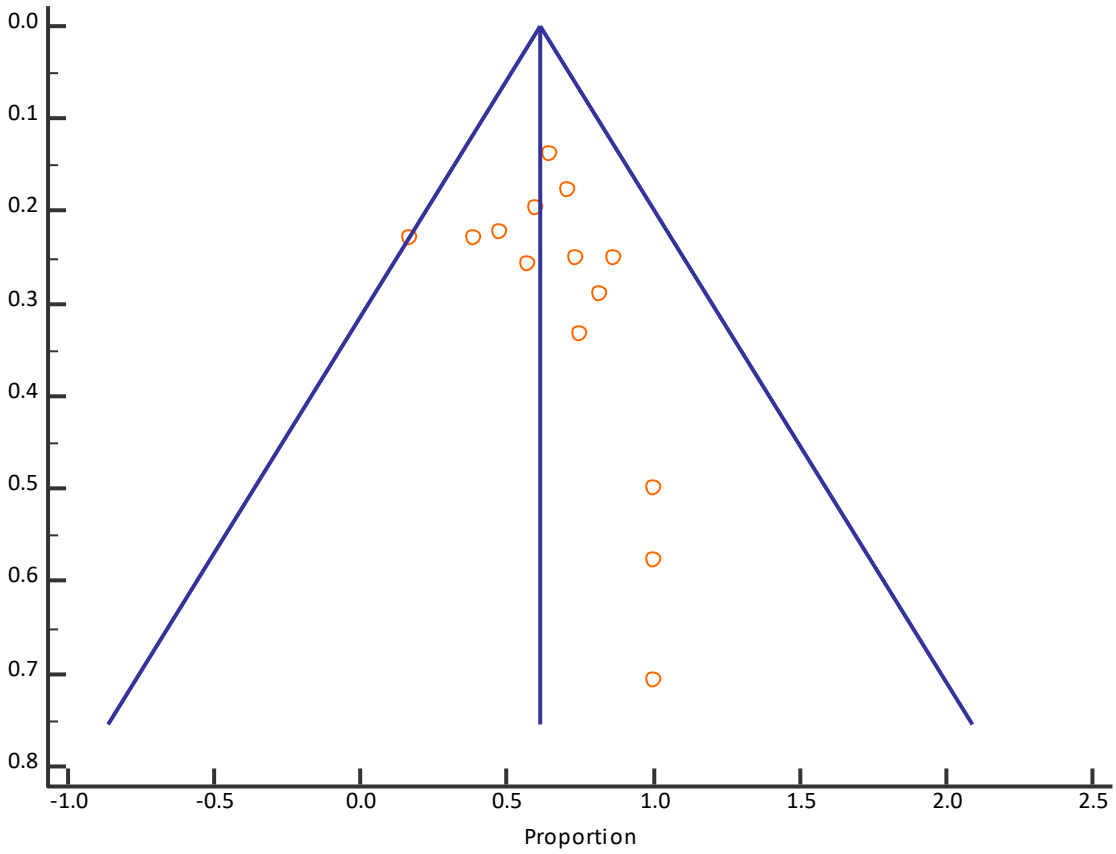
Figure S1. Funnel plot evaluating publication bias in studies reporting survival



Item S1: Detailed Methods

The literature search was done by two independent investigators and involved an exhaustive examination through PubMed, Cochrane, CINAHL, Web of Science, and ScienceDirect databases. The Medical subject headings (MeSH) used were "Inborn Errors of Metabolism" and "CRRT". Results were limited to studies in the English language. Selected articles were exported to Rayyan QCR software, where titles, abstracts, and full texts of the collected studies were reviewed by two independent investigators.

