The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 2, Issue 3, 2024

MEDICATION USE, MANAGEMENT PRACTICES, AND HEALTHCARE CONSULTATION PATTERNS IN ADULT DIABETIC FOOT ULCER PATIENTS:
A CROSS-SECTIONAL STUDY AT GAMBAT INSTITUTE OF MEDICAL SCIENCES, KHAIRPUR, SINDH, PAKISTAN

Farooque Ali Bhatti

Department of Zoology, University of Sindh, Jamshoro Pakistan

alifarooque1@gmail.com

DOI: https://doi.org/10.5281/zenodo.19946918

Keywords
Monotherapy, Combination Therapy, Wagner Grade, Medical Consultation, Hakeem, Comorbidities, Pakistan, Sindh

Article History
Received: 23 November, 2024
Accepted: 20 December, 2024
Published: 28 December,2024

Corresponding Author: *
Farooque Ali Bhatti

Abstract

DFU complications and progression in resource-limited settings are mediated by poor medication compliance, delayed consultation and health-seeking behaviour amongst non-specialist professionals. This is compounded in rural Pakistan by low access to healthcare services, health literacy and a trust in traditional healers.

Objective: The effect of type of medication (monotherapy vs. combination therapy) used to treat diabetes, provider consulted, frequency of follow-up visits, number of comorbidities, impact of psychological distress and association of medication type with Wagner ulcer grade in adult DFU patients.

Methods: A non-selective consecutive cross-sectional survey of 100 adults with DFU at GIMS OPD, Khairpur (June 2021 - January 2022). A questionnaire included medication type, type of health care service provider, consultation frequency, psychopathology and comorbidities. Wagner grading was done via anatomical inspection. Collected data was analysed in SPSS v20.2.0.

Results: 69% took Glucophage only; 28% combination Glucophage/insulin; 3% took a full range of medications. Initially consulted a diabetologist (32%), general physician (31%), orthopaedician (12%) or local Hakeem/wound specialist (25%). 9% attended every month, 48% irregularly. 76% suffered from a comorbidity: nephropathy/systemic (26%), retinopathy (20%), complications of muscle (14%), renal failure (4%), pain in muscle/joint with numbness (12%). 77% worried about being dependent on family. Cross tabulation revealed monotherapy patients were mostly in Wagner Grade 3-5, while those using combination therapy were in Grade 1-2.

Conclusion: Monotherapy, erratic follow-up, non-specialist as first point of care, high burden of other illnesses and high psychological distress in DFU patients describes the situation in rural Sindh. Standardized patient care, cost-effective procurement of combination therapy, and educator-led patients care are needed.

I. INTRODUCTION

Type 2 diabetes mellitus (DMT2) is a relentless progressive disease with lifelong drug therapies needed to ensure glycemic control and avoid complications. Metformin (Glucophage, Pakistan) is universally recommended as initial oral hypoglycemic agent; it curbs hepatic glucose production, and increases peripheral insulin sensitivity and response.

Diabetic foot ulcer (DFU) is a marker of end-organ damage. DFU has results from pre-ulceration, poorly managed or inadequately escalated pharmacotherapy, often for years.4 The medications DFU patients were on prior to their ulceration, and whether those medications were appropriate - is the key to understanding DFU's development, and its progression to advanced Wagner grades. In rural Pakistan, medication management is dramatically hindered by financial, cultural and pharmaceutical availability issues: the high cost of self-administered insulin, cultural beliefs about insulin, sporadic drug supplies, and inertia to escalate medication keep patients on sub-optimal medications for years.5

Factors influencing DFU include consultation behaviours. Initial consultation source determines whether debridement is provided, antibiotics are prescribed, offloading is provided and a referral for specialist treatment is provided. In rural Sindh, Hakeems (traditional healers) are widely respected and sought out as primary health-care providers for foot disease, resulting in considerable lag in starting evidence-based treatment for DFU. Poorer medical care-seeking and follow-up allows uncontrolled hyperglycemia, and the burden of other diabetes-related complications, to accumulate; each case of DFU is complicated by this factor.

The psychological impact of DFU, especially fear of amputation and a fear of becoming a financial burden, is an undercarried, yet crucial barrier to seeking help and undergoing treatment in South Asia.6 This paper, the second of four in the series derived from an MPhil thesis (University of Sindh, 2022) by Farooque Ali Bhatti, examines these aspects in detail for 100 DFU patients at GIMS, Khairpur.

