

RESEARCH ARTICLE

DIABETIC FOOT AMONG INDIVIDUALS WITH DIABETES IN SAUDI ARABIA: A **COMPREHENSIVE REVIEW**

Mohammad Abdullah Aljuhani¹, Wassiem Mohsen Al-Hassan², Mohommad Eid Abdulaal², Majedah Ramadan Alaqabawi², Talal Saud Almutary², Adel Nezar Alakkam², Falah Suaib Almutairi², Amal Nezzar Alakkam³, Abdulmajed Farhan Al Farhan⁴, Mohammad Abdulaziz Althomali⁵, Yasser Ali Alkubaisy⁵ and Sultan Khalaf Almutairi⁶

- 1. Family and Community Medicine Department, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.
- 2. Department of Internal Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.
- Family Medicine Department, National Guard Hospital, Riyadh, Saudi Arabia. 3.
- 4. Department of Pharmaceutical Services, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.
- 5. Department of Ear, Nose, and Throat, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.
- 6. Plastic and Reconstructive Surgery Department, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

..... Manuscript Info

Abstract

..... Manuscript History Received: 25 March 2024 Final Accepted: 30 April 2024 Published: May 2024

Key words:-

Diabetic Foot, Diabetes Mellitus, Management, Saudi Arabia

Diabetic foot ulcers (DFUs) pose a significant health challenge globally, particularly in Saudi Arabia, where the prevalence of diabetes is among the highest in the world. This comprehensive review explores various aspects of DFUs among the Saudi population, including prevalence, risk factors, complications, management strategies, socioeconomic factors, and healthcare expenditure. The review highlights the significant impact of DFUs on healthcare costs and quality of life, emphasizing the need for effective prevention and treatment strategies. It discusses challenges and barriers in DFU management and identifies advances and innovations in care, such as multidisciplinary clinics, telemedicine, and research into novel therapies. Recommendations include implementing educational programs, capacity-building initiatives for healthcare professionals, cost-of-illness studies, and advocacy for public health policies prioritizing diabetic foot care. Overall, this review underscores the importance of tailored approaches to managing DFUs in the Saudi population to improve outcomes and reduce the burden of this debilitating complication of diabetes.

.....

.....

Copy Right, IJAR, 2024,. All rights reserved.

Introduction:-

Diabetes mellitus (DM) is a complex and chronic metabolic disorder characterized by the body's inability to effectively regulate blood glucose (or blood sugar) levels. This dysfunction arises from either a lack of insulin production (type 1 diabetes; T1DM) or insulin resistance, where cells fail to respond adequately to insulin (type 2 diabetes; T2DM). In addition to the two main types, there are other less common forms of diabetes, including gestational diabetes, which develops during pregnancy, and latent autoimmune diabetes in adults (LADA), which shares characteristics of both T1DM and T2DM. T1DM typically presents in childhood and has a strong genetic predisposition. In contrast, T2DM, the more prevalent form, is often associated with factors such as obesity,

Corresponding Author:- Mohammad Abdullah Aljuhani Address:- Family and Community Medicine Department, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

sedentary lifestyle, and advancing age, although it can also affect children and younger adults (1–3). Regardless of the specific type, uncontrolled diabetes can lead to a range of serious health complications, affecting the eyes, kidneys, nerves, and cardiovascular system.

The global burden of diabetes has reached alarming proportions, solidifying its position as a leading public health challenge (1,4,5). Recent decades have witnessed a dramatic surge in diabetes prevalence across developed and developing nations (6–8). Approximately 10% of the global population aged 20 to 79 years, totaling 537 million individuals, currently live with diabetes. Projections indicate that these figures will rise to 643 million by 2030 and 783 million by 2045(9). In 2021, diabetes was responsible for approximately 6.7 million deaths. Financially, diabetes accounted for at least USD 966 billion in health expenditures in 2021, marking a 316% increase over the last 15 years. Additionally, impaired glucose tolerance places an estimated 541 million people at elevated risk of developing T2DM(10–12)

With the highest estimated prevalence of diabetes in the Middle East and North Africa region at 18.1%, Saudi Arabia was found to be among the top ten countries with the highest prevalence of T2DM worldwide(12). The International Diabetes Federation(IDF) projects that by 2035, the incidence in the Gulf region alone will have increased by about 20% (Saudi Arabia: 24.5%; Kuwait: 23.2%; the United Arab Emirates [UAE]: 19.4%)(12). The increase in diabetes cases has a significant impact on the economy. It is estimated that the cost of diabetes-related treatment in Saudi Arabia was 17 billion SAR in 2014. Moreover, the yearly public healthcare spending on people with diabetes is expected to be ten times higher than that of those without the disease (13).

One of the major complications of diabetes that affects 18.6 million individuals globally each year, including 1.6 million in the US, is diabetic foot ulcers (DFU). In patients with diabetes, these ulcers are linked to a higher risk of death and account for 80% of lower extremity amputations. High blood sugar, peripheral vascular disease, and neuropathy—damage to the nerves—are some of the variables that contribute to the disorder(14,15).In Saudi Arabia, 3.3% of diabetic patients were found to have DF problems (16). Among DF patients, vasculopathy was observed in 33.1% (17). Peripheral artery disease (PAD) ranks as the third most common vascular complication among Saudi patients, with a prevalence rate of 2.41%, following cerebral vascular disease (10.2%) and coronary artery disease (23.6%). Moreover, among DFU patients, those with foot ulcers have a prevalence of PAD at 30%, while those with amputations show a higher prevalence at 54% (17).

