**EFFICACY OF MOXIFLOXACIN IN DIABETIC FOOT ULCERS**

**BY**

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**DEDICATION**

**I dedicate these pages to**

**To my Parents, Teachers and all my family members**

**ACKNOWLEDGMENT**

All glory be to Almighty Allah who gave me good health, opportunity and courage to accomplish this study.

I am profoundly indebted to **PROF. DR JAMAL UD DIN MARWAT** who kindly supervised me throughout my work. His guidance, encouragement and keen interest made the completion of this project possible. I am highly grateful to his invaluable help and generous guidance.

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**ABSTRACT**

Chronic hyperglycemia is a hallmark of diabetes mellitus (DM), a metabolic condition that may be brought on by insulin deficiency or insulin resistance. In 2017, 425 million people throughout the world were diagnosed with diabetes mellitus (DM), according to the International Diabetes Federation. Inconsistent data supports the usefulness of moxifloxacin in the treatment of diabetic foot ulcers. Certain confounding variables may influence the findings derived from previous study. The purpose of this inquiry was to come up with a solution to this conundrum. The findings will be useful to practitioners due to the presence of pertinent local evidence. The goal of this study was to determine the efficacy of moxifloxacin in treating diabetic foot ulcers. A descriptive case series research was done at the Khyber Teaching Hospital in Peshawar, Pakistan, to accomplish this purpose. Throughout the event, a total of 195 patients were seen. Each patient got 400 mg of moxifloxacin intravenously for two weeks. Throughout the therapy, blood glucose levels were tested regularly and appropriately treated with insulin as necessary. One and two weeks after the wounds were first opened, they were examined for the presence of granulation tissue on the ulcers. By the conclusion of the second week of moxifloxacin treatment, the ulcer had been entirely filled by granulation tissue, and the granulation tissue culture had returned negative. After treatment, the wound was assessed in size. A proforma was used to collect demographic information about the patient, such as his or her name, age, gender, and place of residence, as well as information on the duration of the patient's diabetes. The 195 patients in the study had an average age of 54 years, with a standard deviation of 10.31 years between them. The average age of the patients was 54 years. Men made up 72% of the total, while females made up 28%. According to the statistics, diabetes had a mean duration of 12 years and a standard deviation of 6.72 years. The individuals had a mean BMI of 30 kg/m2 and a standard deviation of 10.63 kg/m2. There were 43 smokers (22%) among the patients, compared to 152 non-smokers (78%). Alcohol consumption was reported by six persons (3%) but not by 189 patients (97 percent). 84 individuals (43%) had a lesion on their right foot, whereas 111 individuals (57%) had a lesion on their left foot. There were 51 patients with a dorsal lesion, 31 patients with a plantar lesion, 43 patients with a toe lesion, 31 patients with a Malleoli lesion, and 39 patients with a heel lesion. Additionally, the findings indicated that moxifloxacin was beneficial in 162 (84%) of the patients, but was unsuccessful in 31 (16%) of the patients. Additionally, it has been established that the antibiotic moxifloxacin is 84% efficient in the treatment of diabetic foot ulcers.

KEY WORDS: moxifloxacin, diabetic foot ulcers.

# Chapter 1: Introduction

## 1.1 Background;

The metabolic condition known as diabetes mellitus (DM) is defined primarily by the presence of persistent hyperglycemia, which is caused by a lack of insulin production or by insulin resistance. Diabetes affects 425 million people globally, according to the International Diabetes Federation (IDF), according to their 2017 estimates [1].

The chance of having foot issues in diabetics increases throughout the course of their lives, which is estimated to be at a rate of around 25% overall, with a point prevalence of 2% or less. Diabetes-related foot illness affects almost 6% of the population, and it can manifest itself as infection, ulceration, or loss of foot tissues. In addition to negatively impacting patients' quality of life and ability to participate in social activities, this illness can also negatively impair their earning capability. About 0.03 percent to 1.5% of diabetic foot patients necessitate amputation. The majority of amputations begin with ulcers, which can be avoided with proper foot care and screening for foot problems. Along with these consequences, diabetic foot ulceration is related to hospitalization, a prolonged inpatient length of stay, as well as physical and psychological morbidity [2], [3], [4].

Diabetic foot infections (DFIs) are caused by Staphylococcus species, which are the most prevalent pathogens. Compared to patients without the infection, DFI patients with methicillin-resistant Staphylococcus aureus (MRSA) has a higher chance of treatment failure than those without the infection. Polymicrobial infections and wounds, including gram-negative bacilli, typically occurs with antibiotic treatment for more severe infections and wound necrosis. In necrotic wounds and infections of the ischemic foot, anaerobic microorganisms are more prevalent. For the past 20 years, fluoroquinolones have been utilized to treat DFIs effectively. Moxifloxacin is a newer fluoroquinolone with action against the majority of aerobic and anaerobic gram-positive and gram-negative bacteria; it is now approved for the treatment of infections of the skin and skin structure caused by specified susceptible pathogens, but not particularly for DFI [5].

In a clinical trial, moxifloxacin had a 68 percent success rate in treating diabetic foot ulcers, indicating that it might be used as a monotherapy treatment for such infections [6]. Moxifloxacin was shown to be 84% effective in the treatment of diabetic foot ulcers in research conducted at Liaquat University Hospital in Jamshoro, Hyderabad [5].

Moxifloxacin has a 51% effectiveness rate in diabetic foot ulcers, according to Vick-Fragoso et al. [7]. The effectiveness of moxifloxacin in diabetic foot ulcers has been studied in a number of different ways, with varying results. The outcomes of past research may be influenced by several factors. The purpose of this study was to figure out how to remedy this problem. Because of the available evidence in the area, the results will be utilized by practitioners.

# Chapter 2 Literature Review;

The diabetic foot ulcer is a significant consequence of diabetes mellitus and is almost certainly the most prevalent component of the diabetic foot.

Most of the time, wound healing is an intrinsic system of action that works well. A critical element of wound healing is the gradual replacement of lost extracellular matrix (ECM), which accounts for the majority of the dermal skin layer's composition [1]. However, in other circumstances, the healing process is disrupted by a variety of illnesses or physical insults. As an example of a metabolic condition that interferes with wound healing, diabetes mellitus is mentioned. Researchers have found evidence of an extended period of inflammation in diabetic wounds; this, in turn, slows the production of mature granulation tissue and reduces the strength of the wound bed [2].

Blood sugar management, the removal of dead tissue from the lesion and wound dressings are all necessary components of the treatment of diabetic foot ulcers. Although surgery might benefit some patients, hyperbaric oxygen therapy may potentially be beneficial but is costly [3].

As blood sugar levels rise over time, neurons, kidneys, eyes, and blood vessels are damaged. This is known as type 2 diabetes (DM). Nerve cells, kidneys, eyes, and blood vessels in people with type 2 diabetes are damaged by high blood glucose levels over time. It's also possible that diabetes will impair the immune system's ability to protect the body. Organ damage and immune system failure can occur if diabetes is not properly treated. Diabetes is linked to an increased risk of foot problems, which can quickly become more severe [8].

A diabetic who suffers from nerve damage may find it difficult to feel his or her feet correctly as a result of the condition. The skin of the foot is unable to produce the oils and perspiration that keep it lubricated. Due to a combination of these elements, abnormal pressure can be exerted to the skin on the feet and to the bones and joints of the feet while walking, which can result in skin breakdown on the feet. It is possible for sores to form.

Because diabetes has damaged the blood vessels and compromised the immune system, these wounds are difficult to heal. Bacterial infection can then spread to the skin, connective tissues, muscles, and bones. Gangrene can be caused by certain illnesses. Antibiotics are unable to reach the infection because of the inadequate blood flow. Amputation of the foot or leg is often the only therapy for this. The infection can be deadly if it gets into the bloodstream [9].

In order to avoid foot problems, diabetics must be informed of how to prevent them, how to detect them when they do arise, and how to get the proper treatment when they do occur. Prevention, particularly proper blood sugar control, remains the best method to avoid diabetic foot complications despite recent advances in the treatment of diabetic foot disease.

Those who have diabetes should get familiar with the process of self-examination and the early signs and symptoms of diabetic foot issues. There are a number of things they should be taught about how to care for their feet at home, as well as how to tell when a condition is so bad that they need emergency treatment.

## 2.1 Background;

The development of diabetic foot ulcers can be accelerated by a variety of variables, including infection, ageing, diabetes, peripheral vascular disease, smoking, poor glycemic management, previous foot ulcers or amputations, and ischemia of small and large blood vessels [6], [7], [8]. In addition, those who have had a foot ailment, have feet that don't operate the way they should, or have calluses on the regions that get a great deal of pressure are at risk [5], [6]. As a result of several metabolic and neurovascular variables, many diabetics get diabetic neuropathy (DN). Peripheral neuropathy is a condition that results in the loss of pain and sensation in the toes, foot, legs, and arms as a result of distal nerve injury and inadequate blood flow. As a result, pressure or injury to the metatarso-phalangeal joints or the heel may go undetected, causing blisters and sores.

## 2.2 Pathophysiology;

### 2.2.1 Role of Extracellular Matrix;

In multicellular organisms, the extracellular matrix (also known as the "ECM") is the exterior structural framework to which cells connect. The dermis is the layer of skin that lies underneath the epidermis, and these two layers are together referred to as the skin. In this matrix, fibroblasts proliferate and form the dermal skin. Even though the chemical composition of the many ECM species found in connective tissues varies, collagen is almost always the primary constituent.

Extracellular matrix (ECM) and cell membrane interactions assist control a variety of cellular activities through the transmission of anchoring molecules known as "integrin’s" (also known as "integrin ligands") that are found in the ECM. In order for a wound to heal properly, cells must respond to the harm they have been exposed to in a limited manner.

Damaged ECM is broken down and replaced by new ECM, and the number of cells normally increases as a response to the injury. Rebuilding the ECM is done by cells growing on and through the matrix, and the process is triggered by cells reacting to ECM fragments that have been damaged. Due to its role in wound healing, the extracellular matrix is commonly spoken upon as the 'conductor of the wound healing symphony' [11]. When neutrophils and macrophages enter the wound as part of the Inflammatory phase, they attract and activate fibroblasts, which migrate into the wound and deposit new collagen of types I and III during the granulation phase that follows.

The first stages of wound healing are characterized by the predominance of collagen III in the granulation tissue, which is later replaced by collagen I during the remodeling phase, providing the healing tissue with additional tensile strength [12], [13]. Tensile strength, as proven by the known collagen assembly, is mostly due to the fibrillary arrangement of collagen molecules, which self-assemble into micro fibrils in both the longitudinal and horizontal directions and therefore contribute strength and stability [13], [14]. Collagen, which has been metabolized, is known to break down in high-pressure situations. Fibronectin is the primary glycoprotein produced by fibroblasts during the first stages of the creation of extracellular matrix proteins. It is also the most abundant glycoprotein in the body. Chemo attraction for macrophages, fibrinogen cells and endothelial cells is one of its most essential roles.

