A STUDY TO COMPARE THE EFFECTS OF HONEY AND SALINE DRESSING IN THE WOUND HEALING OF CHRONIC FOOT ULCERS

Dissertation submitted for

M.S. DEGREE (Branch I) in General Surgery

April - 2015

The Tamil Nadu Dr. M.G.R. Medical University

Chennai – 600 032.

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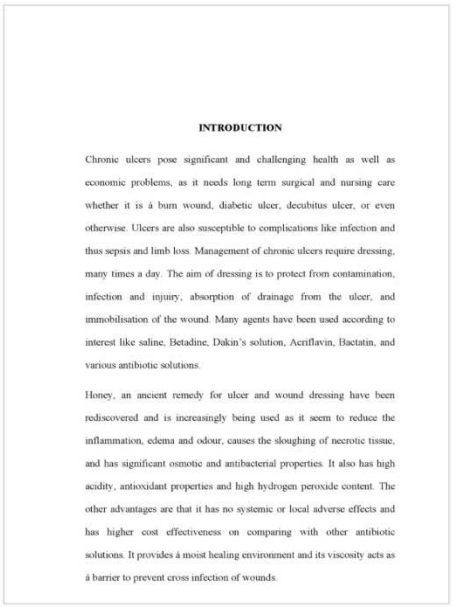
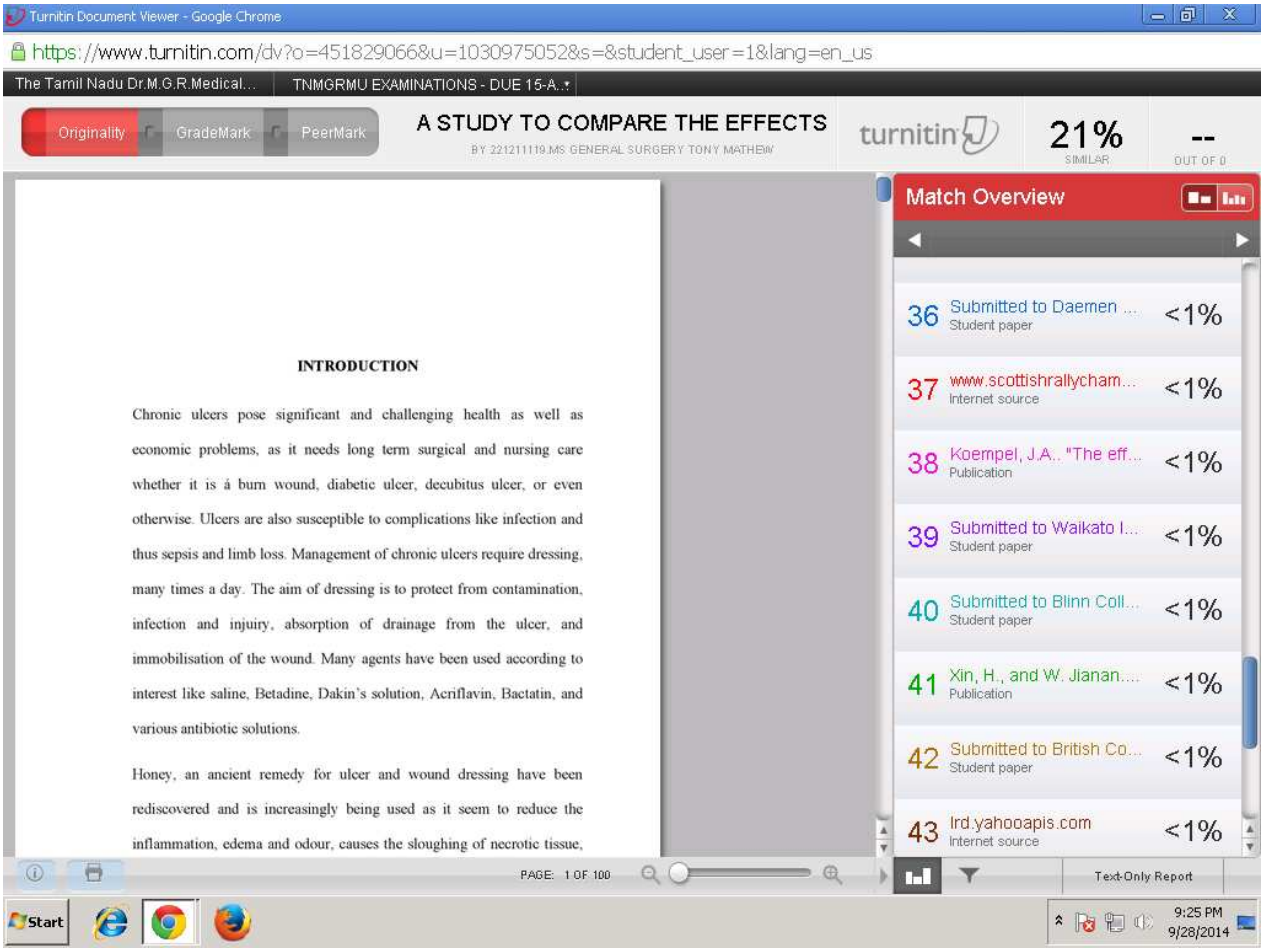


INTRODUCTION

Chronic ulcers pose significant and challenging health as well as economic problems, as it needs long term surgical and nursing care whether it is â burn wound, diabetic ulcer, decubitus ulcer, or even otherwise. Ulcers are also susceptible to complications like infection and thus sepsis and limb loss. Management of chronic ulcers require dressing, many times a day. The aim of dressing is to protect from contamination, infection and injuiry, absorption of drainage from the ulcer, and immobilisation of the wound. Many agents have been used according to interest like saline, Betadine, Dakin's solution, Acriflavin, Bactatin, and various antibiotic solutions.

Honey, an ancient remedy for ulcer and wound dressing have been rediscovered and is increasingly being used as it seem to reduce the inflammation, edema and odour, causes the sloughing of necrotic tissue, and has significant osmotic and antibacterial properties. It also has high acidity, antioxidant properties and high hydrogen peroxide content. The other advantages are that it has no systemic or local adverse effects and has higher cost effectiveness on comparing with other antibiotic solutions. It provides â moist healing environment and its viscosity acts as â barrier to prevent cross infection of wounds.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The Ethics Committee meeting of the Madurai Medical College, Madurai was held on 22nd July 2014 at 10.00 Am to 12.00 Noon at Anaesthesia Seminar Hall at Govt. Rajaji Hospital, Madurai . The following members of the Ethics Committee have attended the meeting.

1.Dr.V.Nagarajan,M.D.,D.M(Neuro) Ph: 0452-2629629 Cell No.9843052029 nag9999@gmail.com.	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2.Dr.Mohan Prasad, MS.M.Ch. Cell.No.9843050822 (Oncology) drbkcmp@gmail.com	Professor & H.O.D of Surgical Oncology (Retired) D.No.32, West Avani Moola Street, Madurai.-1	Member Secretary
3. Dr.L.Santhanalakshmi, MD (Physiology) Cell No.9842593412 dr.l.santhanalakshmi@gmail.com.	Vice Principal, Prof. & H.O.D. Institute of Physiology Madurai Medical College	Member
4.Dr.K.Parameswari, MD(Pharmacology) Cell No.9994026056 drparameswari@yahoo.com.	Director of Pharmacology Madurai Medical College.	Member
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6.Dr.A.Sankaramahalingam, MS., (Gen. Surgery) Cell.No.9443367312 chandrahospitalmdu@gmail.com	Professor & H.O.D. Surgery Madurai Medical College.	Member
7.Mrs.Mercy Immaculate Rubalatha, M.A., Med., Cell.No.9367792650 lathadevadoss86@gmail.com	50/5, Corporation Officer's Quarters, Gandhi Museum Road, Thamukam, Madurai-20.	Member
8.Thiru.Pala.Ramasamy, B.A.,B.L., Cell.No.9842165127 palaramasamy2011@gmail.com	Advocate, D.No.72,Palam Station Road, Sellur, Madurai-20.	Member
9.Thiru.P.K.M.Chelliah, B.A., Cell No.9894349599 pkmandco@gmail.com	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20.	Member

The following project was approved by the committee

Name of the PG Student	Course	Name of the Project	Remarks
Dr.Tony Mathew drmathewtony@gmail.com	PG in MS., (General Surgery) Madurai Medical college & Govt. Rajaji Hospital, Madurai	A study to compare the effects of Honey and Saline dressing in wound healing of chronic foot ulcers.	Approved Indemnity Bond to be obtained from lawyer and shown to the committee

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.
2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance.
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4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

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Ethical Committee

Chairman
Ethical committee

31.7.14
DEAN/Convenor
Madurai Medical College & Govt.
Rajaji Hospital, Madurai.

To
The above Applicant
-thro. Head of the Department concerned

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INDEMNITY BOND

THIS DEED OF INDEMNITY made and executed at ..MADURAI..... an ...05.....on day of August 2014.

By

Mr.Tony Mathew son of Mr. M.P.Mathew, Roman Catholic, aged about 29 years, residing at Madathiparambil, Kanattupara, Pala Taluk in Kottayam District and now doing M.S., General surgery in Govt. Medical College, Madurai. Tamilnadu (hereinafter called as party of FIRST PART/ INDEMNIFIER which expression shall unless it be repugnant to the context be deemed to include his heirs, executors and administrators)

INFAVOUR OF

Dean and Ethical Committee , Govt. Rajaji Hospital , Madurai (hereinafter called as party of SECOND PART which expression shall unless it be repugnant to the context be deemed to include its assigness, executors and administrators)

WHEREAS the party of the FIRST part is doing research in " Comparison of the Efficacy of Honey and Saline Dressing in Healing of Chronic Foot Ulcer" as the part of M.S., General Surgery in Govt.Rajaji Hospital at Madurai.

WHEREAS, during the course of research, the party of the FIRST part, has to take trial with the inpatient of the party of the SECOND part.....

.....

Under these circumstances the party of the first part has executed this indemnity with abundant caution for the protection and to indemnify the party of second part.

WHEREAS the party of the first part, shall at all times hereinafter remain liable for and shall fully and effectually indemnify and keep indemnify the party of the second part, its executors, administrators and assigns against all loss and damage, costs, charges and expenses which the in - patients of the second part may put to or reasonably incur or suffer by reason of any future claim by the party of first part in carrying out the research work with the inpatients of the SECOND part.

In witness thereof, the party of first part has signed this 05.. th day of August 2014 at Madurai mentioned above, in presence of the under mentioned witnesses.

(Dr. TONY MATHEW)

Party of FIRST part

Party of SECOND Part

Secretary,
Ethical committee

5.8.14

Witnesses :

1. N. Aravind
ARAVIND
5/732 KABILAR ST
SATHASIVA NAGAR
MADURAI - 20

BONAFIDE CERTIFICATE
FROM THE DEAN

This is to certify that this dissertation entitled **"A STUDY TO COMPARE THE EFFECTS OF HONEY AND SALINE DRESSING IN THE WOUND HEALING OF CHRONIC FOOT ULCERS"** is the Bonafide Work of **Dr. TONY MATHEW,** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.S Degree (Branch I) General Surgery** examination to be held in **April 2015.**

Captain Dr. B. SANTHAKUMAR,
M.Sc. (F.Sc) , M.D (FM)., PGDMLE., Dip.N.B (FM)
THE DEAN
Madurai Medical College & Government Rajaji Hospital,
Madurai.

BONAFIDE CERTIFICATE
FROM THE HOD

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Dr.A.SANKARAMAHALINGAM, M.S.

Professor and HOD,
Department Of General Surgery,
Government Rajaji Hospital,
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Madurai.

BONAFIDE CERTIFICATE
FROM THE GUIDE

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Dr. S. SELVACHIDAMBARAM, M.S
Professor of Surgery,
Department Of General Surgery,
Government Rajaji Hospital,
Madurai Medical College,
Madurai.

DECLARATION
BY THE CANDIDATE

I, **Dr. TONY MATHEW,** hereby solemnly declare that this Dissertation entitled **"A STUDY TO COMPARE THE EFFECTS OF HONEY AND SALINE DRESSING IN THE WOUND HEALING OF CHRONIC FOOT ULCERS"** is a Bonafide and Genuine Research Work carried out by me.

This is submitted to The Tamil Nadu Dr M.G.R Medical University, Chennai, in partial fulfillment of the regulations for the Award of **MS Degree (Branch I) in General Surgery**.

Place : Madurai

Date : 29.09.2014 **Dr. TONY MATHEW**

ACKNOWLEDGEMENT

It is my honor and privilege to thank Prof. **Dr. S. SELVACHIDAMBARAM**, M.S., Professor of General Surgery, who helped me in choosing the subject, for this study and guided me at every stage. His valuable suggestions and timely advice were of immense help to me throughout all phases of this study.

I express my gratitude towards **Dr. A. SANKARAMAHALINGAM,** M.S., Head of the Department of General Surgery, Madurai medical College, Madurai, for his valuable suggestions and guidance.

I thank Dr. K.G. Subangi, M.S., DGO., Dr. Muniasamy, M.S., Dr. A. Jagadish Singh, M.S., Dr. A.N. Gurumoorthy, M.S, for their encouragement and guidance.

I am very thankful to my colleagues who helped me in preparing this Dissertation.

My 'Sincere Thanks' to all the patients, without whose co-operation this study would have not been possible and last but not the least, I wish to express my gratitude to my family & friends also, without them, this study would have not been possible.

Date: 29-09-2014

Place: Madurai

Dr. TONY MATHEW

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INTRODUCTION

Chronic Ulcers pose significant and challenging health as well as economic problems, as it needs long term surgical and nursing care whether it is á Burn wound, Diabetic ulcer, Decubitus ulcer, or even otherwise. Ulcers are also susceptible to complications like infection and thus sepsis and limb loss. Management of chronic ulcers require dressing, many times a day. The aim of dressing is to protect from contamination, infection and injury, absorption of drainage from the ulcer, and immobilization of the wound. Many agents have been used according to interest like saline, Betadine, Dakin's Solution, Acriflavin, Bactatin and various antibiotic solutions.

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The other advantages are that it has no systemic or local adverse effects and has higher cost effectiveness on comparing with other antibiotic solutions. It provides á moist healing environment and its viscosity acts as á barrier to prevent cross infection of wounds.

The study aims at comparing the effects of commonly used saline dressing and honey dressing in chronic foot ulcers, in patients who are in the surgical wards of Government Rajaji Hospital, Madurai.

AIMS AND

OBJECTIVES

To study “The Efficacy of Application of Honey Dressing in the management of Chronic Foot Ulcers”.

Comparison of the results over the conventional method of Saline Dressing.

REVIEW OF LITERATURE

HISTORY

The most ancient methods of management of chronic wounds were first developed in Egypt. They were crude methods. Skin of frog, animal grease were used to cover raw area. In India, Susrutha was said to have used skin grafts. Jeter used spider-web. Pasteur found out that for wound to heal properly it must be kept covered and dehydrated at all times and the coverings must be changed at regular intervals.

Lumiere was a French Researcher who used cotton gauze soaked in liquid paraffin. He found out that dressing of wounds in this method prevented the stickage of dressing to the wound and helped better wound healing and caused less pain to the patient while dressing were changed. Alginate dressings have been available, since 1984, although the benefits of seaweed have been known for centuries, when it was known as the 'Mariner's Cure'[3]

About 400y B.C. Hippocrates said, “in case of ulcer, it is not expedient to stand” specifically whenever ulcer is situated on the lower limbs”. The Management of any foot ulcer needs multi-disciplinary approach. The standard therapy of Foot Ulcers includes systemic control of diabetic mellitus, infection and local control by debridement, pressure relief and protective dressing[4].

Topical treatment of wounds in an important aspect of wound care, although secondary to surgical and systemic care. Dressing materials come in many forms to suit wound types and preferences. No hard evidence exists to place any one approach above another. All wounds deserve individualized attention and care plans.

Likewise, a plethora of solutions exist to augment dressing materials in cleansing, antibiosis, and debridement. Traditional agents, including Hydrogen Peroxide, Dakin’s solution and Povidone - Iodine, are more tissue toxic than their common usage would indicate[5].

HONEY IN DRESSING

Honey a complex mixture containing mainly Glucose and Fructose was used by ancient Egyptian. Hippocrates, father of modern medicine,

also recommended the use of ‘honey’ as an ointment. Recent years have seen a revival of interest in the use of sugar, sucrose as a dressing material. Honey has an excellent “trace record” over 4000 years of usage as a wound dressing.

In recent times it has been “rediscovered” with various report of clinical studies, care reports and randomized controlled trials showing it takes alongside modern dressing intervals in its effectiveness in managing wounds and has a potent antibacterial activity and it also has a debriding effect anti-inflammatory activities and a stimulatory effect on granulation and epithelialisation.[6]

Compared to the conventional Normal saline dressing for diabetic foot ulcer, so many research studies have shown the effectiveness of honey dressing among diabetic foot ulcer patient. Therefore this motivated the researcher to select this statement.

Honey was investigated and used as a surface agent in treating a variety of conditions for the past 3000 years. The chemical explanation for its variety of properties, have come out only in the near past. It has a wide range of antisepsis and microbicidal properties which are proved by randomized controlled trials.

Study by Moore implied that there is definite biological advantage in using Honey for the treatment of superficial burns but people are less confident in using Honey for this purpose .

In year 2004, Peter Nolan a professor from NewZealand who worked in Honey Reseach Unit at the University of Waikatto, found out in his study that MRSA infections can be treated with honey. Honey has high osmolarity and Hydrogen peroxide activity.

It dehydrates the micro organisms and kill them. It is a saturated mixture made from two different mono-saccharides. It has glucose oxidase enzyme, which produces Hydrogen peroxide. Its concentration in honey is 1mmol/litre. commercially available. Hydrogen peroxide has around 3 percent content.

Most of the glucose in honey is utilized by bacteria rather than the usual amino-acids . The substitution of glucose instead of amino-acids for use by bacteria is responsible for the deodourising action of honey. Honey rapidly deodourises heavily contaminated wounds.

The other properties of honey are :

- Ph of honey ranges between 3.2 to 4.5-Acidic
- Honey contains Inhibins - Hydrogen Peroxide, Phenolic Acid and Flavanoid
- Reduce the swelling and scarring of tissues
- Antiinflammatory action

ANATOMY OF

FOOT[12]

The human foot combines mechanical complexity and structural strength. The ankle serves as foundation, shock absorber and propulsion engine. The foot can sustain enormous pressure (several tons over, the course of a one-mile run) and provides flexibility and resilience.

THE FOOT AND ANKLE CONTAIN[12]

- 26 Bones (one-quarter of the bones in the human body);
- 33 Joints;
- More than 100 muscles, Tendons and Ligaments.
- A network of blood vessels, nerves, skin and soft tissue.

These components work together to provide the body with support, balance and mobility. A structural flaw or malfunction in any one part can result in the development of problems elsewhere in the body.

