Managements for Controlling Inflammation/ Infection in Diabetic Foot Ulcers: A Scoping Review

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Abstract

Aims: This review summarizes the management strategies for controlling inflammation/infection in diabetic foot ulcers based on infection severity and identifies research gaps.

Methods: This scoping review was conducted in accordance with the PRISMA-ScR guidelines. Three databases (PubMed, CINAHL, and Medline) were searched in October 2024 using combinations of keywords related to diabetic foot ulcers, inflammation, infection, osteomyelitis, and management. Two independent researchers screened and extracted data from studies meeting the inclusion criteria: original articles/case reports, studies involving patients with diabetic foot ulcers, and studies on inflammation/infection management.

Results: The search yielded 11201 articles, of which 206 met the inclusion criteria. The included studies were published between 1993 and 2024. Among these, two studies focused on inflammation and reported the beneficial effects of antioxidant vitamin and mineral supplementation and glycemic control. A total of 124 studies addressed infection management strategies, demonstrating the effectiveness of debridement, systemic antibiotic therapy, and adjunctive or innovative therapies. However, quantitative evidence distinguishing interventions based on local and systemic infections remains limited. In addition, 80 studies focused on osteomyelitis, supporting the effectiveness of surgical intervention, systemic antibiotic therapy, and adjuvant therapy.

Conclusion: The management strategies for diabetic foot ulcers include nutritional intervention, antimicrobial treatments, adjuvant therapies, and surgery. While these approaches affect inflammation and infection control, no study has identified the best method for each infection condition. Further research is needed to develop specific recommendations based on the infection severity and skin layers in diabetic foot ulcers.

Keywords: diabetic foot, inflammation, osteomyelitis, wound healing, wound infection

Introduction

Recent projections from the International Diabetes Federation indicate a continuing rise in global diabetes cases, with estimates reaching more than 640 million by 2030 and further increasing by 2045 (International Diabetes Federation, 2025). Diabetic foot ulcers are one of the most common complications associated with diabetes mellitus. It is estimated that approximately 2.5% of individuals with diabetes develop foot ulcers each year, and approximately 14–24% of these cases may ultimately lead to amputation. Globally, lower limbs are lost every 30 seconds due to diabetes, even though 85% of these cases could be prevented, as they are preceded by diabetic foot ulcer (Boulton, 2005). While, it is estimated that nearly 85% of lower limb amputations among patients with diabetes are preceded by the occurrence of diabetic foot ulcers, which if inadequately treated, may progressively worsen through persistent inflammation, tissue necrosis, and severe infection, ultimately necessitating limb amputation (Lepantalo et al., 2011).

The treatment of inflammation and infection in patients with diabetes remains distinct from that in non-diabetic patients due to the unique immunosuppressive and inflammatory states induced by chronic high blood sugar levels. Hyperglycemia weakens the "innate" immune system by inhibiting phagocytosis and glycosylating complement proteins, which can occur in patients with diabetic foot ulcers (Holt et al., 2024). Severe late-stage complications of diabetes, such as infection and ulceration, often occur in diabetic foot ulcers and are continuously associated with delayed healing (Wang et al., 2022).

Inflammatory and infectious treatments in patients with diabetes require specific approaches compared with non-diabetic protocols, as prolonged hyperglycemia promotes immune dysfunction and sustained inflammation. Hyperglycemia weakens the "innate" immune system by inhibiting phagocytosis and glycosylating complement proteins, which are essential for recognizing pathogens. Diabetic foot ulcers have a longer inflammatory phase of wound healing. This extended pro inflammatory state delays wound healing and can lead to the formation of chronic wound (Dasari et al., 2021). Persistent Inflammation and infection inhibiting angiogenesis, disrupting new tissue formation, and increasing the risk of complications such as osteomyelitis or sepsis (Eming et al., 2014; Falanga, 2005; de Gennaro et al, 2024; Wang Q, Liu C, An J, Liu J, 2025).

Therefore, infection control and inflammation management are crucial for the treatment of diabetic foot ulcers. Several wound management strategies are available for diabetic foot ulcers as the treatment of inflammatory or infected wounds, including surgical management, antimicrobial, wound offloading, vascular assessment, glycemic control, negative pressure wound therapy, dressing and topical products, and many more (Everett & Mathioudakis, 2018). Chronic inflammation prolongs the healing process by inhibiting angiogenesis and tissue regeneration, whereas infection exacerbates tissue damage and may lead to serious outcomes, such as osteomyelitis. To address these issues, various wound management strategies have been developed, including surgical intervention, antimicrobial therapy, offloading techniques, vascular assessment, glycemic control, negative pressure wound therapy, advanced dressings, and the use of topical agents. These approaches aim to interrupt the prolonged inflammatory phase, promote tissue repair, and ultimately improve healing outcomes in patients with diabetic foot ulcers (R. G. Frykberg & Banks, 2015; Spampinato, Simona Federica Caruso et al., 2020). The American Diabetes Association has published a few developments in the treatment of ulcerations, including the management of diabetic foot ulcers, and agreed that the management of infection is one of the basic principles of ulcer treatment. Many products have been developed to overcome diabetic foot ulcers such as negative pressure therapy, growth factors, acellular matrix tissue, hyperbaric oxygen therapy, and most recently topical oxygen therapy to prevent inflammation/infection (American Diabetes Association Professional Practice Committee, 2025). However, there are no systematic recommendations for management strategies to control inflammation/infection in diabetic foot ulcers. This gap underscores the need for a comprehensive synthesis of the current evidence to support more targeted and severity-based clinical decision-making. While the goal of these interventions is to shorten the inflammatory phase, limit microbial burden, and promote tissue repair, their application in clinical practice often lacks clear differentiation based on the infection severity of tissue involvement. By summarizing what has been identified regarding the management of inflammation/infection in this review, we aim to propose recommendations that could be utilized to control inflammation/infection in diabetic foot ulcers. The most appropriate question for this scoping review was, What kinds of management strategies can be utilized to control inflammation/infection in patients with diabetic foot ulcers?

