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Digital Ischemia and Gangrene in Neonates and Preterm Infants: A Systematic Review

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Abstract

Digital ischemia and gangrene in neonates and infants born preterm are rarely described, with evidence largely confined to case reports. Objective: To summarize reported clinical circumstances and distinguish preterm-specific observations from those involving term newborns. The review reported searching six information sources for publications from 2013 to 2023. The reported selection process identified 201 records, removed 27 duplicates, screened 174 records, assessed 85 full texts, and included five publications. We examined gestational age, age at presentation, anatomical site, clinical context, and outcomes. Two reports described extremely preterm neonates with catheter-associated ischemia, and one described a former preterm infant presenting later in infancy with sepsis-associated digital ischemia. Two additional reports involved term newborns, one with sepsis-associated digital gangrene and the other with dehydration, disseminated intravascular coagulation, and gangrene. The cases reflect heterogeneous clinical circumstances rather than a single established etiology. Causal inference and risk estimation are not possible from the available case-based evidence; incomplete historical search documentation further limits reproducibility.

Keywords

catheter-associated ischemia, digital ischemia, neonatal gangrene, neonatal sepsis, preterm infant, systematic review.

1. Introduction

Acute digital gangrene refers to tissue necrosis of the fingers or toes, whereas peripheral limb ischemia describes inadequate blood perfusion that may progress to gangrene but may also be reversible. These outcomes must be distinguished when synthesizing neonatal case reports. Both conditions are rarely documented in neonatal care, where infection, hemostatic disturbances, dehydration, and vascular access procedures may coincide with impaired distal perfusion (Ayyad et al., 2019; Sundaram et al., 2021).

Infants born prematurely frequently require invasive monitoring and vascular access. However, not all published reports of neonatal gangrene involve preterm infants. Relevant evidence also

includes term newborns and infants born preterm who develop ischemia beyond the neonatal period. Gestational age at birth and chronological age at the onset of ischemia therefore need to be distinguished.

Several pathophysiological pathways have been proposed. Systemic infection may be accompanied by endothelial activation, microcirculatory dysfunction, and coagulation disturbances. Severe dehydration may compromise systemic perfusion, while peripheral or central vascular catheterization may be associated with vasospasm, arterial injury, or thrombosis (Chang, 2019; Hotchkiss et al., 2016; Papageorgiou et al., 2018). Mechanisms described in the broader literature should not, however, be interpreted as proven causes in individual neonatal cases.

Published cases have sometimes used digital gangrene and potentially reversible digital ischemia interchangeably, or have failed to distinguish preterm birth from the neonatal age period. These differences in population and clinical outcome may lead to conclusions that exceed the underlying evidence.

This review examines five case-based publications identified through the reported search and synthesizes their documented clinical circumstances. Its objectives are to clarify population characteristics, distinguish ischemia from established gangrene, describe associated clinical factors, and identify limitations affecting etiological interpretation.

2. Research Methods

Review design and information sources

The review was reported as using a structured search of Scopus, PubMed/MEDLINE, ScienceDirect, the Cochrane Library, Embase, and Google Scholar, supplemented by reference-list screening. The stated publication period was 2013–2023, with eligibility restricted to English- and Indonesian-language reports. PRISMA 2020 was used as a reporting reference for the presentation of the review (Page et al., 2021).

The archived search documentation available for this report did not include the complete database-specific Boolean strategies, field restrictions, search dates, source-level record counts, or exported search results. Therefore, database-specific yields or dates cannot be verified, and no reconstructed search history is presented. These omissions limit the reproducibility of the reported search and require verification against the original research records.

Population, outcomes and eligibility

The review retained the five publications included in the reported evidence corpus and examined their population characteristics. The population comprises neonates and infants born preterm with digital or distal-limb ischemia or gangrene. This definition includes term newborns and recognizes that infants born prematurely may present more than 28 days after birth. Clinical reports documenting ischemic or gangrenous changes were prioritized over publications that discussed only hypothetical risk factors.

