

Infectious comorbidity among individuals living with type 2 diabetes mellitus: Primary healthcare perspectives of advanced environment health factors in DFU infection management

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Received date: 13th August 2025

Accept date: 4th October 2026

Published: 11th October 2026

Abstract

Background: Diabetic foot ulcers are a devastating and costly complication of diabetes, and most times lead to prolonged hospitalization of such patients, reduce the quality of life, and lead to amputation especially in a situation where the ulcer is associated with a certain environmental exposure. From the primary healthcare perspective, the environment factors play a crucial role in the management of this complex condition DFU.

Context: In a challenging environment, managing an advanced diabetic foot ulcer requires effective and proactive PHC strategies.

Objective: This narrative review discusses environmental determinants such as poor foot care habit, inadequate footwear, and walking barefoot increases the risk of foot ulcers. Prevention and management strategies include patient education, regular foot examination, multidisciplinary care, risk stratified monitoring program by implementing programs to identify and manage high-risk patients.

Significance: Understanding these factors and implementing effective prevention and management strategies, primary healthcare providers will be able to deliver high-quality care and improve patient outcomes. This narrative update focuses on the Primary healthcare perspectives of advanced environment health factor in diabetic foot ulcer.

Conclusion: By addressing these environmental factors, primary healthcare providers can help prevent DFUs, improve healing rates, and reduce complications.

Keywords: diabetes mellitus, immune system, infection, inflammation, neuropathy, oxidative stress, primary healthcare.

1. Introduction

1.1: Overview

Diabetes foot ulcer (DFU) is a severe and debilitating complication of diabetes impacting 26 million people globally each year. Individuals with diabetes face a 25% lifetime risk of developing a foot ulcer, with prevalence rates ranging from 4% to 10%. DFU often results from injury, particularly in the presence of peripheral neuropathy, ischemia, or both, and can be triggered by mechanical stress or thermal trauma. Notably, 50% of DFU occurs on the foot's surface. If left untreated or poorly managed, it can aggravate to chronic, leading to amputation. DFU also significantly burdens healthcare system due to prolonged healing period, reduce quality of life and increased mortality rate (Tran & Haley, 2021)

Diabetes foot ulcers are a significant complication of diabetes, often precipitated by a combination of neuropathy, peripheral artery disease, and environmental factors. From primary healthcare perspective, understanding the advanced environmental health factors contributing to diabetes foot ulcer is important for prevention and management. Environmental factors such as poor foot care habits, inadequate footwear, and walking barefoot increase the risk of foot ulcers. Additional factors such as climate change, which can lead to increased temperatures and humidity, may exacerbate foot condition (Raja et al., 2023).

According to Van Netten et al (2023), stated that the International Working Group on the Diabetic Foot (IWGDF) stated that advanced environmental health factors contributing to DFUs include poor footwear which can cause repeated trauma and abnormal forces, leading to ulceration, physical inactivity (sedentary lifestyle increases the risk of DFU recurrence), smoking, smoking can impair wound healing and reduce blood flow to the feet, and poor glycemic control can as well impede wound healing and increase susceptibility to infection (van Netten et al., 2024). When diabetes is involved, foot ulcer heals very slowly and many advanced countries are concerned about what can be used to improve healing period. The time of healing for men is mostly longer than that for women. The location of the ulcer is also an aspect in the risk factors (Alsabek & Abdul Aziz, 2022).

1.2.-Hyperglycemia and infection

Hyperglycemia occurs when the body's insulin production is insufficient or when the body's cells become resistant to insulin's action. Insulin is a hormone that helps regulate blood sugar levels by allowing glucose to enter cells for energy. The primary cause of hyperglycemia in T2DM is a combination of insulin deficiency and insulin resistances. Insulin deficiency is about the beta cells in

the pancreas of an individual with T2DM, which are responsible for producing insulin, gradually lose their ability to produce enough insulin and this insulin deficiency contributes to hyperglycemia (Sharma et al., 2020).

Diabetes mellitus is recognized as a serious factor in both morbidity and mortality globally, affecting different demographics regardless of their age, gender or location (Donath & Shoelson, 2011). DM has been established to be inseparable from autophagy (Marasco & Linnemann, 2018; Muriach et al., 2014; Nwose & Bwititi, 2021; Turkmen, 2017), which in turn is intricately related with the immune system (Jiang et al., 2019; Kuballa et al., 2012). Hence, DM is complexly and strongly associated with infection including bacteria, fungi, and viruses (Chávez-Reyes et al., 2021).

