“A COMPARATIVE STUDY OF COLLAGEN DRESSING WITH MOIST GAUZE DRESSING IN DIABETIC FOOT ULCERS”

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ABSTRACT

BACKGROUND: Diabetes is one of the most common chronic condition affecting the population across the globe. By 2030 the prevalence of diabetes mellitus is expected to reach 366 million. Collagen dressing promotes wound contraction and facilitates formation of granulation tissue.

OBJECTIVES OF THE STUDY: To compare the clinical efficacy of collagen dressing with moist gauze dressing in the treatment of diabetic foot ulcers.

MATERIALS AND METHODS: All patients attending surgical OPD and/or admitted in BLDE University's Shri B.M.Patil Medical College Hospital and Research centre, Vijayapur with diabetic foot ulcers during the period of October 2013 to June 2015. A prospective interventional study was conducted with 60 patients alternatively assigned to each group i e 30 patients to collagen dressing group and 30 patients to moist gauze dressing group. All patients were examined, necessary investigations were done and appropriate treatment was given. All cases were followed up till discharge of the patient from the hospital or till closure of wound. 'Primary efficacy end point' was complete ulcer closure. 'Secondary efficacy end points' include reduction in ulcer surface area over time, time to achieve ulcer closure by either skin grafting or secondary suturing. All the data was analyzed using the Z-test, student's T-test and the results were tabulated. A "p value" of <0.05 was considered statistically significant.

RESULTS: Most of the patients included in the study were males and majority of them presented with ulcer. The efficacy of the dressing was compared as the percentage of reduction in the surface area of the ulcer, percent of ulcer surface area covered by granulation tissue and mean duration to outcome in the form of skin

grafting, secondary suturing or healing by secondary intention. Granulation tissue fill up of the ulcers and wound contraction was better in collagen dressing group as compared to moist gauze dressing group.

CONCLUSION: Collagen dressing can be considered as a superior option in the management of diabetic foot ulcer. But we advocate further studies with larger sample size to substantiate the findings we made.

Contents

List of Abbreviations

CD	:	Collagen Dressing
MGD	:	Moist Gauze Dressing
HBOT	:	Hyperbaric Oxygen Therapy
VAC	:	Vaccum Assisted Closure
WBC	:	White Blood Cell
TCC	:	Total Contact Cast
TGF	:	Transforming Growth factor
PRP	:	Platelet Rich Plasma
TNF	:	Tumor Necrosis Factor

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Introduction

INTRODUCTION

Diabetes mellitus is one of the most common chronic condition affecting the human across the globe. In 2011 the global prevalence of diabetes was 171 million which is expected to reach 366 million by 2030[1]. The International Diabetes Federation (IDF) estimates the total number of people in India with diabetes to be around 50.8 million in 2010, rising to 87 million by 2030[2].

Diabetes mellitus is associated with various chronic complications like retinopathy, neuropathy, nephropathy and peripheral arterial disease. Diabetic foot ulcer is another devastating chronic complication of Diabetes mellitus, in fact every 30 seconds a limb is lost due to diabetes mellitus across the globe[3].

Diabetic foot is a common term used for diabetic foot ulcers, diabetic Charcot foot and gangrene. Diabetic foot ulcers occur due to interplay of neuropathy, ischaemia and secondary infection. Diabetic foot ulcer commonly affects the toes followed by mid-foot. It usually starts with colonization of neuropathic or ischaemic ulcers, traumatic wounds, small fissures between the toes or nail beds, wounds due to burns or chronic pressure. Diabetic foot ulcers can also develop secondary to cellulitis, necrotizing fasciitis and abscess[4].

Various modalities of wound healing products like growth factors, skin substitutes, extracellular matrix protein, protease inhibitors, vasoactive compounds, platelet therapies and techniques like Negative pressure wound therapy(NPWT),Hyperbaric oxygen therapy(HBO), Autologous bone marrow cultured cell have been described in literature[5].

Collagen granules facilitate wound contraction and formation of granulation tissue by recruiting fibroblasts into the ulcer and thus act as effective tool in the healing of diabetic foot ulcers[6].

This study is undertaken to compare the efficacy of collagen granule dressing with moist gauze dressing in the treatment of diabetic foot ulcers.

Objectives of the study

OBJECTIVES OF THE STUDY

The purpose of this study is to evaluate the clinical efficacy of collagen granule dressing with moist gauze dressing in the treatment of diabetic foot ulcers.

Review of literature

REVIEW OF LITERATURE

Diabetic foot ulcers are a significant health problem affecting more than 1 million patients at some point in their life time. The principles of good wound care includes use of proper footwear, non-weight bearing limb support, use of appropriate antibiotics, debridement, aggressive revascularization, control of serum glucose levels and careful monitoring of the ulcer.[7]

The prevalence of diabetes in adults is about 2.4% in rural and 4.0-11.6% in urban dwellers. High frequencies of impaired glucose tolerance shown by the above studies ranging from 3.6-9.1% indicate the potential for further rise in the prevalence of diabetes mellitus in the coming years.[8]

It is believed that every 30 seconds a lower limb is lost somewhere in the world as a consequence of diabetes.[9]

Laing Patrick (1998) from the department of Orthopedics, Royal Liverpool Hospital, Liverpool, U.K described that Neuropathy and ischemia are the primary underlying risk factors for the development of foot ulcers and their complications.[10]

Pat Phillips et al.,(2000) from North West Adelaide Health Service, Woodville South, South Australia described that treatment of diabetic foot ulcers involves a number of sequential steps. First, prepare the ulcer for healing, ensuring that the blood supply is adequate, there is no infection, pressure is removed and the ulcer is clean. The dressing can then facilitate the healing process.[11]

Robson MC (1997) from the department of Surgery, Divisions of Surgical Research and Plastic Surgery, University of South Florida, USA described that infection in a wound, like infection elsewhere in the body is a manifestation of a disturbed host-bacteria equilibrium in favor of the bacteria, to be able to prevent and manage wound infections requires an understanding of how each prophylactic or therapeutic maneuver works to maintain or reestablish the bacteria-host balance. Only when this equilibrium is in balance can the normal process of wound healing proceed to give a satisfactory healing trajectory [12].

Van Gils Carl, et al., (1999) from the department of Surgery, Veterans Affairs Medical Center, Phoenix, Arizona, USA in their study involving 124 patients described that the effect of foot ulceration on amputation is not disputed. Failure of normal wound healing after cutaneous ulceration is reported to be the best predictor of amputation risk. Amputation is estimated to occur in 6 – 43 % of diabetic patients with foot ulceration, depending on ulcer severity[13].

Crystal H, et al., (2013) from the department of internal medicine, University of Michigan Medical School, Ann Arbor, MI, USA conducted a systematic review of 26 studies reporting collagen dressings used in the treatment of 2386 patients with Diabetic foot ulcers. They concluded that collagen dressing showed an increase in the healing rate of diabetic ulcers[6].

Veves A et al., (2002) from Joslin Beth Israel Deaconess Foot Center, Boston, MA, USA conducted a randomized prospective trial involving 276 patients comparing collagen dressing with standard treatment in the management of diabetic foot ulcers. They concluded that Collagen dressing is an useful adjunct in the management of diabetic foot ulcers, especially in ulcers of less than 6 months duration[14].

Donaghue VM et al., (1998) from Joslin Beth Israel Deaconess Foot Center, Boston, MA, USA evaluated the efficacy of collagen dressing in the management of 76 patients with diabetic foot ulcers. They concluded that collagen dressing caused significant reduction in ulcer size and is an effective mode of dressing in diabetic foot ulcers[15].

Ann Zmuda (2013) from department of Orthopaedics, University of Chicago states that collagen dressings are designed to increase fibroblast production in the ulcer, collagen also inhibits excess matrix matelloproteinases. Collagen is derived from variety of sources such as bovine, equine and porcine[16].

Di Mauro et al., (1991) from Institute of General clinical medicine, University of Catania, Italy in their study involving 40 patients found that Lyophilized type 1 collagen promotes platelet aggregation and adhesion, collagen also acts as chemotactic factor for macrophages thus it significantly improves wound healing[17].

Lazaro-Martinez et al., (2007) from Unidad de Pie Diabetico, Clinica Universitaria de Podologia, Madrid, Spain in their study involving 40 patients confirmed that protease modulating dressings like collagen lead to better tissue regeneration in patients with neuropathic diabetic foot ulcers[18].

Historical aspect of diabetic foot ulcer and its management

The term diabetes mellitus was introduced by William Cullen (1710-1790), In 1769 Cullen published Nosologiae Methodicae in which for the first time a distinction between diabetes mellitus and diabetes insipidus was elaborated.

The association of Diabetes with neuropathy, foot ulcers and gangrene is seen in the writings of Marchial de Calvi(1852), Thomas Hodgkin(1854), Frederick W Pavy (1885), M Laffon(1885), T Davies Pryce(1887), Thomas Buzzard(1890) and others.

FW Pavy described neuropathic signs and symptoms associated with Diabetes foot ulcer.

Laffon in 1885 first described the association between diabetes and neuropathic plantar ulceration.

20th century saw an uprise in awareness of the lower extremity complications of diabetes as well as a distinction between neuropathic, ischemic and neuro-ischemic lesions of feet.

In 1913 Maurice J Lewi founded “The school of Chiropody” of New York now known as the “New York college of Podiatric Medicine”

In 1934, Elliott P Joslin wrote a paper entitled “ The menace of Diabetic Gangrene” in which he observed that gangrene increased with age of patient and duration of Diabetes Mellitus. He described the importance of patient education in foot care, medical nutrition therapy, exercise, prompt treatment of foot infections and specialized surgical care. Under the umbrella of Massachusetts Chiropody Association he established the first foot clinic at the New England Deaconess Hospital in 1928[19].

Anatomy of the foot

ANATOMY OF THE FOOT

The foot can be divided into forefoot, midfoot and hind foot anatomically and functionally. The foot consists of 7 tarsal bones,5 metatarsals and 14 phalanges[20].

Forefoot

The forefoot plays an important role during toe off phase of the gait cycle. Diabetic foot ulcers occur more commonly in the forefoot because due to prominent metatarsal heads and toe deformities secondary to neuropathic changes the plantar pressure in forefoot is increased.

Midfoot

It is at the centre of arch of foot. It consists of 3 cuneiforms, navicular and cuboid bones.

Hind foot

It consists of talus and calcaneum bones. The body weight mostly borne by the calcaneum. Talus articulates with fibula and tibia to form ankle joint.

Arches of the Foot

The bones of the foot do not lie in a horizontal plane. Instead, they form longitudinal and transverse arches relative to the ground, which absorb and distribute downward forces from the body during standing and moving on different surfaces.

Plantar Aponeurosis

The plantar aponeurosis is a thickening of deep fascia in the sole of the foot .It is firmly anchored to the medial process of the calcaneal tuberosity and extends forward as a thick band of longitudinally arranged connective tissue fibers. The fibers diverge as they pass anteriorly and form digital bands, which enter the toes and connect with bones, ligaments, and dermis of the skin.

Arteries

Blood supply to the foot is by branches of the posterior tibial and dorsalis pedis arteries. Lateral plantar artery,a branch of posterior tibial artery anastomosis with dorsalis pedis artery to form deep plantar arch.

Veins

There are interconnected networks of deep and superficial veins in the foot. The deep veins follow the arteries. Superficial veins drain into a dorsal venous arch on the dorsal surface of the foot over the metatarsals.

Nerves

The foot is supplied by the tibial, deep fibular, superficial fibular, sural and saphenous nerves[21].

Muscles of the foot[22]

Muscle on dorsal aspect of foot

Muscle	Origin	Insertion	Innervation	Function
Extensor digitorum brevis	Superolateral surface of the calcaneus first muscle layer in the sole of the foot	Base of proximal phalanx of great toe and lateral sides of the tendons of extensor digitorum longus of toes II to IV	Deep fibular nerve [S1,S2]	Extension of metatarsophalangeal joint of great toe and flexion of toes II to IV
Extensor Hallucis Longus	Calcaneum and Inferior extensor retinaculam	Base of proximal phalanx of Great toe	Deep fibular nerve(S1, S2)	Extension of metatarsophalangeal joint of Great toe
MUSCLES ON PLANTAR ASPECT				
FIRST LAYER				
Abductor hallucis	Medial process of calcaneal tuberosity	Medial side of base of proximal phalanx of great toe	Medial plantar nerve from the tibial nerve [S2,**S3**]	Abducts and flexes great toe at metatarsophalangeal joint

Muscle	Origin	Insertion	Innervation	Function
Flexor digitorum brevis	Medial process of calcaneal tuberosity and plantar aponeurosis	Sides of plantar surface of middle phalanges of lateral four toes	Medial plantar nerve from the tibial nerve [S2,**S3**]	Flexes lateral four toes at proximal interphalangeal joint
Abductor digiti minimi	Lateral and medial processes of calcaneal tuberosity, and band of connective tissue connecting calcaneus with base of metatarsal V Second layer of muscles in the sole of the foot	Lateral side of base of proximal phalanx of little toe	Lateral plantar nerve from tibial nerve [S2,**S3**	Abducts little toe at the metatarsophalangeal joint
SECOND LAYER				
Quadratus plantae	Medial surface of calcaneus and lateral process of calcaneal tuberosity	Lateral side of tendon of flexor digitorum longus in proximal sole of the foot	Lateral plantar nerve from tibial nerve [S1 to S3]	Assists flexor digitorum longus tendon in flexing toes II to V
Lumbricals	First lumbrical-medial side of tendon of flexor digitorum longus associated with toe II; second, third, and fourth lumbricals-adjacent surfaces of adjacent tendons of flexor digitorum longus third layer of muscles in the sole of the foot	Medial free margins of extensor hoods of toes II to V	First lumbrical-medial plantar nerve from the tibial nerve; second, third, and fourth lumbricals-lateral plantar nerve from the tibial nerve [S2,S3	Flexion of metatarsophalangeal joint and extension of interphalangeal joints
THIRD LAYER				
Flexor hallucis brevis	Plantar surface of cuboid and lateral cuneiform; tendon of tibialis posterior	Lateral and medial sides of base of proximal phalanx of the great toe	Lateral plantar nerve from tibial nerve [**S1**,S2]	Flexes metatar-sophalangeal joint of the great toe
Adductor hallucis	Transverse head-ligaments associated with metatarsophalangeal joints of lateral three toes; oblique head-bases of metatarsals II to IV and from sheath covering fibularis longus	Lateral side of base of proximal phalanx of great toe	Lateral plantar nerve from tibial nerve [S2,S3]	Adducts great toe at metatarsopha-langeal joint

Muscle	Origin	Insertion	Innervation	Function
Flexor digiti minimi brevis	Base of metatarsal V and related sheath of fibularis longus tendon Fourth layer of muscles in the sole of the foot	Lateral side of base of proximal phalanx of little toe	Lateral plantar nerve from tibial nerve [S2,S3]	Flexes little toe at metatarsophalangeal joint
FOURTH LAYER				
Dorsal interossei	Sides of adjacent metatarsals	Dorsal expansions and bases of proximal phalanges of toes II to IV	Lateral plantar nerve from tibial nerve; first and second dorsal interossei also innervated by deep fibular nerve [S2,S3]	Abduction of toes II to IV at metatarsophalangeal joints; resist extension of metatarsophalangeal joints and flexion of interphalangeal joints
Plantar interossei	Medial sides of metatarsals of toes III toV	Dorsal expansions and bases of proximal phalanges of toes III to V	Lateral plantar nerve from tibial nerve [S2,S3]	Adduction of toes III to V at metatarsophalangeal joints; resist extension of the metatarsophalangeal joints and flexion of the interphalangeal joints

EXTRINSIC MUSCLES OF FOOT

Muscle	Origin	Insertion	Innervation	Function
Tibialis Anterior	Lateral surface of tibia	Medial cuneiform and base of 1st metatarsal	Deep fibular nerve	Dorsiflexion and inversion of the foot
Extensor Digitorum Longus	Lateral condyle of tibia and medial surface of fibula.	The tendon splits into four each inserting on to proximal phalanx of respective toe.	Deep fibular nerve	Extension of lateral four toes and dorsiflexion of the foot
Extensor Hallucis Longus	Medial surface of the fibular shaft	Base of distal phalanx of great toe	Deep fibular nerve	Extension of great toe and dorsiflexion of the foot
Gastrocnemius	Lateral head originates from the lateral femoral condyle, and medial from the medial condyle	The muscle belly combines with the soleus to from the calcaneal tendon, which inserts onto the calcaneum	Tibial nerve	Plantarflexion at the ankle joint
Plantaris	The lateral supracondylar line of the femur	Its tendon blends with the calcaneal tendon.	Tibial nerve	Plantarflexion at the ankle joint
Soleus	Soleal line of the tibia and proximal fibula	It forms calcaneal tendon which inserts onto the calcaneum	Tibial nerve	Plantarflexion at the ankle joint
Tibialis Posterior	Interosseous membrane between the tibia and fibula	Plantar surfaces of the medial tarsal bones	Tibial nerve	Inversion and plantarflexion of the foot
Flexor Digitorum Longus	The medial surface of the tibia	Plantar surfaces of the lateral four toes	Tibial nerve	Flexion of lateral four toes
Flexor Hallucis Longus	Posterior surface of the fibula	Plantar surface of the proximal phalanx of the great toe.	Tibial nerve	Flexion of the great foe
Fibularis Longus	The superior and lateral surface of the fibula and the lateral tibial condyle.	Medial cuneiform and base of 1st metatarsal	Superficial fibular (peroneal) nerve	Eversion and plantarflexion of the foot
Fibularis Brevis	Inferior and lateral surface of the fibular shaft	Tubercle on 5th metatarsal	Superficial fibular (peroneal) nerve	Eversion of the foot

Wound Healing

WOUND HEALING

Phases Of Wound Healing

Wound healing can be divided into overlapping phases defined by respective cellular populations and biochemical activities. These phases can be broadly classified into

(a) Haemostasis and inflammation

(b) Proliferative phase

(c) Maturation and remodelling.

All wounds progress through these phases of healing to successfully re-establish tissue integrity.

(a) Haemostasis and Inflammation

Haemostasis initiates inflammation due to release of chemotactic factors at the wound site. Disruption of tissue integrity and division of blood vessels exposes extracellular matrix to platelets. Exposure of sub-endothelial collagen to platelets results in platelet aggregation, degranulation and activation of the coagulation cascade. Platelets release a number of wound-active substances such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF), platelet-activating factor, fibronectin and serotonin. In addition to achieving haemostasis, the fibrin clot serves as scaffolding for the migration of inflammatory cells such as polymorphonuclear leukocytes (PMNs or neutrophils) and monocytes into the wound. Cellular infiltration after injury follows a characteristic sequence. PMNs first infiltrate the wound, peaking at 24 to 48 hours. Increased vascular permeability, local prostaglandin release and the presence of chemotactic substances such as complement factors, interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), TGF, platelet factor 4 or bacterial products all stimulate neutrophil migration.

The primary role of neutrophils is phagocytosis of bacteria and tissue debris. PMN's are a major source of cytokines during early inflammation, TNF-α also has a significant influence on subsequent angiogenesis and collagen synthesis.

The second population of inflammatory cell that invade the wound consists of macrophage, which are recognized as being essential to successful healing. Derived from circulating monocytes, macrophages concentrate in the wound by 48 to 96 hours post injury and remain present until wound healing is complete.

Macrophages play a role in wound debridement via phagocytosis. The macrophage's most pivotal function is activation and recruitment of other cells via mediators such as cytokines and growth factors, as well as directly by cell–cell interaction and intercellular adhesion molecules. By releasing such mediators as TGF, vascular endothelial growth factor (VEGF), insulin-like growth factor, epithelial growth factor and lactate, macrophages regulate cell proliferation, matrix synthesis and angiogenesis. Macrophages also play a significant role in regulating angiogenesis and matrix deposition and remodelling.

T lymphocytes comprise another population of inflammatory/immune cells that routinely invade the wound. Less numerous than macrophages, T-lymphocyte numbers peak at about 1 week post injury and truly bridge the transition from the inflammatory to the proliferative phase of healing. The lymphocytes role in wound healing is not fully defined. A significant body of data supports the hypothesis that T lymphocytes play an active role in the modulation of the wound environment and their depletion decreases wound strength and collagen content, whereas selective depletion of the CD8+ suppressor subset of T lymphocytes enhances wound healing.