A recent study at a Saudi Arabian tertiary care institution revealed that the total cost of managing DFU over ten years amounted to 6,618,043.3 Saudi Riyals (SAR), equivalent to 1,764,632.68 US Dollars (USD). This study estimated the annual cost of managing DFU at 661,804.3 SAR (176,481.2 USD), translating to 6,684.9 SAR (1,782.6 USD) per patient year. These figures underscore the considerable financial burden of DFU on healthcare resources and were derived from a patient sample at a single institution (18). Outpatient topical treatments represent approximately 51% of the total cost of DFU management. However, due to the prolonged healing process associated with DFU, surgical intervention may offer a more cost-effective solution. In cases requiring surgical management, surgical intervention accounts for about 95% of the total cost, with antibiotics constituting approximately 4% of the overall expenditure (18).

This review comprehensively examines various dimensions of diabetic foot (DF) complications within the Saudi population. It delves into multiple facets, such as the prevalence and incidence of the condition, associated risk factors, diagnostic methodologies, effectiveness of treatment strategies, socioeconomic influences, avenues for future research, recommendations for optimal approaches, and the consequential impact on both healthcare expenditure and quality of life. By addressing these diverse dimensions, the review seeks to advance the understanding and management of DF complications in Saudi Arabia, ultimately aiming to improve healthcare outcomes and enhance the well-being of affected individuals.

Methodology:-

Our research entailed a thorough exploration of databases, including Medline (via PubMed), Scopus, and Web of Science, employing a set of targeted keywords such as "Saudi Arabia," "Prevalence," "Diabetes," "Diabetic Foot," "Management," "Socioeconomic Factors," and "Healthcare." Inclusion criteria encompassed studies concentrating on the Saudi population, published in English, and comprising research endeavors spanning clinical trials, observational studies, systematic reviews, and meta-analyses, all investigating diverse facets of DF.

Epidemiology of Diabetes in Saudi Arabia

According to the World Health Organization (WHO), Saudi Arabia has the second-highest diabetes prevalence in the Middle East and the seventh-highest worldwide (19). The prevalence of DFU in the IDF Middle East and North Africa Region ranges between 5.0% and 20.0% (12). The prevalence of lower limb amputations (LLA) varied from 0.2% in Saudi Arabia to 60.0% in Jordan, with values often falling below 30.0% (13–16). Studies with sample sizes of fewer than 300 participants indicated higher values for LLA prevalence in this region. These studies might have occurred in specialist clinics or inpatient high-risk settings rather than community settings where one would anticipate a larger sample size(17).

From 2000 to 2011, the number of people aged 20-79 with diabetes increased from 996,700 to 2,759,600. The ageadjusted comparative prevalence of diabetes during this period decreased from 19.6% to 18.7%. In 2021, the number of individuals with diabetes rose to 4,274,100, with a prevalence rate of 20.4%. By 2030, researchers estimate that diabetes will affect approximately 5,631,000 people, with a projected prevalence of 21.4%. They expect that by 2045, the number of individuals with diabetes will further increase to 7,537,300.Diabetes Estimates and Projections in Saudi Arabia (2000-2045) are shown in **Figure 1**.

The IDF reported that in 2021, approximately 4.3 million individuals aged between 20 and 79 years in Saudi Arabia were diagnosed with diabetes, and researchers suggest that the number of diagnosed diabetes cases will reach 5.5 million by 2030. Notably, about 43.6% of people with diabetes in Saudi Arabia remain undiagnosed, and the percentage of diabetes-related deaths among individuals under 60 years old is almost 13.8%(12). Among individuals aged 20 to 79, women are anticipated to experience a slightly lower prevalence of diabetes (10.2% compared to 10.8% in men). The prevalence (%) estimates of diabetes by age and sex, IDF Middle East and North Africa Region in 2021 are shown in **Figure 2**,

Risk Factorsandcomplications of DF

Complications stemming from diabetes can be broadly categorized into two types. Macrovascular problems, involving long-term damage to major blood vessels, contribute to cardiovascular disorders, while damage to small vessels can lead to neuropathy, blindness, and kidney-related diseases (20,21). Diabetic neuropathy, affecting approximately 30% of adults with diabetes, particularly those over 50, damages peripheral nerves, increasing the risk of DFU and lower-extremity amputations (22,23).DFU, arising from multiple factors including peripheral neuropathy, atherosclerotic peripheral artery disease, and mechanical foot architecture modifications, is a significant concern in Saudi Arabia, with a prevalence rate of approximately 2.3% (24,25). Its occurrence is influenced by various factors such as reduced joint mobility, foot abnormalities, pressure or trauma, and peripheral vascular or neuropathic diseases (26).

The prevalence of DFU complications, notably infection, poses a significant risk, with about 25% of DFUs becoming infected and up to 20% of infected cases resulting in amputation (27,28). A cross-sectional study conducted at a tertiary center in Saudi Arabia found that over two-thirds of DFU patients presented with cellulitis and/or osteomyelitis, with a significant correlation between traditional remedies usage and higher Wagner scale grades and osteomyelitis. Furthermore, the study noted the chronic nature of these ulcers, with the mean duration of open wounds being 206.9 days, underscoring the urgency of effective management to prevent progression to gangrene and subsequent amputation (29,30).

In Riyadh, a study revealed that primary care providers lack optimal knowledge about diagnosing and managing DF infections, with only 53.9% performing a probe-to-bone test on DF patients with open wounds, indicating a gap in diagnostic practices (16). Another study highlighted a general lack of awareness among healthcare workers, diabetic patients, and their relatives in Saudi Arabia regarding DFUs, emphasizing the need for improved knowledge dissemination to facilitate early diagnosis and treatment (31). The impact of DFUs extends beyond physical health, significantly affecting patients' quality of life. Factors such as age, gender, education, occupation, smoking habits, duration of diabetes, and associated complications influence patients' perceived health-related quality of life, highlighting the multidimensional burden of DFUs (32).