SKIN OF THE FOOT.[13]

The skin of dorsum of the foot (hirsute) is thin and highly flexible, containing hair follicles, sweat glands and scanty sebaceous gland. Hairs are sparse and thick. It is less then 2mm thick and few fibrous septa penetrate to deeper facial structures. The plantar skin (glabrous) is 5mm thick especially over those points which bear weight viz., heel, ball of big toe and lateral margins of the sole.

It has no hair follicles or sebaceous glands but sweat glands are numerous.

Hypodermis is composed of loose areolar connective tissue, most of this collagenous and elastic fibers running parallel to the surface of the skin but some are continuous with the fibers of dermis. Hypodermis is well supplied with blood vessels and nerve endings. Tactile sensation is exceptionally good in the sole.

The subcutaneous tissue in the sole as in the palm differs from that of the rest of body in being more fibrous, tough and stingy. Fibrous septa divide the tissue into small loculi which are filled with fluid fat under

tension. This makes a shock absorbing pad especially over the heel and over the tips of toes.

Deep fascia: On the dorsum of the foot *(fascia dorsalis pedis)* is the thin layer continuous above with the inferior extensor retinaculum and at the sides of the foot; it blends with plantar aponeurosis, anteriorly it ensheathes the dorsal tendons.

Plantar aponeurosis: Cover the whole length of the sole. It arises posteriorly from the medial and lateral tubercles of the calcaneous and from the back of that bone below the insertion of the tendo-calcaneous. It spreads out over the sole and is inserted by five slips into each of the five toes. A very dense and strong intermediate part is known as plantar aponeurosis.

PARTS OF THE FOOT

Structurally, the foot has three main parts:

i) The Fore Foot

ii) The Mid-Foot

iii) The Hind Foot

The fore-foot: It is composed of the five toes called ‘phalanges’ and their connecting long bones (metatarsals). Each toe (phalanx) is made up of several small bones. The big toe (hallux) has two phalanges, two joints (inter-phalangeal joints) and two tiny, round sesamoid bones that enable it to move up and down. The other four toes each have three bones and two joints. The phalanges are connected to the metatarsals by five metatarsal phalangeal joints at the ball of the foot. The forefoot bears half the body’s weight and balances pressure on the ball of the foot.

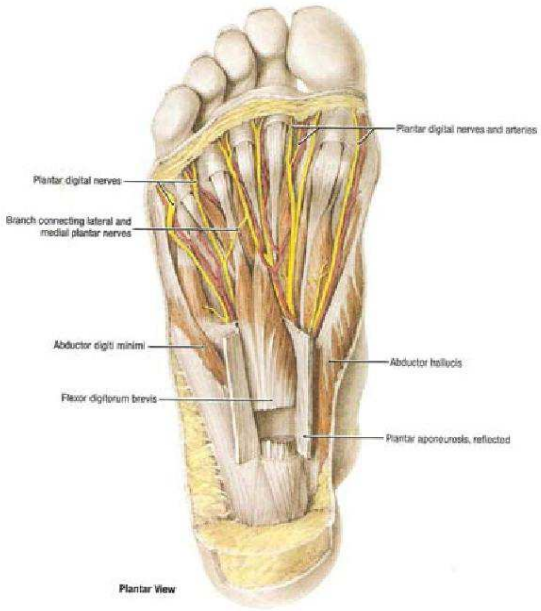
The Mid-Foot: It forms the font’s arch, and serves as a shock absorber. The bones of the mid-foot are cuboid, first, second, third cuneiform and navicular, connected to the fore foot and the hind foot by muscles and the plantar fascia.

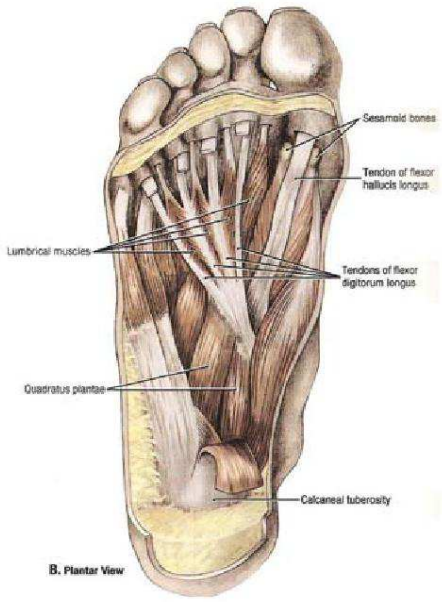
The hind foot: It is composed of three joints and links the mid-foot to the ankle (talus). The top of the talus is connected to the two long bones of the lower leg (tibia and fibula. forming a hinge that allows the foot to move up and down. The heel bone (calcaneus) is the largest bone in the foot. It joins the talus to form the sub-talar joint, which enables the foot to rotate at the ankle. The bottom of the heel bone is cushioned by a layer of fat.

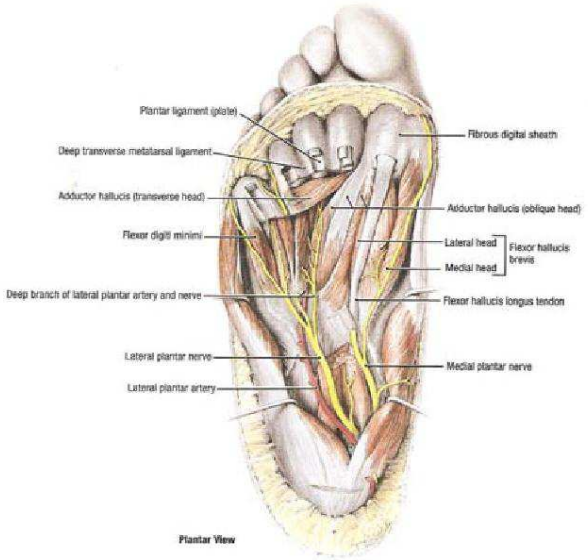
The Arches: The foot has three arches. The medial longitudinal arch is composed of the calcaneus, talus, navicular cuneiforms and the first three metatarsals. The lateral longitudinal arch is composed of the cuneiforms, cuboid and the fourth and fifth metatarsals. The transverse arch is composed of the cuneiforms the cuboid and the five metatarsal bases. The arches of the foot are maintained not only by the shapes of the bones as well as by ligaments; in addition, muscles and tendons play an important role in supporting the arches.

Muscles, Tendons, and Ligaments: There are 20 muscles in the foot that give the foot its shape by holding the bones in position and expand and contract to impart movement. The muscles in the sole of the foot are categorized into four layers: Muscles in the first layer include Flexor digitorum brevis, Abductor hallucis and Abductor digiti minimi. In the second layer are tendon of Flexor hallucis longus, Flexor digitorum accessorius and the Lumbricals. In the third layer are Flexor hallucis brevis, Adductor hallucis and Flexor digiti minimi brevis. In the fourth layer are peroneous longus tendon, Tendon of the tibialis posterior, 4 dorsal interossei and 3 plantar interossei.

FIGURE-1:
MUSCLES OF THE 4 LAYERS OF THE FOOT







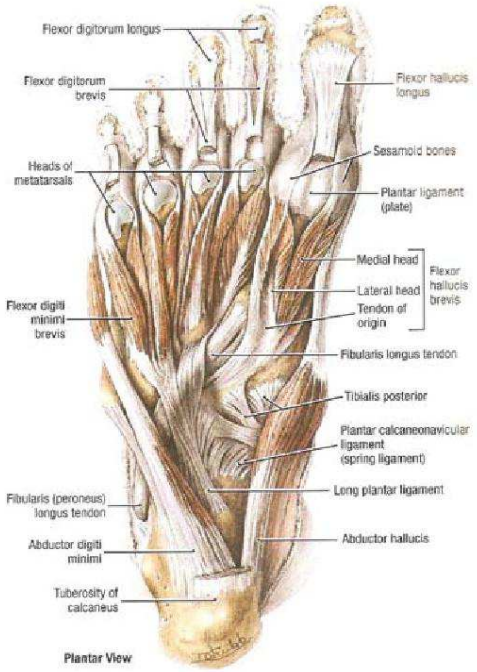


FIGURE-2:
ARTERIES OF THE SOLE OF FOOT

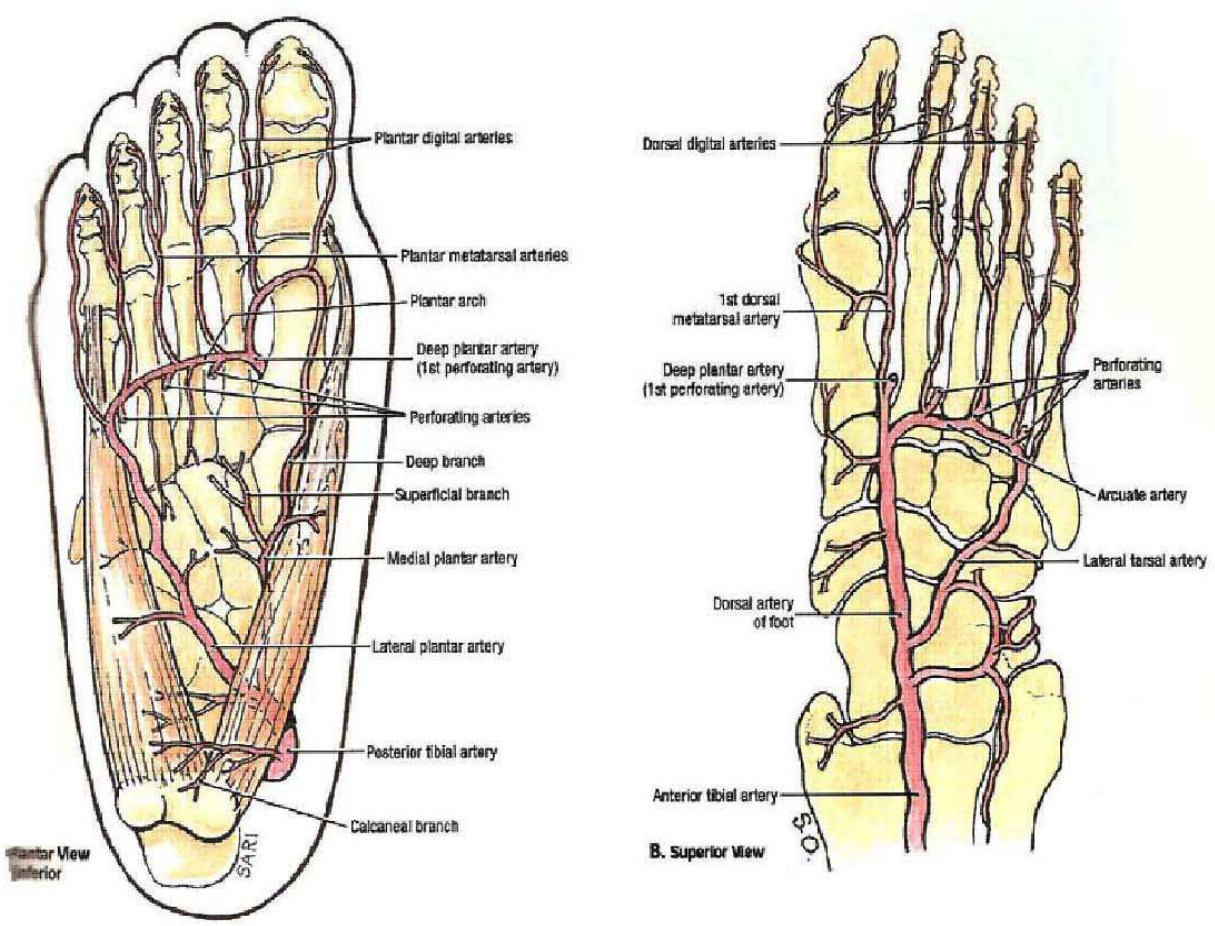
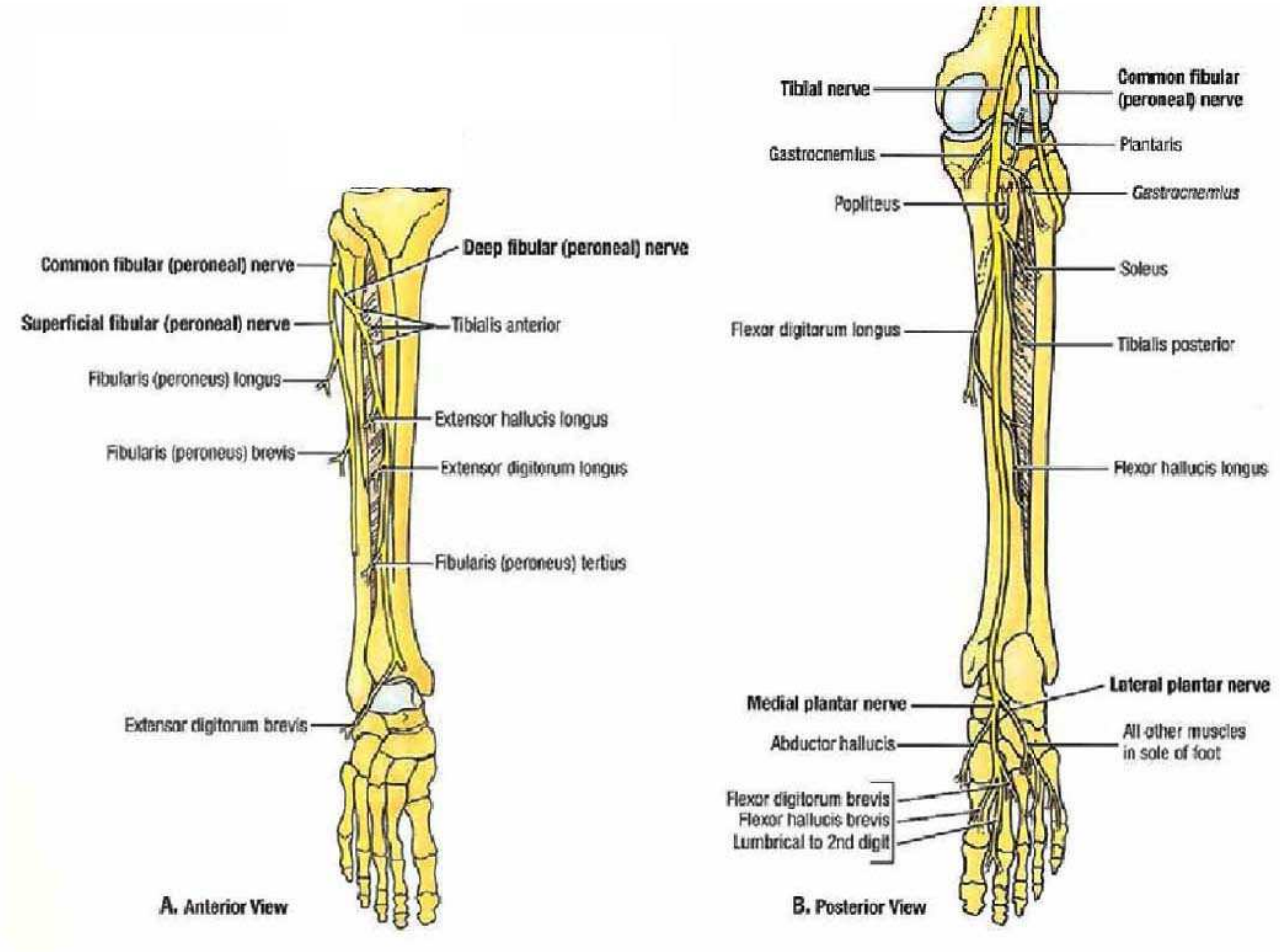


FIGURE-3:
NERVES OF THE FOOT



SKIN[14,15]

Skin is comprised of three layers :

i. The Epidermis (or) Outermost layer,

ii. The Dermis, and

iii. The Sub-cutaneous tissue.

Each Strata plays a critical role.

THE EPIDERMIS

This is the most superficial layer of the skin and is only few millimetre thick. It consists of 3 types of cells and each one described in brief below :

1. **Keratinocyte Cells**

This is the most outermost and protective part of the skin. It originates in the base of epidermis and gradually migrates up, and mixes with the sebum and eventually shed off.

2. **Melanocytes**

These cells produce melanin, the colouring pigment of the skin. This counts to about each one for around 40 keratinocytes.

3. **Langerhans Cells**

These are modified macrophages in the skin and these do the antigen presentation. These cells play key role in the dermal immunity.

DERMIS[15]

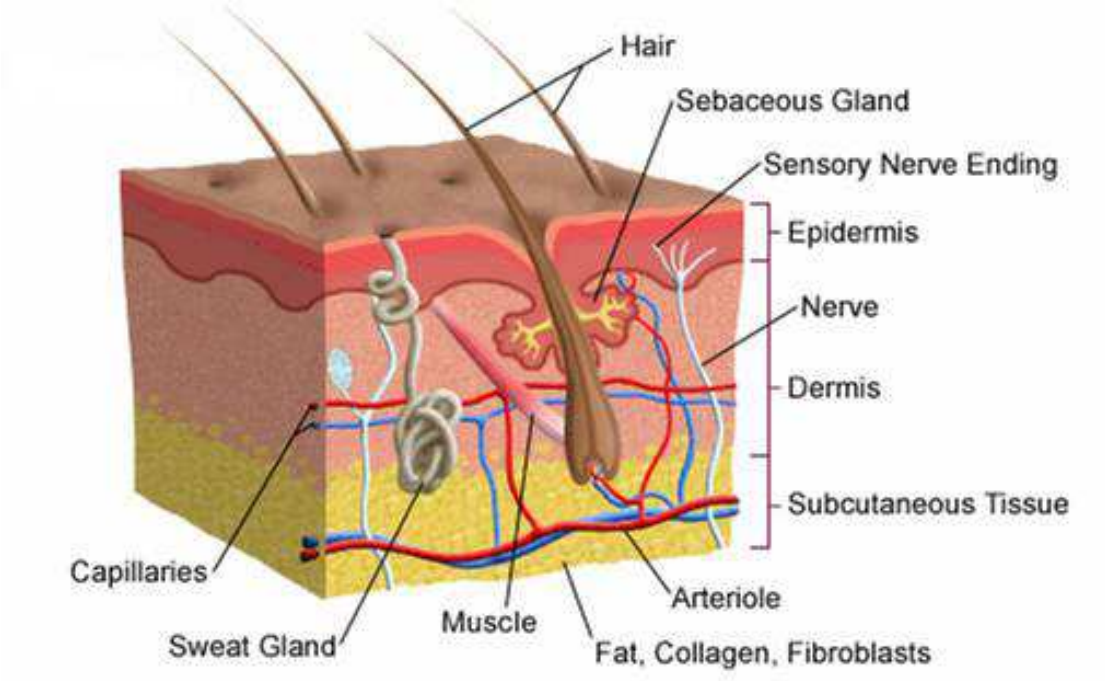
It lies inner to the epidermis and is the thickest layer. It contains collagen fibres, elastin, fibroblast and give the skin its tensile strength and toughness. It also has sebaceous glands. It has langerhans cells and lymphatic and capillary channels which form the channel for lymph glands. With the help of secreted sebum, the skin remains moist.

