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Original Research Article

Effectiveness of Conservative and Definitive Interventions to Enhance Outcomes of Diabetic Foot Ulcer

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Abstract

Background: Diabetic foot ulcer is one of the most commonly encountered complication seen in patients with uncontrolled diabetes. It is most commonly treated with combined approach of debridement with dressings or offloading techniques and use of sking grafts or flaps. We review the various conservative approaches like dressings, offloading, vaccum assisted dressings, use of growth factors, hyperbaric oxygen therapy and definitive modalities like grafting, flaps or the use of integra, to facilitate early wound healing and prevent undergoing amputation.

Methods: 106 patients of age above 35 years with diabetes mellitus suffering from non-healing foot ulcers and infections were selected as per Wegger-Maggit Classification up to Grade 3. Outcomes were compared with patients improving with dressings/ offloading/ VAC dressing vs debridement with skin grafting, integra or flaps.

Results: Surgical complications are more common in men due to their increased susceptibility to trauma, smoking, and tobacco. More than half of the patients had infection in addition to ischemia or neuropathy. This study indicates that all these three factors can be present in a patient with diabetic foot lesions.

Conclusion: Conservative procedures include wound debridement followed by dressing with offloading / VAC dressing, use of PDGF resulted in healing of diabetic foot ulcers. Definitive procedures like Integra implant followed by SSG, or directly SSG or Flap Transfer resulting in healing of diabetic foot ulcers in patient with poor glycemic control or more complications. A multidisciplinary approach involving early intervention with conservative and definitive measures helped in preventing amputation in majority of the patients.

Introduction

Diabetes is one of this century's largest global health emergencies, ranking among the 10 leading causes of mortality together with cardiovascular disease (CVD), respiratory disease, and cancer. [1] Over the past three decades the worldwide burden of diabetes has gradually increased, with India bearing a substantial share of this burden. It is predicted that by 2045, there will be 548 million people with IGT and 700 million people with diabetes, a 51% rise from 2019. [2] In many developing nations, including India, diabetes has reached epidemic levels. [3]

The most costly and disabling complication of diabetes mellitus are diabetic foot ulcers (DFU) which impact 15% of diabetics in their lives. Diabetic foot as defined by the World Health Organization is, "The foot of a diabetic patient that has the potential risk of pathologic consequences, including infection, ulceration, and/or destruction of deep tissues associated with neurologic abnormalities, various degrees of peripheral vascular disease, and/or metabolic complications of diabetes in the lower limb." [4-5]

More than any other diabetic complications, foot ulcers carry a lifetime risk of up to 25%, are the most prevalent reason for diabetic patients to be hospitalized (approximately h30%), and account for around 20% of total healthcare costs. [6, 7] Over 50% of foot ulcers develop an infection that necessitates hospitalization, and 20% of infections lead to amputations. Despite having "foot at risk," the majority of study participants (65–80%) in studies from India were found to not follow any foot care regimens. [6, 8-9]

Early, effective therapy of DFU can lessen the severity of consequences including avoidable amputations and potential mortality and can also enhance the general quality of life. This study

aimed to study the effectiveness of conservative and definitive interventions to enhance outcomes of diabetic foot ulcers to prevent amputation.

Materials and Methods:

This was a hospital based, prospective observational study, conducted by the departments of General Surgery and General Medicine of C.R. GARDI Hospital Ujjain with patients admitted for diabetic foot ulcers for a period of one year after approval by the Institutional review committee and Institute's medical ethics committee. Informed consent regarding the study was taken from the prospective participants.

Patient selection:

All patients above 35 years of age with diabetes mellitus suffering from non-healing foot ulcers and infections who presented to OPD and IPD of C.R.G.H Ujjan as per Wegger-Maggit Classification up to Grade 3 were included in the study. Those with foot infections without diabetes mellitus and patients whose treatment could not be completed due to noncompliance were excluded from the study.

Follow up of the patients was done at 15 days, 1 month, 3 months, and 6 months.

Outcome variable protocol used was as follows:

(i) Patients improving with Conservative approach(Debridement with dressing/ Offloading/ VAC dressing) Yes/ No

(ii) Patient requiring definitive procedures but not willing Yes/ No

(iii) Patients improving with Definitive procedures (Skin grafting / Flap transfer) Yes/ No

Statistical analysis

Categorical data was expressed as frequencies and percentages. Comparison of categorical variables was performed by chi-square test. Continuous variables were expressed as mean and standard deviations. A p value of <0.05 was accepted as statistically significant.