1.1 Aims and Objectives

Objectives: (1) establish the pattern of the usage of medication for TYPE 2 diabetes mellitus (DMT2); (2) determine the initial place of medical consultation for DFU; (3) assess the frequency of follow-up visits; (4) record the patients' co-morbidities; (5) understand the psychological burden of DFU; and (6) test the association of type of medication with the Wagner ulcer category.

II. LITERATURE REVIEW

Metformin has been the initial drug of choice for DMT2 for at least two decades. It is safe, effective, cardiac-neutral and affordable, making it the drug of choice for initial therapy worldwide.2,3 But beta-cell function steadily degrades in DMT2 and studies suggest that lost almost half the patients on metformin monotherapy achieve HbA1c targets after 3 years.7 Therefore, treatment escalation should be expected and prepared for. This is often not the case in Pakistan. Khowaja et al.'s national survey revealed physicians' reluctance to escalate therapy beyond metformin treatment, with insulin delayed 3-5 years beyond when it should be started.8

The ramifications of medication undertreatment are written in the severity of DFU. Poorer glycemic control (reflected in HbA1c values above 8%) is found to be associated with higher Wagner grades at DFU onset, slower healing, and more infection, and is a significant risk factor for amputation.9,10 In contrast, patients receiving multiple-adjunct therapy (including insulin) generally present with lower HbA1c and lower-grade DFU. An Indian study (2008) by Shankhdhar et al. found DFU patients using insulin presented with lower Wagner grades than other patients using oral monotherapy alone, suggesting that the early introduction of insulin is protective.11

DFU patients' initial consultation point may be crucial. GPs may prescribe antibiotics without Wagner grading or ABI measurements; orthoad surgeons may correct the wound without controlling blood sugars; and Hakeems (traditional practitioners) may apply unproven herbal concoctions while delaying use of systemic antibiotics and/or offloading.12 In rural Pakistan where access to specialist diabetologists is low, many patients spend precious weeks of ulceration under the care of non-specialists, in which time the lesion deepens and infection gets established.

Follow-up rates are recognised as a predictor of diabetes outcomes. The ADA recommends

quarterly HbA1c and annual foot-checks for non-euglycemic patients and all diabetics, respectively.3 In Pakistan, compliance with these targets is poor: "only 22% of DMT2 patients attended regularly scheduled follow-ups", according to one Karachi-based study.13 This symptom-driven mode of care allows deterioration in glycaemic control and progression of neuropathy to develop unchecked until the occurrence of complications such as DFU makes the failure of prevention inescapable.

DFU patients with DMT2 have virtually ubiquitous comorbidities. Diabetic kidney disease (20-40% prevalence) narrows the scope of drug therapy, slows healing and creates drug interactions; diabetic retinopathy (up to 35% after 10 years) blinds the sufferer to their own foot inspection; and musculoskeletal complications limit the pain tolerance to comply with wound offloading.14,15 Each of these comorbidities is a result of the cumulative contribution of hyperglycaemia to end-organ damage, which in turn provokes the complexity and cost of treating DFU.

Psychology of DFU is becoming increasingly recognised. Amputation fears, stigma over disability and fears of loss of income are the primary fears in South Asian DFU patients.16 These fears preclude seeking care; reduce compliance with treatment and form a vicious circle of behaviour where the amputation feared is precisely what a non-healing ulcer results in.17

III. MATERIALS AND METHODS

Design and Place of Study

A non-random, consecutive cross-sectional study at the OPD of GIMS, Khairpur, Sindh from June 2021 to January 2022 for an MPhil thesis under the supervision of Prof Dr. Tahira Jabeen Ursani from the Department of Zoology, University of Sindh, Jamshoro.

Participants

A total of 100 consecutive adult diabetics with type 2 diabetes (DMT2) with active DFU or DFU in the past six months were recruited. Five diabetologists, 11 orthopaedicians, 12 general physicians and 7 Hakeems from district Khairpur were also interviewed to validate patient data on their consultations. The details of inclusion and exclusion criteria can be found in Paper 1 of this series.

Data Collection

An electronic questionnaire captured: type of medication(s) for diabetes; first point of contact for medical care; rate of attending the doctor or hospital; other medical conditions; and self-reported psychological distress from fear of burden on the family. Wagner grade (0-5) was allocated at physical examination by the senior researcher by the Meggit-Wagner classification.

