INPLASY

Diagnostic Performance of rK39 Rapid Tests for Visceral Leishmaniasis in Children: A Systematic Review and Diagnostic Accuracy Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 June 2026 and was last updated on 12 June 2026.

INTRODUCTION

Review question / Objective Objective: To evaluate the diagnostic accuracy (sensitivity and specificity) of rapid immunochromatographic tests based on the recombinant rK39 antigen for the detection of visceral leishmaniasis in children and adolescents (<18 years).
Review Question: What is the diagnostic performance of rK39 rapid diagnostic tests compared to the parasitological gold standard or composite reference standards in diagnosing visceral leishmaniasis among pediatric populations in endemic areas?

Rationale Visceral leishmaniasis (VL) is a severe zoonosis with high mortality, disproportionately affecting vulnerable pediatric populations (<18 years). While the gold-standard parasitological diagnosis is highly invasive and risky for children, rK39-based rapid diagnostic tests offer a non-invasive and accessible alternative. However, their diagnostic accuracy exhibits substantial heterogeneity in children due to factors like immature humoral immunity, malnutrition, coinfections, and regional strain variability. This review is justified to consolidate scattered evidence, address diagnostic inconsistencies that delay pediatric treatment, and provide evidence-based recommendations for public health settings.

Condition being studied Visceral leishmaniasis (VL), also known as kala-azar, is a neglected, vector-borne tropical disease caused by intracellular hemoflagellate protozoa of the Leishmania donovani complex. The systemic infection primarily affects the reticuloendothelial system and is characterized by prolonged irregular fever, weight loss, hepatosplenomegaly, and anemia. It is potentially fatal in over 95% of untreated cases and poses a severe public health

threat, particularly to pediatric populations in endemic regions.

METHODS

Search strategy Database: PubMed / MEDLINE.
Search String: ("Leishmaniasis, Visceral"[Mesh] OR "visceral leishmaniasis"[tiab] OR "kala azar"[tiab] OR "kala-azar"[tiab] OR "Leishmania donovani"[tiab] OR "Leishmania infantum"[tiab] OR "Leishmania chagasi"[tiab]) AND (rK39[tiab] OR rk39[tiab] OR rk-39[tiab] OR "rK-39"[tiab] OR "K39 antigen"[tiab] OR immunochromatograph*[tiab] OR "rapid diagnostic test"[tiab] OR "rapid test"[tiab] OR dipstick*[tiab]).
Filters applied: Articles published between 2000 and 2026; Portuguese, English, and Spanish languages; Human population.

Participant or population Children and adolescents (<18 years) with clinical suspicion of visceral leishmaniasis (VL) from endemic areas, regardless of sex, coinfections (such as HIV or helminthiasis), or nutritional status.

Intervention The index test evaluated is the application of rapid immunochromatographic diagnostic tests (RDTs) based on the recombinant rK39 antigen for VL diagnosis, performed using blood, serum, or plasma samples.

Comparator The reference standard includes the parasitological gold standard (direct visualization of the parasite in splenic, bone marrow, or hepatic aspirates) or a composite reference standard (comprising parasitology, PCR, and/or combined clinical-epidemiological criteria).

Study designs to be included Observational diagnostic accuracy studies, specifically cross-sectional or cohort study designs, that perform a comparative application of the index test and the reference standard.

Eligibility criteria Inclusion Criteria:
Studies including pediatric samples (<18 years) with clinical suspicion of VL. Application of the rapid rK39 test against a defined reference standard. Availability of absolute data required to construct 2x2 contingency tables (True Positives, False Positives, False Negatives, True Negatives). Publications in Portuguese, English, or Spanish, published between 2000 and 2026.

Exclusion Criteria:
Studies conducted exclusively in adults or mixed populations without data stratification for pediatric participants (<18 years). Reviews, editorials, case reports, case series without comparator groups, and Phase I/II developmental studies without independent comparative application. Intervention studies (e.g., RCTs) lacking diagnostic accuracy data. Studies lacking a defined reference standard or containing incomplete methodological reporting. Studies with an eligible pediatric sample size of fewer than 10 participants. Duplicate studies or secondary publications derived from the same cohort.

Information sources Comprehensive searches will be conducted in the following electronic databases: PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library (CENTRAL), LILACS/BVS, and Global Index Medicus (WHO). To minimize publication bias, gray literature will be searched via ClinicalTrials.gov, WHO ICTRP, and OpenGrey. Additional eligible studies will be identified through manual screening of the bibliographic reference lists of the included articles. The search will cover publications from 2000 to May 2026.

