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Epidemiological aspects and new perspectives for the prevention of diabetic foot and its consequences

Abstract

Diabetes Mellitus (DM) is a clinical condition characterized as a chronic non-communicable disease, which imposes challenges in the lives of individuals when neglected in the context of community and preventive health. In this context, the identification and description of the consequences acquired by this disease imply greater chances of early diagnosis of bacterial infections and mitigation of the occurrence of antibiotic resistance, developed mainly by people who have complications of DM, such as diabetic foot. This complication leads to a high number of lower limb amputations. As discussed in the article, people who exhibit diabetic foot can resort to alternative therapies such as larval and photodynamic therapy. Therefore, this narrative review aims to cover the main contextual elements of DM in the Brazilian population, microbial infections that affect diabetic foot patients, innovative therapies, and the general implications for the Unified Health System (SUS).

Keywords: bacterial infections, unified health system, diabetes mellitus, ulcers

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Abbreviations: DM, diabetes mellitus; SUS, unified health system; PAD, peripheral arterial disease; WIfI, wound, ischemia, and foot infection; IDSA, infectious diseases society of America; IWGDF, international working group on the diabetic foot; MRI, magnetic resonance imaging; PND, diabetic polyneuropathy; RR, risk ratio; MDRB, multidrug-resistant bacteria; PHC, primary health care; WHO, world health organization; PDT, photodynamic therapy; ROS, reactive oxygen species

Introduction

Diabetes mellitus (DM) is a chronic non-communicable condition that affects millions of people worldwide. It is characterized by the physiological difficulty in producing or properly using insulin, resulting in high blood glucose levels that, when not controlled, can lead to serious complications, including cardiovascular problems, nephropathy, neuropathy, and eye retinopathy. The high prevalence of the disease is a major challenge for public health, requiring strict control, which involves lifestyle changes, constant monitoring of blood glucose, and, in many cases, the use of medications. The seriousness of the issue can be understood through a study carried out in 2021 that analyzed DM mortality in Brazil between 2008 and 2019, in which the excessive number of 74,180 deaths in the country due to the disease became evident. Another important point to be analyzed is that the risk of death from DM tends to be higher in individuals who exhibit ulcers.

Ulcers, especially infected ulcers that are characterized as diabetic foot, depend on greater care by the multidisciplinary team and generate greater expenses for the unified health system. The incidence of these lesions has increased every year, and individuals with diabetes mellitus are more likely to develop ulcers, with or without an infectious process. That said, this article brings the main risk factors for the development of these ulcers, persistent symptoms, prevention, and self-care with the feet and tissues that become essential to avoid more serious complications. As well as the amputation of the lower limbs, which harms the lives of these patients and can lead them to develop emotional problems, in addition, most of these amputations could be avoided with the early detection of ulcers.

From this perspective, the diabetic foot can be affected by a variety of bacteria that trigger infections. In addition, bacterial resistance, an increasingly common problem, occurs when certain strains manage to proliferate even in the presence of high concentrations of antimicrobials, making treatment difficult. A crucial aspect to be discussed is precisely this resistance to antibiotics, which directly impacts therapeutic efficacy and represents a major challenge for the management of infections in patients with diabetic foot. Health services that are well structured can offer appropriate self-care and curative practices; However, in health systems that already have deficiencies in care, the supply of these resources becomes limited. This contributes to a significant increase in risk factors, further aggravating the condition of patients and making it difficult to prevent and properly manage these lesions.

Since the treatment for diabetic foot may not be fully effective and generate high costs, alternative therapies have stood out, as an example we mention larval therapy which has a proven cost-benefit ratio and high efficacy. Thus, the objective of this study is to deepen the knowledge of DM, to know the main pathogens present, what care is performed in this type of wound, as well as the impacts on the individual and the UHS, in addition to the therapies currently used in these patients for healing.

Methodology

This is a narrative literature review study on diabetic feet; new therapies and microbiological aspects were considered. The search was conducted in the PubMed and SciELO libraries, in addition to the Google Scholar page, in search of scientific articles to compose the review, using the keywords: “diabetes”, “bacterial infections”, “ulcers”, and “Unified Health System”. We considered the articles that, after reading the title, abstract, and body of the text, best aligned with the objectives proposed in this study. As an inclusion criterion, only articles with full texts available free of charge, in Portuguese or English, in the last 10 years were considered. Incomplete articles or articles published outside the period defined by the authors were excluded from the study. In addition, documents from international organizations, such as the WHO, were consulted. There were no exclusion criteria.

