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Incidence of acute kidney injury-associated mortality in hospitalized children: a systematic review and meta-analysis

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Abstract

Background Acute kidney injury (AKI) is a significant health concern in hospitalized children and is associated with increased mortality. However, the true burden of AKI-associated mortality in pediatric populations remains unclear.

Objective To determine the pooled incidence of mortality independently associated with AKI in hospitalized children globally.

Data sources Medline and Embase were searched for studies published by March 2024.

Study eligibility criteria The inclusion criteria encompassed observational studies involving hospitalized pediatric patients (< 18 years old) with AKI. Only studies that identified AKI as an independent risk factor for increased mortality in multivariate analysis were considered.

Study appraisal and synthesis methods Studies with at least 100 AKI patients were included in the meta-analysis. Two authors extracted data on the study and patients' characteristics and mortality across AKI stages and assessed the risk of bias. We used a random-effects meta-analysis to generate pooled estimates of mortality.

Results Analysis of 60 studies including 133,876 children with AKI revealed a pooled in-hospital mortality rate of 18.27% (95% CI: 14.89, 21.65). Mortality increased with AKI severity; 8.19% in stage 1, 13.44% in stage 2, and 27.78% in stage 3. Subgroup analyses showed no significant differences across geographical regions, income levels, or AKI definition criteria. The pooled post-discharge mortality rate was 6.84% (95% CI: 5.86, 7.82) in a 1–9-year follow-up period.

Conclusions This meta-analysis demonstrates a substantial global burden of AKI-associated mortality in hospitalized children, with higher mortality rates in more severe AKI stages. These findings highlight the critical need for early detection and intervention strategies in pediatric AKI management.

Clinical trial number Not applicable.

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Introduction

Acute kidney injury (AKI) poses a significant health concern for hospitalized children, leading to adverse outcomes and increased in-hospital and post-discharge mortality rates [1]. In efforts to standardize AKI diagnosis, several classification systems like KDIGO and RIFLE have been introduced to gain better insights into this condition and its effects on children. The lack of consensus on a universally accepted standardized definition for AKI in children has resulted in variations in its incidence and staging [2]. Furthermore, AKI has been significantly associated with short-term adverse outcomes, including prolonged hospital stays and in-hospital mortality [3]. Additionally, AKI has demonstrated links to long-term consequences such as hypertension, proteinuria, and chronic kidney disease in infants and children, potentially leading to post-discharge mortality. This highlights the necessity for comprehensive management strategies [4]. Nevertheless, irrespective of the setting of patients, mortality rates are proved to be higher among patients with AKI compared to those without AKI [1] and there is an ongoing investigation into the incidence of AKI-associated mortality in different pediatric populations.

To devise effective interventions, it is crucial to comprehend the incidence of AKI-associated mortality in diverse groups of children. Studies have indicated that the occurrence of AKI varies, with rates ranging from 5 to 31% in non-critically ill hospitalized children and up to 55% in critically ill hospitalized children [5–8]. Moreover, the burden and causes of AKI vary worldwide, with different resource settings facing distinct challenges. Some studies show low and low-to-middle-income countries experience a higher incidence of AKI due to factors like contaminated water and endemic diseases, such as malaria [4]. In such settings, the mortality of AKI can be worse than high-income countries [4].

Despite the existing literature on AKI mortality, a knowledge gap remains regarding the true burden and mortality rates associated with AKI in children. A previous meta-analysis have reported mortality rates of 11% among hospitalized children with AKI, but these rates have not been statistically proven to be independently associated with AKI via multivariate analysis in many of the included studies [1]. Confounding factors and the complexity of critically ill children contribute to the challenges in attributing mortality solely to AKI. Therefore, our systematic review and meta-analysis aims to determine the overall rate of mortality that is directly linked to AKI in children on a global scale. By synthesizing available evidence, this study intends to enhance our understanding of the impact of AKI on pediatric patients.

Methods

Study design

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines [9] and was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO ID: CRD42024527413). To identify relevant studies, an extensive literature search was performed across Medline (via Pubmed) and Embase in March 18th 2024. In order to optimize search results, tailored search strategies were developed for each database, incorporating pertinent keywords and Medical Subject Headings (MeSH) terms directly related to acute kidney injury (AKI) in the pediatric population (Supplemental material 1). Language restrictions were avoided during the literature search process. Articles in languages other than English were translated using online services such as Doc Translator, and then have them reviewed by an expert translator fluent in both the original language and English to ensure accuracy. Additionally, to enrich our electronic search, we manually scrutinized the bibliographies of eligible studies that met our inclusion criteria.

Study selection

To generate pooled global estimates of AKI mortality, we established rigorous inclusion criteria for selecting relevant studies. Specifically, we only included cohort and cross-sectional studies that reported AKI-related mortality, given that they demonstrated an independent association between AKI and mortality through the application of multivariate analysis. We investigated mortality rates during hospitalization and after discharge, in the pediatric population aged below 18 years. To ensure methodological consistency and the integrity of our analysis, we implemented a series of exclusion criteria. Studies on adults aged over 18 years were excluded from consideration. Additionally, we omitted studies in the form of conference abstracts that did not provide sufficient information for a robust assessment of diagnostic criteria and risk of bias. To achieve an objective screening process, eight authors in pairs independently assessed the titles and abstracts of the electronic records initially. Subsequently, the same authors meticulously evaluated the full texts of relevant articles to determine the final selection of studies for incorporation into our review. In the event of any disagreements between the two authors, a collaborative discussion was undertaken to reach a consensus.

This methodological approach guarantees the quality and reliability of our pooled estimates of AKI mortality in the global pediatric population.

Data extraction and quality assessment

The full set of records was divided into four equal parts, with each part independently screened (title/abstract and full-text) by a pair of authors. Each pair reviewed their assigned portion, discussing and resolving any discrepancies between them. Any unresolved conflicts were addressed with the involvement of a third reviewer (MY). This division and screening process ensured that all records were reviewed independently by at least two authors, as recommended by the PRISMA guidelines, while accommodating the high volume of records.

The data extracted included the first author's name, year of publication, country, data gathering period, study design, clinical setting (e.g., intensive care unit, cardiac surgery, etc.), participants' age, sample size, number of children with AKI and its severity, in-hospital and post-discharge mortality number in AKI patients among each stage, AKI criteria and definition, and follow-up duration. We also extracted data indicating countries' development and overall health status including gross domestic income per capita (GDP) [10], % GDP spent on total health expenditure [11], and maternal mortality ratio (MMR) [12] defined as deaths due to complications from pregnancy or childbirth per 100,000 live births.

Based on KDIGO criteria, we equaled the AKI stages in all studies into 3 stages. For RIFLE, pRIFLE, and nRIFLE, "Risk", "Injury", and "Failure", were considered equivalent to KDIGO stage 1, stage 2, and stage 3, respectively. Since many studies had categorized AKI with merged stages, we reported stage-1 and 2, and stage-2 and 3 together for these studies. To assess the risk of bias in the included studies, we utilized the National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [13].

Statistical analysis

All statistical analyses were conducted using the STATA 18.0 statistical program. To calculate the incidence of mortality among hospitalized patients with AKI, we employed the "meta" package with the random-effect model and reported a pooled incidence with a 95% confidence interval (95% CI). Statistical heterogeneity was assessed using I^2 and Chi-square tests. To explore the potential sources of heterogeneity, we performed subgroup analyses as per severity of AKI, clinical setting, study design, and economic groups of countries classified by World Bank.

To better understand and interpret the results with and without small-study effects on the incidence of AKI-associated mortality, we conducted meta-analyses on studies of any sample size and separately on studies with a minimum of 100 AKI patients. Our findings primarily emphasize the results from the latter group, which are presented in the manuscript. For interested readers, the supplementary material includes a table providing subgroup analysis and meta-regressions that incorporate studies without excluding studies with smaller sample sizes.

Meta-regressions were performed to assess the effects of gross domestic product (GDP) per capita in the year 2022 and % of GDP spent on health expenditure (the year 2020), and maternal mortality ratio (2000–2020) on AKI-associated mortality.

Since only five included studies assessed post-discharge mortality, subgroup analysis and meta-regression was not applicable for post-discharge mortality.

Results

Study selection and characteristics of the included studies

We identified 26,797 records from electronic databases. After screening 363 full-text articles, 96 studies were included in this systematic review [3, 14–108] (Fig. 1). The meta-analysis data comprised 96 in-hospital and 5 post-discharge mortality observations. These studies, from over 24 countries, enrolled a total of 135,448 hospitalized children with AKI. All of these studies reported mortality, which was confirmed to be independently associated with AKI. The characteristics of the included studies are reported in Table 1.

Among 101 observations, 13 reported AKI in children with prematurity-related outcomes, 14 with infections, 9 with cardiac surgery, 7 with non-cardiac surgery, 6 with sepsis/septic shock, 5 with ECMO, 33 with mixed conditions, and 14 with miscellaneous conditions. Twenty-seven of the studies were prospective. The geographical distribution of the studies was as follows: 49 from the Region of the Americas (AMR), 15 from the Western Pacific Region (WPR), 12 from the European Region (EUR), 8 from the African Region (AFR), 7 from the South-East Asia Region (SEAR), and 6 from the Eastern Mediterranean Region (EMR). The remaining studies were multinational. Thirty-eight studies included urine output in their AKI diagnostic criteria, and 33 studies enrolled exclusively neonates.

