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PATHOGENIC BACTERIA IN DIABETIC FOOT ULCERS: MICROBIAL DIVERSITY, RESISTANCE PATTERNS, THERAPEUTIC CHALLENGES, AND PATH TO SUSTAINABLE DEVELOPMENT GOALS

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ABSTRACT

Diabetic foot ulcers (DFUs) are chronic, complex wounds that pose a significant global health care burden, particularly for individuals with poor control of their glycemic index. The current study sheds light on the prevalence of polymicrobial infections that are mostly brought on by drug-resistant bacterial strains by investigating the microbial diversity within DFUs. Additionally, we highlight the resistance mechanisms that hinder curative outcomes and lead to therapeutic failure. The current review highlights the need for localized surveillance and antimicrobial management while also examining regional variations in resistance patterns. Emerging therapeutic approaches such as bacteriophage therapy, antimicrobial peptides, biofilm-disrupting elements, and AI-guided approaches offer beneficial substitutes for conventional antibiotics. The management of DFU is changing due to molecular diagnostic techniques like metagenomics and 16S rRNA sequencing, which may make pathogen-specific treatment strategies possible. The current review placed these innovations within the framework of the United Nations' Sustainable Development Goals, urging responsible antibiotic use, fair and impartial healthcare, developments in technology. Overall, this analysis highlighted the need to integrate new clinical techniques with microbiological insights to enhance the consequences of DFUs and contribute significantly to global health protocols.

Keywords: Diabetic foot ulcers, DFUs, MDR, Biofilm, Antimicrobial resistance, ESBL-producing pathogens, Sustainable Development Goals, SDGs.

1 INTRODUCTION

Diabetic foot ulcers (DFUs) are a serious and progressive complication of diabetes mellitus that imposes a significant global health burden. Worldwide, approximately 537 million people have diabetes mellitus, primarily type 2 diabetes [1, 2], and between 19% and 34% will develop DFUs during their lifetime, with nearly 20% requiring lower-extremity amputations, either minor (below ankle), major (above ankle), or both [3]. Additionally, 10% will die within one year

of their initial diagnosis with diabetic foot ulcers [4, 5]. These ulcers are characterized by skin breakdown and deep tissue injury, which are significant causes of hospitalization, lower-extremity amputation, and increased mortality rates among diabetic patients [3, 6]. Diabetic foot ulcers are typically caused by a combination of peripheral neuropathy, which results in loss of protective sensibility; ischemia, which is caused by peripheral arterial disease, which impairs tissue perfusion; and repetitive trauma, or foot deformity or improperly sized footwear [7, 8]. Poor glycemic control exacerbates the situation by impairing immune function and increasing oxidative stress, thereby slowing wound healing [9, 10]. DFUs are related to increased morbidity rates, including infections, hospitalization, and lower-extremity amputation, and responsible for high mortality rates that reached 70% in severe cases [11]. The burden is especially augmented in low-resource settings, where early intervention and multidisciplinary care are limited [12].

In fact, the microbial landscape of DFUs is complex and frequently polymicrobial, containing both aerobic and anaerobic microorganisms. The most common pathogens include *Staphylococcus aureus* (*S. aureus*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Escherichia coli* (*E. coli*), and *Enterococcus* species, each with their own virulence mechanisms such as toxins, immune evasion, and biofilm production [13]. Biofilms are a serious issue because they form a protective matrix that shields bacteria from antibiotics and host immune responses, resulting in persistent infection and delayed wound healing [14]. The dynamic interplay between host immunity and microbial virulence is a key factor in the chronicity and severity of diabetic ulcers [15]. Antimicrobial resistance has emerged as a significant challenge in the management of DFU. MDR pathogens, such as methicillin-resistant *S. aureus* and extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacilli, are the most common pathogens in chronic wounds [16]. The well-known resistance mechanisms include plasmid-mediated gene transfer and efflux pumps, which help these pathogens persist and spread [17]. Indeed, biofilm formation complicates therapeutic approaches by decreasing antibiotic penetration and efficacy [18]. Despite advances in wound care and antimicrobial agents, DFU therapy remains challenging. Traditional approaches include debridement, offloading, infection management, and, if necessary, revascularization procedures [19]. However, therapeutic outcomes are typically suboptimal, especially in the presence of resistant pathogens or low patient commitment [20]. Emerging therapeutic approaches, such as topical oxygen delivery and autologous platelet-rich patches (Leuco-Patch), along with antimicrobial peptides, provides promising alternatives [21]. The current review aims to highlight the microbial profile of DFUs, reveal the roles of bacterial virulence agents and biofilm formation in infection persistence, assess antimicrobial resistance patterns, evaluate current treatment limitations, and shed light on emerging therapeutic approaches and integrated management strategies to improve clinical outcomes.