Subcutaneous Tissue:

- Adipocyte fat cells, the primary component of subcutaneous tissue, provides warmth, insulation.
- Sweat glands which are important in temperature regulation reside here.

- A system of tiny muscles connected to our hair follicles.
- Cutaneous vessels ultimately arise from underlying named source vessels. These form channels and connect to the deeper vessels which underlie.

FIGURE-4:
THE SKIN



FUNCTIONS OF SKIN

The skin has four major functions:

1. Protection
2. Sensation
3. Thermoregulation and
4. Metabolic Functions

1. Protection : It acts as physical barrier to invasion by microbes, protects from thermal, mechanical and mild radiation injuiry. Acts as the covering for the organs and muscles inside.

2. **Sensation :** The largest sense organ of the body , has receptors for pain, temperature, touch and pressure.

3. **Thermoregulation** : With the help of auto-regulation in the cutaneous network of blood vessels, underlying adipose tissue, it controls heat regulation

4. **Metabolic functions :** Subcutaneous adipose tissue constitutes a major store of energy, mainly in the form of triglycerides.

Vitamin D is synthesized in the epidermis and supplements that derived from dietary sources.

HEALING OF WOUNDS

In wound healing, the process involves stabilisation of the wound both structurally and functionally. The primary objectives in wound healing are :

1. Restore all barriers to control loss of fluid and entry of infection from outside.
2. Mechanical integrity must be maintained.
3. Normal blood flow and lymphatic flow to the injured tissues must be re-established in order for the tissue to survive**.**

Regeneration in its true sense is the ideal process of wound healing but it is theoretically applicable only during development of embryo. It is however found in cases of some lower level organisms such as salamander. It is also found in tissues such as bone and liver. These tissues are capable of regeneration. In adult human species the precision of wound healing is found to be compromised for the speed in repairing the tissues.

All tissues proceed through the same series of events, and for ease of understanding, these are divided into specific stages. However, these phases overlap in both time and activity.

Every wound go through the similar basic steps of tissue repair. There are however differences in the healing between acute wounds and chronic wounds. Acute wound heal in á more proper, orderly way and within á short-time. Chronic wounds are more difficult to treat because it will be stuck in an inflammatory phase and does not immediately give way to spontaneous closure. Wound closures are classified into primary, secondary and tertiary types of healing.

HEALING BY FIRST INTENTION

(PRIMARY HEALING)

It involves clean wounds. They heal by first intention. They involve mainly clean, Uninfected surgical wounds, Graft wounds, Flap cover, Simply sutured clean wounds.

SECONDARY (SPONTANEOUS.)

It includes contaminated wounds. It heals by re-epithelialisation and wound contraction. There is no active mechanism like primary healing.

HEALING BY TERTIARY INTENTION

(DELAYED PRIMARY CLOSURE)

In tertiary intention healing, the wound is initially contaminated. It is stabilised by regular dressings and slough excision. Once the wound is fit for closure and free from slough, it is sutured or skin grafting or flap cover is done .

PHASES OF WOUND HEALING

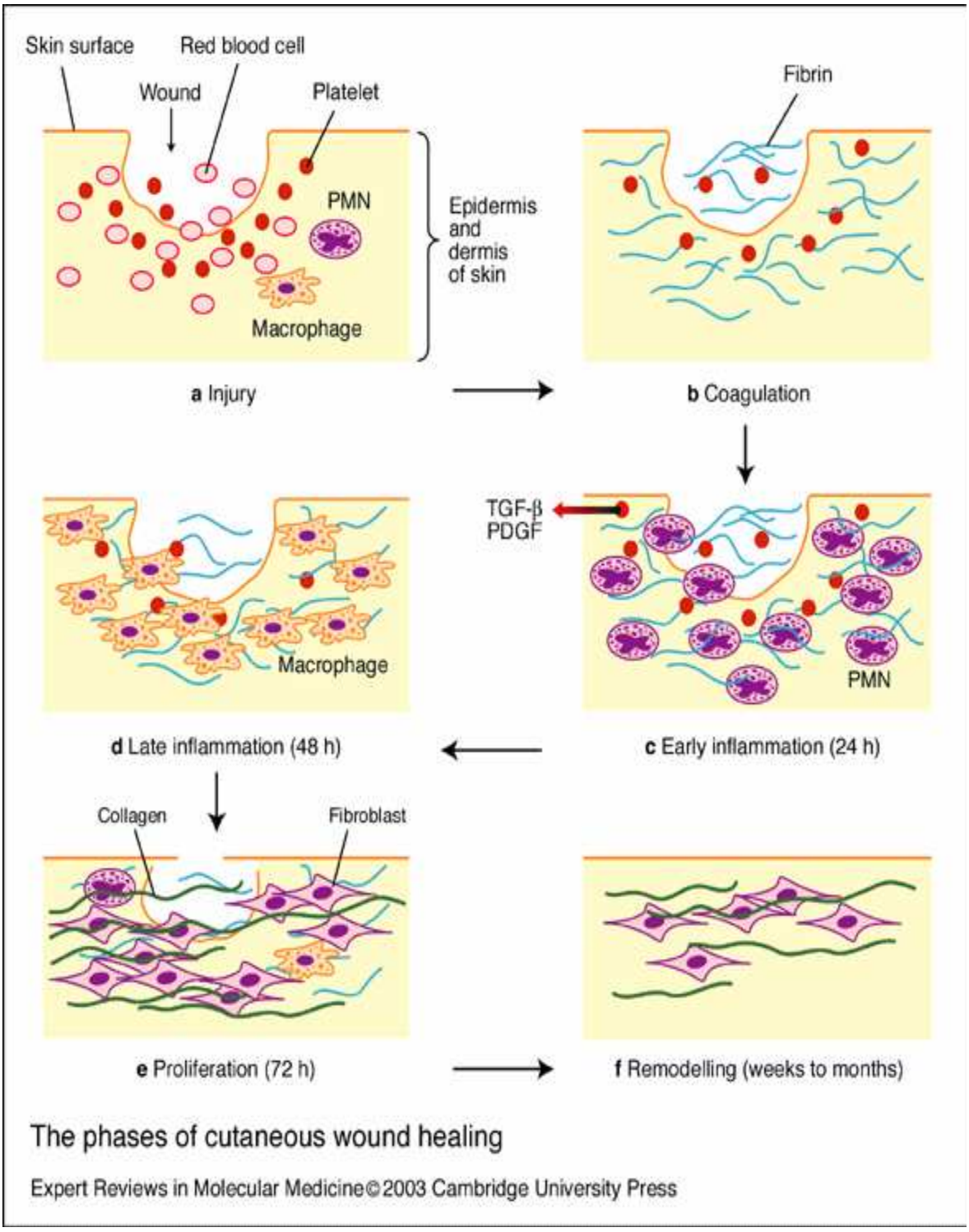
The immediate response to injury is the **inflammatory** (also called reactive) phase. The body's defenses are aimed at limiting the amount of damage and preventing further injury. The **proliferative** (also called regenerative or reparative) phase is the reparative process with re- epithelialisation, matrix synthesis, and neo vascularisation to relieve the ischemia of the trauma itself. The final **maturational** (or remodeling) phase is the period of scar contraction with collagen cross-linking, shrinking, and a loss of edema[18]. The stages are detailed below,

1. **HEMOSTASIS AND INFLAMMATION**

Following injury to tissue, endothelium is damaged and sub-endothelial collagen is exposed. Platelets come in to contact and they undergo aggregation. Coagulation Cascade is then activated. There will be initially reflex vasoconstriction at first. This is followed by vasodilatation.

This increases the permeability of vessels. Then hemorrhage is controlled when the platelets along with the erythrocytes plug up the capillaries Type 4 and type 5 collagen activates the platelets.

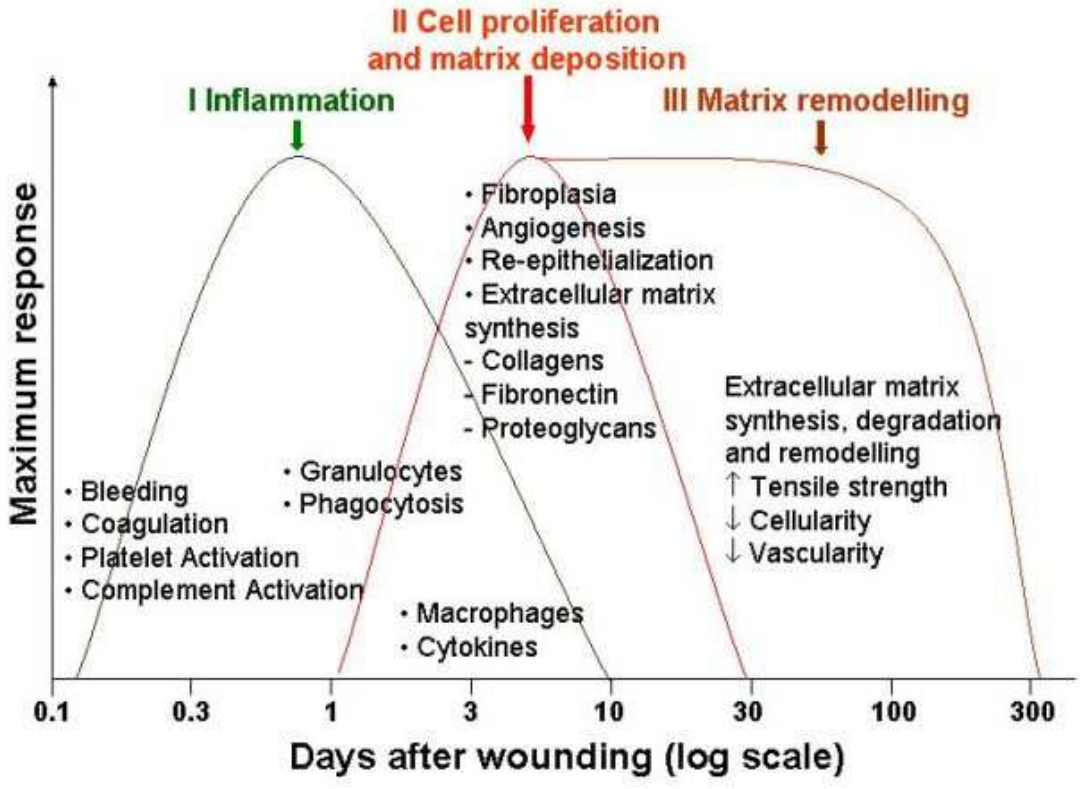
FIGURE-5:
STAGES IN WOUND HEALING



Platelet granules are storage organelles which contain Platelet Derived Growth Factor (PDGF), Transforming Growth Factor (TGF-ß), Insulin-like Growth Factor IGF-1, Fibronectins, Fibrinogen, Thrombospondin, and VonWillibrand factor.

Mast cells are responsible for endothelial permeability. They cause the Plasma leakage. The mediators involved in this process are histamines along with serotonins.

FIGURE-6:
STAGES OF WOUND HEALING WITH THEIR DURATION



The fibrin strands trap red blood-cells, leading to formation of the clot and sealing of wound. Lattice framework which results will be the frame for endothelial cells, inflammatory cells, and fibroblasts. Traction at the leading edge of the cell develops through binding of the integrin followed by translocation of the cell over the adherent segment of the plasma membrane.

Migration of neutrophils into wound site will functionally activate many events such as expression of antigen on the surface of the cell, potentiate cytotoxicity, release and aggregate the cytokines production. Activated polymorphs feed on dead debris, bacterias and foreign body

2. **PROLIFERATIVE PHASE**

On resolution of the acute events in inflammatory response the framework for repair of the wound is laid down. The three stages are angiogenesis followed by Fibroplasia and finally Epithelialisation occurs. It is featured by granulation tissue formation. It involves capillary and fibroblast proliferation. Collagen is loosely laid down on the matrix. It also includes Hyaluronic acid and Fibronectin formation.

A. STAGE OF ANGIOGENESIS

After occurance of injury, the basement membranes of venules are acted upon by activated cells. Gaps occur between these cells through which other cells migrate. This result in formation of new tubules and formation of new vessels (Angiogenesis) takes place Those interactions will result in the up regulation of the expression of cell surface adhesion molecules, like vascular cell surface adhesion molecule VCAM-1. Matrix-degrading enzymes, such as plasmin and the metalloproteinase, are released and will be activated.

Some of the new capillaries differentiate into arterioles and venules, but the others will undergo involution along with apoptosis, and finally ingested by macrophages.

B. STAGE OF FIBROPLASIA

Fibroblasts are specialized cells that gets differentiated from resting mesenchymal cells in connective tissue; they do not arrive in the wound cleft by diapedesis from circulating cells. After injury, the normally quiescent and sparse fibroblasts are chemoattracted to the inflammatory site, where they divide and produce the components of the ECM.

After stimulation by macrophage and Platelet Derived Cytokines and growth factors, the fibroblast, which is normally arrested in the G0 phase, undergoes replication and proliferation. Platelet derived TGF-ß stimulates fibroblast proliferation indirectly, by releasing PDGF.

C. STAGE OF EPITHELIALISATION

The re-epithelialisation of acute wounds begin within just hours after occurence of the insult. At first the wound is sealed by clot formation. Then epithelial cells begin to move across the gap. Kerationocytes from the undamaged epithelium begins to migrate over to the surface of the injured area. Epithelialisation occurs in the wound by,

- Detachment of the Keratinocytes
- Migration
- Proliferation
- Differentiation
- Stratification

Intactness of the basement membrane is an accelerating factor for Epithelialisation

D. EXTRACELLULAR MATRIX FORMATION

The next stage is formation of extracellular matrix. It is composed of complex interaction with

- Fibrin
- Fibronectin
- Fibrinogen
- Vitronectin
- Glucosaminoglycans
- Proteoglycans

E. COLLAGEN SYNTHESIS

Collagens, which are the predominant scar proteins, are the end result. Attachment proteins, such as fibrin and fibronectin, provide linkage to the ECM through binding to cell surface integrin receptors. Stimulation of fibroblasts by growth factors induces the upregulated expression of the integrin receptors, facilitating cell-matrix interactions

After secretion into the ECM, specific proteases cleave the propeptides of the procollagen molecules, forming collagen monomers. These monomers assemble to form collagen fibrils in the ECM, driven by

collagen’s tendency to self-assemble. Covalent cross-linking of the lysine residues provides tensile strength.

F. DEGRADATION OF THE ECM

Proteolysis is tightly regulated. Many are secreted as inactive precursors that are activated when required. In addition, cell surface receptors bind these proteases, ensuring that these enzymes act only on sites where they are needed. Finally, protease inhibitors, such as the tissue inhibitors of metalloproteinase (TIMP), can bind these enzymes and block their activity.

3. PHASE OF MATURATION

It involves contraction of the wound. It involves the in-drawing of the whole of the surrounding skin .Thus the scar area is reduced in size. Extensive contraction of the wound will result in wound contracture. wound contracture will limit the physical movement across the contracted skin. It will result in functional impairment across the area. Examples are joint contracture causing limitation of movement across the joint. Eye-lid

contracture after burns will result in difficulty in closing the eye-lids which will in-turn lead to corneal ulceration

The actin appears at day 6 after wounding and persists at high levels for 15 days and is gone by 4 weeks when the cell undergoes apoptosis. It appears that the stimulated fibroblast develops a contractile ability related to formation of cytoplasmic actin-myosin complexes. When this stimulated cell is placed in the fibroblast-populated collagen lattice, contraction occurs even faster. The tension that is exerted by the fibroblasts' attempt at contraction appears to stimulate the actin-myosin structures in their cytoplasm.

4. **REMODELING PHASE**

Finally, tissue remodeling, in which wound contraction and tensile strength is achieved, occurs in the next 6-12 months. After the third week, the wound undergoes constant alterations, known as remodeling, which can last for years after the initial injury occurred.

Collagen is degraded and deposited in an equilibrium-producing fashion, resulting in no change in the amount of collagen present in the

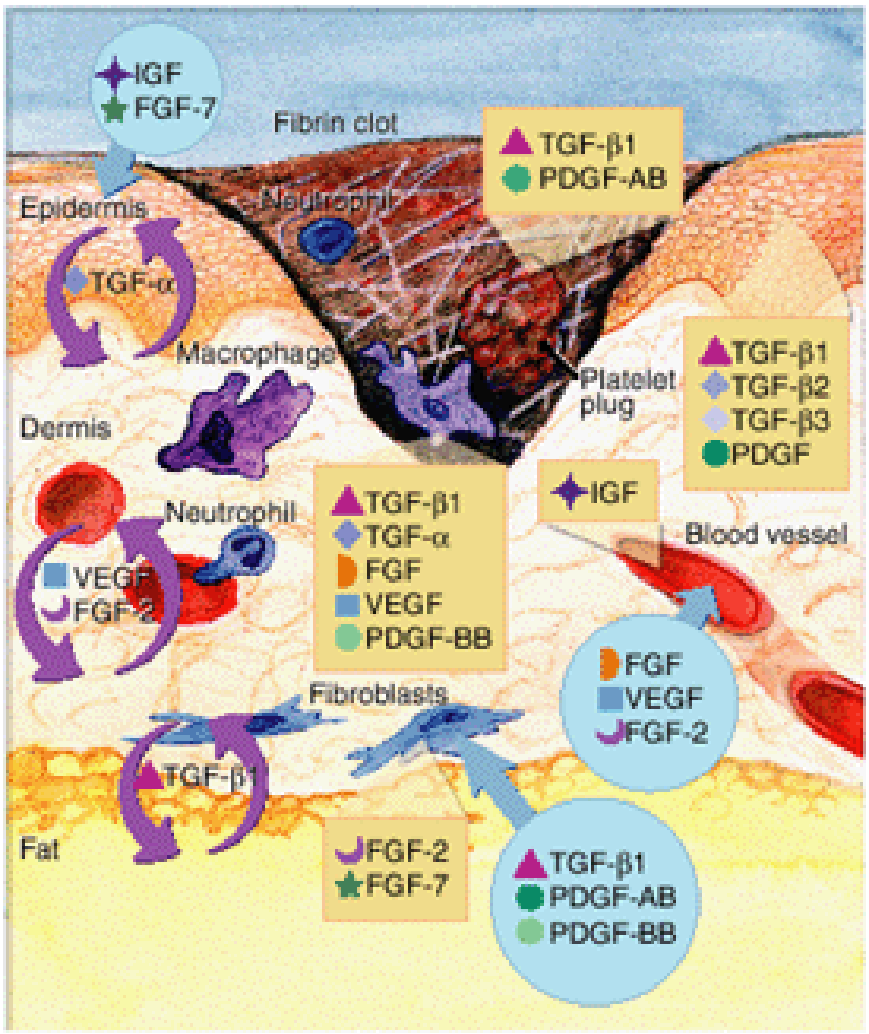
wound. The collagen deposition in normal wound healing reaches a peak by the third week after the wound is created. Contraction of the wound is an ongoing process resulting in part from the proliferation of the specialized fibroblasts termed myofibroblasts, which resemble contractile smooth muscle cells.

