

https://dspace.org/

The use of ultrasonography in the diagnosis and management of Acute Kidney Injury and other forms renal dysfunction in the paediatric population Systematic review protocol

Gontse Leballo; Nabeela Arbee; Moses Kebalepile; Palesa Motshabi

PUBLIC LIBRARY SCIENCE
https://hdl.handle.net/10539/48993
WOS

Downloaded from a DSpace repository. https://dspace.org/

PLOS One

STUDY PROTOCOL

The use of ultrasonography in the diagnosis and management of Acute Kidney Injury and other forms renal dysfunction in the paediatric population: Systematic review protocol

Gontse Leballo☯*, **Nabeela Arbee-Kalidas**☯, **Moses Mogakolodi Kebalepile**☯, **Palesa Motshabi Chakane**☯

Department of Anaesthesiology, Charlotte Maxeke Johannesburg Academic, Hospital, University of the Witwatersrand, Johannesburg, South Africa

☯ These authors contributed equally to this work.
* gontse.leballo@wits.ac.za

Check for updates

OPEN ACCESS

Citation: Leballo G, Arbee-Kalidas N, Kebalepile MM, Chakane PM (2025) The use of ultrasonography in the diagnosis and management of Acute Kidney Injury and other forms renal dysfunction in the paediatric population: Systematic review protocol. PLoS One 20(6): e0325549. https://doi.org/10.1371/journal.pone.0325549

Editor: Gilbert Sterling Octavius, Universitas Pelita Harapan, INDONESIA

Received: September 11, 2024

Accepted: May 14, 2025

Published: June 18, 2025

Copyright: © 2025 Leballo et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data availability statement: No datasets were generated or analysed during the current study. All relevant data from this study will be made available upon study completion.

Abstract

Background

Acute kidney injury remains one of the most prevalent complications in hospitalised patients, with an especially high incidence in the paediatric population. Its diverse pathophysiological aetiologies present significant challenges in its clinical diagnosis. Relying solely on serum creatinine levels and urine output measurements for diagnosis has been shown to be inadequate, particularly for early detection of the disease. The wide range of disease manifestations highlights the importance of exploring diagnostic techniques that can identify patients at risk before disease progression occurs, thereby allowing for the implementation of timely corrective measures. Point-of-care ultrasound is a valuable technique with the potential to aid in the early identification of at-risk patients.

Objective

To describe ultrasound parameters associated with the development of acute kidney injury or renal dysfunction in the hospitalised paediatric patient, and to examine their association with its development. This will include an analysis of the specific ultrasound features that may predict or be associated with the occurrence of acute kidney injury, as well as their potential role in identifying at-risk paediatric patients, facilitating timely interventions to mitigate further kidney damage.

Methods

A systematic review of existing literature will be performed to assess ultrasound modalities currently associated with the diagnosis of acute kidney injury in the

Funding: The author(s) received no specific funding for this work.

Competing interests: NO authors have competing interests.

paediatric population. The protocol for this review has been registered with PROSPERO (CDR42024547614) and was developed in accordance with the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA). A comprehensive search of scientific literature will be conducted across PubMed, Scopus, Cochrane Library, and CINAHL databases. The data search will be performed independently by the primary researchers (GL and NA), with any disagreements resolved by the third and fourth researchers (MK, PMC). The COVIDENCE Systematic Review Software® 2024 will be utilised for article exportation, review, and data extraction. The QUADAS-2 tool will be applied to assess the risk of bias in the diagnostic accuracy of the studies included in the review.

Conclusion

This protocol outlines a systematic review designed to evaluate the application of ultrasonography in identifying paediatric patients at risk of developing acute kidney injury and other forms of renal dysfunction. The review will critically assess the effectiveness of ultrasound techniques, including point-of-care ultrasound, in identifying acute kidney injury in children, with a particular emphasis on early detection. The findings from this review will contribute to a deeper understanding of the role of ultrasonography in clinical practice, with the potential to improve patient outcomes through earlier intervention. The ultrasound techniques identified, including Doppler imaging and flow measurements, will be employed in a subsequent prospective study within the paediatric population to evaluate their role, sensitivity, and accuracy.

Introduction

Acute kidney injury (AKI) is a multifactorial pathophysiological condition characterised by a rapid decline in renal function [1], typically subsequent to an episode of renal insult or stress, often referred to as acute kidney stress (AKS) [2]. In the absence of timely intervention, AKI may progress to renal failure, which can subsequently evolve into chronic kidney disease (CKD) and, in advanced stages, end-stage renal disease (ESRD), as illustrated in Diagram 1 below [3].

AKS is described as the “pre-injury” phase of renal dysfunction [2]. It is identified using novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), a proximal tubule biomarker [4], and cell-cycle arrest biomarkers, such as insulin-like growth factor binding protein (IGFBP-7) and tissue inhibitor of metalloproteinases (TIMP-2) [5]. Elevated urinary levels of NGAL within two hours following cardiopulmonary bypass (CPB) have been directly associated with the severity and duration of AKI [6].

AKI exhibits a high prevalence in hospitalised paediatric patients, particularly among those receiving care in an intensive care unit (ICU). The global incidence of AKI in paediatric patients is estimated to be 21% [7], with 27% of cases occurring in ICUs in low-to-middle income countries (LMICs), and 5% of cases involving