Statistical Analysis

Data analysis done using SPSS (IBM) v20.2.0. Described using frequencies and percentages. Cross-tabulation of ulcer severity (Wagner grade) by medication type to determine relationships between medications and ulcer severity. Data presented without inferential statistics, given a descriptive nature of a cross-sectional study.

Ethical Considerations

All participants given written informed consent. Data from patients completely anonymised. Approval obtained from the administration of GIMS. Ethically conducted as per The Code of Ethics by The World Medical Association.

IV. RESULTS

Table 1: Anti-Diabetic Medication Type Among DFU Patients (n=100)

Medication Type	Frequency (n)	Percentage (%)
Monotherapy: Glucophage only	69	69.0%
Dual therapy: Glucophage + Insulin	28	28.0%

Combination + Supplementary drugs	3	3.0%
Total	100	100.0%

The types of anti-diabetic medications used by the 100 DFU patients are given in Table 1. The overwhelming majority (69 patients; 69%) took a single medication (Glucophage - metformin). 28 patients (28%) were on a double drug therapy with Glucophage and insulin. Few patients (3%) were on a total three drug or supplementary administration of anti-diabetic drugs targeting PVD or neuropathy, as well as Glucophage and insulin.

Table 2: First Point of Healthcare Consultation Among DFU Patients (n=100)

Provider Type	Frequency (n)	Percentage (%)
Diabetologist	32	32.0%
General Physician	31	31.0%
Orthopaedician	12	12.0%
Local Hakeem / Wound Specialist	25	25.0%
Total	100	100.0%

The first kinds of doctors visited by DFU patients is presented in Table 2. Diabetologist (32%), general physician (31%), orthopaedician (12%) and local Hakeem or traditional wound specialist (25%) were the first of visit by patients, respectively. Overall, 68% of the patients did not consult a specialist diabetologist first.

Table 3: Frequency of Doctor/Hospital Visits Among DFU Patients (n=100)

Visit Frequency	Frequency (n)	Percentage (%)
Monthly	9	9.0%
Once every three months	41	41.0%
Irregular / Not regular	48	48.0%
Uncertain	2	2.0%
Total	100	100.0%

Table 3 shows that only 9% of patients were seeing their physician every month, as recommended for DM patients with complications. One-third of participants had seen a doctor once in three months, 48% had seen one randomly and 2% did not know how often they had seen one. These tend to be mainly reactive visits based on DFU severity and related symptoms.

Table 4: Comorbidities Reported Among DFU Patients (n=100)

Comorbidity	Frequency (n)	% of Total (n=100)
No additional comorbidity	24	24.0%
Nephropathy / Multiple systemic	26	26.0%
Retinopathy	20	20.0%
Muscular dystrophy / Muscle pain	14	14.0%
Severe renal failure	4	4.0%
Muscle / joint pain with numbness	12	12.0%
Total with any comorbidity	76	76.0%

As shown in Table 4, 76% (76) of 100 DFU patients had one or more other physiologically-related complications of DMT2. These included: 26% patient with nephropathy and multiple complications, 20% with retinopathy, 14% with sudden muscular dystrophy or abnormal muscle pain, 4% with renal failure, and 12% complained of muscular and joint pain with numbness. Just 24% have DFU as only complication of DMT2.

Table 5: Psychological Burden — Fear of Being a Family Burden (n=100)

Response	Frequency	Percent (%)	Cumulative %
Yes — Worried	77	77.0%	77.0%
No — Not Worried	23	23.0%	100.0%
Total	100	100.0%	—

Table 5 shows the results of the question, "Are you concerned about becoming a family burden because of DFU or amputation?" Seventy seven percent of patients answered yes, and were clearly distressed about this. Only 23% were not worried - some believing it was their destiny. This data is extracted from table 4.1 in SPSS, in the parent thesis.

Table 6: Cross-Tabulation of Medication Type with Wagner Ulcer Grade (n=100)

Wagner Grade	Total (n)	Monotherapy: Glucophage Only (n=69)	Dual: Glucophage + Insulin (n=28)	Combination + Supplementary (n=3)
Grade 0	1	1	0	0
Grade 1	11	5	6	0
Grade 2	32	17	11	3
Grade 3	33	25	7	0
Grade 4	14	13	1	0

Grade 5	8	7	1	0
Total	100	69	28	3

The cross-tabulation of medication type vs. Wagner grade is reported in Table 6 below - directly from the parent thesis data. Among the 69 monotherapy patients: 25 (36.2%) were Grade 3, 13 (18.8%) Grade 4, and 7 (10.1%) Grade 5. By contrast, of the 28 combination therapy patients, 6 (21.4%) had a grade 1 and 11 (39.3%) grade 2 ulcer, with only 2 at grade 4-5 combined. The 3 patients using combination therapy were all at Grade 2 but none at 4-5.