2 MICROBIAL DIVERSITY OF DIABETIC FOOT ULCERS

Unlike other infections DFUs have a viral range of microorganisms including both aerobic and anaerobic bacteria from initial colonization to established infections [22]. Most studies demonstrated that among Gram-positive bacteria *S. aureus* consider the most bacteria that caused DFUs [23-25]. In contrast to theses finding, other studies by Palomo *et al.* in Brazil have revealed that most of DFU Infections caused by gram negative bacilli with 88% while 68% of infection caused by Gram-positive cocci [26]. other recent studies showed almost the same result finding out that most of DFU infection caused by Gram-negative bacteria [27-28]. The microbial diversity is belonged to many several factors such as the variation in bacteria that caused the infection, in addition to the severity and type of infection [29]. This microbial diversity, coupled with the compromised host immunity in diabetic patients, creates a challenging battleground where pathogens can thrive, evade host defenses, and resist antimicrobial interventions.

2.1 Gram-Positive Bacteria

Firmicutes is a major phylum of bacteria, which comprises several *Streptococcus* species (*S. agalactiae*, *S. pyogens*, and *S. mitis*), *Staphylococcus* species (*S. aureus*), and *Enterococcus* species (*E. faecalis*) [23, 30]. *S. aureus*, including its methicillin-resistant strains (MRSA), is still one of the most frequent pathogens isolated from DFU specimens in different geographical regions [31, 32]. Several studies have reported that *S. aureus* is the most prevalent pathogen in DFUs; an investigation included 342 patients with DFUs, and *S. aureus* was the most common Gram-positive bacteria isolated from these diabetic ulcers at a rate of 20.2% of isolates [33].

These findings are relatively alike to the numbers that were recorded in the study of Al Benwan *et al.* [34] and the study of Jneid *et al.* [35], which used different methods (culture and culturomic techniques, respectively) for isolating the microorganisms. The pathogenicity of *S. aureus* belongs to an expansive arsenal of virulence factors, which includes adhesins (fibronectin-binding proteins), toxins (Panton-Valentine leukocidin and alpha-hemolysin), and enzymes that enable tissue invasion and immune evasion [36]. As well, *S. aureus* is a prolific biofilm former, which outstandingly contributes to its perseverance, resistance to antibiotics, and the chronic nature of DFUs [37]. In particular, the presence of MRSA constitutes a substantial clinical challenge due to limited therapeutic options and expanded rates of treatment defeat [24, 38]. In addition to *S. aureus*, *S. epidermidis* was also reported as a dominant bacterial species in DFU specimens, although *S. epidermidis* is normally found in skin but could lead to intense infections if foreign bodies like prosthetic devices and wound infections are present [39, 40].

2.2 Gram-Negative Bacteria

Prevalence of Enterobacteriaceae members (*E. coli*, *K. pneumoniae*, *Morganella morganii* (*M. morganii*), and *Proteus mirabilis* (*P. mirabilis*)) had been documented as a main group of aerobic Gram-negative bacteria in DFUs; As Benwan et al. [34] reported that the average of bacterial pathogens was 1.8 per diabetic wound specimen, 51.2% of these pathogens were Gram-negative, which was very high versus the percent (26.4%) that reported in study of Jneid et al. [35]. This difference may be as a result of prior antibiotic usage by patients, long hospitalization period, and wounds chronicity. As well, *E. coli* was documented as the most frequent Gram-negative pathogen in 342 diabetic cases have ulcers [33]. Several recent investigations have emphasized rising predominance of Gram-negative bacteria in DFUs, especially in tropical climates, low-resource setting, and chronic or formerly treated wounds. Schechter et al. [28] revealed that gram-negative diabetic foot infections are notably more common in tropical regions, with a global prevalence of 68% versus only 43% in temperate regions.

some studies of Rajha et al. [28], conducted in several countries, such as Lebanon and Iran, have shown that Gram-negative bacteria are the main cause of infection and are more resistant to them than gram negative bacteria. Other studies by Khan et al. [27], also showed the same results, finding that a large percentage of bacteria that caused DFU were Gram-negative, such as bacilli, *E. coli* and *P. aeruginosa*.