Wound contraction occurs to a greater extent with secondary healing than with primary healing. Systemic illness and local factors can affect wound healing.

COMMON GROWTH FACTORS INVOLVED IN WOUND HEALING[18]

- Monocyte Chemotaxis - PDGF, FGF, TGF-B
- Fibroblast migration - PDGF, EGF, FGF, TGF-B, TNF'
- Fibroblast proliferation - PDGF, EGF, FGF, TNF'.
- Angiogenesis - VGEF, FGF'
- Collagen Synthesis - TGF-B, PDGF, TNF'.
- Collagenase Secretion - PDGF, FGF, EGF, TNF, TGF-B'.

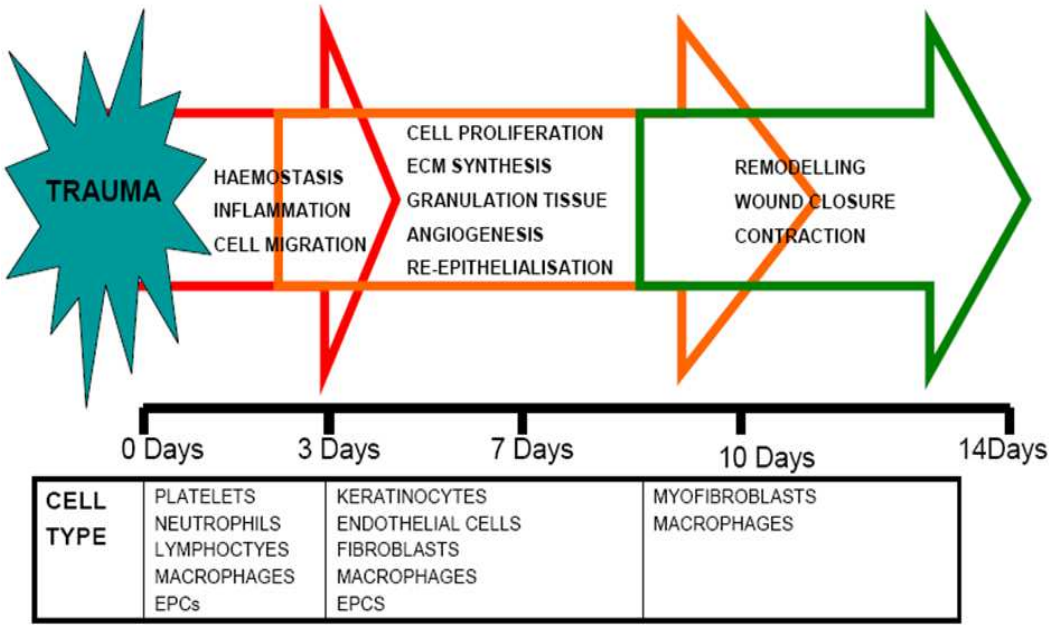
FIGURE-7:
GROWTH FACTORS IN WOUND HEALING



The careful balance between constructive and destructive processes leads to the normal process of wound healing. Many growth factors and cytokines play key role in this process of balancing. If the balance progresses in favour of destruction, delayed healing is the result.

The recent advances have resulted in interacting with this wound healing cascade in multiple ways as to speed up this process and result in early wound healing.

FIGURE-8:
STAGES OF NORMAL CUTANEOUS WOUND HEALING



ULCER[19]

CLASSIFICATION

Two types of classification are made.

1. CLINICAL
2. PATHOLOGICAL

1. CLINICAL CLASSIFICATION

An ulcer can be categorized into three types:

A. Spreading ulcer

B. Healing ulcer

C. Chronic or callous ulcer.

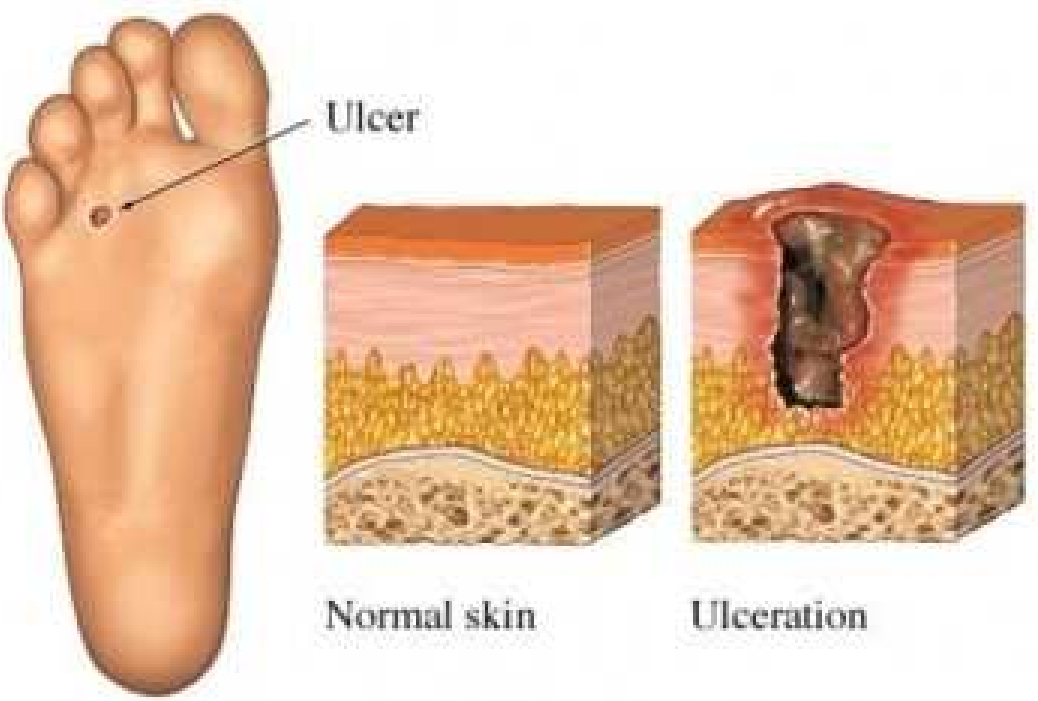
a. SPREADING ULCER: Spreading ulcer has its base filled with slough and absence of granulation tissue. Its edges are destructed, ragged and edematous. The surrounding area is inflammatory and may be contaminated occasionally.

b. HEALING ULCER: A Healing ulcer is in the process of healing, the floor is covered with pink or red granulation tissue.

The edges are red with granulation tissue and the margins appear bluish with growing epithelium.

c. **CHRONIC ULCER:** A Chronic or callous ulcer is that it shows no tendency towards healing. The floor is covered with pale granulation tissue. It shows typical wash leather slough with scanty discharge. The surrounding skin and the edge are indurated.

FIGURE-9:
ULCER



2. PATHOLOGICAL CLASSIFICATION

NON-SPECIFIC ULCERS

These ulcers can be classified into the following categories:

- Traumatic
- Arterial
- Venous
- Trophic
- Tropical
- Other Types : Bazin’s, Martorell’s , Meleney’s

SPECIFIC ULCERS

Ulcers due to specific underlying conditions.

- Tuberculosis
- Syphilitic
- Actinomycotic

PHYSICAL EXAMINATION[20]

TABLE-1:
PHYSICAL EXAMINATION

	VENOUS	ARTERIAL	DIABETIC	VASCULITIC
LOCATION	Medial malleolus, gaiter area	Toes, heels, bony prominences of foot, lateral malleolus, rarely over medial malleolus.	Same as arterial trophic ulcers on pressure points on the plantar foot, especially metatarsal heads.	Pretibial and dorsum of foot but may be anywhere and frequently is also on other areas.
VASCULAR EXAMINATION	Ankle/brachial index greater than 0.9. Pulses present. Plethysmography or Doppler studies show abnormal venous system.	Ankle/brachial index less than 0.9. Pulses decreased. Abnormal pallor of leg with elevation, and subsequent rubor with dependency. Delayed venous filling.	Mixed, usually associated with arterial disease.	Normal
HISTORY	Edema, trauma, rapid onset. Thrombo-phlebitis 20% varicosities	Arteriosclerosis, claudication. Usually >45 yr. Slow progression	Diabetes mellitus; peripheral neuropathy	Association with other systemic disease; rapid onset.

PAIN	Increases with leg dependency, decreases with elevation	Frequently very painful. Decreases with leg dependency, increases with exercise and leg elevation	Painless but associated with paraesthesia, anaesthesia, in constant, mostly at night.	Extremely painful.
TREATMENT	Leg elevation, compression by elastic bandages or stockings, 30 mm Hg, moist wound dressings. Grafts.	Vascular surgical consultation. No compression. Moist wound dressings. Pentoxyphylline	Control diabetes; careful wound care, early intervention for infections; vascular surgical consult.	Control underlying disease; no adherent dressings; oral steroids, ASA, bed rest.
APPEARANCE	Irregularly shaped, surrounded by brown pigmentation with edema or sometimes fibrotic, hard skin (lipodermatosclerosis). Ulcer base has granulation tissue and exudates, and the borders may be hyperkeratotic	Punched out ulcer with round well-demarcated borders and pale or white ulcer bed. Sometimes covered with dry eschar. Surrounding skin cool atrophic and hairless.	Punched out, often surrounded by hyperkeratotic borders; purulent drainage may indicate osteomyelitis.	Palpable purpura, hemorrhagic vesicle, typically small and multiple, with black, gray, or yellow base and minimal or no granulation tissue; may have thin undermined border; surrounding skin shows reticulated vascular pattern

An ulcer can be defined as a break in the epithelial continuity. A prolonged inflammatory phase leads to overgrowth of granulation tissue, and attempts to heal by scarring leave a fibrotic margin. Necrotic tissue often at the ulcer centre is called slough.

A chronic Ulcer, unresponsive to dressings and simple treatments, should be biopsied to rule out neoplastic change, a squamous cell carcinoma known as a Marjolin's ulcer being the commonest.

AETIOLOGY OF LEG ULCERS

- Venous disease leading to local venous Hypertension
  (e.g. Varicose Veins)
- Arterial disease, either large vessel (Atherosclerosis) or
  Small Vessel (Diabetes)
- Arteritis associated with autoimmune disease
  (Rheumatoid Arthritis, Lupus, etc.,)
- Trauma : could be self-inflicted
- Chronic Infection – Tuberculosis / Syphilis
- Neoplastic – Squamous or basal cell Carcinoma, Sarcoma

Effective treatment of any leg ulcer depends on treating the cause, and diagnosis is therefore vital. Arterial and venous circulation should be assessed, as should sensation throughout the lower limb. Surgical treatment is only indicated if non-operative treatment has failed or if the patient suffers from intractable pain.

Meshed skin grafts are more successful than sheet grafts and have the advantage of allowing mobilisation, as any tissue exudate can escape through the mesh. It should be stressed that the recurrence rate is high in venous ulceration, and patient compliance with a regime of hygiene, elevation and elastic compression is essential.

PATHOPHYSIOLOGY[23,24,25]

Rheumatoid arthritis is associated with ulcers both from vasculitis and from immobility of the leg with resultant inadequate venous return.

In sickle cell anemia there is an incidence of ulcers of 25% to 75%, probably from the abnormal rheological properties of the red blood-cells resulting in an ulcer that resembles venous ulcers. Recurrent hemorrhages and infections also play a role.

Other hematologic diseases also share common factors with venous ulcers. Polycythemia vera results in increased viscosity, as do various dysproteinemias.

Pyoderma gangrenosum mostly represents a small vessel vasculitis, although not all cases show vasculitis. It may be associated with ulcerative colitis, rheumatoid arthritis, leukemias, regional enteritis, or may occur without any underlying disease.

Venous ulcers, also known as varicose ulcers, venous hypertension ulcers, venous stasis ulcers, or postphlebitic ulcers are caused by the common mechanism of too much hydrostatic pressure in the superficial venous system of the leg. At least 80% of the time this is caused by incompetent valves in deep veins. Trauma to the leg and rare congenital fistulas can cause arteriovenous fistulas, which also result in venous hypertension.

Arterial ulcers are primarily a result of arteriosclerosis obliterans .Although this accounts for only 5% to 10% of all leg ulcers, by the age of 80, over 90% of patients have an arterial component. In other words, a venous ulcer at age 50 will become a mixed venous and arterial ulcer by the time the patient reaches 80 and treatment will need to be changed to

address the arterial component. Risk factors are diabetes mellitus, smoking, hyperlipidemia, hypertension, and early menopause in women.

Diabetes mellitus results in ulceration from atherosclerosis, peripheral neuropathy and less commonly necrobiosis lipoidica, diabetic dermopathy and bacterial and fungal infections. Hyperemia and capillary hypertension, loss of auto-regulation and neurogenic regulation, disturbed endothelial function, and abnormal rheology also play a part in the abnormal microcirculation of diabetic patients.

Drugs may cause ulcers by a number of mechanisms. Hydroxyurea may cause ulcerative lichen planus or a livedo vasculitis-like picture. Some drugs, such as corticosteroids, alter wound healing, although low anti-inflammatory products (e.g., Cortisone Acetate and Prednisone in oral doses under 10mg. daily) have no appreciable effect on wound healing. Coumarin necrosis is a rare disease caused by an imbalance in the anti-coagulant and procoagulant factors. Inhibition of production of protein C and protein S in hereditary deficiency states or rarely acquired deficiencies associated with disseminated intravascular coagulation, multiple myeloma, and the lupus anticoagulant may disproportionately balance the coagulation system toward thrombosis in early coumarin treatment.

Antibodies to phospholipids cause recurrent thrombosis with a vasculitic appearing ulcer. These antibodies are manifested by false positive VDRL, a lupus anticoagulant, or anticardiolipin antibodies, and may be associated with lupus and lupus-like diseases and livedo vasculitis and may cause their effects through interactions with Protein 'C' or Protein 'S'. It has been proposed that they may promote thrombosis by binding to endothelial cells and impairing Prostacyclin release or damaging platelet adhesiveness.

DETERRENTS OF WOUND HEALING [26,27,28,29]:

Factors that delay the Wound Healing Process	
Local Factors	**Systemic Factors**
• Continued Pressure • Desiccation and dehydration • Trauma and Edema • Infection or Heavy Colonization • Necrosis • Incontinence leading to maceration. • Lack of Oxygen delivery to the tissues	• Old Age • Obesity • Chronic Diseases (e.g., Diabetes, Anemia) • Mal-Nutrition • Vascular Insufficiency • Immuno Deficiency • Smoking • Stress • Poor Health

AGENTS TO OPTIMISE WOUND HEALING

DRESSINGS[36,37,38]

The ideal dressing should be simple, inexpensive, highly absorptive, and non-adherent.

It should achieve moist healing and have antibacterial properties, less frequent dressing changes, an all-in-one dressing that does not require tape or an overlay, and a gentle adhesive that is effective but not injurious to the skin when removed. The simplest dressing is gauze and tape - it is inexpensive, is absorptive, and when used with an ointment, can achieve moist healing. The primary disadvantages are the necessity for frequent dressing changes and the potential for tape irritation and wound desiccation. Other products are classified into films[36], foams, hydrocolloids, hydrogels and absorptive powders. Films are semi-permeable to water, generally made of polyurethane, and non-absorptive. These are useful to achieve a moist wound healing environment over minimally exudative wounds, such as a split-thickness skin graft donor site.

ANTIBIOTICS

- Only when the surrounding tissue is invaded (cellulitis) are systemic antibiotics clearly indicated.

- Antibiotics may be useful in other situations, such as when the granulation tissue has a high bacterial count or in a case of reduced resistance to bacteria, such as in a diabetic foot ulcer.

- The routine use of systemic antibiotics for chronic wounds should be avoided to reduce the development of resistant bacterial strains within the wound.

- Topical antibiotics are frequently used and can be useful

- With most antibiotics, however, resistant organisms emerge quickly and development of allergic, hyper-sensitivity reactions are common.

- Most topical antibiotic ointments should be limited to 3 weeks of therapy to avoid developing a rash or other signs of inflammation as a result of the antibiotic ointment not bacteria.

- The expense is substantial.

DÉBRIDING AGENTS

Collagenases have been used to débride wounds for 20 years and can be a highly effective adjunct in the treatment of chronic wounds with necrotic tissue. These agents are used after surgical débridement to help clean a wound and to avoid a painful mechanical débridement. Collagenases that are combined with antibiotic powder have been proposed as a useful treatment for chronic wounds.

PHARMACOLOGIC AGENTS

Growth Factors: The growth factors with the most evidence for efficacy are PDGF, TGF-β, epidermal growth factor, and members of the FGF family, although IGF1, Interleukin (IL-1, IL-2), Granulocyte-Macrophage Colony - stimulating factor and VEGF have also shown improved rates of healing in animal models. Clinical trials are in progress, and only Becaplermin (PDGF) has been approved by the FDA.

Growth Hormone : It deserves brief mention because it has been used successfully in some situations to reverse the catabolic impact of many severe injuries. Wound healing is a fundamentally anabolic event (creating new tissue), and in the setting of a severe burn, growth hormone

administration significantly accelerates donor site healing, presumably because of its effects in minimizing catabolism.

VACUUM ASSISTED CLOSURE (VAC)

This proprietary treatment involves the application of a moderate vacuum to an occlusive dressing with a sponge to allow wicking of the exudates up into the sponge and out of the wound. The negative pressure results in reduction of wound edema and resulting increase in local tissue perfusion. Continual removal of wound exudates removes the media for bacterial growth and results in removal of the bacterial as well, with a resulting reduction in bacterial burden, and the negative pressure accelerates wound contraction. The VAC has found uses in the treatment of chronic wounds and difficult acute wounds; for adherence of skin grafts; and in recent years in the treatment of open sternotomy wounds and exposed joint prostheses, as well as in a variety of other applications

KEY POINTS

- The inflammatory phase of acute wound healing begins immediately after injury. The initial response to the disruption of blood vessels is bleeding.
- The proliferative phase begins with the formation of a provisional matrix of fibrin and fibronectin as part of initial clot formation.
- The transition from the proliferative phase to the remodeling phase is defined by reaching collagen equilibrium.
- Reconstruction of the epithelial barrier (epithelialization) begins within hours of the initial injury.
- Visible scarring occurs only when the injury extends deeper than the superficial dermis.
- A practical definition of a chronic wound is one that has failed to heal within 3 months. Although there are a variety of underlying causes, most can be categorized as pressure sores, diabetic foot ulcers, or leg ulcers.
- It takes at least 3 weeks for collagen to undergo sufficient remodeling and cross-linking to attain moderate strength.
- A chronic wound is commonly defined as an open wound that has failed to respond to standard care and remains open at 3 months.

ROLE OF HONEY IN DRESSING

Honey was one of the most ancient remedies for wound healing even before the term “Bacteria” was coined. Later in the new era, it is being increasingly rediscovered to have anti bacterial property against multiple bacteria, not only that is also being found to have anti fungal properties, against many of the common fungi which affect the skin like Aspergillus and certain Dermatophytes[38]. The characteristic of this naturally occuring pharmacological product is that it has many biochemical and physiologic properties which provide it to be a healing agent, which is being detailed below.