While peripheral neuropathy is a common risk factor, specific factors contributing to DFU development include genetic predisposition, advancing age, obesity, sedentary lifestyle, and unhealthy dietary habits like smoking (33,34). Addressing these modifiable risk factors through lifestyle modifications and interventions is crucial for preventing DFU occurrence and reducing associated complications.

Management of DFU

To effectively treat DFU, a multifaceted approach is necessary, encompassing various interventions aimed at promoting wound healing and preventing complications. Offloading the wound is paramount, as evidenced by studies (35,36). This involves using regular saline or comparable dressings to maintain wound moisture, along with debridement when necessary. Additionally, antibiotic treatment may be required in cases of osteomyelitis or soft tissue infection, either with or without surgery (37,38). Optimal blood glucose management and assessment and treatment of peripheral arterial insufficiency are also crucial components of DFU management (39). In cases where nonsurgical offloading therapy fails to improve ulcer healing in neuropathic plantar ulcers, more invasive procedures such as joint arthroplasty, Achilles tendon lengthening, or metatarsal head resection may be considered (40,41). While adjunct therapies like recombinant growth factors or hyperbaric oxygen may be beneficial in some cases, caution is advised, especially in the presence of arterial insufficiency (42–44).

Healthcare professionals tasked with treating diabetic patients with ulcers often face challenging decisions regarding treatment strategies. Balancing the need for invasive procedures to salvage limbs against the risks associated with aggressive management in high cardiac-risk patients requires careful consideration (45,46).Legal implications also underscore the importance of prompt diagnosis and thorough treatment of DFUs to prevent adverse outcomes (47,48).

The International Working Group on the Diabetic Foot (IWGDF) plays a pivotal role in developing evidence-based guidelines for the prevention and treatment of DFU-related issues (49). The IWGDF infection guidelines emphasize the importance of prompt and appropriate management of severe infections. In cases of severe infection, prompt assessment for surgical intervention is crucial to remove necrotic tissue, alleviate compartment pressure, and drain abscesses. Examination for PAD is also essential, as immediate medical attention and revascularization may be warranted post-infection control. Broad-spectrum empirical antibiotic therapy via parenteral administration is recommended to combat common gram-positive and gram-negative bacteria, including obligatory anaerobes. Subsequent adjustments to the antibiotic regimen should be made based on culture and sensitivity results and clinical response to empirical therapy. Antibiotic therapy for soft-tissue infections typically spans one to two weeks. However, prolonged treatment may be necessary for severe illnesses or slow-clearing infections. In cases of osteomyelitis, where conservative antibiotic treatment is preferred over incision and drainage, treatment duration should be carefully considered. For minor soft tissue infections with superficial ulcers, prompt removal of necrotic tissue and calluses is essential. Initiation of oral antibiotics without delay is recommended to address common pathogens like Staphylococcus aureus and β-hemolytic streptococci, unless alternative infections are suspected (49,50). The IWGDF 2023 Risk Stratification System and corresponding foot screening frequency are shown in Table 1.

A holistic, team-based approach is essential for the successful prevention and treatment of diabetes-related foot conditions. Annual foot exams for diabetic patients, education on risk reduction strategies, and prompt treatment of infections or ulcers are key components of organized foot care. Access to podiatric care, appropriate footwear, and insoles is critical for mitigating risks (51,52).

The healing of foot ulcers is significantly influenced by ischemia in the lower extremities. Recommendations from the intersocietal IWGDF stress the importance of considering vascular imaging and revascularization in individuals with compromised blood flow (50). Immediate evaluation and management are advised for patients with ankle pressure less than 50 mm Hg or ABI less than 0.4, or in cases of TcpO2 less than 25 mmHg or toe pressure less than 30 mmHg. Revascularization aims to restore blood flow to the affected area, ideally through the artery supplying the injured region. However, careful consideration of individual factors, such as patient co-morbidities and local expertise, is necessary when selecting a revascularization procedure. Post-surgery, perfusion measurement is used to assess the success of revascularization. It is important to emphasize lifestyle modifications and pharmacological interventions to lower cardiovascular risk associated with PAD in diabetic patients, such as smoking cessation, blood pressure and cholesterol management, and the use of certain medications like anti-platelets, SGLT2-inhibitors, or GLP1-agonists.

Offloading is a critical aspect of treating foot ulcers induced by heightened mechanical stress, as outlined in the IWGDF Offloading guidelines (53). For neuropathic plantar ulcers, healthcare providers recommend using a non-removable knee-high offloading device such as a total contact cast or a detachable walker, fitted by a professional.

In cases where a non-removable device is not feasible or tolerated, a removable knee-high or ankle-high offloading device can serve as an alternative. Consistent wear of detachable devices is essential to reap their benefits.

Diabetes-related amputations pose a substantial challenge for the Saudi Ministry of Health. A 2018 Saudi statistical yearbook reported a concerning number of cases, with 1,280 in diabetic males and 765 in diabetic females (54). Addressing this issue necessitates a comprehensive assessment of knowledge, awareness, and practices related to DFU among healthcare staff, patients, and their families (31). Implementation of digital health solutions, such as patient-owned wound surveillance applications, can enhance DFU care by promoting patient engagement, monitoring, and communication with healthcare providers (55). Additionally, novel approaches like immunomodulatory hydrogels show promise in improving wound healing outcomes by addressing hyperglycemia-induced inflammation and reactive oxygen species elevation (56). Effective management of DFU requires addressing healthcare access, DFU risk, and outcomes, emphasizing the necessity of a multimodal approach to tackle these challenges (57).