Other studies by Ramakant et al. [41], showed the same results, finding a high percentage of Gram-negative bacteria *P. aeruginosa*. Recent researches have increasingly identified *P. aeruginosa* as predominant bacteria in DFUs. Coye et al. [42] demonstrated a pooled prevalence at 8.06% for *P. aeruginosa* in DFUs in United States. Yakout and Abdelwahab [43], also highlighted its clinical consequence, they demonstrated that 93% of *P. Aeruginosa* isolates from DFUs were biofilms formers, and expressed principal virulence genes like *algD*, *pelF*, and *pslD*. The global systematic review and meta-analysis of Garousi et al. [30] further emphasized the clinical importance of *P. aeruginosa*, revealed that *P. aeruginosa* accounted for 16.6% of DFUs worldwide. Moreover, Khan et al. [27] reported that *P. aeruginosa* was among the most frequent isolated bacteria from a cohort of DFUs patients in India, and these isolates often associated with multi drugs resistance and persistent infections. The intrinsic resistance mechanisms and biofilms-formation abilities of this pathogen implicated with delayed wounds healing and poor therapeutic outcomes [44].

2.3 Polymicrobial Infection

Diabetic foot infections are included a mixture of bacteria. Thus, producing of various virulence agents like protease, collagenase, and hemolysin that implicate with infections chronicity [40]. Polymicrobial infections are considered more difficult to treat as compared with infections with simpler bacterial constitution and could evolve a complexed and persist infection [45]. It has been revealed that Polymicrobial infections were occurred in 75% of 440 patients had DFUs [35]. In addition, Citron et al., reported that high percent of (83.8%) of examined cultures were polymicrobial, which including both Gram positive and negative bacteria [41]. In Miyan's investigation included 473 cases, 56.87% of DFUs being polymicrobial with a great dominance for Gram-negative bacteria [46]. However, Sánchez et al. had reported relatively lower occurrence rate for polymicrobial infections at 48.3% [47].

2.4 Unexpected Bacterial Species

Although DFUs are predominantly colonized by common pathogens such as *S. aureus*, *P. aeruginosa*, and members of the Enterobacteriaceae family, various studies had identified uncommon bacterial spp. that may engage to infections severity, especially in chronic or previously treated wounds. These include environmental and opportunistic bacteria like *Ralstonia pickettii*, *Serratia marcescens*, *Finegoldia magna*, and species of *Citrobacter*, *Corynebacterium*, *Bacillus*, and *Micrococcus* [40, 23, 48]. While some of these bacterial spp. Are traditionally deem as skin commensals or low-virulence contaminant, but their isolation from deep tissues and osteomyelitic lesions proposes prospective pathogenic impacts in immunocompromised cases and in polymicrobial biofilms [49]. One of normal flora of urogenital and digestive tracts, buccal cavity and skin) is *Finegoldia magna* (*F. magna*), it is an anaerobic Gram-positive bacterium, it is found that these bacteria found as a dominant anaerobe from DFUs at rate of 37.4% [41]. *Ralstonia pickettii*, waterborne Gram-negative bacteria, had been isolated from patients infected with DFUs, it is resistance to disinfectants and has an intrinsic tolerance to antibiotics, thus complicated wounds treatment [23]. Likewise, *Corynebacterium striatum*, once deem as a contaminant, has reported as a MDR pathogen in DFUs, particularly in cases with prolonged hospital duration or previous antibiotics exposure [24]. Additionally, *Porphyromonas* and *Prevotella*, *Aerococcus*, *Helcococcus*, and *Gemella* spp. are slow-growing bacteria that were scarcely isolated from DFUs [50]. The identification of these unexpected bacteria is often missed by traditional culture procedures, while advanced molecular methods like 16S rRNA sequencing and metagenomics have explored their existence and the possible clinical relevance [49].