OSMOTIC EFFECT

Van Ketel in 1896 found the antibacterial property of honey. It was thought that the antibiotic property of honey was entirely due to its high Osmolarity. But honey loses its osmolarity when applied as a wound dressing since it mixes with the wound discharge and gets diluted. One of the most common wound pathogen like Staphylococcus was found to be

getting inhibited ,even after the honey was diluted to its 10-14 times the original Osmolarity[39].

How this happened was the Dilemma which got solved by 1919 when it was found that, on diluting honey an enzyme hydrogen peroxide is released which is highly inhibitory to many of the bacterial species. It acts as an 'Inhibin' which prevent the growth of bacteria in the wound[40]. Hydrogen peroxide as a chemical by itself is one of the wound sterilising agents.

Later in the next stage experiments were conducted comparing honey with saturated sugar solution. These were mainly animal experiments in pigs, buffallos and other animals, and it was found that, compared to the sugar solution, honey had lesser colonies of bacteria[40] and the sugar solution group required multiple change of dressing unlike their counterpart.

HYDROGEN PEROXIDE ACTIVITY[41]

- Hydrogen peroxide was an important antiseptic which was commonly used in the olden era as it had high oxygen radical component.

- But it has lost its importance recently as it causes damage to the tissues and causes inflammation in the wounds
- In honey the concentration of hydrogen peroxide is 1000 times lower than the commonly used 3% H_2O_2.
- And other Anti-oxidants other than H_2O_2 present in honey augments its anti-oxidant property in a favourable manner.
- A steady release is possible when it is released from a Glucose solution rather than the product in isolation.
- A study with E-Coli demonstrated that, it was better inhibited at lower concentrations like 0.02% without damage to fibroblast.

PHYTOCHEMICAL COMPONENT

In the 4th stage, honey was applied and studied after mixing it with 'catalase' the Enzyme which destroys hydrogen peroxide. But even then the anti-oxidant property of honey retained and was higher in Manuka[47] (Leptospermum Scoparium) honey from New Zealand , which was found to have unidentified Phytochemicals which attribute it a higher antibacterial property.

LYMPHOCYTE AND PHAGOCYTIC ACTIVITY

It was found that the wound healing property was not entirely due to anti-bacterial action but also multitude of characteristics of honey, a few of which are mentioned below.

- Honey was found to stimulate the action of B lymphocytes and T lymphocytes in cell culture medium.
- It augments the action of phagocytes.
- It activates the monocytes to release cytokines like TNF Alpha, IL6 and other cytokines
- Due to the acidic pH of Honey (between 3 and 4), the phagocytic activity of honey is augmented by providing a suitable environment.

ANTI-BACTERIAL POTENCY

Varities of honey from different parts of the world are obviously from different floral sources and so they differ in their antibacterial properties. Examples are Manuka honey from New Zealand, lotus honey from India, honey from Jirddin Valley of Dubai, strawberry tree honey of Sardinia.

They vary in their MIC from 25% to 0.25%. And as a result, various studies conducted in different parts of the world takes different time to heal a similar wound as, certain study has the result in 3 to 5 days, but some as long as 2 to 3 weeks. There is no internationally available uniform honey- is the main drawback behind it becoming one of the major pharmacological wound healing substance, and the studies relating to Honey at present varies in its anti-bacterial properties .

LABORATORY STUDIES USING HONEY

Very few studies have been conducted using standardised honeys. Few important points are as follows :

- Manuka honey which was removed of hydrogen peroxide activity was compared with multi-floral standardised honey which retained its hydrogen peroxide activity.
- Antibiotic effects in seven species of bacterial cultures were studied.
- The bacterias which were studied included MRSA, VRE, enterococci and other skin pathogens.
- MIC varied from 0.8 to 10.8% (v/v) in both the honey group

- Apart from enterococci species , there were no significant difference between two honeys used for the study
- On comparing with routine antibiotics, honey had around 56 times antibiotic activity regarding certain pathogens
- Even some antibiotic resistant species were found sensitive to honey.

CLINICAL STUDIES USING HONEY

Though laboratory studies were rarer, plenty of clinical studies had been conducted by using honey. Many types of ulcers and wounds were studied and it included burns, boils, foot ulcers of various etiology, diabetic ulcer, post-traumatic wounds, pressure sores, venous ulcer, post-laparotomy wounds, wounds in children were all studied. Many studies have compared honey with other dressing materials. Most of these studies showed successful healing response in wounds treated with honey.

- A study was conducted in 59 patients of which 51 had bacterial colonization of their wounds and 47 had persistent ulcers lasting for more than a month. Ulcers have been treated with Acriflavin,

Chlorinated lime and Boric Acid. Many ulcers were even increasing in size. After treating with honey, all except one showed signs of healing and the other was a Buruli ulcer.

- This study was conducted in 9 infants with large surgical, infected wounds, which did not show any sign of healing. They were given IV Antibiotics and wounds were dressed with Fusidic Acid[51]. After applying honey, all wounds started signs of healing after just 5 days and all the wounds got closed within 21 days.
- This study was a randomised controlled study. It compared 2 groups of patients with post operative wounds, the first 26 were treated with honey and the second group was treated with Povidone Iodine and alcohol. The group treated with alcohol had earlier healing within half the time required for those in the second group[52].
- Two main studies have compared honey with silver Sulphadiazine[38] in treatment of burn ulcers- partial thickness burns[53,54]. Both the studies showed improved response with honey
- Another study was conducted in Fourniers gangrene patients. 20 of them were treated with honey and second group was treated with conventional methods[42] of wound debridement and secondary suturing. The second group had shorter hospital stay, but the honey treated group had their wounds became disinfected earlier and they

recovered from the morbid state[55] earlier compared with the second group.

- In certain studies, it was showed that wounds infected with resistant pseudomonas species became free of the infection after applying honey and they were able to undergo skin grafting.[56,57]
- Some studies have shown that certain antibiotic resistant strains of bacteria which were resistant to Oxytetracycline, Ampicilin, Chloramphenicol and Gentamycin got cleared of their infection after applying honey for 5 weeks[58].
- Studies have also shown that honey could heal Cavitory wounds infected with MRSA[60,61]

ADVERSE REACTIONS

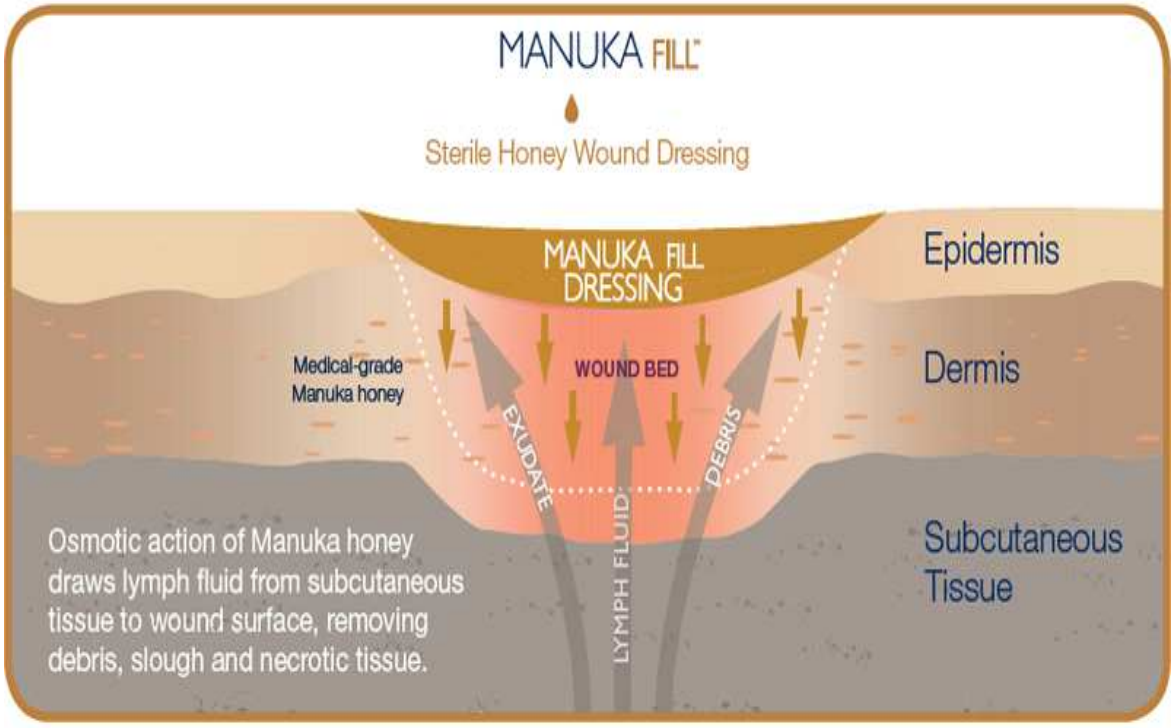
Adverse reactions to honey application are rare to be found :

- Honey for application over wounds is processed by passing through fine filters by causing the pollen[63,64] within to stop contaminating the honey. More than 500 studies conducted have not reported to have any allergic reaction. Thus allergic reactions are rarer.[62]

- Transient stinging sensation was reported by quite few on applying honey over certain wounds and for ophthalmologic purposes[61]. This was found to be due to acidic nature of honey and they were relieved of the stinging sensation, when acidity of honey was neutralized.[67]
- In contrast, larger number of studies shows that, honey application was free of adverse effects[71] and it was pain free[70], soothing[68] and had no irritation[69].
- Many histological studies have also shown that honey application was free of adverse effects[72]
- Practical considerations while using honey on wounds[48]
- Larger amounts of honey are needed for application over single wound.
- On dilution, its viscous property is lost as it may get diluted with discharges from the wound an on exposure to higher temperature of body heat.
- For maximum therapeutic effect, inner parts of wound should be getting more honey and so a reservoir of honey like a pad embedded in honey should be placed on the surface

- Honey available for edible purposes may not be filtered or treated so that, it may be a source for pollen, and clostridial spores. Gamma irradiation[73] to honey, kills these spores and filtering the honey clears it from the pollen, which is available in the market, which could be used for application over wounds. This gamma irradiation does not affect[71] its antibacterial property.
- Examples of those gamma irradiated and processed honey are Manuka honey, which is rated on a UMF scale according to its Phytochemical component and anti-bacterial property. (UMF 15 = 15% Phenol)
- Medihoney, is a product from the pharmacological goods department of Australia, is another example of therapeutically available form of honey which could be used over the wounds.

FIGURE 10
HONEY FILL DRESSING



FACTS TO BE NOTED WHILE USING HONEY CLINICALLY

1. It is better that honey be applied to an adsorbent surface, which being applied to the wounds rather than applying directly over the wound surface to provide a constant supply of honey.

2. In deep, cavitory wounds, a ‘blister’ of honey could be used on an adhesive film and could be applied to the wounds, but in exuding, highly discharging wounds, this is not possible.

3. According to the amount of discharge coming from the wound, the dressing may have to be changed frequently, as the discharge will dilute the honey and its therapeutic effect decreases.

4. Honey may not easily get absorbed on to absorbant surfaces as it is highly viscous, for the same, it may have to be diluted atleast 20 times with sterile water or be heated it properly.

5. Honey will not soak readily into absorbent dressings. Soaking is facilitated by warming the honey to body temperature and/or adding 1 part water to 20 parts honey to make the honey more fluid.

6. As the surrounding portion of the wound may also be infected, honey will have to be applied to the surrounding tissue as well for ideal disinfection.

7. Honey could be easily applied to cavitory wounds and in sinuses with the help of catheter or syringe as it could be easily washed off and that, if any debris remains, is biodegradable.

8. Alginate after getting impregnated with honey becomes a soft gel, and so could be replaced with cotton/ cellulose dressings.

9. A less adherent dressing may be used in between honey dressing and the wound surface. In case of fear, if honey sticks to the wound as that it should be porous to allow seepage of honey particles from the superficial dressing applied above.

10. An occlusive dressing (e.g. Polyurethane film) could be used over the honey dressing in case of heavily discharging wounds. but if another absorbant dressing is used above, it may absorb the honey from the dressing and the wound and the therapeutic effect may be lost

MATERIALS AND METHODS

DESIGN OF THE STUDY

This study is a prospective parallel group and comparative trial among patients admitted with foot ulcer in General Surgery wards in Madurai Medical College, Madurai.

The number of patients included in the study was 80, Out of which 40 were in the test group and 40 were in the control group. Study duration was 1 year. (August 2013 - August 2014)

MATERIALS USED

Normal Saline, Sterilised Honey

ETHICAL CLEARANCE

Ethical Clearance Obtained Consent: Individually written and informed Consent obtained from all 80 Patients enrolled in the Study.

CONFLICT OF INTEREST

NIL

FINANCIAL SUPPORT

NIL

INCLUSION CRITERIA

- Patients aged more than 20 years with foot ulcer of any Etiology.
- Ulcers of Wagner's Grade II – IV.

WAGNER CLASSIFICATION OF DIABETIC FOOT LESIONS

Grade 0: At risk foot no obvious ulcer, thick callus prominent metatarsal heads, claw toes or any bony abnormality.

Grade I : Superficial ulcer, not clinically infected.

Grade II: Deeper Ulcer, often infected but no bone involvement.

Grade III: Deep Ulcer, abscess formation, bony involvement.

Grade IV: Localized Gangrene.

Grade V: Gangrene of the whole foot

EXCLUSION CRITERIA

a) Clinical Signs of infection, Cellulites.

b) Ulcers of Wagner's Grade V.

c) X-ray showing Osteomyelitis.

d) Doppler showing gross atherosclerotic arterial changes and Venous abnormalities like Varicosities.

e) Malnutrition poorly-controlled Diabetes.

f) Other clinically significant medical conditions that would impair wound healing such as various renal hepatic haematological neurological immunological disorders.

g) Patients on corticosteroids immunosuppressive drugs radiation and chemotherapy for the last 1 month prior to entry into the study were excluded from the study

The selected patients underwent screening for a period of one to two weeks, to stabilize the wound and institute appropriate medical and surgical line of treatment like diabetic control, control of infection by initiating appropriate antibiotic based on culture sensitivity report, surgical debridement, correction of anemia and correction of other medical illness.

After the initial screening period the eligible patients who required bed side debridement were divided randomly into test group and control groups.

1. **Test Group :** Received Honey dressing with bedside surgical debridement when ever required for wounds/ulcers which had slough in the floor and till granulation tissue appeared.
2. **Control Group:** Received bedside surgical debridement with conventional normal Saline dressing.

The test medication was applied to test group once every day, making use of á a tongue depressor, medication was applied over entire surface the slough and only superficial slough was removed using bed side surgical debridement when ever required.

Treatment of control group was done with bed side surgical debridement when ever required and conventional Normal Saline dressing, Wounds are treated one-time daily till complete debridement or upto 7 week. The content of necrosed tissue, amount of granulation tissue, overall wound response was assessed all weekly using an visual score.

THE VISUAL SCORES ARE AS FOLLOWS

The score for the percentage of wound covered by slough and non-viable (necrotic) tissues are :

1. 76-100% wound was covered with necrotic tissue.
2. 51-75% wound covered with nonviable tissue.
3. 26-50% wound covered with nonviable tissue.
4. 11-25% wound covered with nonviable tissue.
5. 0-10% wound covered with nonviable tissue.
6. No Necrotic Tissue

The score for the percentage of wound covered by granulation tissues are:

1. No Granulation
2. < 25% of wound covered by Granulation Tissue
3. 25-74% of wound covered by Granulation Tissue
4. 75-100% of wound covered by Granulation Tissue

The reduction of wound size and area measured in cm^2

The final parameters and wound characteristics of the two randomized groups were analyzed using statistical methods and compared.

STATISTICAL METHODS

Chi-Square and Fisher exact tests have been used to test the significance of frequencies of presence of necrotic tissue, Presence of granulation tissue and wound surface area between test group and control group.

1. CHI-SQUARE TEST

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

where O_i is observed frequency and E_i is expected frequency

2. Fisher Exact Text

	Class I	Class 2	Total
Sample 1	a	b	a + b
Sample 2	c	d	c + d
Total	a+c	b+d	n

$$p = \frac{(a + b)!\,(c + d)!\,(a + c)!\,(b + d)!}{n!\,a!\,b!\,c!\,d!}$$

OBSERVATION AND RESULTS

AGE DISTRIBUTION

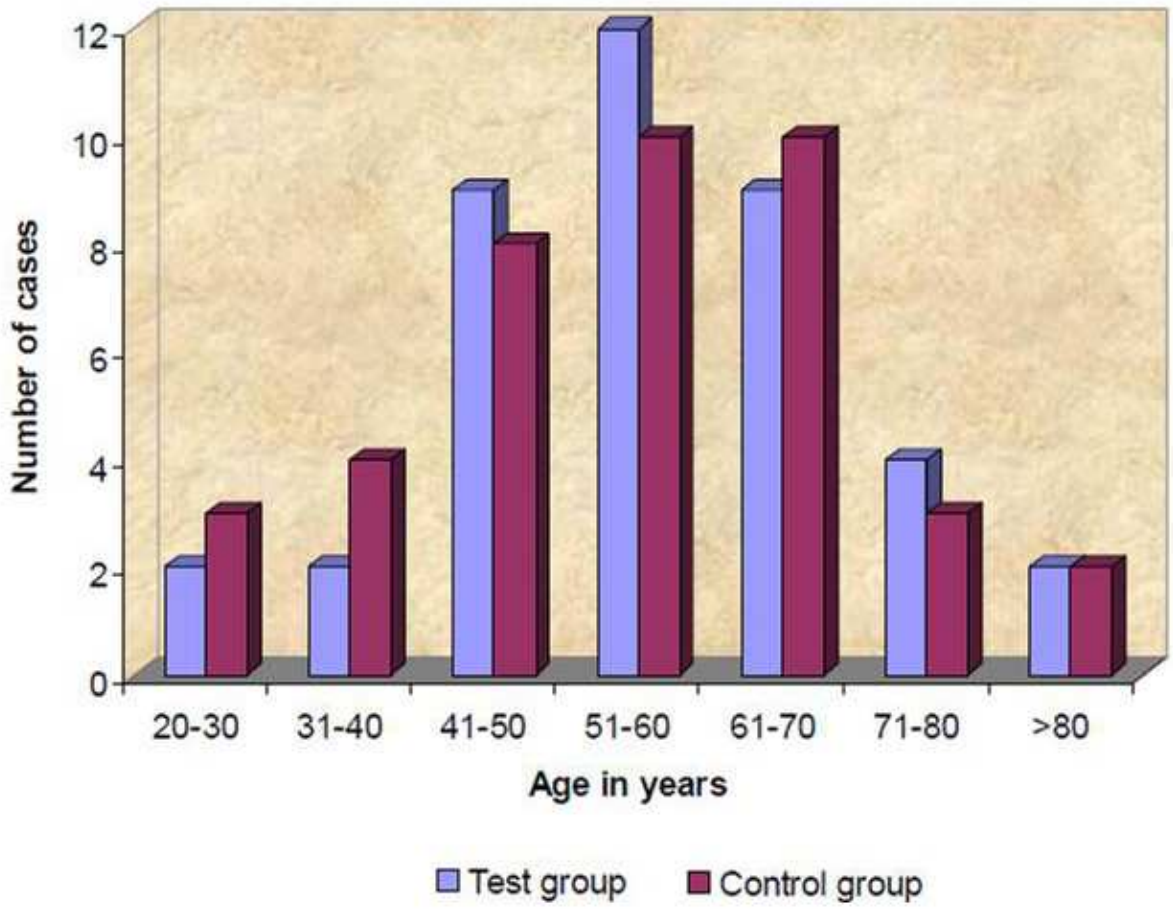
Most of the patients fell in the age group between 40 years to 70 years. The mean ± SD for Test Group is (57.0 ± 14.85) and control is (55.5 ± 14.45). So, age distribution is statistically similar between the two groups with $P > 0.05$.