Risk of bias assessment

In the quality control section, it was noted that the majority of studies did not provide justification for the sample size (item 5). Moreover, the blinding status of the outcome observer was not a concern for causing bias since the outcome measured was mortality (item 12). The proportion of patients lost to follow-up could not be determined or was not reported in some studies (item 13). Most studies exhibited a low risk of bias in other domains (Table 2).

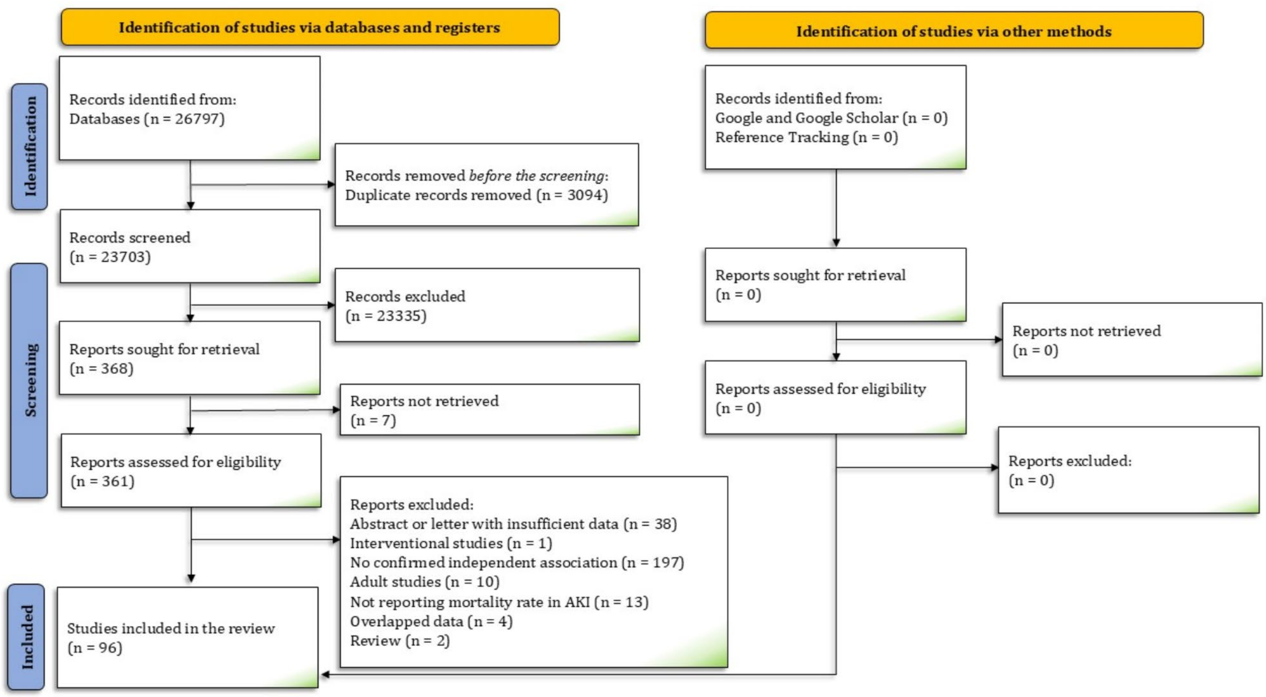

Fig. 1 The PRISMA flow diagram depicts the flow of the study selection process through the different phases of the present systematic review

Meta-analysis of the AKI-associated in-hospital and post-discharge mortality

Since the meta-analysis was conducted using a random-effects model, small studies ($n < 100$) were assigned weights comparable to larger studies ($n \geq 100$), leading to a pronounced small-study effect (Supplementary Fig. 1). To provide more robust and generalizable estimates of AKI-associated mortality across diverse patient- and country-level characteristics, we excluded studies with fewer than 100 AKI patients in the main meta-analysis. For comparison, the pooled AKI-associated in-hospital mortality, including small studies ($n < 100$), is shown in Supplementary Fig. 2.

The pooled incidence of AKI-associated in-hospital mortality (60 studies, 133876 participants) was 18.27% (95% CI: 14.89, 21.65) (Fig. 2). Using a KDIGO-equivalent AKI definition, the pooled AKI-associated mortality rate among patients with AKI stage 1, stage 2, and stage 3 was 8.19% (95% CI: 5.65, 10.73), 13.44% (95% CI: 8.69, 18.19), and 27.78% (95% CI: 21.82, 33.74), respectively, as depicted in Figs. 3, 4 and 5. Some studies reported AKI in merged staging of 1 to 2, and 2 to 3. Pooled mortality in AKI stage 1 to 2 and AKI stage 2 to 3 was 12.54% (95% CI: 8.05, 17.02) and 23.50% (95% CI: 18.62, 28.39), respectively (Supplementary Figs. 3–4). We observed significant heterogeneity in the overall in-hospital mortality pooled estimate ($I^2 = 99.84\%$). Considering that we pooled data from studies with diverse sample sizes, clinical settings, and severities of AKI, some heterogeneity was expected. To explore potential sources of heterogeneity, we performed subgroup analyses and meta-regressions, as reported in Table 3. Compared to AKI stage 1, the mortality rate was significantly higher in AKI stage 3 (meta-regression coefficient = 0.19 [95% CI: 0.12, 0.25]; $p < 0.001$), and from AKI stage 2 to stage 3 (meta-regression coefficient = 0.15 [95% CI: 0.09, 0.20]; $p < 0.001$). The pooled mortality rates were 21.81% (95% CI: 16.84, 80.75) for neonates and 16.56% (95% CI: 12.37, 20.75) for older children. Thirty-nine studies used only a serum creatinine-based definition for AKI, reporting a pooled mortality rate of 18.19% (95% CI: 14.08, 22.30). In comparison, 18 studies using both urine output and serum creatinine-based criteria reported a mortality rate of 17.31% (95% CI: 11.96, 22.66). No differences in the pooled incidence of mortality were observed between prospective and retrospective studies, nor among different geographical regions or countries with different income levels (Fig. 6). AKI-associated mortality rates using KDIGO/mKDIGO and pRIFLE/RIFLE/nRIFLE criteria were 16.76% (95% CI: 13.01, 20.51) and 22.81% (95% CI: 17.46, 33.94), respectively. Meta-regression showed no significant difference (meta-regression coefficient = 0.06 [95% CI: -0.07, 0.19]; $p = 0.634$). The median sampling period was not significantly associated with the incidence of AKI-associated mortality (meta-regression coefficient = -0.007 [95% CI: -0.014, 0.0004]; $p = 0.065$). A meta-regression assessing the effects of GDP, its proportion spent on health, and maternal mortality rate (Supplementary Fig. 5)

Table 1 Summary characteristics of the included studies

Author, year	Country	Study Design	Etioology	Neonates/ Infants & Children	Ad-mis-sion sites	Aki Criteria	AKI (*n*)	Mortality (Overall)	Mortality Assessment
Adegboyega, 2022 [109]	USA	Retrospective	LBW	Only neonate	NICU	KDIGO	116	21	In-hospital
Ahn, 2024 [108]	USA	Retrospective	Hypoxic ischemic encephalopathy	Only neonate	NICU	KDIGO	64	10	In-hospital
Akcan-Arikan, 2007 [107]	USA	Prospective	Mixed	Non-neonate	PICU	pRIFLE	123	18	In-hospital
Al Gharabieh, 2023 [106]	USA	retrospective	Sepsis	Only neonate	NICU	KDIGO	16	7	In-hospital
Algadeeb, 2021 [104]	Saudi Arabia	Retrospective	Mixed	Only neonate	NICU	KDIGO	396	122	In-hospital
Al-Mouqdad, 2021 [105]	Saudi Arabia	Retrospective	LBW	Only neonate	NICU	KDIGO	268	79	In-hospital
Alobaidi, 2019 [103]	Canada	Retrospective	Mixed	Non-neonate	PICU	KDIGO	308	21	In-hospital
Alvarez-Hernandez, 2015 [102]	Mexico	Retrospective	Infection	Neonate and non-neonate	PICU, NICU and ward	NR	14	7	In-hospital
Arruda Moraes, 2023 [15]	Brazil	Retrospective	LBW	Only neonate	NICU	KDIGO	61	22	In-hospital
Bakkaloglu, 2024 [101]	Turkey	Retrospective	Crush-AKI	Neonate and non-neonate	Mix	oligo/anuria or serum creatinine level > 2 times the upper limit of age- and sex-referenced normal levels	314	20	In-hospital
Basu, 2021 [100]	multinational	Prospective	Sepsis/Infectious	Non-neonate	PICU	KDIGO	307	37	In-hospital
Bauer, 2023 [99]	USA	Retrospective	Hematopoietic cell transplantation	Non-neonate	PICU and ward	KDIGO	186	47	In-hospital
Bezerra, 2013 [91]	Brazil	Retrospective	Infectious	Only neonate	NICU	pRIFLE	51	19	In-hospital
Bradshaw, 2019 [98]	USA	Retrospective	Diarrheal illness	Neonate and non-neonate	PICU, NICU and ward	ICD-9-CM	616	4	in-hospital
Chen, 2023 [97]	Taiwan	Retrospective	Prematurity	Only neonate	NICU	mKDIGO	204	55	In-hospital
Coggins, 2021 [96]	USA	Retrospective	Sepsis	Only neonate	NICU	mKDIGO	56	17	In-hospital
Conroy, 2019 [95]	Uganda	Prospective	Malaria	Non-neonate	PICU	KDIGO	168	20	In-hospital and Post-discharge
Conroy, 2022 [94]	Uganda	retrospective	Blackwater fever + Malaria	Non-neonate	PICU and ward	KDIGO	495	20	In-hospital
Cui, 2022 [93]	China	Retrospective	Non-Cardiac surgery	Only neonate	NICU	KDIGO	28	9	In-hospital

