

ISWM

International Scope of Wound Management

Volume 1 | Issue 2

August 2026

e-ISSN 3149-8302

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internationalswm.org



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REVIEW ARTICLE

42 The Fibrin-Nanofat Membrane for Coverage of Raw Wound Surfaces: A Literature Review

Alicia María Tamayo-Carbón, Jorge Berlanga-Acosta, Diana Katherine Cuastumal-Figueroa

ORIGINAL RESEARCH

52 Beyond the Outpatient Clinic: High-Risk Clinical Exposure and Employment Inequities Among Wound, Ostomy and Continence Nurses in Türkiye

Burçin Irmak, Serap Yılmaztürk, Şenay Gül, Ayişe Karadağ, Zehra Göçmen Baykara

64 The Relationship Between Venous Ulcer and Lymphedema: A Recognized but Underreported Topic in the Literature

Ali Cihat Yıldırım

71 Serum Albumin as a Marker of Infection Severity and Clinical Course in Patients with Diabetic Foot Infection

ErMehmet Mert Hıdıroğlu, Ahmet Yavuz, Salih Taha Armağan, Efe Tanar, Salih Uçar, Mustafa Karamustafa, Nursima Ceviz, Zeynep Sezin Bulut, Nurefsan Korkmaz, Mucahit Kaya, Kerim Bora Yılmaz

79 Clinical and Microbiological Characteristics of Diabetes-Related Foot Infections According to the Presence of Osteomyelitis

Hilal Küpeli, Hande Hazır Konya, Ümit Alakuş, Hakan Öztürk, Perçin Karakol

LETTER TO THE EDITOR

92 Wound Care for People Experiencing Homelessness: A Call for Accessible and Integrated Care

Mahmut Çapkın

Content

| COVER IMAGE



The Surgeon by David Teniers the Younger, 1670s.

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The Fibrin-Nanofat Membrane for Coverage of Raw Wound Surfaces: A Literature Review

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ABSTRACT

Chronic and complex wounds, including acute and extensive poor-healing injuries, present a significant challenge in reconstructive surgery. Conventional therapies—such as advanced dressings, negative pressure therapy, skin grafts, flaps, and recombinant growth factors—often fail to restore complete tissue architecture and function due to persistent inflammation, impaired angiogenesis, bacterial colonization, and deficient regenerative responses. To address these limitations, this review examines the regenerative rationale and clinical applications of fibrin-nanofat bioactive membranes as an innovative strategy for managing problematic and chronic wounds. Analysis of the literature on platelet concentrates and adipose tissue derivatives, with a focus on platelet-rich fibrin (PRF) and nanofat, demonstrates that PRF acts as a reservoir for the sustained release of growth factors that orchestrate tissue repair. Mechanically processed nanofat retains adipose-derived stem cells, stromal cells, exosomes, and bioactive mediators that stimulate proliferation, enhance neovascularization, and regulate fibrosis. Recent advances in tissue engineering have successfully integrated the scaffold properties of fibrin with the regenerative potential of nanofat into bioactive membranes. Experimental evidence indicates that these hybrid constructs yield uniform, flexible, and biologically active biomaterials that adapt to tissue defects, support cell adhesion, migration, and survival, and provide a sustained release of growth factors and progenitor cells. Fibrin-nanofat membranes therefore represent a promising regenerative tool in reconstructive surgery, with significant potential to advance chronic wound management by accelerating healing, improving tissue quality, and reducing reliance on complex procedures.

Keywords: Chronic wounds, regenerative medicine, platelet-rich fibrin, nanofat, bioactive membranes

REVIEW ARTICLE

Int Scope Wound Manag.
2026;1(2):42–51

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Received

July 3, 2026

Accepted

August 6, 2026

Published

August 31, 2026

DOI

10.36519/iswm.2026.1254

Suggested Citation

Tamayo-Carbón AM, Cuastumal-Figueroa DK, Berlanga-Acosta J. The fibrin-nanofat membrane for coverage of raw wound surfaces: A literature review. Int Scope Wound Manag. 2026;1(2):42–51.



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INTRODUCTION

Chronic wounds, including diabetic ulcers, pressure injuries, complex traumatic lesions, and poor-healing postoperative wounds, represent a major clinical challenge in reconstructive surgery. Persistent inflammation, impaired angiogenesis, bacterial colonization, and deficient tissue regeneration contribute to delayed healing and increased patient morbidity. Conventional treatments—such as advanced dressings, negative pressure therapy, skin grafts, flaps, and recombinant growth factors have demonstrated utility in many cases. Yet they often fail to fully restore the architecture and functionality of affected tissues (1–3). In light of these limitations, regenerative medicine has emerged as a promising alternative to optimize tissue repair. Among the most extensively studied strategies are platelet concentrates (4,5) and adipose tissue derivatives (6,7), owing to their capacity to modulate inflammation, stimulate angiogenesis, and promote cellular regeneration. Platelet-rich fibrin (PRF), a second-generation platelet concentrate, functions as a biological reservoir of growth factors—including transforming growth factor- β (TGF- β), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF)—which are gradually released to orchestrate the cellular and molecular events underlying wound healing (8).

Nanofat, obtained through mechanical processing of adipose tissue, retains a high concentration of adipose-derived stem cells (ASCs), stromal cells, exosomes, and other bioactive mediators capable of stimulating cell proliferation, promoting neovascularization, and modulating fibrosis. In addition to its use as a filler material, nanofat has been established as an effective regenerative tool in the treatment of cutaneous alterations, scars, and complex tissue defects (9). Recent advances in tissue engineering have enabled the combination of fibrin's biological properties with nanofat's regenerative potential through the creation of bioactive membranes. This association leverages fibrin's role as a three-dimensional scaffold that supports cell adhesion, migration, and survival, while providing sustained release of growth factors. Nanofat contributes progenitor cells and bioactive molecules that enhance tissue repair and regeneration (10). Fakhri Gomez et al. (11) demonstrated that incorporating nanofat into a fibrin membrane yields a uniform, flexible, and easily manipulable biomaterial capable of adapting to tissue defects and serving as a biologically active coverage for chronic wounds. Although this is an incipient methodological approach, the fibrin-nanofat membrane may represent an innovative strategy within regenerative and reconstructive surgery, with the potential to improve wound healing quality, accelerate tissue coverage, and reduce the need for more complex reconstructive

procedures. This review aimed to highlight the regenerative rationale and clinical applications of this hybrid membrane in the management of chronic wounds.

MATERIALS AND METHODS

A comprehensive literature review was conducted using PubMed, Google Scholar, ResearchGate, and SciELO, including publications in both English and Spanish. The search strategy utilized combined descriptors combined with Boolean operators: “AND” was used to connect different terms, while “OR” linked similar concepts.

The main search strings were:

1. Regenerative therapy OR tissue engineering AND nanofat PRF membrane
2. Nanofat PRF membrane AND raw wound surfaces OR coverage defects OR reconstruction
3. Nanofat PRF membrane AND plastic surgery OR reconstructive surgery OR aesthetic surgery

From an initial set of 174 references, 36 articles were selected that met the inclusion criteria: full text availability, originality, bibliographic reviews, meta analyses, and clinical trials published over a 12-year period (2013 to 2025) in English or Spanish. The remaining 138 records were excluded because they consisted of short communications, conference abstracts, letters to the editor, or in press articles.

Development: Preparation and Mechanical Properties of the Nanofat-PRF Membrane

Tissue engineering has driven the development of autologous biomaterials that combine structural support with regenerative biological activity. The nanofat-PRF membrane integrates the cellular and paracrine components of adipose tissue with the biomechanical and bioactive properties of PRF, resulting in a biologically active construct with potential applications in soft tissue regeneration and the coverage of complex wounds (10).

Nanofat, first described by Tonnard et al. (12), is obtained through mechanical emulsification and subsequent filtration of aspirated adipose tissue. This process destroys most mature adipocytes but preserves a high concentration of ASCs, progenitor cells, stromal vascular fraction components, growth factors, cytokines, and extracellular vesicles, including exosomes with recognized regenerative activity. Multiple studies (13–16) have demonstrated nanofat's abundance of cells with angiogenic, immunomodulatory, and extracellular

matrix remodeling capacities, explaining its growing use in regenerative medicine and reconstructive surgery.

The PRF, the second component, is a platelet concentrate obtained by centrifugation of peripheral blood without anticoagulants. This process generates a three-dimensional fibrin matrix that entraps platelets, leukocytes, and plasma proteins. Unlike other platelet concentrates, PRF enables the progressive and sustained release of growth factors—including PDGF, TGF- β , VEGF, epidermal growth factor (EGF), and insulin-like growth factor-1 (IGF-1)—which are essential for angiogenesis, cell proliferation, extracellular matrix synthesis, and tissue repair (17–20).

The hybrid membrane is created by incorporating nanofat into PRF during the initial fibrin polymerization phase. This ensures the homogeneous distribution of progenitor cells, growth factors, and extracellular vesicles within the fibrin network, forming a biologically active and structurally stable biomaterial. Fibrin acts as a natural three-dimensional scaffold that facilitates cell adhesion, fibroblast migration, neovascularization, and the spatial organization of regenerative components. Thus, the membrane functions not only as a physical support but also as a dynamic reservoir of biochemical signals capable of modulating the wound microenvironment (10,21).

Biomechanically, the fibrin network provides viscoelastic properties that distribute mechanical loads and resist moderate tensile forces. The PRF membranes have demonstrated sufficient tensile strength for surgical manipulation, suturing, and fixation, while maintaining flexibility and adaptability to irregular anatomical defects (10,11,22). Incorporation of nanofat further enhances plasticity, improves adaptation to recipient beds, and maintains a moist environment conducive to healing. Residual extracellular matrix from adipose tissue may act as an additional biological reinforcement, promoting internal cohesion and prolonging local bioactive factor availability (13).

Although specific biomechanical characterization of nanofat-PRF membranes remains limited, available studies (10,11,21,22) suggest that combining both components simultaneously enhances structural stability and regenerative potential. Fibrin also functions as a controlled-release system for bioactive molecules. Its three-dimensional network retains proteins, cytokines, and growth factors, enabling their gradual release during physiological degradation. This prolongs local availability of regenerative signals and optimizes interactions between resident cells and progenitor cells derived from nanofat, thereby stimulating key biological processes such as cell proliferation, angiogenesis, collagen

synthesis, extracellular matrix remodeling, and modulation of inflammation (11).

Adipose-derived stem cells and adipose-derived exosomes play a central role in tissue regeneration through paracrine mechanisms. These extracellular vesicles contain proteins, growth factors, mRNA, and microRNA that regulate cell proliferation, fibroblast migration, angiogenesis, and immune modulation. Their incorporation into the fibrin matrix provides a biological platform that enhances local persistence and therapeutic activity (15,23).

Although evidence on the impact of varying proportions of PRF and nanofat within the membrane remains limited, available data suggest that compositional differences directly influence biomechanical properties. A higher proportion of PRF yields a thicker, denser, and more mechanically resistant membrane, useful for areas requiring structural support, though potentially less permeable to immediate cell migration. Conversely, a higher proportion of nanofat produces a more fragile but highly bioactive construct. The optimal balance likely involves PRF acting as a biological “glue” that traps nanofat components, ensuring both surgical manageability and regenerative activity (10).

In summary, the nanofat-PRF membrane can be regarded as a bioactive autologous biomaterial that integrates the mechanical properties of fibrin with the regenerative potential of adipose-derived stem cells, growth factors, and exosomes.

Synergistic Mechanisms of the Nanofat-PRF Membrane

The regenerative potential of the nanofat-PRF membrane lies in the synergistic interaction between ASCs present in nanofat and the three-dimensional fibrin matrix provided by PRF (Figure 1). Rather than a mere physical association, the membrane constitutes a functional unit in which the cellular and molecular properties of each component mutually enhance regenerative activity (10,11).

Adipose-derived stem cells are multipotent cells with the ability to differentiate into fibroblasts, endothelial cells, adipocytes, osteoblasts, and chondrocytes. However, their therapeutic effect is now recognized to depend primarily on paracrine activity. Adipose-derived stem cells secrete a wide variety of growth factors, cytokines, chemokines, and extracellular vesicles that regulate tissue responses to injury. Key molecules include VEGF, hepatocyte growth factor (HGF), basic fibroblast growth factor (bFGF), IGF-1, PDGF, TGF- β , and stromal cell-derived factor-1 (SDF-1), which drive angiogenesis,

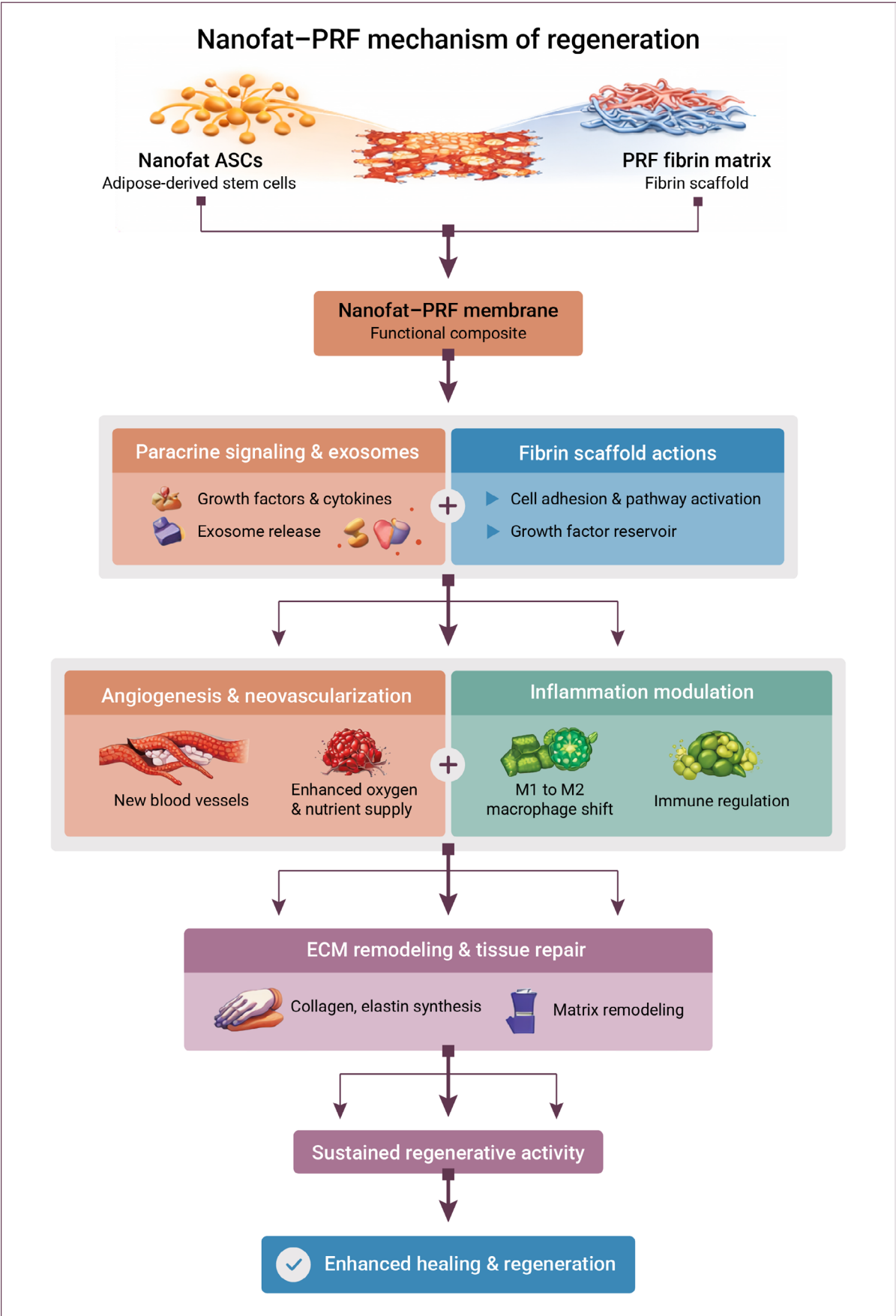


FIGURE 1. Regenerative synergy between nanofat-derived ASCs and PRF in wound healing.

fibroblast migration, and extracellular matrix synthesis. Exosomes released by ASCs are rich in microRNAs and signaling proteins that modulate gene expression in resident cells (24,25).

The fibrin matrix of PRF acts as a dynamic biological scaffold, mimicking early wound-healing events. Its porous architecture facilitates cell adhesion via integrins ($\alpha 5 \beta 1$, $\alpha v \beta 3$), promoting ASC survival, proliferation, and migration. This cell-matrix interaction activates intracellular pathways such as focal adhesion kinase (FAK), phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), and mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK), which regulate proliferation, survival, and synthesis of reparative proteins (26–28). Furthermore, fibrin serves as a molecular reservoir, retaining growth factors from both PRF platelets and ASCs. These molecules are trapped within the fibrillar network and gradually released during physiological degradation, maintaining high local concentrations of bioactive mediators for extended periods (10,11,29). Growth factors such as VEGF, angiopoietin-1 (Ang-1), HGF, and bFGF stimulate endothelial cell proliferation and migration, while fibrin provides a physical guide for capillary formation. This dual mechanism enhances neovascularization, improving oxygen and nutrient supply essential for tissue repair (24,30). Studies confirm that fibrin scaffolds enriched with mesenchymal stem cells exhibit superior angiogenic capacity compared to either component alone (10,11,21,22).

Inflammation modulation is another critical mechanism. Chronic wounds often exhibit persistent pro-inflammatory M1 macrophages producing TNF- α , interleukin-1 β (IL-1 β), and IL-6. Adipose-derived stem cells release IL-10, prostaglandin E2 (PGE2), tumor necrosis factor-stimulated gene-6 (TSG-6), and indoleamine 2,3-dioxygenase (IDO), promoting polarization toward anti-inflammatory M2 macrophages. Fibrin further supports ordered immune cell recruitment (13,31). Extracellular matrix remodeling is facilitated by ASC-induced fibroblast proliferation and synthesis of collagen I/III, elastin, fibronectin, and hyaluronic acid. Concurrent secretion of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) ensures balanced degradation and reconstruction. Fibrin acts as a provisional matrix, progressively replaced by mature functional tissue (32). Ultimately, exosomes derived from ASCs add another layer of regulation. These vesicles contain microRNAs that modulate signaling pathways including PI3K/Akt, Wnt/ β -catenin, Notch, TGF- β /Smad, and MAPK/ERK. Fibrin protects exosomes from rapid degradation, enabling sustained release and prolonged local activity (33,34).

Nanofat-derived adipose stem cells release paracrine signals and exosomes enriched in growth factors and cytokines, which are retained within the fibrin scaffold. The PRF matrix serves as both a reservoir and a structural support, enabling cell adhesion and pathway activation. Collectively, these processes initiate angiogenesis, enhancing oxygen and nutrient delivery to the healing tissue. Simultaneously, immune modulation occurs through a macrophage phenotype shift (M1 to M2), reducing inflammation and promoting a pro-regenerative environment. The composite membrane further drives extracellular matrix remodeling, stimulating collagen and elastin synthesis. These integrated mechanisms result in sustained regenerative activity, leading to accelerated tissue repair and enhanced healing outcomes.