Methods

Design

This scoping review aimed to summarize the available evidence on the management of inflammation/infection in diabetic foot ulcers according to the severity of infection and to identify potential gaps in the current research. Patient, Concept, and Context (PCC) were defined according to the JBI Manual as follows: a patient was an adult with a diabetic foot ulcer, the concept was diabetic foot ulcer inflammation/infection, and the context was none.

Protocol and registration

This review adopted the PRISMA-ScR framework to guide the identification, screening, and reporting of evidence relevant to infection and inflammation management strategies (Tricco et al., 2018). No published or registered protocols were available for this review.

Eligibility criteria

We included studies involving participants of all ages with foot ulcers in any setting. Studies on management for controlling inflammation/infection were included, and we had no limitation on publication years. We limited the search to articles published in English. Originally published articles and case reports were included in this scoping review. Proceedings, conference abstracts, letters to the editor, editorials, guidelines, protocols, literature reviews, and meta-analyses were also excluded.

Information sources

The following bibliographic databases were searched in October 2024: PubMed, CINAHL, and Medline. Search terms and strategies were formulated based on consensus among the research team members. The retrieved citations were imported into Rayyan (Qatar Computing Research Institute, Doha, Qatar), where duplicates were identified and removed by one author (EI).

Search
The search was performed using a combination of search terms, including “diabetic foot ulcer” OR “diabetic foot” OR “diabetic ulcer” OR “diabetic wound” AND “inflammation” OR “inflamed” OR “infection” OR “infected” OR “local infection” OR “localized infection” OR “osteomyelitis” OR “bone infection” OR “systemic infection” OR “sepsis” AND “management” OR “treatment” OR “therapy” OR “intervention”.

Table 1. Search history on 24th October 2024

Source	Search Number	Boolean Search	Result Articles
PubMed	4	((#1) AND (#2)) AND (#3)	4,951
	3	“management” OR “treatment” OR “therapy” OR “intervention”	11,186,552
	2	“inflammation” OR “inflamed” OR “infection” OR “infected” OR “local infection” OR “localized infection” OR “osteomyelitis’ OR “bone infection” OR “systemic infection” OR “sepsis”	2,689,716
	1	“diabetic foot ulcer” OR “diabetic foot” OR “diabetic ulcer” OR “diabetic wound”	20,010
CINAHL	4	(“management” OR “treatment” OR “therapy” OR “intervention”) AND (S1 AND S2 AND S3)	2,189
	3	“management” OR “treatment” OR “therapy” OR “intervention”	2,807,168
	2	“inflammation” OR “inflamed” OR “infection” OR “infected” OR “local infection” OR “localized infection” OR “osteomyelitis” OR “bone infection” OR “systemic infection” OR “sepsis”	425,038
	1	“diabetic foot ulcer” OR “diabetic foot” OR “diabetic ulcer” OR “diabetic wound”	12,575
Medline	4	(“management” OR “treatment” OR “therapy” OR “intervention”) AND (S5 AND S6 AND S7)	5,004
	3	“management” OR “treatment” OR “therapy” OR “intervention”	11,333,839
	2	“inflammation” OR “inflamed” OR “infection” OR “infected” OR “local infection” OR “localized infection” OR “osteomyelitis” OR “bone infection” OR “systemic infection” OR “sepsis”	2,771,861
	1	“diabetic foot ulcer” OR “diabetic foot” OR “diabetic ulcer” OR “diabetic wound”	19,998

Selection of sources evidence
The retrieved records were imported into Rayyan (Qatar Computing Research Institute, Doha, Qatar), and duplicate entries were eliminated. Two reviewers (EI and MO) independently screened the titles and abstracts, excluding studies that did not satisfy the eligibility criteria. Subsequently, the remaining full-text articles were assessed against the inclusion criteria by two independent researchers (EI and AY). Any disagreements during the selection process were resolved through discussions.

Data charting process
A data charting template was designed by one of the authors (EI) to specify the variables to be extracted. Data extraction was conducted by EI and subsequently checked by the co-authors (MO and AY). Any inconsistencies in the extracted information were addressed through discussions among the three authors (EI, MO, and AY).

Data items
The following information was extracted: (a) study authors, year of publication, and country; (b) study design/participants; (c) aims/purpose; (d) characteristics; (e) management method of inflammation/infection; and (f) outcomes related to controlling inflammation/infection.

Synthesis of results
We grouped the studies according to categories of management methods and presented them in three tables: management of inflammation, management of infection, and management of osteomyelitis. Management methods were divided into surgical debridement, adjunctive therapies, dressing, innovative therapies, and antimicrobials according to the guidelines.

Result
Selection of sources evidence
The database search identified 12,144 records in total. After removing duplicates (n=943), 11,201 studies remained for screening. Title and abstract assessments led to the exclusion of 10,856 articles. Subsequently, 345 full-text papers were reviewed in detail, of which 139 were excluded for not meeting the inclusion criteria. Finally, 206 articles were included in this scoping review. The study selection process is illustrated in the PRISMA flowchart (Figure 1).