Main outcome(s) The primary outcomes are the diagnostic accuracy measures of the rK39 rapid tests, specifically: sensitivity, specificity, positive likelihood ratios (LR+), negative likelihood ratios (LR-), diagnostic odds ratio (DOR), and the area under the Receiver Operating Characteristic (ROC) curve.

Additional outcome(s) Additional outcomes include the identification of biological and epidemiological factors influencing test performance (moderator variables) through subgroup analyses, evaluating the impact of commercial brands, HIV coinfection, age groups (<5 years vs. 6-17 years), and geographic regions. Furthermore, the certainty of the synthesized evidence will be established using the GRADE-DTA framework, and clinical applicability in low-resource settings will be qualitatively assessed.

Data management All identified citations will be exported to reference management software (Zotero/Mendeley) for deduplication. The study screening process (title/abstract and full-text) will be conducted independently by two blinded reviewers using the Rayyan QCRI platform. Data extraction will be independently performed using standardized forms. Any disagreements between the two primary reviewers during screening or data extraction will be resolved through consensus or, if necessary, by consulting a third senior reviewer (supervisor).

Quality assessment / Risk of bias analysis The methodological quality and risk of bias of all included studies will be systematically assessed using the QUADAS-2 instrument. This evaluation will encompass four key domains: patient selection, index test, reference standard, and flow and timing. Additionally, publication bias will be evaluated across studies using Deeks' funnel plot asymmetry test.

Strategy of data synthesis Data synthesis will be executed by pooling diagnostic accuracy measures (sensitivity, specificity, likelihood ratios, and DOR) using the bivariate random-effects Hierarchical Summary Receiver Operating Characteristic (HSROC) model. Heterogeneity will be quantitatively evaluated through the I^2 statistic and qualitatively assessed via visual inspection of HSROC curves. Sensitivity analyses will be conducted by systematically excluding studies classified as "High Risk of Bias" in any QUADAS-2 domain. All statistical meta-analytical procedures will be performed utilizing R software (mada package) and/or Stata (midas/metandi modules).

Subgroup analysis Subgroup analyses will be conducted to explore potential sources of heterogeneity based on the following pre-specified variables: type of recombinant antigen utilized (e.g., rK39 vs. rK28), commercial brand of the rapid diagnostic test (e.g., InBios, DiaMed, Cypress, Bio-Rad), presence of HIV coinfection, specific pediatric age groups (<5 years vs. 6-17 years), and geographic region of the study (Latin America, Asia, Africa).

Sensitivity analysis Sensitivity analyses will be performed to evaluate the robustness of the meta-analytical estimates by systematically excluding studies classified as having a "High Risk of Bias" in any of the four domains assessed by the QUADAS-2 instrument.

Language restriction Inclusion is restricted to articles published in English, Portuguese, or Spanish.

Country(ies) involved Brazil.

Other relevant information The certainty of the synthesized evidence will be systematically graded using the GRADE-DTA (Grading of Recommendations Assessment, Development and Evaluation for Diagnostic Test Accuracy) framework. Furthermore, this review adheres strictly to Open Science and FAIR (Findable, Accessible, Interoperable, Reusable) principles; extracted datasets, variable dictionaries, and analytical scripts will be made publicly available in an open-access repository, such as the Open Science Framework (OSF).

Keywords Visceral leishmaniasis; rK39 rapid diagnostic test; pediatric diagnosis; diagnostic accuracy; systematic review.

Dissemination plans The findings of this systematic review will be disseminated through multiple academic channels: (1) Submission of a formal manuscript to a high-impact, peer-reviewed international journal (preferably Q1/Q2) in the fields of Infectious Diseases or Tropical Medicine; (2) Oral and poster presentations at relevant national and international scientific congresses, such as the Brazilian Congress of Infectious Diseases (CBI) and IDWeek; (3) Defense as an undergraduate medical thesis (TCC) at PUCPR; and (4) Deposit of the full dataset and analytical protocols in an open-access repository following FAIR principles.

Contributions of each author

Author 1 - Guilherme Medina - Contributed to the conception and design of the protocol, formulated the search strategy, performed data extraction, and drafted the initial manuscript.
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Author 4 - Philipe Quagliato Bellinati - Acted as the senior methodological supervisor, served as the third independent reviewer to resolve disagreements during the screening process, oversaw the statistical analysis and GRADE-DTA evaluation, and critically revised the final protocol and manuscript for intellectual content.
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