Table 1 (continued)

Author, year	Country	Study Design	Etioology	Neonates/ Infants & Children	Ad-mis-sion sites	Aki Criteria	AKI (*n*)	Mortality (Overall)	Mortality Assessment
Dang, 2022 [92]	China	Retrospective	Mixed	Non-neonate	PICU and ward	KDIGO	419	30	In-hospital
Deep, 2018 [90]	UK	Prospective	Septic shock	Non-neonate	PICU	KDIGO	31	9	In-hospital
Demiroz, 2024 [89]	Turkey	Retrospective	Liver transplant	Non-neonate	PICU and ward	KDIGO	60	27	In-hospital
Dos Santos El Halal, 2013 [88]	Brazil	Prospective	Cardiac surgery	Non-neonate	PICU	pRIFLE	38	7	In-hospital
Downes, 2017 [87]	USA	Retrospective	Antibiotic associ-ated AKI	Non-neonate	PICU	KDIGO	157	7	In-hospital
El-gendy,2023 [85]	USA	retrospective	Diaphragmatic hernia	Only neonate	NICU	ICD9,10	445	239	In-hospital
Elgendy, 2021 [84]	USA	Retrospective	LBW	Only neonate	NICU	NR	19,603	6872	In-hospital
Elgendy, 2024 [86]	USA	retrospective	Hypoxic-ischemic encephalopathy	Only neonate	NICU	ICD9,10	2719	786	In-hospital
Esmaeili, 2024 [83]	IRAN	Retrospective	Cardiac surgery	Non-neonate	PICU	KDIGO	58	16	In-hospital
Fitzgerald, 2016 [82]	multinational	Prospective	Sepsis/Infectious	Non-neonate	PICU	KDIGO	102	53	In-hospital
Fleming, 2016 [81]	milticenter	Retrospective	ECMO	Neonate and non-neonate	PICU and NICU	KDIGO	615	311	In-hospital
Gil-Ruiz, 2014 [80]	Spain	Retrospective	Cardiac surgery	Non-neonate	PICU	pRIFLE	107	16	In-hospital
Hasson, 2024 [79]	USA	retrospective	Cardiac surgery	Only neonate	NICU	mKDIGO	205	18	In-hospital
Hessey, 2018 [78]	Canada	Retrospective	Non-Cardiac surgery	Non-neonate	PICU	KDIGO	355	34	Post-discharge
Hingorani, 2021 [77]	USA	Prospective	LBW	Only neonate	NICU	KDIGO	350	45	In-hospital
Hirabayas-hi, 2022 [76]	Japan	retrospective	Prematurity	Only neonate	NICU	nRIFLE	47	12	In-hospital
Hui, 2013 [75]	Hong Kong	Retrospective	Mixed	Non-neonate	PICU	pRIFLE	71	16	In-hospital
Iamwat, 2021 [74]	Thailand	Retrospective	ECMO	Neonate and non-neonate	PICU and NICU	KDIGO	10	7	In-hospital
Ibrahim, 2023 [73]	Nigeria	Retrospective	Malaria	Non-neonate	Mix	KDIGO	237	19	In-hospital
Imani, 2013 [72]	Uganda	Prospective	Infectious	Non-neonate	PICU	pRIFLE	272	68	In-hospital
Jetton, 2017 [71]	multinational	Retrospective	Mixed	Only neonate	NICU	KDIGO	605	59	In-hospital
Kaddourah, 2017 [70]	Asia, AU, EU, NA	Prospective	Mixed	Non-neonate	PICU	KDIGO	1261	82	In-hospital
Kari, 2017 [14]	Saudi Arabia	Prospective	Mixed	Non-neonate	PICU	KDIGO	511	99	In-hospital
Kasililika, 2020 [69]	Tanzania	Prospective	Mixed	Non-neonate	PICU	KDIGO	53	19	In-hospital

Table 1 (continued)

Author, year	Country	Study Design	Etioology	Neonates/ Infants & Children	Admission sites	Aki Criteria	AKI (*n*)	Mortality (Overall)	Mortality Assessment
Khatana, 2023 [68]	USA	retrospective	Severe Sepsis	Non-neonate	not specified	ICD	45,463	9005	In-hospital
Kriplani, 2016 [67]	USA	Retrospective	Mixed	Non-neonate	PICU	KDIGO	28	8	In-hospital
Kuai, 2022 [17]	China	Prospective	Mixed	Non-neonate	PICU	KDIGO	22	14	In-hospital
Kuai, 2022 [66]	China	Prospective	Mixed	Non-neonate	PICU	KDIGO	247	47	In-hospital
Kumar Sethi, 2024 [65]	multinational	prospective	Continuous kidney replacement therapy	Non-neonate	PICU	KDIGO	308	99	In-hospital
Lazarovits, 2023 [64]	Israel	retrospective	Prematurity	Only neonate	NICU	NIDDK	32	13	In-hospital
Leow, 2022 [63]	Singapore	Retrospective	Acute respiratory distress syndrome	Non-neonate	PICU	KDIGO	64	41	In-hospital
Lobasso, 2021 [62]	USA	retrospective	Cardiac surgery	Neonate and non-neonate	PICU/ NICU	KDIGO	701	80	In-hospital
Lu, 2022 [61]	China	retrospective	Cardiac surgery	Only neonate	CICU, NICU	KDIGO	131	38	In-hospital
Medar, 2015 [60]	USA	Retrospective	Heart failure	Non-neonate	Not specified	pRIFLE	44	4	In-hospital
Mengqi, 2020 [59]	China	Retrospective	Malignancy	Non-neonate	Not specified	KDIGO	1657	90	in-hospital
Moffett, 2022 [58]	USA	Retrospective	Mixed	Non-neonate	Not specified	KDIGO	10,246	590	In-hospital
Mohamed, 2023 [57]	USA	retrospective	Non-Cardiac surgery	Only neonate	NICU	ICD-9 and 10	2625	431	In-hospital
Morgan, 2013 [56]	Canada	Prospective	Cardiac surgery	Only neonate	NICU	AKIN	163	10	Post-discharge
Murdeshwar, 2023 [55]	India	ambispective	Mixed	Non-neonate	PICU/ Ward	ADQI	200	37	In-hospital
Nakwan, 2016 [54]	Thailand	Retrospective	Pulmonary hypertension	Only neonate	NICU	A serum creatinine level of 41.5 mg/dL on two separate occasions at least 12 h apart, while maternal kidney function was normal	31	22	In-hospital
Namazzi, 2022 [53]	Uganda	Prospective	Malaria	Non-neonate	Not specified	KDIGO	271	37	In-hospital and Post-discharge
Özçakar, 2009 [52]	Turkey	Retrospective	Mixed	Non-neonate	Not specified	AKIN	100	33	In-hospital

Table 1 (continued)