Discussion

Diabetes mellitus (DM) encompasses a set of metabolic disorders characterized by hyperglycemia, that is, high blood glucose levels. The condition negatively impacts health, increasing the risk of developing serious and potentially fatal complications. The consequences of DM extend beyond the medical sphere, impacting medical care costs, reducing quality of life and contributing to increased mortality rates (Baena-Díez et al, 2016). The incidence of DM is increasingly prevalent globally. Data from 2017 indicate that the disease affected about 8.4% of adults between 18 and 99 years old, with projections of reaching 9.9% in 2045. In Brazil, the National Health Survey (PNS) shows a significant increase in the prevalence of DM, from 6% in 2013 to 8% in 2019.[1] The main risk factors that predispose to the development of type 2 diabetes consist of advanced age, that is, older people are more likely to acquire diabetes, poor diet, obesity, lifestyle and genetic factors are also included in these factors. With aging, individuals do not usually have a regulated diet and physical activity, eating few meals a day and practicing a sedentary lifestyle throughout the days, resulting in a greater probability of developing DM 2 (Schnurr et al, 2020).

Disability resulting from diabetes mellitus is significantly influenced by its microvascular complications, such as nephropathy, retinopathy, neuropathy, and lower limb amputations, and macrovascular complications, such as coronary heart disease, stroke, and peripheral vascular disease. Studies indicate that 30% to 50% of individuals with diabetes are affected by these complications (Litwak et al, 2018). Therefore, the complications of diabetes, in addition to negatively impacting the quality of life of patients, also generate a substantial increase in the use of health services, raising costs for the health system and social insurance. It is estimated that about 50% of a patient's lifetime health expenditure with diabetes is related to the complications of the disease (Zheng & GBD 2019; Harding et al, 2018).

The scientific literature on the prevalence of diabetes mellitus reveals a significant predominance of cases in women compared to men. About 11.1% of women have diabetes, while only 9.1% of men have the condition. It is observed that the prevalence of diabetes mellitus (DM) has a positive correlation with age, that is, it increases with age. On the other hand, the prevalence of DM shows a negative correlation with the level of education, decreasing in both sexes as the level of education increases (Brazilian Diabetes Society 2024).

Individuals with diabetes mellitus (DM) are more likely to be hospitalized and stay longer when they are at lower socioeconomic levels, advanced age, obese, have a history of smoking and sedentary lifestyle, or when they have inadequate blood glucose control. A study conducted in 2021 analyzed mortality from diabetes mellitus (DM) in Brazil between 2008 and 2019. This study showed that, between 2008 and 2019, there were 74,180 deaths due to DM, which represents 1.48% of the total deaths registered in the country. The mortality rate from DM was estimated at 4.75 per 100,000 population.[2] In addition, the correlation observed between risk of death and some type of diabetic foot ulcer shows that, the first happens more often with individuals that have the second. The complications caused by DM are also related to the causes of death of these patients, with cardiovascular diseases representing 80% of the mortality risk in these individuals.[3]

Diabetic neuropathy, one of the most frequent microvascular complications, can be defined as a dysfunction of the peripheral nerves that affects diabetic patients. This complication can also be related to the mortality of the patients with diabetes, as it can be observed that in about 50% of patients with type 1 and type 2 diabetes, with a prevalence of up to 20% to type 2 diabetes. (Rodrigues et al, 2017; Oh, 2020). Early identification of this complication is essential, as it enables the adoption of preventive measures against the appearance of foot ulcer, reducing the incidence of amputations in people with diabetes (Sebastianes, 2021). Also, diabetic foot syndrome refers to the appearance of infections, ulcerations, and/or damage to the deep tissues of the feet in individuals with diabetes, usually related to neurological dysfunctions and different stages of peripheral arterial disease (PAD). The annual incidence of foot ulcerations in diabetic patients is estimated to be 2%, and over the lifetime of a population, about 34% of this population may be affected by this condition. The prevention of these lesions is crucial to reduce the complications associated with diabetes and minimize the damage to the health of patients (Ministry of Health, 2016).