3 RESISTANCE PATTERNS OF PATHOGENIC BACTERIA IN DFUS

The emergence of numerous antibiotic-resistant strains in diabetic foot ulcers has made treating the disease extremely difficult or created obstacles to treatment. This is due either to the indiscriminate use of medications, which in any case

necessitates prolonged treatment and hospital stays, and may even lead to the risk of amputation. Therefore, it has become essential to understand the mechanisms of resistance to these drugs and microbial susceptibility in order to overcome this problem and find effective treatment methods.

3.1 Antibiotics Resistance in DFUs Pathogens

The resistance of pathogens in DFUs to the antibiotic considered as a serious problem that will affect the treatment it was observed that *E.coli* bacteria that isolate from DFUs infections have completely resistant to the fluoroquinolones antibiotics, And some strains of *P. aeruginosa* also revealed a high rate of resistance to the aminoglycoside and cephalosporin antibiotics [27], Coşkun et al. [50] showed that 58.6% and 66.7% of *Klebsiella* and *E. coli* spp. respectively were former of ESBL, this in turn will limiting the treatment possibilities. The Methicillin resistant of *S. aureus* (MRSA) strains making a serious concern. some studies found that there is a significant increase in resistance with resistance rates exceeding 50% [28]. These findings emphasize the significance of routine susceptibility testing and the requirement for empirical treatment guided by local resistance profiles.

3.2 Mechanisms of emerging Multidrug Resistance strains

Multidrug resistance patterns of pathogenic bacteria are complicating the treatment approaches of DFUs, posing a considerable clinical challenge due to restricted effectual antibiotic options. The mechanisms that drive bacterial MDR strains isolated from DFUs are multifactorial and include both genetic and phenotypic adaptations that enable these pathogens to tolerate exposure to antibiotics.

3.2.1 Genetic Mechanisms of MDR strains

3.2.1.1 Acquisition of resistance genes

Studies indicated a high prevalence of MDR strains in DFUs, with *S. aureus* (including MRSA), *E. coli*, and *P. aeruginosa* being dominant MDR pathogens [16, 51, 52]. Risk factors that lead to the dominance of these MDR strains in DFUs involve former hospitalization, earlier antibiotic therapy, and sizeable ulcers, as well as surgical interventions [16, 52]. The existence of MDR strains complicates treatment and often leads to chronic infections and an escalated risk of amputations, along with increasing mortality rates.