Clinical Evidence of Efficacy and Safety

Recent clinical evidence is encouraging regarding the efficacy and safety of nanofat and PRF, whether used individually or in combination for reconstructive, aesthetic, and complex wound-healing applications. Systematic reviews published between 2023 and 2025 highlight consistent benefits of nanofat in improving skin quality, regenerating soft tissues, treating scars, and correcting volumetric defects (14,35,36). These effects are attributed to the high concentration of stromal cells, pericytes, growth factors, and extracellular vesicles that stimulate angiogenesis and matrix synthesis. However, most studies remain limited to case series or small prospective cohorts, reducing the overall level of evidence. Given the promising therapeutic effects of the nanofat-PRF combination, larger controlled studies are needed based on standardized preparation protocols. Meta-analyses and systematic reviews converge to indicate that PRF formulations (advanced platelet-rich fibrin [A-PRF], injectable platelet-rich fibrin [i-PRF]) significantly enhance tissue healing, angiogenesis, and soft-tissue regeneration through sustained growth-factor release (Table 1). Preliminary clinical improvements have been documented in oral surgery, periodontal regeneration, facial rejuvenation, and wound repair, with superior tissue quality, reduced inflammation, and accelerated healing compared with conventional treatments (10,17,19).

Although clinical studies specifically targeting hybrid nanofat-PRF membranes remain scarce, available data suggest improved tissue regeneration, vascularization, and aesthetic outcomes compared with either component alone (10,11,22). Hence, further studies are needed to provide more consistent and conclusive data on their safety and efficacy. Both nanofat and PRF are autologous, minimizing risks of immune reactions, disease transmission, or tissue rejection. Reported adverse events are mild and transient, including edema,

Table 1. Platelet-rich fibrin variants in wound healing.

Type	Preparation	Form	Growth factor release	Clinical use
Advanced platelet-rich fibrin (A-PRF)	Low speed centrifugation	Solid fibrin membrane	Sustained, prolonged release	Wound coverage, scaffolds, oral/maxillofacial surgery
Injectable platelet-rich fibrin (i-PRF)	Very low speed centrifugation	Liquid, later gels	Rapid, concentrated release	Injectable therapy, mixing with grafts, regenerative infiltration

ecchymosis, local pain, or self-limited inflammation. No major complications have been identified when standardized protocols are followed (10,12,14,19,21).

Nevertheless, methodological limitations persist, including heterogeneity in preparation protocols, differences in application techniques, small sample sizes, and short follow-up periods. The authors emphasize the need for multicenter randomized clinical trials with standardized methodologies to validate efficacy and establish optimal protocols (10,11,22). Overall, available evidence suggests that nanofat-PRF membranes represent a safe and promising regenerative strategy for complex wounds, soft-tissue defects, and skin rejuvenation (10).

Practical Considerations and Applications

Tailoring membrane composition to specific clinical requirements may improve outcomes. For example:

- Formulation for rigidity (coverage in tension zones): Increasing the PRF proportion yields a thicker, denser, and more resistant membrane, useful for mechanical protection, though potentially less permeable to immediate cell migration.
- Formulation for regeneration (ischemic ulcers): Prioritizing nanofat maintains high bioactivity and moisture, facilitating stem-cell release, though with reduced mechanical strength.

Currently, no standardized protocols define exact proportions for specific properties; adjustments remain empirical. A balanced ratio—nanofat emulsified with centrifuged PRF—appears most reliable, with modifications reserved for cases requiring additional mechanical support. Clinical applications reported include temporary coverage of exposed cartilage after nasal reconstruction, early re-epithelialization following rhinophyma surgery, facial fillers, management of chronic wounds resulting from aesthetic complications, and pressure ulcers, all with satisfactory outcomes and absence of major complications (Figure 2).

Limitations and Future Perspectives

Despite the growing interest in the nanofat-PRF membrane as a regenerative medicine tool, the currently available scientific evidence remains subject to significant limitations that must be acknowledged when interpreting reported clinical outcomes. As mentioned, a major constraint is the paucity of randomized, prospective, and controlled clinical trials specifically evaluating this hybrid membrane as a combined product. Most publications consist of case reports, small case series, or observational studies with limited sample sizes, thereby reducing the strength of the conclusions and hindering extrapolation to broader patient populations.

Another critical limitation lies in the lack of standardized protocols for membrane preparation. Considerable variability exists among studies regarding liposuction techniques, nanofat emulsification and filtration methods, centrifugation parameters for PRF isolation, and the strategies used to integrate both components into a single construct. Such methodological heterogeneity may influence the cellular yield, biological composition, and mechanical properties of the final product, complicating direct comparisons across investigations and limiting reproducibility.

Equally important is the incomplete biological characterization of the hybrid membrane. While it is known to combine stromal vascular fraction cells, growth factors, and a three-dimensional fibrin scaffold, data remain scarce on the precise concentration of viable cells, biomolecule release kinetics, long-term cell survival, and the mechanistic basis of the observed *in vivo* effects. This lack of uniformity hampers the establishment of quality control parameters necessary for routine clinical application.

Follow-up periods reported in the literature are generally short, focusing primarily on early wound closure and immediate outcomes (10,11). Consequently, evidence regarding the durability of regenerative effects, long-term stability of repaired tissues, and functional outcomes remains limited.

Table 2. Nanofat-PRF membrane main potential clinical indications, advantages, limitations, and future research directions.

Potential Indications
Chronic wounds (diabetic ulcers, pressure injuries)
Complex traumatic lesions
Poorly healing postoperative wounds
Soft-tissue defects and reconstructive surgery
Facial fillers and aesthetic corrections
Temporary coverage in nasal and facial reconstruction or rhinophyma surgery
Potential Advantages
Key regenerative and clinical benefits observed.
Accelerated epithelial closure and tissue repair
Enhanced angiogenesis and neovascularization
Modulation of inflammation (M1 to M2 macrophage shift)
Improved extracellular matrix remodeling (collagen, elastin)
Autologous origin minimizes immune rejection
Flexible, adaptable biomaterial for irregular defects
Current Limitations
Constraints in evidence and methodology that limit widespread adoption
Few randomized controlled trials; mostly case series
Lack of standardized preparation protocols (liposuction, centrifugation)
Short follow-up periods; limited long-term data
Heterogeneity in biological composition and mechanical properties
Technical complexity requiring specialized equipment and trained personnel
Patient-specific variability (age, comorbidities, and metabolic status)
Future Research Priorities
Conduct multicenter randomized clinical trials with larger cohorts
Standardize harvesting and processing protocols for reproducibility
Define optimal PRF-to-nanofat ratios for mechanical vs regenerative needs
Expand biological characterization (cell viability, release kinetics)
Explore integration with smart biomaterials and controlled-release systems
Investigate novel applications in tissue engineering and organ regeneration

Comparative studies assessing the superiority of nanofat-PRF membranes over other autologous biomaterials or dermal substitutes are also scarce.

From a technical standpoint, membrane preparation requires specialized equipment, trained personnel, and careful

coordination between adipose tissue harvesting and blood processing. These factors may increase procedural complexity and restrict availability in certain centers. Furthermore, product quality may be influenced by patient-specific variables such as age, comorbidities, metabolic status, and the intrinsic quality of adipose and blood-derived tissues (10).

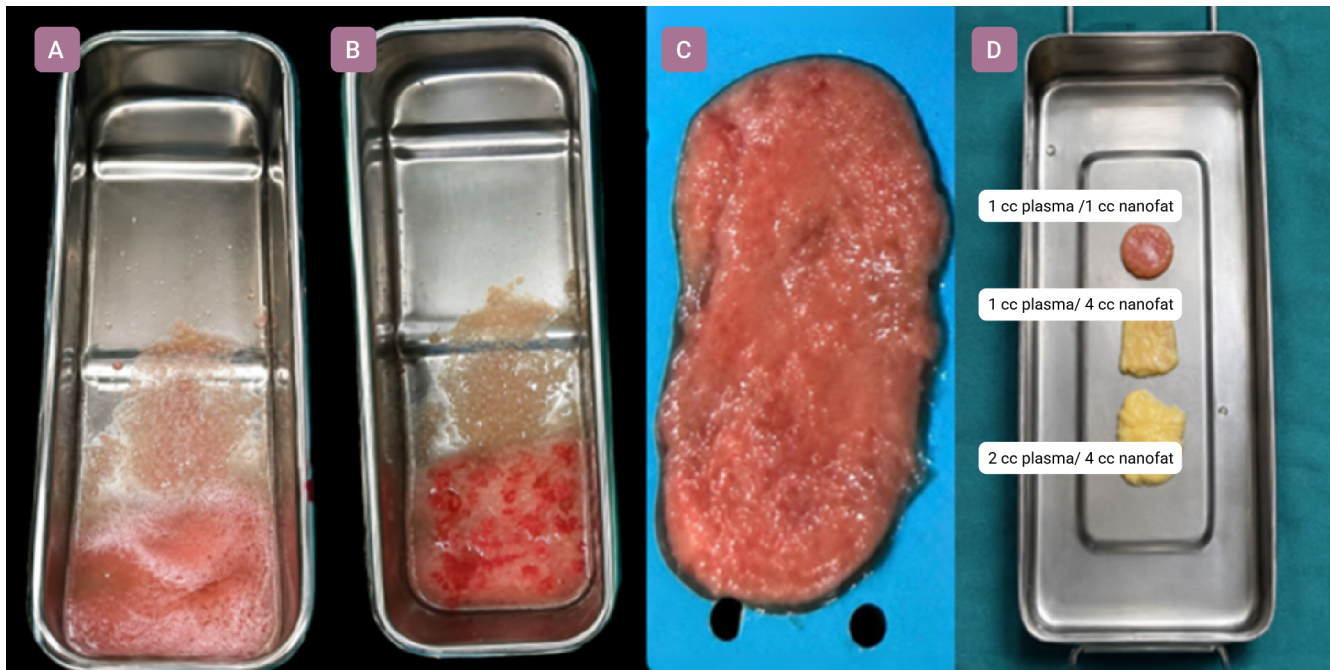


FIGURE 2. Stages of membrane formation.

Note: The content of this image reflects the major steps in the preparation of the membrane variants. **A. Fusion mixture:** Components being mixed. **B. Final result:** Membrane in its final form. **C. Final result:** Final outcome with consistency varying according to the proportions of the components. Picture taken by the lead author in a surgical setting. Plastic and Reconstructive Surgery Service, Hermanos Ameijeiras Hospital.

Although published studies to date suggest a favorable safety profile due to the autologous nature of the product, multicenter investigations with larger cohorts and standardized protocols are essential to more precisely define efficacy, safety, specific indications, and cost-effectiveness. High-level clinical evidence will be pivotal for consolidating the role of nanofat-PRF membranes within reconstructive surgery and regenerative medicine algorithms.

Future perspectives focus on the standardization of harvesting and processing protocols to ensure reproducible biological composition and consistent clinical outcomes. Advances in tissue engineering may further enhance the mechanical and biological properties of the membrane through integration with smart biomaterials, controlled-release systems for growth factors, and biofabrication technologies. Such innovations could expand therapeutic indications to include complex wounds, soft tissue defects, and cutaneous regeneration.

Collectively, the nanofat-PRF membrane represents a promising strategy whose clinical potential will continue to evolve as scientific evidence matures (Table 2).

CONCLUSION

The use of nanofat combined with PRF may represent a potentially effective and safe autologous strategy, particularly for the management of complex and chronic wounds, as multiple studies report accelerated epithelial closure without complications. Although the mechanism of action involves both the release of growth factors and a pro-angiogenic scaffold effect, the precise contribution of adipose-derived stem cells within the membrane remains to be fully characterized. Rigorous clinical trials are necessary to confirm its efficacy in cosmetic indications and to explore novel applications such as peripheral nerve regeneration.

Ethical Approval: Not applicable

Informed Consent: Not applicable

Peer-review: Externally peer-reviewed

Author Contributions: Concept – A.M.T.C., D.K.C.F.; Design – A.M.T.C., D.K.C.F.; Supervision – A.M.T.C., D.K.C.F., J.B.A.; Materials – Not applicable; Data Collection and/or Processing – A.M.T.C., D.K.C.F., J.B.A.; Analysis and/or Interpretation – A.M.T.C., D.K.C.F., J.B.A.; Literature Review – A.M.T.C., D.K.C.F.;

Writing – A.M.T.C., D.K.C.F., J.B.A.; Critical Review – A.M.T.C., D.K.C.F., J.B.A.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

AI Statement: No artificial intelligence-assisted technologies were used in the preparation of this manuscript.

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Beyond the Outpatient Clinic: High-Risk Clinical Exposure and Employment Inequities Among Wound, Ostomy and Continence Nurses in Türkiye

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ABSTRACT

Objective: Wound, Ostomy and Continence Nurses (WOCNs) frequently provide bedside care across multiple hospital settings, including intensive care units and other high-risk clinical environments. However, despite these responsibilities, many are administratively classified as outpatient nurses and may not receive the employment benefits available to staff formally assigned to high-risk units. This study aimed to describe WOCNs' involvement in high-risk clinical settings, their occupational exposures, and their employment benefits in Türkiye.

Methods: A descriptive cross-sectional study was conducted among 100 WOCNs working in seven geographical regions of Türkiye. Data were collected through an online questionnaire assessing demographic characteristics, time spent in high-risk clinical units during the previous month, occupational exposures, compensation status, and perceptions of working in these settings. Ethical approval and institutional permission were obtained prior to data collection. Quantitative data were analyzed using descriptive statistics, while qualitative responses were examined using content analysis.

Results: Participants had worked as WOCNs for a mean of 4.67 ± 4.75 years. During the previous month, WOCNs spent substantial time in high-risk clinical environments, particularly in intensive care units (median 40 [interquartile range (IQR), 10–80] hours), and palliative care centers (median 5 [IQR, 0–38.5] hours). The most frequently reported occupational exposures were blood (93%), feces (89%), and urine (83%). Although WOCNs regularly provided care in high-risk units, 76.0% reported not receiving the additional compensation available to staff officially assigned to these units. Qualitative findings revealed perceived inequities related to compensation, high infection exposure risk, excessive workload, barriers to certification, and assignments outside their area of expertise.

ORIGINAL ARTICLE

Int Scope Wound Manag.
2026;1(2):52–63

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Received

June 1, 2026

Accepted

August 15, 2026

Published

August 31, 2026

DOI

10.36519/iswm.2026.1196

Suggested Citation

Irmak B, Yılmaztürk S, Gül Ş, Karadağ A, Göçmen Baykara Z. Beyond the outpatient clinic: high-risk clinical exposure and employment inequities among wound, ostomy and continence nurses in Türkiye. Int Scope Wound Manag. 2026;1(2):52–63.



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Conclusion: The WOCNs in Türkiye spend a considerable proportion of their working time in high-risk clinical environments. Despite these responsibilities, most do not receive employment benefits comparable to those provided to staff formally assigned to high-risk units. The findings highlight a mismatch between administrative classification and actual clinical practice and support the need for workforce policies and employment regulations that better reflect the scope, risks, and responsibilities of specialist WOC nursing practice.

Keywords: Wound, ostomy and continence nurse, occupational exposure, high-risk units, workforce policy, employment rights, specialist nursing

INTRODUCTION

Wound, Ostomy, and Continence Nurses (WOCNs) constitute an important nursing specialty that encompasses specialized care services in wound care, ostomy care, and continence care (1). The development of WOCN worldwide dates back to the late 1950s. In particular, the enterostomal therapy programs launched at the Cleveland Clinic under the leadership of Dr. Rupert Beach Turnbull and Norma N. Gill, a person with an ileostomy, marked a significant turning point in the professionalization of this field (2). Programs that initially focused solely on the rehabilitation of individuals with stomas have, over time, expanded to include wound and incontinence care. As a result, stoma care nursing has become a multidisciplinary and evidence-based field of expertise (1). Today, through international organizations such as the World Council of Enterostomal Therapists (WCET) and the Wound, Ostomy and Continence Nurses Society (WOCN), educational standards are being established in this field, specialist qualifications are being defined, and care models aimed at improving patients' quality of life are being developed (3,4). In developed countries, WOC nurses perform their duties after obtaining a WOC specialist training certificate from an accredited body, following completion of an undergraduate or postgraduate degree (4).

WOCN development in Türkiye began in the 2000s. The first stoma therapy unit in Türkiye was established at Gazi University Hospital in 2000, marking a significant step toward the systematic provision of stoma care services (5,6). The professional identity of the field was subsequently strengthened by the establishment of the Wound, Ostomy and Incontinence Nurses' Society (Yara Ostomi ve İnkontinans Hemşireleri Derneği [YOIHD]), the development of certified training programs, and the definition of the duties, powers, and responsibilities of the Stoma and Wound Care Nurse in the Nursing Regulations in 2011 (6,7). Founded in Türkiye in 2008, the YOIHD is a professional nursing organization dedicated to supporting and advancing the career development of nurses

specializing in wound, ostomy, and incontinence care. Since 2000, the number of specialist nurses in this field has grown rapidly in Türkiye. The WOCNs in Türkiye obtain their certification by completing a 240-hour theoretical and practical training course approved by the Ministry of Health, in accordance with the Certified Training Standards for the Healthcare Sector (8). The number of Enterostomal Therapy Nursing Training Programs (ETNEP), which stood at zero in 2000, has risen to approximately 10 (9); the number of nurses certified through these programs has exceeded 650; according to YOIHD, the number of stoma therapy units has reached 36 (10), while the number of chronic wound care units reported by the Ministry of Health reached 59 as of May 2026 (11).

Nowadays, stoma and wound care units provide patients with care and rehabilitation services, as well as education and counseling, to reduce complications and improve quality of life (6). The WOCNs assume significant responsibilities within the healthcare team in their roles as caregivers, educators,

HIGHLIGHTS

- Wound, ostomy, and continence nurses (WOCNs) routinely deliver bedside care in intensive care units, isolation rooms, emergency departments, and other high-risk clinical settings.
- Occupational exposure among WOCNs includes frequent contact with blood, feces, urine, and hazardous body fluids.
- Despite working in high-risk environments, 76% of WOCNs reported receiving no additional compensation designated for staff working in high-risk units.
- Administrative classification as outpatient nurses does not reflect the actual scope, responsibilities, or occupational risks of WOC nursing practice.
- The findings of the study support policy reforms to ensure equitable recognition, occupational protection, and compensation for specialist WOCNs.

consultants, researchers, and managers (5,6,12). The WOCNs work across a wide range of areas, from determining the stoma site prior to surgery to postoperative stoma and peristomal skin care, wound care, prevention of complications, and selection of appropriate care products (6,13). In addition, they play an active role in helping patients develop self-care skills (14), adapt to changes in body image (15), and improve their quality of life (13,16). By adopting evidence-based care practices, WOCNs continue to provide patient and family education, support multidisciplinary teamwork, and contribute to improving care outcomes (6,7).

In Türkiye, WOCNs carry out their duties either as an independent unit or as part of a consultation system within health-care institutions. The WOCNs provide stoma and wound care services to patients of all ages in hospitals, not only in stoma therapy, colorectal surgery outpatient clinics, and chronic wound units, but across all departments (17,18). The WOCNs also provide care to patients in areas designated by the Ministry of Health in Türkiye as requiring special attention (19). These units include: operating rooms, angiography units, intensive care units (ICUs), palliative care centers, delivery rooms, neonatal units, pediatric wards, burn units/centers, dialysis units, emergency departments/outpatient clinics, closed psychiatric wards, alcohol and substance use treatment centers, child monitoring centers, isolation rooms, and organ, tissue, and bone marrow transplant units. The WOCNs play a role in patient care in these units and are exposed to high-risk bodily fluids such as blood, urine, feces, and exudate while providing care (20). The risk increases when nursing interventions such as wound culture collection, application of topical agents, mechanical debridement, drain management, and assistance with surgical or chemical debridement are performed.

Furthermore, WOCNs have provided care services during exceptional conditions, such as the COVID-19 pandemic, and have faced numerous physical and psychosocial risks (18,21,22). During the pandemic, WOCNs faced situations that threatened staff safety, such as the risk of exposure to COVID-19—a highly contagious infection—the risk of developing pressure injuries associated with medical devices due to the use of personal protective equipment, and being separated from their families (23,24). All these physical, biological, and psychosocial risk factors to which WOCNs are exposed clearly highlight the demanding nature of their working conditions and the high level of clinical responsibility they take on. For these reasons, appropriate regulations governing the working conditions of WOCNs are warranted.