(b) Proliferative phase

It is the second phase of wound healing and roughly spans days 4 to 12. It is during this phase that tissue continuity is re-established. Fibroblasts and endothelial cells are the last cell populations to infiltrate the healing wound and the strongest chemotactic factor for fibroblasts is PDGF. Fibroblasts that recruit at the wound proliferate and on activation carry out their primary function of matrix synthesis remodelling. This activation is mediated mainly by the cytokines and growth factors released from wound macrophages.

Fibroblasts isolated from wounds synthesize more collagen than non-wound fibroblasts, they proliferate less and they actively carry out matrix contraction. Although it is clear that the cytokine-rich wound environment plays a significant role in this phenotypic alteration and activation, the exact mediators are only partially characterized. Lactate, which accumulates in significant amounts in the wound environment is a potent regulator of collagen synthesis through a mechanism involving adenosine 5'-diphosphate–ribosylation.

Endothelial cells also proliferate extensively during this phase of healing. These cells participate in the formation of new capillaries (angiogenesis) which is essential for successful wound healing. Endothelial cells migrate from intact venules close to the wound. Their migration, replication and new capillary tubule formation are under the influence of such cytokines and growth factors as TNF, TGF and VEGF. Although many cells produce VEGF, macrophages represent a major source in the healing wound and VEGF receptors are located specifically on endothelial cells.

Matrix synthesis

Collagen, the most abundant protein in the body, plays a critical role in the successful completion of adult wound healing. Its deposition, maturation and subsequent remodelling are essential to the functional integrity of the wound.

Although there are at least 18 types of collagen described, the main ones of interest to wound repair are types I and III. Type I collagen is the major component of extracellular matrix in skin. Type III, which is also normally present in skin, becomes more prominent and important during the repair process.

Biochemically, each chain of collagen is composed of a glycine residue in every third position. The second position in the triplet is made up of proline or lysine during the translation process. The polypeptide chain that is translated from messenger RNA (mRNA) contains approximately 1000 amino acid residues and is called proto-collagen. Release of proto-collagen into the endoplasmic reticulum results in the hydroxylation of proline to hydroxyproline and of lysine to hydroxylysine by specific hydroxylases. Prolyl hydroxylase requires oxygen and iron as cofactors, ketoglutarate as co-substrate and ascorbic acid (vitamin C) as an electron donor. In the endoplasmic reticulum, the proto-collagen chain is also glycosylated by the linking of galactose and glucose at specific hydroxylysine residues. These steps of hydroxylation and glycosylation alter the hydrogen bonding forces within the chain, imposing steric changes that force the proto-collagen chain to assume a helical configuration. Three-helical chains entwine to form a right-handed superhelical structure called procollagen. At both ends, this structure contains non-helical peptide domains called “registration peptides”. Although initially joined by weak ionic bonds, the procollagen molecule becomes much stronger by the covalent cross-linking of lysine residues. Extracellularly, the non-helical registration peptides are cleaved by a procollagen

peptidase and the procollagen strands undergo further polymerization and cross-linking. The resulting collagen monomer is further polymerized and cross-linked by the formation of intra and intermolecular covalent bonds.

Collagen synthesis, as well as posttranslational modifications, is highly dependent on systemic factors such as an adequate oxygen supply, the presence of sufficient nutrients (amino acids and carbohydrates), cofactors (vitamins and trace metals) and the local wound environment (vascular supply and lack of infection). Addressing these factors and reversing nutritional deficiencies can optimize collagen synthesis and deposition.

(c) Maturation and Remodelling

The maturation and remodelling of the scar begins during the fibroplastic phase and is characterized by a reorganization of previously synthesized collagen. Collagen is broken down by matrix metalloproteinases and the net wound collagen content is the result of a balance between collagenolysis and collagen synthesis. There is a net shift towards collagen synthesis and eventually the re-establishment of extracellular matrix composed of a relatively acellular collagen rich scar.

Wound strength and mechanical integrity in the fresh wound are determined by both the quantity and quality of the newly deposited collagen. The deposition of matrix at the wound site follows a characteristic pattern, **Fibronectin and collagen type III** constitute the early matrix scaffolding, glycosaminoglycans and proteoglycans represent the next significant matrix component and collagen type I is the final matrix. By several weeks post injury the amount of collagen in the wound reaches a plateau, but the tensile strength continues to increase. Fibril formation and fibril cross-linking result in decreased collagen solubility, increased strength and increased resistance to enzymatic degradation of the collagen matrix. Scar

remodelling continues for many (6 to 12) months post injury, gradually resulting in a mature, avascular and acellular scar. The mechanical strength of the scar never achieves that of the uninjured tissue.

There is a constant turnover of collagen in the extracellular matrix, both in the healing wound, as well as during normal tissue homeostasis. Collagenolysis is the result of collagenase activity, a class of matrix metalloproteinases that require activation. Both collagen synthesis and lysis are strictly controlled by cytokines and growth factors. Some factors affect both aspects of collagen remodelling. For example, TGF increases new collagen transcription and also decreases collagen breakdown by stimulating synthesis of tissue inhibitors of metalloproteinase. This balance of collagen deposition and degradation is the ultimate determinant of wound strength and integrity.

Epithelialization

While tissue integrity and strength are being re-established, the external barrier must also be restored. This process is characterized primarily by proliferation and migration of epithelial cells adjacent to the wound. The process begins within 1 day of injury and is seen as thickening of the epidermis at the wound edge. Marginal basal cells at the edge of the wound lose their firm attachment to the underlying dermis, enlarge and begin to migrate across the surface of the provisional matrix. Fixed basal cells in a zone near the cut edge undergo a series of rapid mitotic divisions and these cells appear to migrate by moving over one another in a leapfrog fashion until the defect is covered. Once the defect is bridged, the migrating epithelial cells lose their flattened appearance, become more columnar in shape and increase

their mitotic activity. Layering of the epithelium is re-established and the surface layer eventually keratinizes.

Re-epithelialization is complete in less than 48 hours in the case of approximated incised wounds, but may take substantially longer in the case of larger wounds, in which there is a significant epidermal/dermal defect. If only the epithelium and superficial dermis are damaged, such as occurs in split-thickness skin graft donor sites or in superficial second-degree burns, then repair consists primarily of re-epithelialization with minimal or no fibroplasia and granulation tissue formation. The stimuli for re-epithelialization remain incompletely defined, however it appears that the process is mediated by a combination of a loss of contact inhibition, exposure to constituents of the extracellular matrix particularly fibronectin and cytokines produced by immune mononuclear cells. In particular, epithelial growth factor, TGF, basic fibroblast growth factor, PDGF and insulin-like growth factor have been shown to promote epithelialization.

Wound contraction

All wounds undergo some degree of contraction. For wounds that do not have surgically approximated edges, the area of the wound will be decreased by this action (healing by secondary intention), the shortening of the scar itself results in contracture. The “myofibroblast” has been postulated as being the major cell responsible for contraction and it differs from the normal fibroblast in that it possesses a cytoskeletal structure. Typically this cell contains smooth muscle actin in thick bundles called stress fibers, giving myofibroblasts contractile capability.

The smooth muscle actin is undetectable until day 6 and then is increasingly expressed for the next 15 days of wound healing. After 4 weeks this expression fades

and the cells are believed to undergo apoptosis. A puzzling point is that the identification of myofibroblasts in the wound does not correspond directly to the initiation of wound contraction, which starts almost immediately after injury.

Fibroblasts placed in a collagen lattice in vitro actively move in the lattice and contract it without expressing stress fibers. It is postulated that the movement of cells with concomitant reorganization of the cytoskeleton is responsible for contraction[23].

Diabetes and wound healing

DIABETES AND WOUND HEALING

Infection is an important contributing factor to the morbidity of diabetic patients with foot problems. It is uncertain if they have a greater susceptibility to infection as a result of impaired resistance or whether reduced blood supply allows infections to become established and the neuropathy permits the infection to go unrecognized.

Diabetes might lead to the impairment of inflammatory and wound healing process by reducing the blood supply to the affected area, the effectiveness of the inflammatory response and the repair process which results in the formation of fibrous tissue.

(a) Impaired blood Supply

Reduced blood supply may not be able to sufficiently permit healing of small wounds and as a result, necrosis and infection follow.In ischemic tissue, the growth of anaerobic organisms is favored, particularly if there is concomitant growth of aerobes.There are several mechanisms by which the micro vascular changes in diabetes could impair the response to injury. Blockage of small vessels might prevent the blood flow from increasing sufficiently to allow healing. In addition the capillary basement membrane thickening might alter the permeability and thus interfere with leukocyte migration and fluid exudation. Wound ischemia is detrimental to all wound healing and may be a contributing factor in the initial formation of chronic wounds. Hypoxia is initially a potent stimulus for fibroblast proliferation and angiogenesis. However wound healing is impeded if hypoxia persists. In an environment of 30 to 40 mmHG of oxygen, fibroblasts cannot replicate and collagen production is severely limited. Wound hypoxia also predisposes the wound to bacterial invasion.

(b) Impaired inflammatory response

There is evidence that various inflammatory stages are impaired in diabetes. Decreased adhesion of polymorphs to vessel wall and reduced rate of escape from vessels. The abnormality is directly related to the level of fasting blood glucose and returned towards normal with treatment. The mobility of white cells towards a chemical stimulus (chemo taxis) is impaired.

The ability of the polymorphs to ingest and kill bacteria is reduced. It is likely that the leucocytes in diabetes patients are less efficient at both engulfing and killing bacteria. Wound infection has been shown to impair wound contraction in both acute and chronic wounds. The mechanism by which this occurs is believed to be the release of bacterial enzymes and metalloproteinases that may degrade fibrin as well as wound growth factors.

(c) Impaired repair mechanism

Goodson and Hunt(1979) demonstrated that the development of strength in an incised wound, which was closely related to the amount of collagen produced in the tissues closest to the wound edge, was decreased in insulin deficiency - Diabetes.

The experiments of Goodson and Hunt demonstrated that granulation tissue formation could be returned to normal if insulin was given soon after wounding. If the insulin replacement was delayed until the time of greatest collagen formation (about 10 days after wounding) there was no increase in the amount of collagen formed[24].

Pathophysiology of diabetic foot

PATHOPHYSIOLOGY OF DIABETIC FOOT

The pathogenesis of diabetic foot is complex and involves the interactive processes of angiopathy, neuropathy and immunopathy.

A) Angiopathy

Diabetic angiopathy is the most frequent cause of morbidity and mortality in a patient with diabetes. Angiopathy can be in the form of macroangiopathy and microangiopathy

Macroangiopathy

Macroangiopathy in a diabetic patient presents as a more diffuse disease than in a nondiabetic patient, with more multisegmental involvement and compromised collateral circulation. It is more often seen bilaterally in the lower extremities. Vascular impairment, evaluated by resting Doppler ankle pressure, was found to correlate with the development of diabetic foot ulcers. Large vessel disease predisposes a patient with diabetes to foot lesions secondary to ischemic skin changes that, in turn lead to ulceration and possible infection.

Microangiopathy

Tooke and Brash discussed the hemodynamic hypothesis of the pathogenesis of diabetic microangiopathy. This hypothesis states that in the early stages, vessel capillaries of diabetic patients have increased microvascular pressure and flow. The increased capillary pressure results in an injury response within the microvascular endothelium. Injury causes release of extravascular matrix proteins, resulting in microvascular sclerosis. Sclerosis is manifested in the arteriole as hyalinosis and in the capillary as basement membrane thickening, the ultrastructural hallmark of diabetic microangiopathy. With increasing duration of diabetes, the sclerotic process

results in limitation of vasodilatation with reduced maximal hyperemia and in loss of autoregulatory capacity. A key observation has been that nailfold capillary pressure is elevated in the early stages of type 1 diabetes. This has been positively correlated with glycemic control, judged by the glycosylated hemoglobin value at the time of pressure measurement. In addition, pressure appears to be particularly high in those individuals at high risk for microangiopathy, yet relatively normal in patients who have avoided the clinical complications of diabetes over many years.

B) Neuropathy

Neuropathy occurs early in the pathogenesis of diabetic foot problems and is the most prominent risk factor for diabetic foot ulcers. There are three components of diabetic neuropathy namely sensory,motor and autonomic neuropathy. The combined effect of this triad is a foot that cannot respond to pain and is biomechanically impaired, with increased foot pressure, limited joint mobility and poorly hydrated skin that cannot appropriately respond to injury.

Sensory neuropathy

The damage from sensory neuropathy affects the large myelinated alpha fibres. Its distribution is usually symmetric in “stocking and glove” pattern as a result, patients are unable to perceive injury to their feet because primary protective or warning systems are defective. This fundamental pathophysiologic impairment is referred to as the “loss of protective sensation”. Affected patients sustain repetitive, unrecognized injuries to their feet that culminate in full thickness ulceration. Ulcer in an insensate foot is usually painless. Neuropathy can have a wide range of severities and symptoms. Loss of protective sensation does not necessarily mean complete absence of sensation or pain. This scenario can also represent damage to both large

myelinated nerves and small unmyelinated nerves, so the patient may have burning sensation because of small fibre damage and deep gnawing pain and numbness because of large-fibre neuropathy.

Motor neuropathy

Often occurs late in course of diabetic peripheral neuropathy and contribute to intrinsic muscle wasting of the feet and hands. Short, weak flexors and extensors that are over powered by long, strong flexors and extensors in the foot contributes to structural foot deformities such as claw toes, dislocated metatarsophalangeal joints and ankle equinus. **Motor neuropathy changes the biomechanics of the foot** and directly contributes to increased shear and pressure under the balls of toes, the most common site of neuropathic foot ulcers. Severe motor neuropathy contributes to the development of 'intrinsic minus' foot, or the appearance of high arch structures because of muscle wasting and weakness.

Autonomic neuropathy

Autonomic dysfunction also occurs early in the course of neuropathy. In the foot, autonomic dysfunction results in shunting of blood through direct arteriole venule communications, diminishing the effectiveness of perfusion. There is loss of hair, sweat and oil gland function, leading to dry, scaly skin that cracks and fissures easily. **Vibration, pain and temperature sensations are affected more than touch or proprioception.**

C) Immunopathy

The contribution of immunopathy to the development of infection in a patient with diabetes is controversial. Most investigators believe that poor glucose control predisposes patients to infection. Humoral immunity in the patient with diabetes appears to be normal. Normal to elevated levels of circulating immunoglobulins and

normal numbers of B lymphocytes are found. The impaired host defense mechanism in the diabetic patient appears to occur at the cellular level where impaired leukocyte function and impaired intracellular killing have been observed. Phagocytosis and the intracellular killing function of the leukocyte appear to be significantly altered in the presence of hyperglycemia. These defects have been partly or completely reversed by improved diabetic control.

Cell-mediated immune responses are also significantly impaired by elevated glucose concentrations. MacCuishet demonstrated a decrease in phytohemagglutinin-induced lymphocyte transformation in poorly controlled diabetic patients, but not in well controlled patients or in healthy subjects. A poor response of lymphocytes to staphylococcal antigen has been demonstrated in diabetic patients, regardless of the degree of glycemic control, T lymphocyte immunodeficiency in type 1 diabetes[25].

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Diabetic Gangrene

This can occur in neuropathic foot where the arterial tree appears perfectly normal and so are the pulsations throughout the limb.

The gangrene is due to primary infection followed by secondary thrombosis of the digital vessels. The gangrene is slowly progressive and generally remains limited to the area of the foot in which it began[26].

Necrotizing Fascitis

It is a rare complication of diabetic foot infection. It is an acute infection of subcutaneous tissue and fascia resulting in its necrosis, along with noncrepitus gangrene of the overlying skin.

It is usually due to streptococcus pyogenes but may occasionally be caused by staphylococcus aureus. The affected area is initially red, hot, swollen and painful and

the inflammation area is the pathogonomonic sign. This can then progress to frank gangrene. Left untreated, this complication can cause death within days[27].

Neuropathic foot

The neuropathic foot is a warm, well-perfused foot with bounding pulses and distended dorsal veins due to arteriovenous shunting. Sweating is diminished so skin and any callus tend to be hard,dry and prone to fissuring. Toes are flexed and the arch of the foot may be raised.

Ulceration commonly develops on the sole of the foot, associated with neglected callus and high plantar pressures. Despite the good circulation, necrosis can develop secondary to severe infection. The neuropathic foot is also prone to bone and joint problems which we refer to as 'Charcot's osteoarthropathy'.

Neuro-ischemic foot

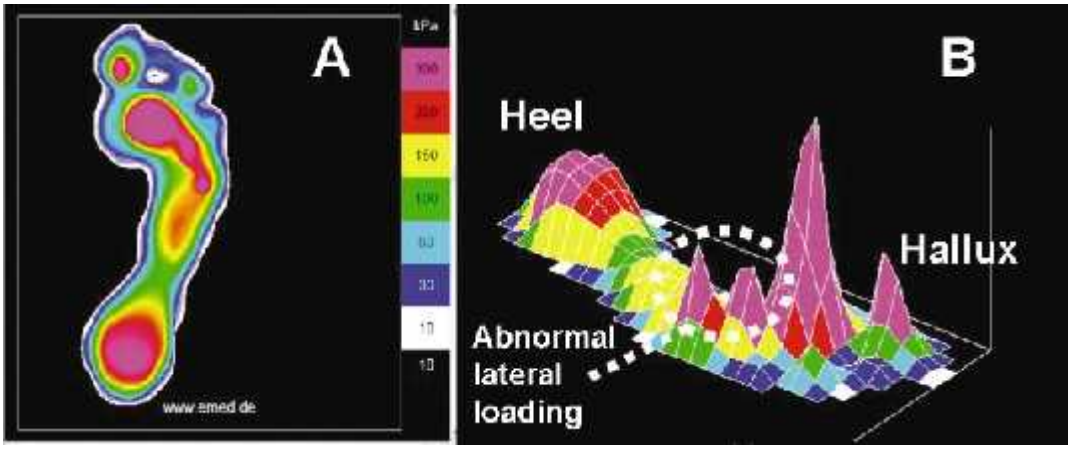
The neuro-ischaemic foot is a cool, pulseless foot with poor perfusion and almost invariably also has neuropathy. The colour of the severely ischaemic foot can be a deceptively healthy pink or red caused by dilatation of capillaries in an attempt to improve perfusion. The neuro-ischaemic foot may be complicated by swelling, often secondary to cardiac failure or renal impairment.

Ischaemic ulcers are commonly seen around the edges of the foot, including the apices of the toes and the back of the heel and are associated with trauma or wearing unsuitable shoes. The neuro-ischaemic foot develops necrosis in the presence of infection or if tissue perfusion is critically diminished. Even if neuropathy is present and plantar pressures are high, plantar ulceration is rare.

Biomechanics of diabetic foot

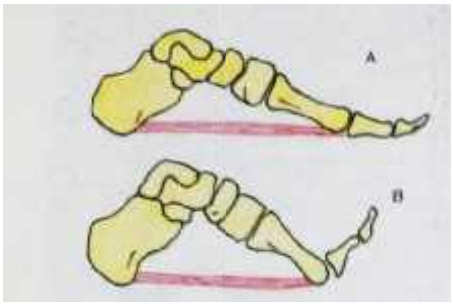
Plantar pressure and shear stress

Normal plantar pressure is 5-30 kPa. These are evaluated using force plate technology. This technology helps in explaining the relationship between plantar pressure, shear stress and ulceration. Plantar force technology is available in the form of in-shoe testing systems. These systems help to evaluate plantar foot pressure.

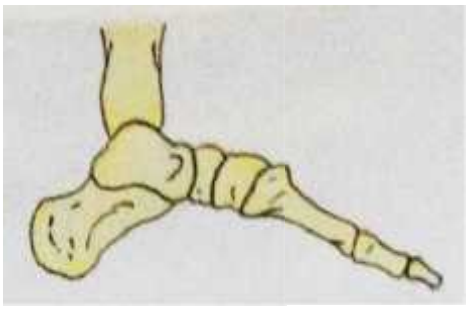


Biomechanical factors for foot ulceration are

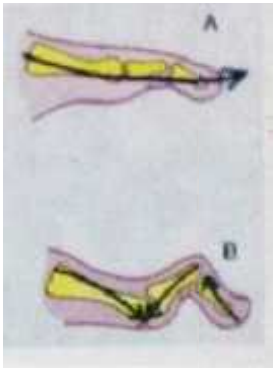
1. Elevated peak shear stress and plantar pressure are major factors
2. Shear stress also contributes to neuropathic injury
3. Reduction in shear stress and plantar pressure helps in healing of ulcers



Longitudinal medial arch of the foot



A. Arch flat
B. Contraction of the plantar aponeurosis resulting in elevation of the arch



A.Normal escape of force from body weight

B.Counter force on the metatarsal heads due to deformities

Callus

Callus acts like a foreign body, exerting concentrated pressure on underlying tissue. Callus is considered to be the most common cause of foot ulceration in patients with diabetes.