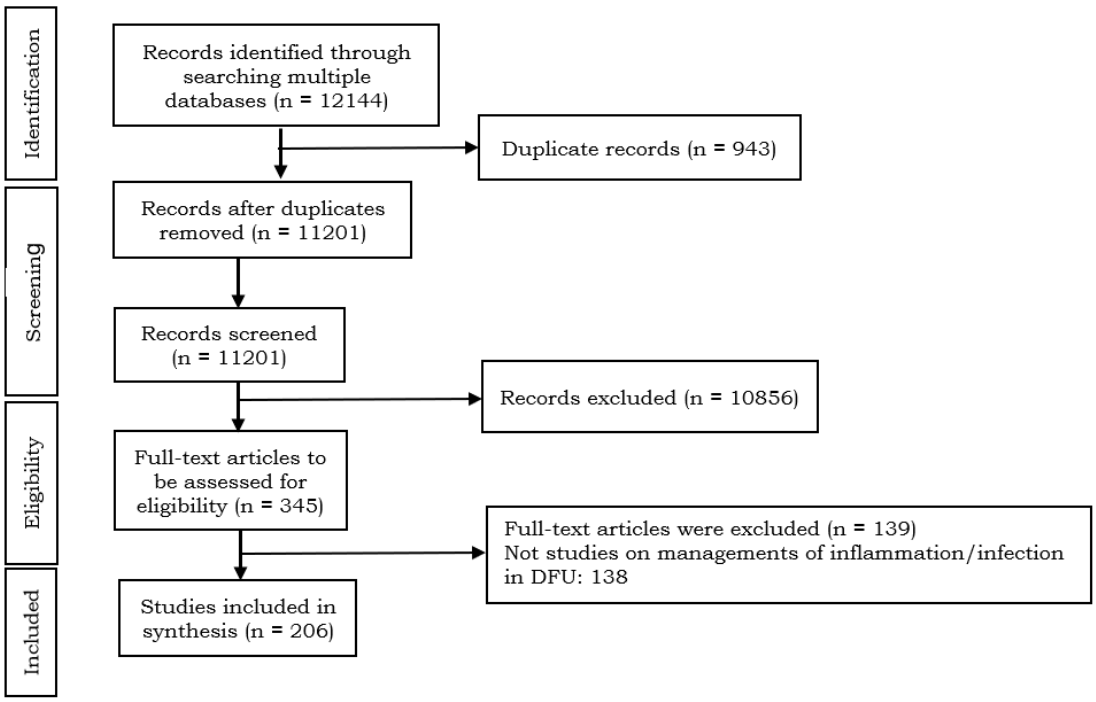

Figure 1. A PRISMA flow chart for this scoping review

Characteristics of sources of evidence
A summary of the management of inflammation/infection in diabetic foot ulcers is presented in Figure 2. Infection management is the most researched, while inflammation management remains underexplored 117 were original articles, 82 were case reports and 7 were case series. The included studies were published between 1993 and 2024 and were conducted by research teams in Argentina, Australia, Belgium, Brazil, Canada, China, Cuba, Cyprus, Czechia, Denmark, Egypt,

France, Germany, Greece, India, Indonesia, Iran, Iraq, Ireland, Israel, Italy, Japan, Korea, Lebanon, Mexico, Netherlands, Poland, Portugal, Saudi Arabia, Serbia, Singapore, Slovenia, Slovakia, Spain, Switzerland, Taiwan, Trinidad and Tobago, Turkey, the United Kingdom, and the United States of America.