Advancements in DFU Management in Saudi Arabia

Saudi Arabia, like many countries worldwide, faces significant health challenges associated with DFUs. However, recent advancements in DFU care, including innovative medications and methods, offer hope for improving patient outcomes. In line with global trends, DFUs remain a major health concern in Saudi Arabia. Yet, the introduction of novel therapies and approaches has led to significant progress in their management. Specialized multidisciplinary clinics dedicated to DFU therapy have emerged, bringing together podiatrists, vascular surgeons, endocrinologists, and infectious disease specialists to provide comprehensive care (29).

The adoption of advanced wound dressings, which offer mechanical protection, bacterial control, and moisture maintenance, has become increasingly popular, creating optimal conditions for healing. Additionally, the utilization of negative pressure wound therapy (NPWT) has gained traction and demonstrated effectiveness in DFU care (72). Some Saudi hospitals now offer hyperbaric oxygen therapy (HBOT), a treatment involving the inhalation of pure oxygen under pressure, which has proven efficacy (73).

The transformation of DFU management in Saudi Arabia has been further facilitated by the growth of telemedicine. Teleconsultations allow patients to receive professional advice and treatment remotely, eliminating the need for inperson hospital visits. Healthcare professionals can remotely monitor patients' wound healing progress, blood sugar levels, and other vital health indicators in real-time, enabling timely adjustments to treatment plans when necessary (74). Tele-education programs equip patients and caregivers with essential knowledge and skills for effective DFU management, thereby reducing complications and the need for amputations (29).

Saudi Arabia is actively engaged in research projects exploring novel therapies such as growth factors and stem cell therapy, as well as studies investigating the underlying causes and consequences of DFUs. Through these coordinated initiatives, Saudi Arabia aims to enhance patient care and outcomes nationwide, refining its DFU management strategy for the benefit of all (31,72).

Challenges and Barriers

Despite significant advancements in diabetes treatment over the past two decades, the management and treatment of DFU still face major barriers within the healthcare system. Addressing these challenges requires careful planning of teaching programs and access points to improve healthcare delivery and reduce disparities (58).

At the individual level, lack of knowledge about DF issues and delays in seeking medical help pose significant obstacles. Patients need to be educated about the importance of prompt medical attention for foot injuries, as diabetes increases the risk of infection and amputation. Moreover, the high costs associated with DFU care highlight the need for comprehensive coverage by safety net insurance providers (59,60).

The patient-provider relationship plays a crucial role in DFU therapy, but challenges in finding suitable healthcare providers and disruptions in continuity of care hinder optimal treatment. Solutions such as increasing the employment of community health workers and improving healthcare assessments can help address these gaps (61,62).

Access to medical equipment is another challenge, with deficiencies in medical supply firms often leading to difficulties in obtaining necessary supplies. Creating partnerships between pharmacies and healthcare providers to provide medical equipment may improve access, especially considering the frequent interaction between patients with diabetes and pharmacists (63,64).

Effective preventative treatment by primary care physicians is essential for limb salvage and the prevention of DFUs. The American Diabetes Association recommends regular foot examinations for diabetic patients at every doctor's appointment and a thorough foot inspection once a year at the latest, emphasizing the importance of identifying risk factors for DFUs (65). Preventive foot care, including self-foot inspection, professional foot examinations, and the use of suitable footwear, should be emphasized to both patients and medical professionals (65).

Furthermore, establishing a defined procedure and care route for initial DFU care is crucial to prevent misdiagnoses and delays in treatment. Educating patients and clinicians about standard protocols is essential to minimize delays in seeking care and improve outcomes (66).

In Saudi Arabia, like many other nations, several challenges hinder the prompt and effective treatment of individuals with DFUs. These challenges include a lack of hospitals, restricted access to specialist care, and insufficient knowledge about DFUs among patients and healthcare professionals (67,68). These factors contribute to delays in diagnosis and treatment, increasing the risk of complications and amputations. Addressing these issues requires attention to insurance and policy matters, alongside efforts to strengthen the healthcare infrastructure. Establishing specialist DF care centers and implementing national guidelines and protocols are essential for providing high-quality care (69). Public education programs are crucial for raising awareness about diabetes and foot care, emphasizing the importance of early ulcer detection (70). Additionally, ensuring comprehensive insurance coverage for podiatry, wound care, and specialty footwear is essential to enable patients to access necessary treatments. Clear reimbursement policies are also necessary to adequately compensate healthcare providers participating in DFU management (71).

Conclusions and Recommendations:-

In Saudi Arabia, DFUs present a significant health concern, especially given the higher prevalence among diabetes patients, often attributed to genetic predispositions, familial history of diabetes, and an aging population. Multidisciplinary care approaches, including sophisticated wound management techniques and specialized clinics, have emerged as crucial components in addressing DFUs. These efforts underline the importance of comprehensive care tailored to the specific needs of DFU patients, reflecting a growing awareness of the complexities involved in managing this condition.

Furthermore, the integration of telemedicine into DFU management signifies a promising advancement, enabling remote consultations and monitoring that enhance accessibility to specialized care, particularly in regions with limited healthcare infrastructure. This innovation not only facilitates timely interventions but also empowers patients and caregivers with essential knowledge for effective DFU management. Additionally, ongoing research initiatives, including investigations into novel therapies and advanced wound care products, demonstrate a commitment to continuously improving DFU treatment outcomes.

