The epidemiology and prognostic factors of mortality in critically ill children with acute kidney injury in Taiwan

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The incidence of acute kidney injury (AKI) in critically ill children varies among countries. Here we used claims data from the Taiwanese National Health Insurance program from 2006 to 2010 to investigate the epidemiological features and identify factors that predispose individuals to developing AKI and mortality in critically ill children with AKI. Of 60,338 children in this nationwide cohort, AKI was identified in 850, yielding an average incidence rate of 1.4%. Significant independent risk factors for AKI were the use of extracorporeal membrane oxygenation, mechanical ventilation or vasopressors, intrinsic renal diseases, sepsis, and age more than 1 year. Overall, of the AKI cases, 46.5% were due to sepsis, 36.1% underwent renal replacement therapy, and the mortality rate was 44.2%. Multivariate analysis showed that the use of vasopressors, mechanical ventilation, and hemato-oncological disorders were independent predictors of mortality in AKI patients. Thirty-two of the 474 patients who survived had progression to chronic kidney disease or end-stage renal disease. Thus, although not common, AKI in critically ill children still has a high mortality rate associated with a variety of factors. Long-term close follow-up to prevent progressive chronic kidney disease in survivors of critical illnesses with AKI is mandatory.

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Acute kidney injury (AKI) is a common complication in critically ill children, occurring in 0.3 to 82% of critically ill patients depending on the criteria and population studied.[1–3] The reported mortality rate of AKI ranges from 8.9 to 70.2% despite considerable advances in medical technology, intensive care practices, and renal replacement therapy (RRT) in the past decades.[4–9] Most survivors will be independent of RRT after an AKI episode;[10] however, children have a high incidence of long-term renal injury.[11,12]

Although many epidemiological studies on AKI in critical illnesses have been conducted in different populations, most of them are from Western countries,[7,10–15] and the epidemiological reports and exact role of pediatric AKI in critical illnesses has not been assessed extensively in Asia. Information on the overall incidence, risk factors, and outcomes in critically ill children with AKI could be useful in the prevention, early detection, and optimized intervention to prevent mortality in children with established AKI. Therefore, we performed this retrospective population-based study using National Health Insurance Research Database (NHIRD) on critical pediatric patients diagnosed with AKI during a 5-year period. The primary objective of this study was to determine the incidence rate, the risk factors for the development, and therapeutic interventions for critical patients with AKI. The secondary objectives were to determine the mortality rate and to identify risk factors associated with mortality, as well as short-term clinical outcomes, of AKI patients. In addition, the impact on developing chronic kidney disease (CKD) in long-term follow-up was evaluated.

RESULTS

Risk factors of AKI

A total of 60,338 critically ill children were admitted to the intensive care unit (ICU) during the 5-year study period. The mean age of all patients was 4.4 ± 5.7 years. AKI was identified in 850 patients during their ICU stay. The yearly incidence rate of AKI is shown in Figure 1. The average

incidence rate of AKI in the ICU was 1.4%. The patients with AKI were older (6.8 ± 6.4 years vs. 4.4 ± 5.7 years, $P<0.001$). Table 1 shows the AKI-associated risk factors. In univariate analysis, undergoing cardiovascular surgery, receiving extracorporeal membrane oxygenation (ECMO), need for mechanical ventilation or vasopressor, presence of sepsis, intrinsic renal disease or past history of hemato-oncological disease, and age older than 1 year were risk factors for the development of AKI. In contrast, the presence of congenital heart disease was not associated with the development of AKI. Variables that were independently associated with developing AKI in a multivariate logistic regression model are shown in Table 2. The risk factors for AKI included the of use of ECMO ($P=0.009$, odds ratio (OR): 1.36, 95% confidence interval (CI): 1.08, 1.70), the need for mechanical ventilation ($P<0.001$, OR: 1.88, 95% CI: 1.56, 2.27), the use of vasopressors ($P<0.001$, OR: 5.54, 95% CI: 4.66, 6.58), intrinsic and postrenal diseases ($P<0.001$, OR: 4.38, 95% CI: 3.55, 5.42), sepsis ($P<0.001$, OR: 2.13, 95% CI: 1.80, 2.52), and age more than 1 year ($P<0.001$, OR: 4.46, 95% CI: 3.74, 5.33). The Akaike's Information Criterion and area under the receiver operating characteristic curve of this model to predict AKI was 7490.3 and 0.84, respectively. Compared with non-AKI patients, total days of ICU stay was longer in patients with AKI, with $P<0.001$.