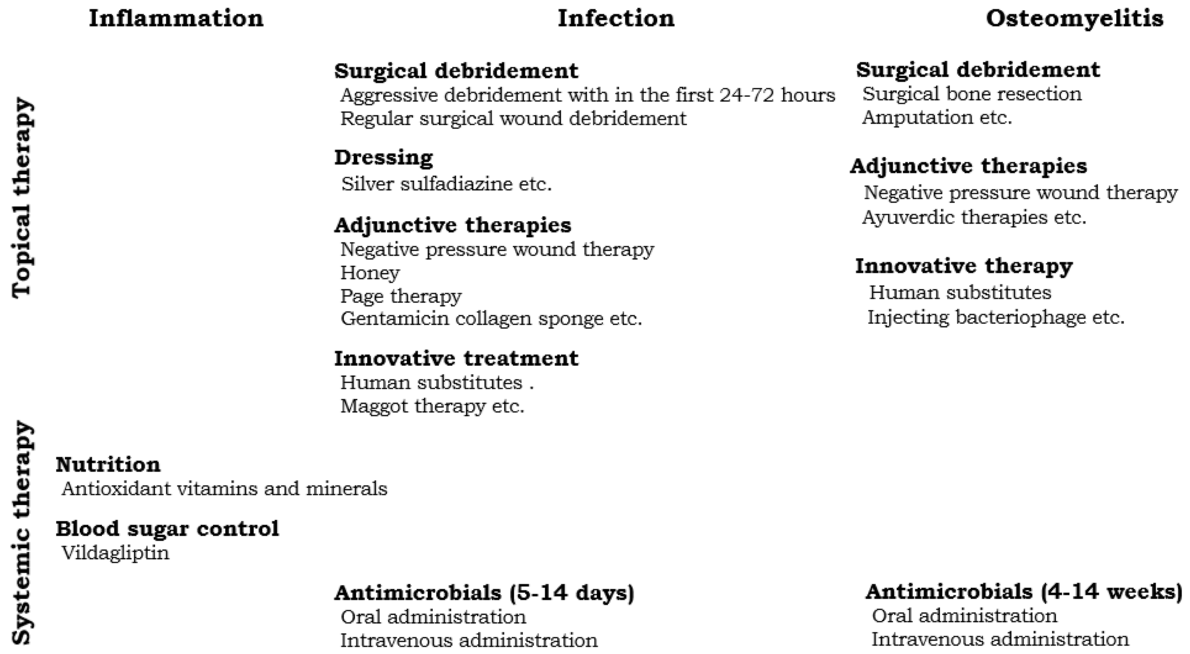

Figure 2. Management of inflammation/infection

Synthesis of result

Management for inflammation

There were two publications related to inflammation, which were published in 2022, the publication was from Switzerland and Australia. Nutritional support plays a crucial role in regulating and reducing inflammation in IBD. Both the control and intervention groups received standard wound care; however, the intervention group was supplemented with antioxidant vitamins and minerals. These nutrients may help reduce chronic inflammatory responses and contribute to improved healing of long-standing wounds. Antioxidants, such as vitamins C, A, and E, and trace elements, including zinc, manganese, and copper, are recognized for their strong anti-inflammatory properties. Levels of inflammatory biomarkers—C-reactive protein, interleukin-6 (IL-6), interleukin-10 (IL-10), and tristetraprolin—were measured at baseline and then every four weeks until wound closure or for a maximum of 12 weeks post-treatment. A significant reduction in mean IL-6 plasma levels was observed in the intervention group, suggesting that nutritional supplementation may be beneficial in controlling inflammation among patients with diabetic foot ulcers (Basiri et al., 2022).

Vildagliptin is an antihyperglycemic agent that is classified as a dipeptidyl peptidase-4 (DPP-4) inhibitor. Human studies investigating its anti-inflammatory effects have reported potential benefits, including reduced oxidative stress and inflammatory activity. In one trial, patients receiving vildagliptin (100 mg/day) in addition to standard care experienced better wound healing outcomes up to 12 weeks than those receiving placebo plus standard care. Biochemical measures and inflammatory markers were assessed at baseline and at weeks 6 and 12, with final analyses conducted at the end of the study period. The vildagliptin group showed decreases in C-reactive protein, white blood cell count, neutrophil levels, and ulcer dimensions (length, width, and surface area) compared to the placebo group. Nevertheless, other inflammatory indicators, such as IL-6, did not differ significantly between the groups(Vangaveti et al., 2022). The management methods used to control inflammation were nutritional supplementation and vildagliptin as an antihyperglycemic medication. (Supplementary Table 1, https://kanazawa-u.repo.nii.ac.jp/records/2003856)

Management for infection

A total of 124 studies examined infection management in diabetic foot ulcers. In 2020, there were fewer publications, presumably due to the impact of the pandemic, but the number of publications related to infections has tended to increase since 2019 (Figure 3). The most common country was the United States of America (23 studies, 18.5%), followed by China (17 studies, 13.7%) and the United Kingdom (14 studies, 11.3%). Several types of surgical debridement have been performed to control infection, including aggressive debridement within the first 24–72 hours (Boey et al., 2023), regular surgical wound debridement (Aybar et al., 2022; Chai et al., 2020; Dai et al., 2023; Derakhshan et al., 2022; Godoy-Santos et al., 2019, 2021; Hajimohammadi et al., 2021; M. H. Kim, 2022; Kunjalwar et al., 2024; Parizad et al., 2022; Vucetic, 2012; Welch & Forder, 2016) where the goals of debridement were source control, limb salvage, and preservation of limb function (Supplementary Table 2, https://kanazawa-u.repo.nii.ac.jp/records/2003856).

Antimicrobials are also essential for infection control and are administered orally or parenterally, tailored to the specific microorganisms causing the infection. Various antimicrobials were administered, such as intravenous amoxicillin 625 mg for 7 days, oral linezolid 600 mg for 5 days, followed by gentamicin 80 mg for 12 days (Kunjalwar et al., 2024), parenteral amoxicillin (1.2 g administered every eight hours, or ceftazidime at a dose of 2.0 g given at the same interval (Fejfarová et al., 2024). Other combinations included flucloxacillin (Mcelvanna et al., 2021), cefuroxime and cloxacillin (Dihari & Pathirage, 2020), ciprofloxacin (Kabbara & Zgheib, 2015; Morley et al., 2013), tigecycline (Arda et al., 2017), and piperacillin/tazobactam (Gough et al., 1997; Harkless et al., 2005; Lipsky et al., 2007; Matthew Malone, 2015; Mccreery et al., 2023; Saltoglu et al., 2010), sulbactam-ampicillin with administration varying from daily to every 6-12 hours depending on the regimen. Antibiotic therapy was administered for durations ranging from 5–14 days, guided by individual patient outcomes.

In addition to antimicrobials, adjunctive therapies are used to control infections in diabetic foot ulcers. Adjunctive therapy is used in addition to primary or main therapy to support, enhance, or complement primary treatment (Smith et al., 2024). In this study, adjunctive therapies included topical treatments such as prabivismane (Lipsky et al., 2024), phenytoin (Tabana et al., 2024), hemoglobin spray (Siafarikas et al., 2024), autologous adipose tissue prepared with minimal processing and applied using 3D bioprinting techniques (Yoon & Song, 2024), LL-37 cream (Miranda et al., 2023), honey (Astrada et al., 2019; Evers, 2011; Faraji et al., 2023; Holubová et al., 2023; Siavash et al., 2011), page therapy (Fish et al., 2016; Young et al., 2023), negative pressure wound therapy with or without instillation,moist exposed burn ointment (Zhan et al., 2021), Dakin solution (Duarte et al., 2020), cadexomer iodine (Malone et al., 2019), gentamicin collagen sponge (Uçkay et al., 2018), pexiganan acetate cream (Lipsky et al., 2008), and pedyphar ointment (Abdelatif et al., 2008).