Of a total of 249 articles gathered after an initial search from multiple databases, only 14 articles met the inclusion/exclusion criteria for survival analysis. Any disagreements regarding selection criteria for data extraction were resolved by a consensus of the two reviewers or by a third reviewer. The studies selected appropriately for inclusion reported survival rates and ammonia levels in pediatric patients with inborn errors of metabolism (IEM) and were given any modality of kidney replacement therapy as an intervention. There was no restriction on the duration or geography of the studies. Studies reporting patients under 18 years old were included in the analysis. Additionally, only original articles consisting of cross-sectional, prospective, case-reports, and retrospective studies were included in the analysis. Literature reviews, systematic reviews, and self-reported outcomes were excluded from this study. Research ethics committee review was not required for this meta-analysis. Informed consent and local research ethics committee approval were obtained in all original studies included in this review.

Based on the quality assessment, a total of 12 studies were observed to be of good quality, while 2 with fair quality (an overall total of 14 studies included for the study of pooled survival). The analysis included efficacy through survival rates, where the proportion of children surviving with KRT intervention was extracted from each of the studies. The degree of between-study heterogeneity attributed to the variance in reported mortality was assessed using the I^2 test, where $I^2 \geq 50\%$ indicated high heterogeneity. The overall (pooled) estimate was calculated with a random effects model for high heterogeneity and a fixed effects model for low heterogeneity. To determine the source of heterogeneity, sensitivity analyses were performed based on the following parameters: age, sample size, geography, and study quality. A p-value <0.05 was considered for statistical significance. A forest plot was used to visualize these outcomes in each study and the combined estimated outcomes with their 95% CI. Publication bias was assessed graphically using funnel plots and Egger's test, where $p<0.05$ was considered statistically significant for small-study bias. All statistical analyses were performed with R software version 3.1.0.

Table S1. General Characteristics of Included Studies

Author	Location	Patients (n)	Age at KRT*	Inborn Errors of Metabolism	Mortality (%)
Ames et al., 2020	USA	19	2 days - 15.6 years	OTC def. (9), CPS-1 def. (4), ASS def. (2), MMA (1), PA (3)	53
Ames et al., 2022	USA	51	3 days (0 days - 11 days)	OTC def. (26), CPS-1 def. (7), ASS def. (6), ASL def (4), MMA (3), PA (5)	35
Celik et al., 2019	Turkey	14	3 days (2 days -10.2 days)†	OTC def. (1), ASS def. (6), ASL def (1), MMA (2), PA (3), Unclear (1)	43
Hakan et al., 2014	Turkey	18	(1 day – 30 days)	UCD (7), MC (8), NKH (3)	83
Hanudel et al., 2014	USA	2	4 days	MMA (1), Unclear (1)	0
Kim et al., 2011	South Korea	1	3 days	OTC def. (1)	0
Lai et al., 2007	Taiwan	8	2 years (11 days – 7 years)	OTC def. (2), CPS-1 def. (1), MMA (4), MSUD (1)	25
Lee et al., 2016	South Korea	11	10 days (1 day – 122 day)	ASS def. (1), Unclear (10)	18
McBryde et al., 2006	USA	18	(2 days -17 years)	OTC def. (5), CPS-1 def. (1), ASS def. (2), ASL def (3), MMA (3), PA (1). IVA (1), Other (2)	61
Mok et al., 2018	Taiwan	3	4 (2 days – 30 days)	OTC def. (1), MMA (1), Unclear (1)	0
Naorungroj et al., 2021	USA	31	(3 days – 7 years)	OTC def. (6), CPS-1 def. (5), ASS def. (10), ASL def (1), MMA (3), PA (3), GA-II (1), Argininemia (1), Unclear (1)	31
Symons et al., 2007	USA	15	(Newborn to 25 years)	Unclear (15)	27
Tsai et al., 2014	Taiwan	15	(7 days – 7 years)	OTC def. (2), CPS-1 def. (1), ASS def. (2), MMA (6) MSUD (4)	13
Yetimakman et al., 2019	Turkey	25	0.66 years (0.21 years – 4.3 years)	ASS def. (1), MMA (9), PA (4), MSUD (4), MC (4), MCADD (1), SCADD (1), Unclear (1)	40