In contrast, some researchers argue that additional factors, such as patient comorbidities and treatment responses, may play a more significant role in predicting major amputation than the WIfI classification alone (Cавон et al., 2024). The Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIfI) classification system is designed to predict wound healing and assess limb threat in patients with diabetic foot ulcers. However, its efficacy in predicting major amputation remains limited.[4,5] Studies show that as WIfI stage increases, the risk of amputation does rise, but the classification is not definitive for major amputation outcomes.[5]

Foot infection in patients with diabetes poses a severe threat to the affected foot and limb, requiring immediate evaluation and treatment. Because all ulcers tend to be colonized by potential pathogens, the diagnosis of infection should be made based on the presence of at least two signs or symptoms of inflammation, such as redness, warmth, induration, pain, or tenderness, or the presence of purulent exudate. However, these signs can be attenuated by neuropathy or ischemia, and systemic signs such as pain, fever, and leukocytosis are often absent in mild to moderate infections. Infections should be classified according to the International Working Group on the Diabetic Foot (IWGDF) / Infectious Diseases Society of America (IDSA) system, as mild (superficial, with minimal cellulitis), moderate (deeper or extensive), or severe (accompanied by systemic signs of sepsis), in addition to being evaluated for the presence of osteomyelitis.[6]

Despite the advancements in imaging techniques, challenges remain in accurately diagnosing diabetic foot complications due to overlapping symptoms and the complexity of the conditions. Further research is needed to refine imaging strategies and improve diagnostic accuracy.[7] Imaging of the diabetic foot is crucial for diagnosing complications such as osteomyelitis and Charcot neuroarthropathy.[8] Various imaging modalities, including conventional and advanced techniques, play a significant role in differentiating these conditions and guiding treatment. Therefore, conventional radiography, Magnetic Resonance Imaging (MRI) and nuclear medicine[9] outline the key imaging modalities and their applications in diabetic foot assessment.

According to the IDF, each year about 26 million people in the world develop foot ulcers and more than 50% of these ulcers suffer the infectious process. The factors that most contribute to the appearance of foot ulceration are sensory neuropathy or diabetic polyneuropathy (PND) and PAD. It is noteworthy that, after 10 years of diagnosis of DM, PND is present in around 50% of patients and about half of these are symptomatic, with greater complaints at night (Zörrer et al, 2022). However, the most common symptoms that these patients may present are numbness, burning, tingling, shock and allodynia in the lower limbs that can reach the distal muscles, as well as neuropathic pain, which is the most frequent involvement, which impacts the daily life

of individuals. By controlling blood glucose and changing lifestyle, it is possible to prevent PND, renovate nerve fibers, and avoid foot disease, making ulceration and amputation impossible (Pop-Busui et al, 2017).

Even when the treatment of an ulcer is successful, the risk of recurrence is 40% in the first year and 65% in the first three years after healing, due to the maintenance of local and systemic risk factors, often seen in poorly controlled diabetics (Jaap et al., 2020). In addition, more than half of lower limb amputations could have been prevented with adequate detection and preventive care before the need for amputation (Tardivo et al., (2014). According to a meta-analysis observed in the current literature, data indicated that the prevalence of amputations among patients with diabetic foot ranged from 1.3% to 66% in the studies reviewed. Thus, the authors also concluded that Diabetes Mellitus was identified as the main risk factor for these amputations and individuals with diabetes have a risk ratio (RR) of 22.3 in relation to non-diabetics for progression to amputation after diabetic foot injuries.[10]

With the microbiological profile and bacterial resistance, together with the appropriate antimicrobial treatment of diabetic foot infections, it is essential to guide the choice of empirical antibiotic therapy. This process is essential to optimize cost-effectiveness measures and reduce the morbidity and mortality associated with these infections. In a study conducted with 141 patients with diabetic foot in Ceará, enterobacteria were the most frequently isolated microorganisms (83.7%), followed by *Staphylococcus aureus* (43.3%). In Belo Horizonte, in a public hospital, the most prevalent bacterial genera were *Acinetobacter* spp (24.4%), *Morganella* spp (24.4%), *Proteus* spp (23.1%) and *Enterococcus* spp (19.2%) (Cardoso, 2016).

The most prevalent group of bacteria is anaerobic, which can be classified as gram-positive and gram-negative. Among the gram-negative bacilli, the genera *Bacteroides*, *Prevotella*, *Porphyromonas* and *Fusobacterium* stand out as the most representative, while the genus *Veillonella* is the main representative among the gram-negative cocci. Gram-positive bacilli are subdivided into spore-forming (genus *Clostridium*) and non-spore-forming (genera *Actinomyces*, *Bifidobacterium*, *Eubacterium*, *Lactobacillus,* and *Propionibacterium*). Gram-positive cocci include genera *Peptostreptococcus*, *Anaerococcus*, *Finegoldia*, *Parvimonas,* and *Peptoniphilus*. Sporulated Gram-positive bacteria are pleomorphic, ranging in morphology from coccoid forms to long, curved filamentous structures. In adverse situations, species such as *Clostridia* enter into sporulation, forming terminal spores that facilitate their identification. The pathogenicity of these microorganisms depends on the genus: while some species maintain a harmless relationship with the host, others can cause serious infections, particularly in immunocompromised people. This group includes the genera *Actinomyces*, *Bifidobacterium*, *Eubacterium*, *Lactobacillus,* and *Propionibacterium*, which belong to the phyla Firmicutes and Actinobacteria, although they are not always phylogenetically close (Hall et al, 2015).