Although WOCNs are frequently perceived as outpatient-based specialists, their clinical practice extends far beyond dedicated wound and stoma care units. In many healthcare settings, WOCNs provide bedside consultation and direct patient care in intensive care units, isolation rooms, emergency departments, palliative care centers, and other environments associated with increased occupational risk. Consequently, their actual workplace exposure may differ substantially from their formal administrative classification. Within the current healthcare system in Türkiye, WOCNs are generally classified as ‘poly-clinic nurses’. As a result, WOCNs are deprived of employment benefits, such as shift allowances and the risk-related components of revolving-fund supplements provided to colleagues formally assigned to units such as ICUs, operating rooms, or emergency departments. However, WOCNs spend a significant portion of their working hours in the hospital’s high-risk and critical care units, managing complex cases directly at the patient’s bedside. As part of their duties in these settings, they work under demanding conditions that involve a high risk of infection, exposure to drug-resistant microorganisms, and the management of complex and open wounds, as well as stoma care—all of which place a heavy physical, biological, and psychological burden on them. Although studies have explored the roles, competencies, and work experiences of WOCNs (25,26), little is known about the extent of their involvement in high-risk clinical environments and whether their employment benefits reflect their actual workplace exposure. To our knowledge, no previous study has quantitatively examined the relationship between WOCNs’ time spent in high-risk units, occupational exposure, and access to employment benefits associated with high-risk clinical work. Addressing this gap is important for workforce planning, occupational health, and the recognition of specialist nursing roles. Understanding the discrepancy between WOCNs’ formal employment classification and their actual clinical exposure is essential for ensuring equitable workforce policies, occupational protection, and recognition of specialist nursing practice.

This study aimed to describe WOCNs’ involvement in high-risk clinical settings, their occupational exposures, and their employment benefits in Türkiye. Specifically, the study addressed the following questions:

1. What is the extent of WOCNs’ involvement in high-risk clinical units?
2. What occupational risks and exposures do WOCNs encounter while delivering care in these settings?
3. Is there a mismatch between WOCNs’ actual clinical exposure and the employment benefits they receive, and how do they perceive this situation?

MATERIALS AND METHODS

Study Design and Sample

This study employed a descriptive cross-sectional design to examine WOCNs' involvement in high-risk clinical environments, occupational exposures, employment benefits, and perceptions regarding their working conditions. Quantitative and qualitative data were collected concurrently through an online survey. The study was conducted online between April 1 and 10, 2023. The study population consisted of nurses working as WOCNs in Türkiye. No formal sampling procedure was used; the study included 100 nurses who were members of YOIHD, were working as WOCNs at the time of the study, and volunteered to participate. At the time of the study, the society had a total of 212 registered members. The study's response rate was 47.17%.

Data Collection Tools

The study used a questionnaire developed by the researchers based on the literature (17,22). The questionnaire was reviewed by researchers experienced in WOC nursing and nursing workforce research to ensure clarity, relevance, and content appropriateness prior to data collection. The questionnaire consisted of three parts and 31 questions. The first part contained nine questions on nurses' demographic characteristics, including age, gender, educational level, years of service, and certification status. The second part consisted of 20 questions, including the amount of time WOCNs had spent working in specialist units during the previous month and the total number of patients they had cared for. The third part contained two open-ended questions: (i) What risks have you been exposed to during your work experience in units with specific characteristics as a WOCN? (ii) What are your views on your work experience in units with specific characteristics as a WOCN?

For the purposes of this study, high-risk units were defined according to the Turkish Ministry of Health regulations identifying clinical areas eligible for additional compensation due to increased occupational risk. These units include ICUs, operating rooms, emergency departments, isolation rooms, burn units, palliative care centers, dialysis units, transplantation units, and other designated specialized clinical settings.

Procedure

The data collection questionnaire was created as an online survey (Google Forms; Google LLC, Mountain View, CA, USA). The online questionnaire was sent to nurses via the WhatsApp (Meta Platforms, Inc., Menlo Park, CA, USA) group comprising

YOIHD members. To prevent nurses from completing the survey more than once, the survey was set to 'Limit to one response'. Data were collected by repeatedly sending messages to the group. It took approximately 5–10 minutes to complete the questionnaire.

Data Analysis

IBM SPSS Statistics, version 20.0 (IBM Corp, Armonk, NY, USA), was used to analyze the data obtained in the study. The research data were analyzed using descriptive statistics (frequencies, percentages, means, standard deviations, minimums, and maximums). The normality of continuous variables was evaluated using the Shapiro-Wilk test. Continuous variables with a normal distribution were expressed as mean and standard deviation, whereas non-normally distributed variables (e.g., time, number of polyclinic visits) were expressed as median and interquartile range (IQR).

The qualitative data obtained from the open-ended survey questions were analyzed using conventional content analysis based on the Miles and Huberman framework (27). In the content analysis, the data were examined independently by two researchers (BI, ŞG), and similar concepts were grouped together to form themes and subthemes. The themes and subthemes developed by the researchers were reviewed by the other members of the research team, and consensus was reached on the final themes and subthemes (28). The Consolidated Criteria for Reporting Qualitative Research (COREQ) guidelines were used to analyze and report the qualitative findings (29).

Ethical Considerations

Ethical approval for the study was obtained from the Gazi University Clinical Non-Interventional Research Ethics Committee on March 21, 2023, with decision no. E-77082166-604.01.02-618184. Institutional permission was obtained via e-mail from the YOIHD. In the first part of the survey questionnaire, participants were provided with preliminary information about the study and provided informed consent. The study was conducted in accordance with the Declaration of Helsinki.

RESULTS

The study findings are presented in two sections: quantitative and qualitative results.

Quantitative Results

The mean age of the participating nurses was 37.49 ± 7.80 , the mean length of service in the nursing profession was

15.94 ± 8.67 years, and the mean length of service as a WOCN was 4.67 ± 4.75 years. Among the participants, 53.0% were aged between 36–49 years, 89.0% were female, and 95.0% held a bachelor's degree or higher. Overall, 37.0% of the nurses worked in the Central Anatolia Region, and 31.0% worked in a stoma and wound care unit. Half of the participants (50.0%) held a WOCN certificate approved by the Ministry of Health. Most participants (76.0%) did not receive the additional compensation provided to staff working in high-risk units (Table 1).

During the previous month, WOCNs spent the most time in intensive care units (median 40 [IQR, 10–80] hours), followed by isolation rooms (median 10 [IQR, 2–30] hours), and the

palliative care center (median 5 [IQR, 0–38.5] hours). The units in which nurses spent the least time were the operating rooms, delivery rooms, angiography units (median 0 [IQR, 0–0] hours), dialysis units, organ, tissue and bone marrow transplantation units (median 0 [IQR, 0–0] hours), and closed psychiatric wards (median 0 [IQR, 0–0] hours) (Table 2).

During the previous month, the highest number of patients cared for by WOCNs was reported in intensive care units (median 40 [IQR, 12.75–103.75] patients), followed by emergency departments or outpatient emergency settings (median 3 [IQR, 0–39] patients), and palliative care centers (median 6.5 [IQR, 0–20] patients). The fewest patients were cared for in dialysis and transplantation units (median 0 [IQR,

Table 1. Demographic characteristics of WOCNs (n = 100).

Variables	n	Variables	n
Age		Unit of employment	
≤35	42	Chronic Wound/Wound Care Unit	39
36–49	53	Stoma and Wound Care Unit	31
≥50	5	Stoma Therapy Unit	5
Gender		General Surgery Clinic	5
Female	89	ICUs	5
Male	11	Diabetic Foot/Wound Outpatient Clinic	2
Education level		Burn and Wound Care Unit	2
High school	5	Endoscopy Unit	2
Bachelor's degree	61	Palliative Care Center	2
Master's/PhD degree	34	Other (Home care unit, internal diseases clinics)	7
Region		WOCNs' certification status	
Central Anatolia Region	37	Yes, approved by the Ministry of Health	50
Marmara Region	32	Yes, approved by other organizations	13
Aegean Region	15	No	37
Mediterranean Region	6	Status of additional payment receipt	
Black Sea Region	4	Yes	24
Eastern Anatolia Region	4	No	76
Southeastern Anatolia Region	2		
		Variables	$\bar{X} \pm SD$ (Min.–Max.)
		Age (y)	37.49 ± 7.80 (23–59)
		Years working in the profession (y)	15.94 ± 8.67 (2–41)
		Years working as a WOCN (y)	4.67 ± 4.75 (1–22)

$\bar{X}$: Mean, SD: Standard deviation, Min: Minimum, Max: Maximum, WOCN: Wound, Ostomy, and Continence Nurse, ICU: Intensive care unit.

Table 2. WOCNs' working hours and the number of patients they cared for in high-risk units over the past month (n = 100).

Units with specific risks	Working hours (hours)	Number of patients under care
	Median (IQR) (Min.–Max.)	Median (IQR) (Min.–Max.)
ICUs	40 (10–80) (0–200)	40 (12.75–103.75) (0–500)
Isolation rooms	10 (2–30) (0–300)	0 (0–0) (0–13)
Emergency department/outpatient clinic	1 (0–32) (0–240)	3 (0–39) (0–900)
Palliative care center	5 (0–38.5) (0–240)	6.5 (0–20) (0–256)
Burn unit/center	0 (0–0) (0–180)	0 (0–0) (0–80)
Operating room/delivery room/angiography unit	0 (0–0) (0–120)	0 (0–0) (0–130)
Dialysis/organ and tissue transplant/bone marrow transplant units	0 (0–0) (0–20)	0 (0–0) (0–13)
Closed psychiatric wards	0 (0–0) (0–30)	0 (0–0) (0–5)

IQR: Interquartile range, Min: Minimum, Max: Maximum, ICU: Intensive care unit.

0–0] patients), closed psychiatric wards (median 0 [IQR, 0–0] patients), and operating rooms, delivery rooms or angiography units (median 0 [IQR, 0–0] patients).

In their daily practice, nurses most frequently reported exposure to blood (93%), feces (89%), and urine (83%) in both stoma and wound care units and in high-risk units. The least frequently reported occupational exposures were sharps injuries (2%), radiation (2%), and scabies (1%) (Table 3).

Qualitative Results

Nurses' views on working in high-risk clinical units were organized into two themes: disadvantages and advantages. The themes and subthemes are presented in Table 4.

Theme 1: Disadvantages

Five subthemes were identified under the theme of disadvantages: high risk of exposure to infectious diseases, lack of additional compensation, excessive workload, barriers to participation in WOCN certification programs, and assignment of certified WOCNs to duties outside their area of expertise.

Table 3. Occupational exposures of WOCNs during their work* (n = 443).

Variables	%
Blood	93
Feces	89
Urine	83
Sweat	80
Saliva	65
Wound exudate	11
Infected wound (purulent drainage, odor)	8
Drainage	6
COVID-19	3
Sharp-object injuries	2
Radiation	2
Scabies	1

WOCN: Wound, Ostomy, and Continence Nurse.

*n was calculated from multiple responses.

Table 4. WOCNs' views on working in specialized units.

Theme	Sub-theme
Disadvantages	• High risk of exposure to infectious diseases
	• Lack of additional compensation
	• Excessive workload
Disadvantages	• Barriers to participation in WOC certification programs
	• Certified WOCNs are being assigned to roles outside their field
Advantages	• WOCNs receiving additional payment

WOCN: Wound, Ostomy, and Continence Nurse.

Subtheme 1: High risk of exposure to infectious diseases

WOCNs who participated in the study reported facing many risks within the hospital. The WOCNs described their experiences related to this subtheme;

'We were at high risk of infection during the pandemic and still are; since we provide care in every department of the hospital, we are exposed to many infections.' (Participant 64, 37 years old, female).

'With blood spurting onto my face, dealing with feces and foul-smelling, infected wound fluids, I continued to perform the care that the patient's spouse, daughter, and mother refused to do—out of self-sacrifice, professional ethics, responsibility, and conscience—under extremely difficult conditions, adhering fully to the ethical guidelines of WOCN because I am so dedicated to this specialty...' (Participant 94, 48 years old, female).

Another participant stated:

'Services are provided to all units. During this process, one is exposed to the risks of all units.' (Participant 100, 36 years old, female)

Subtheme 2: Lack of additional compensation

Participants reported that they did not receive additional compensation from hospital administration despite providing specialized services in high-risk clinical settings. Participants expressed their views as follows:

'Although I provide services in a specialist area, I am treated as an outpatient clinic staff member when it comes to pay. The

treatment we receive is unfair. Although I work 5 hours a day in high-risk ICUs, management ignores this, and assigns us to different areas. Regulations on stoma and wound care are essential.' (Participant 99, aged 45, female)

'As WOCNs, we are the only unit that comes into contact with patients the most, enters the same environment, and performs our duties at the patient's bedside after our colleagues in clinical and ICUs. There must be some recognition for this effort, and additional payment should be made for this.' (Participant 95, 33 years old, female)

'Despite working in high-risk units, we are treated as if we were outpatient clinic nurses and receive the lowest incentive payments; we want improvements in this regard.' (Participant 59, aged 28, female)

Subtheme 3: Excessive workload

Participants noted that WOCNs work across multiple departments in addition to hospital stoma therapy units and described the resulting workload:

'The imbalance between the number of patients and the number of nurses is truly exhausting in terms of workload. The number of nurses should be increased to a certain extent.' (Participant 66, 26 years old, male)

'The work we do is very risky and exhausting; we approach the patient holistically. Our job isn't just about providing education—it involves providing care. All patients in the hospital with wounds or stomas are under our responsibility.' (Participant 81, 52 years old, female)

'As a certified WOCN, I have cared for patients for long hours without distinguishing between clinical units, including those under contact isolation. Even though there are colleagues and units that handle specialized care without even touching the patient, I hope our voices are heard.' (Participant 91, 44 years old, female)

Subtheme 4: Barriers to participation in WOCN certification programs

Some stoma and wound care nurses reported not having a WOCN certificate. One participant described her experience as follows:

'I have been a wound care nurse for 10 years, but I don't have a certificate. I want to enroll in the launched certificate program. As the person who set up the specialist unit, I am being, and

have been, subjected to bullying. I was removed from my post...' (Participant 98, aged 44, female).

Subtheme 5: Assignment of certified WOCNs to duties outside their area of expertise

One participant reported working in a department outside her area of expertise:

'My new place of work is a public hospital, and I am unable to work in a department that matches my qualification.' (Participant 71, aged 40, female)

Theme 2: Advantages

One subtheme was identified under the theme of advantages: receipt of additional compensation by WOCNs.

Subtheme 1: WOCNs receiving additional payment

One participant described her experience as follows: *'About six months ago, I asked my supervisor for a percentage of my working hours in the intensive care units, and my request was approved; I've been receiving it for six months now.'* (Participant 70, 35 years old, female)

DISCUSSION

This study demonstrated that WOCNs in Türkiye routinely provide care in high-risk clinical settings, including intensive care units, isolation rooms, emergency departments, and other specialized settings. Despite their substantial involvement in these environments and their frequent exposure to biological hazards, most participants reported not receiving the employment benefits and additional compensation provided to staff formally assigned to high-risk units.

Most nurses in the study were based in stoma and wound care units or chronic wound care units; however, they also worked in general surgery clinics, intensive care units, diabetic foot clinics, endoscopy units, and palliative care centers (Table 1). A multicenter, cross-sectional study conducted in China involving WOCNs (n = 123) reported that 77.24% of nurses worked in a stoma clinic and only 10.57% worked as full-time WOCNs. The study found that other nurses worked as WOCNs on a part-time basis while also working in the hospital in roles such as clinical nurse, manager, or instructor (25). In another study, 22.90% of WOCNs (n = 218) worked full-time (26). A cross-sectional study conducted in China (n = 247) found that 69.6% of WOCNs worked part-time in clinics, taking on duties

in more than one area (30). These findings are consistent with our research results and demonstrate that WOCNs have diverse areas of practice and employment arrangements. This variation may reflect the absence of standardized national and international frameworks defining the roles, employment settings, and working conditions of WOCNs.

In Türkiye, nurses are generally required to work 40 hours per week, corresponding to approximately 160 hours per month. WOCNs in this study reported spending a median of 40 hours (IQR: 10-80) per month in ICUs, 10 hours (IQR: 2-30) in isolation rooms, and 5 hours (IQR: 0-38.5) in other high-risk units, such as palliative care centre (Table 2). These findings indicate that WOCNs spend a significant percentage of their working hours providing patient care in critical and high-risk environments. The qualitative findings further support this observation, as one WOCN reported: *'...Although I work five hours a day in high-risk ICUs, management turns a blind eye to this, and we are assigned to work in different areas...'* These findings highlight the importance of aligning employment conditions and benefits with the actual clinical environments in which nurses provide care.

In hospitals, WOCNs carry out key interventions including promoting patient self-care, preventing complications, and supporting psychosocial adjustment (31). According to Turkish legislation, wound debridement, identification of the affected body area, pressure ulcer care, and burn/wound debridement are among the procedures that nurses may perform both independently and in collaboration with a doctor (1). When performing these procedures, WOCNs are exposed to physical, chemical, biological, psychosocial, and ergonomic risk factors (32). In our study, WOCNs reported exposure to both physical hazards, including blood, feces, urine, sweat, saliva, exudate, infected wound material, drain contents, COVID-19, sharps injuries, and scabies, in both stoma and wound care units and other specialized units (Table 3). Similarly, the qualitative findings identified a high risk of exposure to infectious diseases as a major disadvantage of working in these settings (Table 4). In a study evaluating wounds resulting from earthquakes, signs of infection were observed in 62.9% of wounds, and exudate was present in 65.0% (20). Similarly, a study of patients attending a wound clinic (n = 158) reported that 43.0% had a small amount of exudate, 15.8% had an infection, and 12.0% had an odor (33). These findings underscore the need to identify occupational hazards encountered by WOCNs and implement appropriate organizational and individual measures to reduce these risks.

During the COVID-19 pandemic, which affected healthcare systems worldwide, WOCNs faced a high risk of infection while providing patient care and were also assigned to duties outside

their usual work units (18,22,34–36). A study conducted in Türkiye reported that 51.3% of WOCNs ($n = 271$) were assigned to units other than their usual workplaces during the COVID-19 pandemic (18). During this period, nurses were exposed not only to SARS-CoV-2 infection but also to the risk of medical device-related pressure injuries associated with the use of personal protective equipment (36,37). Furthermore, the postponement of surgical procedures during the pandemic led to a decline in the number of patients undergoing colorectal surgery, and WOCNs were assigned to different departments by management (36). In the present study, three WOCNs reported exposure to COVID-19 (Table 3). Assigning nurses to duties outside their areas of expertise or without consideration of their preferences may contribute to psychological stress and burnout, reduced organizational commitment, lower work productivity, and interpersonal conflict among staff (38).

Clear regulatory frameworks are important for professional development. In China, the country with the world's second-largest population, the development of legal regulations governing WOC nursing has been recommended (12). In a study conducted with WOCNs in China, 58.30% of nurses reported that there was no performance-based system in place, and 63.80% reported that there was no promotion system for their professional positions. Similarly, 73.90% of nurses reported not receiving additional compensation, which is comparable to the 76% observed in our study (26). Nurses working in public hospitals in Türkiye receive additional payments for working in the specialist units listed in Table 2. However, despite the occupational risks associated with their work, stoma and wound care units are not classified as specialized units, and WOCNs do not receive additional payment (39). Approximately 25% of nurses in our study reported receiving additional compensation, while the rest did not (Table 1). This issue represents an important concern regarding the employment rights and working conditions of WOCNs. A study conducted in Türkiye ($n = 103$) reported that nurses are more likely to choose to work in areas designated as high-risk by the Ministry of Health because of the financial benefits (38). It is recommended to review the definition of high-risk units in Turkish regulations (40). Recognizing stoma and wound care units as specialized units, along with their employment conditions, could support the development of the WOC nursing workforce.