TABLE –2
AGE DISTRIBUTION

Age (in years)	Test Group		Control Group	
	No. of Cases	%	No. of Cases	%
20-30	2	5	3	7.5
31-40	2	5	4	10.0
41-50	9	22.5	8	20.0
51-60	12	30	10	25.0
61-70	9	22.5	10	25.0
71-80	4	10	3	7.5
>80	2	5	2	5.0
Total	40	100.0	40	100.0
Mean ± SD	57.0 ± 14.85		55.55 ± 14.45	
Inference	Age distribution is statistically similar between the two groups.			

P > 0.05 Insignificant

GRAPH-1:
AGE DISTRIBUTION



SEX DISTRIBUTION

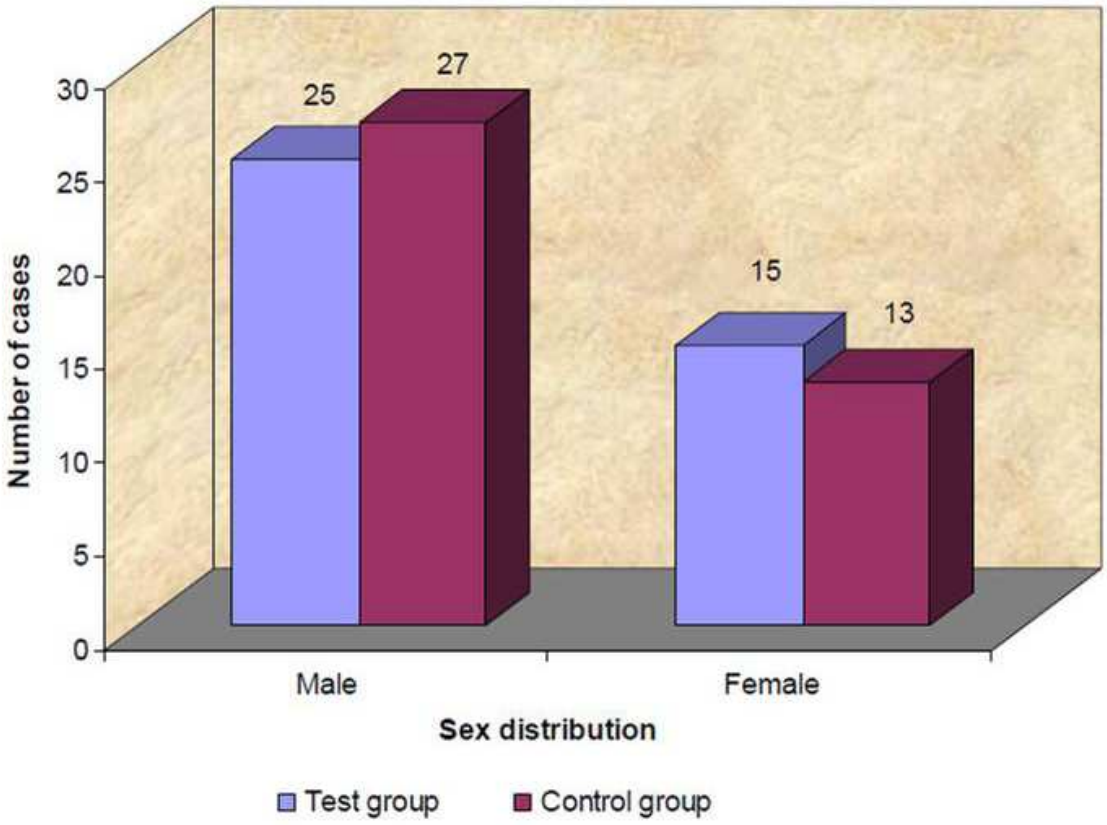
The male and female ratio of the test group is 62.5%: 37.5% and the control group is 67.5%: 32.5%. Hence sex distribution is statistically similar between the two groups with $P > 0.05$.

TABLE –3
SEX DISTRIBUTION

Sex Distribution	**Test Group (n=40)**		**Control Group (n=40)**	
	No	**%**	**No.**	**%**
Male	25	62.5	27	67.5
Female	15	37.5	13	32.5
Total	40	100.0	40	100.0
Inference	Sex distribution is statistically similar between the two groups.			

$\chi^2 = 0.22$ $P > 0.05$ Insignificant

GRAPH-2:
SEX DISTRIBUTION



DIABETES MELLITUS STATUS

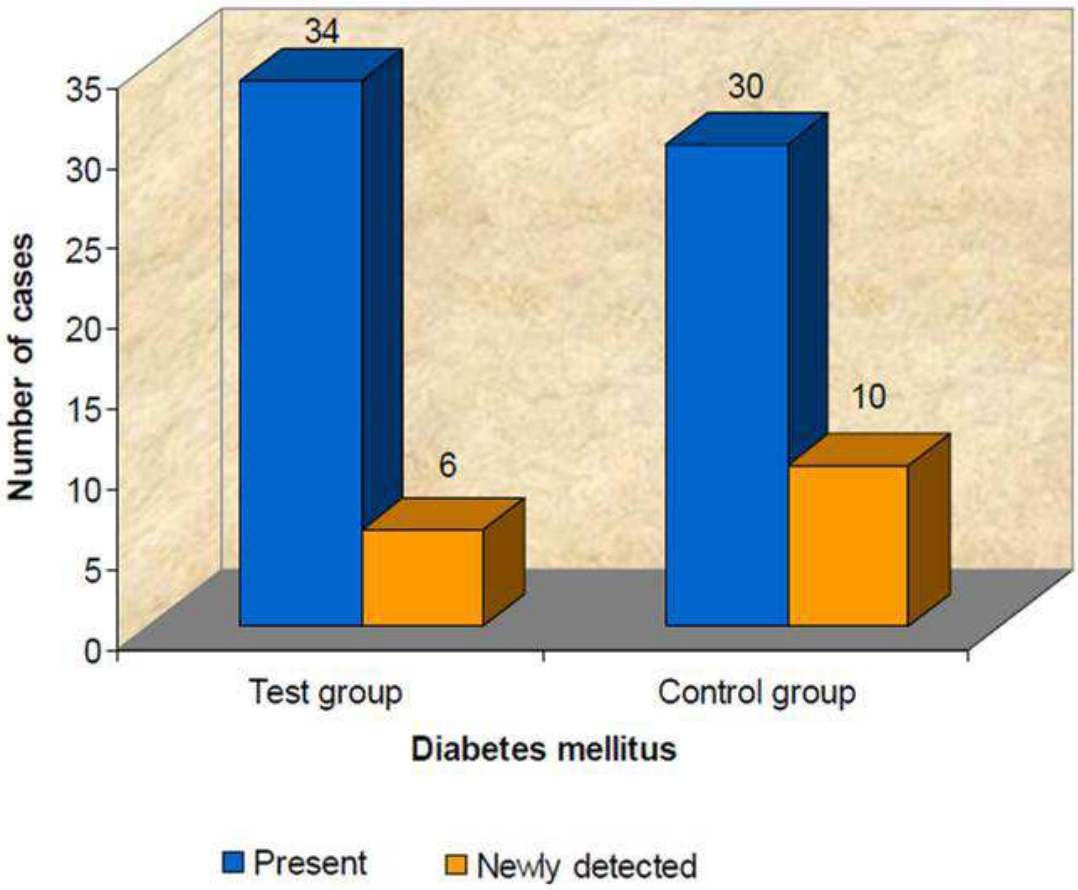
Most of the patients in Test Group (85%) and Control Group (75%) had previous history of diabetes mellitus. The group without diabetes are only 15% and 25% in Test and Control groups respectively

TABLE –4
SEX DISTRIBUTION

Sex Distribution	**Test Group (n=40)**		**Control Group (n=40)**	
	No	**%**	**No.**	**%**
Present	34	85.0	30	75.0
Absent	6	15.0	10	25.0
Total	40	100.0	40	100.0
Inference	Distribution of Diabetes Mellitus is equally likely between the two groups.			

$\chi^2 = 1.25$ P > 0.05 Insignificant

GRAPH-3
DIABETES MELLITUS



DURATION OF DIABETES MELLITUS

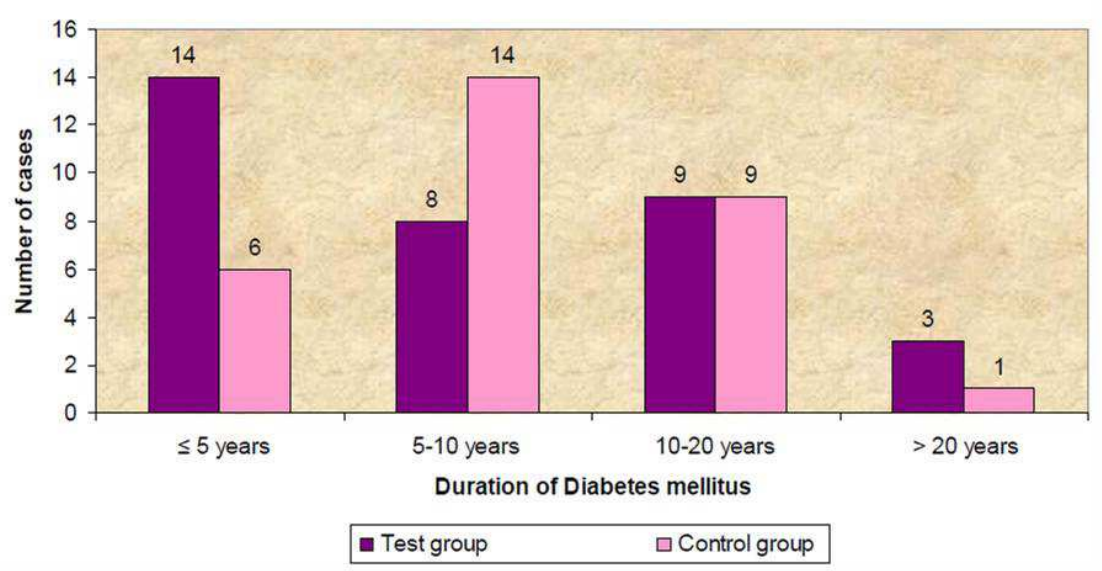
It is observed in our study most of the patients presented with Diabetes Mellitus of duration with Mean ± SD of test group 9.77 ± 6.94 and Control group 10.29 ± 5.61, thus showing long duration of diabetes mellitus patients are prone for diabetic Foot Ulcers.

TABLE -5
DURATION OF DIABETES MELLITUS

Sex Distribution	**Test Group**		**Control Group**	
	No	**%**	**No.**	**%**
≤5 years and absent DM	14	41,1	6	20.0
5-10 Years	8	23.5	14	46.7
10-20 years	9	26.5	9	30.0
> 20 years	3	8.8	1	3.3
Mean ± SD	9.77 ± 6.94		10.29 ± 5.61	
Inference	Distribution of DM is equally likely between the two groups..			

$X^2 = 4.80$ P > 0.05 Insignificant

GRAPH-4:
DURATION OF DIABETES MELLITUS



SIZE OF THE ULCERS

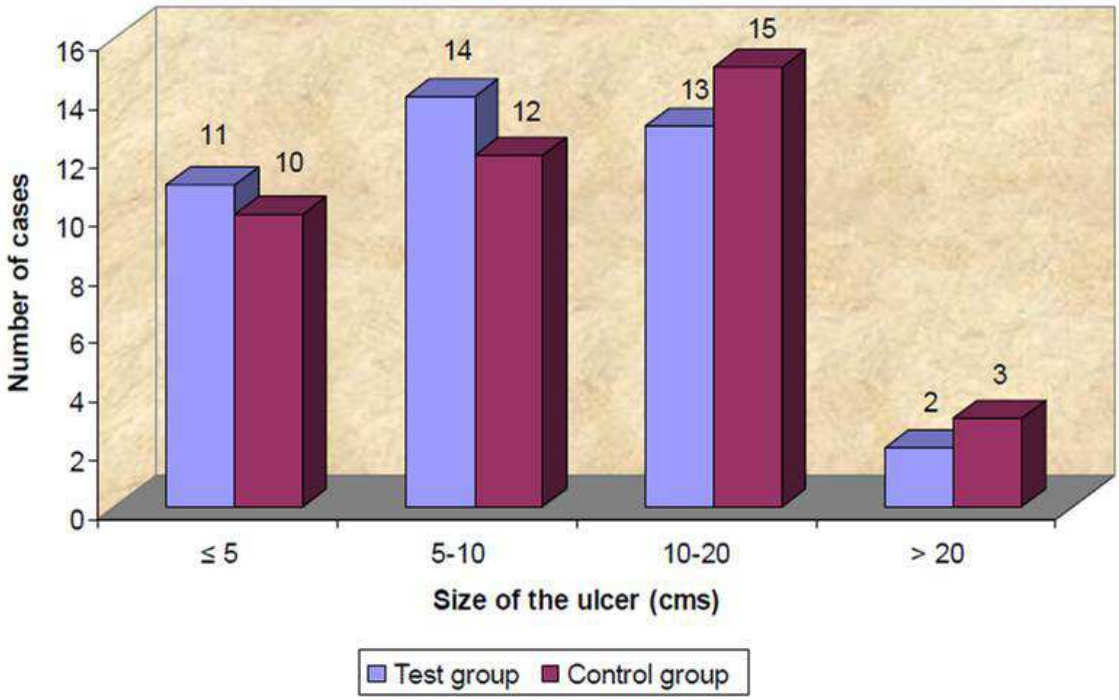
The mean size of the ulcer was 9.82 to 10.32 cm. The mean ± SD of the size of ulcer in test group (9.82 ± 6.80) and in control group (10.32 ± 6.39) is statistically similar between the two groups with $P > 0.05$.

TABLE -6
SIZE OF THE ULCERS

Size of the Ulcer (cms)	Test Group (n=40)		Control Group (n=40)	
	No	%	No.	%
≤5	11	27.5	10	25.0
5-10	14	35.0	12	30.0
10-20	13	32.5	15	37.5
>20	2	5	3	7.5
Mean ± SD	9.82 ± 6.80		10.32 ± 6.39	
Inference	Size of the ulcers is statistically similar between the two groups.			

Z = 0.34 P > 0.05 Insignificant

GRAPH-5:
SIZE OF THE ULCERS



GRADE OF ULCERS

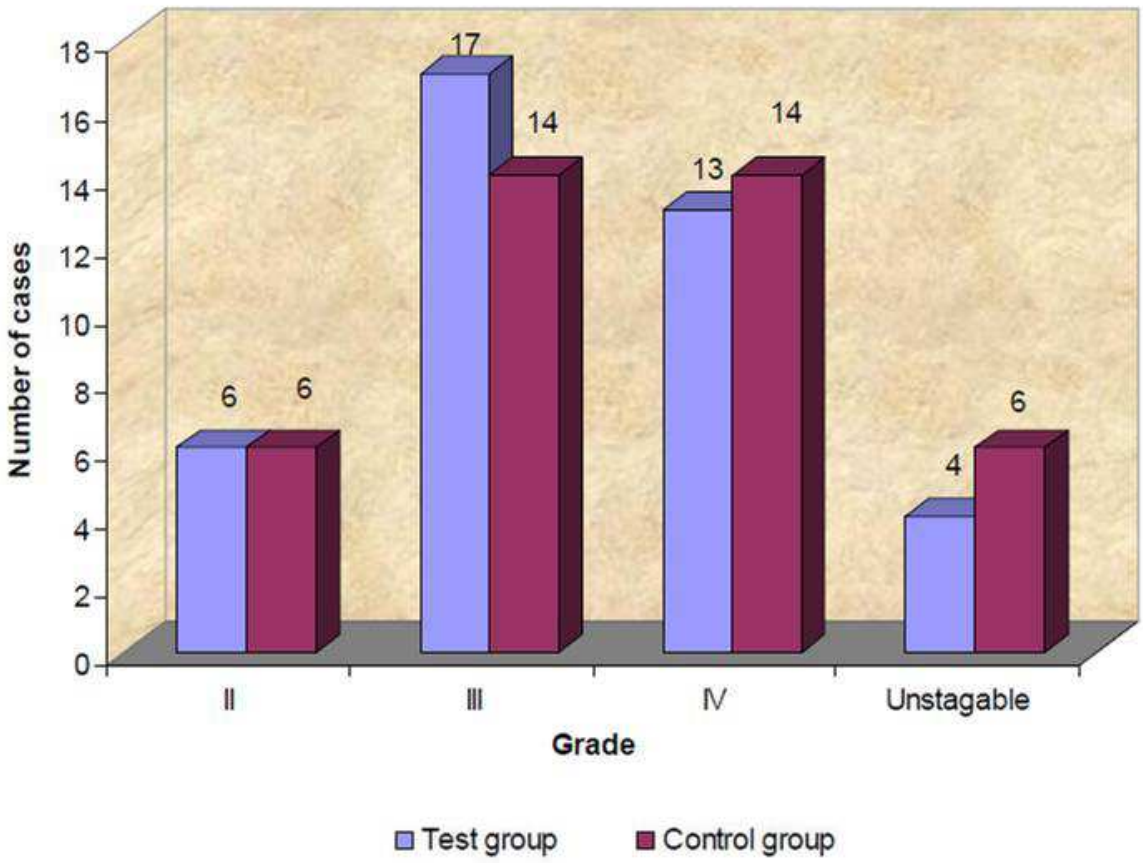
Most of the patients had Grade III and IV Ulcers in both Test and Control groups. The grade of ulcer is statistically similar between the two groups.

TABLE -7
GRADE OF ULCERS

Grade of Ulcer	Test Group (n=40)		Control Group (n=40)	
	No	%	No.	%
II	6	15.0	6	15.0
III	17	47.5	14	35.0
IV	13	27.5	14	35.0
Unstagable	4	10.0	6	15.0

$\chi^2 = 0.73$ P > 0.05 Insignificant

GRAPH-6:
GRADE OF ULCERS



PRESENCE OF NECROTIC TISSUE OR SLOUGH

The number of patients with no necrotic tissue are significantly higher in the test group at 3rd week follow up (P< 0.001), at 4th week (P < 0.001), at 5th week (P< 0.001), at 6th week (P < 0.001) and at the 7th week (P <0.01) when compared to control group as per the Chi-square / Fisher Exact test.