Sheet-forming protein Collagen IV interacts with laminin and proteoglycans in the extracellular matrix. A significant portion of this substance may be found in both the endothelium and basement membranes that divide the epidermis from the dermis. Laminin, perlecan, and nidogen are also found in the epidermal and endothelial basement membranes, in addition to collagen IV. Thirteen and fourteen are two examples of this. In tissues that are wounded or developing, high quantities of hyaluronic acid a pure glycosaminoglycan can be identified. It increases angiogenesis by stimulating macrophage production of cytokines. The membrane of normal skin includes chloride sulphate proteoglycan, but as a wound heals, this protein is enhanced throughout the healing tissue, particularly in the second week of wound repair, when it works as a temporary matrix with a high water-holding capacity [15]. Perlecan has a vital role in wound healing and angiogenesis, as evidenced by the fact that it binds to many growth factors. Perlecan expression may be a factor in the slow healing of diabetic wounds. Gene expression and post-transcriptional modification are likely mechanisms by which high glucose levels might reduce perlecan expression in certain cells [15–16]. Extracellular matrix components undergo a regulated turnover throughout wound healing phases such as granulation, re-epithelization, and remodeling in particular.

### 2.2.2 Altered Metabolism;

Diabetic wound healing has been found to be impaired due to changed protein and lipid metabolism and, as a result, improper granulation tissue development [17]. Diabetes mellitus is considered to be a metabolic condition, and diabetic wound healing deficiencies have been linked to incorrect granulation tissue development as a result of abnormal protein and lipid metabolism. In the absence of glucose in the circulation, a lack of glycosylation enzymes results in an unregulated covalent attachment of aldose sugars to a protein or lipid. They encircle and collect on the surfaces of cell membranes, structural proteins, and circulation proteins, which are all wrapped in these stable molecules. Also known as Amadori products, they are the so-called advanced glycation end products (AGEs). Proteins in the extracellular matrix that have a delayed turnover rate contribute to the formation of AGEs. There are intermolecular covalent connections (or cross-linking) between AGEs and matrix proteins including collagen and vitronectin that modify their properties [18]– [20]. Type I collagen and elastin become stiffer as a result of AGE cross-linking. AGEs have also been shown to stimulate the synthesis of type III collagen, which forms the granulation tissue, in response to a stimuli. Decreased type IV collagen binding, reduced polymer elongation, and reduced heparan sulphate proteoglycan binding are all caused by AGEs on laminin [18].

### 2.2.3 Impaired Nitric Oxide Synthesis;

One of the most well-known stimulators of cell proliferation, maturation, and differentiation is known as Nitric Oxide (NO). Thus, nitric oxide enhances wound healing by promoting fibroblast proliferation and collagen formation. Also required for the proper cross-linking of collagen fibers via proline is nitric oxide (NO), which helps to decrease scarring and improve the tensile strength of regenerated tissue [21]. The pulsatile flow of blood through capillaries activates the enzyme endothelial nitric oxide synthase (ecNOS), which is unique to endothelial cells. Proper blood flow to tissues is maintained by the production of nitric oxide by ecNOS. Also, Angiogenesis is critical to wound healing, and nitric oxide modulates angiogenesis [22]. As a result, L-arginine nitric oxide synthesis in diabetics is impaired. Patients with diabetes who experience ketoacidosis and nitric oxide synthase that is pH dependent have both been suggested as possible explanations [19], [23] for the buildup of the inhibitor of nitric oxide synthase.

### 2.2.4 Structural and Functional Changes in Fibroblasts;

When compared to fibroblasts from age-matched controls, diabetic ulcer fibroblasts exhibit a variety of morphological abnormalities. When compared to the spindle-shaped morphology of diabetic ulcer fibroblasts in age-matched controls, diabetic ulcer fibroblasts are often big and widely distributed in the culture flask in diabetic ulcers. According to transmission electron microscopy studies, they have a dilated endoplasmic reticulum, many vesicular bodies, and no micro tubular structure. As a result, despite high levels of protein synthesis and turnover, secretory proteins in diabetic ulcer fibroblasts were unable to move along microtubules [24], [25]. Wound contraction and healing are both delayed and worsened in diabetic ulcer-derived fibroblasts due to their proliferative impairment [24].

### 2.2.5 Increased Matrix Metalloproteinase (MMP) Activity;

In order to produce mature tissue with sufficient tensile strength, the extracellular matrix must be able to dissolve and remodel as well as be laid down during wound healing [26]. Most extracellular matrix components are known to be degraded by proteases, particularly matrix metalloproteinase. They have been implicated in the migration of fibroblasts and keratinocytes, tissue reorganization, inflammation, and remodeling of injured tissue [2], [26]. Because of the constantly high levels of pro-inflammatory cytokines present in diabetic ulcers, MMP activity has been shown to increase by 30 times compared to that of acute wound healing [2], [27]. MMP-2 and MMP-9 are upregulated in non-healing diabetic ulcers. To maintain MMP activity homeostasis, TIMP is often employed (TIMP). The proteolytic equilibrium is maintained by the ratio of MMP to TIMP, not their individual absolute concentrations, and this ratio is disrupted in diabetic ulcer [29], [30]. There is still a lack of understanding of how diabetes is linked to increased MMP activity. TGF- (transforming growth factor beta) may be considered an active participant in this process. As most MMP genes have a TGF-inhibitory element in their promoter regions, TGF– regulates the production of both MMPs and TIMPs. Cell-cell and cell-matrix contact are critical to wound healing; however, a large range of growth factors and cytokines are involved in all stages of healing. Growth factors, to be exact, facilitate the transition from the early stages of inflammation to the creation of granulation tissue. In diabetic wounds, there is a decrease in growth factors that promote tissue healing, such as TGF. TGF- levels in diabetics are lower, and this results in a decrease in the inhibitory regulatory action on MMP genes, which leads to an increase in the expression of MMPs.

### 2.2.6 Biomechanics;

Patients with diabetes are at risk for a wide range of health issues, including amputations of the lower limbs because of complications in the diabetic foot or foot-ankle complex. Given the fact that diabetic feet display altered locomotion and biomechanics, a greater knowledge of these alterations may benefit in the development and implementation of prevention and therapeutic measures.

In a nutshell, the following are the effects of diabetes on the key components of the foot-ankle complex:

2.2.6.1 Effects on skin: Compression and shear loads are increased on the skin, as well as the soft tissues immediately beneath the skin, which explains the commencement of tissue damage that is so closely associated with traumatic ulceration. Diabetic foot skin is less elastic and hence more susceptible to the effects of mechanical stress due to reduced hydration and a lack of autonomic nerve regulation.

2.2.6.2 Effects on tendons and ligaments: The increased transverse section of tendons and ligaments (i.e. thickening) is induced by protein glycosylation and associated collagen abnormalities. As a result of this surgery, Plantar Fascia and Achilles tendon are particularly sensitive. As a result of both of these variables, the stiffness of such structures is increased.

2.2.6.3 Effects on cartilage: In the same way as tendons and ligaments alter composition owing to the modification of collagen fibers, cartilage also undergoes structural change. In turn, the rigidity of the joint rises, the foot and ankle joints' overall range of motion is reduced, as well.

2.2.6.4 Effects on muscles: There is a deterioration of muscle fiber management in those with diabetes mellitus due to significant nerve conduction impairment. As a result, the foot-ankle complex's intrinsic and extrinsic muscles suffer structural and functional damage (loss of muscle volume) (decrease of muscular strength).

2.2.6.5 Effects on peripheral sensory system: This results in a structural and functional injury to both the foot-ankle complex's intrinsic and extrinsic muscles (decrease of muscular strength). Thermal and mechanical damage, as well as the late discovery of infection processes and tissue disintegration, are all risks for diabetic feet.

2.2.6.6 Effects on foot morphology (deformities): The foot's morphology is significantly altered and the development of foot abnormalities is determined by a severe imbalance in the peripheral muscle and soft tissue. A high longitudinal arch (rigid cavus foot), hammer toes, and hallux valgus are the most frequent diabetic foot abnormalities [34], [35][9], [36][37].

### 2.2.7 Diabetic Foot Ulcer Assessment;

The diabetic foot ulcer examination includes identifying risk factors, such as diabetic peripheral neuropathy, accepting that 50% of patients may not have any symptoms, and ruling out other causes of peripheral neuropathy, such as alcohol intake and spinal injury [6].

When treating an ulcer, it is important to evaluate the ulcer's location as well as its size, shape, and depth, as well as if the tissue is granulating or sloughy. In addition, the existence of malodor, the quality of the wound's border, and palpable bone and sinus development should all be taken into consideration. Grey or yellow tissue, purulent discharge, foul odor, sinus infection, weakening edges, and exposure of bone or tendon are some of the symptoms of infection [38].

The lack of a unique ICD-9 code for diabetic foot and variations in coding techniques make it difficult to identify diabetic foot in medical databases, such as commercial claims and prescription data. The following codes indicate ulcer of the lower limb or foot:

• 707.1 Ulcer of lower limbs, except pressure ulcer

• 707.14 Ulcer of heel and midfoot

• 707.15 Ulcer of other part of foot

• 707.19 Ulcer of other part of lower limb

One or more codes, in combination with a current or prior diagnosis of diabetes may be sufficient to conclude diabetic foot:

* 250.0 Diabetes Mellitus
* 250.8 Diabetes with other specified manifestations

### 2.2.8 Classification;

Diabetes can cause diabetic foot ulcers. There are three types of diabetic foot ulcers [38]: neuropathic, neuroischaemic, and ischemic. An ulcer's severity can be assessed using Wagner grades, which are often used by doctors. It is easier for physicians to track and treat diabetic foot ulcers with the Wagner Grades, which is the goal of this system. A numbering system from 0 to 5 is used to categories diabetic foot ulcers in this method.

There are five levels of Wagner grades: 0 through 5.

0. You do not yet have a Diabetic foot ulcer, but are at high risk to develop one.

1. You have a surface ulcer that involves full skin thickness, but does not yet involve the underlying tissues.

2. You have a deep ulcer that penetrates past the surface, down to the ligaments and muscle. There is no abscess or bone involved yet.

3. You have a deep ulcer with inflammation of subcutaneous connective tissue or an abscess. This can include infections in the muscle, tendon, joint, and/or bone.

4. The tissue around the area of your ulcer (limited to the toes and forefoot) has begun to decay. This is condition is called gangrene.

5. Gangrene has spread from the localized area of the ulcer to become extensive. This involves the whole foot [39].

### 2.2.9 Epidemiology;

Diabetes-related foot ulcers affect about 15% of people [4]. Only approximately half of those who have lower limb amputations survive for more than two years, due to the high risk of ulceration in the lower leg. The non-amputated foot ulcer survivorship rate is 56%. Amputations and foot ulcers have a major negative impact on quality of life. Hospitalizations for diabetes patients for foot difficulties account for approximately 8.8 percent of all hospitalizations [5] and such hospitalizations last approximately 13 days longer than hospitalizations for diabetic patients who do not have foot problems. More than half of all ulcers return after three years, and the recurrence rate might reach 70 percent after five years. Diabetic foot disease is the leading cause of non-traumatic lower limb amputations [6].

## 2.2 Etiology;

Due to various of factors, a person with diabetes is more likely to develop foot problems and diabetic infections in the legs and feet [11].