Plantar fat pad integrity

The planatar fat pad provides the human foot with a custom made,in-built cushioning mechanism. The plantar fat pad is located under the ball of the foot beneath the metatarsal heads and under the calcaneum or heel. When diabetic patients develop clawing or retraction of the lesser digits ,the plantar fat pad under the metatarsal heads migrates and is displaced anteriorly.

Rearfoot biomechanics

Rearfoot varus

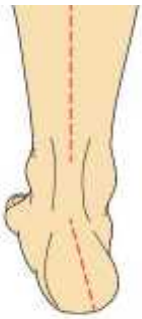
It is a condition where the rearfoot is in an inverted position in relationship to the ground when the subtalar joint is in a neutral position.

In compensated rearfoot varus, the subtalar joint will attempt to compensate for the inverted calcaneal position by pronating beyond the “normal” range to enable the calcaneum to meet the ground and stabilize the foot. In uncompensated rearfoot varus, the subtalar joint doesn’t pronate leaving the heal and the foot in an inverted position during stance.

Right rearfoot
Varus

Rear foot valgus

Rear foot valgus is a condition where the rear foot is in an everted position in relationship to the ground when the foot is in a normal position.

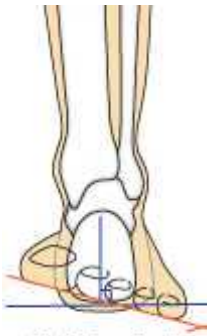


Right rearfoot
Valgus

Forefoot Biomechanics

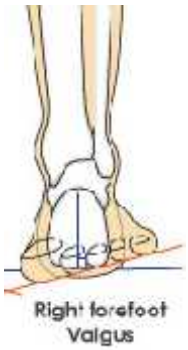
Forefoot varus

Forefoot varus is a condition characterised by fixed, inverted position of the forefoot relative to the rearfoot and to the ground, when the foot is placed in neutral position.



Forefoot valgus

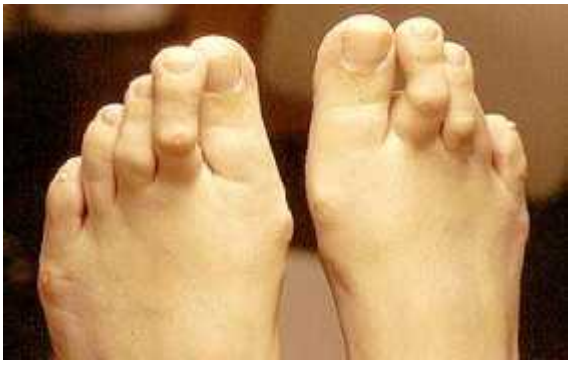
Forefoot valgus is a condition where the forefoot is everted, compared with the rearfoot when the foot is in a neutral position.



Joint deformity

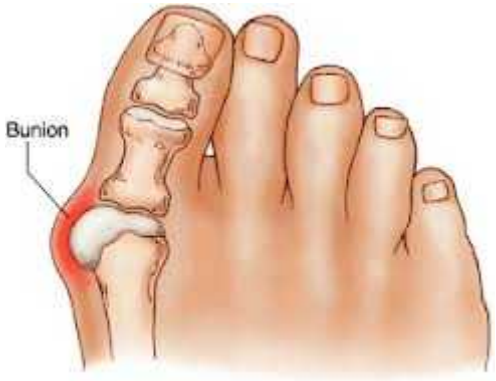
Clawed and retracted toes

Tips of the toes touch the ground with clawing as shown in the figure.



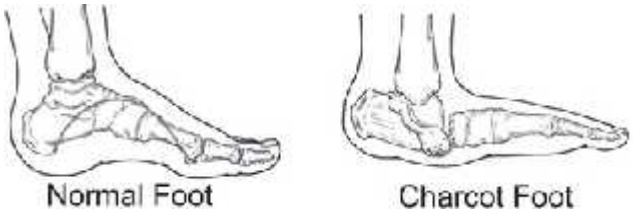
Bunion

It is also known as hallux abducto valgus. Here in there is abducted first metatarsal with prominent first metatarsophalangeal joint.



Charcot foot

It is a condition which occurs in people with diabetes and other conditions associated with peripheral neuropathy. It is characterised by either rocker-bottom foot severely everted ankle with medial protrusion of the malleolus.



Clinical features of diabetic foot

Patients with diabetes are at an increased risk of developing an ulcer on the foot in the presence of established long term complications of the disease. A foot in which arterial disease or neuropathy or both are present is liable to develop major complications.

Presence of sensory neuropathy contributes to the abnormal and prolonged pressure on the foot. Motor neuropathy causes foot deformity, further increasing pressure loading. Loss of innervation to the sweat glands leads to dry skin due to diminished sweating usually in a “stocking” distribution and leads to a dry, cracked skin. These cracks serve as portals of infection that complicate the diabetic neuropathy.

Evidence of neuropathy:

- The posture of the foot, clawing of the toes, callus over pressure areas are definitely due to neuropathic changes.
- Glove and stocking distribution of the deformity.
- Patients complain of cold feet or dead feet describing a sensation of walking on cotton wool. On rare occasions will the foot feel dry and also warm if the blood supply is sufficient.
- Loss of light touch and pain (pin prick) sensation on the toes and foot. In more severe cases this sensory loss may extend to the calf. The loss of the pain sensation my lead to undetected trauma.
- Loss of perception of vibration of foot; at the ankle and at the knee.
- Absence of ankle tendon reflexes and patellar tendon reflexes[28].

Evidence of ischemia:

• A history of intermittent claudication or rest pain.

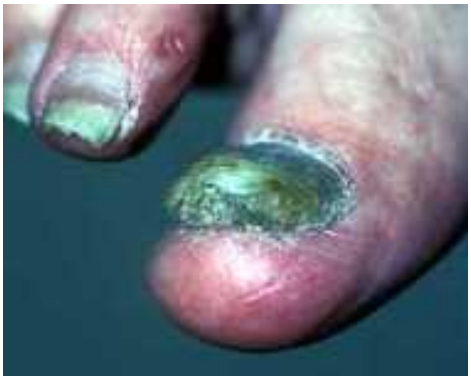
• Coldness of the foot

• Absence of ankle pulses.

Various presentations of diabetic foot

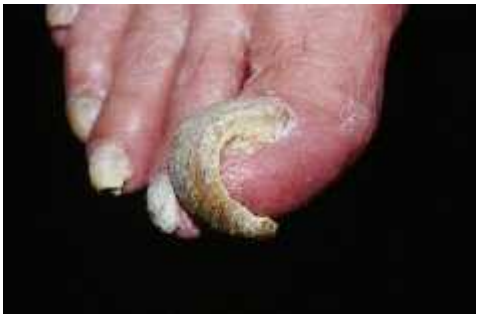
Nail Problems

A.Onychauxis : This is thickening of the nail without deformity, and follows an insult to the nail bed. Without regular reduction onychogryphosis will develop.

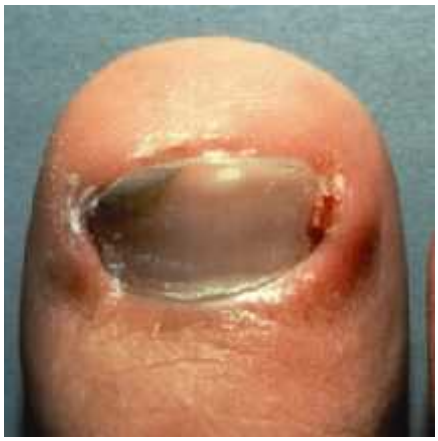


B.Onychogryphosis (Ram's horn nail) : This is thickening of the nail with deformity. Onychogryposis is caused by chronic repetitive trauma particularly to the nails on the great toe. The nails may be grossly thickened, hard and very elongated the deformed nail can press against another toe causing ulcerations.

Treatment: can be palliative or surgical. Palliative treatment consists of regular reduction of excessive thickness of the nail plate



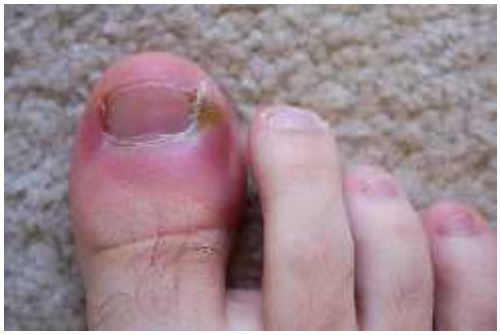
C.Onychocryptosis (ingrowing toe nail): A section of a nail curves into the adjacent flesh and becomes embedded in the soft tissue. Peeling the nail at the edge or rimming it down at the corners is the most common cause. Other causes are wearing tight shoes or socks which press on the sides of the nail making it curve into the skin. An ingrown nail predisposes to local infection (paronychia) as it provides an entry point for pathogens. Nails should be trimmed in a straight line or removed.



D.Paronychia : Inflammation of the nail fold. Paronychia, can be acute or chronic.

Acute paronychia is due to bacterial infection, it is painful and discharges pus. If the margin of the nail plate is pressing on the inflamed area it should be cut back. Collections of pus should be drained. A swab is sent for microscopy and culture and appropriate systemic antibiotics are prescribed.

Chronic paronychia results in the periungual tissues appearing erythematous and oedematous. The infection extends to the nail plate which may develop yellowish-green or yellowish-brown pigmentation. Chronic paronychia is frequently caused by infection with Candida albicans and the treatment is with terbinafine or itraconazole.



E.Onychomycosis (fungal nail): Onychomycosis is a fungal infection of nail. Onychomycosis per se does not cause foot problems, but when it affects the proximal nail it may cause chronic paronychia and serve as a portal for bacteria, resulting in deep tissue infection. It often co-exists with mycosis of the web spaces and it may be superinfected by bacteria, leading to deep tissue infection as well. Treatment with terbinafine hydrochloride, both systemic (tablets 250 mg once daily) and topical (cream), for 3 months with appropriate foot care.

Chronic onychomycosis is classified into two clinical types:

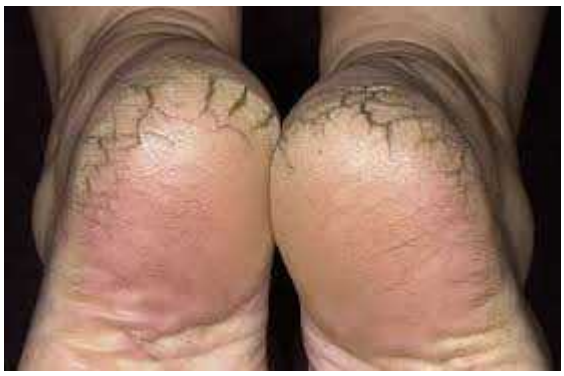
Distal subungual onychomycosis is the most common form.The distal edge of the nail becomes infected and a yellow discoloration, onycholysis and subungual debris develop.

Proximal subungual fungal infection, the second commonest form, Trichophyton rubrum accumulates hyperkeratotic debris under the nail plate and loosens the nail, eventually separating it from its bed.

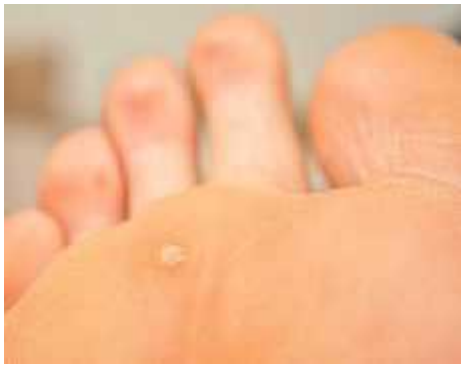
Itraconazole and fluconazole are also effective in the treatment of chronic onychomycosis.

Lesions under the nail can be due to haematoma, necrosis, melanoma, exostosis.

2. **Fissures**: Fissures are moist or dry cracks in epidermis at sites where skin is under tension. Deep fissures may involve dermis. Fissures can occur in dry skin. The treatment involves emollient, such as E45 cream, olive oil or coco butter.

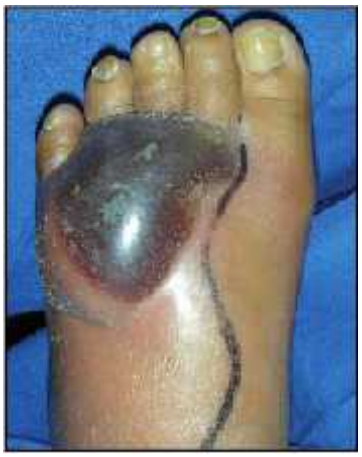


3. **Verrucae**: Warts may occur anywhere on the foot and may be single or multiple and appear as round flattened papules or plaques. Most will resolve within 2 years without treatment. The recommended treatment for ablation of painful or spreading verrucae in people with diabetes is cryotherapy with liquid nitrogen. Sometimes surgical treatment with excision of the wart is required.

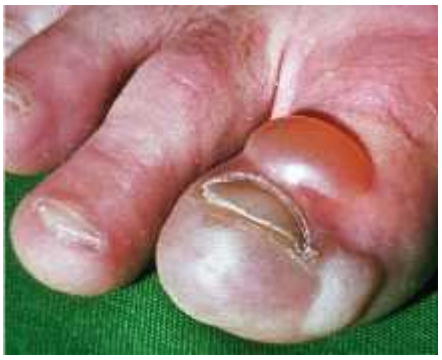


4. **Bullae (blisters)**: These are superficial accumulations of clear fluid within or under the epidermis which develop following trauma to the skin. Common causes include

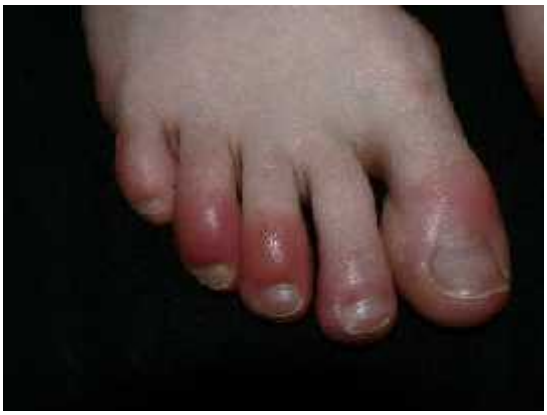
unsuitable shoes, failure to wear socks and walking in wet footwear. Small flaccid bullae can be cleaned and covered with a sterile non-adherent dressing. Large bullae (over 1 cm in diameter) and all tense bullae should be lanced with a scalpel and drained before dressing, aspiration with a syringe is less useful because the hole frequently seals. Fluid accumulates again and unrelieved hydrostatic pressure causes extension of the blister. The cause of blisters should always be ascertained and addressed[29].



5. **Bullosis diabeticorum**: This is a rare condition where diabetic patients present with intraepidermal blisters which are not associated with trauma and heal without scarring. Treatment of bullosis diabeticorurn is as for bullae. This can spread to draining lymph nodes. Suspicious lesions should be biopsied. Treatment is surgical excision.



6. **Chilblains (perniosis)**: These are localized inflammatory lesions, provoked by cold and injudicious reheating. Chilblains are frequently found on the toes.



7. **Hammer toe**: Hammer toe is a complex deformity consisting of contraction (hyperflexion) of the proximal interphalangeal joint, while the metatarsophalangeal joint is either dorsiflexed or in the neutral position. The distal interphalangeal joint may be in the neutral position, hyperextended or in plantar flexion. Hammer toe may be flexible or rigid .It is due to loss of balancing lumbrical functions

8. **Claw toes**: Claw toes are similar to hammer toes, but with more buckling and greater deformity. There is fixed flexion deformity at the interphalangeal Joint, associated with callus and ulceration of the apex and dorsal aspect of the interphalangeal joint. Although claw toes may be related to neuropathy, they are often unrelated, especially when the clawing is unilateral and associated with trauma or surgery of the forefoot. Claw toes may rarely result from acute rupture of the plantar fascia.

9. **Hallux valgus**: Hallux valgus is a deformity of the first metatarsophalangeal joint with lateral deviation of the hallux and a medial prominence on the margin of the foot. This site is particularly vulnerable in the neuroischaemic foot and frequently breaks down under pressure from a tight shoe.

10. **Limited joint mobility (including hallux rigidus)**:Limited joint mobility can affect the feet as well as the hands. The range of motion is diminished at the subtalar and first metatarsophalangeal joints. Limited joint mobility of the first metatarsophalangeal joint results in loss of dorsiflexion and excessive forces on the plantar surface of the first toe causing callus formation and ulceration. It is commonly seen in barefooted and sandal wearing populations.

11. **Charcot foot** : Bone and joint damage in the tarsometatarsal joints and mid-tarsal joints leads to two classical deformities: the rockerbottom deformity, in which there is displacement and subluxation of the tarsus downwards and the medial convexity, which results from displacement of the talonavicular joint or from tarsometatarsal dislocation. Both are often associated with a bony prominence which is very prone to ulceration and healing is notoriously difficult. When the ankle and subtalar joints are involved, instability of the hindfoot can result

12. **Ischemia** : The foot may have a pale white appearance in severe ischemia, especially on elevation. In acute ischemia, the foot is pale, often with purplish mottling. The cause of black appearances is discussed under necrosis.

13. **Necrosis** : Areas of necrosis and gangrene can be identified by the presence of black or brown devitalized tissue. Such tissue may be wet (usually related to infection) or dry. Necrosis can be due to infection, when it is usually wet, or to occlusive macrovascular disease of arteries of leg. Necrosis can involve skin, subcutaneous and fascial layers. In lightly pigmented skin it is easily evident but in the subcutaneous and fascial layers it is not so apparent[30].

Major Infections

1) **Cellulitis**: Patients present with cellulitis of the foot involving distal half or whole of the foot because of necrotising skin and subcutaneous tissue, these patients manifest with edema involving dorsum of the foot with shiny skin.

2) **Abscess**: Abscess may be localized to single toe or multiple toes or in the deep spaces of the sole. Patients may present with or without pain, sometimes even abscess pointing. The most important signs are swelling and redness which can be seen on the dorsum of the web spaces of the foot. However the most characteristic sign is separation of the toes due to diffuse edema of the deep tissues of the foot and always indicates that there is pus deep in the foot.

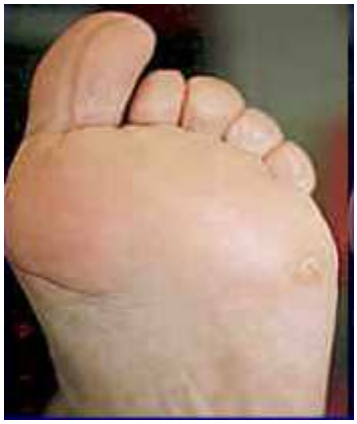
3) **Ulcer**: Ulcer may present on the dorsal or plantar aspect of the foot. Plantar ulcers also called as trophic or penetrating ulcer. They are typically painless and occur over areas that normally carry weight. The earliest change is an area of hyperkeratosis often over a metatarsal head. The commonest site for an ulcer of the toe is on the proximal interphalangeal joint of a clawed toe. Hyperkeratosis or inflammation may precede the breakdown of skin and the development of a small ulcer.

4) **Gangrene**: Gangrene means macroscopic death of tissue with super added putrefaction. There are two kinds of gangrene.

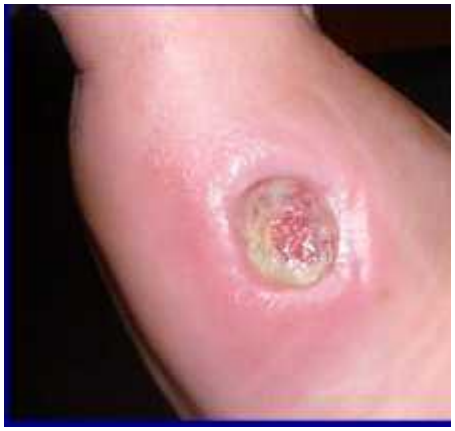
It is caused by a poor blood supply. When not enough blood reaches a part of the foot, the skin and flesh may die and change colour to brown or black. Areas of gangrene may occur on parts of the foot that are exposed to pressure. The common sites are heel, the malleoli and the areas of first metatarsal head medially and the base of the fifth metatarsal. Small areas of gangrene may also occur on the parts of the foot not subjected to pressure because of embolism of atheromatous debris.Gangrenous patches may form in the interdigital clefts[31].