In this study, dressing also plays a crucial role in controlling infection in diabetic foot ulcers by providing a protective barrier, absorbing exudate, and preventing bacterial contamination such as silver sulfadiazine (Anzali et al., 2023; Serrudo et al., 2024) silver (Hosseinpoor et al., 2023), chitosan and nano silver (Abdollahimajd et al., 2022), prontosan (Chai et al., 2020), acidifying antiseptic solution (Fejfarová et al., 2019), silver foam (Lázaro-Martínez et al., 2019), polyhexamethylene biguanide foam (Welch & Forder, 2016), aquacellAg (Torkington-Stokes et al., 2016), antimicrobial exudate transfer dressing (Dhatariya et al., 2016), silver-impregnated hydro fiber dressing (Shen et al., 2016), which promotes a cleaner wound environment conducive to healing.

Innovative treatments are also used to control infections. These therapies refer to new treatments, technologies, or procedures developed through ongoing research (Wendler et al., 2021). In this study, the innovative treatments used include: photodynamic therapy (Mancusi et al., 2024), fufang huangbai fluid hydropathic compress (Yang et al., 2024), growth stimulating factors(Gough et al., 1997; Zhang et al., 2024), autologous cells (Nilforoushzadeh et al., 2021; Sun et al., 2024; Yoon & Song, 2024), vaporous hyperoxia therapy (Abedi et al., 2024), ozone therapy (Anzali et al., 2023; Uzun et al., 2012), platelet rich plasma (Deng et al., 2016; Kim, 2022), polarized light therapy (Taha et al., 2022), low intensity diagnostic ultrasound combined with microbubbles (Zhang et al., 2022), photo bio modulation therapy (Derakhshan et al., 2022), aminolevulinic acid photodynamic therapy (Li et al., 2022), non-thermal gas plasma (Wiegand et al., 2022), maggot therapy (Hajimohammadi et al., 2021, 2023; Malekian et al., 2019; Parizad et al., 2021; Pinheiro et al., 2015; Siddique et al., 2018), waterjet (Liu et al., 2023), bioactive glass (Godoy-Santos et al., 2019), human substitutes (Clerici et al., 2010; Cole, 2016; Frykberg et al., 2011; Frykberg et al., 2017; Yamaguchi et al., 2004), prostaglandin therapy (Chu et al., 2015), superoxidized solution (Paola et al., 2006; Medina et al., 2007; Piaggesi et al., 2010), de Marco formula (Duarte et al., 2010; Duarte et al., 2009), hyperbaric oxygen therapy (C. E. Chen et al., 2010), and intermittent pneumatic foot compression (Armstrong & Nguyen, 2000). Many adjunctive therapies have shown improvements in infection control, although wonder of life (Kalanchoe pinnata) (Cawich et al., 2014), soft candle (Cawich et al., 2014), and intralesional ozone injection (Uzun et al., 2012) showed no significant improvement in infection control. Studies on infection have examined the effectiveness of debridement, systemic antibiotic therapy, and adjunctive therapies.

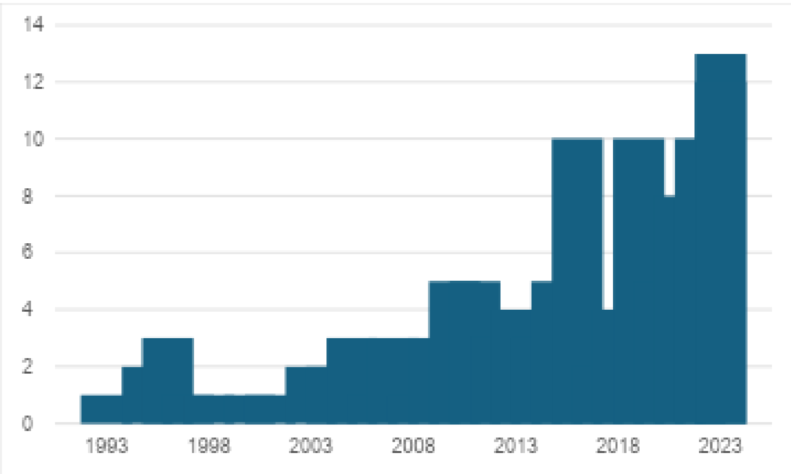

Figure 3. Publication trends in diabetic foot ulcer with infection

Management for osteomyelitis
Eighty studies focused on the control of osteomyelitis. In 2020, there were fewer publications, presumably due to the impact of the pandemic; however, the number of publications related to osteomyelitis has tended to increase since 2019 (Figure 4). The most common country was the United States of America (18 studies, 22.5%), followed by Italy (8 studies, 10.0%) and the United Kingdom (8 studies, 10.0%).