V. DISCUSSION

This study reveals an apparent failure of the diabetes drug treatment of DFU patients in Khairpur, Sindh. The components of our study (type of drug, total consultations, follow up, complications, psychological distress, and relationship between medications used and ulcer severity), are all different teaching points for an average failure of care. Overall they demonstrate how a lack of optimal treatment of DMT2 in the low-resource rural environment leads to the potentially life-threatening ulcers.

Stream of Monotherapy: Drug Fail you can Bank On

The fact that 69% of DFU patients were on Glucophage monotherapy is likely not surprising in itself, in a low-income rural Pakistani community. But when looking at the average HbA1c (described in Paper 3 of this series) of 9.58%, and the fact that 62% of the patients' HbA1c is above 8% (defined as uncontrolled diabetes in literature), it is a concern. The combination of the high proportion on monotherapy, and the relatively high mean HbA1c is a drug gap. Guidelines for diabetes management outline that if the HbA1c is over 7% on metformin, therapy is escalated.2,3 With an average HbA1c of 9.58%, this population is not only a little way off target; they are highly susceptible to glucose intolerance on a drug therapy that they were never going to be adherent to in this stage of disease.

The prevalence of monotherapy is because of a number of factors. First, the most obvious reason is that insulin is unaffordable to this population, since in Pakistan, insulin is more than just insulin, it's insulin, plus syringes and needles, and - crucially - the refrigeration required to store insulin, a rarity in the rural homes of Khairpur. For the 54% of the patients from daily wage families (Paper 1) these costs are beyond their means. Second, the common myths in the rural Sindh about insulin "causes blindness", must be evoked: the reluctance to "start the therapy once started" and "insulin is the last line of treatment" (in all cases invoked to be against the use of insulin)8, are rampant in the rural Sindh and have been reported in Pakistan.8

These impacts of the monotherapy hegemony are seen in Table 6. The proportion of more severe ulcers in the mono therapy group is towards: Grade 3 (36.2%), Grade 4 (18.8%) and Grade 5 (10.1%). In the group who have used combination therapy (methylmetformin and insulin) the distribution is skewed in favour of: Grade 1 (21.4%) and Grade 2 (39.3%). This is no accident. The addition of medications to a metformin-only therapy protocol, by improving the blood glucose, allows for a longer time before the development of pre-diabetic neuropathy (PDN) and pre-diabetic vascular disease (PVD) eventually occurs and thereby the development of foot ulceration. The findings of the current study reinforce the findings from the United Kingdom Prospective Diabetes Study (UKPDS) that was done 20 years ago that showed a 1% reduction in HbA1c is associated with a reduced risk of microvascular complications.19 In this study population with an average HbA1c of 9.58%, the potential therapeutic impact of escalation is huge.

There are implications at several levels. At site level, GIMS and other district hospitals should strive to make HbA1c testing at each visit to their

diabetes OPD a routine (not desirable) practice, with standards on when to escalate medications, and individual accountability. At the system level, the state needs to enter into a discussion to provide insulin at subsidised prices to the district facilities, so that patients on daily wage can afford to use two insulins. At the community level, pharmacists and community health workers need to be engaged to clear the gaps on insulin myths, and compliance. Nothing too sophisticated, affordable, with worked out benefits, and this data.

First consultation the 25% of DFU patients going to Hakeems

The consultation patterns data reveals that 25% of the Khairpur DIU patients consulted a local traditional wound specialist (Hakeem). The role of Hakeems in the rural areas of Sindh is not the result of religious ignorance, but rather an acceptable, accessible and affordable phenomenon and quiteoften very skillful in traditional debridement. Our studies confirm that of these purely herbal medicines the plants used by these Hakeems (Azadirachta indica (neem), Aloe barbadensis (aloe vera), Moringa oleifera, Fagonia arabica, and others), included some species with known in vitro anti-inflammatory and antimicrobial properties. The extract, for instance, is capable of killing in vitro the two most common pathogens in DFU, Staphylococcus aureus, and Pseudomonas aeruginosa.