Wagner's Classification Of Diabetic Foot Wounds

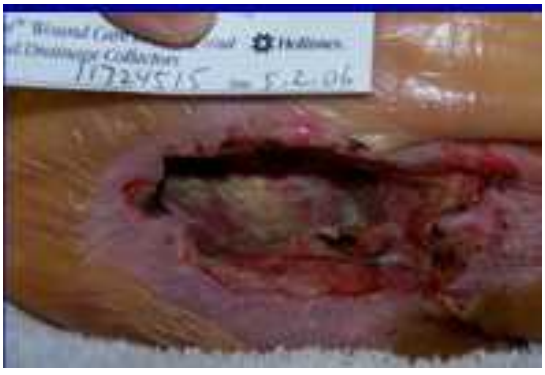
Grade 0 – Pre- or post-ulcerative lesion completely epithelialized. Foot with deformities, hyperkeratosis.



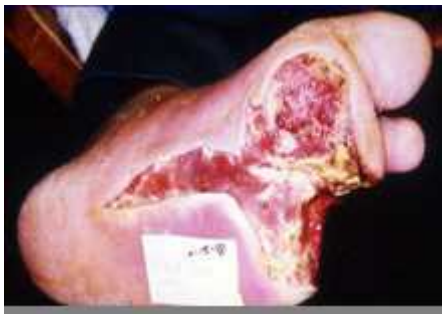
Grade 1 – Superficial, full thickness ulcer limited to the dermis, not extending to the subcutaneous fat layer.



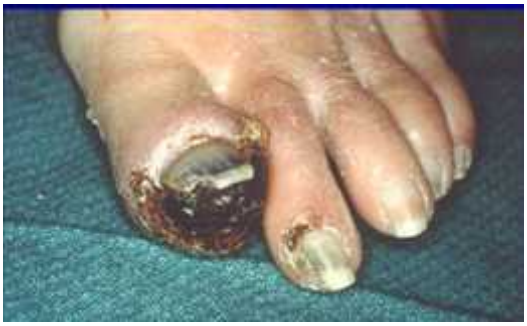
Grade 2 – Ulcer of the skin extending through the subcutaneous tissue with exposed tendon or bone and without osteomyelitis or abscess formation.



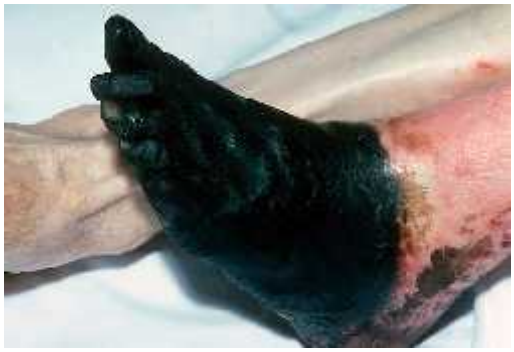
Grade 3 – Deep ulcers with osteomyelitis or abscess formation.



Grade 4 – Localized gangrene of the toes or the forefoot.



Grade 5 – Foot with extensive gangrene[32].



Investigations

INVESTIGATIONS

1.Blood Examination

- Haemoglobin: It is useful investigation to know about general status of the patient and to know about the fitness of the patient for distinctive operative procedures.
- Total WBC count: Indicates defence mechanism of the body.
- Differential WBC count: Will give a clue to diagnosis, like lymphocyte count is increased in tuberculosis, neutrophil reduced in generalized malnutrition, PMN'S is increased in acute inflammation.
- Bleeding time and coagulation time : Altered levels may require correction when contemplating any surgery of the patient.
- Fasting blood sugar : To assess degree of control of diabetes.
- HbA1c to know the previous diabetic status.
- Serum creatinine: It is more sensitive indicator of the renal function, which may be hampered in diabetic nephropathy.
- Blood urea: Also indicates renal function, but may vary with hydration of patient.
- HIV and HBsAG: For universal precautions.

2. Examination of urine

- For Sugar,Albumin
- For Ketone bodies: Diabetic ketoacidosis.

3. Bacteriological

- Examination of the discharge: This investigation is important in inflammation and spreading ulcer. A baseline bacterial culture with sensitivity result is useful. It provides a guideline for appropriate chemotherapy.

4. X-ray of foot

Radiographs of the foot in patients with diabetes commonly reveal a combination of bone alterations, including gross destruction, fragmentation, periosteal new bone formation and pointed bone deformity. If infection is suspected then on plain films defects in soft tissue contour and loss of tissue planes will be seen. Edema or swelling is common.Other findings include osteosclerosis, fragmentation, periositis and radiolucent areas within the soft tissues which may be air as a result of debridement / open wound (or) from production of gas by microorganisms.Calcification of arteries (also known as medial arterial calcification or Monckeberg's arteriosclerosis) is a common findings in patients with diabetes. Usually feet are earliest and most frequent site of involvement.

5. Doppler Ultrasound

Is a useful adjunct to physical examination. Measuring the ankle – brachial ratio is less helpful than in the non – diabetic patient because calcific stenosis may result in artifactually elevated pressures.

The normal Doppler pulse is triphasic, but below a major obstruction it becomes monophasic and this can be readily detected audibly. If all the foot pulses are triphasic, by Doppler then one can assume that the patient does not have significant ischemia. If the pulses are monophasic, then formal non invasive evaluation is indicated.

6. Duplex Imaging : (Duplex Ultrasound scanning)

This is an investigative technique of major importance in vascular disease. A duplex scanner uses 'B' mode ultrasound to provide an image of vessels. This image is created through the different ability of the tissues to reflect the ultra sound beam. A second type of ultrasound, namely Doppler ultrasound is then used to insonate the

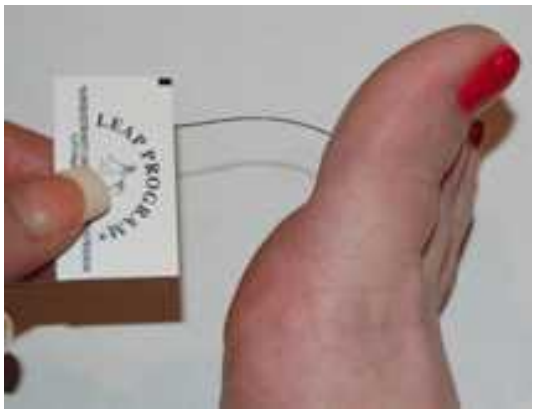
vessels and the Doppler shift is analyzed by dedicated computer in the Duplex scanner itself. Such shifts can give detailed knowledge of vessel blood flow, turbulence. Some scanners have the added sophistication of colour coding which allow visualization of blood flow on the image. The various colours indicate change in direction and velocity of flow points of high flow generally indicate stenosis.

It allows the cross sectional area of arterial lumen to be measured by use of colour, the flow towards or away from the transducer can be easily distinguished so that peripherally running arterial flow (red) can be immediately distinguished from centrally directed venous flow (blue), the intensity of colour increases with the velocity of flow[33].

7. Assessment for neuropathy

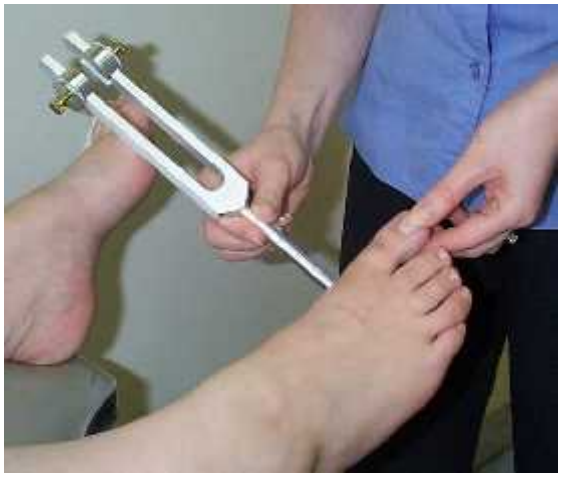
a. Testing with monofilament

Nylon monofilament of 5.07 sizes (thickness), equivalent to 10g of linear forces. It buckles at a given force of 10g. The patient should be able to sense the monofilament by the time it buckles. The patients inability to feel the filament indicates LOPS (Loss of Protective Sensation).



b. 128 Hz tuning fork

Vibratory sensation should be tested using 128 Hz tuning fork over the tip of the great toe bilaterally.



c. Biothesiometer

This helps to further quantify the degree of neuropathy. It delivers a vibratory stimulus which increases as the voltage is raised. It is used for quantitative assessment of the VPT (Vibration Perception Threshold). A VPT more than 25V is strongly predictive of subsequent foot ulcerations.

8. Assessment for vascularity

Its mainly done by using handheld doppler. All diabetic patients with signs and symptoms of vascular disease shoud undergo ABPI (Ankle Brachial Pressure

Index).The ankle and brachial systolic pressures can be measured and the ratio then calculated.ABPI less than 0.9 confirms ischaemia.

9. Testing for high pressure points

This can be done by using plantar force technology as described earlier. Another simple inexpensive technique using Harris mat also gives valuable results. Ink is applied on the other side of mat with the roller, the patient is asked to walk on the mat. While interpreting the footprint darker area indicates a high pressue point.

Treatment

TREATMENT

Prevention of diabetic foot ulcer

Patient education should be regarding the foot hygiene, skin care, nail care and proper footwear.In order to improve compliance and adherence to what is taught the patient should be encouraged to become proactive and participate in the interactive sessions rather than remaining passive. Preventive measures can be in the form of accommodative footwear (MCR- Micro Cellular Rubber, MCP- Micro Cellular Polymer), prophylactic surgery if deformity cannot be accomodated in the footwear, consultation with vascular surgeon and regular followup.

Advises to the patient to prevent diabetic foot ulcer

Diabetic patients should examine their feet on a daily bases. The maceration especially between the toes is usually caused by fungal infection and should be observed carefully. It is recommended to use a mirror in order to better observe the plantar surface of the foot. In case, if the diabetic patient's vision is compromised due to retinopathy or the patient is unable to perform the daily examination of own feet, another individual who is fully trained should do the task for the patient.

The feet should be washed and dry at least once a day. It is important to dry the inter-digital spaces between the toes very carefully.

The temperature of the water used for rinsing the foot should be less than 37 centigrade. This helps to prevent accidental burning of the extremities due to characteristic glove stocking neuropathy in diabetic patients.

The diabetic patients, especially the ones with sensory neuropathy, should not use the heating pads over their bodies. It is also recommended to warn the patient not to place their feet close to the heaters during the winter.

All the patients especially those with diabetic neuropathy or high risk diabetic foot should be instructed to use footwear both indoors and outdoors. It is recommended to wear special shoes with adequate size when the patient is walking indoor on the carpet. The use of the shoes without stockings in diabetic patients should be discouraged. In patients with neuropathy, it is also recommended to use the footwear's with enclosed frontal part in order to prevent the minor trauma to the fore foot.

It is recommended to observe and physically examine inside the patients shoes on a daily basis. This recommendation is given to detect any external objects inside the shoes and to look for pressure effect on different surfaces of the patient's feet. The lateral engorgement of the shoes is an indication of pressure exerted by the first and fifth metatarsals and the swelling observed in the frontal part of the shoes is caused by the pressure of distal phalanges of the first digit.

Diabetic patients due to autonomic neuropathy present with decreased perspiration in lower extremities. As a result, the dryness of the plantar surfaces of the feet and heels is common. The minor trauma combined with the dry skin creates cracks which facilitate the entrance of microorganisms into the skin and consequently foot infection is inevitable. It is recommended to apply lubricants containing urea or salicylates with the ability to penetrate the dry and hyperkeratosis skin.

In diabetic patients it is recommended to change and put on clean socks on a daily bases.

Especially in female diabetics, any kind of manipulation of the nails is not recommended. The nails should not be cut in a rounded fashion.

The patient should be instructed not to use any kind of chemical substances or commercial pads or plasters in order to treat the calluses of the feet.

Debridement

Debridement is widely accepted as the most definitive treatment for the diabetic foot ulcer. Inadequate debridement may lead to prolonged infection, increasing risk for limb amputation.

Sharp debridement of the diabetic foot ulcer stimulates the non migratory edge epithelium, releases growth factors and reduces the local inflammatory and proteolytic environment.

The goal of operative debridement is to remove all hyperkeratotic tissue (i.e callus), necrotic tissue, functionally abnormal senescent cells and infected tissue, all of which inhibit wound healing. In this manner, the remaining tissue, although physiologically impaired, can respond to exogenous topical treatment, (ie, growth factors or cell therapy).

Clinical judgement has traditionally defined the margin of debridement, which is recognized as tissue with punctate bleeding, the margin of debridement of the skin edge should extend to the soft tissue beyond the callus. The depth of debridement of the wound bed should extend to tissue that is free of fibrosis and infection[34].

Infection Control

Diabetic foot infections (DFIs) are usually a consequence of skin ulceration from ischemia or trauma to a neuropathic foot. The compartmentalized anatomy of the foot, with its various spaces, tendon sheaths and neurovascular bundles, allows ischemic necrosis to affect tissues within a compartment or spread along anatomic tissue planes. Recurrent infections are common, 10% to 30% of affected patients eventually require amputation.

Diabetic patients are predisposed to foot infections, not only because of the portal of entry and poor blood supply, but also because of defects in humoral

immunity (e.g., impaired neutrophil chemotaxis, phagocytosis, intracellular killing) and impaired monocyte-macrophage function, which correlate with the adequacy of glycemic control. Cell-mediated immunity and complement function may also be impaired.

Acute infections are usually caused by gram-positive cocci. S. aureus is the most important pathogen in DFIs.

Chronic wounds, recurrent infections and infections in hospitalized patients are more likely to harbour complex flora, including aerobic and anaerobic flora. Among gram-negative bacilli, bacteria of the family Enterobacteriaceae are common and Pseudomonas aeruginosa may be isolated from wounds that have been treated with hydrotherapy or wet dressings. Antibiotic-resistant bacteria, especially MRSA, may be isolated from patients who have received antibiotics previously or who have been hospitalized or reside in long-term care facilities.

Agents that have been shown to be effective for therapy of DFIs in clinical trials include cephalosporins, β-lactamase inhibitor combination antibiotics, fluoroquinolones, clindamycin, carbapenems, vancomycin and linezolid. The optimal duration of therapy for DFIs has not been determined common practice is to treat mild infections for 1 week, whereas serious infections may require up to a 2-week course of therapy. Adequate debridement, resection or amputation can shorten the necessary durations of therapy[35].

Offloading therapy

Neuropathic diabetic foot wounds on the plantar aspect of the foot occur because of a combination of focal pressure and repetitive stress at a given site . The mitigation of either of these variables (pressure or repetitive stress) may reduce risk for ulceration.

Mechanical stress that occurs at right angles to the integument is termed "vertical stress." This tends to damage healthy tissue through repetitive compressive forces. Stress that is imparted parallel to the plantar aspect of the foot is termed "shear." This shearing of soft tissue is equally damaging and is evidenced by the characteristic undermined nature of the periphery of poorly off-loaded diabetic foot wounds. Shear and vertical stress work in tandem in the pathogenesis of a diabetic foot wound. So relieving areas of elevated plantar pressure (off-loading) can prevent and heal plantar ulceration.

Methods to offload the foot include bed rest, the use of a wheelchair, crutch assisted walking, total contact casts, felted-foam, half-shoes, therapeutic shoes, custom splints and removable cast walkers.

Total contact casts (TCCs) are considered the gold standard of the off-loading and treatment of neuropathic ulcers, the technique is called "total contact casting" because it uses a well-moulded, minimally padded cast that maintains contact with the entire plantar aspect of the foot and the lower leg. Total contact casting is effective in treating a majority of non-infected, non-ischemic plantar diabetic foot wounds, with healing rates ranging from 72% to 100% over a course of 5–7 week. Peak plantar pressures are highest in the forefoot and tend to be generally less significant in the hind foot and medial arch TCC is effective because it permits walking by uniformly distributing pressures over the entire plantar surface of the foot. TCCs are effective for a number of other reasons besides their ability to off-load. They may help reduce or control edema that can impede healing and, thus potentially protect the foot from infection[36].

Wound bed preparation

The goal of wound bed preparation is to have well-vascularized granulation tissue with no adjacent slough, discharge. Proper debridement concurrently prepares the wound bed and stimulates the healing process.

The four approaches of wound bed preparation, which address the different pathophysiological abnormalities underlying diabetic foot ulcers, are as follows

(1) Tissue management

(2) Inflammation and infection control

(3) Moisture balance

(4) Epithelial (edge) advancement[37].

Dressings in Diabetic Foot Disease

Wound dressings represent a part of the management of diabetic foot ulceration. Dressings should alleviate symptoms, provide wound protection and encourage healing.

In choosing a dressing for an infected diabetic foot ulcer, several factors have to be taken into account. Infected wounds tend to have a heavy exudate that needs to be controlled to prevent maceration of surrounding tissue. There may be considerable odour associated with infection that may be unpleasant and distressing for the patient and family. A dressing must be comfortable and acceptable for the patient. Ideally, the dressing should also aid in the management of the infection itself.

Desirable characteristics for wound dressings must incorporate the principles of wound healing. For 3 decades, since the work of Winter, Hinman and Maibach, a moist wound environment has been recognized as optimal for healing. Dressings have since been engineered thermally insulate the wound, which allows atraumatic removal. These dressings must also accommodate practical issues such as allowing

observation of the wound and providing mechanical protection at the same time they must also be cost effective .

Classes of dressings for diabetic foot infections.

Dressing	Advantages	Disadvantages
Low-adherence	Simple Hypoallergenic	Minimal absorbency
Hydrocolloids wounds	Absorbent Can be left for several days	Concerns about use for infected
Hydrogels wounds	Absorbent Aid autolysis	Concerns about use for infected
Foams	Thermal insulation Good absorbency	Can adhere to wound Occasional dermatitis with
Alginates	Highly absorbent Bacteriostatic	May need wetting before removal
Iodine preparations	Antiseptic Moderately absorbent	Iodine allergy Discolours wounds
Silver-impregnated	Antiseptic Absorbent	Cost No proven advantage

Non-adherent Or Low-Adherence Dressings

Various types of non-adherent or saline-soaked gauze dressings are often regarded as standard treatment for diabetic ulcers.

These dressings are designed to be atraumatic and to provide a moist wound environment. These simple, relatively inexpensive dressings are not designed specifically for managing infection but can be safely used in conjunction with antibiotic treatments.

Hydrocolloids

Hydrocolloid dressings are semipermeable to vapour, occlusive to wound exudate and absorbent. They are usually presented as an absorbent layer on a film or foam.Examples of commercially available products include Duoderm(Convatec), Granuflex (Convatec), and Comfeel (Coloplast). They are found to be the second most popular choice of dressing (behind non-adherent) for all diabetic foot ulcers in a study of British diabetic specialist nurses and chiropodists. Despite their popularity, their use on infected wounds is controversial. Hydrocolloid materials are designed to be occlusive, trapping exudate within the dressing and hydrating the wound.

Hydrocolloid dressing creates a hypoxic and moist environment that may also facilitate autolysis of necrotic material. Their use for highly exudative wounds can lead to maceration of the surrounding skin. Concerns persist regarding their use for infected wounds. Some evidence suggests that occlusive dressings may reduce the risk of infection developing in a wound by increasing infiltration of poly-morphonuclear leucocytes. Most authorities, however, have expressed concern that hydrocolloids may increase the risk of infection developing within a wound . Hydrocolloid dressings are designed to be left on the wound for prolonged periods (1 week), hence they are useful in clean ulcers but their role in infected ulcers is controversial as infected wounds require repeated inspection of wound.

Hydrogels

Hydrogels are designed to facilitate autolysis of necrotic tissue and they donate moisture to extensively dry wounds. They can lead to maceration when applied to wounds that show moderate to severe exudate. Their use on a diabetic foot lesion should be as an adjunct to sharp debridement of necrotic eschar. Further, they should be applied cautiously on patients with limb ischemia, because dry gangrene

could rapidly progress to wet gangrene, with serious consequences. In vitro studies have shown that hydrogels will not support bacterial growth, although a reluctance to apply gels to infected wound persists. Examples include Aquaform (Maersk Medical) and Intrasite Gel

Foams

Foam-based dressings are another popular choice for diabetic foot ulcers. The dressings have a wide range of absorbency, provide thermal insulation and are easily cut to shape. There have been few published data on their use in diabetic foot ulceration. Examples include Allevyn (Smith and Nephew), Cavicare (Smith and Nephew) and Avance impregnated with bactericidal silver.