TABLE -8:
PRESENCE OF NECROTIC TISSUE OR SLOUGH

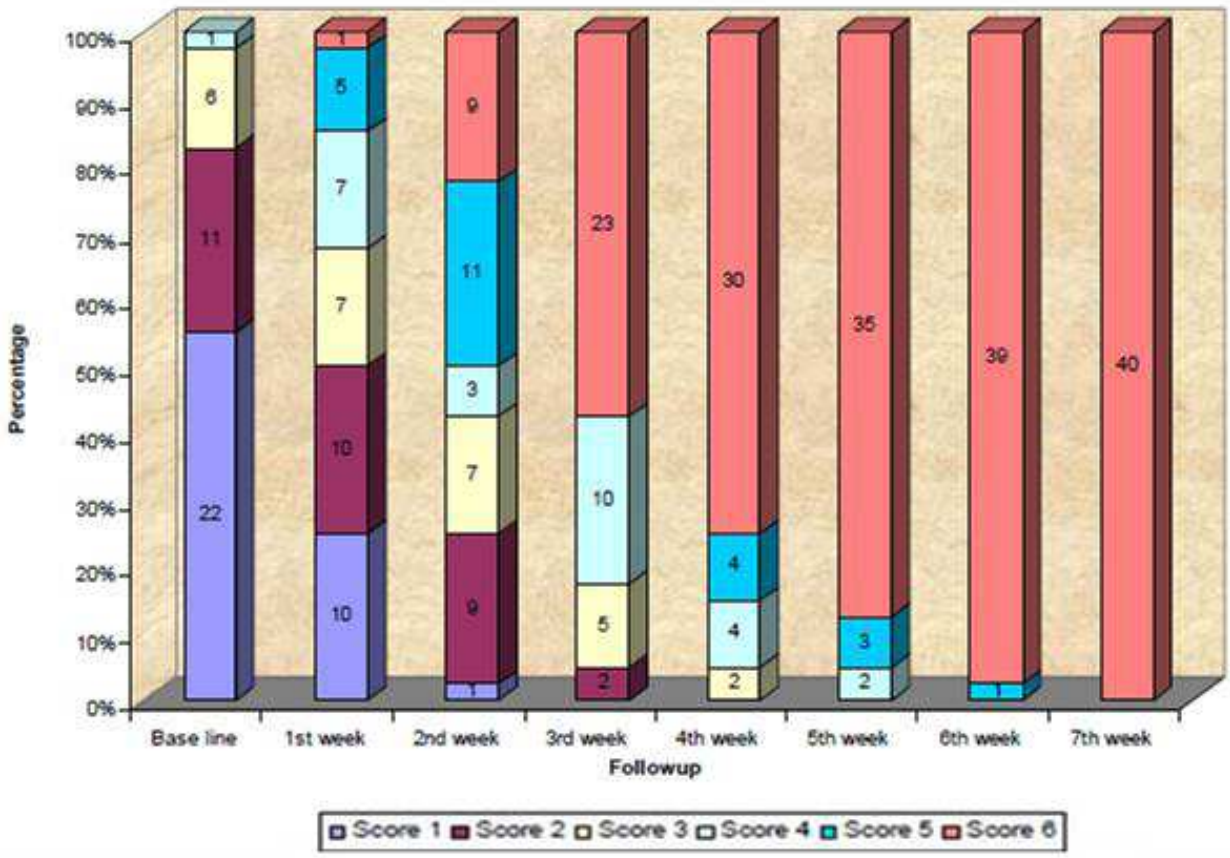
Study Period	Test group (n=40) visual score of slough covering the ulcer						Control group (n=40) visual score of slough covering the ulcer					
	1	2	3	4	5	6	1	2	3	4	5	6
Base Line	22 (55.0)	11 (27.5)	6 (15)	1 (2.5)	-	-	23 (57.5)	10 (25.0)	7 (17.5)	-	-	-
1st Week	10 (25.0)	10 (25.0)	7 (17.5)	7 (17.5)	5 (12.5)	1 (2.5)	20 (50.0)	9 (22.5)	5 (12.5)	3 (7.5)	3 (7.5)	-
2nd Week	1 (2.5	9 (22.5)	7 (17.5)	3 (7.5)	11 (27.5	9 (22.5)	6 (15.0)	17 (42.5)	6 (15.0)	4 (10.0)	2 (5.0)	5 (12.5)
3rd Week	-	2 (5.0)	5 (12.5)	10 (25.0)	0 (0)	23 (57.5.)	2 (5.0)	12 (30.0)	9 (22.5)	4 (10.0)	5 (12.5)	8 (20.0)
4th Week	-	-	2 (5.0)	4 (10.0)	4 (10.0)	30 (75.0)	-	1 (2.5)	14 (35.0)	8 (20.0)	4 (10.0)	13 (32.5)
5th Week	-	-	-	2 (5.0)	3 (7.5)	35 (87.5)	-	-	4 (10.0)	11 (27.5)	9 (22.5)	16 (40.0)
6th Week	-	-	-	-	1 (2.5)	39 (97.5)	-	-	-	6 (15.0)	11 (27.5)	23 (57.5)
7th Week	-	-	-	-	-	40 (100.0)	-	-	-	-	8 (20.0)	32 (80.0)
Infe-rence	Number of patients with No Necrotic tissue are significantly higher in Test Group at 3rd week follow-up (P < 0.001), at 4th Week (P < 0.001), at 5th Week (P < 0.001), at 6th Week (P < 0.001) and at the 7th Week (P <0.01) when compared to control group as per the chi-square / Fisher Exact test.											

Figures in brackets are percentages

VISUAL SCORE

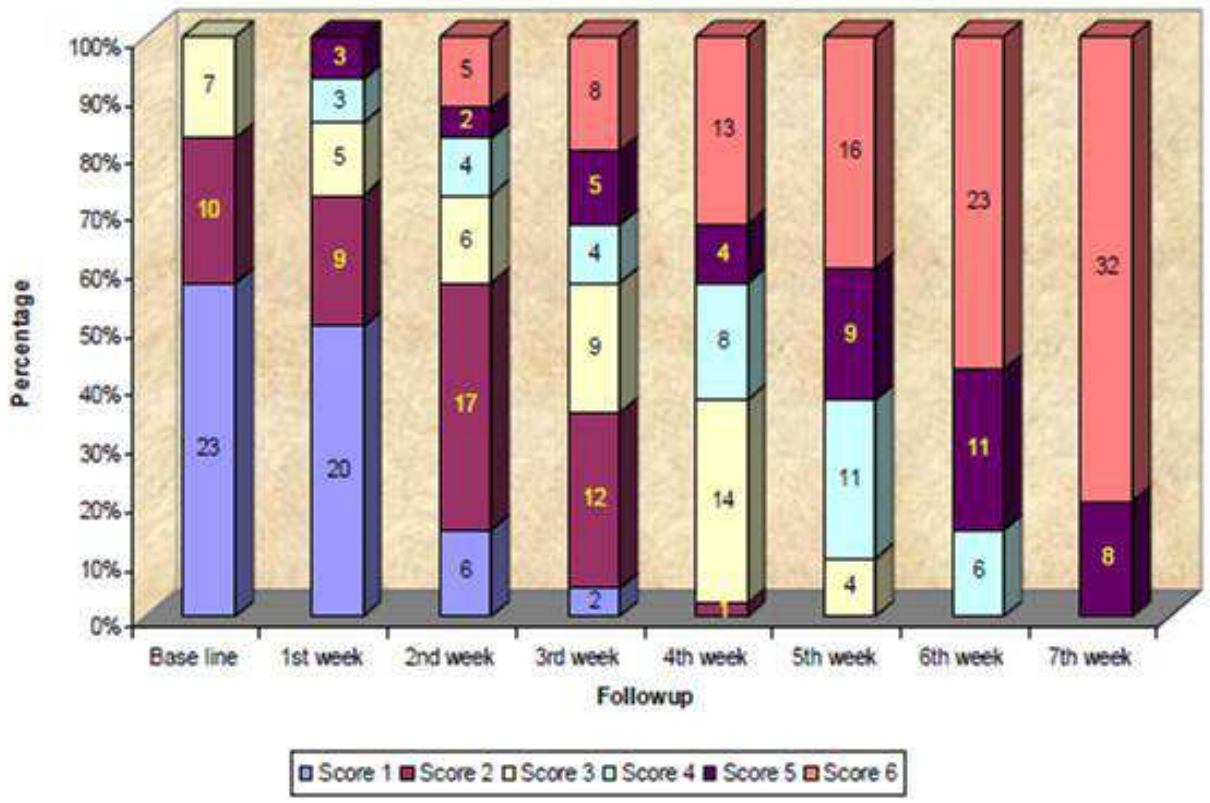
1. = 76-100% wound covered with nonviable tissue
2. = 51-75% wound covered with nonviable tissue
3. = 26-50% wound covered with nonviable tissue
4. = 11-25% wound covered with nonviable tissue
5. = 0-100% wound covered with nonviable tissue
6. = no necrotic tissue

GRAPH-7:
SHOWING THE PRESENCE OF NECROTIC TISSUE OR SLOUGH IN TEST GROUP



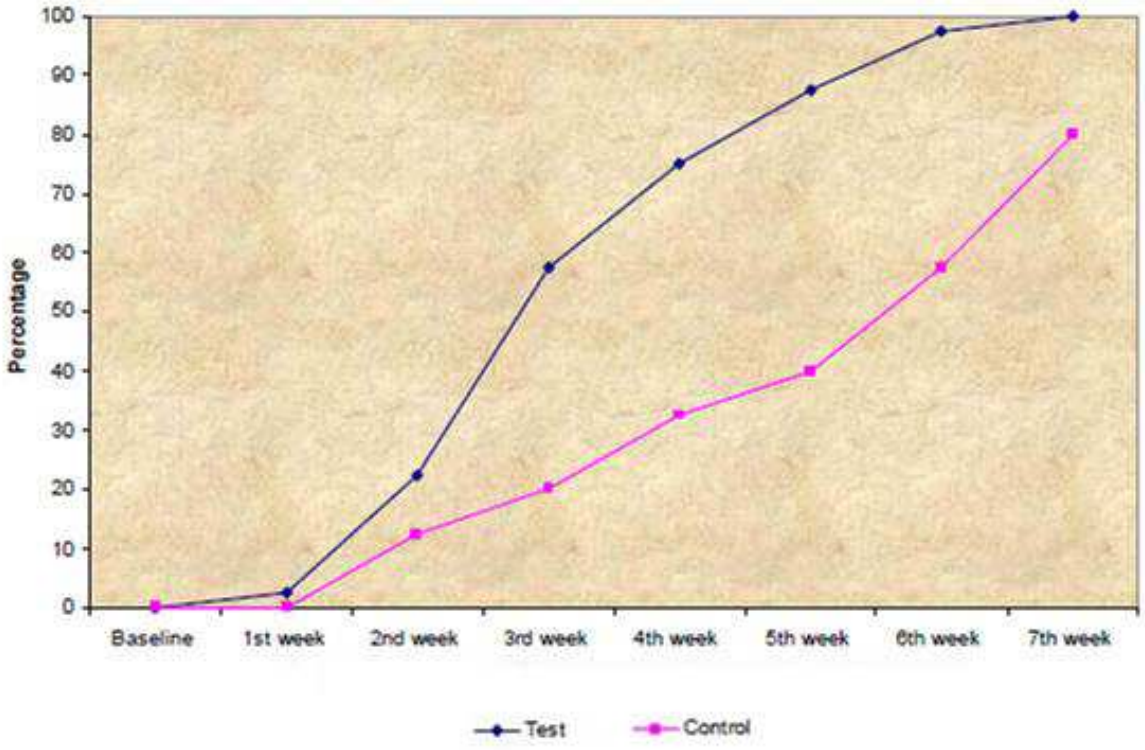
TEST GROUP

GRAPH-8:
SHOWING THE PRESENCE OF NECROTIC TISSUE OR SLOUGH IN CONTROL GROUP



CONTROL GROUP

GRAPH-9:
A COMPARATIVE LINE DIAGRAM



A comparative line diagram showing necrotic tissue or slough in Test and Control group in each week.

PRESENCE OF GRANULATION TISSUE

The number of patients with 75-00% wound filled with granulation tissue are significantly higher in Test group at 3rd week follow up (P<0.001), at 4th week (P < 0.001), at 5th week (P<0.001), at 6th week (P<0.001) and at the 7th week (P<0.05) when compared to control group as per the Chi-Square / Fisher Exact test.

TABLE –9:
PRESENCE OF GRANULATION TISSUE

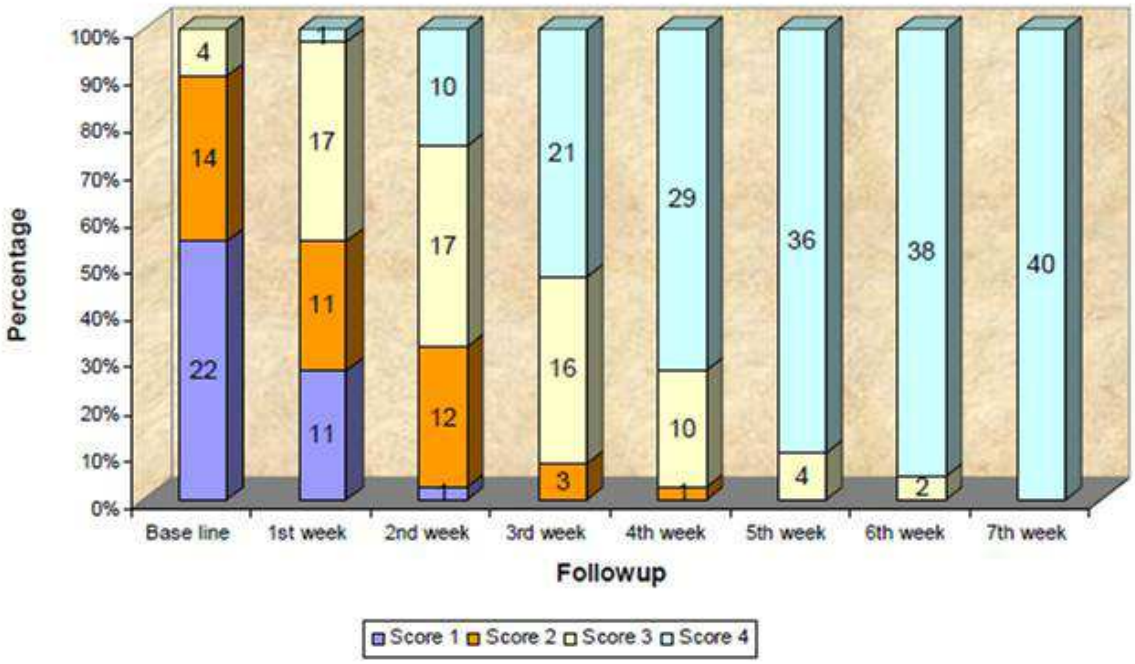
Study Period	Test group (n=40)				Control group (n=40)			
	1	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Baseline	22 (55.0)	14 (35.0)	4 (10.0)	-	23 (57.5)	13 (32.5)	4 (10.0)	-
1st Week	11 (27.5)	11 (27.5)	17 (42.5)	1 (2.5)	23 (57.5)	9 (22.5)	8 (20.0)	-
2nd Week	1 (2.5)	12 (30.0)	17 (42.5)	10 (25.0)	9 (22.5)	17 (42.5)	9 (22.5)	5 (12.5)
3rd Week	-	3 (7.5)	16 (40.0)	21 (52.5)	1 (2.5)	22 (55.0)	9 (22.5)	8 (20.0)
4th Week	-	1 (2.5)	10 (25.0)	29 (72.5)	-	12 (30.0)	16 (40.0)	12 (30.0)
5th Week	-	-	4 (10.0)	36 (90.0)	-	-	24 (60.0)	16 (40.0)
6th Week	-	-	2 (5.0)	38 (95.0)	-	-	21 (52.5)	19 (47.5)
7th Week	-	-	-	40 (100.0)	-	-	5 (12.5)	35 (87.5)
Infe-rence	Number of patients with 75-100% wound filled are significantly higher in Test group at 3rd Week follow-up (P<0.001), at 4th Week (P < 0.001), at 5th week (P < 0.001) at 6th week (P<0.001) and at the 7th Week (P<0.05) when compared to control group as per the Chi-square/Fisher Exact Test.							