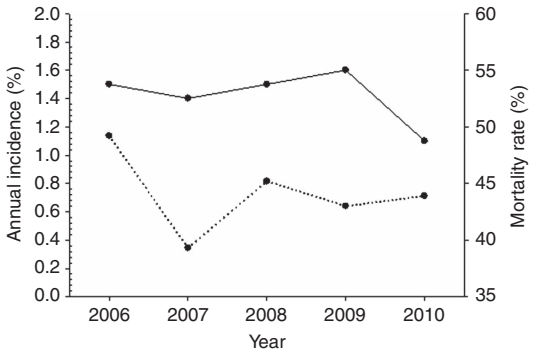

Figure 1 | Yearly incidence and mortality rate of AKI. The yearly incidence (solid line) and mortality rate (dotted line) of acute kidney injury (AKI) in critical children.

Demographics, characteristics, and epidemiological features of the AKI patients

Of the 850 patients with AKI, 438 (51.5%) patients were boys and 412 (48.5%) were girls (male/female ratio, 1.06:1). In all, 63 (7.4%) patients were discharged with a primary diagnosis of AKI. Among 787 patients in whom AKI was not the primary diagnosis, the 2 most frequent primary diagnoses were hematologic and oncologic diseases ($n=112$) and sepsis ($n=69$). The majority (85.5%) of the patients were treated in medical centers, with 13.4% admitted to regional hospitals and 1.1% to district hospitals. The age distribution of the AKI cases is shown in Figure 2. A total of 283 (33.3%) patients were less than 1 year of age. The clinical profiles of the AKI patients are shown in Table 1 and Table 3. Overall, 353 (41.5%) patients received surgical interventions during the admission, of whom 72 patients (8.5%) underwent cardiovascular surgery. The most prevalent comorbidities during the ICU admission for AKI cases were sepsis (46.5%),

Table 2 | Risk factors for developing AKI by multivariate logistic regression

Predictive variables	OR (95% CI)	*P*-value
Use of ECMO	1.36 (1.08–1.70)	*0.009
Need of ventilator support	1.88 (1.56–2.27)	*<0.001
Use of vasopressors	5.54 (4.66–6.58)	*<0.001
Primary renal disease and postrenal disease	4.38 (3.55–5.42)	*<0.001
Sepsis	2.13 (1.80–2.52)	*<0.001
Age more than 1 year	4.46 (3.74–5.33)	*<0.001

Abbreviations: AKI, acute kidney injury; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; OR, odds ratio.
*$P<0.05$.

Table 1 | Characteristics and risk factors for developing AKI by comparison of AKI and non-AKI groups

Variables	All patients $n=60,338$	AKI $n=850$	Non-AKI $n=59,488$	*P*-value
Age at admission (years)	4.4 ± 5.7	6.8 ± 6.4	4.4 ± 5.7	*<0.001
Days of ICU stay	7.2 ± 9.6	13.7 ± 12.0	7.1 ± 9.5	*<0.001
Age older than 1 year	31,895 (52.9%)	567 (66.7%)	31,328 (52.7%)	*<0.001
Comorbidity				
Sepsis	13,915 (23.1%)	395 (46.5%)	13,520 (22.7%)	*<0.001
Congenital heart disease	11,521 (19.1%)	181 (21.3%)	11,340 (19.1%)	0.1
Hemato-oncological disease	3648 (6.0%)	120 (14.1%)	3528 (5.9%)	*<0.001
Primary renal disease and postrenal disease	2250 (3.7%)	165 (19.4%)	2085 (3.5%)	*<0.001
Requiring cardiovascular surgery	2498 (4.1%)	72 (8.5%)	2426 (4.1%)	*<0.001
Use of mechanical ventilation	28,222 (46.8%)	635 (74.7%)	27,587 (46.4%)	*<0.001
Use of ECMO	2198 (3.6%)	115 (13.5%)	2083 (3.5%)	*<0.001
Use of vasopressor	8359 (13.9%)	506 (59.5%)	7853 (13.2%)	*<0.001
Mortality	3915 (6.5%)	376 (44.2%)	3539 (5.9%)	*<0.001

Abbreviations: AKI, acute kidney injury; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.
*$P<0.05$.