Table 1 Etiology of diabetic foot

|  |  |
| --- | --- |
| Foot wear | One of the most prevalent causes of diabetic foot issues is wearing shoes that don't fit properly. |
| If the patient has red spots, sore patches, blisters, corns, calluses, or constant pain associated with wearing shoes, it is critical to obtain new, well-fitting footwear as soon as possible. |
| It may be required to use prescription shoes or shoe inserts if the patient suffers from typical foot issues including flat feet, bunions, or hammertoes. |
| Nerve damage | Diabetics who have had their condition for a long time or who have had it inadequately treated are at danger of nerve damage in their feet. Peripheral neuropathy is the medical name for this. |
| They could be unable to feel their toes because of nerve injury. For this reason, it's possible that they'll have difficulty walking normally or balancing on one foot. It is common for people to notice when they are irritating or straining a certain region of their foot when they are walking. |
| Diabetics may fail to disclose minor injuries (such as cuts, scrapes, and blisters), indicators of abnormal wear and tear (such as calluses and corns), and foot strain. In most cases, a person can tell whether they have a stone in their shoe by feeling it and quickly removing it. A stone may go unnoticed by a diabetic patient. As a result of its persistent friction, it can easily inflame the skin. |
| Poor circulation | The condition known as atherosclerosis is caused by the rapid hardening of the arteries caused by diabetes, particularly when it is not well treated. Injured tissues do not recover effectively if blood flow to them is insufficient. |
| Infections | To avoid more serious bacterial infections that may result from athlete's foot, it is important to treat the illness as soon as possible. |
| The tiny blood arteries in the feet and legs are damaged by smoking any kind of tobacco. Amputations and infections can occur as a result of this injury, which can delay the healing process. It cannot be overstated how critical smoking cessation is. |
| Smoking | The tiny blood arteries in the feet and legs are damaged by smoking any type of tobacco. Infections and amputations can be increased as a result of this damage, which can impede the body's natural healing process. It cannot be emphasised enough how critical smoking cessation is. |

## 2.3 Prognosis;

When it comes to diabetic foot ulcers and diabetic kidney disease, large vessel arteriosclerotic disease of the coronary or renal arteries is a major contributing factor in the mortality of diabetics. If treatment is delayed, limb loss is a serious danger for diabetic foot ulcer patients. Preventable non traumatic amputations of the lower limbs are most prevalent among diabetics. After five years, the likelihood of having a contralateral amputation is 50% due to diabetic foot issues [48].

Despite effective care, 66% of diabetics with neuropathy develop another foot ulcer, with 12% requiring amputation.

## 2.4 Diabetic Foot Management;

### 2.4.1 Diabetic Foot Symptoms and Signs;

* Persistent pain can be a symptom of sprain, strain, bruise, overuse, improperly fitting shoes, or underlying infection.
* It is possible that redness is an indication of infection, particularly when it occurs around a wound, or that it is caused by excessive rubbing of shoes or socks.
* An underlying illness or infection, incorrectly fitted shoes, or inadequate vein circulation can all result in swelling of the feet or legs. Some more symptoms of impaired circulation are as follows [12];
* Walking exacerbates pain in the legs or buttocks, whereas resting alleviates the discomfort (claudication).
* Hair is no longer growing on the lower legs and feet.
* Legs with hard, lustrous skin [12], [14].
* It is possible that localized warmth is an indication of infection or inflammation, which may be caused by wounds that are failing to heal or healing too slowly.
* Skin damage can be caused by a variety of events, including traumas, excessive wear and tear, and infections. A persistent injury to the foot may create the calluses and corns seen in the figure below. All of these conditions can develop to more serious bacterial infections, such as ingrown toenails and athlete's foot.



Figure 1 Describing calluses and cons

* A wound that drains pus is generally an indication of an infection. It is also indicative of a potentially significant foot condition when the bloody leakage persists for an extended period of time.
* Joint issues, significant infection, or incorrectly fitted shoes can all manifest themselves in the formation of a limp or causing troubles in walking.
* Swelling of the foot in conjunction with fever or chills may indicate a potentially fatal condition that should be examined.
* Red streaks from a wound or redness that extends from it is a clear sign of an infection that is advancing.
* Symptoms of diabetic nerve damage, such as numbness in the feet and legs, might appear quickly or continue, which raises a person's chance of developing leg and foot issues [15], [16].

### 2.4.2 Alarming Signs;

If a diabetic has a diabetic foot or leg condition, the following are typical reasons to contact a doctor:

* Any damage to the feet or legs, regardless of its severity, requires medical attention. Even the smallest mishaps might result in fatal illnesses.
* The presence of mild-to-moderate soreness in the feet or legs needs immediate attention. It is not natural to be in constant discomfort.
* A fresh blister, wound, or ulcer with a diameter of less than 1 inch might swiftly deteriorate into a more serious scenario.
* A physician and patient must collaborate to develop a treatment approach for these wounds.
* When someone's feet or legs develop a new region of redness or swelling, this is almost always an indication of an infection. Taking care of them as soon as possible will assist avoid the development of more serious problems.
* Patients with diabetes are more likely to have ingrown toenails, which can lead to foot infections and amputations. For an ingrown toenail, a patient may notice redness or swelling around the nail. The importance of receiving early and proper counselling cannot be overstated.
* Diabetic nerve degeneration (neuropathy) or poor circulation in the legs can also produce tingling or numbness in the feet or legs. Each of them has the potential to result in patient amputations and other life-threatening consequences.
* It is possible to have trouble walking as a result of diabetic arthritis (Charcot's joints), which is frequently caused by excessive pressure and strain on the foot, or by wearing shoes that are too large or too small. Early identification and treatment of more significant problems, for the prevention of conditions including skin breakdown and infections in the lower limbs [17], [18].
* Itching in the feet can be caused by a fungal infection or dry skin, which can lead to an infection.
* The foot should have any calluses or corns properly removed. It is not suggested to remove it from home.
* An urgent visit to the doctor's office should be made in the case of a fever (temperature more than 98.6°F (37°C)), in conjunction with any additional symptoms or even just the presence of fever. The severity of an illness does not necessarily correlate with the degree of fever. Even if a patient has no temperature or a mild fever, they might still be infected. A fever should be taken very seriously by diabetics [19].

Notify the hospital emergency department of the patient's symptoms, current medications, and any known drug allergies. When it comes to diagnosing and treating a patient, this knowledge will be useful [20] [21].

The following are some typical reasons why diabetic foot and limb issues require immediate medical treatment.

* Pain in the feet or legs might be an indication of an infection, a sudden loss of circulation, or a substantial damage to the nerves in the leg (neuropathy).
* In order to speed up the healing process, it is important to clean and treat any lesion on the feet or legs that bleeds profusely and penetrates the skin.
* There is a considerable risk of infection from any substantial puncture wounds to the foot (treading on an unpolished nail or getting attacked by an animal).
* Limb-threatening infections are usually linked to foot or leg wounds or ulcers larger than 1 inch in diameter.
* Redness or red streaks spreading from a lesion or ulcer on the foot or leg may transfer infection.
* An elevated temperature of more than 101.5°F (38.6°C), as well as redness and swelling on the lower legs, may indicate a severe disease. You should seek immediate medical assistance if your fever is more than 101.5°F (38.6°C) without any other signs or symptoms. Because the severity of an infection is not always indicated by the level of fever, diabetics should be aware of low-grade fevers and monitor their condition. Even though viral infections are frequently to account for fevers, the doctor may or may not give antibiotics to the patient [22], [23].
* An altered mental state (confusion) in the presence of a leg wound or foot ulcer may be a sign of a potentially life-threatening infection that might end in the loss of a leg or foot. If there is an illness present, it is also possible to have disorientation as a result of abnormally high or extremely low blood glucose levels.

After inquiring about the patient's symptoms, the physician will examine the patient. This assessment should involve a physical examination of the patient (temperature, pulse, blood pressure, and respiratory rate). When examining an extremity with a diabetic ulcer, look for signs of vascular insufficiency, peripheral neuropathy, and edema, as well as the ulcer itself.

Based on the severity of the soft tissue and bone damage, a comprehensive examination of the feet and legs may be essential to identify how to proceed with treatment for diabetic foot wounds, as well as to establish how to proceed with treatment for the wounds themselves. In the instance of a wound or ulcer on the lower extremities, a blunt probe may be required to determine the depth of the lesion [25], [26].

### 2.4.3 Diabetic Foot Ulcers Differential Diagnosis;

Individuals with diabetes are not the only ones who can have skeletal and soft-tissue infections of the foot; as a result, additional illnesses may need to be considered in the differential diagnosis, depending on the infection and structures affected. A thorough history  is often helpful

Differentials include

1. Gas gangrene
2. Superficial thrombophelibitis
3. Vibrio fulnicus infection
4. Leukoclastic angitis

## 2.5 Workup;

**2.5.1 Laboratory Tests;**

A total blood cell count may be ordered by a clinician to detect the presence and severity of a disease (CBC). A serious infection is indicated by an unusually high or low white blood cell count. The doctor may also do a finger stick or a laboratory test to check the patient's blood sugar. In the midst of a significant illness, the doctor may order kidney function tests, blood chemistry studies, liver enzyme testing, and heart enzyme tests to see if other body systems are operating normally [26], [27].

### 2.5.2 Stains and Cultures of the Wound;

In skin and soft-tissue infections, Gram stain and cultures can be used to determine the aetiology of the infection, whereas blood cultures can be used to identify the organisms that are causing the infection in acute osteomyelitis and cellulitis. In individuals with a soft tissue diabetic foot infection, a tissue specimen for culture should be taken aseptically from the ulcer using curettage or biopsy.

### 2.5.3 Radiology;

X-rays of the feet and legs may be ordered by the doctor to look for evidence of bone degeneration, arthritis, infection, or foreign bodies in the soft tissues. The presence of gas in soft tissues is an indication of gangrene, a life- or limb-threatening illness.

### 2.5.4 Doppler Ultrasound;

Doppler ultrasonography may be ordered by the doctor to examine the flow of blood in the legs' arteries and veins. A non-invasive probe is moved across the blood veins of the lower limbs by a technician, any discomfort throughout the procedure is not felt by the patient.

### 2.5.5 Consultation;

The physician may request that the patient be seen by a vascular surgeon, an orthopedic surgeon, or both. Infections of the lower extremities, difficulties with the bones, and circulation issues can all be treated by these specialists.

* **ANGIOGRAPHY:** Patients with poor circulation in the lower limbs may benefit from an angiography, which the vascular surgeon will order if they are diagnosed with this condition [27], [28]. Angiograms are performed by inserting a catheter into an artery in the groyne and injecting dye while taking x-rays. This enables the surgeon to determine the location of the obstructions and arrange a procedure to bypass them. This treatment is often conducted under local anesthesia with the administration of a mild sedative via a tube put into the patient's vein.