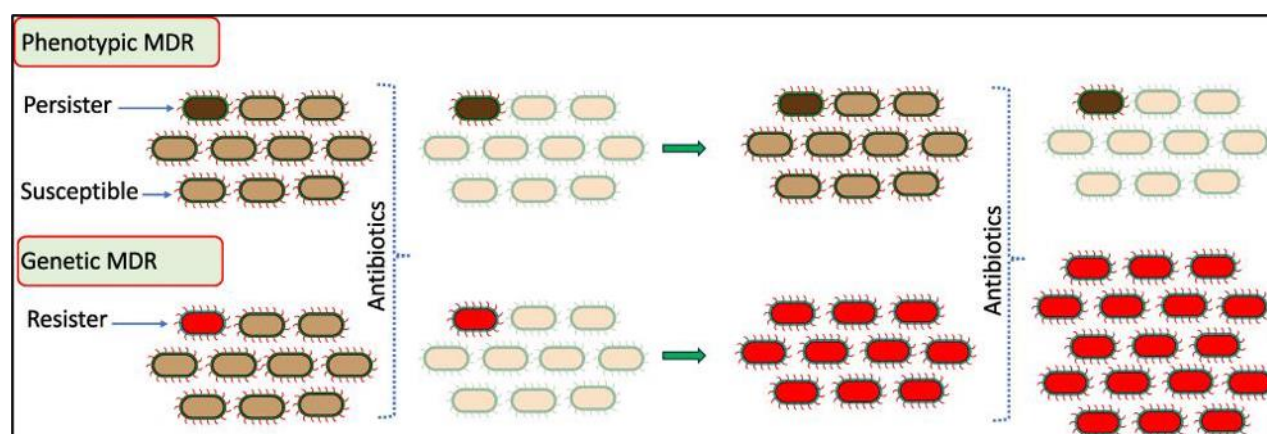


Figure 1: Demonstrative of MDR types. There is a genetic identity between phenotypic MDR bacterial cell and its siblings, but metabolic status of this cell is enabled to survive after 1st exposure of a certain antibiotic (dark grey cell). However, this cell produces its new progeny, where 2nd exposure of a given antibiotics would kill the same number of bacteria as before. In genetic MDR, the mutated bacterium (red cell) likely to resist antibiotics to survive, and the division of these bacteria proceeds. Under exposing to certain antibiotics, majority of susceptible bacteria (light grey cells) die. The reproduction of resistant bacteria proceeds and newly progeny remain on having induced mutation, even in lack the certain antibiotic. The 2nd exposure of a same antibiotic doesn't influence the survival; these bacteria proceed with growing [55].

The MDR strains often possess multiple resistance genes located on mobile genetic elements like plasmids, transposons, and integrons. These genes encode resistance to certain antibiotics, and their cumulating in a single bacterial cell awards resistance to multiple drugs simultaneously. Key resistance determinants include the production of ESBLs genes (such as blaCTX-M, blaTEM, and blaSHV), carbapenemases (such as blaNDM and blaKPC), and MRSA genes (like mecA) in *S. aureus* [53]. Horizontal gene transfer promotes the spreading of these resistance determinants among bacterial populations within the ulcer's environment [54, 55]. The expression of resistance genes occurs against various targets, which can remarkably alter according to varying growth conditions [56].

Oftentimes, bacteria acquired genetic modifications (mutations) in the DNA by phage, plasmid, and other mobile genetic factors [57]. MDR is generally divided into two classes: genetic and phenotypic. The mutation at the antibiotic resistance genes gained from other bacterial types forms genetic MDR. From the clinical view, genetic MDR causes the failure of treatment, so it requires alternative antibiotic usage or different medicinal approaches. Unlike genetic MDR, phenotypic MDR leads to alterations in bacteria and abates within individual cells, with no genetic variations. The phenotypic MDR against a certain antibiotic doesn't permit the whole growth of entire bacterial populations [55], Fig. (1).

3.2.1.2 Overexpression of Efflux pumps

Various MDR strains expand the expression of multidrug efflux pumps, which actively expel a wide range of antibiotics away from bacterial cells, lowering intracellular drug levels below therapeutic levels. This tactic is usual in Gram-negative bacteria such as *P. aeruginosa* and *E. coli* [54, 58].

3.2.1.3 Modifications of antibiotics targets

Bacteria could evolve mutations or acquire genes that change structures of antibiotic targets, thus diminishing drug binding affinity, such as the mutations in penicillin-binding proteins leading to MRSA in *S. aureus* or modifications of ribosomal RNA that give resistance to macrolides and oxazolidinones [58].

3.2.1.4 Enzymatic degradation or modifying of antibiotics

Enzyme production, like β -lactamases, hydrolyzes β -lactam antibiotics, rendering them unavailing. ESBLs and carbapenemases are especially concerns in DFU pathogens, because they confer resistance to a broad range of β -lactams, including carbapenems [58, 59].