The study found that only half of the nurses held a WOCN certificate approved by the Ministry of Health. The literature indicates that ostomy care provided by clinical nurses is inadequate, that nurses lack experience in managing peristomal skin complications, and that ongoing training in this area is required (16,41,42). Care provided by certified WOCNs may improve patient satisfaction, reduce preventable

complications, and enhance the quality of nursing care. The study suggests that the reasons WOCNs do not participate in certification programs include the absence of a stoma care unit in the hospital, insufficient support from hospital management, certification programs being offered in another city, and lack of financial resources.

One key issue highlighted in the study is that WOCNs were assigned to duties outside their areas of expertise. Participants reported that, in addition to their primary responsibilities in wound and stoma care, they were assigned tasks such as clinical nursing, preparing duty rosters, and performing administrative duties. In the qualitative data, this issue was reported as follows: *'My new place of work is Public Hospital A, and I am unable to work in a department that matches my qualification.'* A descriptive study conducted with specialist nurses in Türkiye ($n = 83$) found that 34.9% of nurses were working in a department unrelated to their area of specialization, and that the majority of these nurses (68.97%) had not requested a transfer to a department related to their area of specialization from the hospital management (43). These findings suggest that nurses who have received specialized theoretical and practical training may nevertheless be routinely assigned to roles that do not utilize their specialist competencies. This may reflect organizational staffing requirements, limited opportunities for specialist practice, or nurses' reluctance to challenge administrative decisions. Reports from YOIHD workshops have also emphasized the need to increase the number of certified WOCNs. According to these reports, expanding the number of certified specialists is essential for standardizing specialized care and improving patient outcomes nationwide (39,44).

This study has several limitations. Participation was limited to WOCNs who were members of a professional nursing association and volunteered to participate; therefore, the findings may not fully represent all WOCNs working in Türkiye. In addition, data regarding time spent in high-risk units, occupational exposures, and receipt of additional compensation were based on self-report and were not verified through institutional records, which may have introduced recall and reporting bias. Furthermore, WOCNs who were not members of the professional communication network used for recruitment may not have been reached.

Despite these limitations, the study has several strengths. To our knowledge, this is one of the first studies to examine WOCNs' involvement in high-risk clinical environments, occupational exposures, and employment-related inequities. The study included participants from all seven geographical regions of Türkiye, providing a nationwide perspective on WOC nursing practice and increasing the potential transferability of

the findings across healthcare settings. In addition, participants were actively working in a variety of healthcare institutions, allowing the study to capture real-world experiences from diverse clinical environments. The integration of quantitative and qualitative findings provided a comprehensive understanding of the discrepancy between WOCNs' actual clinical responsibilities and the employment benefits they receive. The findings provide evidence that may inform workforce planning, occupational health policies, and the recognition and compensation of specialist nursing roles.

CONCLUSION

The findings reveal a clear mismatch between the administrative classification of WOCNs and their actual clinical responsibilities and workplace exposures. This discrepancy may

contribute to employment inequities and inadequate recognition of specialist nursing practice. Workforce policies and employment regulations should be reviewed to ensure that compensation, occupational protection, and professional recognition more accurately reflect the scope and risks of WOC nursing practice.

Healthcare organizations should also support the appropriate utilization of certified WOCNs by enabling them to practice within their areas of expertise and recognizing their contributions across high-risk clinical settings. Future multicenter national and international studies are needed to examine further the relationship between specialist nursing roles, occupational exposure, workforce retention, and employment outcomes.

Ethical Approval: Ethical approval for the study was obtained from the Gazi University Clinical Non-Interventional Research Ethics Committee on March 21, 2023, with decision no. E-77082166-604.01.02-618184.

Informed Consent: In the first part of the online survey form, participants were given preliminary information about the research and informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.K., Z.G.B., Ş.G., B.I., S.Y.; Design – A.K., Z.G.B., Ş.G., B.I., S.Y.; Supervision – Z.G.B., A.K.; Funding – B.I., S.Y.; Materials – B.I., S.Y.; Data Collection and/or Processing – B.I., S.Y.; Analysis and/or Interpretation – B.I., Ş.G.; Literature Review – B.I., Ş.G.; Writing – B.I., Ş.G.; Critical Review – Z.G.B., A.K.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Acknowledgements: The authors thank the participating WOCNs and the Wound, Ostomy and Incontinence Nurses Society (YOİHD) of Türkiye for their valuable support.

Scientific Presentation: An abstract of this study was presented as an oral presentation at the 12th National and 1st International Colorectal Surgery Nursing Congress (May 16–20, 2023) in Antalya, Türkiye.

AI Statement: During the preparation of this work, the authors used solely the Grammarly AI tool to check, refine, and improve the language, grammar, and spelling of the manuscript. No AI tools were used to generate, analyze, interpret, or produce any scientific content, data, or text of the study.

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The Relationship Between Venous Ulcer and Lymphedema: A Recognized but Underreported Topic in the Literature

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ABSTRACT

Objective: This study aimed to map the bibliometric profile of publications addressing venous ulceration and lymphedema and to assess the extent to which this relationship is proportionately represented in the literature.

Materials and Methods: A PubMed-derived comma-separated values (CSV) dataset containing publications on venous ulcer and lymphedema was analyzed using descriptive statistics (absolute and relative frequencies) in Hex.tech. Publication year, journal title, authorship fields, digital object identifier (DOI)/PubMed Central identifier (PMCID) availability, and title-based thematic categories were extracted. Titles were manually classified into the following categories: venous ulcer, lymphedema/lymphatic, compression, wound care, guideline/review, interventional, and direct venous ulcer/lymphedema overlap. No inferential statistical tests were performed.

Results: The dataset contained 200 PubMed records published between 1955 and 2026, distributed across 105 journals. A DOI was available for 122 records (61.0%), whereas 26 records (13.0%) were assigned a PMCID. There were 181 unique first authors. The most frequent title-based categories were compression therapy (47 records, 23.5%), lymphedema/lymphatic terminology (41 records, 20.5%), and venous ulcer terminology (31 records, 15.5%). Direct venous ulcer/lymphedema overlap was identified in only five records (2.5%).

Conclusion: The venous ulcer and lymphedema relationship is clinically well recognized but remains underrepresented in publication titles within the analyzed PubMed literature. Future research on venous ulcers should report lymphatic status more explicitly and include edema phenotypes and lymphatic-specific outcomes.

Keywords: venous leg ulcer, lymphedema, lymphatic dysfunction, phlebolymphe-
dema, compression therapy, bibliometric analysis

ORIGINAL ARTICLE

Int Scope Wound Manag.
2026;1(2):64–70

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Received

June 5, 2026

Accepted

July 22, 2026

Published

August 31, 2026

DOI

10.36519/iswm.2026.1214

Suggested Citation

Yıldırım AC. The relationship between venous ulcer and lymphedema: A recognized but underreported topic in the literature. Int Scope Wound Manag. 2026;1(2):64–70.



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INTRODUCTION

Venous leg ulcers are among the most persistent and resource-intensive complications of chronic venous disease. They cause prolonged morbidity, repeated clinical visits, and a marked burden on patients and health systems (1,2). The usual pathophysiologic explanation focuses on venous hypertension, ambulatory venous pressure, microcirculatory inflammation, and impaired tissue repair (1). This framework is essential, but it does not fully describe the chronic edema phenotype seen in many patients. In advanced venous disease, lower-limb swelling is rarely a purely venous event. Persistent capillary filtration may exceed lymphatic transport capacity, producing lymphatic overload, secondary lymphatic damage, and the mixed venous-lymphatic state often described as phlebolymphe¹dema (3,4).

The clinical importance of this overlap is clear. When lymphatic failure is present, edema may become more persistent, lymphorrhea more difficult to control, and tissue fibrosis more established. These changes can contribute to an increased susceptibility to cellulitis, delayed epithelialization, and recurrent ulceration (3,5,6). Compression therapy therefore does more than reduce venous hypertension; it also promotes lymphatic drainage and remains central to both venous and lymphatic care pathways (2,7,8). Despite this, many venous ulcer studies do not formally assess lymphatic dysfunction, report edema phenotype, or identify lymphedema as an outcome modifier. The condition is often recognized clinically but may be underrepresented in the literature (5,9).

This study presents a bibliometric analysis of PubMed-indexed literature on venous ulceration and lymphedema. The aim was not to perform a treatment-effect review but to clarify how often the venous-lymphatic relationship is explicitly reflected in publication titles, journals, and thematic patterns.

MATERIALS AND METHODS

Data Source and Search Basis

A PubMed search was conducted on June 4, 2026, using combined search terms for venous ulcer and lymphedema. The resulting records were exported as a comma-separated values (CSV) file for analysis. The export included publication year, journal title, authorship fields, digital object identifier (DOI), PubMed Central identifier (PMCID), and title fields.

Data Processing and Statistical Analysis

The exported CSV file was analyzed in Hex.tech (Hex Technologies Inc., San Francisco, CA, USA) using Python for data

cleaning, sorting, and tabulation. Descriptive statistics were used to characterize the dataset; results were reported as absolute frequencies, relative frequencies (percentages), and count distributions by year, journal, and thematic category. No inferential statistical tests were performed, as the study aimed to describe the bibliometric profile rather than to test hypotheses. Automated keyword matching was not used; thematic classification was performed by manual review of each record's title according to the predefined category list described below. The unit of analysis was the individual PubMed record.

Thematic Classification

A title-based thematic classification was applied to identify the major themes represented in the literature:

- Direct venous ulcer/lymphedema overlap
- Lymphedema or lymphatic terminology
- Venous ulcer terminology
- Compression therapy
- Wound care or healing
- Guideline, review, or algorithm publications
- Surgical or interventional lymphatic approaches
- Case reports, pilot studies, or clinical trials

RESULTS

Overall Bibliographic Profile

The dataset contained 200 PubMed records published from 1955 to 2026 (as of June 4, 2026), distributed across 105 journals (Table 1). A DOI was available for 122 records (61.0%), while 26 records (13.0%) had a PMCID. There were

HIGHLIGHTS

- Only 2.5% of 200 PubMed records directly linked venous ulcer and lymphedema in their title.
- Compression therapy (23.5%) and lymphedema/lymphatic terminology (20.5%) were the most frequent thematic categories.
- Publication activity increased after 2010, but direct venous ulcer/lymphedema overlap remained consistently low.
- The literature was dispersed across 105 journals and involved 181 unique first authors.
- Future venous ulcer research should systematically report lymphatic status and edema phenotype.

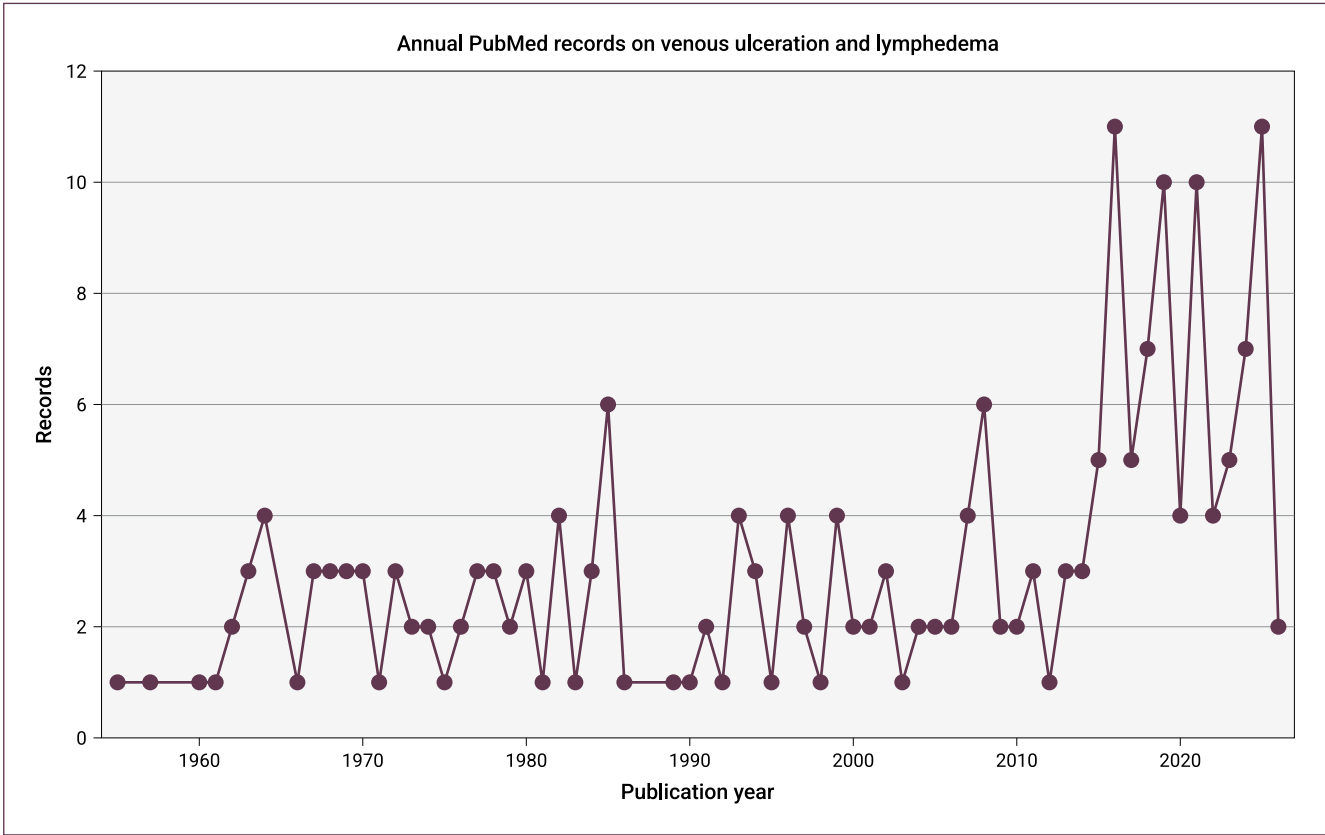


Figure 1. Annual PubMed publication trend for venous ulcer/lymphedema-related records, showing the annual number of records.

181 unique first authors, indicating a dispersed authorship structure rather than the output of a single dominant research group.

Temporal Trend

Publication activity was sparse and irregular before the 1990s and increased more substantially after 2010 (Figure 1). The largest annual totals occurred in 2016 and 2025, with 11 records in each year. Direct title-level overlap between venous ulceration and lymphedema remained consistently low, even in years with higher overall publication activity.

Although overall publication volume increased after 2010, the proportion of records using lymphedema or lymphatic terminology remained variable across decades (Figure 2). In the earliest period (1955–1989), lymphatic terms appeared in only a small fraction of the sparse output. From the 1990s onward, the use of lymphedema or lymphatic terminology became more consistent, with three of four records in 1996, three of 11 records in 2016, and four of 11 records in 2025 containing these terms. The direct venous ulcer and lymphedema overlap was limited to five individual records across

Table 1. Bibliometric profile of the PubMed-derived dataset on venous ulcer and lymphedema.

Indicator	Value
Total records	200
Publication year range	1955–2026
Number of journals	105
Unique first authors	181
Records with a DOI, n (%)	122 (61.0)
Records with a PMCID, n (%)	26 (13.0)
Records with lymphedema/lymphatic terminology, n (%)	41 (20.5)
Records with venous ulcer terminology, n (%)	31 (15.5)
Records with compression terminology, n (%)	47 (23.5)
Direct venous ulcer/lymphedema overlap, n (%)	5 (2.5)
Peak publication years (n, each)	2016, 2025 (11)

DOI: Digital object identifier, PMCID: PubMed Central identifier.

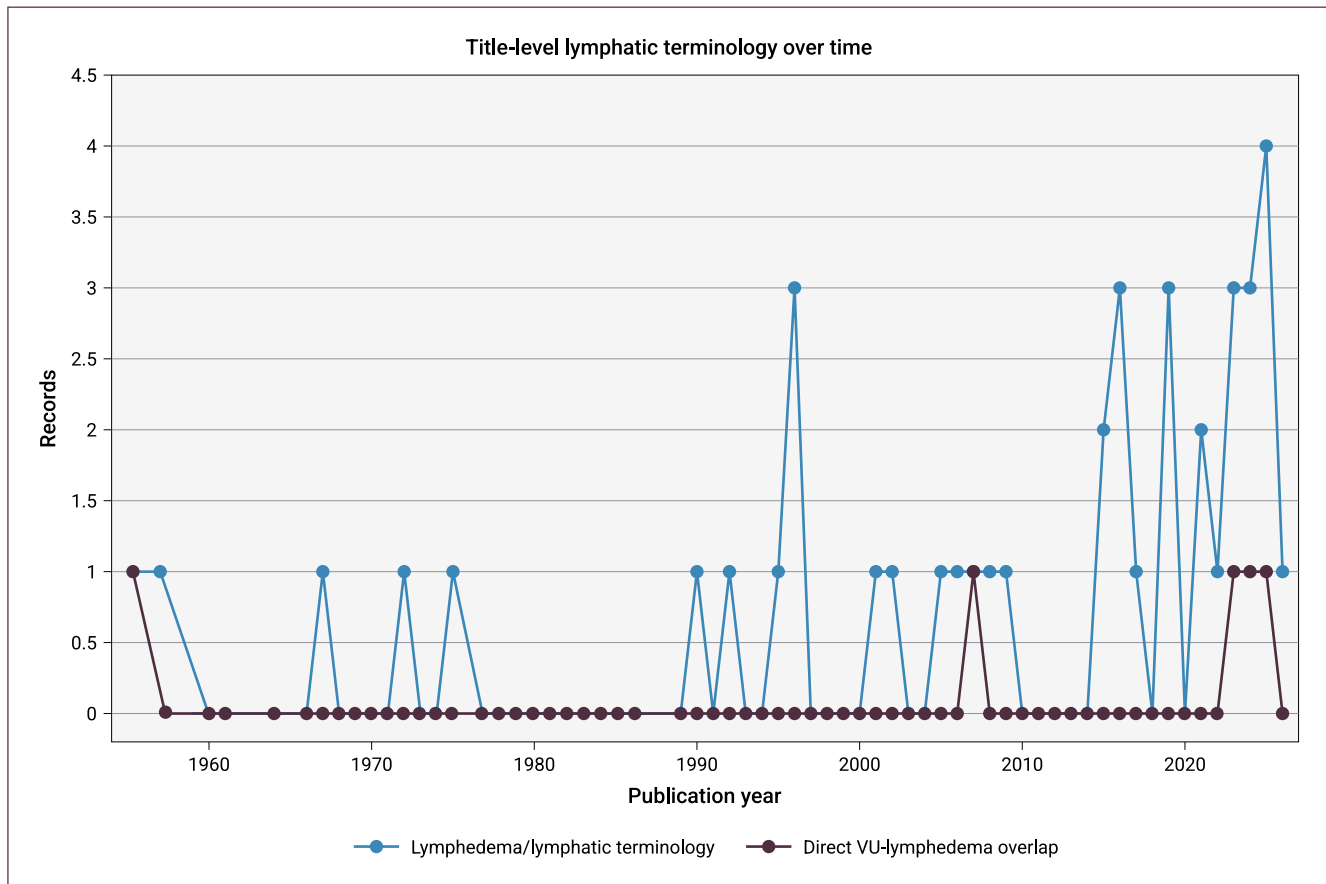


Figure 2. Temporal trends in the use of lymphedema or lymphatic terminology, illustrating the infrequent occurrence of direct venous ulcer/lymphedema overlap in publication titles.

the entire dataset (1955, 2007, 2023, 2024, and 2025), suggesting that the combined topic has only recently begun to appear in publication titles.