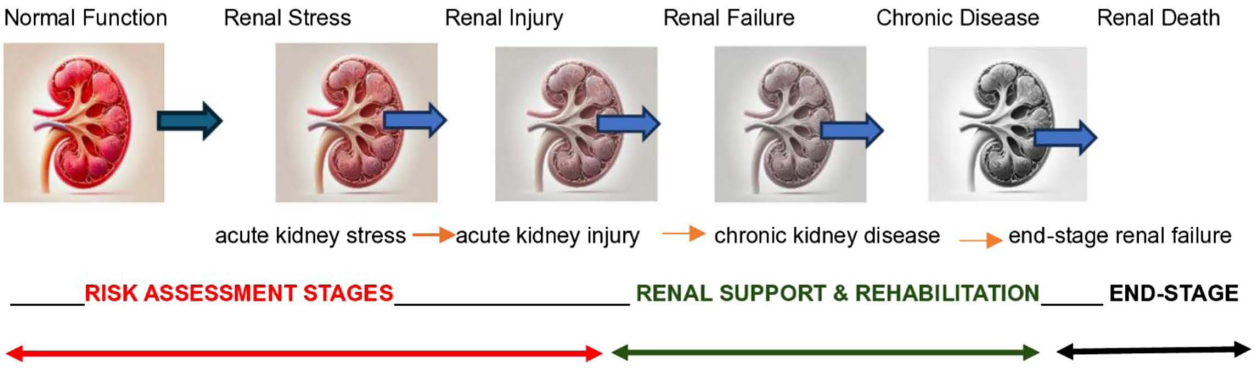


Diagram 1. The spectrum of kidney function.

https://doi.org/10.1371/journal.pone.0325549.d001

non-critically ill paediatric patients [8,9]. One of the key predictors AKI in this population is age, with neonates, infants, and children representing 64%, 52%, and 9.6% to 42% of cases, respectively, and with children less than the age of two-years shown to be at highest risk [10]. This complication is associated with high morbidity and mortality rates [10–13], particularly following cardiac surgery involving the use of CPB [14,15]. In LMICs, the burden of AKI in the paediatric population is substantial, with high morbidity rates often linked to prolonged hospital stays [16,17]. Mortality rates are reported as high as 34%, significantly exceeding the global average of 14% [18]. These high prevalence rates may largely be attributed to disparities in diagnostic tools, limited access to healthcare, and the financial constrains faced by both populations and state healthcare facilities [19].

Validated AKI diagnostic and classification criteria are based on a rise in serum creatinine (SCr) levels and decreasing urine output measurements despite their shortcomings in identifying early kidney injury. A major disadvantage of SCr in AKI diagnosis is the delay in its increase which may take 24–48 hours from the initial renal insult [20]. Its detectable elevations occur only after approximately 50% of renal function has been lost [21]. Changes in SCr levels and urine output measurements consistently lag behind the onset of renal injury, making them ineffective for the early recognition of AKI [22]. In the paediatric population, the Kidney Disease Improving Global Outcomes (KDIGO) criteria and the paediatric Risk Injury Failure Loss and End-Stage (pRIFLE) classification are often employed, with the Acute Kidney Injury Network (AKIN) classification mentioned rarely in some literature [10,23]. The modified pRIFLE criteria utilises glomerular filtration rate (GFR) criteria, which is based on SCr and/or urine output measurements in classifying AKI into different stages [24]. SCr is used to calculate for estimated creatinine clearance (eCCr) by means of the Schwartz formula [10,25].

The multifactorial nature of AKI is underpinned by a complex interplay of diverse pathophysiological mechanisms. The factors contributing to AKI can be broadly categorised into renal pathologies (such as renal obstruction and exposure to exogenous or endogenous toxins), systemic factors (including sepsis, volume depletion, ischemia-reperfusion injury, and heart failure), and surgical factors [26]. This pathophysiological interplay has been demonstrated in various studies, which indicate that alterations in renal blood flow patterns, along with changes in the renal cortex and medullary echogenicity, can be associated with the AKI onset and its progression [27–29].

Aspects of point-of-care ultrasound (POCUS) are emerging as valuable resources in the diagnosis and management of patients with AKI in ICU settings [30]. The Chinese Critical Ultrasound Study Group (CCUSG) developed the Critical Care Ultrasound Guided (CCUSG)-$A_{(AKI)}$BCDE protocol, which provides a comprehensive framework for the risk assessment and diagnosis of AKI in critical care patients [26]. This protocol offers a systematic approach to renal function assessment by evaluating the clinical profile that may contribute to the development of AKI, utilising B-mode ultrasonography for renal structural assessment, employing colour and spectral Doppler imaging of the kidneys, and assessing microcirculation. The

development of this protocol highlights the essential role of renal ultrasound in facilitating the diagnosis and risk stratification of AKI, particularly in resource-constrained environments.

Doppler ultrasound has demonstrated potential as a cost-effective, non-invasive, and a rapid modality for predicting AKI in critically ill paediatric patients by identifying altered renal blood flow patterns [21,31]. Doppler measurements of hepatic, portal, cardiac, and renal vascular parameters have been shown to be associated with AKI in adult patients [32–34]. A study by Guinot et al. demonstrated that right ventricular systolic dysfunction and elevated central venous pressure (CVP) following cardiac surgery were associated with an increased risk of AKI [37]. Similarly, Pettey et al. reported that abnormal hepatic vein flow patterns and ratios, were correlated with AKI in adults undergoing cardiac surgery, with elevated CVP measurements independently associated with AKI [32]. Additionally, tricuspid annular plane systolic excursion (TAPSE) was found to be significantly associated with AKI in critically ill patients [38].

Fluid overload and thus venous congestion leads to an increase in venous pressure, which causes a decrease in renal blood flow and contributes to the occurrence of AKI [35]. The venous excess ultrasound (VExUS) score associated renal venous congestion with AKI [35]. It systematically assesses inferior vena cava (IVC) diameter and Doppler waveforms of hepatic, portal, and intrarenal veins, classifying the severity into Grades I to III [35,36]. Studies on paediatric renal arterial ultrasound parameters are predominantly reporting renal resistive index (RRI), and renal pulsatility index (RPI), with inconclusive and poor results [24,41]. Structural abnormalities on ultrasound typically present late and are not useful in AKI [29,39,40].

Studies utilising POCUS in adults have provided valuable insights, associating renal, hepatic, and cardiac ultrasound parameters to the occurrence of AKI. These findings underscore the potential of ultrasound techniques to improve early detection and monitoring of AKI in high-risk patients, particularly in resource-limited settings, and highlight the need for further research in paediatric populations to optimise diagnostic approaches. This systematic review aims to evaluate renal, hepatic, portal and cardiac ultrasound parameters associated with the development of AKI in paediatric patients.