Looking ahead, future research endeavors in Saudi Arabia should prioritize several key areas to further enhance DFU management. This includes evaluating the effectiveness of educational programs aimed at raising public awareness about DF and preventive measures. Moreover, initiatives to strengthen healthcare professionals' expertise in DFU screening and management, alongside capacity-building efforts in primary healthcare settings, are essential for optimizing patient outcomes and reducing the incidence of DFU-related complications.

Technological advancements, such as molecular-level assessments and innovative therapy modalities, hold promise for transforming DFU care. By exploring cutting-edge technologies and treatment strategies, researchers aim to address the complex challenges associated with DFUs effectively. Additionally, community-based interventions and advocacy for public health policies prioritizing DF care are vital for reducing the prevalence of DFUs and improving the overall quality of life for individuals with diabetes in Saudi Arabia.

In summary, the management of DFUs in Saudi Arabia reflects a multifaceted approach encompassing multidisciplinary care, telemedicine integration, ongoing research initiatives, and community-based interventions. These efforts underscore a concerted commitment to enhancing DFU management strategies, with a focus on improving patient outcomes and reducing the burden of DFU-related complications on individuals and healthcare systems alike.

Risk category	Ulcer Risk	Definition	Suggested
			follow-up
0	Very low	No LOPS, no PAD, no deformity	Once a year
1	Low	LOPS or PAD	Once every
			6-12 months
2	Moderate	LOPS + PAD, or	Once every
		LOPS + foot deformity or	3-6 months
		PAD + foot deformity	
3	High	LOPS or PAD, and one or more of the following:	Once every
		- history of a foot ulcer	1-3 months
		- a lower-extremity amputation (minor or major)	
		- end-stage renal disease	
LOPS = Loss of Protective Sensation; PAD = Peripheral Artery Disease			

Table 1:- The IWGDF 2023 Risk Stratification System and corresponding foot screening frequency (75).







Figure 2:-.Prevalence (%) estimates of diabetes by age and sex, IDF Middle East and North Africa Region in 2021(12).

References:-

1. Abdelhaleem IA, Salamah HM, Alsabbagh FA, Eid AM, Hussien HM, Mohamed NI, et al. Efficacy and safety of imeglimin in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized clinical trials. Vol. 15, Diabetes and Metabolic Syndrome: Clinical Research and Reviews. 2021.

2. Ebada MA, Fayed N, Fayed L, Alkanj S, Abdelkarim A, Farwati H, et al. Efficacy of alpha-lipoic acid in the management of diabetes mellitus: A systematic review and meta-analysis. Iran J Pharm Res. 2019;18(4):2144–56.

3. Ko JH, Kim TN. Type 2 Diabetes Remission with Significant Weight Loss: Definition and Evidence-Based Interventions. J Obes Metab Syndr. Korean Society for the Study of Obesity; 2022 Jun;31(2):123.

4. Al-Lawati JA. Diabetes mellitus: A local and global public health emergency! Vol. 32, Oman Medical Journal. 2017. p. 177–9.

5. Al Hayek AA, Al-Saeed AH, Alzahrani WM, Al Dawish MA. Assessment of Patient Satisfaction with On-Site Point-of-Care Hemoglobin A1c Testing: An Observational Study. Diabetes Ther. 2021 Sep;12(9):2531–44.

6. Patterson CC, Harjutsalo V, Rosenbauer J, Neu A, Cinek O, Skrivarhaug T, et al. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989–2013: a multicentre prospective registration study. Diabetologia [Internet]. 2019 Mar 28;62(3):408–17. Available from: http://link.springer.com/10.1007/s00125-018-4763-3

7. Wang L, Gao P, Zhang M, Huang Z, Zhang D, Deng Q, et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in China in 2013. JAMA [Internet]. 2017 Jun 27;317(24):2515. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2017.7596

8. Dwyer-Lindgren L, Mackenbach JP, van Lenthe FJ, Flaxman AD, Mokdad AH. Diagnosed and Undiagnosed Diabetes Prevalence by County in the U.S., 1999–2012. Diabetes Care [Internet]. 2016 Sep 1;39(9):1556–62. Available from: https://diabetesjournals.org/care/article/39/9/1556/37094/Diagnosed-and-Undiagnosed-Diabetes-Prevalence-by

9. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. Elsevier; 2022 Jan;183:109119.

10. Magliano DJ, Chen L, Islam RM, Carstensen B, Gregg EW, Pavkov ME, et al. Trends in the incidence of diagnosed diabetes: a multicountry analysis of aggregate data from 22 million diagnoses in high-income and middle-income settings. lancet Diabetes Endocrinol. Lancet Diabetes Endocrinol; 2021 Apr;9(4):203–11.

11. Manne-Goehler J, Geldsetzer P, Agoudavi K, Andall-Brereton G, Aryal KK, Bicaba BW, et al. Health system performance for people with diabetes in 28 low- and middle-income countries: A cross-sectional study of nationally representative surveys. PLoS Med. PLoS Med; 2019 Mar;16(3).

12. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels, Belgium; 2021.

13. Al Sifri S, Aldahash R, de Luis Roman DA, Amin A, Camprubi-Robles M, Kerr KW, et al. Optimizing Diabetes Management Using a Low-Calorie Diet in Saudi Arabia: A Cost-Benefit Analysis. Diabetes Ther. Springer; 2024 Jan;15(1):155.

14. Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic Foot Ulcers: A Review. JAMA. JAMA; 2023 Jul;330(1):62–75.

15. McDermott K, Fang M, Boulton AJM, Selvin E, Hicks CW. Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers. Diabetes Care. Diabetes Care; 2023 Jan;46(1):209–11.