*Data reported as median (range) or (range), as appropriate

† Data reported as median (IQR)

Abbreviations: OTC def., ornithine transcarbamylase deficiency; ASS def., argininosuccinate synthetase deficiency (aka citrullinemia); CPS-1 def., carbamoyl phosphate synthetase 1 deficiency; ASL def, argininosuccinate lyase deficiency (aka argininosuccinate acidemia); MMA, methylmalonic acidemia; PA, propionic acidemia; GA-II, glutaric aciduria type II; IVA, isovaleric acidemia; MC, mitochondrial cytopathy; MSUD, maple-syrup urine disease; NKH, nonketotic hyperglycinemia; SCADD, short-chain acyl-CoA dehydrogenase deficiency; MCADD, medium chain acyl-CoA dehydrogenase deficiency; KRT, kidney replacement therapy; and IEM, inborn errors of metabolism.

Table S2. Inborn errors of metabolism disorders among 231 children reported across gathered studies

Inborn Errors of Metabolism		Patient Sample (n)	Proportion (%)
Urea cycle disorder	OTC def.	53	22.9
	ASS def.	30	13.0
	CPS-1 def.	19	8.2
	ASL def.	9	3.9
	Argininemia	1	0.4
Organic acidemia	MMA	33	13.0
	PA	19	8.0
	GA-II	1	0.4
	IVA	1	0.4
	MC	12	5.2
	MSUD	9	3.9
	NKH	3	1.3
	SCADD	1	0.4
	MCADD	1	0.4
	Other	2	0.9
	Not specified	37	16.0

Abbreviations: OTC def., ornithine transcarbamylase deficiency; ASS def., argininosuccinate synthetase deficiency (aka citrullinemia); CPS-1 def., carbamoyl phosphate synthetase 1 deficiency; ASL def, argininosuccinate lyase deficiency (aka argininosuccinate acidemia); MMA, methylmalonic acidemia; PA, propionic acidemia; GA-II, glutaric aciduria type II; IVA, isovaleric acidemia; MC, mitochondrial cytopathy; MSUD, maple-syrup urine disease; NKH, nonketotic hyperglycinemia; SCADD, short-chain acyl-CoA dehydrogenase deficiency; MCADD, medium chain acyl-CoA dehydrogenase deficiency; and IEM, inborn errors of metabolism.

Table S3. Survival among children with an inborn error of metabolism

Study	Survival population size	Sample size	% Proportion (95% CI)	Random Weight (%)
Ames et al., 2022	33	51	64.7 (50.1 - 77.6)	10.66
Naorungroj et al., 2021	22	31	71.0 (52.0 - 85.8)	9.70
Ames et al., 2020	9	19	47.4 (24.5 - 71.1)	8.50
Celik et al., 2019	8	14	57.1 (28.9 - 82.3)	7.66
Yetimakman et al., 2019	15	25	60.0 (38.7 - 78.9)	9.20
Mok et al., 2018	3	3	100.0 (29.2 – 100.0)	3.67
Lee et al., 2016	9	11	81.8 (48.2 - 97.7)	6.98
Hakan et al., 2014	3	18	16.7 (3.6 - 41.4)	8.36
Hanudel et al., 2014	2	2	100.0 (15.8 – 100.0)	2.97
Tsai et al., 2014	13	15	86.7 (59.5 - 98.3)	7.86
Kim et al., 2011	1	1	100.0 (2.5 – 100.0)	2.15
Lai et al., 2007	6	8	75.0 (34.9 - 96.8)	6.07
Symons et al., 2007	11	15	73.3 (44.9 - 92.2)	7.86
McBryde et al., 2006	7	18	38.9 (17.3 - 64.3)	8.36
Total (random effects)	142	231	63.4 (52.4 - 73.7)	100.00

Abbreviation: CI, confidence interval