## 2.6 Treatment Modalities;

In diabetes, foot ulcers require multidisciplinary examination, a diabetic nurse specialist, a tissue viability nurse, podiatrists, diabetes specialists, and surgeons frequently undertake this procedure [38]. Aiming to enhance glycemic control, the goal of treatment is to slow down the progression of the disease if it is insufficient [6]. Indications of osteomyelitis, suspected Charcot neuroarthropathy, or ulcers that don't heal after four weeks of standard care and evidence that the exudate is of synovial membrane origin are all indications of a condition known as "probe to bone". An MRI scan should be performed if osteomyelitis is suspected but not evident on an x-ray [38].

In the case of infected foot ulcers, the presence of bacteria alone does not indicate infection. The most conclusive signs of a present infection are inflammation and purulence. Staphylococcus aureus is the most often infected organism [5]. Debridement, proper dressings, management of peripheral arterial disease, the treatment includes proper antibiotic medication (against pseudomonas aeruginosa, staphylococcus, streptococcus, and anaerobe strains), as well as arterial revascularization [5].

### 2.6.1 Antibiotics;

Antibiotic regimens can last anywhere from one week to six weeks or longer, depending on the severity of the sickness and whether or not a bone infection is present. When there is evidence of an infection, antibiotics should only be administered until the infection has been eliminated, rather than until the ulcer has healed, according to current guidelines. Local bacterial strains that cause ulcers influence antibiotic selection. Oral swabs, according to the researchers, are of little help in identifying the infectious strain. In situations of osteomyelitis, a microbiological examination is beneficial [38]. Multiple bacteria are involved in the majority of ulcer infections [5].

### 2.6.2 Dressings for Wounds;

Dressings made of absorbent fillers, hydrogels, and hydrocolloids are only a few of the many varieties used to treat diabetic foot ulcers [40]. There is no evidence that one approach of dressing diabetic foot ulcers is better than another [41]. Consideration should be given to the cost of a product when selecting bandages for chronic wounds that do not heal [42].

Despite the fact that hydrogel dressings may have a modest benefit over traditional dressings, the quality of the study remains unknown [43]. Neither silver-containing dressings nor creams [44] nor alginate dressings [45] have been thoroughly investigated. Hydrogel and hydrocolloid-based bioactive bandages need more research to determine their efficacy [40].

### 2.6.3 Total Contact Casting;

Total contact casting (TCC) is a kind of cast that is particularly designed to support the weight of the foot in patients with DFUs (off-loading). In DFU therapy, lifting the weight of the foot off the wound has proved to be quite efficient at reducing pressure on the lesion. People who have diabetes in the United States are more likely to have to have their lower legs amputated because of DFUs. 85% of diabetics who have their lower legs amputated had a DFU first [46]. For individuals with neuropathic DFUs, It is estimated that the 5-year mortality rate among diabetics following amputation will be around 45% [46].

Since the mid-1960s, TCC was first introduced in the United States to aid in the off-loading of DFUs, and it is now widely considered as the "reference standard" for off-loading DFUs on the bottom surface (sole) of the foot in this nation [47].

TCC allows patients to retain their lifestyle. In order to maintain their activity level, patients should encase their whole foot — including the toes and lower leg in a specialized cast that redistributes weight and pressure from the foot to the lower leg during regular movements [48]. TCC's pressure redistribution preserves the wound, allowing injured tissue to regenerate and heal [49]. Additionally, TCC prevents the ankle from turning when walking, hence preventing shearing and twisting forces from aggravating the wound [50].

Effective offloading is a critical component of treating DFUs, particularly those involving nerve injury in the foot (peripheral neuropathy). TCC, in conjunction with infection control and vascular evaluation, is a critical component in properly managing DFUs [50]. TCC is the most successful and dependable approach for DFU disposal [51], [52], and [53].

A meta-analysis done in 2013 by the Cochrane Collaboration indicated that casts, therapeutic shoes and dressings, detachable orthotic devices, and surgical therapies were all beneficial in reducing pain. Treatment of diabetic foot ulcers using non-removable pressure relieving treatments, such as non-removable casts with an Achilles tendon lengthening component, was found to be more effective than treatment with therapeutic shoes and other pressure releasing procedures in terms of healing success [54].

### 2.6.4 Hyperbaric Oxygen;

At 6 weeks, a Cochrane review found that hyperbaric oxygen therapy decreased amputation risk and improved healing in persons with diabetic foot ulcers, published in 2015. However, the quality of the assessed studies was insufficient to draw significant conclusions [55].

### 2.6.5 Negative Pressure Wound Therapy;

In order to remove extra fluid and cellular debris from a wound, suction is frequently used to extend the inflammatory phase of wound healing. Despite the fact that negative pressure wound therapy has a straightforward mechanism of action, some research have revealed inconsistent results (NPWT). Pressure intensity, intervals between treatments, and precise timing of negative pressure therapy must be studied further in the case of chronic wound healing [56].

### 2.6.6 Other Treatments;

People with diabetes may benefit from ozone treatment, however there is just little and poor-quality evidence to support this claim [57].Diabetic foot ulcers may heal more quickly and completely if growth hormones are used taken in account [58].

A technique known as Continuous Diffusion of Oxygen (CDO), on the other hand, involves the delivery of continuous oxygen to an occluded, wet wound site at significantly lower flow rates of 3–12 mL/h for 24 hours per day, seven days per week, for up to many weeks or months, depending on the wound status [59]. A vascular surgeon or podiatrist should examine each diabetic foot ulcer patient to see if debridement, revision of bone architecture, vascular reconstruction, or soft tissue covering is required [41], [62].

### 2.6.7 Patient Self Care;

The following are precautioning a diabetic should do: [30], [31].

Table 2 Precautions for diabetic foot

|  |  |
| --- | --- |
| **Foot examination** | Keep an eye out for any irregularities or injuries, no matter how little, on your feet on a daily basis. Any irregularities should be reported to your physician. Using a water-based moisturizer every day is the best approach to avoid dry skin and cracking (except between your toes). Cotton or wool socks are preferred. Elastic socks and hosiery can impede blood flow, so avoid them if you want to keep your feet warm. |
| **Eliminate obstacles** | Move or eliminate anything that might cause you to trip or bump your feet. Maintain an orderly appearance on the floor. Indoor and outdoor paths should be illuminated at night. |
| **Toenail trimming** | Never use scissors to trim your nails. They should be cut across the grain with plenty of space between them. Let the doctor or a family member handle it if one has trouble seeing or using your hands. |
| **Footwear** | The feet should be protected by wearing durable, comfortable shoes whenever possible. Also, it beneficial to consult with a podiatrist (foot doctor) for shoe fitting advice, or shop at shoe retailers that specialize in fitting persons with diabetes. To identify local shoe retailers, ask your endocrinologist for a reference. One may require prescription footwear or shoe inserts if he/she has flat feet, bunions, or hammertoes. |
| **Exercise** | Regular exercise improves the health of the bones and joints of the feet and legs, as will leg circulation and the stability of blood sugar. It is recommended that to consult a doctor before commencing any fitness program [32], [33]. |
| **Smoking** | One of the greatest ways to avoid foot issues is to stop smoking tobacco of any kind. Smoking has the ability to hasten the deterioration of blood vessels, especially the smaller ones, and as a result of this, foot infections and, eventually, amputations, become more typical. |
| **Diabetes control** | Healthy eating, taking prescribed medications, frequent blood sugar monitoring, regular physical exercise, and open lines of contact with your doctor are the best ways to manage diabetes. Individuals with diabetes whose blood sugar levels have been out of control for a lengthy period of time risk damaging their nerves, kidneys, eyes, and blood vessels. |
| **Antibiotics** | Treatment for infections or possible infections, such as a cat-bite wound, requires the use of antibiotics, which the doctor prescribes after determining the wound or ulcer has become infected. A complete course of antibiotics must be completed by the patient exactly as advised by the doctor. In the majority of cases, the patient will see some healing in two to three days, but improvement may occur as early as the day of therapy. IV antibiotics will be administered to patients with life-threatening illnesses, which necessitates hospitalization. With over-the-counter medications, outpatient care may not be necessary for some infections. In the clinic or emergency room, prior to commencing pills, the doctor may deliver a single dosage of antibiotics through shot or IV [35], [36]. |
| **Referral to wound care center** | Wound treatment services at community hospitals are becoming more readily available to treat patients with diabetic ulcers and sores on the lower limbs. At these facilities, treatment regimens for leg ulcers and chronic wounds can be developed in collaboration with the patient and the patient's medical professional by a multidisciplinary team of medical specialists. Special dressings, antibiotics, and surgical debridement of the wound are all possible treatment options. A number of different therapies may be included in the strategy. |
| **Referral to podiatrist** | Bone, toenail, corn and callus, hammertoe and bunion problems can all be sent to one of these specialists by a doctor. They can also help with heel spurs and arthritis. They not only create shoe inserts, but also prescribe footwear, remove calluses, and are bone surgery specialists. Additionally, their skill in good daily foot care can be highly beneficial [9], [37]. |
| **Home health care** | A home health nurse may aid with wound care and bandaging, blood sugar monitoring, and prescription delivery or assistant assigned by the patient's doctor. |

Numerous factors contribute to the development of diabetic foot ulcers, including mechanical alterations foot's bone architecture and peripheral neuropathy, as well as atherosclerotic disease of the peripheral artery system, all of which occur more frequently and intensely in diabetics[38], [39].



Figure 2 Before and after wound care for a diabetic ulcer on the medial surface of the left first toe.



Figure 3 Left fourth toe diabetic ulcer coupled with minor cellulitis.

## 2.7 Diabetes-Related Atherosclerosis;

It is more common for diabetics to suffer from atherosclerosis, capillary fibrosis and endothelial proliferation than for individuals without the illness. Diabetics are also more prone to calcification and thickening of the arterial media (Mönckeberg sclerosis), however their effect on the circulatory system is unknown.

As is the case with non-diabetics, diabetics can develop atherosclerosis of the main and medium arteries, including aortoiliac and femoropopliteal atherosclerosis. On the other hand, in the diabetic population, severe atherosclerotic disease of the infrapopliteal segments is unusual. When combined with an infected lesion, Substantial illness of the digital arteries can result in the entire loss of digital collaterals and the development of gangrene [63], [64].

Patients with diabetes are more likely to develop this kind of vascular disease because of a number of metabolic abnormalities, such as higher plasma LDL and VLDL levels, elevated plasma von Willebrand factor, inhibition of prostacyclin synthesis, and elevated plasma fibrinogen and platelet adhesiveness.

## 2.8 Diabetic Peripheral Neuropathy;

A lack of myoinositol is assumed to be the source of the pathophysiology of diabetic peripheral neuropathy, which affects myelin synthesis and ATPase function, chronic hyperosmolarity, edema in the nerve trunks is caused by excessive levels of sorbitol and fructose in the blood [40], [41].

In the absence of sensation in the foot, recurrent stress results in unreported foot injuries and fractures, structural foot abnormalities such as hammertoes, bunions, metatarsal deformities, or Charcot foot, increased stress, and eventual tissue collapse are all possibilities. Blisters and ulceration can occur as a consequence of an injury caused by a blunt or sharp object left in the shoe as a result of unexpected exposure to extreme heat or cold. When paired with insufficient vascular supply, these variables significantly increase the risk of limb loss in diabetes patients.