Alginates

A wide range of different alginate, or seaweed products are currently available. They are highly absorbent provide haemostasis and are atraumatic at dressing change (but may require wetting). It is important to ensure that all dressing is removed from a wound, because retained dressing may be a source for further infection. The dressings may have some bacteriostatic properties. Calcium alginate dressing inhibited growth of Staphylococcus aureus in vitro, with no increase in growth of Pseudomonas, Streptococcus pyogenes, or Bacteroides fragilis.

Alginates should be safe to use on infected foot ulcers, provided there are regular and thorough dressing changes. Examples include Kaltostat (Convatec) and Sorbsan (Maersk Medical).

Iodine Preparations

Antiseptics such as iodine-based preparations are commonly used on wounds, although there is no evidence to support a beneficial effect. Typically they are applied to locally infected wounds, usually in combination with systemic antibiotics.

Iodine comes in 2 main preparations: cadexomer- iodine and povidone-iodine.Iodine is bactericidal in vitro, with maximal activity at 0.1%–1% . Povidone-iodine has long been used as a skin antiseptic, but its antimicrobial effect on wounds is debatable. Furthermore, some data have shown iodine solutions to be toxic to fibroblasts and keratinocytes.

A randomized controlled trial of cadexomer- iodine versus saline-soaked gauze on clean foot ulcers showed no significant difference in healing between the groups. Certain iodine dressings are highly absorbent and therefore useful in preventing skin excoriation in moderately exudating ulcers. In our own clinical practice, Cadexomer-iodine pastes are used for wounds and povidone-iodine gauze for superficial ulcers. Despite the lack of evidence, many consider iodine preparations to be appropriate dressings for infected diabetic foot ulcers.

Silver-Impregnated Dressings

The use of silver as a topical antimicrobial for acute and chronic wounds is well established. It has been traditionally delivered as silver nitrate or as silver sulfadiazine. Silver nitrate has cytotoxic effects on host cells, a property often exploited in the treatment of hypergranulating tissue, but its application can be uncomfortable. Silver sulfadiazine, which has the antimicrobial actions of both silver and sulfadiazine, is used on burns and chronic wounds and is generally well tolerated. The antimicrobial effects of silver are complex, including direct inhibition of bacterial cell respiration, inactivation of intracellular enzymes and alterations to the cell

membrane. Silver-coated dressings that use elemental silver may be more efficacious at killing bacteria than is silver sulfadiazine or silver nitrate . New silver-impregnated dressings may be suitable for use for infected diabetic foot ulcers. Examples include Megaheal and Hydroheal.

There have been no randomized controlled clinical trials of these dressings in diabetic foot ulceration. However, reports of accelerated wound reepithelialization and beneficial antibacterial action in the treatment of burns are encouraging[38].

Biological dressings

Biological Therapy (e.g., bilayered keratinocytes and fibroblasts and platelet-derived growth factor) must be used when patients fail to improve after the approaches described above have been applied for 3 weeks. Biological therapy should be implemented only if wound size cannot be decreased by more than 10 percent within a 3-week time period.

Diabetic foot ulcers exhibit a decreased production of growth factors within the wound. Cell therapy, also known as biological therapy, presents an appropriate treatment option in some cases. Biological therapy is an ideal treatment for diabetic foot ulcers, because it adds cells that release growth factors to a growth factor-dependent environment, increases cytokines and matrix proteins and promotes angiogenesis. Thus accelerating healing time decreases the risk of wound infection. The biological therapy consists of “The bilayer biologically active skin construct”, composed of a surface layer of allogenic human keratinocytes over a layer of allogenic human fibroblasts suspended within a collagen matrix. The “Bilayer cell therapy” has been shown to increase the healing rate of diabetic foot ulcers not complicated by osteomyelitis or ischemia. Fibroblasts synthesize collagen and secrete a matrix of growth factors and matrix proteins in physiological concentrations

essential for wound healing and epitheliazation. Biological therapy is usually performed after a debridement and after achieving proper haemostasis. Often wounds require several applications, as the biological effect from the cell therapy lasts only up to 6 weeks[39].

Hyperbaric oxygen therapy (HBOT)

Hyperbaric oxygen therapy is based on the premise that the delivery of supraphysiological concentrations of oxygen to diseased tissues will result in beneficial physiological changes.

The therapy is based on achieving an atmospheric pressure of 2–3 atmospheres pressure which is administered using a sealed polyethylene bag over the affected area and administering 100 percent oxygen to a pressure between 20 and 30 mmHg. Treatment lasts for 2 to 2 ½ hours.

HBOT can be offered to patients who have diabetic foot ulcers for whom at least 30 days of standard wound care has failed and who have a Wagner grade III lesion or higher. (meaning the ulcer must penetrate to tendon, bone or joint and may be associated with deep abscess, osteomyelitis, gangrene, or septic arthritis) In diabetic foot ulcer, it is believed both that the function of phagocytic cells is improved, assisting in the fight against any infection and that wound healing is independently aided through effects on cellular processes. Thus, it has been suggested that HBOT is useful for the treatment of infection and for the healing of chronic diabetic wounds[41].

Growth Factors

PDGF-beta (becaplermin; available as Regranex) has been developed as a topical therapy for the treatment of noninfected diabetic foot ulcers. It is applied in the form of a once-daily gel along with debridement on a weekly basis.

Platelet-rich plasma (PRP) is an autologous product, extracted from the patient's plasma, which includes a high platelet concentration in a fibrin clot that can be easily applied to the ulcer area. The fibrin clot is absorbed during wound healing within days to weeks following its application . There are a few studies reporting a shorter closure time and higher healing percentage in patients using PRP and platelet-derived products.

Granulocyte colony stimulating factor (GCFS) when applied on diabetic foot ulcer cause faster resolution of the infection and faster healing.

Basic fibroblast growth factor (b FGF) is known to be beneficial in the formation of granulation tissue and normal healing.

Epidermal growth factor (EGF) acts on epithelial cells, fibroblasts and smooth muscle cells to promote healing[42,46] .

Bioengineered Skin Substitutes

Tissue-engineered skin substitutes are classified into

- Allogenic cell-containing
- Autologous cell-containing
- Acellular matrices.

The first two types of matrix contain living cells such as keratinocytes or fibroblasts, while acellular matrices are free of cells and act by releasing growth factors to stimulate neovascularization and wound healing. Accumulating evidence shows that bioengineered skin substitutes may be a promising therapeutic adjunct therapy to the standard wound care for the management of non-infected diabetic foot ulcers.

Extracellular matrix Protein is a semisynthetic ester of hyaluronic acid which facilitates the growth and movement of fibroblasts and controls hydration[43].

Topical negative pressure

The practice of exposing a wound to sub-atmospheric pressure for an extended period to promote debridement and healing was first described by Fleischmann et al in 1993 following the successful use of this technique in 15 patients with open fractures. The science behind topical negative pressure dressings is to apply a sub atmospheric pressure over the wound bed and maintain the negative pressure environment by means of a semi permeable occlusive coverage. Since the wound is occluded from the surrounding environment it is also called " Limited access dressing".

Usage of a subatmospheric pressure causes

- Fourfold increase in blood flow in the local wound environment. (As measured by a laser Doppler technique.)
- Induces mechanical stress which causes an increase in cellular activity.
- Increase in the rate of granulation tissue formation and reduction in the bacterial load in the wound.
- Clinically TNP removes large amounts of fluid from wounds especially acute wounds. The resulting reduction in oedema is thought to aid in the enhancement of blood and nutrient flow into the wound.
- The mechanism behind the ability of the TNP to decrease bacterial count may be attributable to three properties increased blood flow, decreased interstitial edema and removal of harmful enzymes from the wound bed[44,45].

Collagen dressing

Diabetic foot ulcers take a longer time for healing as there are elevated levels of matrix metalloproteinases, which result in increased proteolytic activity and inactivation of the growth factors involved in the wound healing process. The use of collagen dressing has been found to inhibit the action of metalloproteinases. Collagen is a biomaterial that encourages wound healing through deposition and organization of freshly formed fibres and granulation tissue in the wound bed. Collagen when applied to a wound, not only promotes angiogenesis, but also enhance repair mechanisms. Collagen helps to reduce oedema and loss of fluids from the wound site, along with facilitation of migration of fibroblasts into the wound and enhancing metabolic activity of the granulation tissue.

Glycemic control

According to Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study , tight control of blood glucose will decrease rates of retinopathy, nephropathy and neuropathy. Lowering HbAlc may reduce the risk of myocardial infarction and cardiovascular death. The control of glucose levels should be as strict as possible and blood glucose levels above 10mmol/L must be avoided, as they are associated with impaired function of the leucocytes, both polymorphonuclear and mononuclear cells[40].

Amputation

The indications for amputations are as follows:

- Infective gangrene
- Trauma – Crush injury with tissue loss
- Frostbite.
- Ischaemic gangrene of the toes, or forefoot, from peripheral arterial occlusive disease

Ray amputation

The most common amputation in the foot is a ray amputation of the affected toe with the distal half of the associated metatarsal. This also allows good drainage of infected deep spaces of the foot

Transmetatarsal, Tarsometatarsal And Midtarsal amputations

These are also satisfactory amputations for distal gangrene with adequate perfusion of the hindfoot and leave a patient with a weight-bearing heel.

Syme's Amputation

This classical ankle amputation, first described by Syme in 1842, produces a durable weight bearing stump. It consist of a bone section at the distal tibia and fibula 0.6 cm proximal to the periphery of ankle joint and passing through the dome of ankle centrally.

Below-Knee Amputations

These operations are most commonly performed for diabetic with peripheral arterial occlusive disease and the standard technique is designed to maximize the use of well-perfused tissue. It is not always possible to retain the ideal 15 cm of tibia, but if stump is less than 8 cm then there will be difficulty in fitting a satisfactory prosthesis.

Disarticulation Through The Knee

This amputation produces a stump which is functionally satisfactory and which can sustain end weight-bearing. A through-knee amputation has advantages in children in order to preserve final femoral length.

Above-Knee Amputation

These are common amputations for ischaemia . In general, the longer the stump the better the control of the prosthesis and ideally 70 per cent of the femur (or around 25–30 cm as measured from the tip of the greater trochanter) should be retained[47].

Materials and methods

MATERIALS AND METHODS

Source of data

All patients attending the surgery OPD and/or admitted patients in B.L.D.E.U's Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijaypur with diabetic foot ulcer during the period of October 2013 to June 2015 were taken for the study.

Method of collection of data

- Period of study was from October 2013 to June 2015.
- The patients were allocated to study group and control group alternatively.
- A Proforma was used to collect all the relevant data from the patients.
- Detailed history was taken, thorough clinical examination and investigations were performed in both the groups
- All cases were followed up to discharge and subsequently for a follow up till wound healing.
- 'Primary efficacy end point' is complete ulcer closure. 'Secondary efficacy end points' include a reduction in ulcer surface area over time, time to achieve ulcer closure by either skin grafting or secondary suturing.

Sampling

- Prospective, interventional study.
- The life time risk for a person with Diabetes developing foot ulcers is 15%. The
- allowable error is 10%.

- Formula for estimating sample size :

$$n = \frac{z2\alpha pq}{E2}$$

Where : n = Sample size to be estimated.

$Z\alpha$ = Z value at α% level of significance

p = Prevalence rate.

q = 1 – prevalence

E = Allowable error is 10%.

- Calculated sample size was 60.
- In this study 60 cases were studied, in each group 30 cases, which were allocated alternatively.

Statistical Analysis

- Statistical tools like “measure of Central tendency” and “dispersion” are used to describe the data
- Statistics like “Z statistics” are used for the analysis of data and to draw valid conclusion.

Inclusion Criteria

- All cases of diabetic foot ulcers presented to the hospital during the study period with Wagner’s grade 1 – 3

Exclusion Criteria

- Diabetic patient with foot ulcers resulting from electrical, radiation burns and those with collagen vascular disease.
- Patients on medications such as corticosteroids, immunosuppressive medications, or chemotherapy.
- Pregnant or nursing mothers.

Procedure

After thorough debridement of the ulcer, collagen granule dressing is applied to grade 1 to 3 diabetic foot ulcers in case group and moist gauze dressing is applied to control group . Then the wound is assessed for reduction in surface area of ulcer, granulation tissue fill up of wound after 7,14,21,28 days in both the groups.

Results

RESULTS

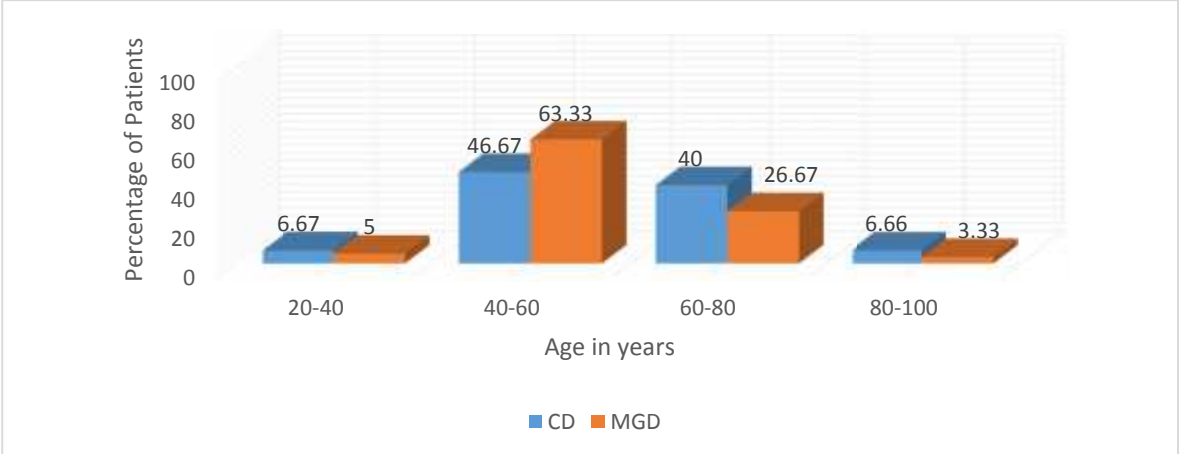
The 60 patients were divided in collagen dressing group and moist gauze dressing alternatively. The patient characteristics in both groups were well matched as shown below.

Distribution of patients according to age

Table no 1: Frequency and percentage distribution of patients according to age

AGE(Yrs)	CD	CD	MGD	MGD	TOTAL
	Frequency	%	Frequency	%	
20-40	3	6.67	2	5	5
41-60	15	46.67	19	63.33	34
61-80	10	40	8	26.67	18
81-100	2	6.66	1	3.33	3
Total	30	100	30	100	60

Figure no 1: Percentage distribution of patients according to age



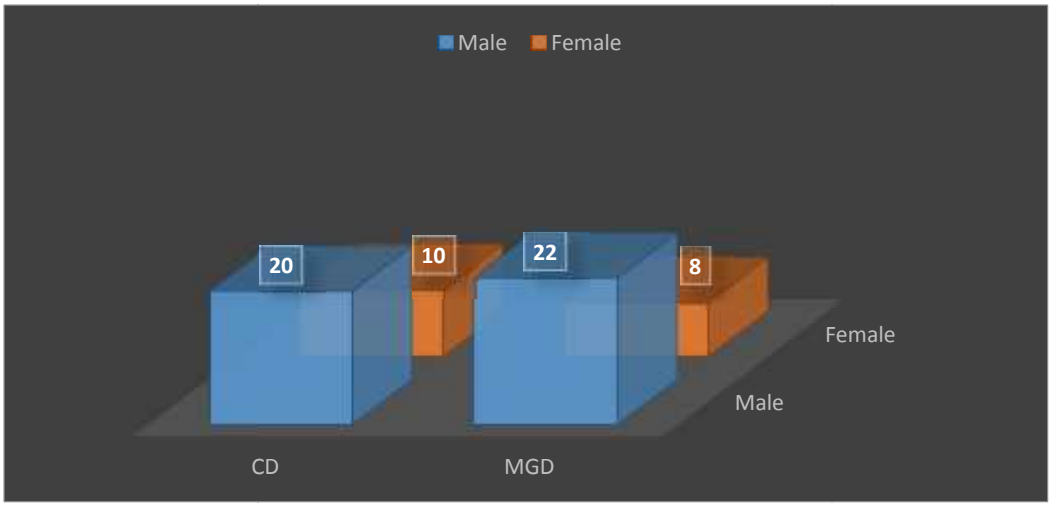
The mean age in CD group was 58(standard deviation of 13.5),the mean age in MGD group was 58.4(standard deviation of 10.7)

Distribution of patients according to sex

Table no 2: Distribution of patients according to sex

SEX	CD	MGD	TOTAL
MALE	20	22	42
FEMALE	10	8	18
TOTAL	30	30	60

Figure no 2: Distribution of patients according to sex



Male: Female in CD group is 20:10

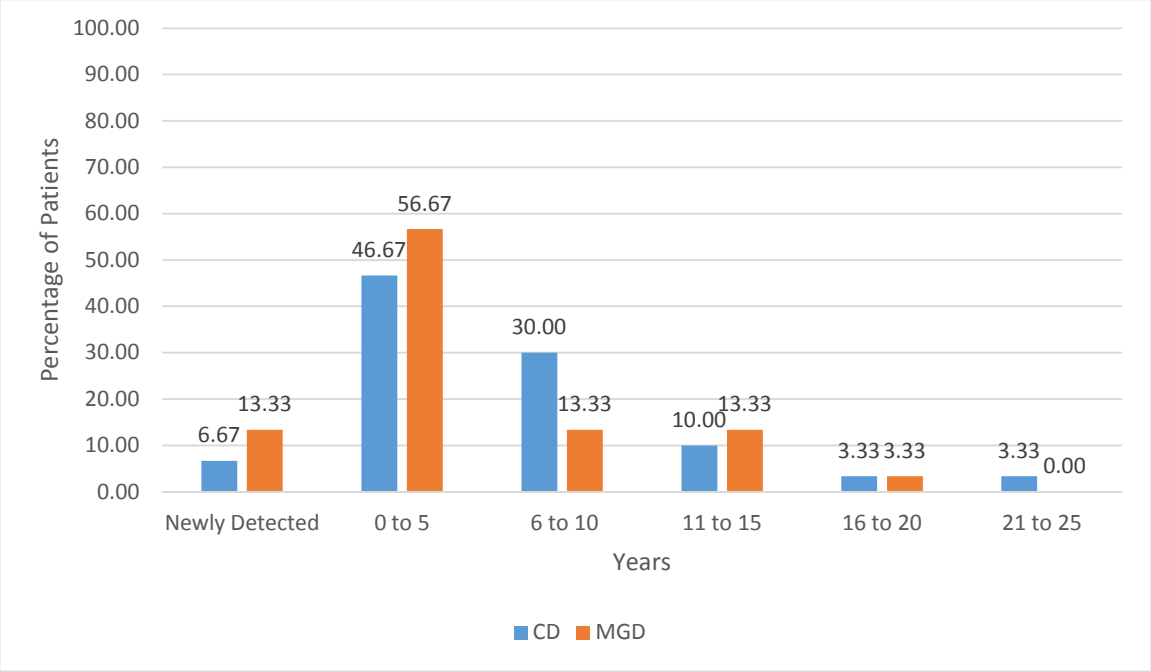
Male: Female in MGD group is 22:8

Distribution of patients according to duration of Diabetes Mellitus

Table no.3: Distribution of patients according to duration of Diabetes Mellitus

Duration of diabetes (Yrs.)	CD	MGD	Total
Newly detected	2	4	6
0-5	14	17	31
6-10	9	4	13
11-15	3	4	7
16-20	1	1	2
21-25	1	0	1
Total	30	30	60

Figure no.3: Percentage distribution of patients according to duration of Diabetes mellitus



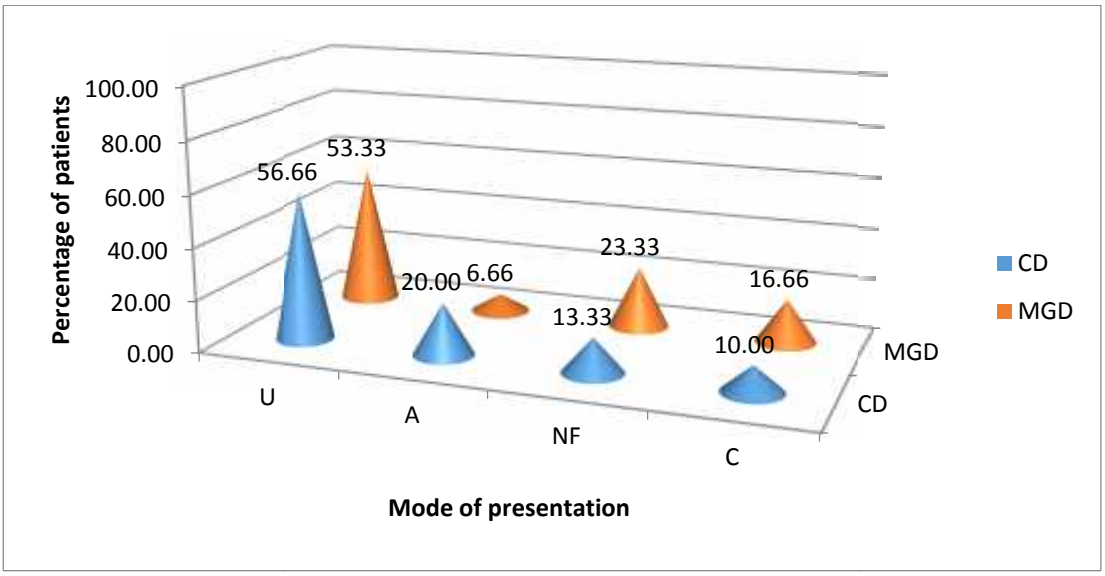
The study included patients suffering from diabetes mellitus for various durations. Some had regular treatments and others on irregular treatments.