Recommendations by the Enhanced Recovery after Cardiac Surgery (ERAS-Cardiac) support efforts to explore robust and cost-effective methods of early identification of renal stress following cardiac surgery, particularly ultrasound techniques that can quantify renal congestion [41]; and to employ Goal Directed Fluid Therapy (GDFT) practises to achieve required haemodynamic goals thus promoting oxygen delivery and end-organ perfusion [41,42].

Aim

The aim of this review protocol is to outline the process for investigating clinically relevant ultrasound parameters (B-mode, Doppler and waveform ultrasound patterns) associated with the development of AKI in hospitalised paediatric patients.

Objectives

The objective of this systematic review is to describe ultrasound parameters associated with the development of AKI or renal dysfunction in the hospitalised paediatric patient.

Methodology

Study design

The protocol is developed according to the recommendations from the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) guidelines (Fig 1) (PRISMA-P checklist- Appendix A, S1) [43,44]. It is registered on the International Prospective Register of Systematic reviews (PROSPERO 2024, CDR42024547614). While ethical clearance is not required for this review, the associated large-scale study has received approval from the Human Research Ethics Committee (HREC) Medical of the University of the Witwatersrand, South Africa (Reference number:

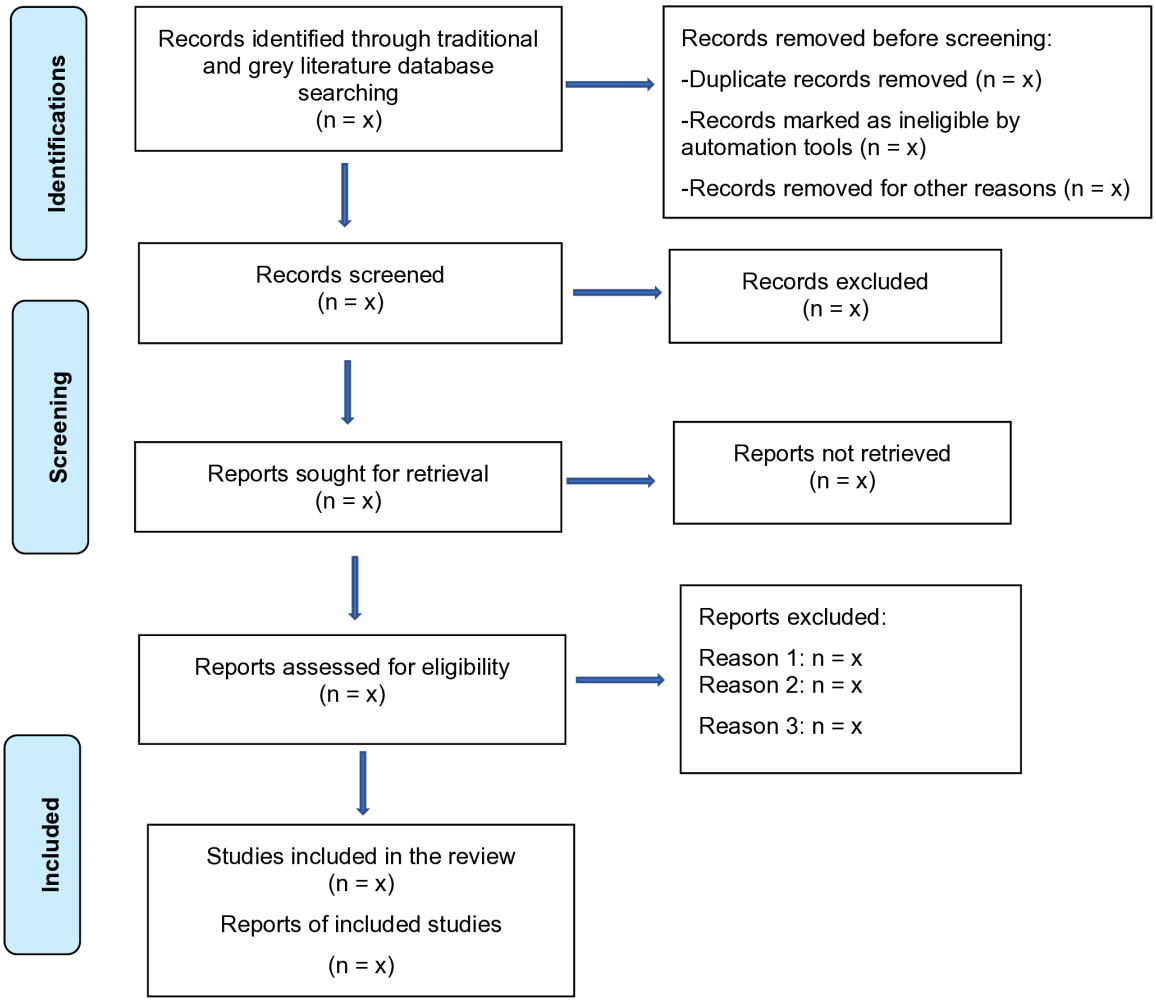


Fig 1. A PRISMA flow diagram showing a schematic representation of how literature screening will occur for the systematic review.

https://doi.org/10.1371/journal.pone.0325549.g001

M231003 M240423-A-0001).This protocol is designed to conduct a comprehensive systematic review of the literature on ultrasound modalities associated with the diagnosis of AKI or renal dysfunction in the paediatric population. All studies describing various ultrasound parameters such as renal structural findings, Doppler patterns, and waveform parameters explored clinically to identify paediatric patients with AKI will be included.

The following research assumptions are made: **paediatric patient:** a patient less than the age of 18 years; **acute kidney injury:** it will be inclusive of AKI, acute renal failure (ARF), renal injury, and renal dysfunction; **acute kidney injury diagnostic criteria:** in this study AKI will be defined according to the paediatric Risk, Injury, Failure, Loss, and End-Stage renal function (pRIFLE) criteria, Kidney Disease Improving Global Outcomes (KDIGO) criteria, and the Acute Kidney Injury (AKIN) network; and **ultrasound parameters:** they will include Doppler haemodynamic flow patterns (renal, hepatic, and cardiac), and renal morphological, or anatomic structural changes.

