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The diagnostic value of clinical and laboratory parameters in distinguishing between invasive bacterial infections and vaso-occlusive crisis in pediatric inpatients with sickle cell disease – A scoping review

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - Piloting of the study selection process.

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 5 August 2026 and was last updated on 5 August 2026.

INTRODUCTION

Review question / Objective To identify and map the clinical and laboratory parameters that influence the diagnosis of IBI and management of ABT in hospitalized pediatric patients with sickle cell disease experiencing vaso-occlusive crisis.

Background Sickle cell disease (SCD) causes vaso-occlusive crises (VOC) in pediatric patients. VOC are accompanied by fever and elevated inflammatory markers This makes it difficult to distinguish between an infection and a non-infectious condition and to decide whether or not to prescribe antibiotic therapy (ABT). Prolonged broad-spectrum ABT without confirmed infection risks adverse events and selects resistant pathogens. No consensus exists on how clinical, laboratory and microbiological findings should guide diagnosis of invasive bacterial infection (IBI) and management of ABT in this setting.

Rationale In pediatric patients with sickle cell disease experiencing vaso-occlusive crises, distinguishing invasive bacterial infection from sterile inflammation remains a major clinical challenge because both conditions frequently present with fever and elevated inflammatory markers. This diagnostic uncertainty often leads to empiric broad-spectrum antibiotic therapy, despite the absence of confirmed infection, increasing the risk of adverse events and antimicrobial resistance. A comprehensive overview of the clinical, laboratory, and microbiological parameters currently used to guide diagnostic and therapeutic decision-making is lacking, highlighting the need to systematically map the available evidence.

METHODS

Strategy of data synthesis Articles are searched in Pubmed/MEDLINE, Scopus and Web Of Science. Data is systematically extracted using a predefined charting form capturing study characteristics, patient population, relevant clinical, laboratory and microbiological findings. Extraction

is performed independently by two blinded reviewers, with a third blinded reviewer resolving disagreements.

Eligibility criteria This scoping review includes peer-reviewed studies that examine the detection of bacterial infections in hospitalized pediatric patients (aged 0–18 years) with SCD during VOC defined as admission because of pain or fever ≥38.0°C. Eligible sources of evidence are observational studies, clinical trials, retrospective chart reviews, case series, and clinical guidelines that report on the clinical, laboratory and findings influencing the diagnosis of IBI. In this context, IBI are defined as bacteremia (with or without signs of sepsis and organ dysfunction), bacterial pneumonia, pyelonephritis, or osteomyelitis. A subgroup of microbiologically confirmed IBI (cIBI) must be provided.
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Articles published in English and German will be considered to ensure accessibility and accurate interpretation of findings. No publication date restrictions will be applied in order to capture all relevant literature from the earliest available evidence to the present.
Studies focusing exclusively on adult populations, non-hospitalized settings, or infections unrelated to VOC will be excluded. Moreover, studies that only focus on the population of patients with acute chest syndrome (ACS) but not VOC in general will be excluded. Review articles, editorials, and conference abstracts without sufficient methodological detail will also be excluded.
The rationale for these criteria is to ensure the inclusion of studies that directly address the diagnosing process of IBI and antibiotic decision-making within the specific clinical context of pediatric SCD and VOC, while maintaining methodological rigor and relevance to inpatient management practices.

Source of evidence screening and selection
The selection of sources of evidence follows a two-step process:

1. Screening
• Titles and abstracts of all retrieved articles are independently screened by two reviewers to identify potentially relevant studies.
• Studies that do not meet the inclusion criteria or are clearly irrelevant are excluded at this stage.
2. Eligibility Assessment
• Full texts of potentially relevant articles are assessed for eligibility based on predefined inclusion and exclusion criteria by three reviewers. The following excluding reasons are defined:
• Po = Population (Age >18 years, ACS only)
• Or = Original data not provided (e. g. guidelines, reviews)
• Ci = cIBI trough microbiological testing not provided
• Di = Differentiation between VOC and cIBI not investigated
• Ac = Accessability
• La = Language (other than English, German)
• Discrepancies between reviewers were resolved through discussion.

Data management Data from the included studies are systematically extracted using a predefined data charting form developed and calibrated by the review team prior to use. The form represents a summary of findings tool and captured key information on study characteristics (e.g., author, year, country, study design), patient population, and clinical, laboratory and microbiological findings. Data charting is performed independently by two blinded reviewers. In cases of disagreement, a third independent blinded reviewer makes the final decision. Where information was unclear or missing, attempts are made to contact study authors to obtain or confirm relevant data.

The following variables are extracted from the included studies:

1. Study characteristics: Author, year of publication, country, study design
2. Sample size of subgroups: VOC, cIBI
3. Clinical findings: Temperature, Hemodynamic instability (defined as hypotension or persistent tachycardia requiring fluid resuscitation or inotropic drugs), Hypoxemia (defined as SpO2 <92%), Central venous catheter (CVC), Previous hospital admissions, Previous days of fever, Upper respiratory symptoms
4. Laboratory findings: White blood count (WBC), Absolute neutrophile count (ANC), Segmented granulocyte count (SGC), Absolute band count (ABC), Hemoglobin (HGB), Platelet count (PLT), C-reactive protein (CRP), Procalcitonin (PCT), Interleukin-6 (IL-6), IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, IL-17a, Interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α).

Reporting results / Analysis of the evidence For all studies, data is extracted as reported, including medians or means, ranges, without further transformation unless explicitly stated. In cases where data is missing or unclear, attempts are made to contact study authors; if this is

unsuccessful, the variable is recorded as “not reported.”.

Presentation of the results Data is presented in tables showing the results of the available evidence for each investigated parameter by kind of study (retrospective/prospective). Furthermore, results are presented as text. Where appropriate, Forrest plots are performed to visualize and compare effect sizes.

Language restriction Only articles in English and German are screened.

Country(ies) involved Germany.

Keywords vaso-occlusive crisis; VOC; sickle cell crisis; invasive bacterial infection; IBI; pediatric; children.

Dissemination plans Publication in a peer reviewed journal.

Contributions of each author

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