Author, year	Country	Study Design	Etioology	Neonates/ Infants & Children	Ad-mis-sion sites	Aki Criteria	AKI (*n*)	Mortality (Overall)	Mortality Assessment
Patel, 2023 [51]	USA	retrospective	Mixed	Neonate and non-neonate	PICU/NICU/ward	KDIGO	528	138	In-hospital
Pedersen, 2008 [50]	Denmark	Retrospective	Cardiac surgery	Neonate and non-neonate	PICU and NICU	need for dialysis after surgery	130	26	In-hospital
Pillon, 2019 [49]	Italy	Retrospective	Malignancy	Non-neonate	PICU	KDIGO	17	12	In-hospital
Piyapha-nee, 2020 [48]	Thailand	Retrospective	Mixed	Non-neonate	PICU	KDIGO	169	53	in-hospital
Plumb, 2023 [47]	UK	retrospective	Mixed	Only neonate	NM	KDIGO	712	59	In-hospital
Plumb, 2023 [47]	UK	retrospective	Mixed	Non-neonate	NM	KDIGO	4900	150	In-hospital
Prodhan, 2012 [46]	USA	Retrospective	Trauma	Non-neonate	PICU	pRIFLE	52	10	In-hospital
Raina, 2022 [45]	USA	retrospective	Covid/infectious	Non-neonate	PICU	KDIGO	274	21	In-hospital
Raina, 2023 [44]	USA	retrospective	Mixed	Neonate and non-neonate	NM	ICD-10	2424	11	In-hospital
Robinson, 2021 [43]	Canada	Retrospective	Mixed	Neonate and non-neonate	Not speci-fied	ICD-9 and 10	1688	113	Post-discharge
Rozmiarek, 2004 [42]	USA	Retrospective	Diaphragmatic hernia	Only neonate	NICU	NR	14	10	In-hospital
Sainathan, 2022 [41]	USA	Retrospective	LBW	Non-neonate	Not speci-fied	ICD-10	98	8	In-hospital
Sainathan, 2022 [41]	USA	Retrospective	Fontan Operation	Non-neonate	PICU and ward	NR	97	8	In-hospital
Sanchez-Pinto, 2015 [40]	USA	Retrospective	Mixed	Non-neonate	PICU	KDIGO	974	246	in-hospital
Schneider, 2010 [39]	USA	Retrospective	Mixed	Non-neonate	PICU	pRIFLE	339	104	In-hospital
Schueller, 2017 [38]	USA	Retrospective	ECMO	Only neonate	NICU	KDIGO	15	7	In-hospital
Selewski, 2014 [37]	USA	Retrospective	Mixed	Non-neonate	PICU and CICU	KDIGO	737	83	In-hospital
Selewski, 2023 [36]	multinational	prospective	mixed	Non-neonate	PICU	KDIGO	1258	78	In-hospital
Shalaby, 2018 [35]	Saudi Arabia	Prospective	Mixed	Only neonate	NICU	nKDIGO	120	34	In-hospital
Sharma, 2022 [34]	India	Retrospective	Covid/infectious	Non-neonate	Not speci-fied	NR	12	9	In-hospital
Singh, 2022 [33]	India	Prospective	Mixed	Non-neonate	PICU	KDIGO	44	14	In-hospital
Slagle, 2021 [32]	USA	Prospective	Non-Cardiac surgery	Only neonate	NICU	mKDIGO	33	8	In-hospital

Table 1 (continued)

Author, year	Country	Study Design	Etioology	Neonates/ Infants & Children	Admission sites	Aki Criteria	AKI (*n*)	Mortality (Overall)	Mortality Assessment
Smith, 2009 [31]	USA	Retrospective	ECMO	Neonate and non-neonate	PICU and NICU	pRIFLE	32	23	In-hospital
Srinivasan, 2018 [30]	USA	Retrospective	LBW	Only neonate	NICU	mAKIN	89	25	In-hospital
Stanski, 2023 [29]	USA	Prospective	Mixed	Non-neonate	PICU	KDIGO	77	14	In-hospital
Starr, 2020 [28]	USA	Prospective	septic shock	Non-neonate	PICU	KDIGO	176	27	In-hospital
Stojanović, 2017 [27]	Serbia	Retrospective	LBW	Only neonate	NICU	mAKIN	57	35	In-hospital
Umapathi, 2020 [26]	USA	Retrospective	Drowning	Non-neonate	PICU and ward	NR	752	403	In-hospital
Üstün, 2021 [25]	Turkey	Retrospective	LBW	Only neonate	NICU	KDIGO	102	34	In-hospital
Varadarajan, 2022 [24]	India	Prospective	Multisystem Inflammatory syndrome	Non-neonate	PICU and ward	KDIGO	34	22	In-hospital
Vincent, 2023 [23]	USA	Retrospective	Mixed	Only neonate	NICU	KDIGO	100	14	In-hospital
Wang, 2022 [22]	China	Retrospective	Metabolic Acidosis	Non-neonate	PICU and SICU (Surgical ICU)	pROCK	181	22	In-hospital
Wei, 2021 [21]	China	Retrospective	Mixed	Non-neonate	PICU	pROCK	257	32	In-hospital
Wingert, 2021 [20]	USA	Retrospective	Non-Cardiac surgery	Neonate and non-neonate	PICU, NICU and ward	KDIGO	288	23	in-hospital
Xu, 2018 [18]	China	Retrospective	Mixed	Non-neonate	PICU and ward	KDIGO	19,908	842	In-hospital
Xu, 2023 [19]	China	Retrospective	Mixed	Only neonate	NICU	Cys-C based criteria	6336	96	In-hospital
Zwiers, 2013 [16]	Netherlands	Prospective	ECMO	Only neonate	NICU	RIFLE	153	43	In-hospital

ADQI: Acute Dialysis Quality Initiative; AKIN: Acute Kidney Injury Network; CICU: Cardiac Intensive Care Unit; Cys-C: Cystatin C; ECMO: Extracorporeal Membrane Oxygenation; ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; KDIGO: Kidney Disease: Improving Global Outcomes; LBW: Low Birth Weight; mAKIN: Modified Acute Kidney Injury Network; NICU: Neonatal Intensive Care Unit; NR: Not Reported; nKDIGO: Neonatal Kidney Disease: Improving Global Outcomes; PICU: Pediatric Intensive Care Unit; pRIFLE: Pediatric Risk, Injury, Failure, Loss, End-Stage Renal Disease; pROCK: Pediatric Reference Operative Check for Kidney Dysfunction; SICU: Surgical Intensive Care Unit

revealed no significant associations with AKI mortality rate ($p = 0.491$, $p = 0.662$, and $p = 0.308$, respectively). The pooled post-discharge mortality rate associated with AKI (from 5 studies including 2,556 participants) was 6.84% (95% CI: 5.86, 7.82) with a median follow-up ranging from 1 to 9 years, as shown in Fig. 7. Subgroup analyses and meta-regressions for all studies including the ones with less than 100 AKI patients are presented in Supplementary Table 1.

Discussion

This meta-analysis, encompassing 60 studies and 133,876 hospitalized children with AKI, reveals a substantial global burden of mortality. The pooled in-hospital mortality rate was 18.27% (95% CI: 14.89, 21.65) among studies with at least 100 AKI patients, increasing from 8.19% in stage 1 to 27.78% in stage 3. Subgroup analyses showed no significant differences across geographical regions, income levels, or AKI definition criteria. Meta-regression

Table 2 Risk of bias assessment by NHLBI tool in included studies

Study	Item 1	Item 2	Item 3	Item 4a	Item 4b	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14
Adegboyega, 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Ahn, 2024	Yes	Yes	CD	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Akcan-Arikan, 2007	Yes	No	CD	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	NR	Yes
Al Gharabieh, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Algadeeb, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Al-Mouqdad, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Alobaidi, 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes
Alvarez-Hernandez, 2015	Yes	Yes	CD	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Arruda Moraes, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Bakkaloglu, 2024	Yes	Yes	CD	Yes	CD	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	NR	Yes
Basu, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Bauer, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Bradshaw, 2019	Yes	Yes	Yes	Yes	CD	No	Yes	CD	NR	No	CD	Yes	NA	Yes	No
Chen, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Coggins, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Conroy, 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	Yes
Conroy, 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	CD	Yes	NA	Yes	Yes
Cui, 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Dang, 2022	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Bezerra, 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Deep, 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Demiroz, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Dos Santos El Halal, 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Downes, 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Elgendy, 2024	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	NR	CD	CD	Yes	NA	Yes	Yes
Elgendy,2023	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	NR	CD	CD	Yes	NA	Yes	Yes
Elgendy, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	NR	CD	CD	Yes	NA	Yes	Yes
Esmaeili, 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	CD	Yes	NA	Yes	Yes
Fitzgerald, 2016	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	CD	Yes	NA	Yes	Yes
Fleming, 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes
Gil-Ruiz, 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Hasson, 2024	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Hessey, 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Hingorani, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Hirabayashi, 2022	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	Yes
Hui, 2013	Yes	Yes	CD	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Iamwat, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Ibrahim, 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	CD	Yes	NA	Yes	Yes
Imani, 2013	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	Yes

Table 2 (continued)

Study	Item 1	Item 2	Item 3	Item 4a	Item 4b	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14
Jetton, 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Kaddourah, 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	CD	Yes	NA	Yes	Yes
Kari, 2017	Yes	Yes	CD	Yes	Yes	No	Yes	Yes	Yes	Yes	CD	Yes	NA	CD	Yes
Kasililika, 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Khatana, 2023	Yes	Yes	CD	Yes	Yes	No	Yes	CD	CD	CD	CD	Yes	NA	CD	Yes
Kriplani, 2016	Yes	Yes	CD	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	CD	Yes
Kuai, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Kuai, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Kumar Sethi, 2023	Yes	Yes	CD	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NA	CD	Yes
Leow, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Lobasso, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Lu, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Medar, 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	No	Yes	NA	Yes	No	CD	Yes
Mengqi, 2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Moffett, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Mohamed, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	No	Yes	NA	Yes	No	CD	Yes
Morgan, 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Murdeshwar, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Nakwan, 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes
Namazzi, 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Özçakar, 2009	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	Yes	Yes	NA	Yes	No	CD	Yes
Patel, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Pedersen, 2008	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Pillon, 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Piyaphanee, 2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	No	Yes
Plumb, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Prodhan, 2012	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	Yes	Yes	NA	Yes	No	CD	Yes
Raina, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Raina, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Robinson, 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes
Rozmiarek, 2004	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	No	Yes	NA	Yes	No	CD	Yes
Sainathan, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Sanchez-Pinto, 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Schneider, 2010	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Schueller, 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	CD	No	Yes	NA	Yes	No	CD	Yes
Selewski, 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Selewski, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Shalaby, 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes
Sharma, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes

Table 2 (continued)

Study	Item 1	Item 2	Item 3	Item 4a	Item 4b	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14
Singh, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Slagle, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	No	Yes	NA	Yes	No	Yes	Yes
Smith, 2009	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Srinivasan, 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Stanski, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	No	Yes
Starr, 2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	No	Yes
Stojanović, 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	CD	Yes	Yes	NA	Yes	No	CD	Yes
Umapathi, 2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Üstün, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	No	Yes
Varadarajan, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Vincent, 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Wang, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes
Wei, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Wingert, 2021	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Xu, 2023	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	NA	Yes	No	CD	Yes
Xu, 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	CD	Yes
Zwiers, 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes

CD, cannot determine; NA, Not applicable; NR, not reported

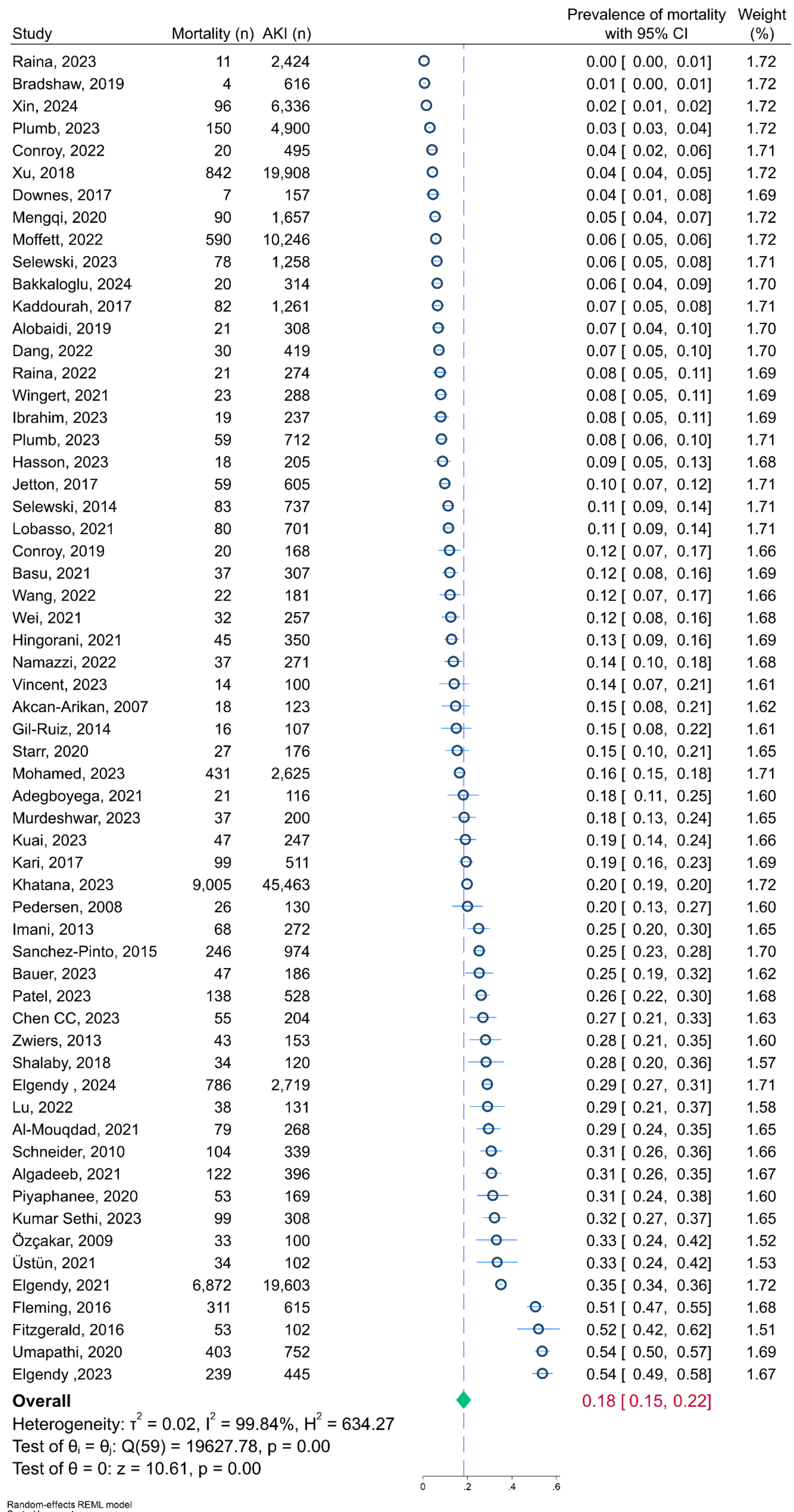

Fig. 2 The forest plot for the incidence of in-hospital mortality among hospitalized children with acute kidney injury

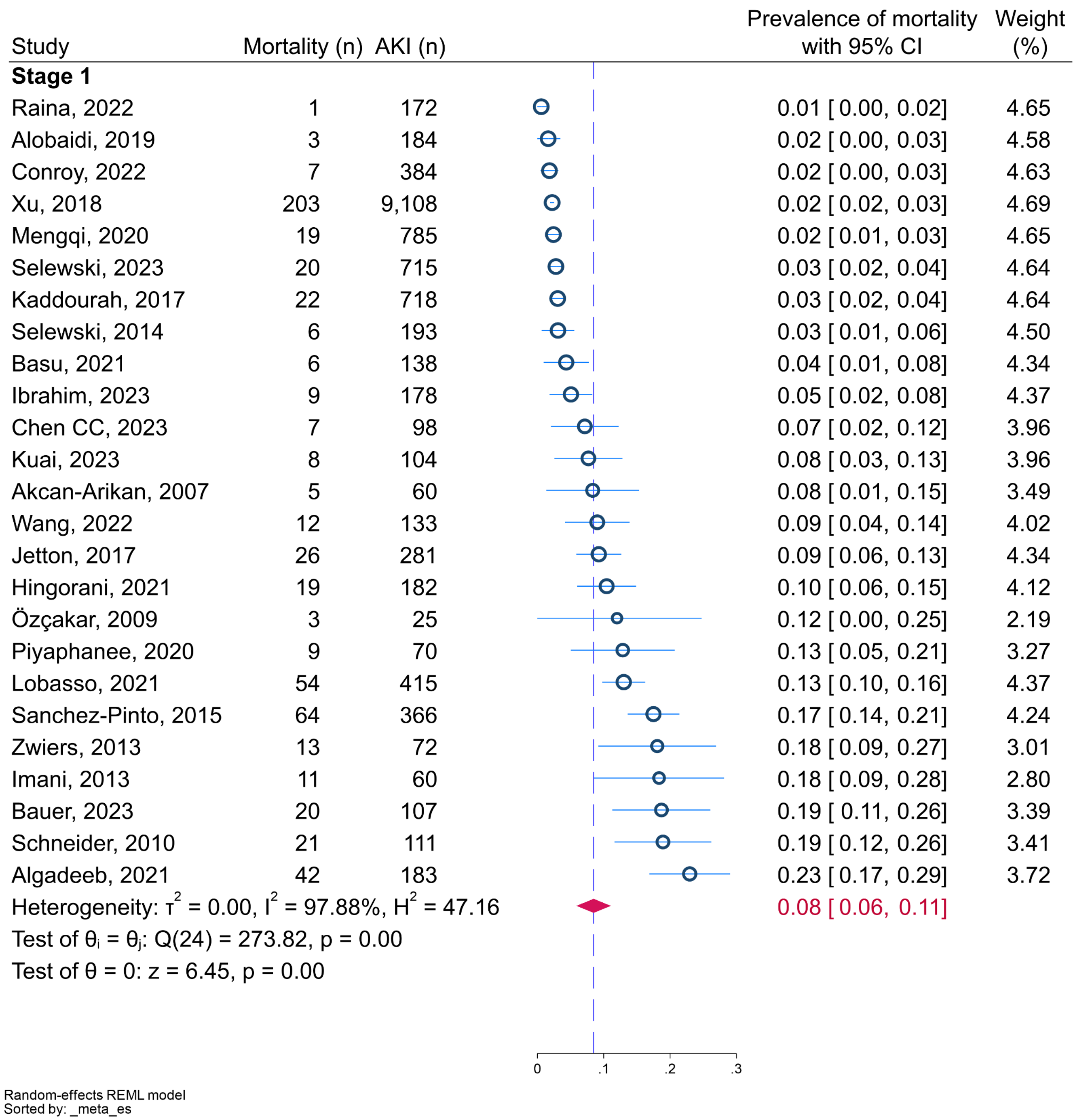

Fig. 3 The forest plot for the incidence of in-hospital mortality among hospitalized children with stage 1 acute kidney injury

analyses found no significant associations between AKI-associated mortality and factors such as GDP, healthcare expenditure, or maternal mortality ratio. The pooled post-discharge mortality rate was 6.84% (95% CI: 5.86, 7.82) in a 1–9-year follow-up period. These findings provide crucial insights into the global impact of pediatric AKI mortality and set the stage for discussing potential interventions and policy implications.