Journal Distribution

The most frequent journals were *J Wound Care* and *Phlebologie*, with 18 records each, followed by *Br J Community Nurs* and *Br J Nurs*, with nine records each (Figure 3). Nursing, vascular, dermatology, wound care, and microsurgical journals were all represented among the leading sources, reflecting the multidisciplinary nature of the topic.

Thematic Structure

The most frequent title-based categories were compression therapy (47 records, 23.5%), lymphedema/lymphatic terminology (41 records, 20.5%), and venous ulcer terminology (31 records, 15.5%) (Figure 4). Direct venous ulcer/lymphedema overlap was identified in five records (2.5%) using the title-overlap definition. Wound care/healing terminology appeared in 18 records (9.0%), guideline/review publications

in 10 records (5.0%), surgical/interventional approaches in 14 records (7.0%), and case reports, pilot studies, or clinical trials in 14 records (7.0%).

DISCUSSION

Three practical areas dominate the literature. The first is compression therapy, which remains the shared foundation of venous and lymphatic management (2,7,8). The second is wound care, where publications address exudate, healing, dressings, and chronic ulcer management, but often without formally phenotyping lymphatic dysfunction (1,6,9). The third is a smaller interventional field focused on lymphatic surgery, including lymphovenous bypass and lymphovenous anastomosis, mainly in selected chronic or refractory cases (10–13). Importantly, treatment-pattern analyses suggest that lymphatic therapy may be undervalued for patients with phlebolymphe-
dema and venous leg ulcer (14). This distribution may reflect daily practice: many clinicians manage both the wound and the edema, but the lymphatic component is not always separately identified, measured, or reported. The limited explicit representation of this relationship in the

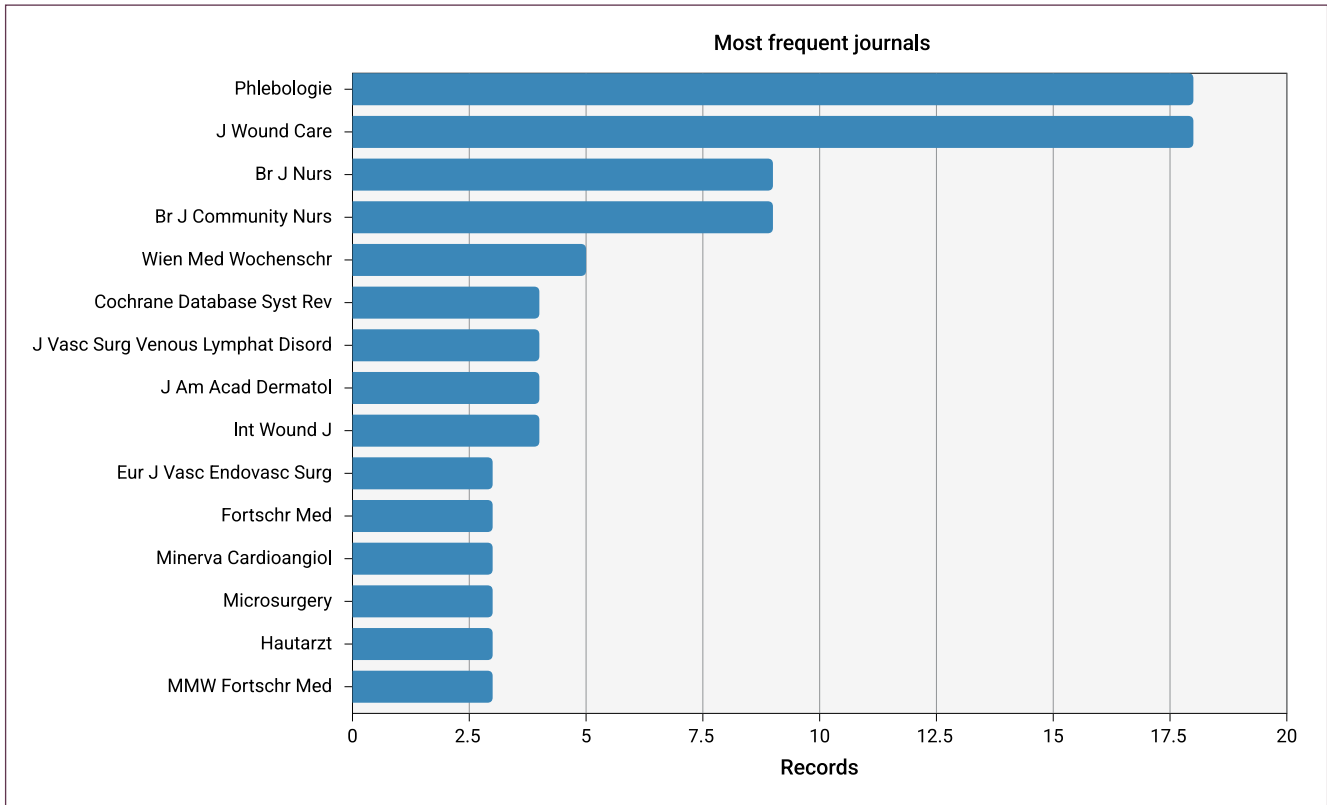


Figure 3. Leading journals publishing on the venous ulcer/lymphedema topic, showing the total number of records by journal.

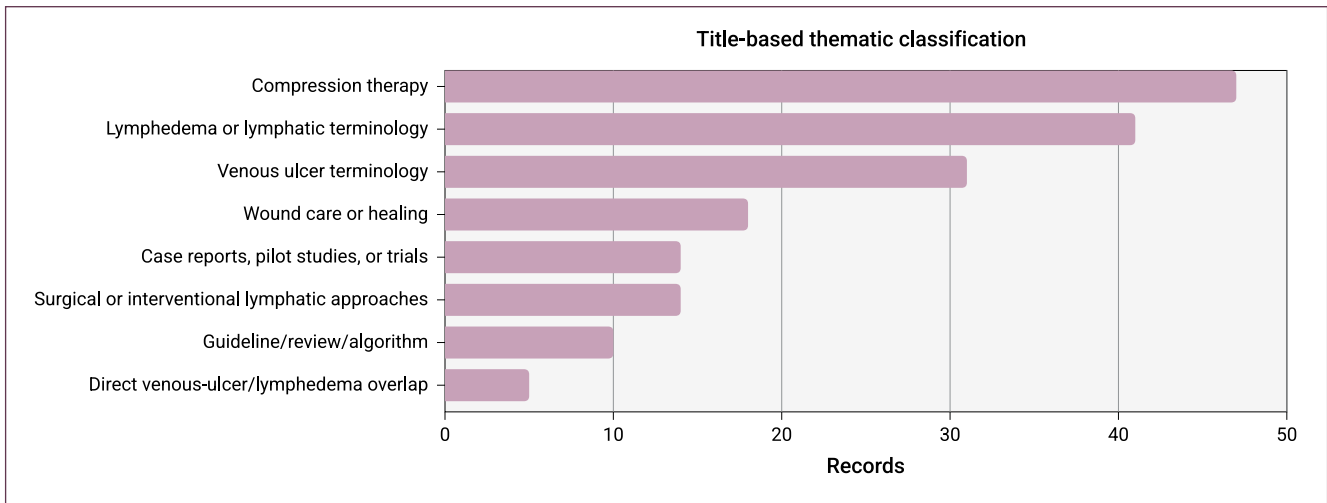


Figure 4. Title-based thematic distribution of the literature, showing the frequency of direct venous ulcer/lymphedema overlap compared with broader themes, including venous ulceration, lymphedema/lymphatic disease, and compression therapy.

literature is not merely a bibliometric detail. Lymphedema may alter prognosis, compression tolerance, infection risk, and response to standard venous ulcer care (5). Patients with persistent lymphatic failure may need more than venous correction and conventional compression. In selected cases, management may require structured edema staging, lymphatic-specific compression, manual lymphatic drainage, cellulitis

prevention, skin-care protocols, lymphorrhea control, lymphatic imaging, or surgical consultation (7,8,10–15). If lymphatic status is not recorded, its influence cannot be accounted for, and clinically meaningful heterogeneity may remain unrecognized.

Future venous ulcer studies should therefore treat lymphatic dysfunction as an important clinical variable rather than an

incidental observation. Baseline reporting should include edema phenotype, suspected or confirmed lymphatic insufficiency, history of cellulitis, lymphorrhea, fibrosis or skin changes, compression tolerance, and recurrence. Prospective cohorts could test whether lymphatic impairment predicts delayed healing or relapse after venous intervention. Trials of compression systems and wound care technologies should include lymphatic subgroup analyses. Finally, lymphatic imaging and microsurgical approaches require structured evaluation beyond isolated case reports.

This study has several limitations. First, the analysis was based on PubMed records only; inclusion of additional databases such as Embase, CINAHL, or Scopus might yield a larger or differently structured dataset. Second, the title-based thematic classification relied on keyword presence and did not capture themes discussed within abstracts or full texts where the venous-lymphatic relationship may have appeared without being named in the title. Third, the dataset includes records across seven decades with evolving terminology; earlier records may have used different terms for overlapping

concepts, potentially underestimating the true overlap. Fourth, bibliometric metadata do not capture the depth of clinical discussion; a study may address lymphatic impairment extensively in its text without including relevant terminology in the title. Finally, the search was conducted at a single time point, and newly published or indexed records may alter the distribution.

CONCLUSION

Venous ulceration and lymphedema are closely connected in clinical practice, but their explicit overlap remains underrepresented in publication titles within the PubMed literature. This limited representation matters because lymphatic dysfunction may influence healing, recurrence, infection risk, and response to compression-based care. Venous ulcer research should move beyond a purely venous framework and report lymphatic status more systematically, including edema phenotype and lymphatic-specific outcomes, especially in patients with chronic edema, lymphorrhea, recurrent cellulitis, fibrosis, or refractory wounds.

Ethical Approval: Not applicable.

Informed Consent: Not applicable.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.C.Y.; Design – A.C.Y.; Supervision – A.C.Y.; Funding – A.C.Y.; Materials – A.C.Y.; Data Collection and/or Processing – A.C.Y.; Analysis and/or Interpretation – A.C.Y.; Literature Review – A.C.Y.; Writing – A.C.Y.; Critical Review – A.C.Y.

Conflict of Interest: The author declared no conflict of interest.

Financial Disclosure: The author declared that this study has received no financial support.

AI Statement: During the preparation of this work, the author used Hex.tech for statistical analysis and Liner AI for language editing and proofreading. After using these tools, the author reviewed and edited the content as needed and takes full responsibility for the content of the publication.

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Serum Albumin as a Marker of Infection Severity and Clinical Course in Patients with Diabetic Foot Infection

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ABSTRACT

Objective: This study aimed to evaluate the association between admission serum albumin levels, infection severity, and clinical outcomes in patients hospitalized and managed surgically for diabetic foot disease.

Materials and Methods: This retrospective, single-center observational cohort study included adult patients hospitalized for diabetic foot wounds who underwent surgical treatment (debridement or amputation) and received enteral nutritional support at a tertiary training hospital between January and April 2025. Clinical data, including length of hospital stay, duration of enteral nutrition, and duration of intravenous antibiotic therapy, together with laboratory parameters such as admission and discharge serum albumin levels, were obtained from medical records. Infection severity was assessed using the infection component of the PEDIS classification system. Patients were categorized into the low-to-moderate severity (PEDIS Infection Grades 1–2) and advanced severity (PEDIS Infection Grade 3) groups for comparative analyses.

Results: A total of 69 patients were included in the study. The mean age of the study population was 66.6 ± 10.6 years, and 75.4% of the patients were male. Median serum albumin levels increased significantly during hospitalization, from 3.1 g/dL (2.1–4.5) at admission to 3.3 g/dL (1.6–4.3) at discharge ($p = 0.001$). Patients with PEDIS Infection Grade 3 disease had significantly lower admission serum albumin levels than those with PEDIS Infection Grades 1–2 (2.8 g/dL [2.1–3.7] vs. 3.2 g/dL [2.5–4.5], $p = 0.001$). In addition, patients with advanced disease had significantly longer hospital stays (16 days [3–86] vs. 8 days [3–33], $p = 0.004$), longer durations of enteral nutritional support (14 vs. 7 days, $p = 0.001$), and prolonged intravenous antibiotic therapy (15 vs. 7 days, $p = 0.004$). No significant differences were observed between groups regarding HbA1c, hemoglobin, platelet count, or C-reactive protein levels (all $p > 0.05$).

Conclusion: Low admission serum albumin levels were associated with advanced infection severity in patients with diabetic foot infection. Advanced disease severity was accompanied by longer hospitalization, prolonged antibiotic therapy, and increased nutritional support requirements. Serum albumin may serve as a practical and readily available biomarker for assessing disease severity and monitoring the clinical course in patients with diabetic foot disease.

Keywords: Diabetic foot, albumin, PEDIS, nutritional status, wound infection, prognosis

ORIGINAL ARTICLE

Int Scope Wound Manag.
2026;1(2):71–8

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Received

June 9, 2026

Accepted

July 15, 2026

Published

August 31, 2026

DOI

10.36519/iswm.2026.1218

Suggested Citation

Hıdıroğlu MM, Yavuz A, Armağan ST, Tanar E, Uçar S, Karamustafa M, et al. Serum albumin as a marker of infection severity and clinical course in patients with diabetic foot infection. Int Scope Wound Manag. 2026;1(2):71–8.



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INTRODUCTION

Diabetic foot ulcers represent a complex clinical condition influenced by the combined effects of neuropathy, ischemia, infection, impaired glycemic control, and the patient's systemic reserve (1). In these patients, wound healing is closely associated not only with local wound care and surgical interventions but also with infection control, metabolic regulation, and adequate nutritional support. Particularly in infected diabetic foot wounds, the increased inflammatory response and catabolic state increase the protein and energy requirements necessary for tissue repair, thereby affecting clinical outcomes, length of hospital stay, and treatment response.

Although numerous adjunctive treatment modalities—including regenerative products, skin grafts, negative pressure wound therapy, and hyperbaric oxygen therapy—are currently used to shorten treatment duration in diabetic foot management, the success of these approaches is largely influenced by the patient's systemic condition and nutritional reserve (2–4). Nutritional status is one of the key determinants of wound healing in diabetic foot disease. Adequate protein and energy intake are essential for collagen synthesis, granulation tissue formation, angiogenesis, immune regulation, and epithelialization (5,6). Therefore, assessment of nutritional reserve in patients with diabetic foot disease is important not only for planning supportive treatment but also for providing prognostic information regarding infection severity and the clinical course. In general surgical practice, this assessment is often based on practical, readily available, and reproducible laboratory parameters.

Serum albumin is one of the most commonly used biochemical markers for evaluating nutritional reserve in clinical practice. However, albumin levels reflect not only nutritional status but also systemic inflammatory activity and are influenced by several factors, including the inflammatory response, catabolic state, fluid balance, and hepatic synthetic capacity. Consequently, low serum albumin levels should be considered not only an indicator of malnutrition but also a marker of ongoing inflammatory and catabolic processes (7,8). In this respect, albumin may provide practical information regarding both nutritional status and the systemic impact of the disease in patients with diabetic foot infection.

Previous studies have suggested that low serum albumin levels in patients with diabetic foot disease may be associated with delayed wound healing, increased infectious burden, prolonged hospitalization, and unfavorable clinical outcomes (9). However, this relationship may not be uniform across all patient populations and should be interpreted in conjunction with disease severity. Unlike C-reactive protein (CRP) and

white blood cell (WBC) count, serum albumin may provide additional clinical information by reflecting both nutritional reserve and inflammation-related systemic burden in patients with diabetic foot infection. The PEDIS classification is widely used to assess diabetic foot ulcers based on key clinical components, including perfusion, extent, depth, infection, and sensory loss (10). Therefore, evaluating serum albumin levels together with PEDIS Infection Grade, length of hospital stay, duration of intravenous antibiotic therapy, and duration of enteral nutritional support may contribute to the clinical management of patients with diabetic foot infection.

Nevertheless, studies investigating the relationship between serum albumin levels and PEDIS Infection Grade, as well as treatment-related clinical parameters in patients with diabetic foot infection, remain limited. The present study aimed to evaluate the association between admission serum albumin levels, infection severity, and clinical outcomes in patients hospitalized for diabetic foot infection.

MATERIALS AND METHODS

Study Design and Patient Selection

This single-center observational cohort study was designed as a retrospective analysis of patients hospitalized for diabetic foot wounds and treated surgically (debridement or amputation) in the Department of General Surgery at Gülhane Training and Research Hospital between January and April 2025.

Among patients hospitalized for diabetic foot wounds and managed surgically in our clinic, those with inadequate oral intake requiring enteral nutritional support were included in the study.

HIGHLIGHTS

- Lower serum albumin levels were associated with advanced PEDIS Infection Grades.
- Patients with PEDIS Infection Grade 3 disease required longer hospitalization and intravenous antibiotic therapy.
- Advanced infection severity was associated with longer durations of enteral nutritional support.
- Serum albumin levels increased significantly during hospitalization.
- Serum albumin may be a practical biomarker for assessing infection severity in patients with diabetic foot disease.

Adult patients hospitalized and treated for diabetic foot disease were eligible for inclusion. Patients with incomplete clinical or laboratory data were excluded. Patients who did not undergo surgical debridement in the operating room or did not require operative intervention were not included. Patients with inadequate oral intake requiring intensive care unit follow-up and parenteral nutritional support were excluded. Patients undergoing day-case surgical procedures, those receiving corticosteroid therapy, immunosuppressed individuals, and patients with concomitant immunosuppressive conditions (such as malignancy or rheumatologic diseases) were also excluded. Patients with known chronic renal failure, end-stage renal disease, severe chronic liver disease, or hepatic failure were also excluded from the study.

Ethical approval was obtained from the University of Health Sciences Gülhane Training and Research Hospital Non-Interventional Scientific Research Ethics Committee on April 2, 2026, with decision number 2026/95.

Data Collection and Variables

Demographic characteristics (age and sex), clinical variables (length of hospital stay, duration of enteral nutrition, and duration of intravenous antibiotic therapy), and laboratory parameters including glycated hemoglobin (HbA1c), serum albumin, C-reactive protein (CRP), white blood cell (WBC) count, hemoglobin, and platelet count, were retrospectively collected from the medical records. Serum albumin levels were recorded at both admission and discharge, and changes in albumin levels during hospitalization were evaluated.

Assessment of Infection Severity

The infection component of the internationally recognized PEDIS classification categorizes diabetic foot infections into four grades based on clinical severity, ranging from Grade 1 (no clinical signs of infection) to Grade 4 (infection associated with systemic inflammatory response syndrome [SIRS]). In the present study, disease severity was assessed using this infection component. For analysis, patients were categorized into two groups based on clinical severity: PEDIS Infection Grades 1–2, representing low-to-moderate infection severity, and PEDIS Infection Grade 3, representing advanced infection severity. Clinical and laboratory parameters were compared between these groups.

Patients classified as PEDIS Infection Grade 4, characterized by SIRS or severe sepsis, were excluded because serum albumin levels in these patients are substantially influenced by systemic inflammation, capillary leakage, aggressive fluid

resuscitation, and critical illness in addition to the severity of the local diabetic foot infection. To specifically evaluate the association between serum albumin levels and localized diabetic foot infection severity while minimizing the confounding effects of systemic critical illness, only patients with PEDIS Infection Grades 1–3 were included.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 27.0 for Windows (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using visual methods and the Kolmogorov-Smirnov test. Normally distributed variables were expressed as mean $\pm$ standard deviation, whereas non-normally distributed variables were presented as median (minimum–maximum). Categorical variables were expressed as frequencies and percentages.