The study aims to identify and emphasise evidence-based bedside ultrasound parameters that are correlated with the diagnosis of AKI or renal dysfunction in paediatric patients. The study will follow a seven-step methodological framework based on the PRISMA guidelines [45].

Step 1: Identifying the research question. The population, exposure, and outcome (PEO) framework (Table 1) will be applied. The proposed systematic review will address the following research question:

Which bedside ultrasound techniques can clinicians utilise for risk assessment of AKI in hospitalised paediatric patients?

Step 2: Eligibility criteria for considering studies for inclusion in this review. The inclusion of the identified studies will be conducted independently by two primary reviewers (GL and NA), with the third (MK) and fourth reviewers (PMC) consulted in cases of discordance. The selected studies will be systematically reviewed by GL and NA, and the relevant data (Table 2) will be presented in alignment with the research question and the PEO framework (Table 1). Searches will be performed for English-language literature, along with unpublished and grey literature, spanning the past 40 years (1984–2024). The inclusion and exclusion criteria are detailed in Table 2. Only studies conducted in accordance with established methodological standards will be included.

Step 3: Information sources and search strategy for the identification of relevant studies. The literature search will encompass the following databases: MEDLINE (PubMed), Scopus, Cochrane Library, and CINAHL. In addition to the electronic database search, the reference lists of eligible articles will also be reviewed.

A search strategy for data collection from these databases is outlined in Table 3 below. Medical Subject Headings (MeSH) terms and relevant keywords such as “paediatric patient,” “ultrasound,” and “acute kidney injury” will be employed during the search.

The results of the search will be managed using the EndNote™ 20 [Endnote 20.6 (2001–2020), Clarivate Analytics (US) LLC, Philadelphia, PA] reference management tool. Eligible studies will be exported to the Covidence [Covidence systematic review software (2024), Veritas Health Innovation, Melbourne, Australia] data extraction software for systematic data extraction.

Step 4: Study selection and eligibility. The study search and selection of eligible articles will follow a multistep process, independently conducted by primary reviewers GL and NA, adhering to the PRISMA guidelines as illustrated in Fig 1.

The screening process will be implemented as follows:

i. **Title screening:** The aforementioned databases (PUBMED, Scopus, Cochrane Library, and CINHAL) will be utilised to identify eligible studies, with primary reviewers applying predefined inclusion and exclusion criteria during the

Table 1. The population, exposure, and outcomes (PEO) framework.

Population	**Paediatric patients (< 18 years of age)**
Exposure of interest or Intervention	B-mode ultrasound, Doppler flow patterns and wave-length patterns (renal/ hepatic/ portal), right heart chamber measurements associated with AKI diagnosis
Comparator or Control	none
Outcomes	Acute kidney injury or renal dysfunction

https://doi.org/10.1371/journal.pone.0325549.t001

Table 2. Inclusion and exclusion criteria for this systematic review.

	Inclusion criteria	**Exclusion criteria**
Population	Paediatric patients (age ≤ 18 years)	Duplicate studies
Study design	Cohort studies, case control studies, *RCTs, grey literature, master’s, and PhD Thesis	
Outcome	*AKI diagnosis (or any phrase utilised to describe renal dysfunction) utilising bedside ultrasound techniques or *POCUS	Non-English studies
Publication type	Full text in English	

*RCT: randomised control trials; *AKI: acute kidney injury; *POCUS: point-of-care-ultrasound.

https://doi.org/10.1371/journal.pone.0325549.t002

Table 3. Databases search strategy according to the population, exposure, and outcomes (PEO) framework.

Database	PEO Framework	MeSH terms/ Phrases
PubMed/ MEDLINE	**Population**	((((((((((((pediatrics[MeSH Terms]) OR ("paediatric patient*"[Text Word])) OR ("pediatric patient*"[Text Word])) OR ("paediatric patient*"[Title/Abstract])) OR ("pediatric patient*"[Title/Abstract])) OR (child[Text Word])) OR (children[-Text Word])) OR (neonate*[Text Word])) OR (child[Title/Abstract])) OR (children[Title/Abstract])) OR (neonate*[Title/Abstract])) OR (infant*[Title/Abstract])) OR (infant*[Text Word])
	Exposure of interest	((((acute kidney injury[MeSH Terms]) OR ("acute renal failure"[Text Word])) OR ("acute renal failure"[Title/Abstract])) OR ("acute kidney insufficiencies"[Text Word])) OR ("acute kidney insufficiencies"[Title/Abstract])
	Outcomes	"ultrasound"[Title/Abstract] OR "ultrasonograph*"[Title/Abstract] OR "POCUS"[Title/Abstract] OR "ultrasonogra*"[Title/Abstract] OR "echocardiogra*"[Title/Abstract] OR "echocardiograph*"[Title/Abstract] OR "doppler"[Title/Abstract] OR "portal ultrasound"[Title/Abstract] OR "renal ultrasound"[Title/Abstract] OR "hepatic ultrasound"[Title/Abstract] OR "cardiac ultrasound"[Title/Abstract] OR "resistive index"[Title/Abstract] OR "portal vein pulsatility index"[Title/Abstract] OR "portal vein velocity"[Title/Abstract] OR "hepatic vein Doppler"[Title/Abstract] OR "hepatic vein velocity"[Title/Abstract] OR "inferior vena cava diameter"[Title/Abstract] OR "ejection fraction"[Title/Abstract] OR "EF"[Title/Abstract] OR "LVEF"[Title/Abstract] OR "tricuspid annular plane systolic excursion"[Title/Abstract] OR "TAPSE"[Title/Abstract] OR "mitral annular plane systolic excursion"[Title/Abstract] OR "MAPSE"[Title/Abstract] OR "cardiac output"[Title/Abstract] OR "cardiac index"[Title/Abstract] OR "parenchymal echogenicity"[Title/Abstract] OR "RRI"[Title/Abstract] OR "renal circulation"[MeSH Terms] OR "renal blood flow, effective"[MeSH Terms] OR "renal ultrasound"[Text Word] OR "renal resistive index"[Text Word] OR "renal doppler"[Text Word]
Scopus	(TITLE-ABS-KEY ("acute kidney injury" OR "acute renal failure" OR "renal dysfunction" OR "AKI") AND TITLE-ABS-KEY ("pediatric*" OR "paediatric*" OR "infant" OR "neonate") AND TITLE-ABS-KEY ("ultrasound" OR "doppler" OR "ultrasonogra*" OR "renal ultrasound" OR "renal resistive index" OR "RRI" OR "hepatic ultrasound" OR "cardiac ultrasound" OR "FATE" OR "hepatic vein ratio")) AND (LIMIT-TO (SUBJAREA, "MEDI")) AND (LIMIT-TO (EXACTKEYWORD, "Human") OR LIMIT-TO (EXACTKEYWORD, "Acute Kidney Failure") OR LIMIT-TO (EXACTKEYWORD, "Infant, Newborn") OR LIMIT-TO (EXACTKEYWORD, "Child") OR LIMIT-TO (EXACTKEYWORD, "Newborn") OR LIMIT-TO (EXACTKEYWORD, "Infant") OR LIMIT-TO (EXACTKEYWORD, "Humans")) AND (LIMIT-TO (LANGUAGE, "English")) AND (EXCLUDE (DOCTYPE, "re") OR EXCLUDE (DOCTYPE, "ch"))	
Cochrane Library	(Paediatrics AND Acute kidney injury OR AKI OR Acute renal failure OR acute renal dysfuntion):ti,ab,kw AND ("POCUS" OR "Renal resistive index" OR "RRI" OR "hepatic doppler" OR "hepatic vein ratio" OR "echocardiograph" OR "FATE"):ti,ab,kw NOT (adult):ti,ab,kw	
CINHAL	TI (acute kidney injury or acute renal failure or aki or acute kidney failure) AND AB (ultrasound or sonography or sonogram or ultrasonography) AND AB (paediatric or pediatric or children	