Distribution of patients according to mode of presentation

Table no.4: Distribution of patients according to mode of presentation

MOP	CD	MGD	Total
Ulcer(U)	17	16	33
Abscess(A)	6	2	8
Necrotizing fasciitis(N.F)	4	7	11
Cellulitis(C)	3	5	8

Figure no.4: Percentage of patients according to mode of presentation



Ulcers are the most common presentation in diabetic foot as observed in CD and MGD treatments.

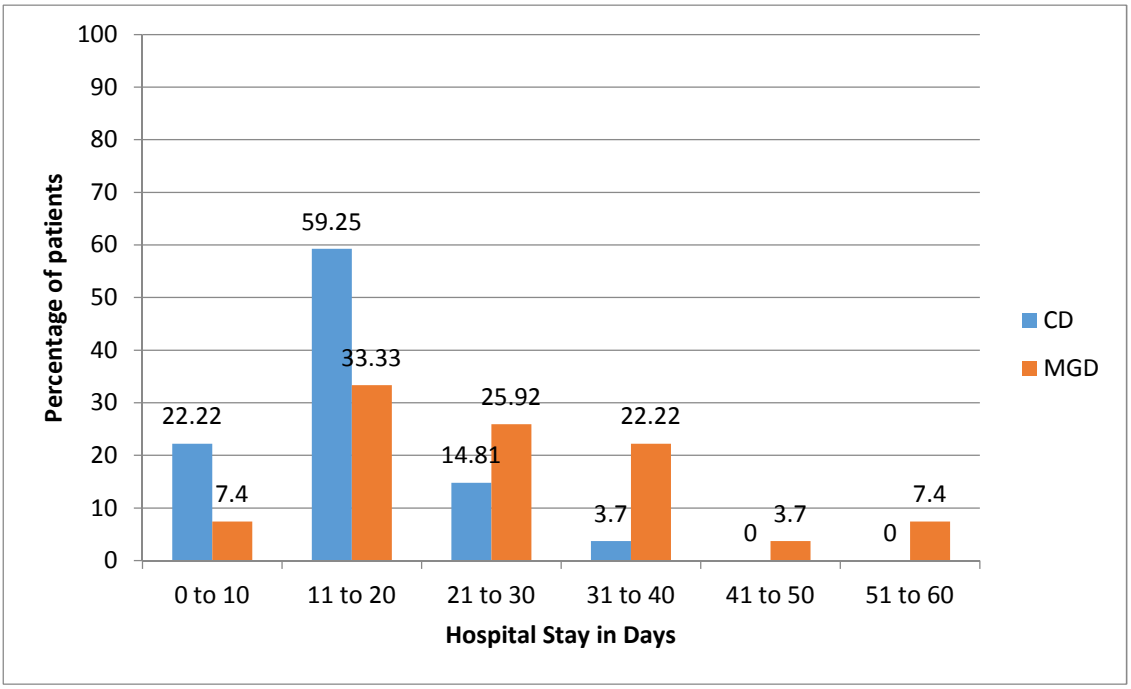
Distribution of patients according to duration of hospital stay

Table no 5: Distribution of patients according to duration of hospital stay

DAYS	CD	MCD	TOTAL
0 to 10	6	2	8
11 to 20	16	9	25
21 to 30	4	7	11
31 to 40	1	6	7
41 to 50	0	1	1
51 to 60	0	2	2
Total	27	27	54

6 patients attending the OPD were included in the study

Figure no 5: Distribution of patients according to duration of hospital stay



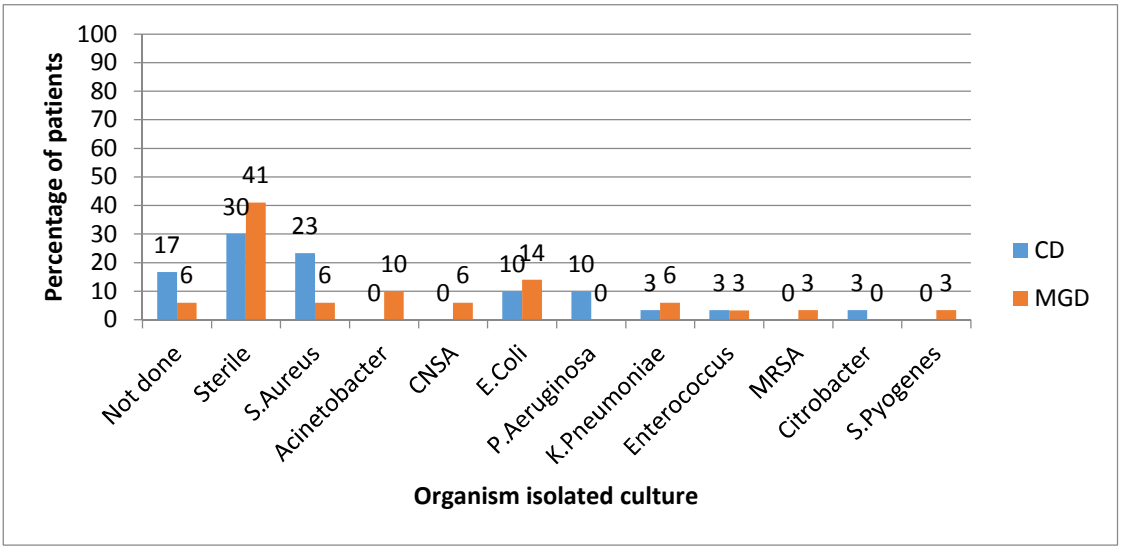
Majority of patients i.e 48% patients stayed for 11-20 days.

Distribution of patients according to organism isolated

Table no 6: Distribution of patients according to organism isolated

Bacteria	CD	MGD	Total
Not done	5	2	7
Sterile	9	12	21
S.Aureus	7	2	9
Acinetobacter	0	3	3
CNSA	0	2	2
E.Coli	3	4	7
P.Aeruginosa	3	0	3
K.Pneumoniae	1	2	3
Enterococcus	1	1	2
MRSA	0	1	1
Citrobacter	1	0	1
S.Pyogenes	0	1	1
Total	30	30	60

Figure no 6: Percentage of patients according to organism isolated



The most common organism isolated from the ulcers was Staphylococcus aureus followed by E.Coli.

Granulation tissue fill up of wound in various durations

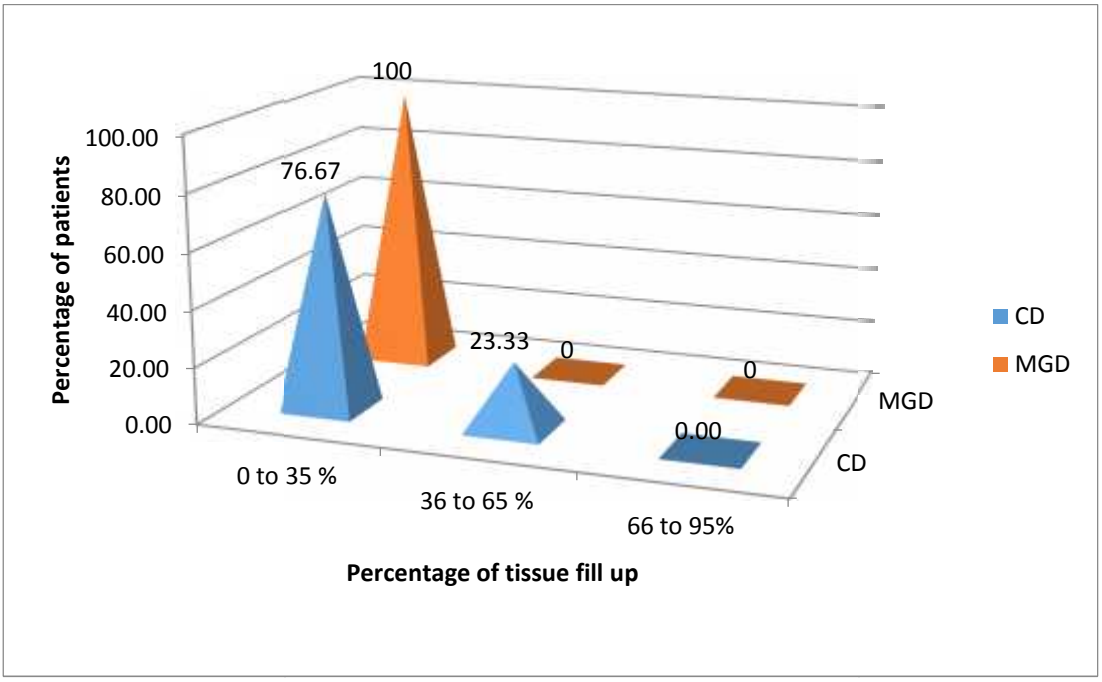
Tissue fill up is complete when the skin growth is complete and wound doesn't require any further dressings. The observations are done after a week, 2 weeks, 3 weeks and 4 weeks.

Distribution according to granulation tissue fill up at 7 days

Table no 7 : Distribution according to granulation tissue fill up at 7 days

Granulation tissue	CD	MGD	Total
0 to 35 %	23	30	53
36 to 65 %	7	0	7
66 to 95%	0	0	0
Total	30	30	60

Figure no 7: Percentage distribution according to granulation tissue fill up at 7 days



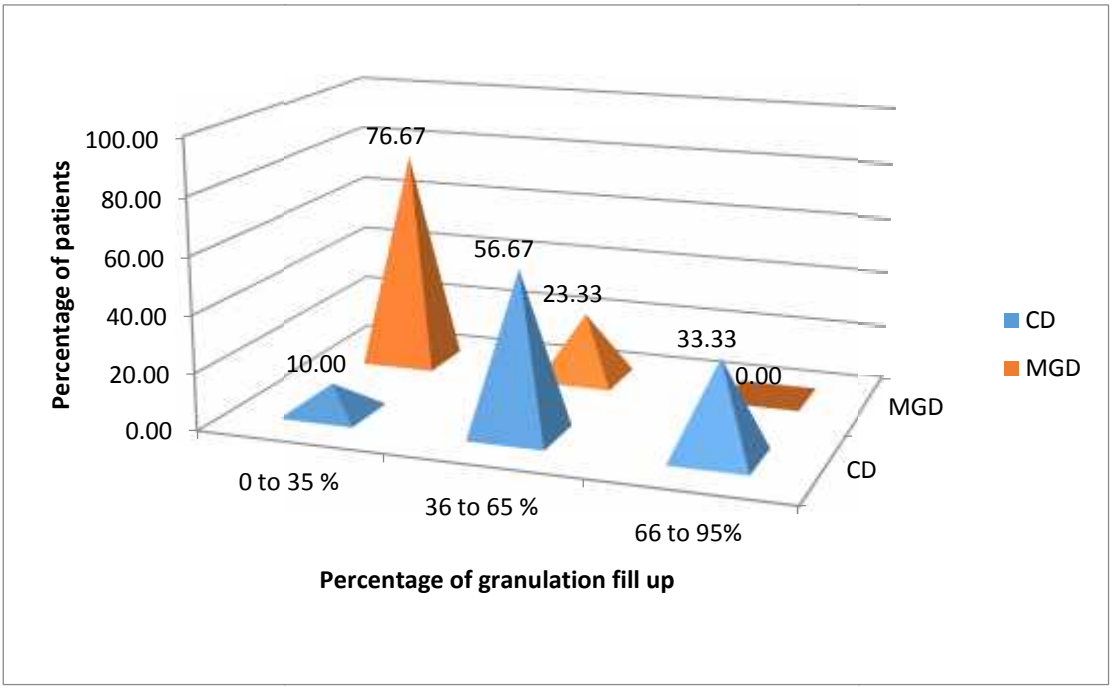
p=0.001

Distribution according to granulation tissue fill up at 14 days

Table no 8: Distribution according to granulation tissue fill up at 14 days

Granulation tissue	CD	MGD	Total
0 to 35 %	3	23	26
36 to 65 %	17	7	24
66 to 95%	10	0	10
Total	30	30	60

Figure no 8: Percentage Distribution according to granulation tissue fill up at 14 days



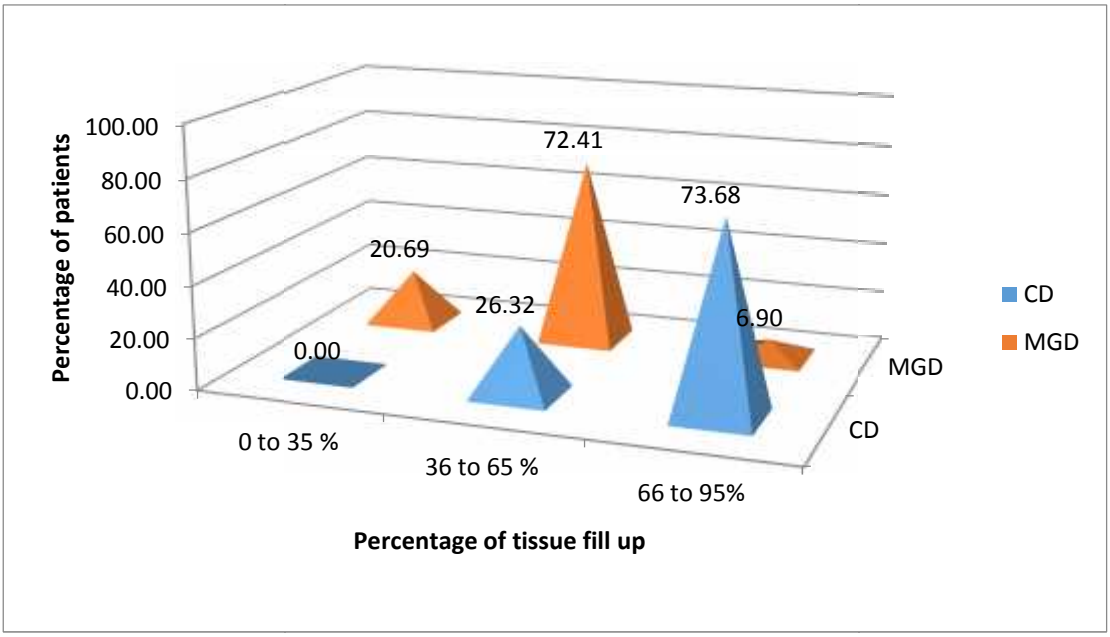
p=0.002

Distribution according to granulation tissue fill up at 21 days

Table no 9: Distribution according to granulation tissue fill up at 21 days

Granulation tissue	CD	MGD	Total
0 to 35 %	0	6	6
36 to 65 %	5	21	26
66 to 95%	14	2	16
Total	19	29	48

Figure no 9: Percentage Distribution according to granulation tissue fill up at 21 days



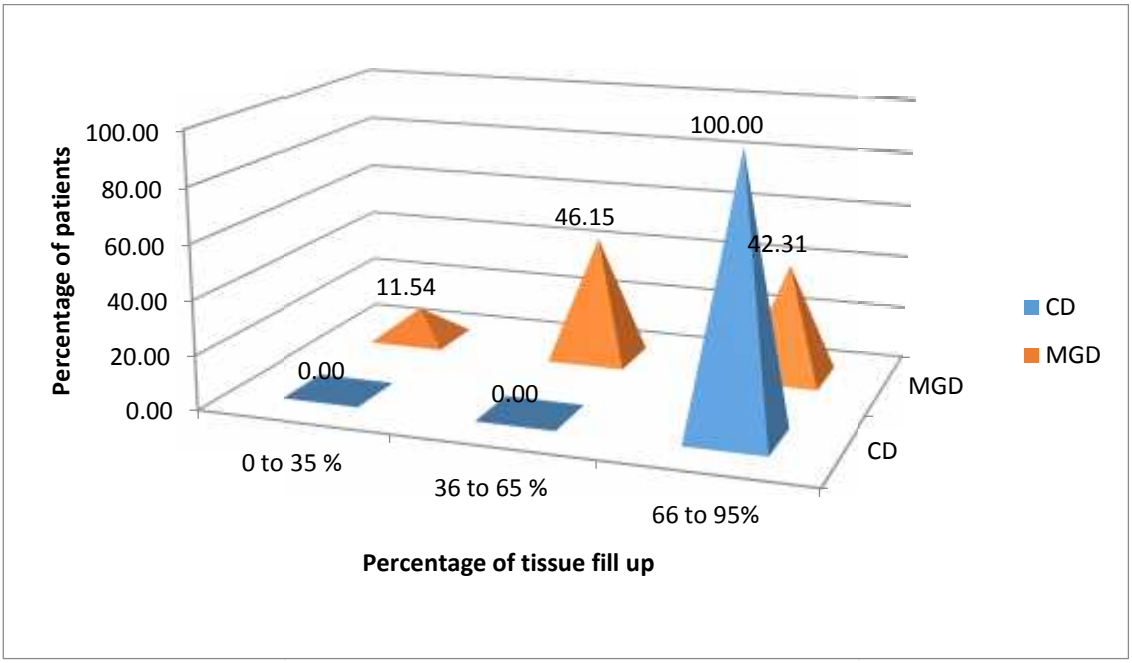
p=0.001

Distribution according to granulation tissue fill up at 28 days

Table no 10: Distribution according to granulation tissue fill up at 28 days

Granulation tissue	CD	MGD	Total
0 to 35 %	0	3	3
36 to 65 %	0	12	12
66 to 95%	8	11	19
Total	8	26	34