Another important aspect is bacterial resistance, which occurs when strains manage to proliferate even at high concentrations of antimicrobials, making it difficult to treat bacterial infections with the available therapeutic resources. Infections caused by microorganisms, including bacteriosis, are highly prevalent in hospital settings, where they are known as bloodstream infections. These infections can affect patients in different sectors, such as intensive care units, neonatology, and operating rooms. A significant incidence of these infections is observed in the elderly, due to the fragility of the immune system in this age group.[11]

Antibiotic resistance is an important issue that must be addressed, as it affects the effectiveness of treating diabetic foot infection. The prevalence of multidrug-resistant bacteria (MDRB) varies between 15% and 66%, depending on the region analyzed. The presence of MDRB can be linked to an increase in recovery time, greater need for surgical procedures and high treatment costs. Furthermore, antimicrobial resistance results in a higher demand for protein intake, increased oxygen consumption, dysregulation of glycemic control, and reduced hemoglobin levels. Considering that these infections are polymicrobial, the use of broad-spectrum antibiotics is recommended initially in severe cases, with subsequent adjustments based on the results of the antibiogram.[6]

Performing regular culture and antibiogram tests in hospitals helps identify the microbiota found in patients. This information is useful for creating local guidelines in order to start antibiotic treatments. It improves treatment success and reduces costs by encouraging careful and step-by-step use of antibiotics (Sonmerzer et al., 2015). On the other hand, improper use of antibiotics can worsen infections and lead to bacterial resistance, compromising the treatment of diabetic foot infections (Oliveira et al., 2014). Regular self-care practice is essential for the prevention and early detection of lesions that can progress to diabetic foot ulcerations. Thus, it is a cost-effective and efficient way to manage health and can be delivered with the innovative One Health approach.[10] Foot care is a key part of self-care for people with diabetes mellitus (DM), and it is essential to implement educational programs on the subject, especially in the context of primary health care (PHC) (Rezende et al, 2017).

While significant advancements have been made in understanding and treating diabetic wounds, challenges remain in achieving timely healing (Pathania et al., 2024). Future research should focus on integrating personalized medicine and novel biotechnologies to further enhance treatment outcomes. Thus, understanding pathogenesis (eg. immune dysregulation),[12] molecular targets (MicroRNAs and signaling pathways),[13,14] and treatment strategies for enhancing wound is crucial for developing effective treatment strategies of healing in diabetic patients.[12]

Dressings represent an effective alternative in the management of colonized, non-infected ulcers or ulcers that are not associated with diabetic foot. They are made from materials with different compositions, whose main functions are wound cleaning, debridement of devitalized tissues, creation of a favorable environment for tissue healing and repair, and controlling the balance of the bacterial flora in the ulcer bed (Armstrong & Meyr, 2019). Although the level of evidence currently available is not considered to be of high intensity, silver-based dressings are often used in the treatment of infected lesions. Case reports indicate that these dressings have significant potential as agents of healing, and as a preventive strategy for bacterial resistance to antibiotics (Durnville et al, 2017).

In wealthy regions with well-established health systems, patients with diabetes have access to a range of services, such as foot care education programs, periodic checkups, follow-ups by multidisciplinary health teams, and early treatment of lesions that may precede ulcer formation. In contrast, in areas with poor or limited health systems, access to these services is often compromised, resulting in difficulties in accessing preventive interventions for the development of diabetic foot ulcers (Avilés et al, 2020). In regions with limited access to health services, such as in parts of Africa and Asia, the main risks for developing diabetic foot ulcers (DFUs) include loss of protective sensation, peripheral arterial disease, foot deformities, history of previous ulceration, and late initiation of medical follow-up

(Aliyu et al., 2023). In addition, people with diabetes play a crucial role in lowering the risk of ulcers by practicing proper foot self-care (Oni, 2020).

In 2002, the World Health Organization (WHO) characterized palliative care as a method focused on enhancing the quality of life for patients and their families in situations of life-threatening diseases. Through this approach, it seeks to prevent and alleviate human suffering (Abrão et al, 2019). The epidemic of chronic diseases has had serious consequences for individuals, families, and communities, as well as overwhelming health systems (Malta et al, 2017). According to data from the World Health Organization (WHO), of the 58 million deaths annually in the world, 34 million are caused by disabling and incurable chronic-degenerative diseases. In Brazil, approximately one million deaths are recorded per year, 650 thousand of which are due to chronic diseases. About 70% of these deaths occur in a hospital environment, especially in intensive care units (Gomes & Othero, 2016).