Digital gangrene was defined as reported distal tissue necrosis. Digital or peripheral ischemia included impaired perfusion, discoloration, or threatened gangrene without documented irreversible necrosis. Non-digital necrosis was considered only when it occurred alongside distal-limb involvement in the same patient. Adult diabetic limb disease and isolated neonatal soft-tissue infection without distal ischemia were not included in the five-publication synthesis.

Screening and study-selection accounting

The reported study-selection sequence comprised 201 identified records, 27 duplicates removed, 174 titles or abstracts screened, 89 records excluded, 85 full texts assessed, 80 full texts excluded, and five publications included. These totals are arithmetically consistent, but their source-level accuracy cannot be independently established without the original screening log. In particular, verified mutually exclusive reasons for the 80 full-text exclusions were unavailable; reason-specific counts have therefore not been inferred.

Data extraction and appraisal boundaries

For each included publication, the following information was examined where reported: study design, gestational age, birth weight, chronological age at presentation, anatomical site, suspected or documented mechanism, diagnostic evidence, management, and outcome. Information was identified as not verified when the available source did not permit reliable confirmation. Patient-level findings were distinguished from etiological factors mentioned only as background considerations in the source publication.

The evidence was synthesized descriptively. The study designs did not permit pooled risk estimation or comparisons with unexposed populations. Reporting limitations were examined narratively using domains relevant to JBI guidance for case reports and case series, including patient characteristics, event chronology, diagnostic support, and outcome reporting (Moola et al., 2020). A complete independent, item-by-item JBI appraisal was not documented, and no formal quality scores are reported.

3. Results and Discussion

Identification and selection of publications

The reported selection process yielded five publications: four individual case reports and one case-series article. The latter, by Bhat et al. (2014), describes multiple atypical manifestations of neonatal sepsis, of which only one case involved digital gangrene. Accordingly, the five publications should not be regarded as five clinically equivalent preterm neonatal cases.

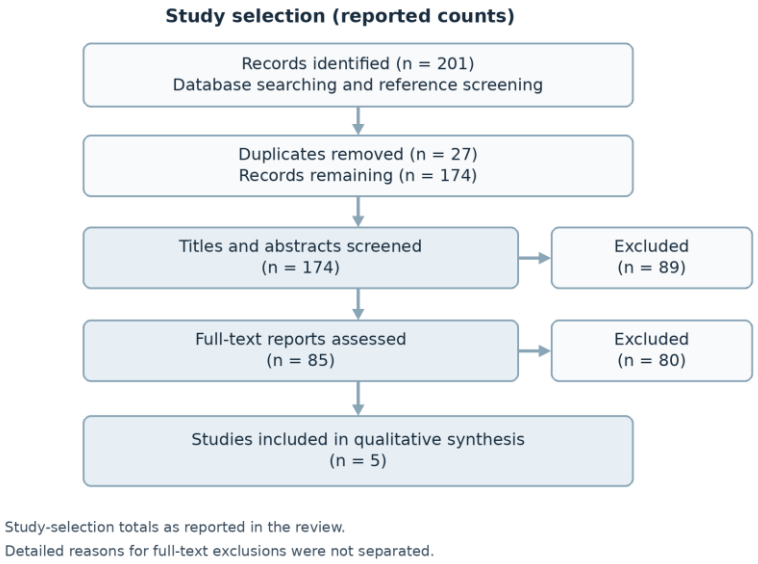


Figure 1. Study-selection flow based on the reported screening totals. Detailed full-text exclusion reasons and database search exports were unavailable for independent reconciliation.

Case characteristics and population verification

Table 1 distinguishes gestational age at birth from postnatal age at presentation and summarizes the anatomical site, documented clinical context, and outcomes. The anatomical findings in the Jadhav and Bhat reports were checked against the corresponding case descriptions.