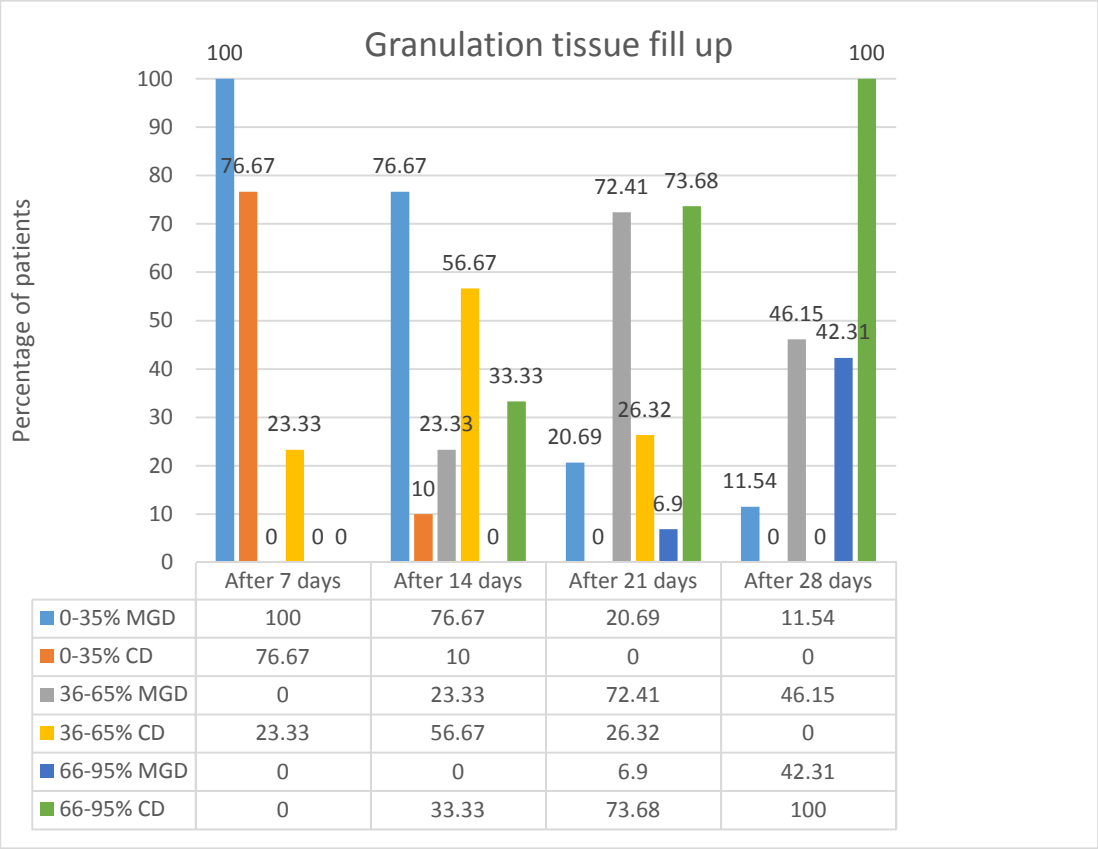
Figure no 10: Percentage Distribution according to granulation tissue fill up at 28 days



p=0.001

Summary of granulation tissue fill up comparing MGD and CD

Figure no 11: Summary of granulation tissue fill up comparing MGD and CD



	After 7 days	After 14 days	After 21 days	After 28 days
0-35% MGD	100	76.67	20.69	11.54
0-35% CD	76.67	10	0	0
36-65% MGD	0	23.33	72.41	46.15
36-65% CD	23.33	56.67	26.32	0
66-95% MGD	0	0	6.9	42.31
66-95% CD	0	33.33	73.68	100

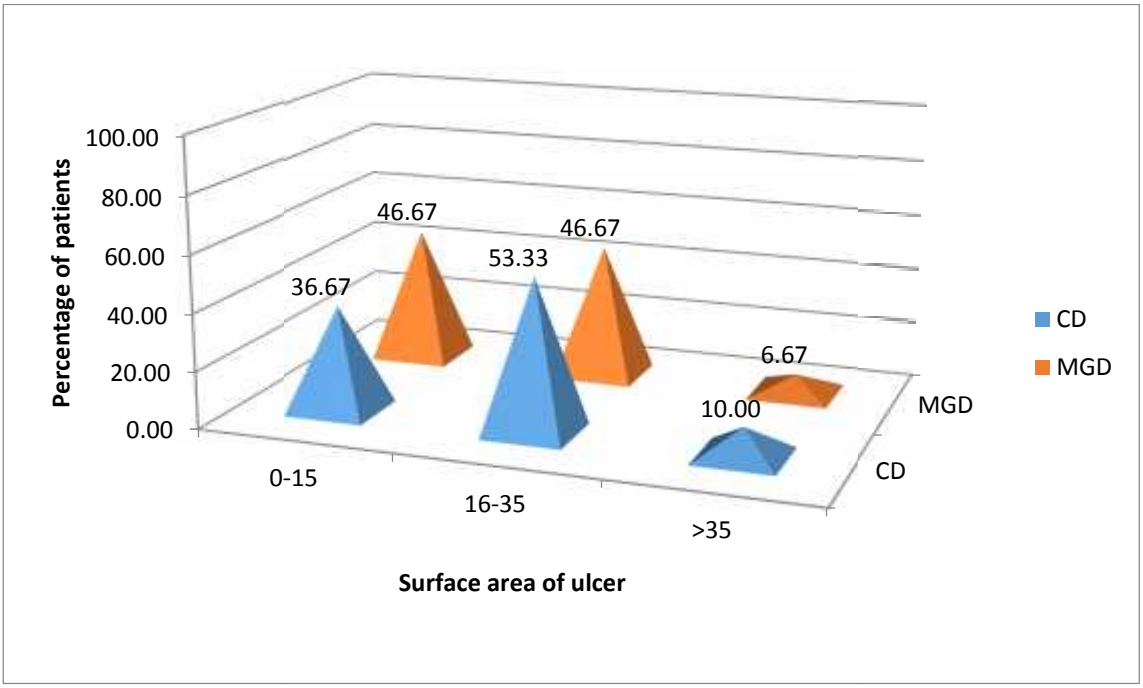
Figure no 11 shows that CD group shows a faster rate of granulation tissue fill up as compared to moist gauze dressing group.

Distribution of patients according to Surface area of ulcer

Table no 11: Distribution of patients according to Surface area of ulcer

Surface area of Ulcer (Sq cm)	CD	MGD	Total
0-15	11	14	25
16-35	16	14	30
>35	3	2	5
Total	30	30	60

Figure no 12: Percentage Distribution of patients according to Surface area of ulcer



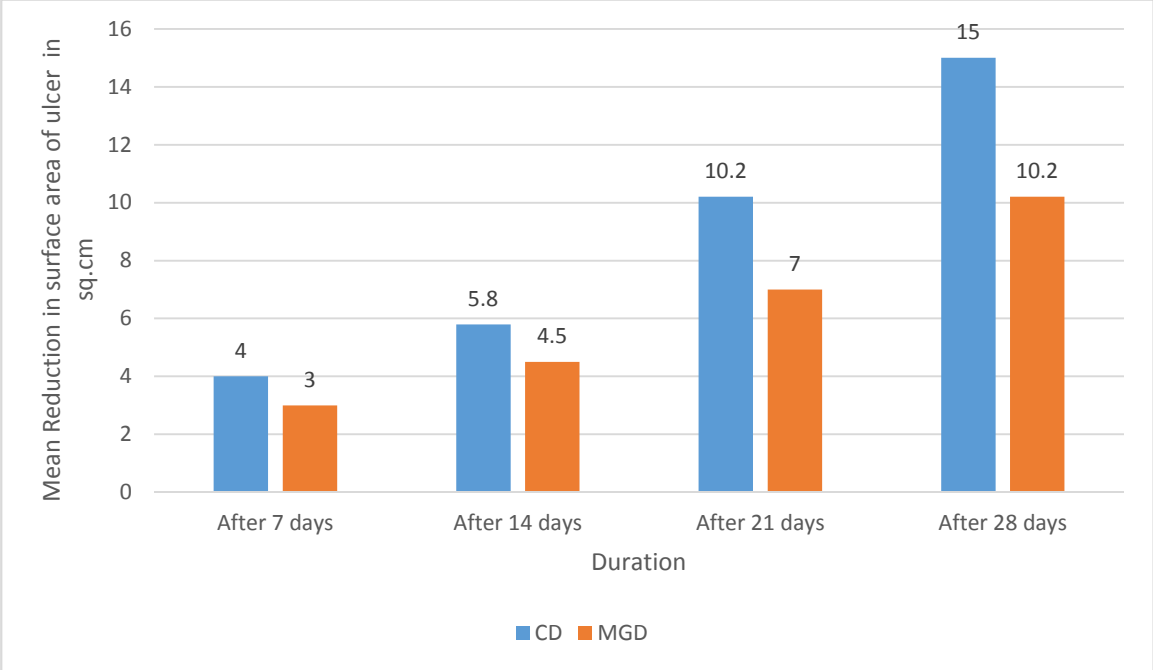
About 50% ulcers in our study groups had surface area of 16-35 sq.cm

Mean and Standard Deviation of reduction in the surface area of ulcers

Table no 12: Mean and Standard Deviation of reduction in the surface area of ulcer in sq.cm

Reduction in Surface area of Ulcer (sq.cm)	CD		MGD	
	Mean	S.D	Mean	S.D
After 7 days	4	2.5	2	0.5
After 14 days	5.8	3.5	3	1.2
After 21 days	10.2	5	4.1	1.7
After 28 days	15	4	7.2	3

Figure no 13: Mean reduction in the surface area of ulcers



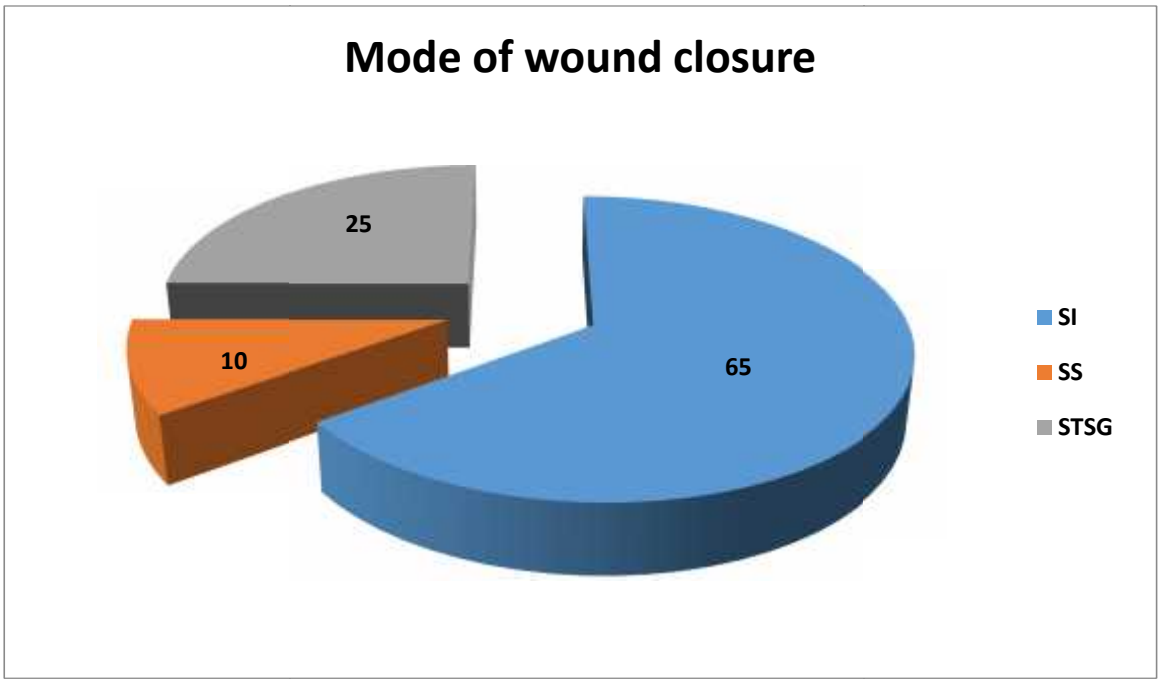
From the above figure it can be concluded that, there is significant reduction in the surface area of collagen treated diabetic foot ulcers as compared to diabetic foot ulcers treated with moist gauze dressing.

Distribution of patients according to mode of wound closure

Table no 13: Distribution of patients according to mode of wound closure

Mode of wound closure	CD	MGD	Total
Secondary Intention Healing	20	19	39
Secondary Suturing	2	4	6
Split Thickness Skin Grafting	8	7	15
Total	30	30	60

Figure no 14: Percentage of patients according to mode of wound closure



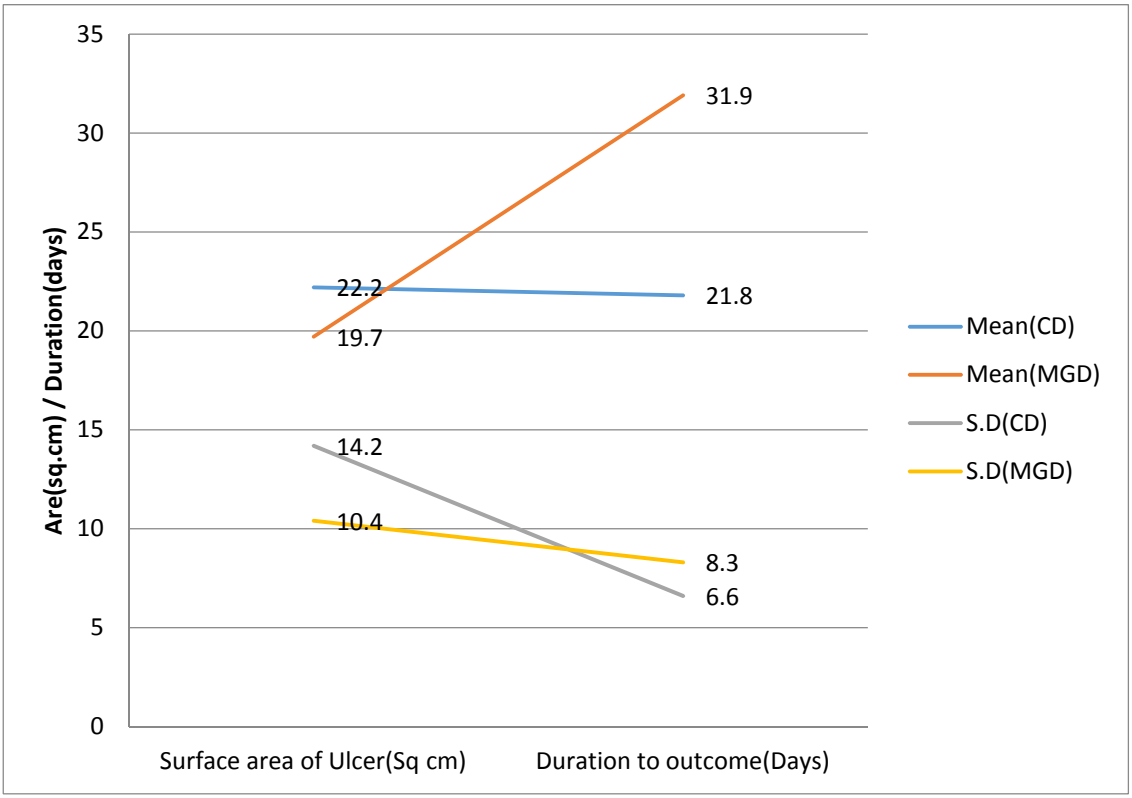
65% ulcers in our study groups healed by secondary intention.

Mean and Standard deviation of size of ulcer and duration to outcome

Table no 14: Mean and Standard deviation of size of ulcer and duration to outcome

Parameters	CD		MGD	
	Mean	S.D	Mean	S.D
Surface area of Ulcer(Sq.cm)	22.2	14.2	19.7	10.4
Duration to outcome(Days)	21.8	6.6	31.9	8.3

Figure no 15: Mean and Standard deviation of size of ulcer and duration to outcome



The figure shows surface area of the ulcers considered for the study are similar, but the final outcome of the treatment using CD is advantageous over MGD.

Discussion

DISCUSSION

Collagen based dressing is an effective tool in the healing of diabetic foot ulcers. Collagen is a biomaterial that encourages wound healing through deposition and organization of freshly formed fibres and granulation tissue in the wound bed thus creating a good environment for wound healing. Collagen granules promote angiogenesis by facilitating migration of fibroblasts and keratinocytes into the ulcer.

The demographic profile was statistically analysed and found to be comparable. The mean age of the patients in our study group was comparable to the study done by Veves A et al., as shown in the table.

	Our study		Veves A et al	
	CD	MGD	CD	MGD
Mean age of the patients (Years)	58	58.4	58	59

The sex distribution of patient in our study was comparable to the study conducted by Holmes et al. and Veves A et al.

	Our study		Veves A et al		Holmes et al	
	Male	Female	Male	Female	Male	Female
Sex distribution (Percentage)	70	30	73.5	26.5	78	22

The mean surface of ulcer was 22 sq.cm in collagen dressing group and 19.7 in moist gauze dressing group this was comparable to study conducted by Harish Rao et al. and Holmes et al.

	Our study		Holmes et al		Harish Rao et al	
	C.D	M.G.D	C.D	M.G.D	C.D	M.G.D
Surface area of ulcer(Sq.cm)	22	19.7	18	16.4	6.49	8.63

The average time for appearance of healthy granulation tissue in CD group was 10 days and MGD was 15 days this was comparable to study conducted by Donaghue VM et al.

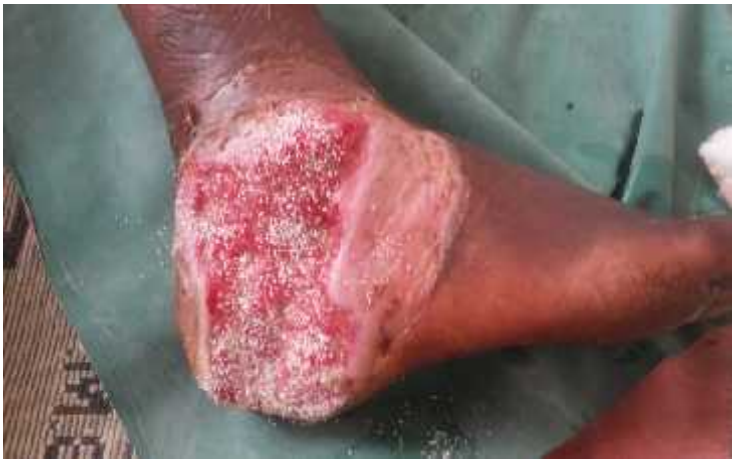
	Our study		Donaghue VM et al.	
	CD	MGD	CD	MGD
Average time to granulation tissue fill up (days)	10	15	8	14

The percentage reduction in surface area of the ulcer after 4 weeks was 68.18% in CD group and 36.5% in MGD group. This was comparable to study done by Veves A et al.

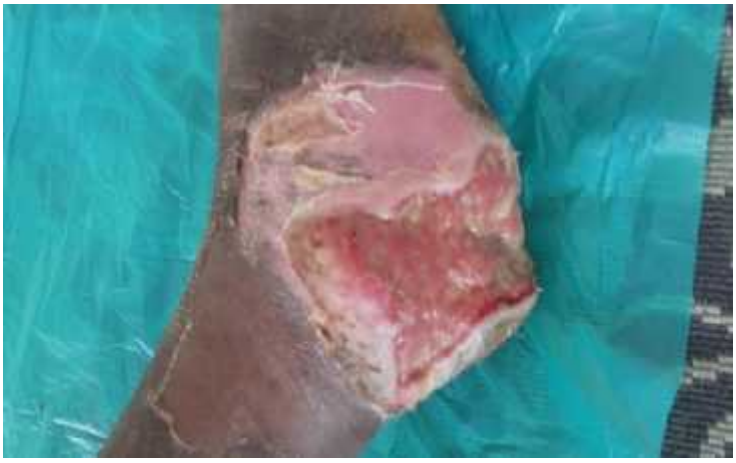
	Our study		Veves A et al.	
	CD	MGD	CD	MGD
Percentage reduction in surface area of the ulcer	68.18%	36.5%	82%	25%

The mean duration to outcome in CD was 21.8(S.D of 6.6) and in MGD was 31.9(S.D of 8.3) this was comparable to study conducted by Harish Rao et al. and Lazaro-Martinez et al.