3.2.2 Phenotypic Mechanisms and Environmental Determinants of DFUs

3.2.2.1 Biofilms formation

Bacteria causing infections in DFUs often found within biofilms, which are complex communities embedding in a protective matrix. Biofilms lessen antibiotics penetration and enable phenotypic tolerance, a non-genetic form of resistance, where bacteria can tolerate temporary antibiotics exposure without genetic modifications [55]. Among the dominant pathogens, *S. aureus* (especially MRSA strains) appeared a vigorous biofilms-forming ability, which driven by surface adhesins and *ica* operon [60, 61]. These biofilms implicated with chronic wounds persistence and notably hinder antibiotics penetration. Notably, biofilms associated *S. aureus* required antibiotic concentrations up to 1000-folds higher than those required for planktonic cells, with agents like ceftaroline and gentamicin exhibiting only partial effectiveness [62]. Yakout and Abdelwahab [43] revealed that 93% of *P. aeruginosa* strains that isolated from DFUs were biofilm formers, leading to persistent infection and poor healing. *K. pneumoniae*, *P. mirabilis*, and *E. coli* which are members of the Enterobacteriaceae family isolated from DFUs frequently and are characterized by their pattern of MDR resistance and biofilms mediated virulence [14,17]. *K. pneumoniae* utilizes fimbria adhesins and extracellular polysaccharides to form biofilms, these strains carried plasmid-encoded resistance genes that complicated antimicrobial treatment [17, 62]. Biofilms produced by *P. mirabilis* enable it to evade host defenses and the traditional antibiotic, inducing tissue necrosis and detained healing of wound [63]. ESBL strains of *E. coli* escalate resistance by enhancing heterogeneity of biofilms through the horizontal gene transferring within the wound's microenvironment [14,27]. Characterized with hyperglycemia, diabetic milieu in general lessening the immune functions and boosts biofilms formation and persistence [31]. Such environment commonly requires combination approaches of treatment in addition to new anti-virulence strategies exploration. These pathogens shed lights on the necessity of targeted diagnostics and integrated treatments approaches that improve the clinical outcomes in DFUs treatment combating biofilm associated resistance.

3.2.2.2 Stress-induced tolerance

Environmental stresses like hypoxia and immune pressures in the microenvironment of diabetic ulcer has the potential to induce phenotypic adaptations that decrease bacterial susceptibility to antibiotics provisionally [55].

3.3 Global Trending and Regional Differences in Antibiotic Resistance in DFUs

Pathogens resistance patterns entailed with DFUs differ vastly across geographical areas, due to usage practices of antibiotics, healthcare infrastructures, and socioeconomic influences. Makeri *et al.* indicated that in Africa *S. aureus* and *P. aeruginosa* were the dominant pathogens in DFUs cases, featuring MDR rates of 26.4% and 41.8%, respectively [64]. Meanwhile, Baral *et al.* demonstrated that 82.97% were gram negative of DFUs isolates in South Asia, and the most common with widely resistant to ampicillin was *K. pneumoniae* [65]. It was documented in Middle East that *P. aeruginosa* especially in ischemic ulcers has the high ESBL prevalence among Enterobacteriaceae and carbapenem resistance additionally the three most frequently found among aerobes Gram negative bacteria were *S. aureus* followed by *P. mirabilis* then *E. coli* [28,66]. In contrary, Gram-positive pathogens like MRSA was prevalent in the global west

despite the decline in MRSA prevalence rates, from 25% before 2010 to 9% henceforth [67]. Geographic disparities showcase the weight of localized surveillance and streamlined programs of antimicrobial management for overcoming resistance effectively.

4 THERAPEUTIC CHALLENGES AND STRATEGIES

4.1 Limitations of Conventional Antimicrobial Therapies

DFUs infections management is convoluted by limitations of traditional antimicrobial therapies as typical antibiotics were unsuccessful in managing pathogens protected by biofilms that stand as physical and biochemical barriers to medication penetration. Cells in biofilms were 10 to 1000 more tolerant to antibiotics than planktonic cells [14]. Moreover, the emergence of MDR pathogens has been accelerated due to the indiscriminate utilization of broad spectrum antibiotics in treatments [27]. Such pathogens persist despite using systemic and topical antibiotics in managing infections, in return this results in extended infection and impaired healing, which exacerbates the risk of amputation. Mainstream therapies lack the ability of distinguish between colonization and true infections convoluted therapy plans that promotes overuse of antibiotic [14].