Observation and results:

Age and Gender distribution of the cases

One hundred and six patients, suffering from non-healing foot ulcers and infections were enrolled. The mean age of the cases was 54.45±9.46 years and a great proportion of them were in 4th to 6th decade. There were 61(57.5%) males and 45(42.5%) were females in the study. There was no significant association between age groups and gender of the cases with p>0.05 (Table 1).

Table:1 Age and Gender distribution of the cases

Age groups	Gender		Total
	Female	Male	
< =40years	2	2	4
	4.4%	3.3%	3.8%
41 -50years	9	21	30
	20.0%	34.4%	28.3%
51 -60years	22	29	51
	48.9%	47.5%	48.1%
61 -70years	6	5	11
	13.3%	8.2%	10.4%
> 70years	6	4	10
	13.3%	6.6%	9.4%
Total	**45**	**61**	**106**
	100.0%	**100.0%**	**100.0%**
Chi-Square=3.92,p=0.421			

Out of 106 cases majority of cases 68(64.2%) had>10 years duration of DM, 38(35.9%) had <10 years duration, 66(62.3%) cases were treated by OHA, 21(19.8%) were treated by insulin, and 19(17.9%) were treated by both OHA and insulin. 37(34.9%)cases were smokers and 44 (41.5%) cases were tobacco chewer.

Mean FBS levels were 204.32±59.19, PPBS were 264.75±83.56 and HbA1C were 7.81±1.20.

Ulcers:

77(72.6%) cases had a pure tropic ulcer and 29(27.4%) had a neuroischemic ulcer. Majority 82(77.4%) of the ulcers were in forefoot, 13(12.3%) ulcer site is mid-foot and 11(10.4%) ulcer is hind-foot. Stage of ulcer and frequency as per W-M Classification with maximum frequency of ulcers being stage 2 ulcer (Table 2).

Table 2: Stage and frequency of ulcers

Stage of ulcer (WM Classification)	Frequency	Percent
1	12	11.3
2	61	57.5
3	33	31.1
Total	**106**	**100.0**

Procedure and complications:

Most common procedure in a DFU was debridement followed by VAC dressing (25.4%) followed by debridement followed by dressing with offloading and Debridement followed by VAC dressing followed by PDGF (both 19.8%) (Table 3)

Table 3: Distribution of procedures

Procedure	N	%
Debridement followed by VAC Dressing	27	25.4
Debridement followed by dressing with offloading	21	19.8
Debridement followed by dressing with offloading followed by flap transfer	07	6.6
Debridement followed by dressing with offloading followed by SSG	01	0.9
Debridement followed by VAC dressing followed by Graft (INTEGRA)	16	15.1
Debridement followed by VAC dressing followed by PDGF	21	19.8
Debridement followed by VAC dressing followed by SSG	12	11.3
Debridement followed by VAC dressing followed by flap Transfer	01	0.9
Total	**106**	**100**

Distribution of complication according to cases were as follows: 63(59.4%) had developed infections, 67(63.2%) had ischemia and 46(43.4%) developed peripheral neuropathy.

Follow up:

In the first follow up 29(27.4%) were treated with dressing with offloading and 77(72.6%) by VAC dressing.

In second follow up 4(3.8%) treated with dressing with offloading, 29(27.4%) by VAC dressing, 8(7.5%) flap transfer, 16(15.1%) by INTEGRA 21(19.8%) by PDGF, 7(6.6%) by SSG and 21(19.8%) were healed.

In third follow up 3(2.8%) treated with dressing with offloading, 5(4.7%) by VAC dressing, 23(21.7%) by SSG and 75(70.8%) were healed. (Figure 1)