## 2.9 Risk Factors;

Neuropathy [6], vascular disease [7], hypertension [8], and foot deformity [9] are all possible causes of diabetic ulceration. Microvascular disease and inadequate glycemic management also add to the risk of foot ulceration in diabetics, with 60% of diabetics and 80% of diabetics with foot ulcers having diabetic peripheral neuropathy [41], [42].

### 2.9.1 Charcot Foot;

Foot sensory neuropathy can develop as a result of unrecognized trauma events caused by improperly fitted shoes. By generating intrinsic muscle weakening and foot splaying during weight bearing, motor neuropathy exacerbates this damage. As a result, the foot is convex in form and seems to have a rocker bottom. Numerous fractures go unnoticed until significant bone and joint issues develop. The most common cause of Charcot foot (neuropathic osteoarthropathy) is diabetes mellitus, which affects around 2% of diabetic people [43], [44].

The medial portion of the navicular bone and the inferior aspect of the cuboid bone are particularly vulnerable to ulceration if a Charcot foot is ignored. The sinus tubes grow into the deeper planes of the foot and into the bone as a result of ulcerations. Additionally, Charcot alteration can have an effect on the ankle, moving the mortise and resulting in ulceration, which may need amputation.

## 2.10 Epidemiology;

Diabetes affects around 16 million people in the United States, with millions more thought to be at risk. More than 16 million people in the United States have diabetes, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Hospitalizations due to diabetic foot lesions are the most common of any severe complication of diabetes. Between 12 and 24 percent of diabetics who develop a foot ulcer require amputation. According to the American Diabetes Association, diabetes is the most common cause of non-traumatic lower extremity amputations in the United States. Each year, around 5% of diabetics have foot ulcers and amputations [46], [47].

### 2.10.1 Age Distribution for Diabetic Ulcers;

In the United States, diabetes affects about 3-6 percent of the population. Type 1 diabetes affects 10% of the population, with most cases occurring in those under the age of 40. Diabetes affects around 10% of Medicare-eligible persons over the age of 65. (Of these, 90 percent have type 2 diabetes). Neuropathy develops 10 years after the onset of diabetes, causing deformity and ulceration of the diabetic foot.

### 2.10.2 Prevalence of Diabetic Ulcers by Race;

African-Americans [10], Native Americans [11], and Latino populations in the Eastern United States are at increased risk of developing diabetic foot disease, since they have the greatest prevalence of diabetes among all ethnic groups in this country.

## 2.11 History;

It's important to look for symptoms that could be signs of peripheral neuropathy or peripheral arterial insufficiency in the history [49], [50].

### 2.11.1 Symptoms of Peripheral Neuropathy;

Peripheral neuropathy manifests itself in the following ways:

* Hypoesthesia
* Hyperesthesia
* Paresthesia
* Dysesthesia
* Radicular pain
* Anhydrosis

### 2.11.2 Symptoms of Peripheral Arterial Insufficiency;

When the lower extremities have atherosclerosis, the majority of people are asymptomatic; nevertheless, some persons experience ischemia symptoms. As a result, some patients mistakenly believe that their inability to walk is just a sign of old age. Chronic pain, non-healing ulcers on the foot or even complete ischemia are among symptoms that may be present in patients who are clinically symptomatic [51], [52].

Interruption of major muscle groups in one or both lower limbs after walking a certain distance. Resting for a few minutes can alleviate this feeling, which worsens with ambulation until walking is no longer feasible. Walking at a faster pace or uphill or upstairs may lead to claudication earlier than walking at a normal pace.

Infrainguinal occlusive disease usually causes claudication in the calf muscles. Having tibioperoneal atherosclerotic occlusions in the calves or feet is a typical occurrence among diabetics, as they are more likely to have this condition. There is also a possibility of calf muscle atrophy. Aortoiliac occlusive disease is indicated by symptoms in the buttocks or thighs. In diabetic patients, rest discomfort is less prevalent. In some situations, the initial symptom of perfusion loss is a fissure, ulcer, or other disruption in the integrity of the skin envelope. It is common for a diabetic patient to develop gangrene because of an infection [54], [55].

## 2.12 Physical Examination;

There are three basic areas of physical examination for diabetic ulcers on the lower limb:

* Ulcer and extremity examination.
* An examination to determine the risk of vascular insufficiency.
* Possible peripheral neuropathy assessment.

It is important to remember that diabetes is a systemic illness. Because of this, it is critical to undertake a comprehensive physical examination of the whole individual.

### 2.12.1 Examination of Extremity;

When it comes to diabetic ulcers, they tend to manifest themselves in places that are subjected to a great deal of weight bearing. The heel, the plantar metatarsal head, prominent toe tips (often the first or second toe), and hammer toe tips are all examples of prominent toe tips (ulcers also occur over the malleoli because these areas commonly are subjected to trauma). The dorsal portion of the foot is particularly sensitive if you have hammer toes.

Other physical findings include the following:

* Hypertrophic calluses
* Brittle nails
* Hammer toes
* Fissures

### 2.12.2 Assessment of Possible Peripheral Arterial Insufficiency;

Peripheral pulses are missing or decreased when measured below a specific level, according to physical examination. The presence of normal or missing femoral pulse at the level of the inguinal ligament distinguishes infrainguinal illness from aortoiliac disease, which is distinguished by the presence of decreased or nonexistent femoral pulses distal to the inguinal ligament. A proximal superficial femoral artery blockage, in particular, results in the loss of the femoral pulse right below the inguinal ligament. The proximal superficial femoral artery is blocked, causing the femoral pulse to be absent right below the inguinal ligament. Popliteal pulse is absent due to adductor canal anomalies [56], [57].

When the distal popliteal artery or its trifurcation is diseased, there is a loss of pedal pulses. The absence of the dorsalis pedis pulse, on the other hand, is a common anatomic variation that affects around 10% of the pediatric patient population. But 99.8% of children and young adults under the age of 19 have a posterior tibial pulse. Peripheral vascular disease can be diagnosed more accurately when both pedal pulses are absent.

A bruit heard above the iliac or femoral arteries is another indicator of atherosclerotic disease, as is skin atrophy, loss of pedal hair growth, cyanosis of the toes, ulceration or ischemic necrosis, and pallor of the afflicted foot followed by dependent rubor after 1-2 minutes of elevation above heart level are some other signs.

### 2.12.3 Assessment of Possible Peripheral Neuropathy;

Excessive callous development, particularly on pressure sites such as the heel, is one of the signs of peripheral neuropathy. Other signs include loss of vibratory and position awareness, loss of deep tendon reflexes (particularly loss of the ankle jerk), trophic ulceration, foot drop, muscular atrophy, as well as excessive callous formation [58], [59].

The nylon monofilament test can be used to identify sensory neuropathy in the hands. The soles of the feet are gently stroked with a 10-gauge monofilament nylon to bend the wire. This test is positive for neuropathy if the patient cannot feel the wire at four or more of the ten locations listed above. From the NIH or from Semmes-Weinstein, the practitioner can get filaments for use in the treatment of diabetes and kidney disease.

## 2.14 Diagnostic Considerations;

Bullosis diabeticorum, eruptive xanthoma, necrosis lipoidica and granuloma annulare are distinct from the classic diabetic ulcer in terms of diabetes-related skin disorders [59], [65].

There are a number of other possible reasons of lower leg pain, including arthritis and radicular pain as well as spinal cord compression and thrombophlebitis. Peripheral arterial disease's leg pain must be differentiated from these other possible causes. Diabetic neuropathy should be distinguished from other types of neuropathy, which include vasculitic neuropathies, metabolic neuropathies, autonomic neuropathies, radiculopathy, and several other types of neuropathy.

### 2.14.1 Approach Considerations;

The diabetic ulcer patient workup includes blood tests, pulse volume recording, ultrasonography, ankle-brachial index, radiography, computed tomography, magnetic resonance imaging, bone scans, and angiography [66], [67].

#### 2. 14.1.1 Blood Tests;

A complete blood count is recommended. Elevated leukocyte counts may suggest infection in the foot or other areas of the body. Anemia hinders wound healing. When anemia is paired with underlying vascular insufficiency, rest discomfort can occur. The levels of glycated hemoglobin and creatinine in diabetic patients can be used to assess the effectiveness of both acute and chronic glycemic control, as well as the state of renal function in diabetic patients. A normal hemoglobin A1C level, which should be included in all blood tests, can be used to monitor wound healing.

#### 2. 14.1.2 Pulse-Volume Recording;

With pneumatic cuffs enclosing the thighs, calves, ankles, feet, and, rarely, toes, pulse-volume recording (PVR), also known as plethysmography, measures variations in segmental volume with each pulse beat. At each level, the tracings that arise give valuable information regarding the hemodynamic repercussions of the artery disease. Tran’s metatarsal tracings may become almost flat in severe illness. PVR tracings may seem normal at rest in patients with moderate illness, particularly in those affecting the aortoiliac region, and become aberrant only after the patient moves until symptoms arise [68], [69].

It is possible to repeat PVR tests often to monitor the overall hemodynamic response to medication or surgical therapy. In most cases, arterial assessment PVR does not offer any relevant information if pedal pulses are adequate.

#### 2. 14.1.3 Ultrasonography;

Simultaneous Doppler flow velocity measurement and duplex ultrasonography can both give images of arterial segments that can be utilized to locate the extent of sickness. It's much easier to see aortic and popliteal aneurysms using duplex scanning. Generally, it is advisable to leave the decision of whether or not to employ this technique to the discretion of the vascular specialist. There are several ways to employ a handheld Doppler scanner in the assessment of arterial signals, such as locating arteries to simplify probing, or determining the loss of Doppler signal in the vicinity of the blood pressure device. [70], [71]. There have also been Laser Doppler investigations used, however these may not always be accurate.

#### 2. 14.1.4 Ankle-Brachial Index;

The ankle-brachial index (ABI) is a measure of vascular compromise that is calculated by dividing the systolic pressure in the posterior artery by the systolic pressure in the lower extremities. Ordinarily, ABI is 1.0. An ABI less than 0.9 suggests atherosclerotic disease, and it has a sensitivity of around 95%. Distal ischemic ulcers are unlikely to heal if the ABI is below 0.3. As is frequent in diabetics, a high ABI might be misleading and consequently inaccurate if the underlying arteries are substantially calcified[71], [72].

#### 2. 14.1.5 Plain Radiography;

On conventional radiographic examinations of the diabetic foot, the presence of osteomyelitis, demineralization, and the Charcot joint can all be observed seldom, as can the existence of the Charcot joint. Plain radiographs of peripheral artery occlusive disease are not typically obtained in the course of the disease. Atherogenesis insipida (AID) cannot be detected only by looking at plain radiographs since arterial calcification does not necessarily indicate the presence of AID in the body. The presence of calcification in the arterial media does not necessarily indicate the existence of atherosclerosis, and even the presence of calcium in the artery intima does not always imply hemodynamically significant stenosis.

#### **2.** 14.1**.6 Computed Tomography and Magnetic Resonance** **Imaging;**

In most cases, a qualified physician can diagnose a plantar abscess only on the basis of physical examination. If a plantar abscess is suspected but not physically obvious, an imaging test such as a CT or MRI may be conducted.