4.2 Emergence of Treatment Approaches: Biofilm, Phage Therapy, and Novel Antibiotics

Innovative approaches have been explored to overcome treatment challenges, one of the effective and targeted approaches is using bacteriophages therapy, viruses utilized to target bacterial cells and lysing them consequently, as phages has the ability of penetrating biofilms and eradicate MDR pathogens selectively without harming the normal flora of the host. Researches have revealed the effectiveness of phage-antibiotics combination therapy in reduction biofilms biomass and restore antibiotics sensitivity in *P. aeruginosa* and *S. aureus* infections [68, 69]. Furthermore, enzymes that derived from phages like endolysins and depolymerases exhibit ability to degrade biofilms matrices and intensifying the antimicrobial penetration. Other ongoing approaches involving antimicrobial peptides, inhibitors of quorum sensing, and biofilms-disrupting factors that pick out bacterial communications and adhesion mechanisms. Novel antibiotics like sucrose octasulfate dressings, nitric oxide-emission compounds, and engineered nanoparticles are under investigations for their capacity to change the wounds microenvironment and enhance healing [20, 70]. Moreover, 3D-engineered skin models and hydrogel-based delivery systems are developed to mimic DFU conditions and improve drugs delivery as studies results revealed that a gel formula containing live cells of *L. plantarum* L40 that remained viable for 18 days and showed antibacterial activity against *S. aureus*, *K. pneumonia*, *P. mirabilis*, and *P. aeruginosa*. The results suggest the possibility of using bacteriocin-producing *Lactobacillus plantarum* viable cells as an effective probiotic to manage some pathogens of the skin such as diabetic foot ulcer pathogens [71,72].

4.3 The Clinical Relevance of Personalized Medicine to Manage Resistant Infections

Personalized management provides a transformative approach to treat resistant pathogens engaged with infections of DFUs by designing treatment program that compatible and match with the patient's unique microbial profile, genetic makeup, and immunological status. The evolution of molecular diagnostics techniques that includes whole genome sequencing, metagenomics, and 16S rRNA sequencing, imparts precise pathogens and resistance gene diagnosis that expedite the targeted antimicrobial therapy [28, 73]. This approach enhances the clinical outcomes in addition to decrease undue antibiotics exposure. Furthermore, approaches in host directed treatment (HDT) adapt the immune response including macrophages phenotypic polarization and cytokines regulation being explored to boost tissue repair and wound healing in diabetic individuals [74]. Besides, enhancing predictive capabilities and diagnostic accuracy by AI and generative AI are transforming DFU management and guide therapeutics decisions [75].

5 ALIGNING WITH SUSTAINABLE DEVELOPMENT GOALS

The current review on microbial landscape and therapeutic challenges in DFUs provides potent relevance with the United Nations Sustainable Development Goals (SDGs), especially in building resilient and robust health systems. Stripped to its essence, the work directly boosts 3rd SDG: Good Health and Well-being through enrichment our understanding of infections control, antimicrobial resistance, and personalized therapy approaches that may minimize preventable complications such as limb amputations. Through processing the MDR pathogens and enhancing diagnostics-driven therapies, the current review supports 12th SDG: Responsible Consumption and Production via its assertion on rational antibiotics utilization and administration practices that block environmental contamination and increasing resistance.

Also, our discussion on the emerging innovations mechanisms that include phage therapy, molecular diagnostics, and AI-guided wounds treatment links clinical microbiology with 9th SDG: Industry, Innovation, and Infrastructure; underlining the impacts of cutting-edge solutions in shifting the chronic wounds management. Additionally,

investigating the global outlook on resistance trending and the demand for regional surveillance highlights the 17th SDG: Partnerships for Goals; encourages cross-sector collaboration and data sharing to fight a common health threat.

6 CONCLUSION

Diabetic foot ulcers still an enormous clinical and microbiological challenge, mostly as a result of their polymicrobial nature, high prevalence of MDR strains, and the protective impacts of biofilms in chronic infections. The present review underscores the valuable understanding microbial diversity and resistance pathways to enrich targeted diagnostics and guide empirical therapy. Today the need for innovative therapeutics approaches became inevitable owing to the limitation of traditional antibiotics as an alarming difference in resistance profiles repeatedly appears in global trends, making localized surveillance, interdisciplinary collaborations, and sustainable treatment strategies a necessity.

Aligned with SDGs, especially those deals with health equity, responsible antibiotic usage, and technological innovations, our review invites for a paradigm shifting from reactive antibiotics giving to proactive, diagnostics-guided management. By combining molecular insights with emerging therapy platforms, we can't only reduce the burden of DFUs, but as well sharing meaningfully to global health protocols.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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