https://doi.org/10.1371/journal.pone.0325549.t003

screening process. The results from the database searches will be exported to EndNote™ 20 [Endnote 20.6 (2001–2020), Clarivate Analytics (US) LLC, Philadelphia, PA], and subsequently transferred to Covidence [Covidence systematic review software (2024), Veritas Health Innovation, Melbourne, Australia] for further study screening. Covidence will automatically remove duplicate entries. Both reviewers will review all study titles against the established eligibility criteria. Any disagreements regarding study inclusion during title screening will be resolved by the third and fourth reviewers (MK and PMC) prior to proceeding to the studies abstract screening.

ii. **Abstract screening:** Upon completion of the title screening stage and resolution of any disagreements, the primary reviewers will independently screen the abstracts of the included studies in parallel within Covidence software. Studies whose titles and abstracts do not meet the predefined inclusion criteria will be excluded. Any discrepancies encountered by the primary reviewers during this process will be addressed and resolved by the third and fourth reviewers.

iii. **Full article screening:** Full-text articles of studies included during the abstract screening phase will be imported into Covidence software for full-text screening. Similar to the previous stages (title and abstract screening), the primary reviewers will independently assess the full-text articles of the included studies. A thorough evaluation of each study will determine the inclusion of relevant studies and the exclusion of those that do not meet the eligibility criteria. Any discrepancies between the primary reviewers will be resolved by the third and fourth reviewers.

Step 5: Data extraction. Upon completion of the full-text article screening phase, primary reviewers (GL and AN) will independently extract data from all included studies. To minimise bias, inter-rater variability, and data extraction errors, the

Table 4. Data collection template for the systematic review.

1. Study identification
Sponsorship source:
Country:
Setting:
Comments:
2. Authors' details
Name:
Institution:
Email address:
Physical Address:
3. Study period and other
Start date:
End date:
Single centre:
Multicentre:
4. Methods
Study design:
5. Criteria
Inclusion:
Exclusion:
6. Population
Mean age (years) ‡SD:
Medical/ non-surgical cases/ admissions:
Surgical Cases/ admissions:
Sample size:
7. Intervention (ultrasound technique utilised for diagnosis)
Renal parameters (RRI/ RPI/other):
Cardiac parameters (CVP/ IVC/ TAPSE/ RV-pressure/ other):
Hepatic parameters (HVR/ other):
Portal parameters (PVP index/ other):
8. Outcome (acute renal dysfunction diagnosis: dichotomous outcome)
Acute kidney injury/ Acute renal failure/ Other:
9. Serum Creatinine/ Urine Output/ Biomarker parameter also utilised
KDIGO:
pRIFLE:
AKIN:
GFR:
NGAL:
Cystatin C:
TIMP-2/ IGFBP-7:
Other:
None:
10. Statistical analysis
- Continuous measures
standard deviation (mean/ SD/ N):
confidence intervals (mean/ CI/ N):
- Dichotomous measures
percentage of participants with event (N/ %):
number of participants with event (n/ N)

https://doi.org/10.1371/journal.pone.0325549.t004

data extraction process will be performed separately by each reviewer using a pre-established data extraction template (Table 4), which was developed prior to the commencement of the screening process in Step 4. The extracted data from eligible articles will be verified by the third (MK) and fourth (PMC) reviewers and categorised as follows (as outlined in Table 4: Data Collection Table):

i. **General study details**: including author(s), year of publication, study title, country of study, and main conclusions.

ii. **Participant characteristics**: such as sample size, patient selection criteria, gender, type of hospital admission (e.g., medical ICU or post-surgery ICU), and presence of AKI or renal dysfunction.

iii. **Study methods**: including study design (e.g., cohort, observational, pilot, or RCT) and whether the study was single or multicentre.

iv. **Ultrasound parameters employed**: renal Doppler ultrasound parameters, inclusion of hepatic or cardiac ultrasound, and renal structural measurements.

v. **Standard AKI diagnostic criteria**: utilisation of SCr and/or urine output measurements as the standard diagnostic criterion, including KDIGO, pRIFLE, and AKIN criteria.

vi. **Renal biomarkers:** data from studies that mention the use of renal biomarkers will also be extracted; their method of measurement, and their relevance to the diagnosis or monitoring of AKI or other forms of renal dysfunction. The data will be categorised according to the type of biomarkers (e.g., serum, urinary, or molecular markers) and any associated outcomes, such as diagnostic accuracy or prognostic value.

vii. **Outcomes**: including AKI diagnosis, other forms of renal dysfunction, associated complications, and mortality rates.