16. Alsheikh S, AlGhofili H, Alageel R, Ababtain O, Alarify G, Alwehaibi N, et al. Diabetic Foot Care: A Screening on Primary Care Providers' Attitude and Practice in Riyadh, Saudi Arabia. Medicina (B Aires). Multidisciplinary Digital Publishing Institute (MDPI); 2023 Jan;59(1).

17. Altoijry A, AlGhofili H, Alanazi SN, AlHindawi DA, AlAkeel NS, Julaidan BS, et al. Diabetic foot and peripheral arterial disease. Saudi Med J. Saudi Medical Journal; 2021 Jan;42(1):49–55.

18. Alshammary S, Othman SA, Alshammari E, Alarfaj MA, Lardhi HA, Amer NM, et al. Economic impact of diabetic foot ulcers on healthcare in Saudi Arabia: a retrospective study. Ann Saudi Med. King Faisal Specialist Hospital and Research Centre; 2020 Sep;40(5):425.

19. Tan SY, Mei Wong JL, Sim YJ, Wong SS, Mohamed Elhassan SA, Tan SH, et al. Type 1 and 2 diabetes mellitus: A review on current treatment approach and gene therapy as potential intervention. Diabetes Metab Syndr. Diabetes Metab Syndr; 2019 Jan;13(1):364–72.

20. Zhang X, Hou A, Cao J, Liu Y, Lou J, Li H, et al. Association of Diabetes Mellitus With Postoperative Complications and Mortality After Non-Cardiac Surgery: A Meta-Analysis and Systematic Review. Front Endocrinol (Lausanne). Frontiers Media S.A.; 2022 May;13.

21. Lunder M, Janić M, Šabovič M. Prevention of Vascular Complications in Diabetes Mellitus Patients: Focus on the Arterial Wall. Curr Vasc Pharmacol. Curr Vasc Pharmacol; 2019 Feb;17(1):6–15.

22. Basra R, Papanas N, Farrow F, Karalliedde J, Vas P. Diabetic Foot Ulcers and Cardiac Autonomic Neuropathy. Clin Ther. Clin Ther; 2022 Feb;44(2):323–30.

23. Walton DM, Minton SD, Cook AD. The potential of transdermal nitric oxide treatment for diabetic peripheral neuropathy and diabetic foot ulcers. Diabetes Metab Syndr. Diabetes Metab Syndr; 2019 Sep;13(5):3053–6.

24. Lazzarini PA, Cramb SM, Golledge J, Morton JI, Magliano DJ, Van Netten JJ. Global trends in the incidence of hospital admissions for diabetes-related foot disease and amputations: a review of national rates in the 21st century. Diabetologia: 2023 Feb;66(2):267–87.

25. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis[†]. Ann Med. Taylor & Francis; 2017 Feb;49(2):106–16.

26. Badahdah HM, Alshammari SF, Jassomah OM, Alharbi AJ, Alsiwed DT, Althagafi AA, et al. Knowledge, Attitude, and Practice of Foot Care and the Risk of Foot Ul cers in Diabetic Patients in Jeddah, Saudi Arabia: A Cross-Sectional S tudy. Cureus. 16(3 LB-badahdah2024knowledge).

27. Liu C, Shi WL, You JX, Li HY, Li L. An internet-based algorithm for diabetic foot infection during the COVID-19 pandemic. J Foot Ankle Res. Wiley-Blackwell; 2020 Jun;13(1).

28. The American Diabetes Association Releases the Standards of Care in Diabetes—2024.

29. Edrees KM, Alqahtani AI, Alkhatieb MT. Use of Traditional Remedies for Treatment of Diabetic Foot Ulcers: A Cross-Sectional Study at a Tertiary Center in Saudi Arabia. Int J Low Extrem Wounds. Int J Low Extrem Wounds; 2023;

30. Wang Y, Wang Y, Wang X, Zhao Y, Ruan S, Cao H. Effect of leukocyte-platelet fibrin-rich wound reconstruction followed by full-thickness skin grafting in the treatment of diabetic foot Wagner grade 4 ulcer gangrene (toe area). Platelets. Platelets; 2023;34(1).

31. Alsaigh SH, Alzaghran RH, Alahmari DA, Hameed LN, Alfurayh KM, Alaql KB. Knowledge, Awareness, and Practice Related to Diabetic Foot Ulcer Among Healthcare Workers and Diabetic Patients and Their Relatives in Saudi Arabia: A Cross-Sectional Study. Cureus. Cureus Inc.; 2022 Dec;14(12).

32. Ayed M Al, Ababneh M, Robert AA, Misfer N Al, Cruz M, Austria HC, et al. Factors Associated With Health-Related Quality of Life in Patients With Diabetic Foot Ulcer: A Cross-Sectional Study From Saudi Arabia. Cureus. Cureus Inc.; 2020 Jun;12(6).

33. Al-Ayed M, Moosa SR, Robert AA, Al Dawish M. Anxiety, depression and their associated risk factors among patients with diabetic foot ulcer: A two center cross-sectional study in Jordan and Saudi Arabia. Diabetes Metab Syndr. Diabetes Metab Syndr; 2021 Jan;15(1):237–42.

34. Metwally AS, Aljohani ZA, Maashi MI, Alrehaili AA, Alhejaili BM, Aljabri AM, et al. Knowledge, Attitude, and Practice Regarding the Risk of Diabetic Feet Among Diabetic Patients in the Madinah Region, Saudi Arabia. Cureus. Cureus; 2023 Dec;15(12).

35. Chatwin KE, Abbott CA, Boulton AJM, Bowling FL, Reeves ND. The role of foot pressure measurement in the prediction and prevention of diabetic foot ulceration-A comprehensive review. Diabetes Metab Res Rev. Diabetes Metab Res Rev; 2020 May;36(4).

