fatal, but can be reduced with prevention measures. Clinical treatment should be based on constant monitoring of renal function, as well as preventive measures, such as the choice of non-nephrotoxic drugs, prevention of dehydration and/or hypovolemia, and monitoring of nitrogenous slag from the beginning of hospitalization. It is of paramount importance to identify the etiology early, so that appropriate

interventions can be made, aiming at management focused on reducing risks. Abandonment of these measures may lead to increased prevalence and worsening prognosis.

The severity of AKI, associated with the multifactorial etiology, has a variable mortality, which can reach more than 60%. From an epidemiological point of view, there is still a significant lack of robust studies on the incidence, prevalence, and outcomes of AKI in the pediatric population.

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