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A study to assess the efficacy of local applicants to prevent complications of diabetic foot

Arvind Kumar Shukla[1], Avinash Gautam[2], Jujar Kapadia[3], Saranshi Shrivastava[4], Rahul Tayal[5], Rajesh Maida[6], Sagar Arora[7], Ankit Chorma[8], Paramhans D[9]

[1]Associate Professor, [2,8]Assistant Professor, [3,5,6,7]Postgraduate Resident, [4]Senior Resident, [9]Consultant, Department of General Surgery, MGM Medical College and M.Y. Hospital, Indore, Madhya Pradesh, India

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ABSTRACT

Background: Diabetes is one of the most common comorbid illnesses in our community. Diabetes is associated with numerous complications related to microvascular, macrovascular, and metabolic etiologies. One of its complications in long course is diabetic foot ulcer and the associated morbidity and mortality is a major health issue. **Aims and Objectives:** This study was conducted to describe the lesions we treat, study and compare outcomes and to identify measures to decrease morbidity and mortality due to diabetic foot disease. **Materials and Methods:** All patients who attended general surgery outpatient department at M.Y. Hospital (M.P.) India between July 1st 2021 and June 30th, 2022 were included in this study with nonhealing Diabetic foot Ulcer Wagners Stage 3 for more than 2 weeks without any other comorbidities. **Results:** Majority of the patients presented with higher grade and with poor glycemic control at the time of presentation. Conservative management with antibiotics was useful in a small subset of the patients. Majority of the patients needed surgical treatment in the form of debridement to amputations. **Conclusion:** Diabetic limb disease is more prevalent in male sex commonly in 51–60 years of age group. 74% of patients presented with foot ulcer and *Staphylococcus aureus* was found the most common microorganism in pus culture from wounds. Local applicants are effective in controlling ulcers. In our study, hydrogel with colloidal silver was most effective followed by silver nitrate. Early and aggressive treatment of these ulcers can prevent the rate of amputation.

Key words: Diabetes; Ulcers; Antibiotics; Amputation

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INTRODUCTION

Four categories of diabetes are recognized. Type 1, formerly insulin-dependent diabetes mellitus (IDDM), is an autoimmune disease affecting the pancreas. Individuals with type 1 diabetes are prone to ketosis and unable to produce endogenous insulin. Type 2, formerly non IDDM, accounts for 90–95% of cases diagnosed. Type 2 diabetes is characterized by hyperglycemia in the presence of hyperinsulinemia due to peripheral insulin resistance. Gestational as well as genetic defects and endocrinopathies are recognized as other types of diabetes.[1] Diabetes is associated with numerous complications related to microvascular, macrovascular, and metabolic etiologies. These include cerebrovascular, cardio-vascular, and peripheral arterial disease; retinopathy; neuropathy; and nephropathy. Currently, cardiovascular complications are the most common cause of premature death. Diabetes continues to be one of the most common underlying causes of non-traumatic lower extremity amputations.

Mean age at diagnosis of diabetic foot and mean age at major amputation was significantly lower as compared to Western literature. This should be the sole reason to explain the favorable results seen in the Indian series especially in reference to survival at 2 years after major amputation,

Address for Correspondence:
Dr. Jujar Kapadia, Post Graduate Resident, Department of General Surgery, MGM Medical College and M.Y. Hospital, Indore - 452 001, Madhya Pradesh, India. **Mobile:** +91-8770029942. **E-mail**: jujar.kapadia123@gmail.com

contralateral limb amputation rate, above knee to below knee amputation rate. Older patients reported in Western literature are more likely to have advanced atherosclerotic disease involving heart, cerebral circulation, peripheral circulation, and renal circulation thus adversely affecting mortality and contralateral limb amputation rate. Above knee amputation was common in the Western population and the above knee to below knee amputation ratio was 1:2 versus. 1:17 in Western versus Indian series.

Majority of Indian patients have infection as a dominant feature in non-neuro ischemic foot. In such cases, local debridement, control of infection and diabetes, certainly improves the limb salvage. If the infection is fulminant, minor or at the most below knee amputation is enough to stop the advancing infective process. As against this in Western patients, where old age and neuro ischemic limbs are common, advanced atherosclerosis, and multi-system involvement makes above-knee amputation perhaps the right choice to reduce the overall mortality.