#### 2. 14.1.7 Bone Scans;

Bone scans produce a large proportion of false positives and false negatives, making them problematic in their use. A recent study suggests using Technetium-99m-labeled ciprofloxacin as an osteomyelitis marker [71].

#### 2. 14.1.8 Conventional Angiography;

The amount and importance of atherosclerotic disease must be determined by angiography if vascular or endovascular surgery is proposed. Due to the puncture and contrast agent administration, traditional contrast-injection angiography has the most hazards.

## 2.15 Technique;

An infrarenal aorta contrast injection is often performed retrogradely by a femoral puncture, with the contrast being delivered through a catheter into the infrarenal aorta. The contrast is traced down both feet when the films are taken. When an aortic aneurysm is present, it may not be possible to access the aorta by the femoral approach. This may need the interventionist using an alternative entry route, such as the brachial or axillary arteries (interventional cardiologist, vascular surgeon, or interventional radiologist). Sheath diameters of 5F (1.6mm) and smaller are used to insert the arterial catheter into the patient's artery. Although it may only measure 6-10 mm in diameter, the femoral artery has been pierced by this large hole. For approximately 30 minutes following removal of the catheter, mild pressure must be given to the puncture site. A tiny device (referred to as a "closure device") may be used by the physician doing the angiography in order to help with the closure of the puncture site in the majority of cases. It is no longer necessary to apply pressure for an extended period of time when these devices are successfully deployed [72].

### 2.15.1 Puncture-Related Complications;

The dangers of catheter insertion include hemorrhage, pseudo aneurysm formation, and clotting or dislodgment of an intimal flap. Clotting or dislodgment of an intimal flap might abruptly occlude the artery at or near the entrance site. Reduced complication rates have been attributed to the use of percutaneous closure devices on the puncture sites.

### 2.15.2 Contrast-related risks;

Contrast material used in angiography is nephrotoxic. Patients with preexisting renal insufficiency, as well as those who have diabetes, are at the greatest risk of developing acute renal failure. Contrast angiography-induced acute renal failure occurs in 30% of patients with these two risk factors. As a result, before to elective angiography, it is necessary to establish that the serum creatinine level is appropriate. The use of contrast angiography should be avoided in individuals with any substantial renal impairment. It is essential to utilize the least amount of contrast material possible if contrast angiography is absolutely necessary despite renal impairment. Additionally, it is critical to maintain appropriate hydration prior to, during, and after the surgery is completed. According to early studies, patients at risk of contrast-induced nephropathy may benefit from taking the antioxidant acetyl cysteine (Mucomyst) the night before and again shortly before angiography [73].

### 2.15.3 Metformin Warning;

To reduce the risk of fatal lactic acidosis, the drug metformin (Glucophage) should not be used shortly after contrast angiography. Shortly after contrast angiography, diabetic patients on metformin (Glucophage) should avoid taking this medicine. Following confirmation of normal renal function, patients may continue taking their medicine 1-2 days after being exposed to contrast.

### 2.16 Alternatives to Conventional Angiography;

### 2.16.1 Magnetic Resonance Angiography;

A magnetic resonance angiography (MRA) procedure can be used in patients who are allergic to iodinated contrast material. MRA is not a harmless procedure. Acute renal damage, pseudo hypocalcemia, and in people with renal insufficiency, nephrogenic systemic fibrosis has been linked to gadolinium chelates, the contrast agents used in MRA. Patients who have implanted hardware, such as hip prosthesis or pacemakers, should avoid MRA.

Infrapopliteal artery reconstructions may necessitate the use of MRA, although the resolution provided by MRA may be insufficient for the vascular surgeon, particularly in the smaller arteries.

### 2.16.2 Multi Detector CT Angiography;

Avoiding artery puncture is possible with multidetector CT angiography (MDCT). An angiographic picture with outstanding resolution and acquisition speed may be generated by multidetector (16 or 64 channel) CT scanners employing properly timed intravenous contrast injection. The dangers of contrast-related MDCT angiography are outlined above.

### 2.16.2 Carbon Dioxide Angiography;

The use of carbon dioxide angiography for patients with renal insufficiency is an option; however, it is not commonly accessible and needs the use of extra iodinated contrast material in order to generate usable pictures.

### 2.16.3 Transcutaneous Tissue Oxygen Studies;

Because of this, transcutaneous tissue oxygen studies are used only when the advisability of an arterial bypass surgery operation is in dispute.

**Staging;**

Soft tissue and osseous involvement in diabetic foot lesions are classified according to their depth. Any lesion that looks to track into or is deeply lodged in subcutaneous tissues should be suspicious of Osteomyelitis; if bone is contacted, the diagnosis of osteomyelitis should be considered.

**Approach Considerations;**

Diabetes foot ulcers can be treated with a combination of measures, including wearing correct shoes, using saline dressings on a regular basis, and performing debridement surgery. Other measures include using antibiotics, monitoring blood glucose levels, and having peripheral arterial insufficiency diagnosed and repaired [18], [21].

If there is no evidence of vascular insufficiency, wound closure using cultured human cells or heterogeneous dressings/grafts, injection of recombinant growth hormones, and hyperbaric oxygen therapy may also be beneficial.

To save a limb, diabetic patients with ulcers may need to be treated with potentially risky operations like angiography or bypass surgery, but doctors must weigh the risks and benefits of these procedures in light of their patients' high risk of heart disease. In general, the most significant legal concerns are associated with failing to detect diabetic ulceration promptly, failing to aggressively debride and treat infection, and failing to maintain the wound with care once it has been diagnosed. Patients who appear with a new diabetic foot ulcer should be cared for by doctors, surgeons, podiatrists, and pedorthotists who are actively involved in the management of this complex issue.

## 2.17 Management of Systemic and Local Factors;

It is necessary to address a variety of systemic and local parameters in order to effectively treat diabetic foot ulcers. Precision in diabetes management is essential not only for healing the existing wound but also for reducing the likelihood of a recurrence. Critically important is the control of systemic variables such as hypertension, hyperlipidemia, atherosclerotic heart disease (including obesity), and renal insufficiency (including renal failure) [32], [33]. Managing vascular insufficiency, treating infection with appropriate antibiotics, unloading the ulcerated area, and wound care are other critical issues.

### 2.17.1 Wound and Foot Care;

A moist but not wet wound bed is the fundamental premise of topical wound treatment.

### 2.17.2 Wound Coverage;

After debridement, treat the wound site with a wet sodium chloride dressing or isotonic sodium chloride gel (e.g., Normlgel, IntraSite gel) or a hydro active paste (e.g., Duoderm). For effective wound coverage, wet-to-damp dressings that encourage autolytic debridement, absorb exudate, and preserve surrounding healthy skin are necessary. Plastic film dressings like Tegaderm and TegaSite are semipermeable to oxygen and moisture but impenetrable to bacteria. Suitable for wounds that are neither too dry nor highly exudative, these dressings can be used. The following are wound-covering rules for a range of wound conditions.

• Dry wounds: Oxygen and moisture cannot pass through hydrocolloid dressings like DuoDERM or IntraSite Hydrocolloid, which keeps the surrounding area moist. In the case of wounds that are extremely dry, they are a wonderful choice.

• Exudative wounds: Exudative wounds are best treated with a calcium alginate dressing like Kaltostat or Curasorb, which is very absorbent. In certain cases, alginates are available in rope form, which makes them particularly useful for packing large wounds.

• Very exudative wounds: Some of the most efficient treatments for wounds that are very exudative include impregnated gauze or hydro fiber dressings (for example, Mesalt). It may be essential to change the dressings twice a day in certain circumstances.

• Infected superficial wounds: If the patient is not sensitive to sulfa medications, Silva Dene (silver sulfadiazine) can be used to treat infected superficial wounds; if the patient is allergic to sulfa drugs, either bacitracin-zinc or Neosporin ointment can be used as an alternative. A hydro fiber-silver dressing (Aquacel-Ag) can be used to treat wounds that are both exudative and possibly colonized in the presence of heavy bacterial contamination of deeper wounds for a limited period of time when heavy bacterial contamination is present.

• Wounds covered by dry eschar: When a wound is covered with dry eschar, the best course of action may be to merely shield the site until the eschar dries and separates on its own. This kind of treatment may be most appropriate for an uninfected, dry heel ulcer in a well-perfused foot that has been painted with povidone iodine (Betadine).

• Areas that are difficult to bandage: In order to bandage a difficult anatomical site, such as around a heel ulcer, a very thin hydrocolloid is needed; whereas a conformable hydrocolloid, such as the wafer kind, is needed to hold a dressing in a highly moist demanding place, such as around a sacrococcygeal ulcer.

• Fragile periwound skin: It is helpful to employ hydrogel sheets and non-adhesive forms when the surrounding skin is at risk of being injured in order to keep a wound dressing in place.

In addition to these topical medicines, the following are others that may be effective in the therapy of diabetic foot ulcers on occasion.

• Platelet-derived growth factors (PDGF): In the case of wound healing, platelet-derived growth factors (PDGF) are shown to have a mildly positive impact when given topically to the skin. For diabetic foot ulcers, the Food and Drug Administration has approved the use of becaplermin gel 0.01 percent (Regranex), a genetically engineered recombinant human PDGF, for treatment [68]. Regranex is contraindicated when given to a healthy granulating wound foundation rather than a necrotic wound foundation. It is also contraindicated when applied to a spot where a skin cancer has been previously identified.

• Enzymatic debridement: When necrotic soft tissues in chronic wounds include collagen, the enzyme collagenase, generated from the fermentation of Clostridium histolyticum, helps remove nonviable tissue from the wound surface. Although it can be used to treat a severely necrotic wound, it is not a replacement for surgical excision of the wound.

• Miscellaneous topical agents: Sugar, antacids, and vitamin A and D ointment are some of the other topical medications that have been used to treat wounds in the past, and they are all effective.

Cytotoxic compounds that should be avoided include hydrogen peroxide, povidone-iodine, acetic acid, and Dakin solution (sodium hypochlorite) on wounds unless they are specifically indicated above under infected wounds.

### 2.17.3 Vacuum-Assisted Closure;

Negative pressure applied beneath an occlusive wound covering to clean but non-healing deep cavity wounds might produce positive results after several treatments. (Vacuum-assisted closure [VAC]).

### 2.17.4 Hydrotherapy;

The use of saline pulse lavage under pressure to treat intractable, infected cavity wounds has been shown to help in certain cases (PulsEvac).

## 2.17.5 Treatment of Charcot Foot;

Immobilization with special shoes or braces initially treats Charcot foot, but surgery such as ostectomy and arthrodesis may be required in the long run.

#### 2.17.5.1 Surgical Care;

To determine the appropriate course of therapy for diabetic foot ulcer patients, a vascular surgeon and/or a podiatrist should analyses the patient's bone architecture, vascular reconstruction, and soft tissue covering.