Insulin resistance In T2DM, the body's cells become resistant to insulin's action. This means that even when insulin is present, cells cannot effectively take up glucose from the bloodstream, as a result, glucose levels remain high (Yaribeygi et al., 2020). The IDSA model is based on the principle of microbiology spectrum in immunocompromised hosts are at increased risk for infection. It is known that individuals living diabetes are susceptible to the spectrum of bacterial, fungal and viral infections (Chávez-Reyes et al., 2021). However, the range of spectrum have yet to be articulated to inform primary healthcare practice.

1.3: Objective of review:

The purpose of this document is to review the primary healthcare perspectives of advanced environment health factors in DFU, and Infection comorbidity among individuals living with type 2 diabetes mellitus.

2. Literature review method

2.1: Design.

This review is about a mixed narrative approach on primary healthcare perspectives of advanced environment health factors in DFU, and other factors associated with DM. A discretionary quick search for diabetes-related infections was done on PubMed.

14 eligible articles indicated a spectrum of common and uncommon infectious microbes (Asai et al., 2019; Guarro et al., 1999; Gupta et al., 2005; Jayatilake et al., 2009; Kriesel et al., 1994; Lafont et al., 2017; Mehta & Dutt, 2016; Pararajasingam & Uwagwu, 2017; Pichon et al., 2020; Porco & Visconte, 1995; Ribes et al., 2000; Rus et al., 2022; Sendi et al., 2008; Tokimatsu, 2008), which are not limited to wounds but also in blood, foot and sinuses (Fig 1). 2/14 (14.29%) articles include DFU, and both indicate onychomycoses (Gupta et al., 2005; Jayatilake et al., 2009).



Fig 1. Spectrum of microbes found in individuals living with diabetes

It has been known that major infections common among with diabetes include bacteria, fungi and virus (Casqueiro et al., 2012). Therefore, findings on Fig 1 expounds on the knowledge of diabetes infections, especially to emphasize fungi and uncommon infectious agents.

2.2: Risk factors of developing hyperglycemia in T2DM.

Age (The risk of T2DM increases with age, particularly after age 45), obesity (Excess body fat, especially around the abdomen, is a major risk factor for people with type -2 Diabetes mellitus), Family history(a family history of with type -2 Diabetes mellitus increases the risk of developing the disease), Physical inactivity(lack of regular physical activity increases the risk of individuals with type -2 Diabetes mellitus).Race and ethnicity (certain racial and ethnic groups, such as African Americans, Hispanic Americans, and Native Americans, are at higher risk of developing T2DM (Mouri & Badireddy, 2025).

2.3: Symptoms of hyperglycemia in Diabetes mellitus.

The Symptoms of hyperglycemia in individuals with T2DM include; Frequent urination which may occur at night, excessive thirst, increased hunger, unexplained weight loss, fatigue, blurred vision, slow-healing wounds, and frequent infections (Mouri & Badireddy, 2025). The longer the condition is kept untreated, the more severe it may get. Chronic hyperglycemia can lead to a variety of serious complications including damage to nerves leading to numbness, tingling, and pain in the hands, feet, and legs, as well as nephropathy (this is the damage to kidneys) leading to kidney failure (Čugalj Kern et al., 2022).The goal of hyperglycemia management in T2DM according to is to lower blood

sugar levels to a safe range. This can be achieved through the Lifestyle modifications healthy nutritional habit and physical activities of daily living; as well as adherence to both medication and medical check for monitoring blood sugar levels (CDC, 2024a; Johnson et al., 2020; Nwose et al., 2021).

2.4: Neuropathy and infection

Neuropathy is a term used for different conditions that affects the peripheral nervous system (it can affect multiple nerves). It can affect any part of the body, but it is most common in the hands and feet. Neuropathy can be caused by a variety of factors, including diabetes, injury, infection, and certain medications. There are different types of neuropathies, and one common classification system is based on the cause of neuropathy. Thus, diabetes peripheral neuropathy, which occurs in up to 50% of individuals with DM and increase the risk of DFU and infection (Bragg et al., 2024).

2.5: Symptoms and diagnosis of neuropathy

The symptoms of neuropathy vary depending on the type and severity of the condition. However, some symptoms are common (Fig 2). The diagnosis of neuropathy is often based on a medical history, physical examination, and neurological testing. Neurological testing can help to assess the function of the nerves and identify which nerves are affected. Other tests, such as blood tests and imaging studies, may also be used to rule out other possible causes of the symptoms (Bragg et al., 2024).