To our knowledge, this meta-analysis represents the most comprehensive systematic evaluation of AKI-associated mortality in the pediatric population to date. Our literature review revealed two prior meta-analyses. Notably, Susantitaphong et al.'s study [109], which searched the Medline database for 2004–2012, included 11 studies employing a KDIGO-equivalent definition of AKI and found a pooled all-cause mortality rate of 13.8% (95% CI, 8.8 to 21.0). However, that analysis lacked studies from low and lower-middle-income countries, limiting its global generalizability. Our study addresses these

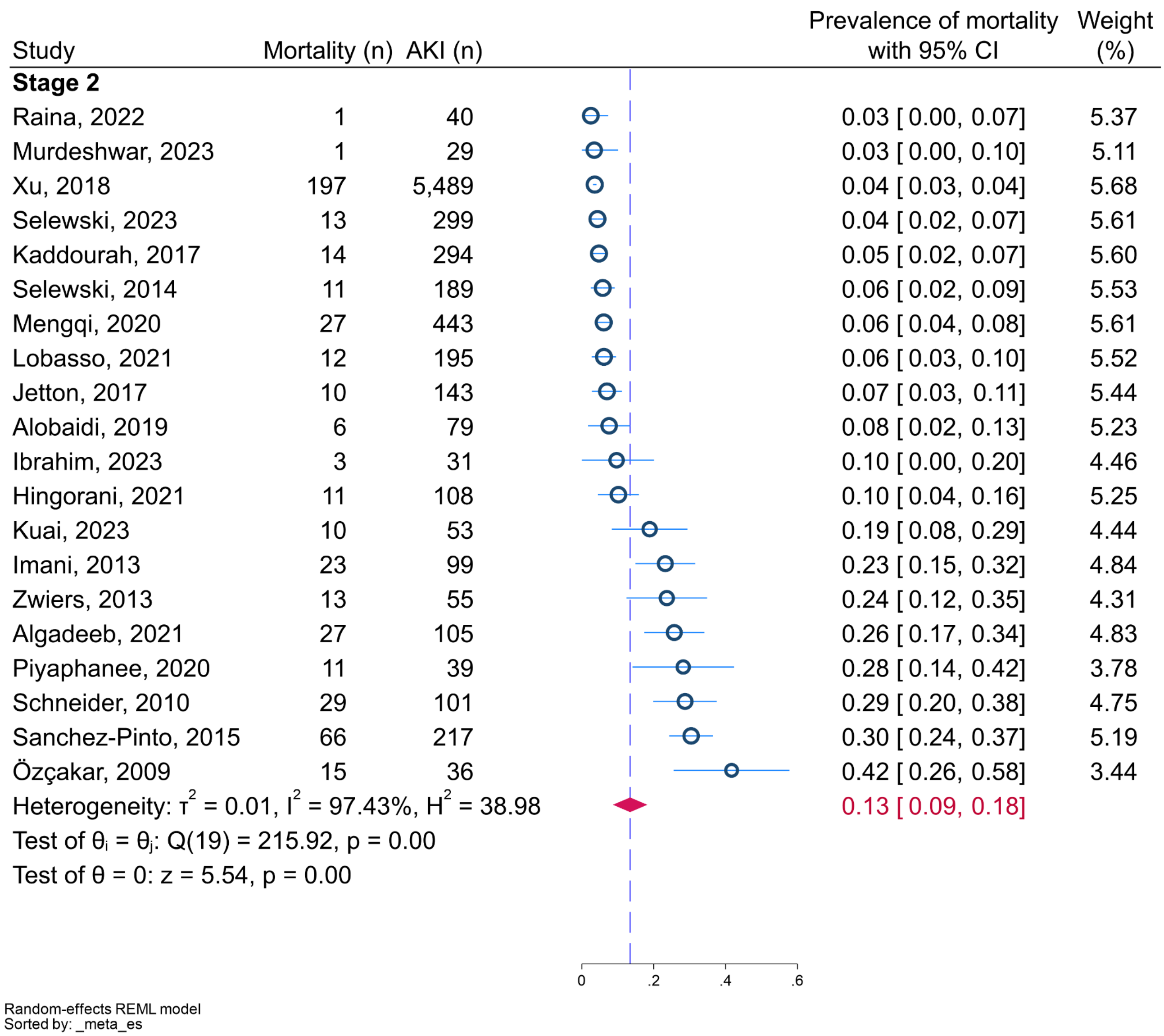

Fig. 4 The forest plot for the incidence of in-hospital mortality among hospitalized children with stage 2 acute kidney injury

limitations, providing a more inclusive and globally representative analysis of pediatric AKI mortality.

The second meta-analysis by Meena et al. [1] searched Medline, Embase, and Web of Sciences from March 2012 to January 2022. Analyzing 60 studies using KDIGO criteria and excluding neonates, they found a pooled AKI-associated all-cause hospital mortality of 11% (95% CI: 9–13). Like our study, they restricted analysis to studies with over 100 patients. However, their analysis was limited to studies using KDIGO criteria and excluded neonate patients, potentially limiting its scope and generalizability.

Our systematic review and meta-analysis demonstrate several key methodological strengths that address limitations of previous studies. First, the study rigorously addresses potential confounding factors by exclusively including studies that demonstrated an independent association between AKI and mortality through multivariate analysis. To mitigate the small study effect, the analysis focused on studies with over 100 patients. The comprehensive approach to assessing different AKI criteria, coupled with subgroup analyses, ensured the inclusion of all relevant studies and facilitated valuable comparisons. Notably, the inclusion of neonates and the subsequent age-based subgroup analysis allowed for a nuanced comparison of mortality incidence between neonates and older children, filling an important gap in the literature.

Our analysis demonstrates a clear association between AKI severity and mortality risk. The mortality rates increased progressively from stage 1 AKI to stage 3 AKI, highlighting the critical importance of early intervention