#### 2.17.5.2 Debridement;

Surgery treating ulcers can involve a variety of techniques, including skin grafting, revascularization, and removal of nonviable and contaminated tissue. When it comes to surgical care of ulcers, callus excision, curettage of underlying osteomyelitis, and skin grafting are all viable choices. It is commonly performed surgically to debride and probe the wound in the first few days after using this test, doctors can determine how widespread an infection is and whether or not bone or joint structures are affected. Having visible or palpable bone in the affected location increases the likelihood of developing osteomyelitis.

#### 2.17.5.3 Revisional surgery;

Pressure points may need the use of bone-revision surgery to eliminate them [36]. Resection of metatarsal heads or ostectomy are two examples of such interventions.

#### 2.17.5.4 Vascular Reconstruction;

Intractable foot ulcers and approaching or current gangrene are all symptoms that a patient needs vascular surgery. In extreme situations, intermittent claudication is very occasionally debilitating and persistent enough to necessitate surgical intervention [9].

2.17.6 Options for Tissue Coverage of Clean Non-HealingWound;

One must decide whether to let natural healing or have the wound surgically expedited after it has achieved a stable clean condition. The optimal care in each case is determined by clinical experience and monitoring of the healing process. There are a number of surgical options that can be used, including skin grafting and the use of bioengineered skin substitutes [37].

#### 2.17.6.1 Skin Grafts;

A feasible coverage of the partial thickness wound with an autologous skin transplant is the gold standard when it comes to covering wounds. Harvesting the graft is an outpatient surgery that can be performed under local anesthetic. Serum and blood drainage is improved by meshing the graft.

It is possible to utilize an allograft to cover wounds following surgery if the wound bed does not appear adequate for an autologous skin transplant to be put as a result, allograft is just a short-term solution [38].

#### 2.17.6.2 Tissue-Cultured Skin Substitutes;

A cryopreserved human fibroblast–derived dermal replacement, a dermatology product, Dermagraft (Smith and Nephew), may be produced by seeding newborn foreskin fibroblasts onto a bioabsorbable polyglactin mesh scaffold and then freezing the resultant product. Dermagraft is useful in the treatment of full-thickness diabetic foot ulcers that have been persistent for a long period of time. Infected ulcers, bone or tendon ulcers, and ulcers containing sinus passages are all contraindicated [39].

Dermagraft had a substantially higher 12-week healing rate (30%) compared to controls (17%) in a multicenter trial of 314 patients. There have been reports of allergic responses to the bovine protein component [60].

Organogenesis' Apligraf (human skin replacement) is a two-layered, living organism. It is not advised to treat an infected ulcer or one that contains tendons or bones. It is not advised if you have an ulcer with sinus tracts. There have been reports of allergic responses to the agarose shipping medium or its bovine collagen component [61]. Due to the fact that the mechanism of action of bioengineered skin replacements is unclear, their effectiveness is uncertain, and they are expensive [41], the usage of these products has been questioned.

#### 2.17.6.3 Xenograft;

One of Health point’s products is Oasis (healthpoint.ltd.), an extracellular matrix and natural growth factor-rich collagen matrix made from the small intestine of swine. As a result, wound healing can be induced using this scaffold. This product should not be used on people who are allergic to porcine products [62], [63].

#### 2.17.6.4 Surgical Wound Closure;

A chronic wound must have well-vascularized clean tissues and tension-free apposition in order to heal properly once it has been opened; in most situations, skin flaps or myofascial flaps must be created to underpin and mobilize neighboring tissue planes [64], [74].

#### 2.17.6.5 Hyperbaric Oxygen Treatment;

Despite the fact that hyperbaric oxygen treatment is infrequently employed, it should be noted that it is not a replacement for revascularization [40]. In some circumstances, hyperbaric oxygen therapy can help cure an unhealed lesion with concomitant irreversible ischemic vascular damage. In Löndahl et al study, 52% of patients who had 40 hyperbaric oxygen treatments (85 minutes per day, five days per week for eight weeks) had their chronic diabetic foot ulcers completely healed. At the one-year follow-up, 29 percent of patients in the placebo group showed full recovery. Inconclusive studies on hyperbaric oxygen treatment for ischemia and pressure ulcers, beneficial results in diabetic chronic foot ulcers have been identified [41], [42].

### 2.17.7 Non-Pharmacological Treatment Options

#### 2.17.7.1 Dietary Changes

It is recommended that people with diabetes eat a diet that is low in saturated fat and low in sugar.

#### 2.17.7.2 Restriction of Activity;

It is critical to remove the ulcerated region. This may necessitate immediate bed rest. Complete contact casting (fibreglass shell with walking bar on the bottom) is required for persons who are mobile. It is critical to remove the ulcerated region. This may necessitate immediate bed rest. For individuals who are mobile, a custom clamshell orthosis (for severe abnormalities) or complete contact casting (a fibreglass shell with a walking bar on the bottom) is necessary [43], [44].

## 2.18 Measures for Prevention of Diabetic Ulcers;

Routine preventive podiatric treatment, suitable footwear, and patient education can reduce diabetes is associated with an increased risk of ulceration and amputation in patients. It is imperative that all diabetic patients have their sensory and vascular systems screened at their local diabetic clinics. About 85% of diabetic foot ulcers may be prevented with the right preventative treatment, including these measures: [45], [46]

• Foot examination every day

• Cleansing with soap and water

• Using a moisturizer on the skin

• For proper support and fit, the shoes should be checked as follows: Custom shoes are covered by Medicare if the patient has sufficient physician paperwork demonstrating that they are at risk for ulceration.

• Medical attention should be sought as soon as possible for minor wounds.

• The correction of high-risk foot abnormalities with preventative podiatric surgery may be required.

• Hot soaks, heated pads, and irritating topical treatments should all be avoided.

### 2.18.1 Glycemic Control;

The Diabetes Control and Problems Trial Research Group conducted a study on long-term implications in people with insulin-dependent diabetes mellitus [47]. Diabetes microvascular consequences, such as nephropathy, neuropathy, and retinopathy, can be reduced or even prevented if blood sugar levels are properly controlled[48], [49]

Hypertension and high cholesterol levels should be managed with smoking cessation and a healthy diet [50].

## 2.19 Objective of the Study;

The study objective is to find the efficacy of moxifloxacin in treating diabetic foot ulcers.

## 2.20 Operational Definitions to Consider;

Gradesofdiabeticfootulcers;

These were wounds on the feet or legs of a diabetic patient that had been present for more than 2 weeks and were classified as Grade 1 or 2 according to the Wagner Ulcer Classification System. Physical examination was used to examine the wound.

Table 3 Grades indicating diabetic foot ulcers

|  |  |
| --- | --- |
| Grade | Classification |
| 0 | No visible signs of infection. |
| 1 | Superficial diabetic ulcer |
| 2 | Extension of the ulcer into the ligament, tendon, joint capsule, or deep fascia in the absence of an abscess or osteomyelitis |
| 3 | Osteomyelitis, joint sepsis, or deep ulcer with abscess. |
| 4 | Infected forefoot or heel with localized gangrene |
| 5 | The entire foot eel is infected with gangrene. |

Effect of Moxifloxacin in diabetic foot ulcers: It was described as 100 percent granulation tissue on the ulcer, light red or dark pink in color, and a negative culture from that granulation tissue at the end of the second week after starting intravenous moxifloxacin.

Smoking:Smoking was defined as consuming more than ten cigarettes per day over the preceding three years.

Alcohol: Three years of consistent alcohol use led to the patient being classified as an alcoholic.

Obesity**:** BMI (body mass index) more than 30.0 was considered as obesity (weight in kilograms divided by height in meters2).

# CHAPTER 3 Materials and Methodology;

## 3.1 Materials and Methods;

Table 4 Depicts materials and methods adopted for the study

|  |  |
| --- | --- |
| **Setting** | Department of Medicine, Khyber Teaching Hospital, Peshawar |
| **Study duration** | 6 months |
| **Design of study** | Descriptive mode |
| **Technique of sampling** | Consecutive non-probability sampling. |
| **Sample size** | The research comprised 195 individuals with diabetic foot ulcers, and the efficacy rate was 51%, a confidence interval of 95%, and a margin of error of 7% based on the WHO sample size calculator. |
| **Inclusion Criteria** | Either gender. |
| Age 20 to 60 years. |
| Diabetic patients with grade 1 or 2 diabetic foot ulcers as defined in operational definitions. |
| Ulcers of any size > 2 cm and present for more than 2 weeks  Diabetic patients with Hb% ≥ 10 g/dl |
| **Exclusion Criteria** | Ulcers associated with osteomyelitis. |
| Immuno suppressed patients |
| Patients on steroid therapy |
| Patients with any malignancy or in intensive care unit |

## 3.2 Process for Collecting Information;

Through a written agreement, all diabetic patients who presented to the department of medicine with diabetic foot ulcers (grades 1 and 2) had their cases included in the research following CPSP approval. All the usual investigations were performed, including a history, clinical examination, and laboratory tests. Prior to treatment, the size of the wound was observed. The kind of wound (grade 1 or 2), the side of the lesions (left or right), the size of the lesion, and the location of the lesion were all recorded. For a period of two weeks, all of the patients got 400 mg of moxifloxacin intravenously every day. Controlled insulin dosages ensured that blood glucose levels were kept in check throughout the course of the treatment. During the first and second weeks, the wounds were checked for signs of granulation tissue. At the end of the second week of therapy with moxifloxacin, the ulcer had healed to 100% granulation tissue and had no granulation tissue culture. After treatment, the size of the wound was observed. On a proforma specifically prepared for this purpose, demographic information such as name, age, gender, and address was entered. It was important to note things like BMI and hypertension, as well as smoking and drinking. Each patient's data was entered into a proforma.

## 3.3 Analyzing the Data;

Statistical Package for the Social Sciences (SPSS) was used to analyze the gathered data. Gender, smoking, drinking, wound type (grade 1 or 2), side of the lesions (left or right), and location of the lesion (dorsum, foot (plantar aspect), toes, malleoli, heel) were all categorical variables that were reported in frequencies and proportions. For continuous variables such as age, BMI, the size of the wound before treatment, the duration of diabetes, and the size of the wound following treatment, mean values with standard deviations were determined. The chi-square test was used to examine variations in categorical characteristics between patients. Before therapy, ulcer healing was stratified by age group, BMI, gender, smoking, alcohol usage, wound type, size of the lesions, and size of the wound. The chi-square test was used after stratification. A P-value of 0.05 was judged statistically significant. Tables and graphs were used to display all of the data.

# Chapter 4: Results and Discussion;

## 4.1 Results;

In this study age distribution among 195 patients was analyzed as 14(7%) patients were in age range 20-40 years, 181(93%) patients were in age range 41-60 years. Mean age was 54 years with SD ± 10.31 as seen in Table 1& figure 3.

Table 5 Age distribution

|  |  |  |
| --- | --- | --- |
| **AGE** | **FREQUENCY** | **PERCENTAGE** |
| **20-40 years** | 14 | 7% |
| **41-60 years** | 181 | 93% |
| **Total** | **195** | **100%** |
|  |  |  |
| Mean age was 54 years with SD ± 10.31 | | |

Figure 3 Age distribution

Gender distribution among 195 patients was analyzed as 140(72%) patients were male and 55(28%) patients were female as shown in figure 4.