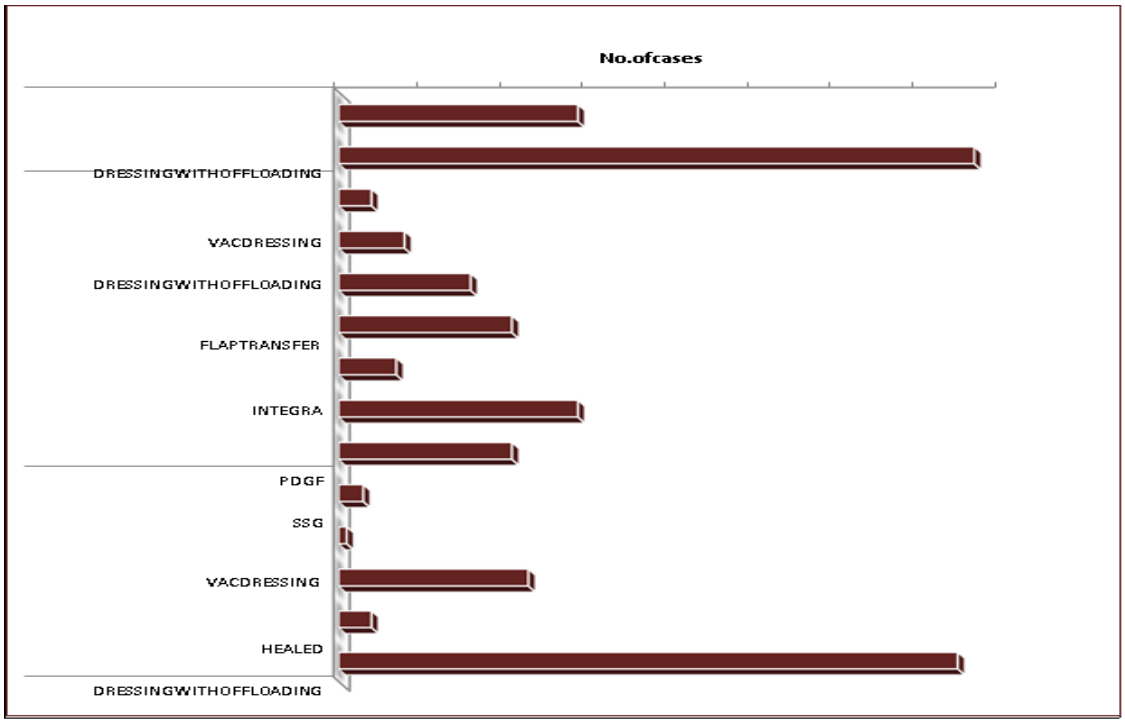


Figure 1: Follow up

Outcome and its associations:

p-value holds a significance in determining the

association between outcomes and complications, if p value is 0.05 or lower, the result is trumpeted as significant, but if it is higher than 0.05, the result is non-significant and tends to be passed over in silence.

Out of 106 cases graft rejection were seen in 8(7.5%) cases, re-infection in 7(6.6%) and 91(85.8%) were healed and amputation were done in 16(15.1%) cases.

There was no significant association observed between complications (peripheral neuropathy, ischemia, infection) and outcomes (graft rejection, healed, re-infection) of diabetic foot ulcer.

Table 4 shows Association between Outcome and Complications

		OUTCOME						p
		GRAFT REJECTION		HEALED		RE-INFECTION		
		N	%	N	%	N	%	
Peripheral Neuropathy	Yes	7	87.5%	32	35.2%	7	100.0%	0.000
	No	1	12.5%	59	64.8%	0	0.0%	
Ischemia	Yes	8	100.0%	52	57.1%	7	100.0%	0.006
	Yes	0	0.0%	39	42.9%	0	0.0%	
Infection	Yes	7	87.5%	49	53.8%	7	100.0%	0.014
	Yes	1	12.5%	42	46.2%	0	0.0%	

There was no significant association observedbetween addiction (smoking and tobacco) and the outcome of the cases with p>0.05 (Table 5)

Table:5 Association between Outcome and Addiction

		OUTCOME						p
		GRAFT REJECTION		HEALED		RE INFECTION		
		N	%	N	%	N	%	
Smoking	Yes	3	37.5%	32	35.2%	2	28.6%	0.928
	No	5	62.5%	59	64.8%	5	71.4%	
Tobacco	Yes	3	37.5%	37	40.7%	4	57.1%	0.675
	No	5	62.5%	54	59.3%	3	42.9%	

According to management methods, graft rejection was observed in 8(20.5%) cases in the definitive method and 31(79.5%) were healed. Re- infection in 7(10.4%) cases in the conservative method and 60(89.6%) were healed in the conservative method. (Table 6)

Table 6: Distribution of Outcome according to management method

OUTCOME	Management method		Total
	Definitive	Conservative	
Graft Rejection	8	0	8
	20.5%	0.0%	7.5%
Healed	31	60	91
	79.5%	89.6%	85.8%
Re-Infection	0	7	7
	0.0%	10.4%	6.6%
Total	**39**	**67**	**106**
	100.0%	**100.0%**	**100.0%**

According to management methods, graft rejection was observed in 8(20.5%) cases in the definitive method and 31(79.5%) were healed. Re- infection in 7(10.4%) cases in the conservative method and 60(89.6%) were healed in the conservative method. This indicates both definitive and conservative methods are almost effectively same for healing of diabetic foot ulcer; however Re-infection in a diabetic foot ulcer are more commonly seen with conservative approaches.