However, their in vitro anti-microbial effect do not necessarily translate in to wound healing properties in the environment of DFU - so now the wounds are worse, the blood (and nerve) supply is compromised and the immune system has failed. More significantly, however, the Hakeem consultation delays the initiation of systemic antibiotics, blood glucose, correction and wound offloading the mainstay of best practice DFU treatment and can't be replaced with herbal extracts. Each week in the care of a Hakeem before the patient is able to access an allopathic system to care for the wound is a week of biofilm-encrusted wound margins and bone. This might have been an important contributor to the grades of ulcer (3-5) at first visit to allopathic care among the patients in this research.

Policy makers here are not to keep Hakeem care out of the process (that is impossible now as it does not fit with the culture), but to include it. A series of training sessions with traditional wound healers on how to refer allopathic care in emergencies (local pain, fever, bad smell, obvious bone, erythema and its quick development) may continue their role as a first contact person for their patients and refer to their care timely. This has been done in similar settings in South Asia and Africa and should be explored by the Province of Sindh.

The 31% of patients who went to a general physician first is another concern. General physicians are medical practitioners, but may have little training in DFU in particular (Wagner grading, ankle-brachial index and monofilament testing) and offloading protocols (standard of care in the DFU clinic under the podiatrist), as the formal DFU clinic. The general physician then administers antibiotics for a Grade 3 DFU, not realising the need for revascularisation (arterial disease, ischaemia) for the antibiotics to work in healing the wound. This could be circumvented at a very low cost with a DFU attending physicians' competency module in the general practitioners' continuing medical education program in Khairpur district.

Irregular Attendance: 48% No Schedule

Perhaps the most important finding of this study is 48% of patients were not regularly followed (nobody had monthly follow-up, as recommended). Irregular follow-up is the link for other "management problems": the patient who doesn't have regular follow-up also doesn't have an HbA1c test to increase the dose of medication, a foot examination to check for a callus, or a discussion about medication to change the dose. The fact that patients did not receive regular follow-up is not a clinical finding of the effect on DFU, but a system finding of the health system.

Perhaps, the reason(s) for irregular follow-up in this group can be modified. Primary structural factors are financial factors: fees, time and tests

(for people who will lose wages if they take time off work). Geographical factors - such as waiting time and crowding at GIMS OPD, lack of evening and weekend clinics, lack of recall and reminder system (to send SMS telling people about their appointment) are secondary. Cultural barriers - people should not go to seek medical advice for an illness that they don't feel is chronic - are tertiary, but long-standing.

Evidence-informed strategies include: mobile diabetes camps to rural communities (free transport for the farthest), appointment reminder by SMS (all you need is a feature phone), and others such as integration of diabetes monitoring into the already-nade well functioning (with high follow up rates) maternal-child health systems in rural Pakistan. These don't require a lot of money, or technology, but will require political will.

Multimorbidity: An Over-burdened System

The presence of one or more of the co-morbidities in 76% is the manifestation of the microvascular complications of sub-optimal diabetes treatment. 26% of patients with external complications of diabetes (nephropathy) and 20% with external complications of diabetes (retinopathy) and 26% with internal complications of diabetes (bone-joint-pain) are not coincidental but the effect of hyper-glycemia on all organs. The occurrence of these in patients with DFU is important from a medicine perspective as it means the treatment of DFU is not just wound care, it is management of renal disease, visual impairment (affecting foot self-exam) and musculoskeletal pain (affecting mobility and adherence to the need for offloading).

Medically, the complications present some constraints: metformin has to be dose adjusted or stopped in patients with an eGFR (estimated Glomerular Filtration Rate) less than 45 mL/min/1.73m^2, thus limiting the use of the main oral anti-hyperglycemic medication in patients developing nephropathy. Some of the antibiotics used to treat infected DFU (e.g. amoxicillin) require dosing adjustment for renal dysfunction. These drug interactions require some degree of pharmacist knowledge (check for renal functionality before prescribing, dose adjustment based on eGFR) that may not be available in primary health care in rural Sindh, without specific training and/or facilities for measuring renal function. A capacity to screen for renal function (at district hospital level) would not only help DFU, but all other complications of DMT2.

Mental Health and its Impact on Health

Establishing that 77% express fear of being a burden on their families is the most human, and probably the most critical of our findings for redesigning care and coverage options. In the Khairpur socioeconomic milieu, of which 74% of DFU sufferers are male, 54% daily wage earner and who frequently have no source of income when amputated, it makes sense to fear the loss of a family bread winner. It is an appraisal of a valid risk. But this fear drives behaviours that would hasten amputation: delay in seeking help, discounting pain and discomfort, beginning and then stopping treatment when the wound is better (even if not completely healed), and not attending follow up appointments, from which an amputation might be recommended.