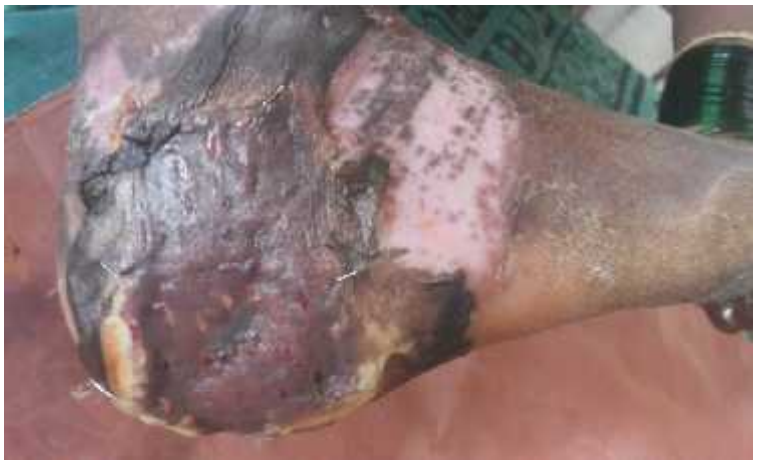
	Our study		Harish Rao et al.		Lazaro-Martinez et al.	
	CD	MGD	CD	MGD	CD	MGD
Mean duration to outcome (days)	21	31	28	42	23.3	40.6



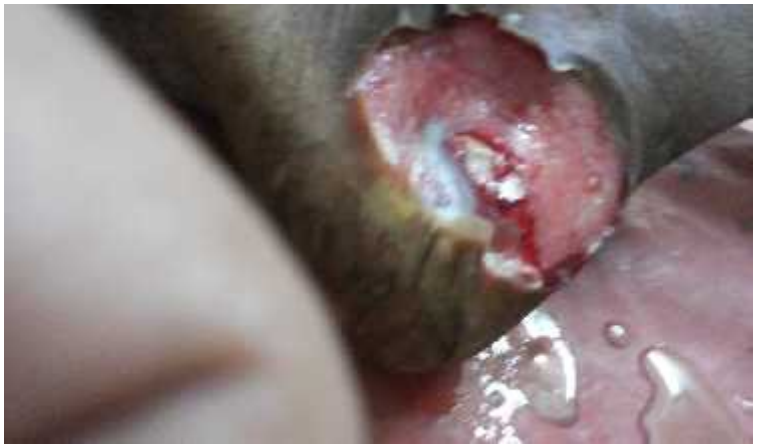
Collagen dressing being done for ulcer over the lateral aspect of the foot



Reduction in the surface area of the ulcer after 2 weeks

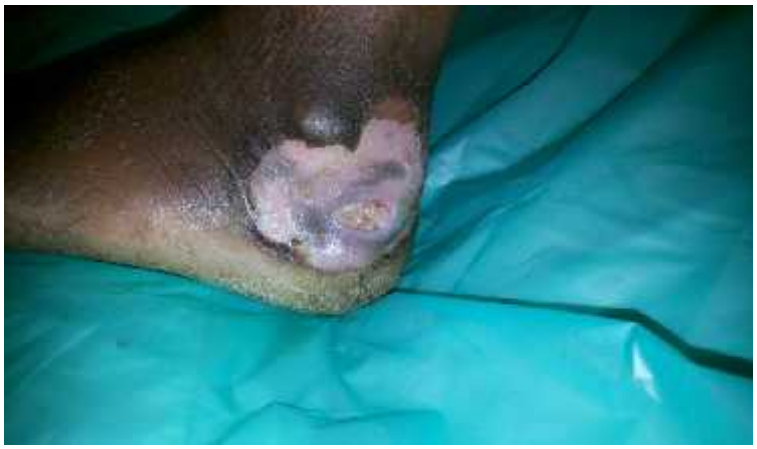


Ulcer ready for skin grafting after 3 weeks of collagen dressing



Abscess over lateral aspect of the foot, incision and drainage done

Collagen dressing being done for the ulcer



Ulcer contracted by size and healed by secondary intention after 4 weeks

Limitations of this study

- Smaller sample size
- The cost effectiveness of collagen dressing was not taken into consideration
- Post interventional parameters like quality of life, graft uptake are not included in the present study

Summary

SUMMARY

- Collagen dressing facilitates faster granulation tissue fill up
- Collagen dressing causes significant reduction in surface area of ulcer in a shorter duration
- Diabetic foot ulcer patients treated with collagen dressing showed faster recovery time and lesser duration of hospital stay.

Conclusion

CONCLUSION

Collagen dressing can be considered as a superior option in the management of diabetic foot ulcer. But we advocate further studies with larger sample size to substantiate the findings we made.

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Annexures

ANNEXURE 1

SAMPLE INFORMED CONSENT FORM

BLDEU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR- 586103

TITLE OF THE PROJECT COMPARATIVE STUDY OF COLLAGEN DRESSING WITH MOIST GAUZE DRESSING IN TREATMENT OF DIABETIC FOOT ULCERS

PRINCIPAL INVESTIGATOR Dr MALLAPPA.V.HUGGI

GUIDE Dr. MANJUNATH.S.KOTENNAVAR
M.S. (GENERAL SURGERY)
PROFESSOR
DEPARTMENT OF SURGERY

Purpose of research:

I have been informed that this study is comparison of Collagen dressing with Moist Guaze dressing. I have also been given a free choice of participation in this study. This study will help in proper understanding, regarding treatment outcome of Diabetic Foot Ulcers

Risk and discomforts:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

Benefits:

I understand that my participation in this study will have no direct benefits to me other than the potential benefits of diagnosis & treatment which is planned to reduce my pain. The major potential benefit is to find out which treatment is more effective.

Alternatives:

I understand that the two modes of treatment being studied are standard ways of treating my problem that is Diabetic foot ulcers.

Confidentiality:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

Request for more information:

I understand that I may ask more questions about the study at anytime. Dr. Mallappa Huggi is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

Refusal or withdrawal of participation:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. Mallappa Huggi may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

Injury Statement:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____ _____

Dr. Mallappa Huggi Dr. Manjunath S. Kotennavar Date

(Investigator) (Guide)

Study subject consent statement

I confirm that Dr. Mallappa Huggi has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

Participant / Guardian Date

_____ _____

Witness to signature Date

Annexure II

SCHEME OF CASE TAKING:

Name:	CASE NO:
Age:	IP NO:
Sex:	DOA:
Religion:	DOD:
Occupation:	
Residence:	

Chief complaints with History of presenting illness

Past History:

- Diabetes mellitus
- Hypertension
- History of any drug intake

Personal History :	Diet	Appetite
	Sleep	Habit

Family History:

General Physical Examination

Vitals

PR:

BP:

RR:

Temp:

Local Examination

- Inspection:
  - Site
  - Size
  - Shape
  - Surrounding skin
  - Foot deformity
- Palpation
  - Sensation
  - Pulsation

Clinical diabetic foot Grading

Other Systemic Examination

- Respiratory System.
- Cardiovascular System.
- Central Nervous System
- Per Abdomen Examination.

Investigations

1) Blood: Hb% TC DC
   ESR BT CT
2) Urine: Albumin Sugar Microscopy Ketone bodies.
3) HIV: HBSAg:

4) Random blood sugar:

   Fasting blood Sugar Post prandial blood sugar HBA1C:

5) Blood Urea Serum creatinine

6) Pus culture and sensitivity

7) Colour Doppler

8) X-ray foot – AP and Oblique view.

9) ECG.

10) Echocadiography whenever necessary.

Final Digonsis

Follow up :

1st Week

2nd Week

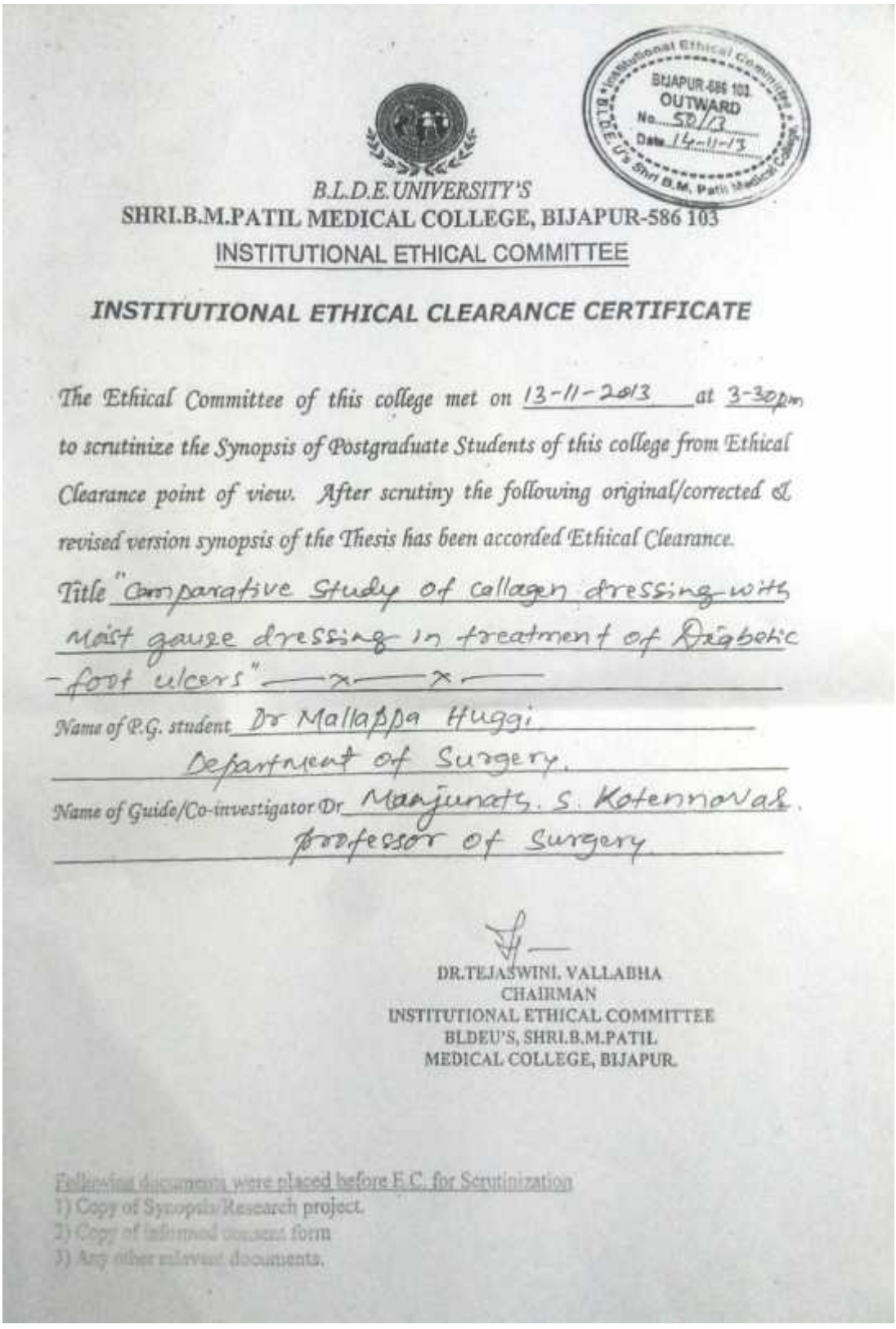
3rd Week

4th Week

Comments:

Annexure III

Ethical Clearance Certificate



B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2013 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "Comparative Study of collagen dressing with Moist gauze dressing in treatment of Diabetic foot ulcers" —x— x—

Name of P.G. student Dr Mallappa Huggi.
Department of Surgery.

Name of Guide/Co-investigator Dr Manjunath. S. Kotennavar.
Professor of Surgery.

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

KEY TO THE MASTER CHART

IP. NO	: In Patient Number
DOA	: Date Of Admission
DOD	: Date Of Discharge
ND	: Newly Detected
U	: Ulcer
A	: Abscess
C	: Cellulitis
NF	: Necrotizing Fascitis
P A	: Pseudomonas Aeruginosa
SA	: Staphylococcus Aureus
EC	: E Coli
A	: Acinetobacter
KP	: Klebsiella Pneumoniae
E	: Enterococcus
Ci	: Citrobacter
MRSA	: Methicillin Resistant Staphylococcus Aureus
CNSA	: Coagulase Negative Staphylococcus Aureus
SAU	: Surface Area of Ulcer
SI	: Secondary Intention healing
SS	: Secondary Suturing
STSG	: Split Thickness Skin Graft

Master Chart Group I (Collagen Dressing)

Sl. No.	Name	Age (Yrs)	Sex	IP No.	Duration of Diabetes Mellitus (Yrs)	MOP	DOA	DOD	Bacterial Growth	SAU	Granulation tissue fill up				Outcome	Duration to outcome (days)
											After 7 days	After 14 days	After 21 days	After 28 days		
1.	Renuka	25	F	64/2014	8	C	01/01/14	16/01/14	Sterile	12	36-65%	66-95%	-	-	SI	16
2.	Saraswati	65	F	1758/2014	2	A	18/01/14	30/01/14	SA	9	36-65%	66-95%	-	-	SI	14
3.	Krushideban	58	F	4451/14	6	U	14/02/14	26/02/14	SA	15	0-35%	36-65%	66-95%	-	SI	21
4.	Ayyappa	87	M	5883/14	22	U	01/03/14	14/04/14	SA	50	0-35%	36-65%	36-65%	66-95%	STSG	30
5.	Mallapa	45	M	6453/14	5	U	06/03/14	21/03/14	EC	8	36-65%	66-95%	-	-	SI	14
6.	Dulesab	51	M	17063/15424	2months	U	27/05/14	25/06/14	PA	60	0-35%	36-65%	66-95%	-	STSG	24
7.	Parappa	65	M	20965	12	C	17/07/14	15/08/14	KP	60	0-35%	36-65%	66-95%	-	STSG	24
8.	Sumathi Sajjanar	49	F	276265	15	U	20/08/14		Sterile	12	36-65%	66-95%	-	-	SI	16
9.	Abdul Sattar	62	M	21816	5	C	25/07/14	19/08/14	PA	18	36-65%	66-95%	-	-	SS	18
10.	Paravati	60	F	26741	3	U	07/09/14	22/09/14	Sterile	15	0-35%	36-65%	-	-	SS	14
11.	Pradeep	47	M	27615	8	U	14/09/14	22/09/14	EC	20	-	0-35%	0-35%	36-65%	SI	28
12.	Sangangouda	70	M	430/15	4	U	05/01/15	24/01/15	SA	20	0-35%	36-65%	-	-	STSG	16
13.	Shreemanth Metri	65	M	1488	2	A	14/01/15	22/01/15	Sterile	20	0-35%	36-65%	66-95%	66-95%	SI	29
14.	Kashipati M	65	M	3480	1	U	01/02/15	10/02/15	EC	15	0-35%	36-65%	36-65%	66-95%	SI	28
15.	Babusab Sheikh	85	M	49521	20	U	08/02/15		Sterile	30	0-35%	0-35%	36-65%	66-95%	SI	30
16.	Basavanthray	70	M	1612	ND	U	15/01/15	21/01/15	Sterile	30	0-35%	36-65%	66-95%	-	SI	29
17.	Channabasappa	65	M	2123	3	U	20/01/15	03/02/15	Sterile	20	0-35%	36-65%	66-95%	-	SI	26
18.	Janabai	50	F	4079	3months	U	06/02/15	16/03/15	Ci	30	0-35%	36-65%	66-95%	66-95%	SI	30
19.	Venkanna	58	M	73278	4	U	26/02/15		Sterile	6	36-65%	66-95%	-	-	SI	10
20.	Gangamma B	75	F	5632	1	U	02/02/15	20/02/15	Sterile	55	36-65%	66-95%	-	-	STSG	13
21.	Devendra P	56	M	7577	ND	A	19/02/15	24/03/15	SA	30	0-35%	36-65%	66-95%	-	STSG	27
22.	Kamalabai	35	F	7356	6	A	07/03/15	18/03/15	EC	16	0-35%	36-65%	66-95%	-	SI	18
23.	Devakamma	45	F	9791	2	NF	28/03/15	05/06/15	SA	32	0-35%	36-65%	66-95%	-	STSG	21
24.	Shanta	58	F	12247	10	A	18/04/15	25/04/15	Sterile	16	0-35%	36-65%	66-95%	-	SI	19
25.	Ramesh	70	M	128045	8	U	10/04/15		Sterile	24	0-35%	36-65%	66-95%	66-95%	SI	28
26.	Ummayya	39	F	12629	8	NF	21/04/15	03/05/15	Sterile	20	36-65%	66-95%	-	-	STSG	18
27.	Mashak	55	M	13975	4	NF	02/05/15	18/05/15	EC	16	0-35%	36-65%	66-95%	66-95%	SI	31
28.	Kashiraya	60	M	15586	5	A	16/05/15	27/05/15	SA	8	0-35%	36-65%	36-65%	66-95%	SI	30
29.	Siddappa	52	M	16040	4	U	20/05/15	22/05/15	Sterile	6	36-65%	66-95%	-	-	SI	14
30.	Shrishail	52	M	16465	2	U	24/05/15	29/05/15	Sterile	12	36-65%	66-95%	66-95%	-	SI	19

Master Chart Group II (Moist Gauge Dressing)

Sl. No.	Name	Age	Sex	IP No.	Duration of Diabetes Mellitus	MOP	DOA	DOD	Bacterial Growth	SAU	Granulation tissue fill up				Outcome	Duration to outcome (days)
											After 7 days	After 14 days	After 21 days	After 28 days		
1.	Somasing	60	M	866/2014	15	U	09/01/14	27/01/14	Sterile	12	0-35%	36-65%	66-95%	-	SS	16
2.	Akkanagamma	52	F	5244/14	1	NF	27/12/13	18/02/14	A	32	0-35%	0-35%	36-65%	66-95%	STSG	32
3.	Ansabai	50	F	2736/14	2	A	28/01/14	07/02/14	CNSA	24	0-35%	36-65%	36-65%	66-95%	SS	30
4.	Sunanda	50	F	8306/14	8	C	24/03/14	14/05/14	SA	24	0-35%	0-35%	36-65%	36-65%	SI	42
5.	Hanamanth rao	58	M	15092	8d	U	23/05/14	11/06/14	EC	15	0-35%	36-65%	36-65%	66-95%	SI	28
6.	Mahaveer	50	M	19059	4	C	30/06/14	10/08/14	KP	50	0-35%	36-65%	36-65%	66-95%	STSG	34
7.	Shankreppa	55	M	26297	2	U	03/09/14	02/10/14	Sterile	12	0-35%	36-65%	36-65%	66-95%	SI	27
8.	Mallawwa	60	F	27163	6months	C	10/09/14	08/10/14	EC	30	-	0-35%	0-35%	36-65%	SI	43
9.	Ningangouda B	60	M	213/15	6months	U	02/01/15	27/01/15	Sterile	30	-	-	-	-	SI	38
10.	Annarao J	64	M	37625	15	U	30/12/14	24/01/15	EC	20	-	0-35%	36-65%	36-65%	STSG	24
11.	Basappa Kori	62	M	4399	10	U	09/02/15	24/02/15	Sterile	6	0-35%	0-35%	36-65%	66-95%	SI	26
12.	Mahadev More	50	M	4396	8	U	09/02/15	16/02/15	Sterile	12	0-35%	0-35%	36-65%	66-95%	SI	26
13.	Shrimath	52	M	3425	ND	NF	31/01/15	22/02/15	Sterile	16	0-35%	0-35%	36-65%	66-95%	SI	29
14.	Tammanna	65	M	4746	2	U	12/02/15	07/04/14	A	30	-	0-35%	36-65%	36-65%	STSG	40
15.	Shenkreppa	56	M	5541	5	U	19/02/15	03/03/15	Sterile	6	0-35%	36-65%	66-95%	-	SI	24
16.	SubhashP	50	M	84935	2	U	07/03/15		Sterile	12	0-35%	0-35%	36-65%	66-95%	SI	28
17.	Dareppa	60	M	5175	2	U	16/02/15	12/03/15	EC	12	0-35%	0-35%	36-65%	36-65%	SI	32
18.	Shamrao	82	M	6575	ND	C	28/02/15	04/04/15	MRSA	40	0-35%	0-35%	36-65%	36-65%	STSG	29
19.	Shantappa	77	M	10816	2	C	06/04/15	02/06/15	KP	50	-	0-35%	0-35%	36-65%	SI	40
20.	Shrishail	52	M	13178	ND	NF	25/04/15	08/05/15	Sterile	24	0-35%	0-35%	36-65%	36-65%	SI	40
21.	Gangabai	70	F	147795	12	U	25/04/15		Sterile	12	0-35%	0-35%	36-65%	66-95%	SI	28
22.	Irappa	55	M	12128	2	NF	17/04/15	25/05/15	CNSA	30	0-35%	0-35%	0-35%	36-65%	SI	45
23.	Gurangouda	80	M	14952	20	U	11/05/15	13/06/15	Sterile	20	0-35%	0-35%	36-65%	66-95%	STSG	30
24.	Yallawwa	61	F	14287	2	U	05/05/15	08/06/15	Sterile	12	0-35%	0-35%	36-65%	-	SS	24
25.	Iqbal	60	M	15001	2	NF	12/05/15	22/06/15	A	24	-	-	-	0-35%	SI	48
26.	Jubeda	35	F	15483	1	NF	15/05/15	03/06/15	Sterile	16	-	-	0-35%	0-35%	SI	42
27.	Afighussain	40	M	16140	2	U	25/05/15	08/06/15	SA	12	0-35%	36-65%	-	-	SS	13
28.	Ashok	50	M	19720	ND	A	21/06/15	02/07/15	Sterile	12	0-35%	0-35%	36-65%	36-65%	SI	35
29.	DrSahebgouda	75	M	19574	10	NF	20/06/15	02/07/15	E	24	0-35%	0-35%	36-65%	36-65%	STSG	35
30.	Laxmi U	60	F	20350	12	U	26/06/15	03/07/15	Sterile	06	0-35%	0-35%	36-65%	36-65%	SI	29