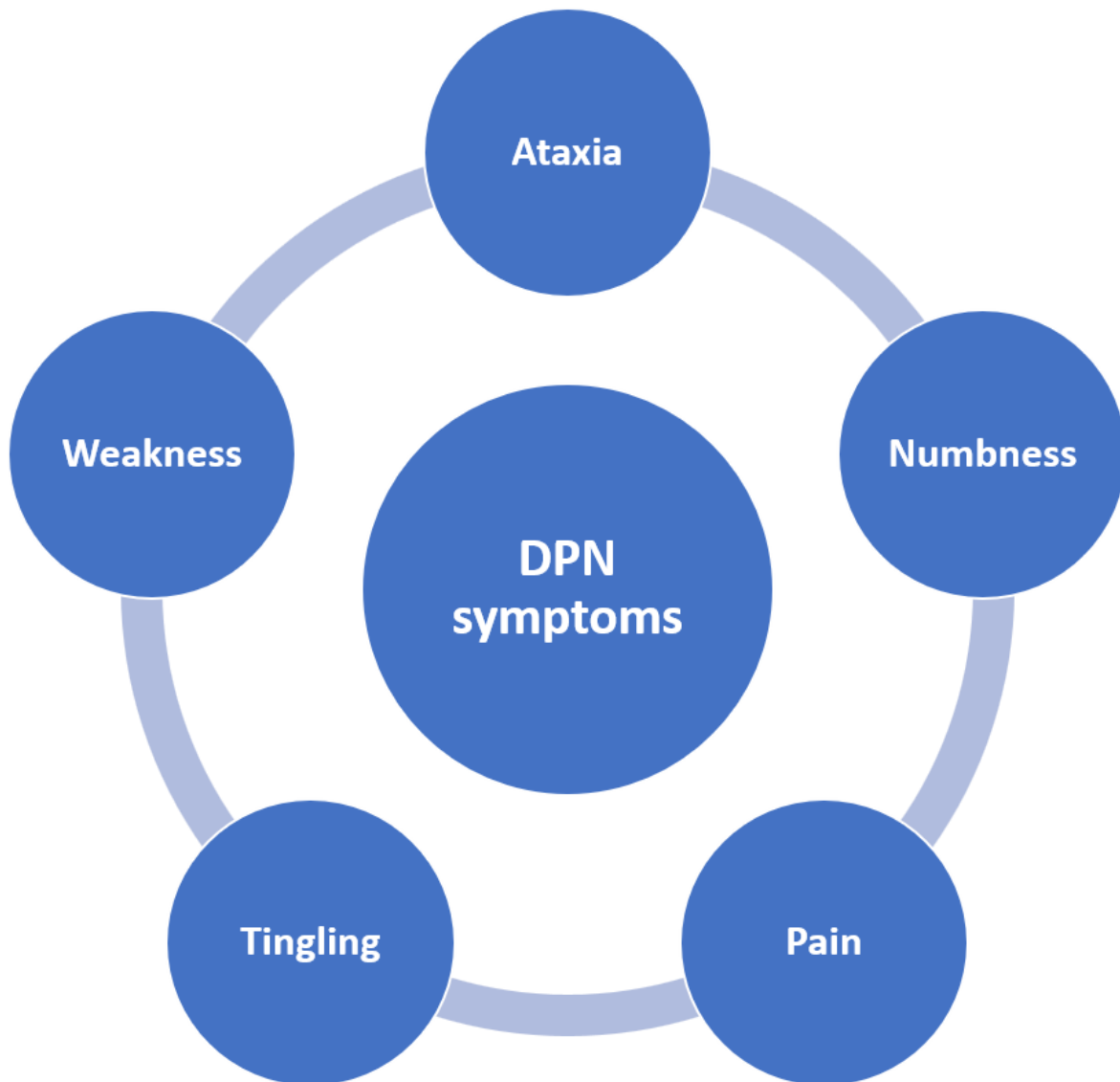


Fig 2:

Common symptoms of diabetic peripheral neuropathy

Treatment of neuropathy depends on the cause of the condition. In some cases, treating the underlying cause of the neuropathy may be enough to improve or resolve the symptoms. For instance, controlling blood sugar levels can help to prevent or slow the progression of DPN. In other cases, treatment may focus on managing the symptoms of neuropathy, such as medications to relieve pain, physical therapy to improve strength/coordination, and assistive devices to help with daily activities and lifestyle change, amongst others (Tesfaye, 2019).

From the primary healthcare perspective, preventive management is the regimen. Prevention of neuropathy has several options including management of blood pressure, healthy dietary habit,

limiting alcohol intake, and attention to foot health care, amongst others (CDC, 2024a). Report has indicated behaviour as a major factor (Johnson et al., 2020), hence health promotion in primary healthcare targeting behavioural change wheel is yet another preventive medicine regimen.