36. Lazarou I, Fiska V, Mpaltadoros L, Tsaopoulos D, Stavropoulos TG, Nikolopoulos S, et al. Stepping Forward: A Scoping Systematic Literature Review on the Health Outcomes of Smart Sensor Technologies for Diabetic Foot Ulcers. Sensors (Basel). Sensors (Basel); 2024 Mar;24(6).

37. Chen Y, Wang X, Tao S, Wang Q, Ma PQ, Li ZB, et al. Research advances in smart responsive-hydrogel dressings with potential clinical diabetic wound healing properties. Mil Med Res. Mil Med Res; 2023 Dec;10(1).

38. Sathyaraj WV, Prabakaran L, Bhoopathy J, Dharmalingam S, Karthikeyan R, Atchudan R. Therapeutic Efficacy of Polymeric Biomaterials in Treating Diabetic Wounds-An Upcoming Wound Healing Technology. Polymers (Basel). Polymers (Basel); 2023 Mar;15(5).

39. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. Ann N Y Acad Sci; 2018;1411(1):153–65.

40. Wendland DM, Kline PW, Bohnert KL, Biven TM, Sinacore DR. Offloading of Diabetic Neuropathic Plantar Ulcers: Secondary Analysis of Step Activity and Ulcer Healing. Adv Skin Wound Care. Adv Skin Wound Care; 2023 Apr;36(4):194–200.

41. Hochlenert D, Bogoclu C, Cremanns K, Gierschner L, Ludmann D, Mertens M, et al. Sensor-Assisted Wound Therapy in Plantar Diabetic Foot Ulcer Treatment: A Randomized Clinical Trial. J Diabetes Sci Technol. J Diabetes Sci Technol; 2023;

42. Capó X, Monserrat-Mesquida M, Quetglas-Llabrés M, Batle JM, Tur JA, Pons A, et al. Hyperbaric Oxygen Therapy Reduces Oxidative Stress and Inflammation, and Increases Growth Factors Favouring the Healing Process of Diabetic Wounds. Int J Mol Sci. Multidisciplinary Digital Publishing Institute (MDPI); 2023 Apr;24(8).

43. Chen RF, Lin YN, Liu KF, Lee CC, Hu CJ, Wang CT, et al. Compare the effectiveness of extracorporeal shockwave and hyperbaric oxygen therapy on enhancing wound healing in a streptozotocin-induced diabetic rodent model. Kaohsiung J Med Sci. Kaohsiung J Med Sci; 2023 Nov;39(11):1135–44.

44. Kuo Y-R. Comparing Extracorporeal Shockwave and Hyperbaric Oxygen Therapy in Enhancing Wound Healing in a Streptozotocin-Induced Diabetic Rodent Model. Plast Reconstr Surg Glob Open. Wolters Kluwer Health; 2022 Oct;10(10 Suppl):26–26.

45. Mens MA, de Geus A, Wellenberg RHH, Streekstra GJ, Weil NL, Bus SA, et al. Preliminary evaluation of dual-energy CT to quantitatively assess bone marrow edema in patients with diabetic foot ulcers and suspected osteomyelitis. Eur Radiol. Springer; 2023 Aug;33(8):5645.

46. Ding X, Yuan Y, Xu H, Jing Z, Lu H, Wang Y, et al. Analysis of Risk Factors for in-hospital Death in Elderly Patients with TEXAS Stage 3 and 4 Diabetic Foot Ulcers after Tibial Transverse Translation: A Case–Control Study. Orthop Surg. Wiley-Blackwell; 2023 Dec;15(12):3272.

47. Ferreira G, Bernardo AC, Carvalho A, Pereira MG. Relax to Heal? Perspectives of Patients with Diabetic Foot Ulcers and Health Professionals on Relaxation Sessions for Wound Healing. Adv Skin Wound Care. Adv Skin Wound Care; 2023 Jun;36(6):1–10.

48. Brennan MB, Allen GO, Ferguson PD, McBride JA, Crnich CJ, Smith MA. The Association Between Geographic Density of Infectious Disease Physicians and Limb Preservation in Patients With Diabetic Foot Ulcers. Open Forum Infect Dis. Oxford University Press; 2017 Nov;4(1).

49. Lipsky BA, Senneville É, Abbas ZG, Aragón-Sánchez J, Diggle M, Embil JM, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. Diabetes Metab Res Rev; 2020 Mar;36 Suppl 1(S1).

50. Fitridge R, Chuter V, Mills J, Hinchliffe R, Azuma N, Behrendt CA, et al. The intersocietal IWGDF, ESVS, SVS guidelines on peripheral artery disease in people with diabetes mellitus and a foot ulcer. J Vasc Surg. J Vasc Surg; 2023 Nov;78(5):1101–31.

51. Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ, Lipsky BA. Practical Guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev. Diabetes Metab Res Rev; 2020 Mar;36 Suppl 1(S1).

52. van Netten JJ, Raspovic A, Lavery LA, Monteiro-Soares M, Paton J, Rasmussen A, et al. Prevention of foot ulcers in persons with diabetes at risk of ulceration: A systematic review and meta-analysis. Diabetes Metab Res Rev. Diabetes Metab Res Rev; 2024 Mar;40(3).

53. Bus SA, Armstrong DG, Gooday C, Jarl G, Caravaggi C, Viswanathan V, et al. Guidelines on offloading foot ulcers in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. Diabetes Metab Res Rev; 2020 Mar;36 Suppl 1(S1).

54. Alharbi M, Sulaiman A. Foot care knowledge, attitude and practices of diabetic patients: A survey in Diabetes health care facility. J Fam Med Prim Care. Medknow; 2022;11(7):3816.