Table 1. Core patient characteristics and reported clinical context of the five included publications

Report	Gestational age / birth weight	Age at event and site	Documented context	Outcome / interpretation
Choudhary et al. (2021)	26+3 weeks; 685 g; girl	Neonatal period; toes of left foot	Black discoloration appeared after peripheral IV catheter insertion; sepsis screen negative; Doppler showed flow.	Digital gangrene improved after catheter removal and topical nitroglycerin; temporal association does not itself prove mechanism.
Jadhav et al. (2021)	26 weeks; 490 g; boy	At 18 weeks postnatal age; right index finger, with additional digital changes	Sepsis-associated digital ischemia / presumed septic emboli; the affected extremity was not cannulated.	Impending gangrene improved; the event occurred beyond the neonatal period despite preterm birth.
Bhat et al. (2014)	Full term; birth weight not confirmed; girl weighed 2.7 kg at admission	About day 5–10 of life; fingers, later a toe	Culture-positive Klebsiella sepsis and coagulopathy; maternal antiphospholipid antibodies were negative.	Gangrenous fingertip loss was described; the source is a series of unusual sepsis cases, not a cohort of preterm gangrene.
Mackintosh et al. (2022)	25+0 weeks; birth weight not verified	Neonatal period, following PICC insertion; left hand fingertips	PICC-associated inadvertent arterial cannulation supported by subsequent Doppler findings.	Perfusion improved after line removal and care, but distal tip of index finger was ultimately lost.
Tamene et al. (2022)	40+1 weeks; 3,000 g; boy	Day 10–12 of life; distal limbs, left fifth finger and nasolabial region	Severe hypernatremic dehydration with coagulation abnormalities consistent with DIC; possible sepsis treated.	Extensive dry gangrene with fatal clinical outcome; this was a term neonate, not a preterm infant.

Clinical contexts represented by the evidence

Two reports describe ischemia temporally associated with vascular access. Choudhary et al. (2021) reported digital changes after peripheral intravenous catheter placement in a very preterm infant. Mackintosh et al. (2022) described left-hand ischemia after peripherally inserted central catheter (PICC) placement in an extremely preterm neonate, with abnormal Doppler findings supporting arterial compromise. The reports differ in diagnostic evidence and tissue outcomes.

Jadhav et al. (2021) described digital ischemia in a former 26-week preterm infant in the setting of suspected systemic infection. The ischemic event occurred at 18 weeks of postnatal age, and no catheter had been inserted into the affected extremity. This episode should not be classified as neonatal-onset ischemia or attributed to local catheter misplacement.

Bhat et al. (2014) described a term infant with culture-positive sepsis and evolving digital necrosis within a broader case series of atypical neonatal sepsis presentations. Other cases in that publication should not be counted as additional instances of digital gangrene. Tamene et al. (2022) reported a term newborn with severe hypernatremic dehydration, coagulation abnormalities, and gangrene affecting distal extremities and facial tissue. Neither report supports an interpretation limited to premature newborns.

Why population and outcome definitions matter

The included publications involve clinically different populations. Two clearly concern term-born infants, whereas another describes an infant born preterm whose ischemic event occurred after the neonatal period. Restricting the review to preterm neonates would therefore misrepresent the published evidence. The broader population definition aligns the research question with the available case descriptions but does not extend the underlying evidence base or resolve limitations of the historical search.

A further distinction concerns potentially reversible ischemia versus established tissue necrosis. Some reports describe threatened gangrene that improved with intervention; others document irreversible tissue loss. Combining these outcomes without qualification would imply unjustified clinical and etiological equivalence. The review therefore uses the terms ischemia and gangrene as appropriate, with case-specific outcomes described in Table 1.

Infectious and coagulation-related mechanisms

Sepsis may be accompanied by inflammatory endothelial injury, impaired perfusion, and coagulation abnormalities that contribute to distal ischemia (Chang, 2019; Hotchkiss et al., 2016; Papageorgiou et al., 2018). Nevertheless, isolated cases cannot establish the independent causal contribution of these pathways. Culture-positive infection in Bhat et al. (2014) differs from the presumptive septic-embolic mechanism discussed by Jadhav et al. (2021). In Tamene et al. (2022), severe dehydration and disseminated intravascular coagulation (DIC) are central features; the presentation should not be attributed exclusively to infection.