Hence this study demonstrated that a multidisciplinary approach comprising of Conservative methods (Dressings) followed by Definitive procedures (SSG/ Integra/ Flap) have a higher chances of healing in diabetic foot ulcer.

Discussion

The most costly and disabling complication of diabetes mellitus, diabetic foot ulcers (DFU) impact 15% of diabetic patient's lives.

Early, effective therapy of DFU can lessen the severity of consequences including avoidable amputations and potential mortality and can also enhance the general quality of life. Due to the need for a comprehensive approach to wound management, the management of DFU should be optimized by employing a multidisciplinary team. Studies suggest that DFU therapy should always include procedures for unloading, wound debridement, and better dressings. [10,11]

In our study, we found most of the patients having diabetic foot ulcers had a bimodal peak, the first peak was in those having been diagnosed with diabetes in the last 5 years. As diabetes is a silent disease, it gets diagnosed after years of hyperglycemia getting undiagnostic till some early complication presents or is screened serendipity. The second peak is after 10-15 years of diagnosis. Similar observations have also been seen by Sayuta et al [12] where the first peak was observed with the median duration of diabetes being 6 years while a second peak was observed after themean 12 years of diagnosis. Additionally, they discovered a strong connection between Wagner's classification of DFU degrees and the duration of diabetes (p =0.018). A similar observation has also been quoted by Al-Rubean et al [13] in their study.

Age also plays an important risk factor in diabetic patients in the development of foot ulcers. The mean age in our study was 53.538 years. A study by Yazdanpanah et al [10] also found the mean age in their study to be 53.52 years, Sayulita et al (12) found a mean age of 56.38 in their study on diabetic foot ulcers. A study by Jeyaraman et al. [14] concluded that there was a correlation between age (with a median age of 64 years) and the occurrence of DFUs. Age has been demonstrated to increase the risk of angiopathy. Age >40 years seems to increase the risk of having angiopathy. Regardless of the type of diabetes, Katsilambros N et al have found that the risk of ulceration and amputation in diabetic individuals increases by two to four times with age and duration of diabetes.[15]

According to studies various studies [15-16], men were shown to have a much higher overall and gender-specific prevalence of diabetic foot ulcers, gangrene, and amputations than women. In our study also 57.5 % of the subjects were males. This finding can be explained by the fact that men are known to have lower joint mobility and higher foot pressure. Males are more likely to have peripheral insensate neuropathy and higher mean heights, which may explain the discrepancy. Men exhibit fear and negative views, but women are more engaged in taking care of their bodies and are more self-aware. In addition to this, men frequently wear improper footwear, and they are more vulnerable to trauma. [17]

Studies have shown a clear and significant relationship between the three diabetic foot conditions and the degree of glycaemic control [13,18-19] which is consistence with the observation that, poor glycaemic control was associated with a two-fold increase in the risk of foot lesions among diabetic patients. This observation is seconded by our study also, patients developing diabetic foot ulcers had mean FBS and mean PPBS which is on the higher side.

The Ankle Brachial Index (ABI) is the ratio of the ankle's systolic pressure to the arm's systolic pressure. It has been demonstrated to be a reliable and sensitive indicator of peripheral artery disease (PAD). The typical ABI lies between 1.0 and 1.4. A result less than 0.9 is regarded as PAD diagnostic.[20-21] In our study, 50 % of patients had ABI between0.6–1,which implied the presence of peripheral vascular disease, and hence had developed ulcers. Studies also concluded that low ABI is associated with a worse Wagner type of ulcer and predicts adverse outcomes. [22-24]