Step 6: Assessment of study quality and risk of bias. Assessment of risk of bias of the included studies in this review paper will be performed using the Quality Assessment of comparative Diagnostic Accuracy Studies (QUADAS) −2 tool (Appendix B) [46]. It is a tool recommended for evaluation of risk of bias of diagnostic accuracy. The GRADE guidelines [47], will be used to evaluate publication bias and selective reporting of included studies and be presented as plots of outcome variables against sample size.

Step 7: Data synthesis and analysis of results. Extracted data addressing the objectives will be presented in tables. Where data allows, a meta-analysis of outcome will be conducted and reported in the form of mean differences for continuous outcomes, odds ratios for dichotomous data, 95% confidence intervals and two-sided p-values for each outcome. A p-value < 0.05 will be considered statistically significant. A narrative synthesis will provide evidence of the pooled prevalence, corresponding standard error and 95% confidence intervals of age, setting and acute AKI diagnosed using ultrasound parameters.

Should a meta-analysis be feasible, fixed effect and random effect models will be used to pool data from individual prevalence and incidence rate estimates from the studies. The heterogeneity of studies included in the meta-analysis will be assessed through the Cochran's Q test (P value <0.05) and I^2 (>50%). The inverse-variance weighting techniques will be used to adjust for publication bias due to study size.

The results will be presented in the form of summary tables and flowcharts, which will be included in the final manuscript. The outputs of this review will be disseminated through publications in peer-reviewed journals, conference presentations, and reports for relevant stakeholders.

Differences between protocol and review

In accordance with the published protocol, we will conduct a review and document any discrepancies from the protocol. Any modifications will be reflected by updating the PROSPERO record and detailing these changes in a section titled "*Differences Between the Protocol and the Review*" in the published systematic review results article.

Ethical considerations

This review article forms part of a broader research initiative investigating perioperative AKI in paediatric cardiac patients. The ultrasound parameters identified and validated through this systematic review will be employed in a large-scale

prospective study aimed at identifying paediatric patients at risk for AKI. This will involve comparing the identified ultrasound parameters—specifically Doppler flow patterns, blood flow resistance ratios in the liver and kidneys, as well as right-sided cardiac pressures—with an established AKI diagnostic criterion (KDIGO), which is based on serum creatinine (SCr), urine output measurements, and renal molecular biomarkers (including serum Cystatin C, IGFBP-7, and TIMP-2).

Study data

Raw data collected from all eligible studies will be exported to Microsoft Excel (Microsoft Corporation, 365). This data will be made publicly available without any restrictions and will be submitted as part of the Supporting Information Files upon submission of the completed study to the journal.

Conclusion

This systematic review, with the potential for meta-analysis, aims to critically assess the use of ultrasound parameters that are associated with paediatric patients diagnosed with AKI based on established diagnostic criteria. The primary objective is to delineate the at-risk population for AKI and to identify specific ultrasound characteristics that effectively aid in its diagnosis. Furthermore, the review will examine the limitations associated with the application of these ultrasound modalities.

Supporting information

S1 Appendix A. PRISMA-P checklist 2015 checklist: recommended items to address in a systematic review protocol.
(DOCX)

Author contributions

Data curation: Gontse Leballo, Moses Mogakolodi Kebalepile, Palesa Motshabi Chakane.

Formal analysis: Moses Mogakolodi Kebalepile.

Investigation: Gontse Leballo, Nabeela Arbee-Kalidas.

Supervision: Moses Mogakolodi Kebalepile, Palesa Motshabi Chakane.

Writing – original draft: Gontse Leballo.

Writing – review & editing: Gontse Leballo, Palesa Motshabi Chakane.

References

1. Makris K, Spanou L. Acute Kidney Injury: Definition, Pathophysiology and Clinical Phenotypes. Clin Biochem Rev. 2016;37(2):85–98. https://pubmed.ncbi.nlm.nih.gov/28303073/ PMID: 28303073
2. Katz N, Ronco C. Acute kidney stress--a useful term based on evolution in the understanding of acute kidney injury. Crit Care. 2016;20:23. https://doi.org/10.1186/s13054-016-1184-x PMID: 26796793
3. Kellum JA, Romagnani P, Ashuntantang G, Ronco C, Zarbock A, Anders H-J. Acute kidney injury. Nat Rev Dis Primers. 2021;7(1):52. https://doi.org/10.1038/s41572-021-00284-z PMID: 34267223
4. Kwiatkowski DM, Sutherland SM. Acute kidney injury in pediatric patients. Best Pract Res Clin Anaesthesiol. 2017;31(3):427–39. https://doi.org/10.1016/j.bpa.2017.08.007 PMID: 29248148
5. Meersch M, Schmidt C, Van Aken H, Rossaint J, Görlich D, Stege D, et al. Validation of cell-cycle arrest biomarkers for acute kidney injury after pediatric cardiac surgery. PLoS One. 2014;9(10):e110865. https://doi.org/10.1371/journal.pone.0110865 PMID: 25343505
6. Bennett M, Dent CL, Ma Q, Dastrala S, Grenier F, Workman R, et al. Urine NGAL predicts severity of acute kidney injury after cardiac surgery: a prospective study. Clin J Am Soc Nephrol. 2008;3(3):665–73. https://doi.org/10.2215/CJN.04010907 PMID: 18337554
7. Lameire N, Van Biesen W, Vanholder R. Epidemiology of acute kidney injury in children worldwide, including developing countries. Pediatr Nephrol. 2017;32(8):1301–14. https://doi.org/10.1007/s00467-016-3433-2 PMID: 27307245