In one population-based study in Sweden[2] the cost of treating foot ulcers was US$ 14,627 as compared to US$ 500 in our patients. The cost of treatment in patients undergoing amputation was US$ 73,702 in Sweden as compared to US$ 2000 in Indian patients. This difference in the cost of treatment is obviously due to marked economic disparity between two populations. Although the cost of private treatment in India is less, majority of our patients have to bear the entire cost of the treatment as they are not medically insured and for them even this cost is substantial.

In India, the number of amputations in diabetic patients is bound to increase due to several factors such as increasing prevalence of diabetes, longer survival, more ageing population, continuous use of tobacco, barefoot walking, careless home surgical attempt, late reporting to medical centers and poor hygienic conditions. Unless urgent steps are taken, India might emerge as a country with the highest rate of amputations for diabetic foot.

Aims and objectives

This study was conducted to describe the lesions we treat, study and compare outcomes and to identify measures to decrease morbidity and mortality due to diabetic foot disease.

MATERIALS AND METHODS

This study was conducted in the Department of General Surgery, M.Y. Hospital, Indore, (M.P.), India. The Institute receives 100 patients which follow inclusion criteria between July 1st, 2021, and June 30th, 2022. Patients with nonhealing Diabetic foot Ulcer Wagners Stage 3 for more than 2 weeks without any other comorbidities which affect healing including malnutrition, tuberculosis, human immunodeficiency virus, carcinoma, immune compromised state, and previous amputations were also included in the study. Patients were recruited from the surgical outpatient department. Data were collected by detailed history, clinical examination, wound or ulcer and were recorded in the pre-designed proforma. Age, gender, socioeconomic status, clinical examination, routine investigation, blood investigations, renal function test, X-ray and treatment provided, pus culture sensitivity, and histopathological examination were collected.

The study of various new local applicants over ulcer such as aminoglycosides, cephalosporins, and penicillin derivatives will also be considered with its effect on wound healing and a comparison also be done.

Statistical analysis

The data were initially entered into the customized pro forma and then transferred to Microsoft Excel for analysis. Statistical software IBM SPSS was used for calculating the P values. Chi-square test was applied for comparing the groups. A $P<0.05$ was taken as statistically significant. The final data were presented in the form of tables and graphs.

RESULTS

The incidence of diabetic foot was present in nearly all age groups but the maximum no of patients were from 41 to 60 years of age group. The youngest patient was of 17 years and the eldest patient was of 80 years.

Minimum patients were from the age group of 0–20 years.

In this study 84% were male and 16% were female.

Diabetic foot patients mainly presented in three modes, ulcers, cellulitis, and both. 74% of patients presented with ulcer.

Cultural sensitivity showed that the main organism was *Staphylococcus aureus*, followed by Proteus.

The local applicant which was used: Hydrogel with colloidal silver, Silver nitrate, hydrogel dressing, collagenase, drez, and Mupirocin Ointment.

Faster wound healing, de-sloughing efficiency, and granulation promotion properties were analyzed and it was found that hydrogel with colloidal silver was efficient in 6 out of 10 cases followed by silver nitrate which was 10 patients out of 26 cases.

DISCUSSION

Diabetes is associated with complications in its long run. Foot infection and subsequent amputation of a lower extremity are one of the most common reasons for hospitalization as shown in Table 2. As observed in our study, it is more common in males as shown in Table 1. More common age group is between 51 and 60 years in our study. The hallmark of diabetic foot is its gross infection and major contributing factors for late presentation are poor knowledge about the disease, undetected diabetes, trust in faith healers, and barefoot walking.