Diagnosis and comprehensive treatment plans, including antimicrobial therapies such as calcium sulfate, were applied 1–2 days post-surgery (Arissol & Newsholme, 2024; Hutting et al., 2019; Patil et al., 2021). Oral antibiotics such as rifampicin (10 mg/kg, max 600 mg/day) were used for up to 3 months (Goyal et al., 2024; Senneville et al., 2001), calcium sulfat antibiotic beads (Qin et al., 2019), oral rifampicin (600 mg daily) (Papaetis et al., 2023), dalbavancin 1000 mg followed by 500 mg weekly (Navarro-Jiménez et al., 2022), rifampin therapy within 6 weeks (Wilson et al., 2019), a regimen consisting of oral fusidic acid 500 mg three times per day and ciprofloxacin 500 mg twice per day (Bamberger et al., 1987; Memis et al., 2014), oral ofloxacin every 12 hours (Lipsky et al., 1997) and intravenous antibiotics like teicoplanin (10 mg/kg daily) (Papaetis et al., 2023), imipenem/cilastatin (1 g every 8 hours) followed by ertapenem (1 g daily) (Papaetis et al., 2024), dalbavancin 1.5 g every two weeks (Loupa et al., 2020), daptomycin was given intravenously at a daily dose of 500 mg (approximately 4 mg/kg/day) (Dos Remedios, 2009), were choices depend on the result cultured. Intravenous fosfomycin is a potential treatment option (Wong et al., 2021). Treatment durations varied, with some regimens lasting 4-6 weeks, and others as long as 12-14 weeks depending on the patient's condition.

Innovative therapies such as cerament-G (Karr, 2011; Niazi et al., 2019; Vasukutty et al., 2022; Wokhlu & Vasukutty, 2021; Zhong et al., 2024), platelet-rich plasma (Alrayes et al., 2024), autologous human bone marrow stem cells (Humenik et al., 2024), topical ozone therapy (Dadfar et al., 2023), bioactive glass (Panunzi et al., 2022), carbon dioxide foot bathing (Hihara et al., 2022), human skin substitutes (Caruso et al., 2022; Marston et al., 2019; Nilforoushzadeh et al., 2021; Raphael & Gonzales, 2017), smartphone applications (Kong et al., 2021), platelet rich fibrin (Crisci et al., 2018), injecting bacteriophage (Fish et al., 2016), CO2 laser treatment (Monami et al., 2017), topical oxygen (Cahn & Kleinman, 2014), low-frequency ultrasound (Amini et al., 2013), photodynamic antimicrobial chemotherapy (Tardivo & Baptista, 2009), Kritter's close instillation system (Connolly et al., 2000) were explored. The adjunctive therapies used in this study included negative pressure wound therapy with or without instillation (Enodien et al., 2021; Ramanujam & Zgonis, 2010; Raphael & Gonzales, 2017; Zhong et al., 2024), medicinal leech therapy (Bopparathi & Narasimha, 2023), triphala decoction cleansing, jatyadi tail dressing and leukocyte platelet (Bopparathi & Narasimha, 2023), that have been shown to contribute to control diabetic foot ulcer with osteomyelitis.

Surgical interventions, including surgical debridement (Aliakbar et al., 2019; Alkhatieb et al., 2021; Aragón-Sánchez et al., 2012; Beieler et al., 2012; Chow et al., 2024; Herbert, 2013; Hutting et al., 2019; Mendivil et al., 2016) surgical bone resection (Lavery et al., 2024; Qin et al., 2019) and amputation (Mendivil et al., 2016; Petithomme-Nanrocki et al., 2024; Schöni et al., 2023; Yoho et al., 2008) were crucial for successful management of osteomyelitis. Surgical bone resection is an important intervention for diabetic foot ulcers complicated by osteomyelitis. This procedure involves excising infected or necrotic bone to achieve infection control, limit inflammatory processes, and support wound healing while maintaining maximal preservation of limb function. The success of bone resection is often measured by the absence of bone reinfection (Qin et al., 2019). Another surgical intervention is transverse tibial bone transport, an advanced limb-salvage technique that is also employed in patients with chronic osteomyelitis, extensive bone loss, or severe ischemia. This technique, based on the Ilizarov method, promotes new bone formation and enhances blood flow to the affected limbs. Following a 10-day latency phase, distraction was initiated, and the bone segment was gradually compressed for 28 days. The external fixator was removed once radiographic imaging confirmed adequate healing, and the patients were permitted to bear weight throughout the course of treatment. Wound healing was considered complete 20 weeks after the start of tibial bone transport (Yang et al., 2024). Studies on osteomyelitis have demonstrated the effectiveness of systemic antibiotics and adjuvant therapies (Supplementary Table 3, https://kanazawa-u.repo.nii.ac.jp/records/2003856).