Figure 4 Gender distribution

Duration of diabetes among 195 patients was analyzed as 60(31%) patients had duration of diabetes <12 years while 135(69%) patients had duration of diabetes >12 years. Mean duration of diabetes was 12 years with SD ± 6.72 as seen in Table No 2& figure 5.

Table 6 Duration of diabetes

|  |  |  |
| --- | --- | --- |
| **DURATION** | **FREQUENCY** | **PERCENTAGE** |
| **≤ 12 years** | 60 | 31% |
| **> 12 years** | 135 | 69% |
| **Total** | **195** | **100%** |
| Mean duration of diabetes was 12 years with SD ± 6.72 | | |

Figure 5 Duration of diabetes

Status of BMI among 195 patients was analyzed as 88(45%) patients had BMI <30 Kg/m2 while 107(55%) patients had BMI >30 Kg/m2. Mean BMI was 30 Kg/m2 with SD ± 10.63. (Table No 4). Smoking status among 195 patients was analyzed as 43(22%) patients were smokers and 152(78%) patients were nonsmokers as seen in Table No 3.

Table 7 Status of BMI

|  |  |  |
| --- | --- | --- |
| **BMI** | **FREQUENCY** | **PERCENTAGE** |
| **≤ 30 Kg/m2** | 88 | 45% |
| **> 30 Kg/m2** | 107 | 55% |
| **Total** | **195** | **100%** |
| Mean BMI was 30 kg/m2 with SD ± 3.02 | | |
| Mean weight was 82 kgs with SD ± 10.63 | | |
| Mean height was 1.5 meters with SD ± 1.08 | | |

Figure 6 Status of smoking

Status of alcohol used among 195 patients was analyzed as 6(3%) patients had used alcohol and 189(97%) patients didn’t used alcohol as seen in Figure no 7.

Figure 7 Alcohol Use

Type of wound among 195 patients was analyzed as 129(66%) patients had severity of wound (grade 1) and 66(34%) patients had severity of wound (grade 2) as seen in Figure no 8.

Figure 8 Wound type

Side of foot involved among 195 patients was analyzed as 84(43%) patients lesion on left foot and 111(57%) patients lesion on right foot as seen in Figure no 9.

Figure 9 Side of the lesions

Site of lesion among 195 patients was analyzed as 51(26%) patients lesion at dorsum, 31(16%) patients lesion at plantar aspect, 43(22%) patients lesion at toes, 31(16%) patients lesion at Malleoli, 39(20%) patients lesion at Heel as seen in Table No 4, figure no 10.

Table 8 Site of the lesion

|  |  |  |
| --- | --- | --- |
| **SITE OF THE LESION** | **FREQUENCY** | **PERCENTAGE** |
| **Foot (dorsum),** | 51 | 26% |
| **Foot (plantar aspect)** | 31 | 16% |
| **Toes** | 43 | 22% |
| **Malleoli,** | 31 | 16% |
| **Heel** | 39 | 20% |
| **Total** | **195** | **100%** |

Figure 10 Site of the lesion

Size of the wound before treatment among 195 patients was analyzed as 37(19%) patients size of the wound <4cm and 158(81%) patients size of the wound >4cm as seen in figure no 11.

Figure 11 Size of wound before treatment

Efficacy of moxifloxacin (in term of wound healing) among 195 patients was analyzed as moxifloxacin was effective in 164(84%) patients and was not effective in 31(16%) patients as seen in Figure no 12.

Figure 12 Efficacy of moxifloxacin

Stratification of efficacy of moxifloxacin with age groups, BMI, gender, smoking, alcohol use, wound type, side of the lesions & size of the wound before treatment is given in table no 5-14.

Table 9 Stratification of efficacy of moxifloxacin on the basis of age distribution

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **20-40 years** | **41-60 years** | **Total** | **P value** |
| **Yes** | 10(71%) | 154(85%) | 164 | 0.178 |
| **No** | 4(29%) | 27(15%) | 31 |
| **Total** | **14** | **181** | **195** |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **Male** | **Female** | **Total** | **P value** |
| **Yes** | 120(86%) | 44(80%) | 164 | 0.326 |
| **No** | 20(14%) | 11(20%) | 31 |
| **Total** | 140 | 55 | 195 |

Table 10 Stratification of efficacy of moxifloxacin on the basis of gender distribution

Table 11 Stratification of efficacy of moxifloxacin on the basis of duration of diabetes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **≤12 years** | **>12 years** | **Total** | **P value** |
| **Yes** | 49(82%) | 115(85%) | 164 | 0.535 |
| **No** | 11(18%) | 20(16%) | 31 |
| **Total** | 60 | 135 | 195 |

Table 12 Stratification of efficacy of moxifloxacin on the basis of BMI

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **≤ 30 Kg/m2** | **> 30 Kg/m2** | **Total** | **P value** |
| **Yes** | 72(82%) | 92(86%) | 164 | 0.429 |
| **No** | 16(18%) | 15(14%) | 31 |
| **Total** | 88 | 107 | 195 |

Table 13 Stratification of efficacy of moxifloxacin on the basis of Smoking

|  |  |  |  |
| --- | --- | --- | --- |
| **EFFICACY** | **Smokers** | **Non smokers** | **Total** |
|
|
| **Yes** | 36(84%) | 128(84%) | 164 |
| **No** | 7(16%) | 24(16%) | 31 |
| **Total** | 43 | 152 | 195 |

Table 14 Stratification of efficacy of moxifloxacin on the basis of Alcohol use

|  |  |  |  |
| --- | --- | --- | --- |
| **EFFICACY** | **Yes** | **No** | **Total** |
| **Yes** | 3(50%) | 161(85%) | 164 |
| **No** | 3(50%) | 28(15%) | 31 |
| **Total** | 6 | 189 | 195 |

Table 15 Stratification of efficacy of moxifloxacin on the basis of wound type

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **Grade 1** | **Grade 2** | **Total** | **P value** |
| **Yes** | 105(81%) | 59(89%) | 164 | 0.148 |
| **No** | 24(19%) | 7(11%) | 31 |
| **Total** | 129 | 66 | 195 |

Table 16 Stratification of efficacy of moxifloxacin on the basis of side of the lesions

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **Left foot** | **Right foot** | **Total** | **P value** |
| **Yes** | 73(87%) | 91(82%) | 164 | 0.352 |
| **No** | 11(13%) | 20(18%) | 31 |
| **Total** | 84 | 111 | 195 |

Table 17 Stratification of efficacy of moxifloxacin on the basis of site of the lesions

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **EFFICACY** | **dorsum** | **plantar aspect** | **Toes** | **Malleoli** | **Heel** | **Total** | **P value** |
| **Yes** | 42(82%) | 26(84%) | 36(84%) | 26(84%) | 34(83%) | 164 | 0.982 |
| **No** | 9(18%) | 5(16%) | 7(16%) | 5(16%) | 5(17%) | 31 |
| **Total** | 51 | 31 | 43 | 31 | 39 | 195 |

Table 18 Stratification of efficacy of moxifloxacin on the basis of site of the lesions before treatment

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EFFICACY** | **< 4 cm** | **≥4 cm** | **Total** | **P value** |
| **Yes** | 33(89%) | 131(83%) | 164 | 0.347 |
| **No** | 4(11%) | 27(17%) | 31 |
| **Total** | 37 | 158 | 195 |

## 4.2 Discussion;

Insulin insufficiency and insulin resistance are the primary causes of diabetes mellitus (DM), a metabolic condition that results in long-term hyperglycemia. In 2017, the International Diabetes Federation (IDF) reported 425 million persons worldwide with diabetes [1]. Diabetics have a lifetime risk of foot complications of around 25%, with a prevalence of about 2% at any given moment. Infection, ulceration, and tissue damage are all symptoms of foot illness that affect roughly six percent of diabetics. This condition can have a negative impact on the quality of life of patients and their ability to participate in social activities as well as their earning capacity. Amputation is required in 0.03 percent to 1.5 percent of diabetic foot patients. The majority of amputations begin with ulcers, which may be avoided with proper foot care and screening to determine the risk of foot problems. Along with these consequences, diabetic foot ulceration is related with hospitalization, an extended duration of time in the hospital, and physical and psychological morbidity [2]–[4].

The study shows that among 195 patients mean age was 54 years with SD ± 10.31. 140(72%) patients were male and 55(28%) patients were female. Mean duration of diabetes was 12 years with SD ± 6.72. Mean BMI was 30 Kg/m2 with SD ± 10.63. 43(22%) patients were smokers and 152(78%) patients were nonsmokers. 6(3%) patients had used alcohol and 189(97%) patients didn’t used alcohol. 84(43%) patients lesion on left foot and 111(57%) patients lesion on right foot. 51(26%) patients lesion at dorsum, 31(16%) patients lesion at plantar aspect, 43(22%) patients lesion at toes, 31(16%) patients lesion at Malleoli, 39(20%) patients lesion at Heel. More over moxifloxacin was effective in 164(84%) patients and was not effective in 31(16%) patients.

# CONCLUSION;

Over the years, different groups of antibiotics are being used for the treatment of chronic wounds caused by diabetes, particularly for the treatment of DFUs, which are a global health issue and pose a big burden on a patient’s quality of life. However, in current years, a greater resistance of microorganisms to many antibiotics has been noted. Therefore, a descriptive case series research has been done at the Khyber Teaching Hospital in Peshawar, Pakistan, to assess the efficacy of moxifloxacin in treating the diabetic foot ulcers. Throughout the event, a total of 195 patients have been seen who receive 400 mg of moxifloxacin intravenously for two weeks. Throughout the therapy, blood glucose levels are monitored regularly and insulin therapy is gauged accordingly. The wounds are examined for the presence of granulation tissue on weekly basis during the therapy. Towards the end of the second week of moxifloxacin treatment, the ulcer has been entirely filled by granulation tissue, and the granulation tissue culture yields no growth. The average age of the sample is 54 years, with a standard deviation of 10.31 years. Men accounts for 72% of the total with  females accounting for  28%.Statistics show that diabetes has a mean duration of 12 years with a standard deviation of 6.72 years . The individuals have a mean BMI of 30 kg/m2 and a standard deviation of 10.63 kg/m2.Smoking is reported  among the patients (22 percent), compared to 152 non-smokers (78 percent ). There are six people (3 percent) who acknowledged drinking alcohol, whereas 189 patients deny drinking alcohol (97 percent. On the right foot, 84 individuals (43% of the total) have the lesion, whereas the left foot is affected by 111 individuals (57%).51 patients have dorsal lesions, 31 patients have plantar lesions, 43 have toe lesions, 31 had ve Malleoli lesions, and 39 have heel lesions, as depicted from the results of the study. Furthermore, the findings indicates that moxifloxacin is effective in 162 (84 percent) of the patients, but is ineffective in 31 (16 percent) of the patients .Hence, Moxifloxacin when given intravenously for two weeks is found to be 84% effective in treating the diabetic foot ulcers . Further studies are required to establish the real benefits of Moxifloxacin against the emerging resistant pathogens of DFUs. These results may help to standardize the treatment of DFUs in the most effective way possible, thereby granting a better quality of life to the patient and their family.

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