According to the international working group on the diabetic foot, infection is the invasion and multiplication of pathogenic microorganisms within tissues of the body.[3] Diabetic foot infections (DFI's) increase morbidity and can lead to limb amputation. Infections in diabetic foot ulcers are frequent and serious complications of ulcers as shown in Table 3.[4,5] It is estimated that 50% of diabetic foot ulcers are infected upon presentation as shown in Table 4,[4,5] and 80% of non-traumatic lower-limb amputations are a consequence of diabetic foot ulcer infection.[4,5] Patients with DFI's are usually hospitalized multiple times and are often exposed to multiple courses of antibiotics.[6] Wound infections are a factor in the delay in the healing process, and, if they are not treated properly, they could lead to systemic compromises.[4,5] Various aspects of wound microbiology are responsible for the development of foot infection. These include microbial load, the diversity of microbes, the existence of infective organisms, and the synergistic association amongst microbial species as shown in Table 4. Infection is said to occur when the microbial load is $>10^5$ organisms per gram of tissue.[7] The exposed tissue left by diabetic foot ulcers then becomes a target for skin commensal bacteria that can colonize the wound, even though, since colonizing does not have a proper host immunological response, it cannot be called an infection.[8] These factors can be physical, chemical, and mechanical. Ischemia, neuropathy, edema, infection, and a poor immune response trigger a complex and are very difficult to heal wounds or ulcers[9] that are predisposed to infections in the diabetic foot. It is critical to assess ulcer infection based on the advice of the Infectious Diseases Society of America and the classification of DFI.[10] The diagnosis of infection is performed by clinical observation and is based on the presence of at least two of the following signs: inflammation, induration, erythema perilesional, hyperesthesia, pain, local heat, and purulent exudate.[11] It is documented that 78% of patients with diabetic foot ulcers also have pads.[12] Endothelial cell dysfunction is the most important feature of microcirculation dysfunction, as it leads to a decrease in vasodilators, particularly in the synthesis of nitric oxide. Furthermore, plasma thromboxane a2 levels become elevated with consequent persistent vasoconstriction and plasma hypercoagulation, leading to an increased risk of ischemia and ulceration.[10,13]

Table 1: Socio-demographic characteristics of the patients

Age group	Number	Percentage
0–20	5	5
21–40	17	17
41–60	51	51
>60	27	27
Total	100	100

Table 2: Sex prevalence

Sex	Number of cases	Percentage
Male	84	84
Female	16	16

Table 3: Mode of presentation

Mode	No of cases	Percentage
Ulcer	74	74
Cellulitis	11	11
Ulcer+Cellulitis	15	15

Table 4: Incidence of pathogen found in the ulcers

Pathogen	Number	Percentage
Escherichia coli	14	14
Klebsiella pneumonae	18	18
Proteus	16	16
Staphylococcus aureus	52	52

Table 5: Type of newer applicants used

Applicants	Percentage
Hydrogel with colloidal silver	26
Silver nitrate	10
Hydrogel dressing	19
Collagenase	14
(Povidine Iodine+Metronidazole) Ointment	9
Mupirocin Ointment	16
Tetrachlorodecaoxide	6

Vacuum-assisted closure (VAC) is an alternative method of wound management, which uses the negative pressure to prepare the wound for spontaneous healing or by lesser reconstructive options. Method of VAC application includes thorough debridement, adequate hemostasis, and application of sterile foams dressing. A fenestrated tube is embedded in the foam and the wound is sealed with adhesive tape to make it airtight. The fenestrate tube is connected to a vacuum pump with a fluid collection container. The machine delivers continuous or intermittent suction, ranging from 50 to 125 mmHg. Negative pressure

Table 6: Efficacy of local applicants

Applicants	Peripheral epithelisation with healthy red granulation tissue		Healthy red granulation tissue		Pale granulation tissue		Total
	Number	Percentage	Number	Percentage	Number	Percentage	
Hydrogel with colloidal silver	10	38.4	13	50	3	11.5	26
Silver nitrate	6	60	3	30	1	10	10
Hydrogel dressing	4	28.57	4	21.05	11	57.8	19
Collagenase	4	21.05	4	28.57	6	42.8	14
Povidone iodine, tinidazole and sucralfate ointment	1	11.1	2	22.2	7	77.7	9
Mupirocin oint ment	2	12.5	5	31.25	9	56.25	16
Tetrachlorodecaoxide	2	33.3	4	66.6	0	0	6

therapy stabilizes the wound environment, reduces wound edema/bacterial load, improves tissue perfusion, and stimulates granulation tissue and angiogenesis. The compression of tissue by negative pressure causes tissue hypoxia due to decreases perfusion beneath the foam which stimulates angiogenesis, and local vasodilatation due to the release of nitric oxide. This occurs during the "suction off" periods of VAC therapy. Therefore, the intermittent mode of VAC is more effective as compared to continuous mode. Hypobaric interstitial pressure and increased permeability of vessels following injury lead to the formation of edema.16 VAC causes increased tissue pressure which leads to compression of vessels and increased velocity of the intravascular fluid (principle of continuity) which reduces the intravascular hydrostatic pressure (Bernoulli's principle). Both the factors cause less efflux of intravascular fluid and decreased edema. In addition, higher blood velocity draws extracellular fluid into the vessel (venturi principle). In addition, the compressive forces of negative-pressure wound therapy physically force edema away from the injured tissues. All these mechanisms result in less interstitial hydrostatic pressure and improved oxygenation of cells. VAC therapy causes immobilization of wound which also aids in healing. All this improves the possibility of primary closure of wounds and reduce the need for plastic procedures.