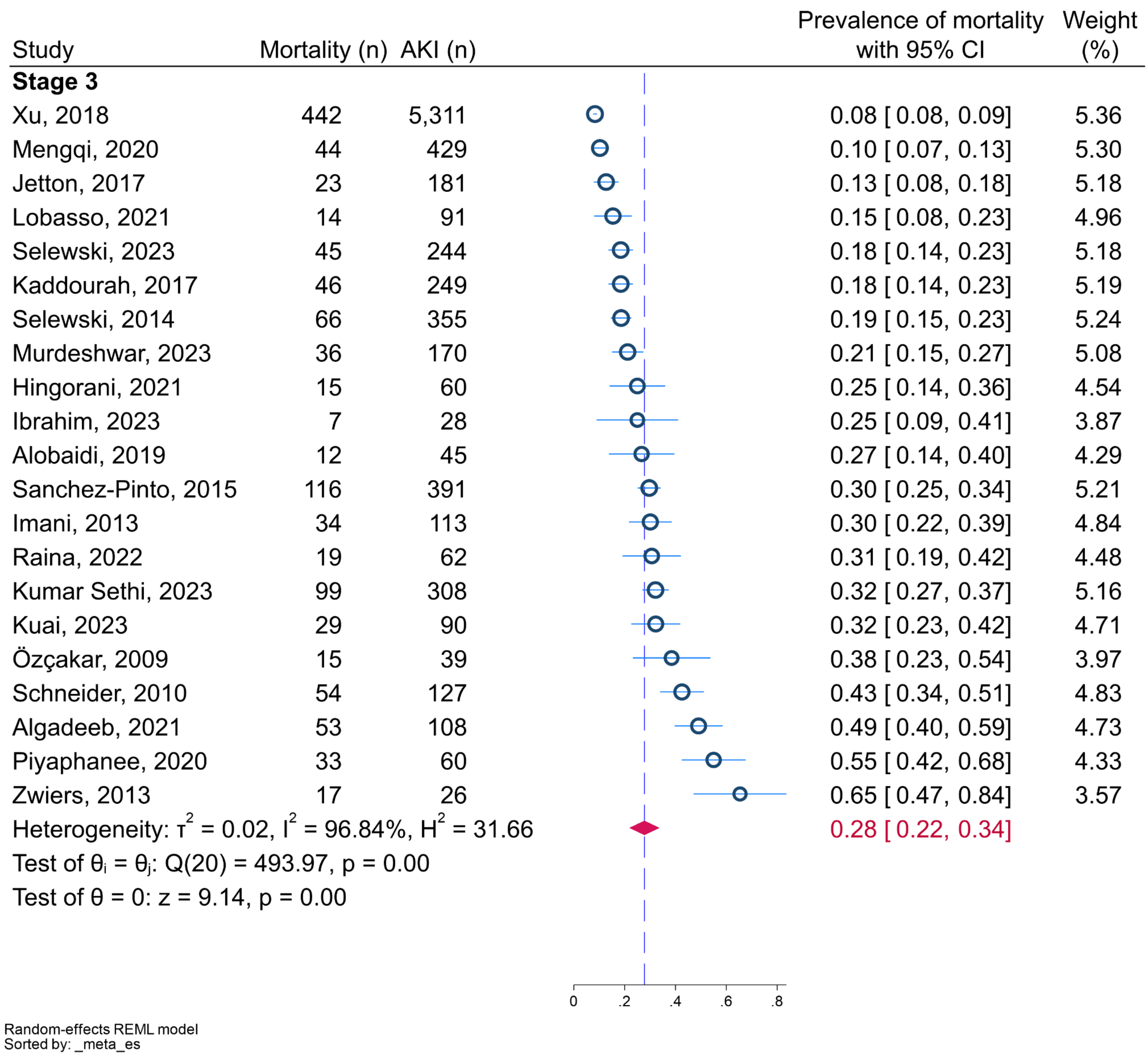

Fig. 5 The forest plot for the incidence of in-hospital mortality among hospitalized children with stage 3 acute kidney injury

to prevent AKI progression. This observation aligns with previous studies that have shown a correlation between AKI severity and adverse outcomes in both adult and pediatric populations [1, 106, 109, 110]. However, our findings highlight the limited availability of data on the utilization of renal replacement therapy (RRT) for severe AKI in pediatric populations. For example, the ASPIRE study reported a mortality rate of 32.1% in children with severe dialysis-dependent AKI, primarily treated with peritoneal dialysis [65]. Unfortunately, such data remain sparse, leaving a significant gap in understanding the specific role of RRT modalities in pediatric AKI mortality.

Our study found neonatal AKI-associated mortality of 21.81% (16.84 to 20.75%), lower than the 30% (27 to 33%) reported in Meena et al.'s meta-analysis of neonates [111]. Both rates exceed those for pediatric patients older than one month. However, our meta-regression couldn't establish a statistically significant difference in mortality between neonates and older pediatric patients. The high mortality in neonates with AKI likely reflects their vulnerability to severe illnesses and complications [111].

Our subgroup analyses showed no significant differences in mortality rates across geographical regions or income levels, contrasting with previous reports suggesting worse outcomes in low and middle-income countries [1, 112]. This indicates that AKI-associated mortality in children is a global challenge transcending economic boundaries, emphasizing the need for universal strategies. However, caution is warranted when interpreting results from low-income countries, as reliable

Table 3 Subgroup analysis and meta-regression for incidence of in-hospital AKI-associated mortality (excluding smaller studies with < 100 AKI patients)

Subgroups	Studies (participants)	Incidence of mortality (%), (95 CI)	Heterogeneity (I^2), *P*	Coefficient (95 CI)	Subgroup differences (*P*)
Severity of AKI					
AKI stage 1	26 (14843)	8.19 (5.65, 10.73)	97.8, < 0.001	Reference	
AKI stage 2	20 (8044)	13.44 (8.69, 18.19)	97.4, < 0.001	0.049 (-0.015, 0.113)	0.136
AKI stage 3	21 (8487)	27.78 (21.82, 33.74)	96.8, < 0.001	0.187 (0.123, 0.252)	< 0.001
AKI stage 1 and 2	20 (21780)	12.54 (8.05, 17.02)	99.3, < 0.001	0.040 (-0.023, 0.104)	0.211
AKI stage 2 and 3	28 (17040)	23.50 (18.62, 28.39)	98.2, < 0.001	0.146 (0.088, 0.205)	< 0.001
Age					
< 1 month	18 (35190)	22.81 (16.84, 20.75)	99.57, < 0.001	Reference	
> 1 month	34 (93070)	16.56 (12.37, 20.75)	99.78, < 0.001	-0.062 (-0.138, 0.013)	0.107
Study design					
Prospective study	15 (5627)	19.34 (13.66, 25.03)	97.67, < 0.001	Reference	
Retrospective study	44 (128049)	17.88 (13.70, 22.07)	99.90, < 0.001	-0.016 (-0.096, 0.064)	0.691
Country income classification (as per gross national income per capita)					
Low income	5 (1443)	12.31 (5.44, 19.17)	94.80, < 0.001	Reference	
Lower-middle income	1 (200)	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Upper-middle income	12 (29821)	15.65 (8.87, 22.44)	99.8, < 0.001	0.033 (-0.097, 0.163)	0.623
High-income	35 (97956)	18.88 (14.56, 23.20)	99.8, < 0.001	0.064 (-0.052, 0.181)	0.279
Region					
AFR	5 (1443)	12.31 (5.44, 19.17)	94.8, < 0.001	Reference	
AMR	28 (92635)	18.66 (13.12, 24.20)	99.9, < 0.001	0.062 (-0.060, 0.184)	0.320
EMR	4 (1295)	26.69 (21.01, 32.37)	80.3, < 0.001	0.145 (-0.025, 0.315)	0.095
EUR	8 (6518)	17.77 (9.41, 26.13)	98.5, < 0.001	0.054 (-0.090, 0.199)	0.462
SEAR	2 (369)	24.73 (12.13, 37.33)	87.7, < 0.001	0.124 (-0.089, 0.337)	0.255
WPR	9 (29340)	12.64 (6.35, 18.94)	99.8, < 0.001	0.004 (-0.137, 0.145)	0.956
AKI criteria					
KDIGO/mKDIGO	40 (50717)	16.76 (13.01, 20.51)	99.6, < 0.001	Reference	
RIFLE/pRIFLE/nRIFLE	5 (994)	22.81 (16.28, 29.34)	83.5, < 0.001	0.059 (-0.068, 0.186)	0.364
AKIN/mAKIN	1 (100)	Insufficient data	Insufficient data	Insufficient data	Insufficient data
ICD-9/ICD-10	6 (54292)	19.91 (4.05, 35.77)	100.0, < 0.001	0.030 (-0.085, 0.145)	0.610
Miscellaneous	8 (27773)	19.96 (8.15, 31.76)	99.8, < 0.001	0.031 (-0.071, 0.134)	0.549
AKI criteria based on					
SCr	39 (124124)	18.19 (14.08, 22.30)	99.9, < 0.001	Reference	
SCr + UOP	18 (6376)	17.31 (11.96, 22.66)	98.0, < 0.001	-0.008 (-0.079, 0.063)	0.831
Predisposing condition					
Prematurity-related outcomes	6 (20643)	25.88 (18.63, 33.13)	94.9, < 0.001	Reference	
Sepsis/septic shock	3 (45946)	16.06 (11.21, 20.90)	86.5, < 0.001	-0.102 (-0.279, 0.076)	0.262
Infections	8 (2435)	14.94 (4.02, 25.86)	99.4, < 0.001	-0.112 (-0.248, 0.024)	0.108
Cardiac surgery	5 (1274)	16.27 (9.48, 23.06)	90.0, < 0.001	-0.093 (-0.246, 0.061)	0.235
Non-cardiac surgery	3 (3358)	25.98 (-1.48, 53.44)	99.6, < 0.001	-0.001 (-0.178, 0.176)	0.992
ECMO	2 (768)	39.54 (17.53, 61.55)	96.6, < 0.001	0.137 (-0.069, 0.344)	0.193
Mixed etiology	25 (53178)	14.61 (10.55, 18.67)	99.8, < 0.001	-0.112 (-0.227, 0.003)	0.056
Miscellaneous [a]	8 (6274)	21.00 (9.03, 32.97)	99.4, < 0.001	-0.050 (-0.186, 0.086)	0.475

CI, confidence interval; AFR, African Region; AMR, Region of the Americas; EMR, Eastern Mediterranean Region; EUR, European Region; SEAR, South-East Asia Region; WHO, World Health Organization; WPR, Western Pacific Region; KDIGO, Kidney Disease: Improving Global Outcomes; mKDIGO, modified KDIGO; RIFLE, Risk, Injury, and Failure; and Loss; and End-stage kidney disease; pRIFLE, pediatric RIFLE; nRIFLE, neonatal RIFLE; AKIN, Acute Kidney Injury Network; mAKIN, modified AKIN; ICD, The International Classification of Diseases; SCr, serum creatinine; UOP, urine output; ECMO, extracorporeal membrane oxygenation

[a] Miscellaneous predisposing conditions include crush injury, hematopoietic cell transplantation, IV antibiotics, hypoxic-ischemic encephalopathy, continuous kidney replacement therapy, malignancy, drowning, and metabolic Acidosis