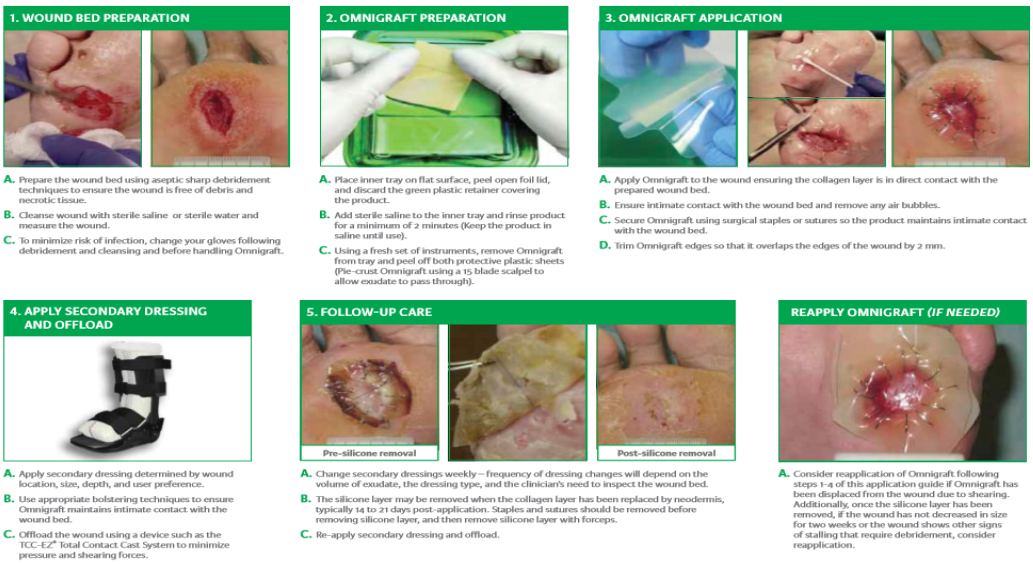
Negative pressure wound therapy(VAC Dressing)

In our study, the forefoot (77.4% cases) was the most common location of DFU, study by Ellis et al

(60% cases) [25] and Oyibo et al (77.8 % cases) had the forefoot as the most common location of DFU. This is because the fore foot is having metatarsal pressure head areas and more precarious vessels with peripheral vascular disease. Trophic ulcers are pressure sores that develop on a part of the body that is already weak from disease, vascular insufficiency, or the loss of afferent nerve fibers. They can be classified based on causes such as neurogenic or vascular. [26] In our study trophic ulcers were maximum of 72.6 % of cases. A study by Meloni et al [27] also reported trophic ulcers were the maximum in their study.

An improved bilayer matrix for skin regeneration is called Omnigraft/ INTEGRA/ Dermal Regeneration Matrix. The dermal replacement layer is made up of a porous, three-dimensional matrix with controlled porosity and a set degradation rate made of bovine collagen and chondroitin6-sulfate. A thin polysiloxane (silicone) layer serves as the temporary epidermal layer, which is used to cover wounds temporarily and prevent moisture loss from them.

When used in conjunction with routine diabetic ulcer management, Omnigraft is suggested for the treatment of partial and full-thickness neuropathic diabetic foot ulcers lasting longer than six weeks and without any exposed bone, tendon, or capsule. Omnigraft should be removed in situations of infection, chronic inflammation, allergic reaction, or significant redness, discomfort, or swelling.



Omnigraft/ INTEGRA/ Dermal Regeneration Matrix

Local flaps usually consist of skin and the underlying fat or skin, fat, and the underlying fascia. They, however, can also include the muscle.

Skin Grafting is one of the simplest of all coverage techniques with the only prerequisite being wound with a bed of healthy granulation tissue. To ensure that there is little to no bacterial contamination within the interstices of the granulation buds, the top layer of granulation tissue is removed. Preferable donor sites include the ipsilateral thigh, leg, or instep. The size of the defect is measured to determine the amount of skin graft needed. The area needed is then drawn on the donor site. Then after obtaining the graft from the donor site, it is meshed and placed appropriately.

It is important to carefully preplan the flap by first accurately determining the size of the defect after debridement. The flap should be designed in the area in which the tissue is the most mobile. The ratio of length to width is critical for the survival of

the tip of the flap. Because the blood flow to the skin in the foot and ankle is not as developed as in the face, the length-to-width ratio should not exceed a 1:1 or 1:1.5 ratio. Local flaps are very useful in the coverage of foot and ankle wounds because they only need to be of sufficient size to cover the exposed tendon, bone, or joint. The rest of the wound can then be covered with a simple skin graft.

Flaps in wound coverage

High-concentration oxygen delivery could hasten wound healing in diabetics [28]. The intermittent delivery of 100% oxygen at a pressure higher than that at sea level is a component of hyperbaric oxygen therapy. The procedure is carried out in a chamber with the patient intermittently breathing 100% oxygen while the ambient pressure is raised to 2-3 atmospheres for 1-2 hours. A whole course consists of 30–40 sessions. Hyperbaric oxygen can be applied as an adjunctive therapy for patients with severe soft-tissue foot infections and osteomyelitis who have not responded to conventional treatment.