Comparisons between groups were performed using the chi-square test for categorical variables, the independent-samples Student's t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous variables. Admission and discharge serum albumin levels were compared using the Wilcoxon signed-rank test. A p-value of < 0.05 was considered statistically significant.

Univariable logistic regression analyses were first performed to evaluate factors associated with advanced infection severity, defined as PEDIS Infection Grade 3 versus PEDIS Infection Grades 1–2. Variables with a p-value < 0.05 in the univariable logistic regression analysis were subsequently entered into the multivariable logistic regression model to identify independent predictors of advanced infection severity. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs).

RESULTS

A total of 69 patients with diabetic foot infection were included in the study. The mean age of the patients was 66.6 ± 10.6 years, and 75.4% of the cohort were male. The median length of hospital stay was 10 days (3–86), the median duration of enteral nutrition was 8 days (2–57), and the median duration of intravenous antibiotic therapy was 9 days (2–86). The median HbA1c level was 8.2% (5–16).

The median serum albumin level at admission was 3.1 g/dL (2.1–4.5), which increased to 3.3 g/dL (1.6–4.3) at discharge. The median C-reactive protein (CRP) level at admission was 129 mg/L (1–410). According to the infection component of the PEDIS classification, 20.3% of patients

were classified as Grade 1, 47.8% as Grade 2, and 31.9% as Grade 3 (Table 1). These categories included 14, 33, and 22 patients, respectively.

When patients were compared according to PEDIS Infection Grade, those in the PEDIS Infection Grade 3 group, representing advanced disease severity, had significantly longer hospital stays, longer durations of enteral nutritional support, and longer durations of intravenous antibiotic therapy than those in the PEDIS Infection Grades 1–2 group ($p = 0.004$, $p = 0.001$, and $p = 0.004$, respectively). In addition, admission serum albumin levels were significantly lower (2.8 vs. 3.2 g/dL; $p = 0.001$), whereas white blood cell counts were significantly higher in the PEDIS Infection Grade 3 group ($p = 0.048$). CRP levels did not differ significantly between the groups, although median values were numerically higher in patients with PEDIS Infection Grade 3 (147 vs. 103 mg/L; $p = 0.059$). No significant differences were observed between

the groups regarding HbA1c, hemoglobin, or platelet counts (Table 2).

Across the entire cohort, the median serum albumin level increased from 3.1 g/dL at admission to 3.3 g/dL at discharge, and this increase was statistically significant ($p = 0.001$).

Univariable logistic regression analysis was performed to identify factors associated with advanced infection severity, defined as PEDIS Infection Grade 3 versus PEDIS Infection Grades 1–2. Length of hospital stay (OR = 1.070, 95% CI: 1.019–1.123; $p = 0.007$), duration of enteral nutrition (OR = 1.099, 95% CI: 1.030–1.174; $p = 0.005$), duration of intravenous antibiotic therapy (OR = 1.071, 95% CI: 1.019–1.125; $p = 0.007$), and admission serum albumin level (OR = 0.050, 95% CI: 0.009–0.291; $p = 0.001$) were significantly associated with advanced infection severity (Table 3). Variables with a

Table 1. Demographic, clinical, and laboratory characteristics of patients with diabetic foot disease.

Variable	Value
Age (years), mean $\pm$ SD	66.62 $\pm$ 10.59
Sex, n (%)	
Female	17 (24.6)
Male	52 (75.4)
Duration of enteral nutrition (days), median (min–max)	8 (2–57)
Duration of IV antibiotic therapy (days), median (min–max)	9 (2–86)
Length of hospital stay (days), median (min–max)	10 (3–86)
HbA1c (%)	8.2 (5–16)
Admission albumin (g/dL), median (min–max)	3.1 (2.1–4.5)
Discharge albumin (g/dL), median (min–max)	3.3 (1.6–4.3)
WBC ($\times 10^9$ /L), median (min–max)	11 (4–28)
Hemoglobin (g/dL), median (min–max)	10.8 (8.8–14.0)
Platelet count ($\times 10^9$ /L), median (min–max)	346 (134–782)
CRP (mg/L), median (min–max)	129 (1–410)
The infection component of the PEDIS Infection Grade, n (%)	
PEDIS Infection Grade 1	14 (20.3)
PEDIS Infection Grade 2	33 (47.8)
PEDIS Infection Grade 3	22 (31.9)

IV: Intravenous, HbA1c: Glycated hemoglobin, WBC: White blood cell, CRP: C-reactive protein; PEDIS: Perfusion, Extent, Depth, Infection, and Sensation.

Table 2. Comparison of clinical and laboratory parameters between PEDIS Infection Grades 1–2 and PEDIS Infection Grade 3.

Variable	PEDIS Infection Grade 1–2 (n=47)	PEDIS Infection Grade 3 (n=22)	p-value
Sex, n (%)			
Female	11 (64.7)	6 (35.3)	*0.769
Male	36 (69.2)	16 (30.8)	
Age (years), mean $\pm$ SD	67.55 $\pm$ 9.89	64.64 $\pm$ 11.94	**0.290
Length of hospital stay (days), median (min–max)	8 (3–33)	16 (3–86)	***0.004
Duration of enteral nutrition (days), median (min–max)	7 (2–32)	14 (3–57)	***0.001
Duration of IV antibiotic therapy (days), median (min–max)	7 (2–32)	15 (3–86)	***0.004
HbA1c (%), median (min–max)	7.9 (5–16)	9.1 (5–13)	***0.119
Admission albumin (g/dL), median (min–max)	3.2 (2.5–4.5)	2.8 (2.1–3.7)	***0.001
WBC ($\times 10^9$ /L), median (min–max)	10.7 (4–28)	11.5 (8–28)	***0.048
Hemoglobin (g/dL), median (min–max)	11.0 (8.8–14.0)	10.7 (8.8–12.0)	***0.344
Platelet count ($\times 10^9$ /L), median (min–max)	333 (134–782)	373 (134–782)	***0.647
CRP (mg/L), median (min–max)	103 (1–410)	147 (12–410)	***0.059

IV: Intravenous, **HbA1c**: Glycated hemoglobin, **WBC**: White blood cell, **CRP**: C-reactive protein; **PEDIS**: Perfusion, Extent, Depth, Infection, and Sensation.

Note: Percentages for sex are calculated within each sex category (row percentages).

*Chi-square test (used for categorical variables).

**Student's t-test (used for normally distributed continuous variables).

***Mann–Whitney U test (used for non-normally distributed continuous variables).

A p-value < 0.05 was considered statistically significant.

p-value < 0.05 in the univariable analysis were included in the multivariable logistic regression model.

In the multivariable logistic regression analysis, only admission serum albumin remained independently associated with advanced infection severity (OR = 0.101, 95% CI: 0.015–0.665; $p = 0.017$). In contrast, length of hospital stay, duration of enteral nutrition, and duration of intravenous antibiotic therapy were no longer significantly associated with advanced infection severity after adjustment (Table 4).

DISCUSSION

Diabetic foot ulcers represent a complex clinical condition that should be evaluated not only according to local wound characteristics but also in relation to infection severity, vascular status, metabolic control, tissue repair capacity, and the patient's systemic reserve. Current guidelines recommend the assessment of diabetic foot infections based on clinical findings and

the severity of infection (1,10). In the present study, disease severity was evaluated using the infection component of the PEDIS classification, and several parameters reflecting the clinical course differed significantly between patients with low-to-moderate and advanced infection severity.

In our study, the length of hospital stay, duration of enteral nutritional support, and duration of intravenous antibiotic therapy were significantly longer in the PEDIS Infection Grade 3 group than in the PEDIS Infection Grades 1–2 group. This finding suggests that advanced PEDIS stages reflect not only more severe local wounds or infections but also a greater need for intensive treatment and prolonged hospitalization. PEDIS Infection Grade 3 is associated with more complex infectious features, including deep tissue involvement, extensive cellulitis, abscess formation, gangrene, and involvement of muscle, tendon, joint, or bone structures. Therefore, prolonged antibiotic therapy, increased nutritional support requirements, and longer hospitalization in patients with advanced-stage

Table 3. Univariable logistic regression analysis of factors associated with PEDIS Infection Grade 3.

Variable	B	OR (95% CI)	p-value
Sex	-0.205	0.815 (0.256–2.589)	0.728
Age (years)	-0.027	0.974 (0.927–1.023)	0.287
Length of hospital stay (days)	0.067	1.070 (1.019–1.123)	0.007
Duration of enteral nutrition (days)	0.095	1.099 (1.030–1.174)	0.005
Duration of IV antibiotic therapy (days)	0.068	1.071 (1.019–1.125)	0.007
HbA1c (%)	0.118	1.125 (0.907–1.395)	0.284
Admission albumin (g/dL)	-2.998	0.050 (0.009–0.291)	0.001
WBC ($\times 10^9/L$)	0.074	1.077 (0.992–1.168)	0.076
Hemoglobin (g/dL)	-0.220	0.803 (0.528–1.220)	0.304
Platelet count ($\times 10^9/L$)	0.001	1.001 (0.997–1.004)	0.705
CRP (mg/L)	0.005	1.005 (1.000–1.010)	0.071

Reference category for sex: Female, OR: Odds ratio, CI: Confidence interval, IV: Intravenous; HbA1c: Glycated hemoglobin, WBC: White blood cell, CRP: C-reactive protein.

disease are clinically expected findings (1,10). From a general surgical perspective, this observation suggests that the infection component of the PEDIS classification may serve not only as a descriptive grading system but also as a practical tool for estimating treatment intensity and healthcare resource utilization. Similarly, a previous study from our institution demonstrated that elevated HbA1c levels were associated with more advanced PEDIS infection stages and an increased need for surgical intervention. These findings support the concept that systemic biomarkers may be closely associated with disease severity in diabetic foot disease (11).

In the present study, admission serum albumin levels were significantly lower in patients with PEDIS Infection Grades. Although albumin is commonly used in clinical practice as a marker of nutritional reserve, it is also a negative acute-phase reactant whose concentration decreases in the presence of infection and inflammation (7,8). During the acute-phase response, positive acute-phase reactants such as CRP increase, whereas negative acute-phase reactants, including albumin, prealbumin, and transferrin, decrease. Consequently,

Table 4. Multivariable logistic regression analysis of factors associated with PEDIS Infection Grade 3.

Variable	B	OR (95% CI)	p-value
Length of hospital stay (days)	-0.896	0.408 (0.039–4.283)	0.455
Duration of enteral nutrition (days)	0.080	1.083 (0.957–1.225)	0.205
Duration of IV antibiotic therapy (days)	0.885	2.423 (0.235–24.965)	0.457
Admission albumin (g/dL)	-2.294	0.101 (0.015–0.665)	0.017

OR: Odds ratio, CI: Confidence interval, IV: Intravenous.

low serum albumin levels in patients with infected diabetic foot ulcers may reflect not only malnutrition but also inflammatory burden, catabolic response, and reduced systemic reserve. Increased cytokine release, protein catabolism, and hepatic acute-phase responses observed in more severe diabetic foot infections may contribute to lower serum albumin levels. Therefore, low serum albumin levels may indicate not only inadequate protein intake but also the systemic inflammatory burden associated with the disease process.

For this reason, patients with PEDIS Infection Grade 4 were intentionally excluded from the present study. In these patients, serum albumin concentrations are affected by systemic inflammatory response syndrome, severe sepsis, capillary leakage, fluid resuscitation, and critical illness, making it difficult to distinguish the effects of localized diabetic foot infection from those of generalized systemic inflammation. Restricting the study population to PEDIS Infection Grades 1–3 allowed a more homogeneous evaluation of the relationship between serum albumin and infection severity. Consequently, our findings should not be extrapolated to patients with PEDIS Infection Grade 4.

The finding of lower albumin levels in the PEDIS Infection Grade 3 group supports the association between advanced disease severity and both reduced nutritional reserve and a greater systemic inflammatory response. Likewise, the higher white blood cell counts observed in the PEDIS Infection Grade 3 group further support the presence of a more pronounced systemic inflammatory response in advanced infections. CRP levels did not differ significantly between the groups, although median values were numerically higher in patients with advanced infection severity. Therefore, no conclusion was

drawn based on CRP, and this finding should be interpreted cautiously in light of the relatively limited sample size. Accordingly, serum albumin should be interpreted not as a substitute for CRP or WBC, but as a complementary and readily available marker that reflects both nutritional reserve and inflammatory burden in patients with diabetic foot infection. This information may help general surgeons and wound care specialists during early clinical assessment and decision-making, particularly by identifying patients who may require closer monitoring, early nutritional assessment, and more intensive inpatient management.

Our findings partially align with those reported by Cheng et al. (12), who demonstrated an association between serum albumin levels and postoperative wound healing outcomes in patients with diabetic foot ulcers. However, unlike that study, the present study did not evaluate direct wound healing endpoints. Therefore, our results should be interpreted as supporting the association between lower serum albumin levels and greater infection severity and treatment intensity during hospitalization, rather than as evidence of impaired wound healing.

In the present study, all patients received enteral nutritional support during hospitalization, and serum albumin levels increased significantly from admission to discharge. Importantly, this does not indicate that enteral nutritional support was applied universally to all patients with diabetic foot infection as standard care; rather, the study cohort was limited to patients who were clinically identified as having inadequate oral intake and requiring enteral feeding. This selected cohort and structured nutritional support may partly explain the significant improvement in discharge albumin levels, together with surgical source control, antibiotic therapy, and resolution of the inflammatory response. This finding supports the importance of early nutritional assessment in diabetic foot patients and the provision of appropriate nutritional support in individuals with inadequate oral intake or at risk of malnutrition. Previous studies have shown that diabetes health literacy is often inadequate among diabetic foot patients and is associated with educational status, which may influence disease management, treatment adherence, and implementation of nutritional recommendations (13).

Furthermore, malnutrition has been reported to be highly prevalent among hospitalized diabetic foot ulcer patients and associated with prolonged hospitalization. In the study by Ran et al. (14), the prevalence of malnutrition was reported as 38.36%, and malnutrition was associated with an

approximately threefold increase in the likelihood of prolonged hospital stay. Additionally, the current literature on nutritional support in diabetic foot ulcers emphasizes that malnutrition is a common and frequently overlooked problem in patients with chronic wounds and that protein, amino acid, and micro-nutrient supplementation may play important biological roles in wound healing processes (15).

Because albumin is a negative acute-phase reactant, the increase in albumin levels observed in our study should not be attributed solely to enteral nutritional support. Improvements in albumin levels may also reflect infection control, resolution of inflammation, antibiotic therapy, and overall clinical recovery following surgical treatment. Therefore, serum albumin may be considered a practical parameter for assessing nutritional and inflammatory status and monitoring the clinical course in patients with diabetic foot disease.

The main limitations of this study include its retrospective design, single-center setting, relatively small sample size, and the inability to assess nutritional status using more detailed clinical nutritional assessment tools. Although patients with known chronic renal failure, end-stage renal disease, severe chronic liver disease, or hepatic failure were excluded, overt proteinuria was not systematically evaluated as a separate variable because of the retrospective design. Therefore, unrecognized or undocumented proteinuria may have acted as a potential residual confounder affecting serum albumin levels. In addition, postoperative wound healing outcomes were not evaluated. Therefore, our findings should be interpreted as reflecting the association between serum albumin levels, infection severity, and short-term clinical course during hospitalization rather than long-term wound healing outcomes or prognosis.

CONCLUSION

Low serum albumin levels were associated with advanced PEDIS Infection Grades in patients with diabetic foot disease. Patients with advanced PEDIS Infection Grades had longer hospital stays, prolonged intravenous antibiotic therapy, and extended durations of enteral nutritional support. The significant increase in serum albumin levels observed during hospitalization may reflect the combined effects of nutritional support, infection control, and clinical recovery, supporting the importance of early nutritional assessment and appropriate nutritional intervention in this patient population. Serum albumin may serve as a practical biochemical parameter for evaluating infection severity and monitoring clinical progress in patients with diabetic foot disease.

Ethical Approval: Ethical approval was obtained from the University of Health Sciences Gülhane Training and Research Hospital Non-Interventional Scientific Research Ethics Committee (Decision No: 2026/95, Date: April 2, 2026).

Informed Consent: Owing to the retrospective design of the study, informed consent was waived by the Ethics Committee.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.M.H., A.Y., S.T.A., E.T.; Design – S.U., M.Kar., N.C., Z.S.B., N.K.; Supervision – M.K., K.B.Y.; Funding – M.M.H., A.Y.; Materials – S.T.A., E.T.; Data Collection

and/or Processing – S.U., N.C.; Analysis and/or Interpretation – Z.S.B., N.K.; Literature Review – M.K., K.B.Y.; Writing – S.T.A., E.T., S.U., M.Kar., N.C., Z.S.B., N.K.; Critical Review – M.M.H., A.Y., M.K., K.B.Y., M.Kar.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

AI Statement: The authors declared that no artificial intelligence (AI) tools were used in the preparation of the manuscript.

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Clinical and Microbiological Characteristics of Diabetes-Related Foot Infections According to the Presence of Osteomyelitis

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ABSTRACT

Objective: This study aimed to compare clinical characteristics, classification scores, microbiological pathogen distribution, and antimicrobial resistance profiles among patients with diabetes-related foot infection according to the presence of osteomyelitis.

Materials and Methods: This retrospective study included adult patients diagnosed with diabetes-related foot infection at a secondary-care hospital between April 15, 2025, and April 15, 2026. Patients were divided into two groups: those with diabetes-related foot infection with concomitant osteomyelitis and those without concomitant osteomyelitis. Demographic data, clinical risk factors, laboratory findings, Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth (SINBAD) and Wound, Ischemia, and foot Infection (WIFI)/International Working Group on the Diabetic Foot (IWGDF) classification parameters, microbiological growth patterns, and antimicrobial resistance profiles were compared between groups.

Results: A total of 95 patients were included; 49 had osteomyelitis, and 46 did not have osteomyelitis. Recurrent foot infection, previous osteomyelitis, previous peripheral vascular intervention, antibiotic use within the previous month, neuropathy, and isolation of resistant microorganisms were significantly more frequent in the osteomyelitis group, whereas C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were significantly higher in this group ($p < 0.05$). Antimicrobial resistance was also more frequent in patients with osteomyelitis (59.2% vs. 34.8%, $p < 0.05$). Among culture-positive patients, polymicrobial growth was more common in the osteomyelitis group than in the non-osteomyelitis group (34.7% vs. 16.1%). *Staphylococcus aureus* was the most frequently isolated pathogen in both groups. Multidrug-resistant (MDR) Gram-negative isolates and methicillin-resistant *S. aureus* (MRSA) were numerically more frequent in the osteomyelitis group; however, these differences did not reach statistical significance.

ORIGINAL ARTICLE

Int Scope Wound Manag.
2026;1(2):79–91

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Received

June 15, 2026

Accepted

August 14, 2026

Published

August 31, 2026

DOI

10.36519/iswm.2026.1229

Suggested Citation

Küpeli H, Hazır Konya H, Alakuş Ü, Öztürk H, Karakol P. Clinical and microbiological characteristics of diabetes-related foot infections according to the presence of osteomyelitis. Int Scope Wound Manag. 2026;1(2):79–91.



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Conclusion: Osteomyelitis in diabetes-related foot infection was associated with recurrent infection, previous osteomyelitis, peripheral vascular intervention, neuropathy, recent antibiotic exposure, elevated inflammatory markers including CRP and ESR, polymicrobial growth, and increased antimicrobial resistance. These findings support individualized, empirically based treatment decisions informed by prior antibiotic exposure, healthcare-related risk factors, and local microbiological resistance patterns.