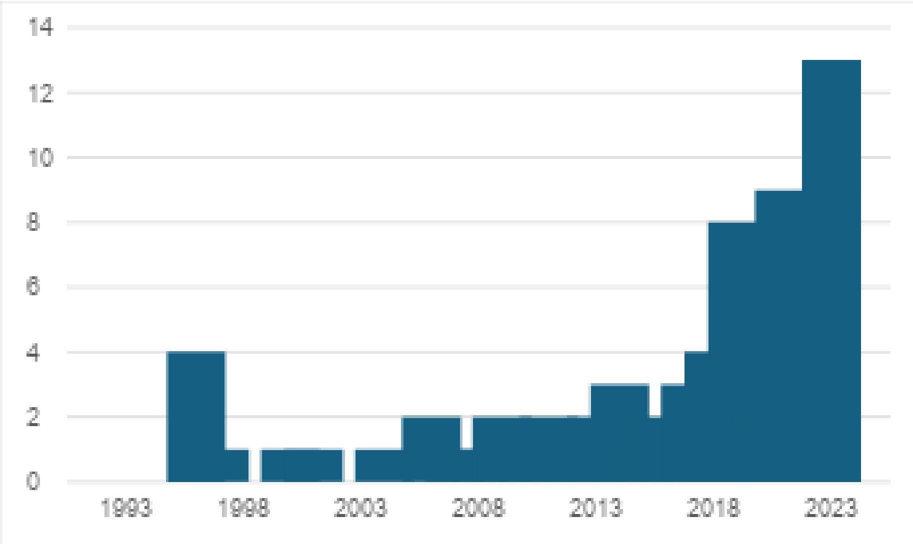

Figure 4. Publication trends in diabetic foot ulcer with osteomyelitis

Discussion

Summary of evidence

This review highlights the imbalance of evidence in DFU care, where infection-focused interventions are well documented, whereas inflammation-targeted strategies remain limited and require further investigation. The available literature shows a clear imbalance, with a substantially greater focus on infection management than on inflammation control. A total of 206 articles were identified, of which 117 were original studies, 82 were case reports, and seven were case series published between 1993 and 2024. Studies on inflammation have demonstrated the effectiveness of antioxidant vitamin and mineral supplements and blood glucose control, and studies on osteomyelitis have demonstrated the effectiveness of systemic antibiotics and adjuvant therapies, such as negative pressure wound therapy and human skin substitutes. In contrast, studies on infection have examined the effectiveness of debridement, systemic antibiotics, and adjunctive therapies. However, despite the predominance of infection-focused studies, limited attention has been given to clearly distinguishing or integrating treatment strategies targeting local versus systemic inflammatory and infectious processes.

Management for inflammation

This study indicates that effective inflammation control in diabetic foot ulcers can be achieved through a synergistic approach combining nutritional intervention, optimal glycemic control using antihyperglycemic agents, and appropriate antibiotic therapy, initially empirical and subsequently guided by culture and sensitivity results from tissue sampling. Inflammation is a critical phase of wound healing that is highly energy-dependent and requires substantial metabolic resources to support cell proliferation, protein synthesis, angiogenesis, and enzymatic activity (Worsley et al., 2023). Therefore, adequate intake of energy, protein, macronutrients, electrolytes, and micronutrients is essential, as undernutrition in patients with diabetic foot ulcers prolongs inflammation, impairs neovascularization and collagen synthesis, and reduces tissue tensile strength (H. Chen et al., 2025; Wild et al., 2010). Early prevention of protein–energy malnutrition and timely micronutrient supplementation have been shown to accelerate wound healing and limit inflammatory persistence (Kurian SJ, Baral T et al., 2023).

Concurrently, antihyperglycemic therapies play a complementary role in modulating inflammation by stabilizing the metabolic homeostasis. Recent evidence highlights that achieving optimal glucose regulation through antihyperglycemic therapies, such as metformin, glucagon-like peptide-1 receptor agonists, and dipeptidyl peptidase-4 inhibitors, provides benefits beyond blood sugar control. These agents also modulate key inflammatory and tissue repair mechanisms, including pathways involving AMP-activated protein kinase, mechanistic target of rapamycin, and vascular endothelial growth factor signaling (Omotosho et al., 2025). Available evidence suggests that sustained glycemic control, supported by continuous glucose monitoring and consistent adherence to antihyperglycemic therapy, can improve the efficacy of the antibiotic treatment. This effect may occur through enhanced immune cell activity and decreased bacterial pathogenicity, ultimately promoting the resolution of inflammation and facilitating wound healing (Maghsoodloo et al., 2025; Pantazopoulos et al., 2025).

Management for infection

The management of diabetic foot infections necessitates a multidisciplinary approach encompassing antimicrobial therapy, adjuvant therapy, surgical intervention, and comprehensive wound care to address the complex nature of these infections (Maity et al., 2024).

Antimicrobial therapy

Antimicrobial therapy is a cornerstone of diabetic foot infection management and is almost always required in such cases. Initial antibiotic selection is typically empirical and is determined by factors such as the severity of infection, previous antibiotic use, local antimicrobial resistance trends, and individual patient risk characteristics (Selva Olid et al., 2015). Antibiotic therapy should provide adequate activity against Staphylococcus aureus, the most frequent and aggressive pathogen in diabetic foot infection. Once culture and sensitivity data are obtained, the regimen should be tailored to improve the outcomes and reduce resistance (Adesanya et al., 2023). Attention is warranted for resistant organisms such as *Pseudomonas aeruginosa* and multidrug-resistant gram-negative bacteria, which complicate treatment and necessitate targeted antibiotic strategies (Lipsky, 2007).

Wound dressings

Wound dressings are widely used in diabetic foot ulcer management strategies by protecting the wound environment and supporting infection control and healing (Wu et al., 2015). Dressing selection should be guided by wound characteristics, including the presence of infection, exudate level, and tissue condition of the wound. Antimicrobial dressings are commonly employed in infected ulcers to reduce bioburden while maintaining a moist wound environment (Ivory JD & C, 2018). In addition to their antimicrobial effects, certain dressings may exert anti-inflammatory effects that contribute to improved healing outcomes (Zhao et al., 2024). Cost, availability, and ease of use are important considerations when choosing a dressing. (Jiang et al., 2023)

Adjuvant therapies

Adjuvant therapy plays a crucial role in managing infections in diabetic foot ulcers by enhancing the effectiveness of primary treatment (Monami et al., 2025). These approaches aim to reduce bacterial load, modulate the wound microenvironment, and stimulate tissue regeneration (Shahid et al., 2024). Techniques such as biological debridement, negative pressure wound therapy, and the use of acellular or bioengineered matrices support wound healing by improving perfusion, managing exudates, and promoting cellular responses. Growth factor–based therapies and tissue replacement strategies further stimulate angiogenesis and extracellular matrix formation. Overall, these diverse adjuvant therapies address the complex nature of diabetic foot ulcer infections by promoting a more effective healing environment (Pandey et al., 2025).