Catheter-associated vascular compromise

The vascular access reports emphasize the importance of procedure chronology and objective perfusion findings. Mackintosh et al. (2022) documented absent distal arterial flow on Doppler assessment after PICC placement, supporting an arterial mechanism. Choudhary et al. (2021) reported a temporal association with peripheral intravenous access, although the precise vascular mechanism was not established. These cases support careful monitoring of distal perfusion but cannot quantify the population-level risk of catheter-related ischemia or gangrene.

Dehydration, circulatory compromise and differentials

Severe hypernatremic dehydration and coagulation abnormalities were prominent in the term newborn described by Tamene et al. (2022). This case broadens the spectrum of associated clinical circumstances beyond infection and vascular access, but it does not establish the relative importance of competing mechanisms. Distal ischemic necrosis should also be distinguished from primary infectious soft-tissue necrosis at other anatomical sites. Evidence derived from adult diabetic gangrene should not be treated as direct neonatal etiological evidence.

Certainty, appraisal boundaries and research implications

The evidence consists of isolated case descriptions and a small case series without comparator groups, population denominators, uniform diagnostic criteria, or consistently reported gestational age and follow-up. It cannot support pooled risk estimates, causal attribution, or a ranking of etiological

factors. Clinical mechanisms discussed only in the introductions of the primary reports were not treated as documented exposures in the corresponding patients.

Reporting completeness differs across sources. Gestational and chronological ages or procedure-related timelines are more clearly documented in some reports than others, while the structure of the Bhat case series requires particular care to avoid counting unrelated presentations as digital gangrene. The narrative appraisal considers these reporting limitations but does not constitute a completed formal JBI quality-rating exercise (Moola et al., 2020).

An additional limitation concerns the original search documentation. Although the reported screening totals are internally consistent, the source-level search exports and detailed reasons for excluding 80 full-text reports remain unavailable. The reproducibility of the systematic search and the completeness of PRISMA reporting cannot therefore be independently established (Page et al., 2021).

Future studies should report gestational age and chronological age separately, document catheter characteristics and insertion events, describe microbiological and coagulation findings, distinguish threatened ischemia from established gangrene, and report serial outcomes. Prospective multicenter registries and well-designed observational studies would be more informative than isolated case reports for examining risk associations. Improvement after treatment in an individual report should not be interpreted as proof of comparative effectiveness.

4. Conclusion

The five included publications describe heterogeneous cases of digital or distal-limb ischemia and gangrene among neonates and infants born preterm. Reported clinical contexts include catheter-associated arterial compromise, suspected or documented infection, coagulation abnormalities, and severe hypernatremic dehydration. The evidence does not consist exclusively of preterm neonatal cases, and potentially reversible ischemia must be distinguished from established gangrene. Case-based reports cannot determine attributable risks, rank etiological factors, or establish treatment efficacy. Complete search records and higher-quality observational evidence are needed to strengthen future etiological conclusions.

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Publication Declarations

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Ethics and Consent : This study is a systematic review of previously published clinical reports concerning digital ischemia and gangrene in neonates and preterm infants. It did not involve the recruitment of new participants, direct patient contact, or the collection of new identifiable patient data. Accordingly, ethical approval and informed consent for participation in this review were not applicable. The authors relied on published reports and acknowledge the importance of protecting patient confidentiality in the presentation and interpretation of clinical information.

Data Availability : The evidence supporting this review is derived from the five publications included in the review and the other sources cited in the manuscript. The selection counts and clinical characteristics reported in the article reflect the information presented in the manuscript. However, the historical search documentation is incomplete, which limits the independent reproducibility of the search and selection process. Any additional data-extraction materials retained by the authors may be requested from the corresponding author, subject to availability and applicable confidentiality requirements.

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