Keywords: Diabetic foot, osteomyelitis, antimicrobial resistance

INTRODUCTION

With the increasing prevalence of diabetes, diabetic foot ulcers are being encountered more frequently. It has been reported that infection develops in more than half of patients with diabetes-related foot ulcers, and that amputation is required in approximately 20% of moderate to severe cases (1). Diabetic foot infections most commonly arise in the setting of these ulcers and encompass a broad clinical spectrum, ranging from superficial soft tissue infections to deep tissue infections, osteomyelitis, and necrotizing infections. Due to the wide clinical spectrum, accurate patient assessment and determination of infection severity are critical for planning appropriate treatment strategies. Bone involvement during diabetes-related foot infection is a serious complication associated with an increased risk of amputation, prolonged antibiotic therapy, and hospitalization. Current clinical guidelines recommend systematic classification of infection severity to provide a standardized approach to the management of diabetic foot infections (2–4).

Diabetes-related foot infections are often polymicrobial, and the duration of treatment varies depending on patient-specific factors (5). Complications such as osteomyelitis frequently require prolonged and broad-spectrum antibiotic therapy; however, this approach may contribute to the development of antimicrobial resistance. In addition, patient-specific risk factors may influence the diversity of microbiological pathogens, which limits the suitability of a single empirical treatment approach for all cases (6).

Studies evaluating the relationship between the presence of osteomyelitis and clinical findings, classification systems, and microbiological characteristics in combination are limited in the literature. In particular, the literature needs to better characterize the clinical and microbiological features associated with osteomyelitis. Therefore, in this study, clinical characteristics, risk factors, antimicrobial resistance profiles, and Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth (SINBAD) and Wound, Ischemia, and foot Infection (WIFI) classification parameters were compared according to the pres-

ence of osteomyelitis in patients with diabetes-related foot infection.

MATERIALS AND METHODS

Study Design and Patient Selection

This retrospective study included patients who presented to the outpatient clinic or were hospitalized with a diagnosis of diabetes-related foot infection at a secondary-care hospital between April 15, 2025, and April 15, 2026. Patients with clinically diagnosed diabetes and an infected foot lesion from whom at least one microbiological sample was obtained during the evaluation process were included in the study. Patients were divided into two groups according to the presence of concomitant osteomyelitis: those with diabetes-related foot infection with osteomyelitis and those without concomitant osteomyelitis. Thereafter, these groups were referred to as the osteomyelitis and non-osteomyelitis groups, respectively. The groups were compared in terms of demographic characteristics, clinical risk factors, wound classification parameters, laboratory findings, microbiological pathogen distribution, and antimicrobial resistance profiles.

The unit of analysis for demographic, clinical, laboratory, and classification variables was the individual patient.

In cases where the same patient had multiple hospitalizations or infection episodes, each episode was considered an independent infection, provided that clinical recovery had been achieved after the previous infection and at least 30 days had elapsed, or that a new focus of infection had developed. Previous antibiotic exposure was defined as systemic antibiotic use within one month before admission for the current diabetes-related foot infection episode. Demographic and clinical data were obtained from electronic medical records.

The study was approved by the Non-Interventional Clinical Research Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine on June 18, 2026, with decision no. 2026/240.

Inclusion Criteria

1. Age ≥ 18 years.
2. Admission to our hospital with a diagnosis of diabetes-related foot infection between April 15, 2025, and April 15, 2026.
3. Having been diagnosed with a diabetic foot infection according to the International Working Group on the Diabetic Foot (IWGDF) criteria and having had the severity of infection graded.
4. Diagnosis of osteomyelitis established in accordance with IWGDF recommendations based on clinical findings, imaging methods (plain radiography or magnetic resonance imaging), and, when necessary, surgical findings or histopathological evaluation results.
5. Availability of an aspiration, deep tissue, or bone sample obtained from the wound for microbiological examination.
6. Availability of sufficient clinical and laboratory data for analysis in electronic medical records.

Exclusion Criteria

1. Age < 18 years
2. Absence of an aspiration, deep tissue, or bone sample obtained from the wound site
3. Microorganism isolates considered contaminants or not clinically significant
4. Repeated culture samples from the same infection episode
5. Patients with missing or incorrect clinical or laboratory data
6. Patients presenting with infections or foot lesions other than diabetes-related foot infection
7. Individuals experiencing homelessness
8. Patients with immunodeficiency
9. Patients diagnosed with vasculitis

Diagnosis of Osteomyelitis and Wound Classification

In patients with diabetic foot infection, **wound and infection classifications** were used to evaluate the clinical characteristics and severity of the lesion, as recommended by the International Working Group on the Diabetic Foot/Infectious Diseases Society of America (IWGDF/IDSA) guidelines. Osteomyelitis was diagnosed in accordance with the same guidelines through the combined evaluation of clinical, laboratory, and radiological findings (4,7). Scores were calculated based on the clinical assessment at the time of initial admission.

Surgical Sampling Procedure

Microbiological samples were obtained intraoperatively or at the bedside, depending on the patient's clinical status. Under sterile conditions, any necrotic tissue present in the wound area was debrided using appropriate surgical techniques. Following debridement, deep tissue, aspirate, or bone specimens were collected from the clinically infected area using sterile instruments. Superficial swab cultures were excluded from the analysis. The specimens were transported to the microbiology laboratory under sterile conditions for further analysis.

Microbiological Analysis

From the prepared fluid suspension of the specimen, 0.05 mL was inoculated onto 5% sheep blood agar and MacConkey agar plates using a sterile loop under aseptic conditions. The inoculated plates were incubated aerobically at 35°C and examined for microbial growth after 24 hours. If no growth was observed, the plates were re-incubated and reassessed at 48 hours post-inoculation.

Bacterial identification was performed using conventional biochemical methods. Upon detection of microbial growth, isolates were initially evaluated by Gram staining. Gram-negative organisms were identified based on standard biochemical characteristics, including glucose, sucrose, and lactose fermentation; citrate utilization; motility; urease and indole production; ornithine decarboxylase activity; and oxidase reaction. Gram-positive organisms were identified according to catalase activity, hemolytic patterns, coagulase production, susceptibility to optochin, bacitracin, and trimethoprim-sulfamethoxazole, as well as growth on bile esculin agar and in media containing 6.5% sodium chloride. Anaerobic cultures could not be performed.

Microbiological pathogen distribution and antimicrobial resistance profiles were evaluated on an isolate basis. Because more than one microorganism could be isolated from patients with polymicrobial growth, the number of isolates exceeded the number of patients.

Antibiotic Susceptibility Testing

Bacterial identification was performed using conventional biochemical methods. Antimicrobial susceptibility testing was performed and interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Methicillin-resistant *Staphylococcus aureus* (MRSA) was identified using the cefoxitin disk diffusion method in accordance

with EUCAST criteria. Ampicillin-resistant enterococci were identified according to EUCAST breakpoints (8).

Extended-spectrum beta-lactamase (ESBL)-producing isolates were defined, in accordance with EUCAST recommendations, as isolates showing reduced susceptibility to third-generation cephalosporins and, when necessary, confirmed phenotypically. The presence of inducible beta-lactamase (IBL), including AmpC beta-lactamase, was evaluated according to EUCAST expert rules and susceptibility patterns (8).

Multidrug-resistant (MDR) microorganisms were defined as isolates resistant to at least three different antimicrobial classes, in accordance with the criteria recommended by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) (9,10).

Statistical Analysis

The assumption of normal distribution for quantitative variables was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were presented as mean $\pm$ standard deviation for normally distributed quantitative variables, median (25th–75th percentile) for non-normally distributed variables, and frequency (%) for categorical variables. For independent group comparisons, the independent samples t-test was used for normally distributed variables, and the Mann-Whitney U test was used for non-normally distributed variables. Associations between categorical variables were

evaluated using the chi-square test. A p value of < 0.05 was considered statistically significant.

RESULTS

Osteomyelitis was detected in 49 of the 95 patients included in the study, while 46 patients had no evidence of osteomyelitis. Patients were divided into two groups according to the presence of osteomyelitis and analyzed accordingly.

When categorical variables were examined, the rate of recurrent foot infection in the osteomyelitis group (77.6%) was significantly higher than that in the non-osteomyelitis group (52.2%) ($p = 0.009$). The proportion of patients with a previous history of osteomyelitis was significantly higher in the osteomyelitis group (53.1%) than in the non-osteomyelitis group (13.0%) ($p < 0.001$). In addition, the rate of previous peripheral vascular intervention was significantly higher in the osteomyelitis group (69.4%) than in the non-osteomyelitis group (28.3%) ($p < 0.001$). The rate of antibiotic use within the previous month was also significantly higher in the osteomyelitis group (91.8%) than in the non-osteomyelitis group (76.1%) ($p = 0.035$). Detailed data for all variables are presented in Table 1.

The neuropathy rate was significantly higher in the osteomyelitis group (85.7%) than in the non-osteomyelitis group (61.4%) ($p = 0.07$). The rate of antimicrobial resistance was also significantly higher in the osteomyelitis group (59.2%) than in the non-osteomyelitis group (34.8%) ($p = 0.017$). When laboratory

Table 1. Demographic and clinical characteristics of patients with diabetes-related foot infection according to the presence of osteomyelitis.

	Without osteomyelitis	With osteomyelitis	p	Achieved power (1– β)
Age	66.15 $\pm$ 9.90	62.43 $\pm$ 10.87	0.085	-
Sex				
Male	31 (67.4)	37 (75.5)	0.381	-
Female	15 (32.6)	12 (24.5)		
Type of diabetes				
Type 1	1 (2.2)	5 (10.2)	0.205	-
Type 2	45 (97.8)	44 (89.8)		
Smoking				
Absent	36 (78.3)	38 (86.4)	0.315	-
Present	10 (21.7)	6 (13.6)		
Duration of diabetes	20.00 (10.75 – 27.50)	18.00 (12.00 – 25.00)	0.372	-

Table 1. Demographic and clinical characteristics of patients with diabetes-related foot infection according to the presence of osteomyelitis. (*Continued.*)

	Without osteomyelitis	With osteomyelitis	<i>p</i>	Achieved power (1–β)
HbA1c	7.40 (6.25 – 8.35)	7.80 (6.53 – 9.15)	0.295	-
Duration of diabetic foot	35.00 (25.00 – 75.00)	55.00 (30.00 – 90.00)	0.217	-
Comorbidity				
Absent	18 (39.1)	19 (38.8)	0.972	-
Present	28 (60.9)	30 (61.2)		
Previous hospitalization				
Present	27 (58.7)	36 (73.5)	0.128	-
Absent	19 (41.3)	13 (26.5)		
Recurrent foot infection				
Present	24 (52.2)	38 (77.6)	0.009	0.782
Absent	22 (47.8)	11 (22.4)		
Previous osteomyelitis				
Present	6 (13.0)	26 (53.1)	<0.001	0.985
Absent	40 (87.0)	23 (46.9)		
Previous debridement				
Present	10 (21.7)	10 (20.4)	0.874	-
Absent	36 (78.3)	39 (79.6)		
Previous amputation				
Present	6 (13.0)	10 (20.4)	0.338	-
Absent	40 (87.0)	39 (79.6)		
Previous peripheral vascular intervention				
Present	13 (28.3)	34 (69.4)	<0.001	0.980
Absent	33 (71.7)	15 (30.6)		
Renal failure				
Present	8 (17.4)	13 (26.5)	0.283	-
Absent	38 (82.6)	36 (73.5)		
Dialysis				
Present	2 (4.3)	4 (8.2)	0.678	-
Absent	44 (95.7)	45 (91.8)		
Antibiotic use within the previous month				
Present	35 (76.1)	45 (91.8)	0.035	0.578
Absent	11 (23.9)	4 (8.2)		

Descriptive statistics are presented as median (25th–75th percentile) or frequency (%). The Mann-Whitney U test was used for quantitative variables, the independent samples t-test was used for the age variable, and the chi-square/Fisher's exact test was used for categorical variables. **HbA1c:** Glycated hemoglobin.

findings were evaluated, both C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were significantly higher in the osteomyelitis group than in the non-osteomyelitis group ($p = 0.007$ and $p = 0.003$, respectively). Detailed data are presented in Table 2.

Patients with positive cultures were additionally analyzed by dividing them into two groups according to antimicrobial resistance status. The mean age was significantly lower in the group with antimicrobial resistance (60.76 ± 10.23) than in the group without antimicrobial resistance (67.36 ± 9.87) ($p = 0.002$).

When categorical variables were evaluated, the rate of a previous history of osteomyelitis was significantly higher in the group with antimicrobial resistance (44.4%) than in the group without antimicrobial resistance (24.0%) ($p = 0.035$). No statistically significant differences were found between the

groups with respect to other clinical characteristics ($p > 0.05$). Detailed data are presented in Table 3.

As shown in Table 4, the infection classification score was significantly higher in the group with antimicrobial resistance than in the group without antimicrobial resistance ($p = 0.003$). When laboratory findings were evaluated, CRP levels were significantly higher ($p = 0.018$), whereas hemoglobin (Hb) levels were significantly lower in the group with antimicrobial resistance ($p = 0.028$).

In the microbiological evaluation, microbial growth was detected in all patients in the osteomyelitis group, whereas no growth was observed in 15 of the 46 patients in the non-osteomyelitis group. Among patients with positive cultures, polymicrobial growth was more frequent in the osteomyelitis group (34.7%) than in the non-osteomyelitis group (16.1%).

Table 2. Wound classification, laboratory findings, and resistance status according to the presence of osteomyelitis.

	Without osteomyelitis	With osteomyelitis	<i>p</i>	Achieved power (1- β)
Wound classification (according to IWGDF)	2.00 (2.00 – 3.00)	3.00 (2.00 – 3.00)	0.255	-
Presence of ischemia				
Present	26 (60.5)	36 (76.6)	0.099	-
Absent	17 (39.5)	11 (23.4)		
SINBAD score	4.00 (3.00 – 5.00)	4.00 (4.00 – 5.00)	0.096	-
Infection classification (according to IWGDF)	3.00 (3.00 – 3.50)	3.00 (3.00 – 4.00)	0.028	0.607
Neuropathy				
Present	27 (61.4)	42 (85.7)	0.007	0.764
Absent	17 (38.6)	7 (14.3)		
Resistance status				
Absent	30 (65.2)	20 (40.8)	0.017	0.663
Present	16 (34.8)	29 (59.2)		
Leukocyte count	9.65 (7.98 – 12.80)	11.30 (8.45 – 13.30)	0.282	-
CRP	61.00 (20.50 – 118.75)	120.00 (55.25 – 198.75)	0.007	0.793
Hb	10.91 $\pm$ 1.95	10.28 $\pm$ 1.56	0.083	-
ESR	63.0 (42.3–92.0)	92.0 (73.0–110.0)	0.003	0.890

Descriptive statistics are presented as mean $\pm$ standard deviation, median (25th–75th percentile), or frequency (%). The independent samples t-test was used for normally distributed quantitative variables, the Mann-Whitney U test was used for non-normally distributed quantitative variables, and the chi-square test was used for categorical variables.

IWGDF: International Working Group on the Diabetic Foot, **SINBAD:** Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth, **CRP:** C-reactive protein, **ESR:** Erythrocyte sedimentation rate, **Hb:** Hemoglobin.

Table 3. Demographic and clinical characteristics according to antimicrobial resistance status.

	No resistance	Resistance present	<i>p</i>	Achieved power (1- β)
Age	67.36 $\pm$ 9.87	60.76 $\pm$ 10.23	0.002	0.936
Sex			0.204	-
Male	33 (66.0)	35 (77.8)		
Female	17 (34.0)	10 (22.2)		
Type of diabetes			0.418	-
Type 1	2 (4.0)	4 (8.9)		
Type 2	48 (96.0)	41 (91.1)		
Smoking				
Absent	41 (83.7)	33 (80.5)	0.694	-
Present	8 (16.3)	8 (19.5)		
Duration of diabetes	20.00 (13.50 – 30.00)	15.00 (10.00 – 25.00)	0.090	-
HbA1c	7.90 (6.80 – 8.70)	7.30 (6.10 – 8.70)	0.277	-
Duration of diabetic foot	30.00 (25.00 – 60.00)	60.00 (30.00 – 100.00)	0.054	-
Comorbidity				
Absent	16 (32.0)	21 (46.7)	0.143	-
Present	34 (68.0)	24 (53.3)		
Previous hospitalization				
Present	33 (66.0)	30 (66.7)	0.945	-
Absent	17 (34.0)	15 (33.3)		
Recurrent foot infection				
Present	33 (66.0)	29 (64.4)	0.874	-
Absent	17 (34.0)	16 (35.6)		
Previous osteomyelitis				
Present	12 (24.0)	20 (44.4)	0.035	0.558
Absent	38 (76.0)	25 (55.6)		
Previous debridement				
Present	8 (16.0)	12 (26.7)	0.203	-
Absent	42 (84.0)	33 (73.3)		
Previous amputation				
Present	5 (10.0)	11 (24.4)	0.060	-
Absent	45 (90.0)	34 (75.6)		
Previous peripheral vascular intervention				
Present	20 (40.0)	27 (60.0)	0.052	-
Absent	30 (60.0)	18 (40.0)		

Table 3. Demographic and clinical characteristics according to antimicrobial resistance status. (*Continued.*)

	No resistance	Resistance present	<i>p</i>	Achieved power (1–β)
Renal failure				
Present	10 (20.0)	11 (24.4)	0.602	-
Absent	40 (80.0)	34 (75.6)		
Dialysis				
Present	2 (4.0)	4 (8.9)	0.418	-
Absent	48 (96.0)	41 (91.1)		
Antibiotic use within the previous month				
Present	41 (82.0)	39 (86.7)	0.533	-
Absent	9 (18.0)	6 (13.3)		

Descriptive statistics were presented as median (25th–75th percentile) or frequency (%). The Mann-Whitney U test was used for quantitative variables, and the chi-square test or Fisher's exact test was used for categorical variables.

HbA1c: Glycated hemoglobin.

Table 4. Wound classification and laboratory findings according to antimicrobial resistance status.

	No resistance	Resistance present	<i>p</i>	Achieved power (1– β)
Wound classification (according to the IWGDF)	2.50 (2.00 – 3.00)	2.00 (2.00 – 3.00)	0.952	-
Presence of ischemia				
Present	31 (66.0)	31 (72.1)	0.775	-
Absent	16 (34.0)	12 (27.9)		
SINBAD score	4.00 (3.00 – 5.00)	4.00 (4.00 – 6.00)	0.063	-
Infection classification (according to IWGDF)	3.00 (3.00 – 3.00)	3.00 (3.00 – 4.00)	0.003	0.855
Neuropathy				
Present	36 (73.5)	33 (75.0)	0.983	-
Absent	13 (26.5)	11 (25.0)		
Leukocyte level	9.65 (8.08 – 12.60)	11.30 (8.15 – 14.55)	0.323	-
CRP	63.00 (20.50 – 144.50)	104.00 (56.50 – 214.75)	0.018	0.664
Hb	10.96 $\pm$ 1.91	10.15 $\pm$ 1.52	0.028	0.613
ESR	80.5 (44.0–97.0)	86.0 (60.0–108.0)	0.303	-

Descriptive statistics were presented as mean $\pm$ standard deviation, median (25th–75th percentile), or frequency (%). For quantitative variables with a normal distribution, the independent samples t-test was used; for quantitative variables without a normal distribution, the Mann-Whitney U test was used; and for categorical variables, the chi-square test was used.

IWGDF: International Working Group on the Diabetic Foot, **SINBAD:** Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth, **CRP:** C-reactive protein, **ESR:** Erythrocyte sedimentation rate, **Hb:** Hemoglobin.