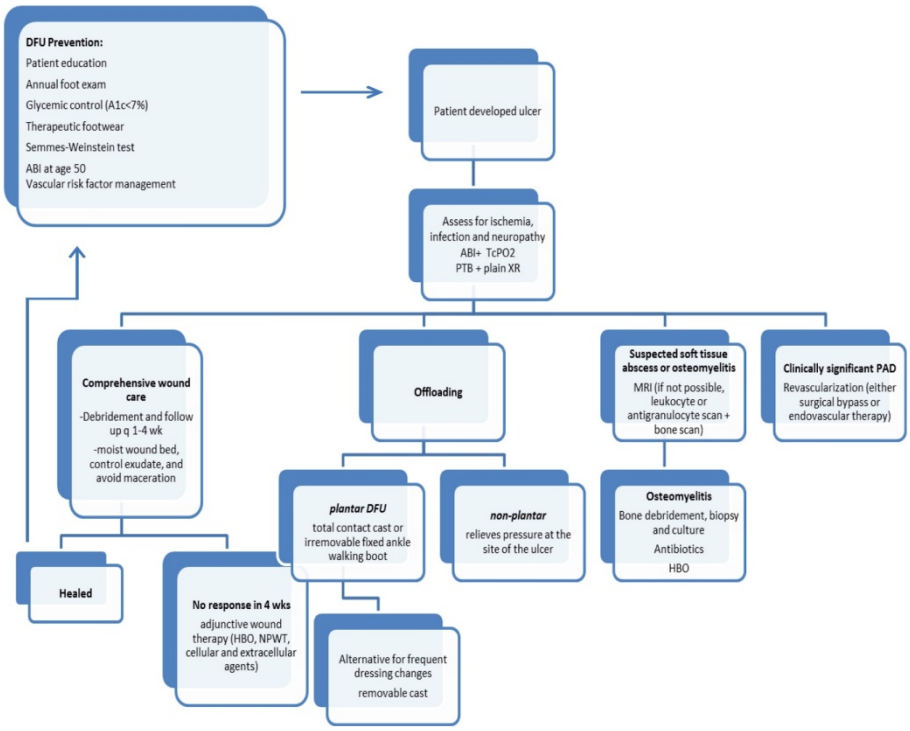
In our study amputation rate was 15.1%, study by The wjitch aroenetal [29] in Thailand with a follow-up of 5 years reported that major amputations were 4.6 % while minor amputations were 22.3 %.A meta- analysis by Lin et al [30] identified the male sex, a smoking history, a history of foot ulcers, osteomyelitis, gangrene, a lower body mass index, and a higher white blood cell count as risk factors of amputation in DFU. Overall, persons with diabetes had a 15 times higher rate of lower limb amputation than those without the disease.DFU is thought to be the cause of between 50% and 70% of all lower limb amputations. Additionally, it is stated that one limb is amputated owing to DFU globally every 30 seconds. [31-32]

The primary cause of diabetic foot sore is pressure combined with cycles of recurrent stress, which causes skin and soft tissue to collapse. The proper debridement of nonviable tissue and sufficient pressure relief form the basis of any therapeutic strategy for neuropathic diabetic foot ulcers (off-loading). Observations in our study (36.8% cases) are also in line with these observations by Armstrong G et al. [33]

Lifestyles habits like smoking and tobacco chewing have shown mixed results in association with outcomes, studies by Jiang Y et al [34], Robinson et al [35], and Tseng C-H [36] have shown a positive association with the adverse outcome while studies have found no association [36-39]. Our study aligns with the latter group finding no significant association ($p>0.05$).

Infection, gangrene, and amputation are the most dreaded complications of diabetic foot ulcers [40]. In our study, infection was noted in59.4 %of cases while gangrene/ischemia in 63.2 % while amputation was done in 15.1% of cases. Our rate of complication is very high as compared to other studies such as the retrospective cohort done by Al-Rubeaanetal [13] who had an overall 3.3 % rate of complication, this can be due to selection and attrition bias in our study. [41]

Management Algorithm



Conclusion

DFU is a significant cause of morbidity and a primary reason for hospitalization in diabetic patients. Education, blood sugar management, wound debridement; advanced dressing, offloading, surgery, and clinically applied advanced therapies are the key management pillars that can ensure successful and quick healing of DFU.

Multidisciplinary teams must have a thorough understanding of risk variables and how they affect amputation outcomes to design care and treatment regimens for patients with DFU, even though some risk factors are difficult to change. Early identification of at-risk patients, early intervention in the form of preventive measures and aggressive management can only help to prevent grave consequences/amputation.

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