The World Health Organization (WHO) emphasizes the urgent need for nursing staff to develop humanization practices that encompass not only cancer treatment, but also other chronic diseases. Palliative care should be offered to all patients with conditions with no prospect of cure, seeking to provide a better quality of life from diagnosis to the end of life, always focusing on the humanization of care (Araújo et al., 2022). It is essential that attention and care be focused on the needs and limitations of patients in the terminal process, based on the biopsychosocial and spiritual well-being, both of the patient and their families, in order to facilitate acceptance and minimize suffering in the final phase of the disease (Provinciatto et al, 2019).

Currently, in some cases, alternative therapies are used as a complement to the treatment of diabetic foot wounds or when drug treatment becomes insufficient or expensive for patients. In this context, larval therapy, also known as fly larvae therapy, has stood out as a promising alternative for the treatment of chronic wounds, presenting superior results to the traditional methods often used in hospital protocols. Consistent studies demonstrate that larval therapy promotes faster healing compared to other therapeutic options.[15] In addition to proven efficacy, larval therapy has a lower cost compared to traditional pharmacological therapies, providing an excellent cost-benefit ratio. Despite the growing international scientific evidence, the development of research on larval therapy in Brazil is still elementary. Thus, most studies focus on the states capitals, with a limited number of studies in rural or distant regions of the country. Therefore, the expansion of research and the dissemination of knowledge about this innovative technique are crucial for the optimization of chronic wound treatment in Brazil.[16]

Furthermore, there is photodynamic therapy (PDT) which consists of an auxiliary therapeutic approach in the treatment of infected wounds. This technique aims to eliminate microbial agents in skin lesions through the combination of electromagnetic radiation, photosensitizer, and tissue oxygen (Sun et al., 2019). The treatment begins with the application of a light source, such as a low-intensity laser, which transfers energy to the photosensitizer. This agent reacts with intracellular substrates, generating free radicals that, when interacting with molecular oxygen, form Reactive Oxygen Species (ROS). As a result, singlet oxygen is formed, a key element in the oxidative process of PDT, which has a significant antimicrobial effect, favoring the elimination of pathogenic microorganisms and accelerating wound healing. In this way, PDT stands out as a promising therapy, contributing not only to infection control but also to tissue regeneration (Nesi-Reis, 2018).

While photodynamic therapy shows promise as a treatment for diabetic foot ulcers,[17,18] the current evidence is insufficient to warrant its approval. Case studies and small trials have reported significant reductions in ulcer size and bacterial load, suggesting that PDT could enhance wound healing and reduce the need for antibiotics and amputations.[19] Thus, the need for large, well-designed RCTs is critical to establish its efficacy and safety conclusively. Until such evidence is available, PDT remains an experimental treatment option, and its use should be considered cautiously within clinical trials or as an adjunct to conventional therapies.[20] Available studies suggest that PDT is generally safe, with no significant device-related adverse events reported.[20]

During the article we address several themes, presenting the problem, its implications and solutions. The topic addressed is essential to draw the attention of people and public agencies to the importance of controlling diabetes mellitus and diabetic foot infection caused by its lack of control, in addition when DM favors this condition, several other consequences arise, as mentioned, for example, the group of bacteria and infections that affect the diabetic foot, Still from this perspective, when the diabetic foot infection becomes strong and resistant and the use of antibiotics becomes frequent, the patient develops antibiotic resistance due to the multipurpose of these drugs. Regarding this concern, we also address the alternative therapies used for a second option or complementary treatment for diabetic foot infection.[21–36]

Conclusion

The present study concludes that the Unified Health System still has barriers concerning the control of Diabetes Mellitus and diabetic foot infection, requiring a greater distribution of human and material resources, especially in primary health care. In addition, it is essential to adopt strict measures regarding self-care and predisposition to ulcers to prevent health problems in patients who have DM. However, funding alone is not enough, health professionals must invest in continuing education with the assisted population so that they avoid habits associated with the risk factors of this disease. Thus, it is necessary to observe the attention of government agencies to the prevention of damage from DM, because, with greater funding for prevention, expenses with damage from the disease such as hospitalizations and expenses with surgeries decrease. Therefore, professionals must keep up to date on diabetes mellitus, methods for preventing the disease, and current therapies that help in wound recovery and improve the quality of life of affected patients.

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Conflicts of interest

The author declares there is no conflict of interest.

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