Staff working in DFU clinics need to be trained in not only wound care but some of the basic psychosocial components of DFU care: to recognise and acknowledge the fear of amputation, rather than being dismissive, to provide the patient with logical and accurate information about the risk of amputation (and not just saying "death" or "disability") as part of the clinic examination, and to involve families in the care plan (so the patient doesn't feel so alone), and if possible, connect with others who have overcome DFU without amputation. These are not "feel-good" things; they are things to enhance compliance, the acceptance of appointments (and the ability to schedule them) and, most importantly, improve wound healing. The inclusion of a psychosocial intervention in the care of DFU patients in the GIMS DFU clinic would be a low-cost supplement to existing strategies to improve care.

VI. CONCLUSION

This study provides a data-based overview of favourable and unfavourable medication use, patterns and pathways of medical consultation, regularity of follow-up, presence of other diseases and psychological status of the DFU patients in rural Sindh. The major clues: 69% were taking a single medication, despite the mean HbA1c level of 9.58%, 25% came for their first visit to traditional healers, 48% had irregular follow-up, 76% were suffering with other disease and 77% felt psychologically scared of being have to go to the family, describe a population in whom diabetes is under-management, episodically, in all aspects.

The best evidence of medication association with Wagner grade is the table cross tabulation of medication with Wagner grade. The progression of DFU can be prevented by continually bringing-on medication therapy (based on HbA1c) and process of regular medical and nursing follow-up, referral to specialist doctors and inclusion of psychological support. DFU can be prevented in Khairpur. To achieve the potential, actions from awareness and skills building in clinicians, to health systems and policy managers and policy makers in Sindh must begin.

Curable DFU requires us to undertake a coordinated journey of reflection in the practice of care, health systems management and policy-making in all earnestness that takes up the gauntlet of curable DFU in Sindh.

REFERENCES

Mishra SC, Chhatbar KC, Kashikar A. Diabetic foot. BMJ. 2017;359(Suppl):j5064.

American Diabetes Association. Standards of medical care in diabetes. Diabetes Care. 2021;44(Suppl 1):S1-S232.

International Diabetes Federation. IDF Diabetes Atlas. 9th ed. Brussels: IDF; 2019.

Rossyid FN. Etiology, pathophysiology, diagnosis and management of diabetic foot. Int J Res Med Sci. 2017;5(90):4206-4213.

Global Report on Diabetes. Geneva: World Health Organization; 2016.

Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217-228.

Tesfamichael GM, Alemayehu A, Tesfaye E, et al. Prevalence of diabetic foot ulcer and associated factors. J Diabetes Res. 2017;2017:2879249.

Khowaja LA, Khuwaja AK, Cosgrove P. Cost of diabetes care in out-patient clinics of Karachi, Pakistan. BMC Health Serv Res. 2007;7:189.

Artegon MM, Redkop WK, Niessen LW. Cost-effectiveness of prevention and treatment of the diabetic foot. Diabetes Care. 1999;22(3):382-387.

Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Diabetes Care. 1990;13(5):513-521.

Shankhdhar K, Shankhdhar LK, Shankhdhar U, Shankhdhar S. Diabetic foot problems in India: an overview and potential future developments. Curr Diab Rep. 2008;8(6):452-458.

Bolton AJM. The diabetic foot. Manchester: Elsevier; 2014.

Khowaja LA, et al. BMC Health Serv Res. 2007;7:189.

Lazzarini PA, Hurn SE, Fernando ME, et al. Prevalence of foot disease and risk factors in general populations. BMJ Open. 2015;5(11):e008544.

Williams DRR. Hospital admissions of diabetic patients. Diabet Med. 1985;2(1):27-32.

Centers for Disease Control and Prevention. National Diabetes Fact Sheet. Atlanta: US Dept of Health and Human Services; 1998.

Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration. Ann Med. 2017;49(2):106-116.

Kumar S, Ashe HA, Parnell LN, et al. Prevalence of foot ulceration and its correlates in type 2 diabetic patients. Diabet Med. 1994;11(5):480-484.

UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352(9131):837-853.

Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in treatment and prevention. Int J Med Sci. 2014;11(11):1185-1200.

Mishra SC, et al. BMJ. 2017;359(Suppl):j5064.