8. Kaddourah A, Basu RK, Bagshaw SM, Goldstein SL, AWARE Investigators. Epidemiology of Acute Kidney Injury in Critically Ill Children and Young Adults. N Engl J Med. 2017;376(1):11–20. https://doi.org/10.1056/NEJMoa1611391 PMID: 27959707
9. McGregor TL, Jones DP, Wang L, Danciu I, Bridges BC, Fleming GM, et al. Acute Kidney Injury Incidence in Noncritically Ill Hospitalized Children, Adolescents, and Young Adults: A Retrospective Observational Study. Am J Kidney Dis. 2016;67(3):384–90. https://doi.org/10.1053/j.ajkd.2015.07.019 PMID: 26319754
10. Yuan S-M. Acute kidney injury after pediatric cardiac surgery. Pediatr Neonatol. 2019;60(1):3–11. https://doi.org/10.1016/j.pedneo.2018.03.007 PMID: 29891225
11. Morgan CJ, Zappitelli M, Robertson CMT, Alton GY, Sauve RS, Joffe AR, et al. Risk factors for and outcomes of acute kidney injury in neonates undergoing complex cardiac surgery. J Pediatr. 2013;162(1):120-7.e1. https://doi.org/10.1016/j.jpeds.2012.06.054 PMID: 22878115
12. Blinder JJ, Goldstein SL, Lee V-V, Baycroft A, Fraser CD, Nelson D, et al. Congenital heart surgery in infants: effects of acute kidney injury on outcomes. J Thorac Cardiovasc Surg. 2012;143(2):368–74. https://doi.org/10.1016/j.jtcvs.2011.06.021 PMID: 21798562
13. Li S, Krawczeski CD, Zappitelli M, Devarajan P, Thiessen-Philbrook H, Coca SG, et al. Incidence, risk factors, and outcomes of acute kidney injury after pediatric cardiac surgery: a prospective multicenter study. Crit Care Med. 2011;39(6):1493–9. https://doi.org/10.1097/CCM.0b013e31821201d3 PMID: 21336114
14. Shi Q, Hong L, Mu X, Zhang C, Chen X. Meta-analysis for outcomes of acute kidney injury after cardiac surgery. Medicine (Baltimore). 2016;95(49):e5558. https://doi.org/10.1097/MD.0000000000005558 PMID: 27930561
15. Sharma A, Chakraborty R, Sharma K, Sethi SK, Raina R. Development of acute kidney injury following pediatric cardiac surgery. Kidney Res Clin Pract. 2020;39(3):259–68. https://doi.org/10.23876/j.krcp.20.053 PMID: 32773391
16. Ademola AD, Asinobi AO, Alao MA, Wade AW. Paediatric Dialysis at a Tertiary Hospital in South-West Nigeria: A 4-Year Report. Blood Purif. 2022;51(12):1015–21. https://doi.org/10.1159/000523746 PMID: 35483325
17. Abdelraheem MB. Acute kidney injury in low- and middle-income countries: investigations, management and prevention. Paediatr Int Child Health. 2017;37(4):269–72. https://doi.org/10.1080/20469047.2017.1386816 PMID: 29216816
18. Olowu WA, Niang A, Osafo C, Ashuntantang G, Arogundade FA, Porter J, et al. Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: a systematic review. Lancet Glob Health. 2016;4(4):e242-50. https://doi.org/10.1016/S2214-109X(15)00322-8 PMID: 27013312
19. Hoste EAJ, Kellum JA, Selby NM, Zarbock A, Palevsky PM, Bagshaw SM, et al. Global epidemiology and outcomes of acute kidney injury. Nat Rev Nephrol. 2018;14(10):607–25. https://doi.org/10.1038/s41581-018-0052-0 PMID: 30135570
20. Greenberg JH, Zappitelli M, Devarajan P, Thiessen-Philbrook HR, Krawczeski C, Li S, et al. Kidney Outcomes 5 Years After Pediatric Cardiac Surgery: The TRIBE-AKI Study. JAMA Pediatr. 2016;170(11):1071–8. https://doi.org/10.1001/jamapediatrics.2016.1532 PMID: 27618162
21. de Carvalho AV, Ferraz I de S, de Souza FM, Brandão MB, Nogueira RJN, Alves DFS, et al. Acute kidney injury in critically ill children: predictive value of renal arterial Doppler assessment. Pediatr Res. 2023;93(6):1694–700. https://doi.org/10.1038/s41390-022-02296-1 PMID: 36075988
22. Awdishu L, Wu S. Acute kidney injury. Renal/Pulmonary Critical Care. 2017;2:7–26.
23. Kourelis G, Kanakis M, Samanidis G, Tzannis K, Bobos D, Kousi T, et al. Acute Kidney Injury Predictors and Outcomes after Cardiac Surgery in Children with Congenital Heart Disease: An Observational Cohort Study. Diagnostics (Basel). 2022;12(10):2397. https://doi.org/10.3390/diagnostics12102397 PMID: 36292086
24. McCaffrey J, Dhakal AK, Milford DV, Webb NJA, Lennon R. Recent developments in the detection and management of acute kidney injury. Arch Dis Child. 2017;102(1):91–6. https://doi.org/10.1136/archdischild-2015-309381 PMID: 27496911
25. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20(3):629–37. https://doi.org/10.1681/ASN.2008030287 PMID: 19158356
26. Liu L, Liu D, Hu Z, Wang X, Chao Y, Wu J, et al. Renal hemodynamic evaluation protocol based on the pathophysiological mechanism of acute kidney injury: Critical Care UltraSound Guided-A(KI)BCDE. Ren Fail. 2023;45(2):2284842. https://doi.org/10.1080/0886022X.2023.2284842 PMID: 37994455
27. Matejovic M, Ince C, Chawla LS, Blantz R, Molitoris BA, Rosner MH, et al. Renal Hemodynamics in AKI: In Search of New Treatment Targets. J Am Soc Nephrol. 2016;27(1):49–58. https://doi.org/10.1681/ASN.2015030234 PMID: 26510884
28. Kellum JA, Prowle JR. Paradigms of acute kidney injury in the intensive care setting. Nat Rev Nephrol. 2018;14(4):217–30. https://doi.org/10.1038/nrneph.2017.184 PMID: 29355173
29. Beland MD, Walle NL, Machan JT, Cronan JJ. Renal cortical thickness measured at ultrasound: is it better than renal length as an indicator of renal function in chronic kidney disease?. AJR Am J Roentgenol. 2010;195(2):W146-9. https://doi.org/10.2214/AJR.09.4104 PMID: 20651174
30. Connor-Schuler R, Suarez J. POCUS in Intensive Care Nephrology. POCUS J. 2022;7(Kidney):51–8. https://doi.org/10.24908/pocus.v7iKidney.15016 PMID: 36896116
31. Shen H, Na W, Li Y, Qu D. The clinical significance of renal resistance index (RRI) and renal oxygen saturation (RrSO2) in critically ill children with AKI: a prospective cohort study. BMC Pediatr. 2023;23(1):224. https://doi.org/10.1186/s12887-023-03941-2 PMID: 37149642
32. Pettey G, Hermansen JL, Nel S, Moutlana HJ, Muteba M, Juhl-Olsen P, et al. Ultrasound Hepatic Vein Ratios Are Associated With the Development of Acute Kidney Injury After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2022;36(5):1326–35. https://doi.org/10.1053/j.jvca.2021.07.039 PMID: 34419361