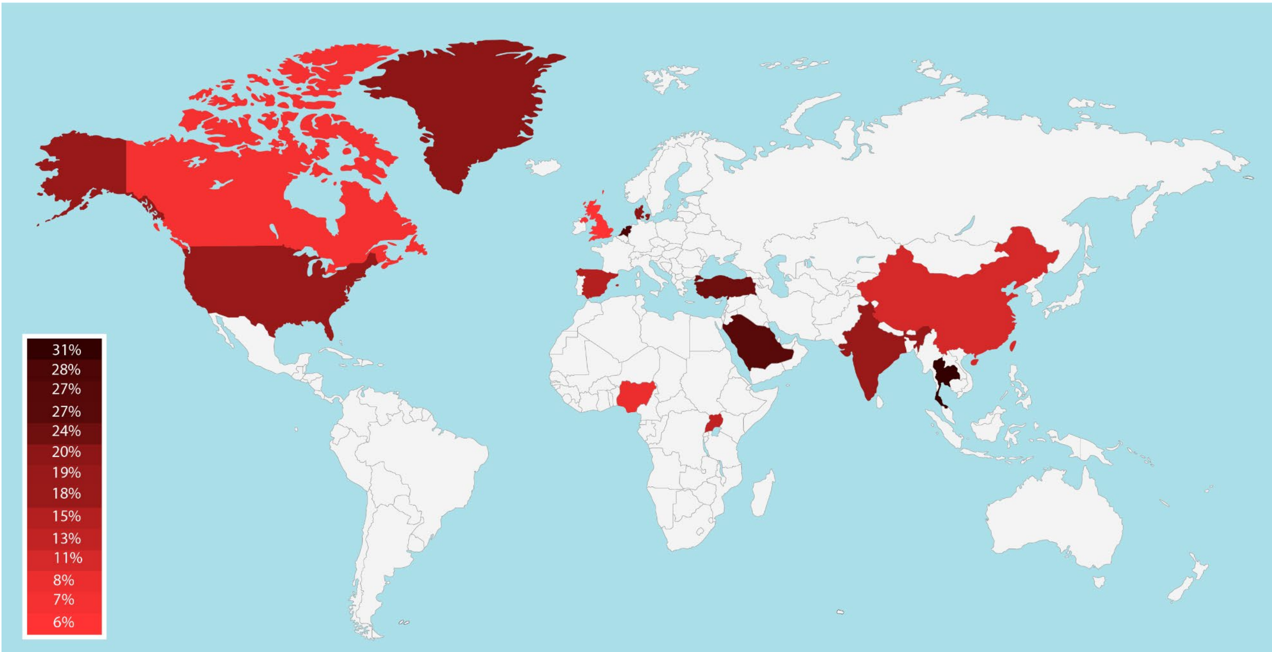

Fig. 6 The map illustrates the incidence of acute kidney injury-associated mortality among hospitalized children across various countries

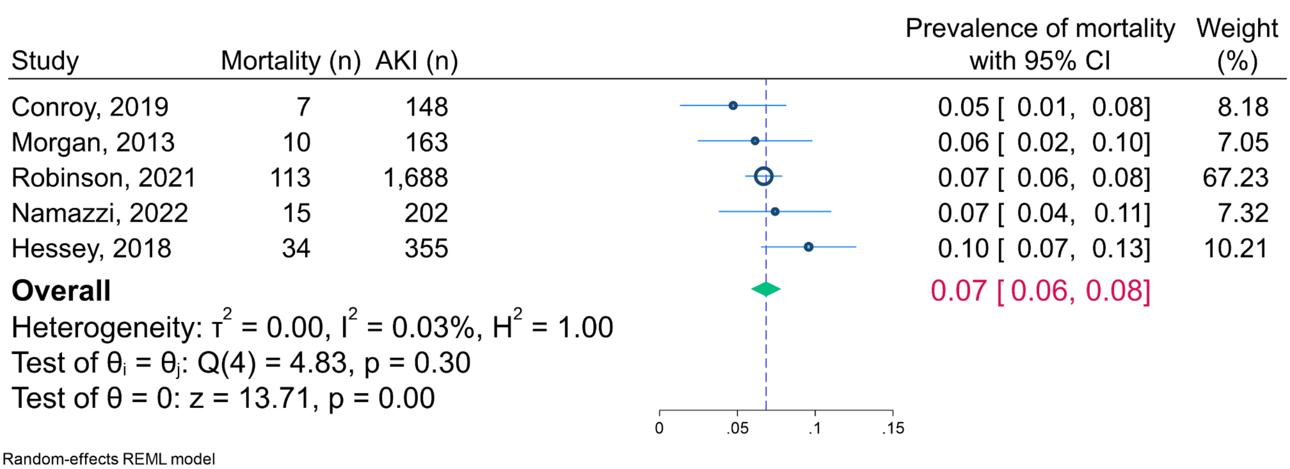

Fig. 7 The forest plot depicting the incidence of post-discharge mortality among hospitalized children with acute kidney injury

epidemiological data on childhood AKI is scarce in these regions [112], and the population samples may be subject to selection bias.

The criteria for defining AKI have evolved from RIFLE to pRIFLE, AKIN, KDIGO, and mKDIGO (neonates). The main differences between these criteria lie in their measurement methods (creatinine, estimated clearance, or GFR), time frames (48 h or 7 days), and use of absolute or relative changes. While these differences can affect the detection of mild AKI cases, the criteria generally align well in identifying more severe cases [61, 106, 113]. Our analysis of different AKI classification systems (KDIGO/mKDIGO vs. pRIFLE/RIFLE/nRIFLE) showed no significant difference in reported mortality rates, supporting the comparability of these widely used classification systems in pediatric populations.

The similar mortality rates observed between studies using only serum creatinine-based AKI definitions (18.19%), and those incorporating both urine output and serum creatinine criteria (17.31%) suggest that serum creatinine alone may be a sufficient marker for identifying high-risk AKI cases in children.

Furthermore, our findings of a 6.84% (95% CI: 5.86, 7.82) post-discharge mortality rate align with Knappett et al.'s meta-analysis, which reported a 4.4% (95% CI: 3.5–5.4%) six-month post-discharge mortality risk in low and low-middle Sociodemographic index (SDI) countries [114]. These results underscore the importance of long-term follow-up for children who have experienced AKI during hospitalization.

Limitations

This study has several limitations that should be considered when interpreting the results. Firstly, despite comprehensive subgroup analyses and meta-regressions, significant variability persisted among the included studies. This heterogeneity likely reflects differences in study populations, clinical settings, AKI definitions, and healthcare systems across countries. Secondly, limited data on post-discharge mortality restricted our ability to perform subgroup analyses and meta-regressions for this outcome, hindering a deeper understanding of long-term effects. Thirdly, our funnel plot analysis revealed asymmetry around the axis, raising potential concerns about publication bias. However, evidence suggests that conventional funnel plots may not accurately assess publication bias in proportional meta-analyses, as asymmetry can occur even in the absence of true bias [115, 116].

Additionally, by including only studies that reported an independent association between AKI and mortality, our analysis may have been biased toward studies involving higher mortality rates and/or sicker AKI cases. Our intention with this selection criteria was to ensure robust findings by focusing on studies that controlled for confounding variables, strengthening the causal interpretation of AKI-associated mortality. However, we acknowledge that this approach might inflate pooled estimates. Furthermore, while our study incorporated data from multiple countries, some regions—particularly low- and low-middle-income countries—were underrepresented. This underrepresentation limits the global generalizability of our findings and is particularly concerning given that mortality rates in these regions are likely higher.

Lastly, the inclusion of studies that demonstrated a statistical association between AKI and mortality, while methodologically robust, may have introduced selection bias toward studies with higher mortality rates or severe AKI cases. This approach ensures a focus on AKI-specific mortality but may not fully capture the broader spectrum of AKI-associated mortality. Future studies should address this gap by including a wider range of studies, regardless of statistical association, to provide a more comprehensive understanding of AKI-related mortality. Additionally, the heterogeneity in AKI etiologies, which often depend on the child's or neonate's age, adds complexity to interpreting the results. Future studies should aim to address these gaps by including diverse populations and systematically reporting long-term outcomes and regional disparities.

Conclusion

This comprehensive systematic review and meta-analysis provides valuable insights into the global incidence of acute kidney injury (AKI)-associated mortality in hospitalized children. Our findings demonstrate that AKI is independently associated with a substantial mortality rate of 18.27% among hospitalized children, with higher mortality rates observed in more severe stages of AKI. This underscores the critical nature of AKI as a significant health concern in pediatric populations worldwide and the crucial need for early detection and intervention strategies. Future research should focus on developing and validating risk prediction models, implementing targeted prevention strategies, and exploring long-term outcomes in pediatric AKI survivors.

Supplementary Information

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Supplementary Material 1

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Author contributions

Study design and conceptualization: MY, MH, NA. Data gathering: HZ, AA, AA, AR, HT, SRD, NS, AD. Data analysis: HZ, MY. Interpretation of the results: HZ, AA, MY. Drafting the manuscript: HZ, AA. Revising, editing, and confirming the final version: All authors.

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Data availability

The dataset generated and analyzed during the current study is available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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