55. Lo ZJ, Chong B, Tan E, Ooi D, Liew H, Hoi WH, et al. Patients, carers and healthcare providers' perspectives on a patient-owned surveillance system for diabetic foot ulcer care: A qualitative study. Digit Heal. SAGE Publications; 2023 Jan;9.

56. Qi X, Cai E, Xiang Y, Zhang C, Ge XX, Wang J, et al. An Immunomodulatory Hydrogel by Hyperthermia-Assisted Self-Cascade Glucose Depletion and ROS Scavenging for Diabetic Foot Ulcer Wound Therapeutics. Adv Mater. Adv Mater; 2023 Nov;35(48).

57. Bonnet JB, Sultan A. Social Deprivation, Healthcare Access and Diabetic Foot Ulcer: A Narrative Review. J Clin Med. Multidisciplinary Digital Publishing Institute (MDPI); 2022 Sep;11(18).

58. Tan TW, Crocker RM, Palmer KNB, Gomez C, Armstrong DG, Marrero DG. A qualitative study of barriers to care-seeking for diabetic foot ulceration across multiple levels of the healthcare system. J Foot Ankle Res. BioMed Central Ltd; 2022 Dec;15(1):1–8.

59. Crocker RM, Tan TW, Palmer KNB, Marrero DG. The patient's perspective of diabetic foot ulceration: A phenomenological exploration of causes, detection and care seeking. J Adv Nurs. J Adv Nurs; 2022 Aug;78(8):2482–94.

60. Fayfman M, Schechter MC, Amobi CN, Williams RN, Hillman JAL, Alam MM, et al. Barriers to diabetic foot care in a disadvantaged population: A qualitative assessment. J Diabetes Complications, J Diabetes Complications; 2020 Dec;34(12).

61. Bubun J, Yusuf S, Syam Y, Hidayat W, Majid S. Validity and Reliability Diabetic Foot Check-up as a Simple Screening Test of Diabetic Foot Ulcers in a Community. Int J Low Extrem Wounds. Int J Low Extrem Wounds; 2023;

62. Gray KE, Hoerster KD, Taylor L, Krieger J, Nelson KM. Improvements in physical activity and some dietary behaviors in a community health worker-led diabetes self-management intervention for adults with low incomes: results from a randomized controlled trial. Transl Behav Med. Transl Behav Med; 2021 Dec;11(12):2144–54.

63. Nabulsi NA, Yan CH, Tilton JJ, Gerber BS, Sharp LK. Clinical pharmacists in diabetes management: What do minority patients with uncontrolled diabetes have to say? J Am Pharm Assoc. Elsevier B.V.; 2020 Sep;60(5):708–15.

64. Dellogono A, Dawson A, Piers-Gamble M, Varghese J, Lewicki L. Lost in Transition: Pharmacist Roles in Identifying and Evaluating Medication-Related Problems During Hospital Discharge Follow-up Visits in a Primary Care Setting. https://doi.org/101177/2150132720917297. SAGE PublicationsSage CA: Los Angeles, CA; 2020 May;11.

65. Association AD. 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes. Diabetes Care. 2020;43(Supplem:S135–51.

66. Mekonen EG, Gebeyehu Demssie T. Preventive foot self-care practice and associated factors among diabetic patients attending the university of Gondar comprehensive specialized referral hospital, Northwest Ethiopia, 2021. BMC Endocr Disord. BMC; 2022 Dec;22(1).

67. Alslamah T, Abalkhail A. The National Strategies for and Challenges in Infection Prevention and Control of the Healthcare System in the Kingdom of Saudi Arabia (Review Study). Vaccines. Multidisciplinary Digital Publishing Institute (MDPI); 2022 Aug;10(8).

68. Gurajala S. Healthcare System in the Kingdom of Saudi Arabia: An Expat Doctor's Perspective. Cureus. Cureus Inc.; 2023 May;15(5).

69. Zhu X, Lee ES, Lim PXH, Chen YC, Chan FHF, Griva K. Exploring barriers and enablers of self-management behaviours in patients with diabetic foot ulcers: A qualitative study from the perceptions of patients, caregivers, and healthcare professionals in primary care. Int Wound J. Wiley-Blackwell; 2023 Sep;20(7):2764.

70. Casagrande SS, Park J, Herman WH, Bullard KM. Health Insurance and Diabetes. Diabetes Am. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); 2023 Dec;

71. Jafary M, Amini M, Sanjari M, Aalaa M, Goudarzi Z, Najafpour Z, et al. Comparison home care service versus hospital-based care in patients with diabetic foot ulcer: an economic evaluation study. J Diabetes Metab Disord. J Diabetes Metab Disord; 2020 Jun;19(1):445–52.

72. Alkalash SH, Alnashri FH, Alnashri AI, Alghubayshi KA, Alsumaydi MA, Alzubaidi WS, et al. Knowledge, Attitude, and Practice of Adult Diabetics Regarding Diabetic Foot Ulcers: A Cross-Sectional Study in Saudi Arabia. Cureus. Cureus Inc.; 2024 Feb;16(1).

73. Tabanjeh SF, Al-Malki T, Alhazzani AR, Robert AA. Management of Diabetic Foot Ulcers Using Topical Oxygen Therapy: A Case Series. Curr Diabetes Rev. Curr Diabetes Rev; 2022 Oct;18(6).

74. Yammine K, Estephan M. Telemedicine and diabetic foot ulcer outcomes. A meta-analysis of controlled trials. Foot. Churchill Livingstone; 2022 Mar;50:101872.

75. Home - IWGDF Guidelines.