33. Hermansen JL, Pettey G, Sørensen HT, Nel S, Tsabedze N, Hørlyck A, et al. Perioperative Doppler measurements of renal perfusion are associated with acute kidney injury in patients undergoing cardiac surgery. Sci Rep. 2021;11(1):19738. https://doi.org/10.1038/s41598-021-99141-y PMID: 34611205

34. Beaubien-Souligny W, Benkreira A, Robillard P, Bouabdallaoui N, Chassé M, Desjardins G, et al. Alterations in Portal Vein Flow and Intrarenal Venous Flow Are Associated With Acute Kidney Injury After Cardiac Surgery: A Prospective Observational Cohort Study. J Am Heart Assoc. 2018;7(19):e009961. https://doi.org/10.1161/JAHA.118.009961 PMID: 30371304

35. Bhardwaj V, Vikneswaran G, Rola P, Raju S, Bhat RS, Jayakumar A, et al. Combination of Inferior Vena Cava Diameter, Hepatic Venous Flow, and Portal Vein Pulsatility Index: Venous Excess Ultrasound Score (VEXUS Score) in Predicting Acute Kidney Injury in Patients with Cardiorenal Syndrome: A Prospective Cohort Study. Indian J Crit Care Med. 2020;24(9):783–9. https://doi.org/10.5005/jp-journals-10071-23570 PMID: 33132560

36. Beaubien-Souligny W, Rola P, Haycock K, Bouchard J, Lamarche Y, Spiegel R, et al. Quantifying systemic congestion with Point-Of-Care ultrasound: development of the venous excess ultrasound grading system. Ultrasound J. 2020;12(1):16. https://doi.org/10.1186/s13089-020-00163-w PMID: 32270297

37. Guinot PG, Abou-Arab O, Longrois D, Dupont H. Right ventricular systolic dysfunction and vena cava dilatation precede alteration of renal function in adult patients undergoing cardiac surgery: An observational study. Eur J Anaesthesiol. 2015;32(8):535–42. https://doi.org/10.1097/EJA.0000000000000149 PMID: 25192267

38. Mukhtar O, Lal A, Tabi M, Jentzer J, Kashani K. Clinical and Echocardiographic Predictors of Recovery of Moderate-to-severe Sepsis-associated Acute Kidney Injury in Critically Ill Patients. J Community Hosp Intern Med Perspect. 2023;13(2):7–17. https://doi.org/10.55729/2000-9666.1159 PMID: 37168057

39. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE, et al. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International Supplements. 2013;3(1):1–150. https://doi.org/10.1038/kisup.2012.73

40. Petrucci I, Clementi A, Sessa C, Torrisi I, Meola M. Ultrasound and color Doppler applications in chronic kidney disease. J Nephrol. 2018;31(6):863–79. https://doi.org/10.1007/s40620-018-0531-1 PMID: 30191413

41. Gregory AJ, Grant MC, Manning MW, Cheung AT, Ender J, Sander M, et al. Enhanced Recovery After Cardiac Surgery (ERAS Cardiac) Recommendations: An Important First Step-But There Is Much Work to Be Done. J Cardiothorac Vasc Anesth. 2020;34(1):39–47. https://doi.org/10.1053/j.jvca.2019.09.002 PMID: 31570245

42. Beaubien-Souligny W, Denault A, Robillard P, Desjardins G. The Role of Point-of-Care Ultrasound Monitoring in Cardiac Surgical Patients With Acute Kidney Injury. J Cardiothorac Vasc Anesth. 2019;33(10):2781–96. https://doi.org/10.1053/j.jvca.2018.11.002 PMID: 30573306

43. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71 PMID: 33782057

44. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015;350:g7647. https://doi.org/10.1136/bmj.g7647 PMID: 25555855

45. Mulrow CD. Rationale for systematic reviews. BMJ. 1994;309(6954):597–9. https://doi.org/10.1136/bmj.309.6954.597 PMID: 8086953

46. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529–36. https://doi.org/10.7326/0003-4819-155-8-201110180-00009 PMID: 22007046

47. Reitsma JB, Rutjes AW, Whiting P, Yang B, Leeflang MM, Bossuyt PM, et al. Assessing risk of bias and applicability. Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy. 2023:169–201. https://doi.org/10.1002/9781119756194.ch8