2.6: Epidemiology

DPN is a common and debilitating complication with an estimated 50% prevalence among individuals living with T2DM (Wang et al., 2022), which can significantly impact their quality of life. The development is a complex process involving multiple factors such as hyperglycemia, insulin resistance, oxidative stress, and inflammation. Additional factors are, age, obesity, hypertension and dyslipidemia can also contribute to the development of DPN. Despite the availability of effective treatment, DPN remains a significant burden to individuals and healthcare system. It is imperative to prioritize prevention, and early intervention means to reduce the incidence. Early detection, comprehensive management and by prioritizing these efforts, we can improve the outcome and enhance the quality of life for individuals with T2DM (Hicks & Selvin, 2019).

3: Advanced environment health factors in diabetes

3.1: Oxidative stress

Oxidative stress is a condition in which there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify them. ROS are highly reactive molecules that can damage cells and tissues. The body has a number of antioxidant defenses that help to neutralize ROS, but when these defenses are overwhelmed, oxidative stress can occur. ROS are produced by a number of normal cellular processes such as autophagy, mitochondrial respiration, inflammation, exposure to environmental toxins (Nwose & Bwititi, 2021).

3.2: Effects and consequences of oxidative stress.

Oxidative stress can damage cells and tissues in a number of ways such as ROS directly damaging DNA, RNA, and proteins, leading to mutations and functional impairments, or attacking lipids in cell membranes leading to lipid peroxidation and cell membrane damage – re: typically, the case in red blood cells in the concept of erythrocyte oxidative stress and impaired red cell deformability (Gyawali et al., 2015; Nwose et al., 2007).

Consequences of oxidative stress have been implicated in a number of diseases situations which contribute to the development and the progression of various diseases. Prolonged exposure to oxidative stress can lead to several disease situations. For instance, in **cardiovascular disease**, diabetes-induced oxidative stress can damage blood vessels and contribute to high blood viscosity that impairs blood flow to tissues (Nwose et al., 2007). further, diabetes-induced ROS could activate

apoptosis and transcription factor synthesis leading to the release of pro-inflammatory cytokines that amplifies inflammation and damaging of surrounding tissues (Nyamadzawo et al., 2025).

3.3: Impaired immune function in T2DM

Individuals with T2DM often experience impaired immune function, making them more susceptible to infections. chronic hyperglycemia has been identified as a key factor contributing to immune dysfunction in diabetes. As previously reported:

The pathophysiology of infection in T2DM is complex and multifactorial. Hyperglycaemia, which is a hallmark of T2DM, impairs the function of immune cells, such as neutrophil and macrophages, making it difficult for the body to fight off infections. Chronic inflammation and oxidative stress are common in T2DM, and they can further impair immune function and increase the risk of infections (Geerlings, 2008; Geerlings & Hoepelman, 1999). In patients with T2DM, insulin resistance and abnormal insulin secretion leads to hyperglycaemia. Some studies have also shown that metabolic disturbance like T2DM, increase the risk of cognitive decline and Alzheimer dementia, as Alzheimer dementia is also a risk factor for T2DM (Mouri & Badireddy, 2025). The impaired immune functions in T2DM can lead to a range of infections, including urinary tract infections, pneumonia, and skin and soft tissue infections (Mattina et al., 2024; Zhou & Lansang, 2024). These infections can be severe and life threatening and may require hospitalization and aggressive treatment. Infections can exacerbate hyperglycaemia and worsen diabetes control, creating a vicious cycle of infection and hyperglycaemia. In addition, to impaired immune function, other factors can contribute to increased risk of infections in T2DM, including poor wound healing, neuropathy, and cardiovascular disease. These factors can increase risk of infection by providing a portal of entry for pathogens and impairing the body's ability to fight infections (Joseph-Shehu & Ncama, 2019; Joshi et al., 1999).

It suffices that there is “framework for understanding and managing infectious diseases in immunocompromised patients (Risi & Tomascak, 1998). The model articulated the concepts of recognition and preventive measures (Figure 1). The report from Germany on healthcare workers' hand hygiene practices adds to the concept, especially in DFU management (von Lengerke et al., 2017), and this is further supported by recommendations “on infection prevention and control for immunocompromised individuals in health care facilities” (Commission for Hospital Hygiene and Infection Prevention (KRINKO), 2022). This is because their immune systems are not able to fight off infections as effectively as the immune systems of healthy people (Dropulic & Lederman, 2016)”.