As shown in Table 5 various topical agents are used for the management of diabetic ulcers there is a growing trend of using hydrogel with colloidal silver and silver nitrate topically. Hydrogel with colloidal silver has silver ions which act as anti-microbial agent. It kills microorganisms by destroying their cell wall. It has an anti-inflammatory action which reduces swelling and pain. Hydrogel with colloidal silver is a gel-based topic agent it promotes healing by retaining moisture on the skin.

Silver nitrate also acts as a broad-spectrum antimicrobial agent, it also results in faster granulation tissue formation which improves the quality of graft bed.

As shown in Table 6 in our study, faster wound healing, de-sloughing efficiency, and granulation promotion properties were analyzed and it was found that hydrogel with colloidal silver has efficiency in 6 out of 10 cases followed by silver nitrate, i.e., 10 patients out of 26 cases.

Wunderlich et al., conducted randomized placebo-controlled clinical trials in which large diabetic populations would further lend credence to the presumption that HBO therapy improves clinical outcomes. Given the relatively high cost of this treatment modality, perhaps a more acute awareness of the medical literature would reduce the economic burden that HBO therapy imposes on care providers that are financially at risk.

Similarly in a study of Flynn MD diabetic foot ulceration is both preventable and treatable. The management of diabetic foot disease is best achieved through the implementation of local protocols involving the primary care team, community care, and the multidisciplinary diabetic team. It is important that the feet are assessed as part of the overall assessment of a diabetic patient at any clinical presentation. The initial management of the acute diabetic foot may present to a general practitioner or general physician and involves the urgent assessment and treatment of infection, foot elevation, wound debridement, and where appropriate, referral for urgent vascular assessment in a specialist center.

Limitations of the study

Study was done for a limited period of one year on a limited number of patients. We were comparing the efficacy of different topical applications.It was a single centre study so berkson's bias could not be eliminated.

CONCLUSION

Diabetic limb disease is more prevalent in male sex commonly in 51–60 years of age group. 74% of patients presented with foot ulcer and *S. aureus* was found the

commonest microorganism in pus cultural wounds. Local applicants are effective in controlling ulcers. In our study hydrogel with colloidal silver was most effective followed by silver nitrate. Early and aggressive treatment of these ulcers can prevent the rate of amputation.

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Authors Contribution:
AKS- Concept and design of the study, interpreted the results, reviewed the literature and manuscript preparation; **AG-** Concept of the study, statistical analysis, coordination; **JK-** Prepared first draft of manuscript, statistical analysis and interpretation, reviewed the literature, manuscript revision; **SS-** Reviewed the literature, manuscript preparation, preparation of draft; **RT-** Reviewed the literature, manuscript preparation, manuscript revision; **RM-** Manuscript preparation, statistical analysis and interpretation; **SA-** Manuscript preparation, statistical analysis and interpretation; **AC-** Manuscript preparation, statistical analysis and interpretation; **PD-** Concept of the study, statistical analysis, coordination.

Work attributed to:
Department of General Surgery, MGM Medical College and M.Y. Hospital, Indore - 452001, Madhya Pradesh, India.

Orcid ID:
Dr. Arvind Kumar Shukla - https://orcid.org/0000-0001-6441-0701
Dr. Avinash Gautam - https://orcid.org/0000-0002-0644-6965
Dr. Jujar Kapadia - https://orcid.org/0009-0004-2657-8246
Dr. Saranshi Shrivastava - https://orcid.org/0000-0002-9790-1811
Dr. Rahul Tayal - https://orcid.org/0009-0007-3110-5592
Dr. Rajesh Maida - https://orcid.org/0009-0006-3393-379X
Dr. Sagar Arora - https://orcid.org/0009-0005-4792-6294
Dr. Ankit Chorma - https://orcid.org/0009-0004-9294-1082

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