Surgical debridement

Surgical debridement is a crucial intervention for achieving source control and eliminating necrotic tissue, particularly in the presence of deep or advanced infections. By removing necrotic and devitalized tissue, debridement reduces the bacterial burden, enhances antibiotic penetration, and restores the wound’s capacity for granulation and re-epithelialization. It also alleviates mechanical pressure in callused or nonviable areas, thereby supporting infection control and wound healing. Therefore, surgical debridement remains a foundational component of comprehensive diabetic foot ulcer management (Kim et al., 2023).

Management for osteomyelitis

The last category is the management of osteomyelitis in diabetic foot ulcers. Diabetic foot osteomyelitis remains difficult to diagnose and manage, and many adverse outcomes are often associated with delayed detection, late specialist referral, and inappropriate treatment decisions (Martínez et al., 2019). This study found that there are several management strategies that can be used to address osteomyelitis, including systemic antimicrobial, local antimicrobial and surgical intervention (Lipsky et al., 2020). While each approach has demonstrated effectiveness in selected contexts, combined antibiotic and surgical therapy remains the gold standard for many patients, particularly when there is extensive bone involvement or concomitant soft tissue infection, as it simultaneously achieves source control and eradicates residual infection (Jing et al., 2025; Luis et al., 2019).

Systemic antimicrobial

Systemic antibiotics remain the foundation of treatment and may be used with or without bone resection, depending on the disease extent and patient factors. Consistent with the International Working Group on the Diabetic Foot (IWGDF) guidance, medical therapy without surgery can be considered for patients with diabetes who have uncomplicated forefoot osteomyelitis and no other indications for operative management. In selected cases, adjunctive systemic agents (e.g., oral rifampin) may be used at the discretion of infections specialists to address biofilm-related infection, reflecting the recognition that biofilms can contribute to persistence and recurrence (Lipsky et al., 2008).

Local antimicrobial

Local antimicrobial delivery is increasingly used as an adjunct to systemic therapy and/or surgery, particularly to achieve high antimicrobial concentrations at the infected site while potentially reducing the reliance on systemic delivery in patients with compromised perfusion. Local options include antibiotic-impregnated bone cement and synthetic bone void fillers (e.g., gentamicin-loaded calcium sulfate/hydroxyapatite composites) that provide structural support and may promote bone regeneration while delivering antimicrobial effects. Additional carrier systems (e.g., polymer-based gels/cements) and antimicrobial peptides have also been explored as local delivery modalities (Metaoy et al., 2024). Emerging loaded biocomposite materials are specifically framed as a strategy to sustain antimicrobial concentrations above the minimum inhibitory concentration directly at the infected tissue, reduce systemic toxicity risk, and potentially shorten therapy duration, thereby supporting antimicrobial stewardship and resistance mitigation (Craven et al., 2025).

Surgical intervention

Surgical intervention remains central to osteomyelitis management because it provides source control by removing infected and devitalized bones and addressing structural or soft-tissue compromise. Importantly, current guidance emphasizes that surgery should be actively considered when osteomyelitis is associated with expanding soft-tissue infection, poor soft-tissue coverage, progressive bone destruction on imaging, or ulcer-related bone exposure, as these features indicate a greater likelihood of failure with antibiotic therapy alone (Lipsky et al., 2020).

In the management of inflammation, infection, and osteomyelitis in diabetic foot ulcers, evidence supports a multimodal approach integrating antimicrobial therapy, nutritional support, glycemic control, local wound care, and surgical intervention when indicated. Inflammation management centers on optimizing the metabolic and nutritional status. Infection control relies on timely debridement and targeted antimicrobial therapies. Osteomyelitis treatment most strongly favors the combination of antibiotics and surgical source control, with local antimicrobials as adjuncts. However, despite the consensus on the need for integrated care, standardized evidence-based guidelines defining the optimal combination and sequencing of these strategies remain lacking, highlighting an important gap in clinical practice.

Limitations

The limitations include the heterogeneity of the study designs, which may affect the consistency and comparability of the results. Additionally, many studies had small sample sizes, limiting the generalizability of the findings and the possibility of publication bias. Variability in treatment protocols, outcome measures, and the lack of stratification based on infection severity further complicate drawing definitive conclusions.

Contribution to Global Nursing Practice

This review highlights the central leadership role of nurses in preventing and managing inflammation and infection in diabetic foot ulcer patients. As frontline clinicians, nurses lead evidence-based wound care through early infection recognition, debridement, and coordination of antimicrobial therapy while continuously monitoring wound progress and adjusting care plans. They play a key role in optimizing healing by addressing nutrition and glycemic control and safely integrating innovative therapies, such as bioactive dressings and photodynamic therapy. Equally important, nurses lead patient education in foot care and infection prevention, promote self-management, and coordinate multidisciplinary care, thereby reducing complications, preventing amputation, and improving patient outcomes.

Conclusion
This scoping review synthesizes the evidence on management strategies for controlling inflammation and infection in diabetic foot ulcers. The main approaches include nutritional interventions, antimicrobial therapy, adjuvant treatment, and surgical procedures. Although these interventions are effective, the evidence remains insufficient to determine the optimal strategy for different infection severities. Future research should focus on developing stratified, evidence-based clinical guidelines to support individualized management.

Author contribution
All authors take full responsibility for the content of the manuscript. EI contributed to the analysis, investigation, and preparation of the original manuscript. AY and MA were involved in the investigation, reviewing, and editing of the manuscript. KM supervised and reviewed the editing process. MO contributed to supervision, manuscript review and editing, and funding acquisition. All the authors have reviewed and approved the final version of the manuscript.

Conflict of interest
The authors declare no conflicts of interest.

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