4. Implications for primary healthcare

4.1: Overview

The primary healthcare service is generally focused on educational health promotion, preventive medicine and treatment (Uzochukwu, 2017). The concepts of health promotion and preventive medicine are most often interwoven around the impact of diabetes on immune system functions (Fig 3). However, the empirical data could be assessed to monitor the activities and achievements (Table 1).

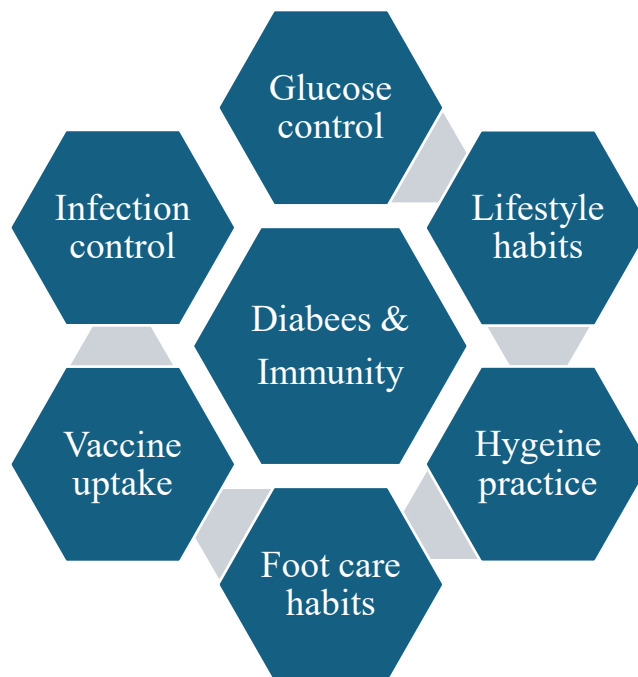


Fig 3: Concept of immune system and diabetes for primary healthcare (CDC, 2024b)

Table 1: Recommended care plan (CDC, 2024a).

Frequency	Activity
Daily	blood glucose test
	foot care
	Lifestyle
	Medication
Quarterly or biannual	HbA1c test
	GP consultation
Yearly	Vaccination
	full medical check*

*1. Lab tests - lipid profile, RFT; 2. Others - eye, foot, periodontal, & hearing.

4.2: Diagnosis of immune system dysfunction and management

The diagnosis of immune system dysfunction can be challenging, as it often involves ruling out other possible causes of the symptoms. A doctor will typically conduct a thorough medical history and physical examination, and may order a variety of tests, such as blood tests, imaging studies, and allergy testing (Grammatikos et al., 2020).

The treatment of immune system dysfunction depends on the type of dysfunction and the severity of the symptoms. In some cases, treatment may not be necessary. However, in other cases, treatment can involve medications, surgery, or other therapies. There is no way to completely prevent immune system dysfunction. However, there are several things that can be done to reduce the risk of developing the condition. These include maintaining a healthy lifestyle, vaccinating to protect against certain infections that can damage the immune system, managing stress, as well as regular medical check-up proper diagnosis and treatment (CDC, 2024a). Perhaps, it is pertinent to reiterate to importance of behaviour (Chin et al., 2019), especially because there are cases of individuals refusing to take up available medical services (Johnson et al., 2020).

4.3: Glycemic control

There is no gain saying that glycemic control is the optimal is the management of blood sugar levels, and poor glycemic control is a significant risk factor for various complications associated with T2DM including DFU (Abuhay et al., 2022; Chin et al., 2019; Johnson et al., 2020). Primary healthcare workers have major role to play (Dettori et al., 2005; International Diabetes Federation, 2022; Ugwu et al., 2020), including clinicians involved in prescription and administration of necessary medications (Bekele & Chelkeba, 2020).

Lifestyle modifications including nutritional therapy is part of diabetes self-management (Bekele & Chelkeba, 2020; International Diabetes Federation, 2022; Ugwu et al., 2020). In a study that investigated the effect of concomitant ‘education and dietary’ interventions on individuals living with DFU, results “showed that nutrition supplementation plus nutrition education significantly accelerated wound healing in DFU patients compared to those who just received a standard-of-care regimen” (Basiri et al., 2020). Another corroborating study emphasized micronutrient deficiency and recommends “assessment, through the development of a clinical-nutritional evaluation as part of wound management, could correct the nutritional status of the patient and an adequate feeding regimen according to the stage of evolution and clinical complications” (Sierra-Carrero Leandro et al., 2023).

5. Conclusion

This opinion paper draws attention to factors that influence infections in DFU. The role of environmental factors in exacerbating immune system dysfunction and oxidative stress among individuals living with diabetes is emphasized. The implications for primary healthcare including the need for health promotion to advance behavioural change in diabetes self-management is indicated.

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