The isolate-based microorganism distribution and antimicrobial resistance rates according to the presence of osteomyelitis are presented in Table 5. In the isolate-based evaluation, Gram-negative bacteria accounted for 56.8% of isolates and Gram-positive bacteria for 43.2% in the non-osteomyelitis group. The most frequently isolated pathogens in this group were *S. aureus* (18.9%), *Klebsiella pneumoniae* (13.5%), and *Pseudomonas aeruginosa* (13.5%). In the osteomyelitis group, Gram-negative bacteria accounted for 56.7% of isolates and Gram-positive bacteria for 43.3%. The most frequently isolated pathogens in this group were *S. aureus* (22.4%), *Escherichia coli* (11.9%), and *P. aeruginosa* (10.4%). No statistically significant difference was found between the groups in terms of the overall distribution of Gram-positive and Gram-negative bacteria. Among the individual microorganisms, only *Acinetobacter* spp. was significantly more frequent in the non-osteomyelitis group than in the osteomyelitis group ($p = 0.043$). No statistically significant differences were detected between the groups for the other microorganisms or antimicrobial resistance patterns.

When resistance profiles were evaluated, the MDR rate among Gram-negative isolates was 33.3% in the non-osteomyelitis group and 44.7% in the osteomyelitis group. Extended-spectrum beta-lactamase production was observed only in the non-osteomyelitis group (9.5%), whereas IBL production was detected only in the osteomyelitis group (5.3%). Among Gram-positive pathogens, the MRSA rate among *S. aureus* isolates was numerically higher in the osteomyelitis group than in the non-osteomyelitis group (66.7% vs. 42.9%). Similarly, methicillin resistance among coagulase-negative staphylococcal isolates was numerically higher in the osteomyelitis group than in the non-osteomyelitis group (75.0% vs. 50.0%). Among *Enterococcus* spp. isolates, ampicillin resistance was detected only in the non-osteomyelitis group (25.0%). However, these differences in antimicrobial resistance patterns were not statistically significant.

DISCUSSION

In this study, the relationship between the presence of osteomyelitis and clinical characteristics, as well as microbiological resistance profiles, and clinical classification scores was evaluated in patients with diabetes-related foot infections. Our findings showed that osteomyelitis was associated with recurrent foot infection, a history of previous osteomyelitis, previous peripheral vascular intervention, neuropathy, and antibiotic use within the previous month.

In our study, a history of peripheral vascular intervention was more frequent in the osteomyelitis group. In diabetes-related foot infection with osteomyelitis, inadequate local circulation

due to peripheral vascular disorders may hinder the achievement of sufficient antibiotic concentrations at the site of infection, thereby making the control of infection more difficult (11). This condition may contribute to the chronicity of infection and predispose patients to the development of osteomyelitis through recurrent infections. In addition, neuropathy was more frequent in the osteomyelitis group. Diabetic neuropathy facilitates the development of recurrent trauma and ulceration by causing the loss of protective sensation, and this process predisposes patients to the development of osteomyelitis through the spread of infection to deeper tissues (12). This finding suggests that neuropathy may play an important role not only in the development of ulcers but also in the progression of infection to bone involvement.

The literature indicates that inflammatory markers such as CRP have limited sensitivity and specificity for the diagnosis of osteomyelitis and that these markers are more useful in distinguishing infectious from non-infectious foot pathologies (13). In our study, both CRP and ESR levels were significantly higher in patients with osteomyelitis than in those without osteomyelitis. This finding suggests that patients with bone involvement had a greater systemic inflammatory burden. In the literature, ESR has been reported to be more closely associated with diabetic foot osteomyelitis than CRP (14). However, inflammatory markers alone are insufficient to establish the diagnosis of osteomyelitis, and current recommendations emphasize their interpretation alongside clinical findings, probe-to-bone test results, imaging, and microbiological or histopathological evidence, when available (4). Therefore, the elevated ESR and CRP levels observed in our study should be interpreted as supportive group-level findings rather than independent diagnostic markers for osteomyelitis.

In the microbiological evaluation, polymicrobial growth was more frequent in the osteomyelitis group than in the non-osteomyelitis group. This finding is consistent with studies reporting that infection in diabetes-related foot infections with concomitant osteomyelitis may be associated with complex microbial communities rather than a single pathogen. A study in which bone samples from cases of diabetes-related foot infection with osteomyelitis were examined using molecular and microscopic methods demonstrated that polymicrobial communities and biofilm structures can frequently be observed in these cases. Therefore, the more frequent detection of polymicrobial growth in the osteomyelitis group in our study may reflect the deeper, more chronic, and more complicated nature of bone infection (15).

The finding that *S. aureus* was the most frequently isolated pathogen in both groups is consistent with the literature

Table 5. Isolate-based microbiological pathogen distribution and antimicrobial resistance profiles according to the presence of osteomyelitis.

	With osteomyelitis n/N(%)	Without osteomyelitis n/N(%)	Total n/N (%)	<i>P</i>
Gram-positive	29/67 (43.3)	16/37 (43.2)	45/104 (43.3)	0.997
<i>Staphylococcus aureus</i>	15/67 (22.4)	7/37 (18.9)	22/104 (21.2)	0.678
Methicillin-sensitive	5/15 (33.3)	4/7 (57.1)	9/22 (40.9)	0.376
Methicillin-resistant	10/15 (66.7)	3/7 (42.9)	13/22 (59.1)	0.376
Coagulase-negative staphylococcus	4/67 (6.0)	4/37 (10.8)	8/104 (7.7)	0.451
Methicillin-sensitive	1/4 (25.0)	2/4 (50.0)	3/8 (37.5)	1.000
Methicillin-resistant	3/4 (75.0)	2/4 (50.0)	5/8 (62.5)	1.000
<i>Enterococcus</i> spp.	6/67 (9.0)	4/37 (10.8)	10/104 (9.6)	0.741
Ampicillin-resistant	0/6 (0.0)	1/4 (25.0)	1/10 (10.0)	0.400
<i>Streptococcus</i> spp.	4/67 (6.0)	1/37 (2.7)	5/104 (4.8)	0.653
Gram-positive resistant bacteria	13/67 (19.4)	6/37 (16.2)	19/104 (18.3)	0.687
Gram-negative	38/67 (56.7)	21/37 (56.8)	59/104 (56.7)	0.997
<i>Klebsiella</i> spp.	9/67 (13.4)	5/37 (13.5)	14/104 (13.5)	1.000
<i>Klebsiella pneumoniae</i>	4/67 (6.0)	5/37 (13.5)	9/104 (8.7)	0.275
<i>Klebsiella oxytoca</i>	4/67 (6.0)	0/37 (0.0)	4/104 (3.8)	0.294
<i>Klebsiella</i> spp.	1/67 (1.5)	0/37 (0.0)	1/104 (1.0)	1.000
<i>Pseudomonas aeruginosa</i>	7/67 (10.4)	5/37 (13.5)	12/104 (11.5)	0.751
<i>Proteus</i> spp.	5/67 (7.5)	4/37 (10.8)	9/104 (8.7)	0.718
<i>Proteus mirabilis</i>	1/67 (1.5)	4/37 (10.8)	5/104 (4.8)	0.053
<i>Proteus vulgaris</i>	4/67 (6.0)	0/37 (0.0)	4/104 (3.8)	0.294
<i>Escherichia coli</i>	8/67 (11.9)	1/37 (2.7)	9/104 (8.7)	0.153
<i>Enterobacter</i> spp.	2/67 (3.0)	0/37 (0.0)	2/104 (1.9)	0.537
<i>Citrobacter</i> spp.	1/67 (1.5)	1/37 (2.7)	2/104 (1.9)	1.000
<i>Serratia marcescens</i>	2/67 (3.0)	1/37 (2.7)	3/104 (2.9)	1.000
<i>Morganella morganii</i>	4/67 (6.0)	1/37 (2.7)	5/104 (4.8)	0.653
<i>Stenotrophomonas maltophilia</i>	0/67 (0.0)	0/37 (0.0)	0/104 (0.0)	-
<i>Acinetobacter</i> spp.	0/67 (0.0)	3/37 (8.1)	3/104 (2.9)	0.043
Gram-negative MDR bacteria	17/38 (44.7)	7/21 (33.3)	24/59 (40.7)	0.393
ESBL-producing Gram-negative bacteria	0/38 (0.0)	2/21 (9.5)	2/59 (3.4)	0.123
IBL-producing Gram-negative bacteria	2/38 (5.3)	0/21 (0.0)	2/59 (3.4)	0.534
Total MDR bacteria	32/67 (47.8)	15/37 (40.5)	47/104 (45.2)	0.479

MDR: Multidrug-resistant, ESBL: Extended-spectrum beta-lactamase, IBL: Inducible beta-lactamase, MRSA: Methicillin-resistant *Staphylococcus aureus*.

reporting this microorganism as one of the principal pathogens in diabetes-related foot infections and with recent multicenter data on diabetic foot osteomyelitis (16). While the MRSA rate among *S. aureus* isolates was reported as 20.8% in that study, the higher MRSA rate observed in the osteomyelitis group in our study may be related to center-specific resistance characteristics and antibiotic use within the previous month. One study reported that, in addition to *S. aureus* being frequently isolated in diabetic foot infections, it can persist in the chronic wound environment and may undergo genomic changes over time (17). This finding supports the view that, particularly in chronic and complicated cases, *S. aureus* is not only a common pathogen but also an important microorganism in terms of patient follow-up and treatment.

One of the notable findings of this study was that both antimicrobial resistance and antibiotic use within the previous month were significantly higher in the osteomyelitis group. The literature indicates that previous antibiotic use and the presence of osteomyelitis may be associated with multidrug-resistant microorganisms; in addition, discordance between soft tissue and bone cultures in diabetes-related foot infections with concomitant osteomyelitis has been reported to contribute to the development of resistance by increasing the use of broad-spectrum antibiotics (18,19). In a prospective multicenter study conducted in Türkiye, resistant bacterial growth was detected in 43% of diabetes-related foot infection cases; antibiotic use within the previous 30 days was identified as an independent risk factor for resistant bacterial growth, and resistant bacterial growth was found to be associated with treatment failure and increased antibiotic costs (20). Similarly, another study from Türkiye reported an MDR rate of 47.9% in diabetes-related foot infection and demonstrated that MDR growth was associated with polymicrobial growth and a history of hospitalization (21). Recent cohort data have also emphasized that antimicrobial-resistant pathogens complicate the management of diabetes-related foot infection and may be associated with poor clinical outcomes (22). These findings support the possibility that the high resistance rates observed in the osteomyelitis group in our study may be related to previous antibiotic exposure, the polymicrobial nature of the infection, and complicated clinical characteristics. Although the higher rate of resistant microorganism isolation in the younger age group was a notable finding in our study, this observation does not fully align with the classical risk factors described in the literature. A meta-analysis found no significant association between age and multidrug-resistant organism (MDRO) infection; however, previous hospitalization, antibiotic use, osteomyelitis, ulcer size, vascular disease, and a history of surgical intervention were identified as more consistent risk factors (23). Therefore, the high resis-

tance rates observed in younger patients and the elevated prevalence of MDROs in our study are consistent with the literature when considered in the context of recent antibiotic use and healthcare exposure rather than as a direct effect of age.

Although bone biopsy (histology and culture) is considered the gold standard for the diagnosis of osteomyelitis, the diagnostic process generally begins with clinical evaluation. Accurate identification of the causative microorganism is critical for treatment. However, studies evaluating the diagnostic value of clinical and laboratory findings remain limited (24).

In the evaluation of clinical classification systems, no significant association was found between osteomyelitis and either the SINBAD score or the IWGDF wound classification. Although the literature has shown that the SINBAD score is associated with adverse clinical outcomes such as amputation, hospitalization, and secondary infection, its role in predicting deep infections such as osteomyelitis remains unclear (25). In contrast, the WIfI classification was developed primarily to predict limb prognosis because it simultaneously evaluates wound, ischemia, and infection components, and therefore has the potential to reflect outcomes related to the depth of infection (4). However, studies directly evaluating the performance of these classification systems in predicting the presence of osteomyelitis remain limited in the current literature.

Our study has several limitations. First, anaerobic cultures could not be performed. Therefore, we were unable to determine the role of anaerobic microorganisms in diabetes-related foot infections. In addition, the limited number of patients and the small number of isolates in some subgroups made the interpretation of subgroup analyses, particularly those involving MRSA, ESBL, AmpC/IBL, and enterococcal resistance, more challenging. Because the microbiological analyses presented in Table 5 were performed on an isolate basis, multiple isolates obtained from the same patient or infection episode could be included in the analysis. Therefore, these observations may not have been statistically independent, and within-patient or within-episode clustering may have affected the variance estimates and p values. Accordingly, the statistical comparisons presented in Table 5 should be interpreted with caution. Another limitation is that comorbidities were evaluated as an overall variable rather than being analyzed separately according to individual conditions or secondary infection foci.

Nevertheless, our study also has several strengths. These include the comparison of diabetes-related foot infections with and without osteomyelitis not only in terms of clinical

characteristics but also with respect to microbiological pathogen distribution, antimicrobial resistance profiles, laboratory findings, and classification systems. Furthermore, the separate analysis of patients according to the presence of resistant microorganism growth contributed to the identification of clinical characteristics associated with antimicrobial resistance. The use of real-world data and the reflection of secondary care hospital practice enhance the relevance of our findings for everyday clinical practice.

In conclusion, in patients with diabetes-related foot infection, concomitant osteomyelitis was associated with recurrent foot

infection, a history of previous osteomyelitis, previous peripheral vascular intervention, neuropathy, antibiotic use within the previous month, elevated CRP and ESR levels, and resistant microorganism growth. Microbiologically, *S. aureus* was the most frequently isolated pathogen, while polymicrobial growth, the rate of Gram-negative MDR organisms, and the MRSA rate appeared to be higher in the osteomyelitis group. These findings support the need for individualized empirical treatment decisions in diabetes-related foot infections with concomitant osteomyelitis, taking into account the patient's previous antibiotic use, healthcare exposure, risk of antimicrobial resistance, and local microbiological data.

Ethical Approval: The study was approved by the Non-Interventional Clinical Research Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine on June 18, 2026, with decision no. 2026/240.

Informed Consent: N/A

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.K., P.C., H.H.K.; Design – H.K., P.C., H.H.K.; Supervision – H.K., Ü.A., H.H.K.; Funding – H.K., Ü.A., H.Ö.; Materials – H.K., Ü.A.; Data Collection and/or Processing – H.K., Ü.A., H.H.K.; Analysis and/or Interpretation – H.K., H.Ö.; Literature Review – H.K., H.Ö., H.H.K.; Writing – H.K.; Critical Review – H.K., P.C.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Scientific Presentation: This manuscript has not been previously presented at any scientific meeting and has not been published elsewhere.

AI Statement: Artificial intelligence (AI)-enabled technologies (such as large language models [LLMs], chatbots, or image creators) were not used in the production of this work.

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Wound Care for People Experiencing Homelessness: A Call for Accessible and Integrated Care

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DEAR EDITOR,

Homelessness is not merely the absence of housing; it is a multidimensional social determinant that directly affects access to healthcare, adherence to treatment, and continuity of care. People experiencing homelessness are at increased risk of foot and lower-extremity problems because of limited access to hygiene facilities, appropriate footwear, and dressing supplies, exposure to trauma, chronic disease, and structural barriers within healthcare systems. Ulcers, infections, and other foot problems are common in this population, while delayed presentation may lead to preventable complications and hospital admissions (1,2).

A major dimension of the problem is that healthcare systems are often designed around assumptions of a fixed address, scheduled appointments, referral pathways, and regular follow-up. People experiencing homelessness are underrepresented in primary care and may rely disproportionately on emergency departments for healthcare (3,4). Wound care therefore cannot be approached solely as a clinical intervention; comprehensive models are needed that address housing, transportation, communication, trust, health literacy, and continuity of care within the same framework. Recent evidence, particularly among people experiencing homelessness with diabetes, suggests that fragmented services create substantial gaps in care and supports the need for integrated models (5). In light of these challenges, I propose the following measures to improve wound-care access and continuity for people experiencing homelessness:

Institutional Organization and Service Delivery Models

1. Dedicated Access and Wound Care Centers: Dedicated low-threshold centers should provide timely wound assessment and treatment and may reduce avoidable emergency-department use.

LETTER TO THE EDITOR

Int Scope Wound Manag.
2026;1(2):92–4

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Received

August 25, 2026

Accepted

August 27, 2026

Published

August 31, 2026

DOI

10.36519/iswm.2026.1332

Suggested Citation

Çapkın M. Wound care for people experiencing homelessness: a call for accessible and integrated care. Int Scope Wound Manag. 2026;1(2):92–4.



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2. Interinstitutional Communication Networks: Public and private health services and social-care providers should be linked through effective communication pathways to support coordinated care.

3. Walk-in and Mobile Health Services: Walk-in access and multidisciplinary mobile teams should deliver screening and early treatment where high-risk groups are concentrated, helping to prevent complications and prolonged admissions.

Healthcare Staff Training and Communication

1. Anti-Stigma and Trauma-Informed Care: Health professionals should receive training in trauma-informed, stigma-sensitive care, as discrimination and previous negative experiences may delay presentation.

2. Welcoming Physical Environments: Calm, safe, welcoming settings offering basic refreshments and practical support may encourage attendance and help rebuild trust.

Education and Health Literacy

Health literacy should be improved through targeted education so that people will be better at identifying early signs of wound problems, looking after themselves, and seeking help in a timely manner.

Transportation, Technology, and Stakeholder Collaboration

1. Transportation and Communication Support: Free or subsidized transportation and practical communication support should be considered; carefully designed mobile applications may help connect vulnerable individuals with services.

2. Third-Sector/Non-governmental Organization (NGO) Collaboration: Partnerships with trusted non-governmental and

third-sector organizations can improve access, continuity, and trust.

3. Co-Production: People with lived experience of homelessness should participate in service design and research so that care pathways reflect real-world needs.

Clinical Processes, Follow-up, and Standardization

1. Integrated Follow-up Systems: Shared digital systems could coordinate care before admission, during hospitalization, and after discharge across health and social-care partners.

2. Evidence-Based Wound Care Programs and Guidelines: Evidence-based, patient-centered wound care programs should include education and be supported by national or local clinical guidance.

3. Integration of Safe Accommodation: Safe accommodation during and after treatment should be incorporated into care planning when needed to support healing.

4. Continuous Monitoring and Preventive Measures: Care pathways should include ongoing follow-up, preventive interventions, and timely referral to specialist services.

Successful wound care for people experiencing homelessness depends not only on selecting the appropriate dressing or surgical treatment, but also on whether patients can access care and remain engaged in care. Community-based wound care algorithms, early identification of at-risk individuals, preventive foot and wound care, and the integration of health and social services should therefore become explicit priorities. Wound care for people experiencing homelessness is an important test not only of a healthcare system's clinical capacity, but also of its commitment to accessibility and health equity.

Ethical Approval: Not applicable.

Informed Consent: Not applicable.

Peer-review: Not applicable.

Author Contributions: Concept – M.Ç.; Design – M.Ç.; Supervision – M.Ç.; Funding – M.Ç.; Materials – M.Ç.; Data Collection and/or Processing – M.Ç.; Analysis and/or Interpretation – M.Ç.; Literature Review – M.Ç.; Writing – M.Ç.; Critical Review – M.Ç.

Conflict of Interest: The author declared no conflict of interest.

Financial Disclosure: The author declared that this study has received no financial support.

AI Statement: The author declared that no artificial intelligence (AI) or AI-assisted technologies were used in the preparation, writing, or analysis of this manuscript.

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