Figures in brackets are percentages

Visual score

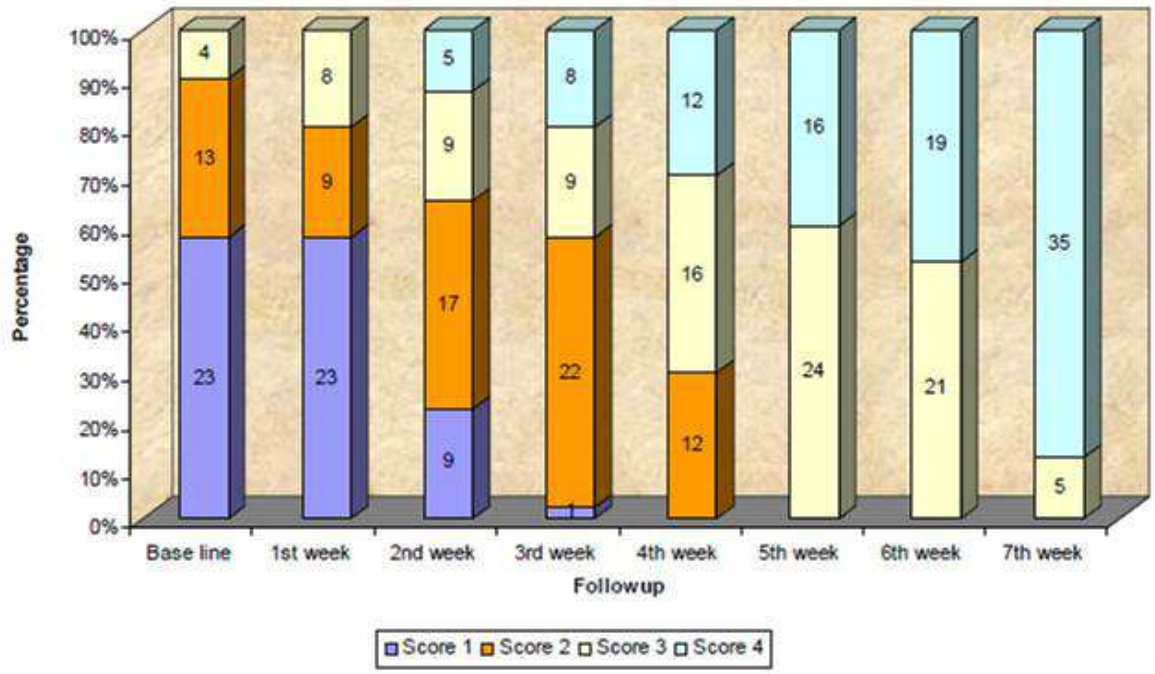
1. = no granulation present
2. = < 25% of wound filled
3. = 25-74% of wound filled
4. = 75-100% of wound filled

GRAPH-10:
SHOWING THE GRADUAL PROGRESS OF GRANULATION TISSUE IN TEST GROUP IN EACH WEEK



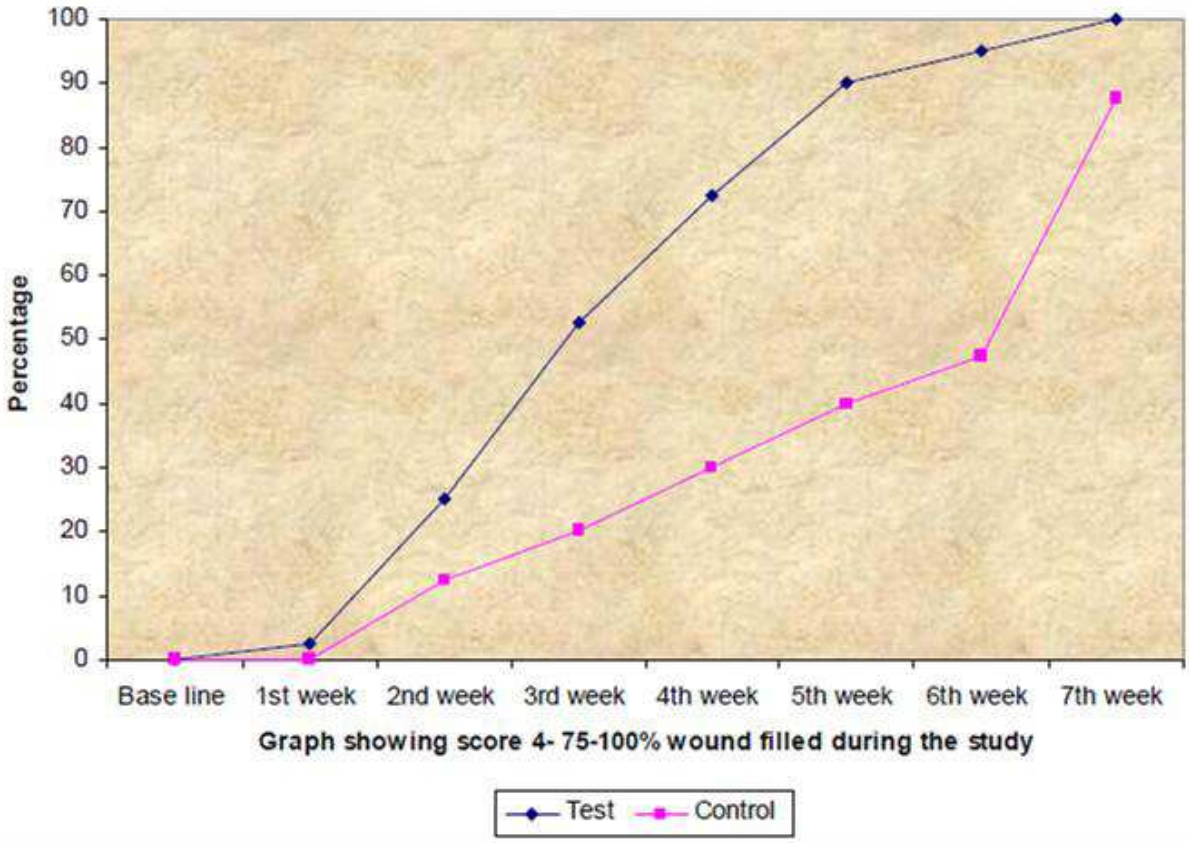
TEST GROUP

GRAPH-11:
SHOWING THE GRADUAL PROGRESS OF GRANULATION TISSUE IN CONTROL GROUP IN EACH WEEK



CONTROL GROUP

GRAPH-12:
LINE DIAGRAM SHOWING COMPARATIVE STUDY OF PROGRESS OF GRANULATION TISSUE IN TEST AND CONTROL GROUPS.



WOUND SURFACE AREA

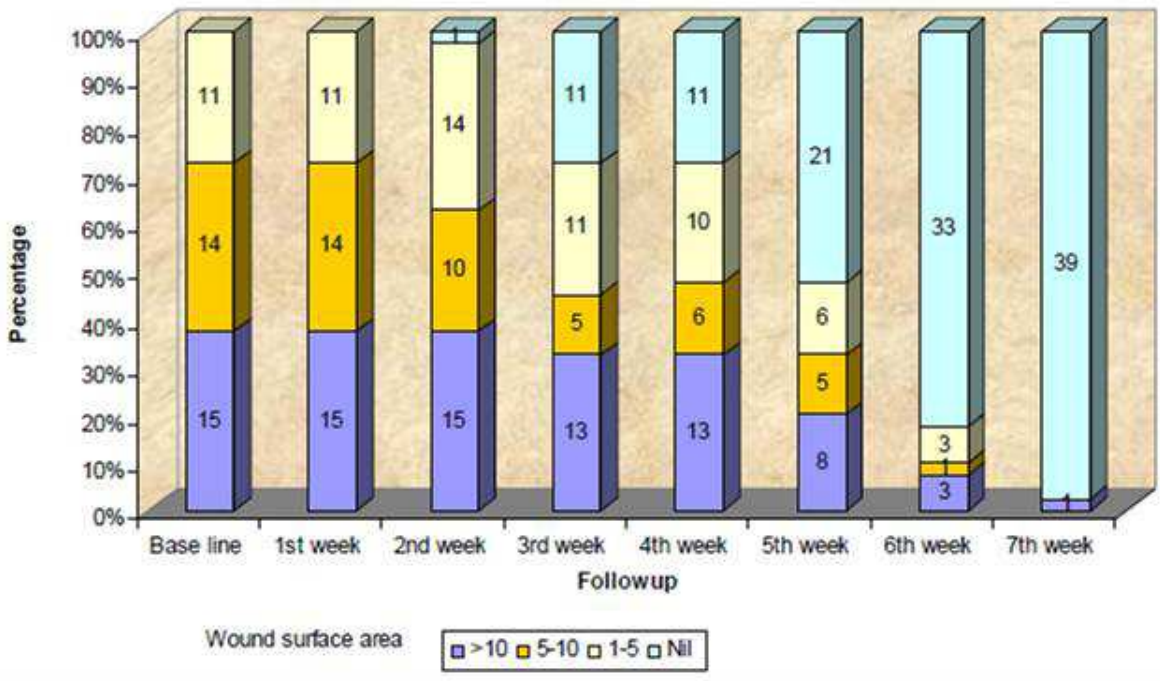
The number of patients with No wound surface (Nil) are significantly higher in Test group at 3rd week follow up (P< 0.05), at 4th week (P <0.05), at 5th week (P < 0.05), at 6th week (P < 0.001) and at the 7th week (P<0.001) when compared to control group as per the Chi-square / Fisher Exact test.

TABLE –10:
WOUND SURFACE AREA

Study period	Test group (n=40)				Control group (n=40)			
	Wound Surface Area (cm^2)							
	> 10	5-10	1-5	Nil	>10	5-10	1-5	Nil
Baseline	15 (37.5)	14 (35.0)	11 (27.5)	-	18 (45.0)	12 (30.0)	10 (25.0)	-
1st Week	15 (37.5)	14 (35.0)	11 (27.5)	-	19 (47.5)	12 (30.0)	9 (22.5)	-
2nd Week	15 (37.5)	10 (25.0)	14 (35.0)	1 (2.5)	21 (52.5)	9 (22.5)	10 (25.0)	-
3rd week	13 (32.5)	5 (12.5)	11 (27.5)	11 (27.5)	20 (50.0)	8 (20.0)	10 (25.0)	2 (5.0)
4th Week	13 (32.5)	6 (15.0)	10 (25.0)	11 (27.5)	21 (52.5)	6 (15.0)	11 (27.5)	2 (5.0)
5th Week	8 (20.0)	5 (12.5)	6 (15.0)	21 (52.5)	20 (50.0)	6 (15.0)	9 (22.5)	5 (12.5)
6th Week	3 (7.5)	1 (2.5)	3 (7.5)	33 (82.5)	19 (47.5)	8 (20.0)	4 (10.0)	9 (22.5)
7th Week	1 (2.5)	-	-	39 (97.5)	14 (35.0)	6 (15.0)	5 (12.5)	15 (37.5)
Inference	Number of patients with No-wound Surface (Nil) are significantly higher in Test group at 3rd Week follow-up (P<0.05), at 4th Week (P < 0.05), at 5th Week (P < 0.05), at 6th Week (P < 0.001) and at the 7th Week (P < 0.001) when compared to control group as per the Chi-Square/ Fisher Exact test.							

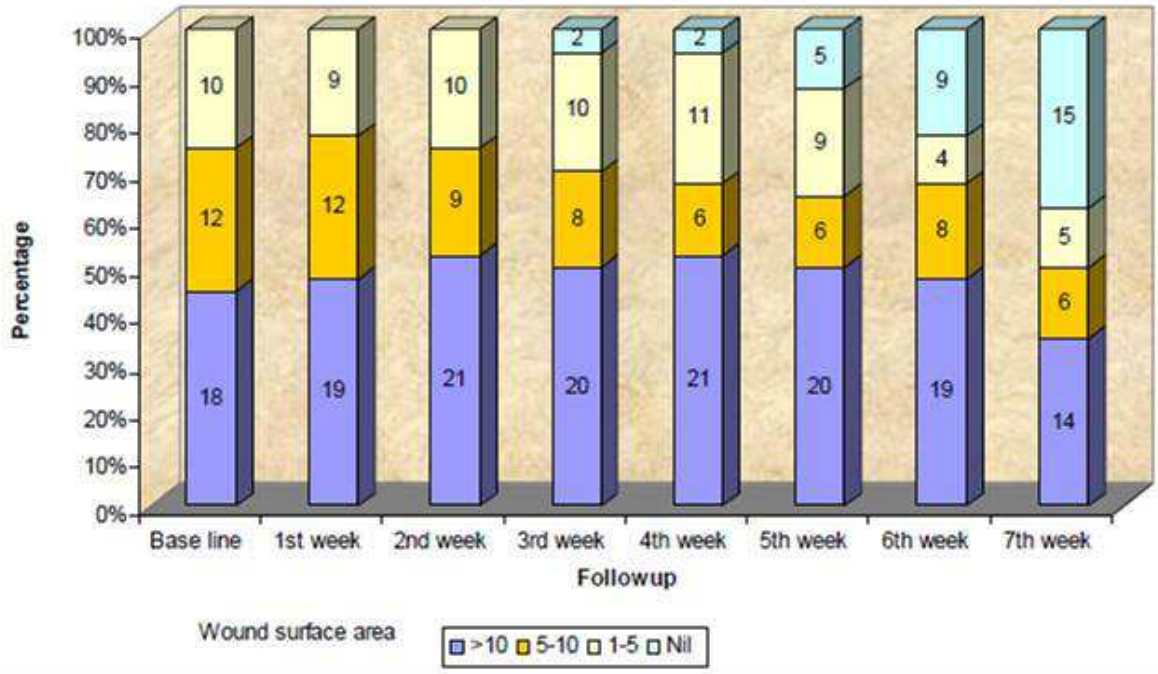
Nil – Flap, Heeled, SSG and Suturing

GRAPH-13:
SHOWING SHRINKING OF WOUND SURFACE AND THEIR FINAL TREATMENT LIKE SECONDARY SUTURING, SSG, FLAP AND COMPLETE WOUND HEALING (NIL)



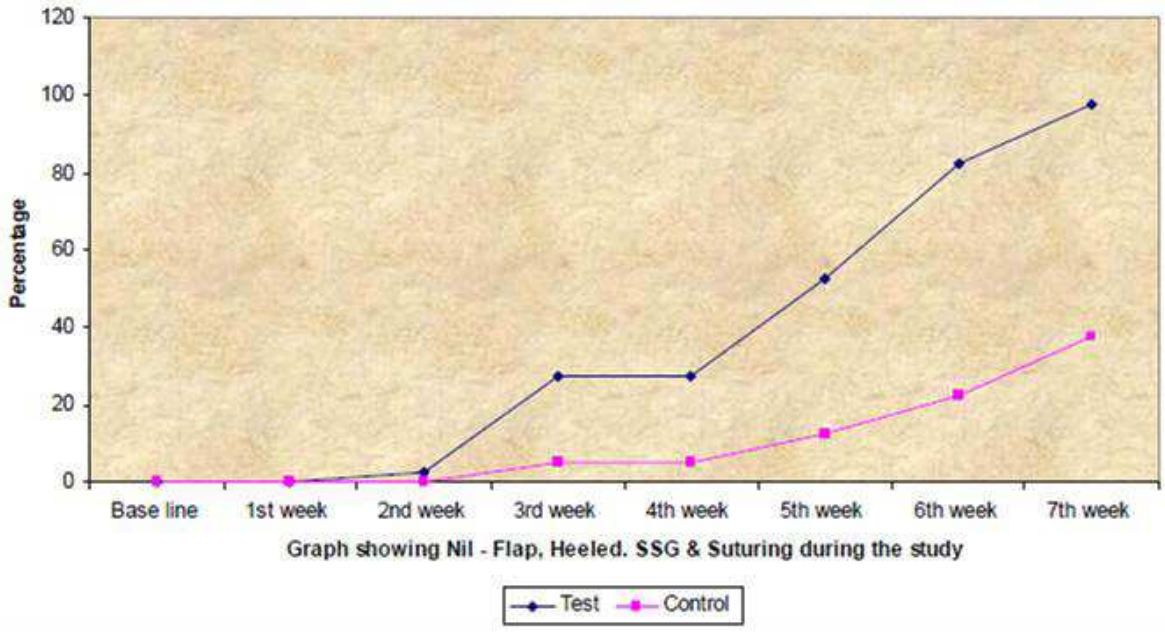
(TEST GROUP)

GRAPH-14:
SHOWING SHRINKING OF WOUND SURFACE AND THEIR FINAL TREATMENT LIKE SECONDARY SUTURING, SSG, FLAP AND COMPLETE WOUND HEALING (NIL)



(CONTROL GROUP)

GRAPH-15:
A COMPARATIVE LINE DIAGRAM SHOWING WOUND SHRINKAGE AND THEIR FINAL TREATMENT



A comparative line diagram showing wound shrinkage and their final treatment like secondary suturing, SSG, flap and complete wound healed.

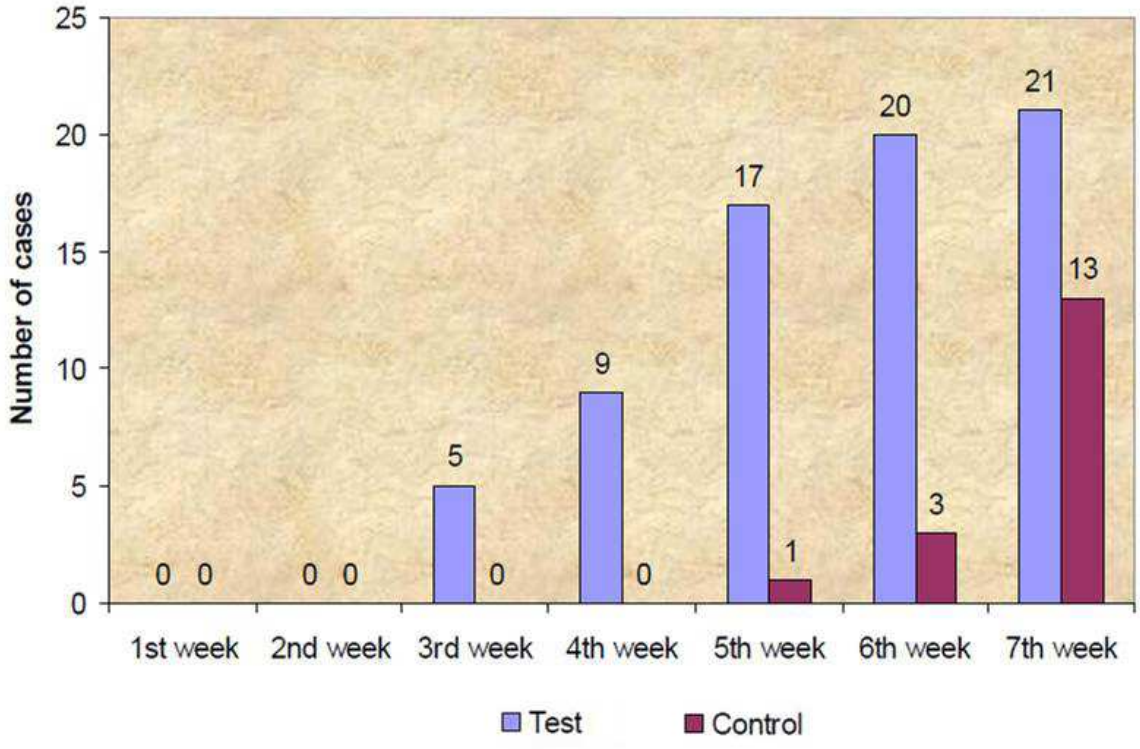
SPLIT SKIN GRAFT

Patients in test group are subjected to the skin graft as early as 3rd week, were as the patients in control group underwent skin graft only in 5th week. At the end of 6th week totally 21 patient in test group underwent S.S.G compare to the control group were only 3 patients.

TABLE -11:
SPLIT SKIN GRAFT

	Test	**Control**
1st week	Nil	Nil
2nd week	Nil	Nil
3rd week	5	Nil
4th week	9	Nil
5th week	17	1
6th week	20	3
7th week	21	13

GRAPH-16:
SHOWING SPLIT SKIN GRAFT IN TEST AND CONTROL GROUP



DISCUSSION

The number of patients studied was 80 and randomly divided into test group (40) and control group (40). Both the test and control groups were matched regarding their age, sex, diabetic status, nutritional status, and grade of ulcer.

In addition, there was no significant difference between the two groups with respect to baseline ulcer size and amount of nonviable tissue / slough.

The number of patients with no necrotic tissue is significantly higher in Test group at 3^{rd} week follow up ($P< 0.001$), at 4^{th} week ($P <0.001$), at 5^{th} week ($P <0.001$), at 6^{th} week ($P < 0.001$) and at the 7^{th} week ($P<0.01$) when compared to control group. There is minimal loss of viable tissue in the test group compared to that of control group this is because the number of bedside surgical debridement required is less and done superficially to remove dead tissue only.

The number of patients with 75-100% wound filled by granulation tissue is significantly higher in Test group at 3rd week follow up (P<0.001), at 4th week (P <0.001), at 5th week (P <0.001), at 6th week (P <0.001) and at the 7th week (P< 0.05) when compared to control group.

The number of patients with no wound surface (nil) is significantly higher in Test group at 3rd week follow up (P<0.05), at 4th week (P <0.05), at 5 week (P <0.05), at 6th week (P < 0.001) at the 7th week (P < 0.001) when compared to control group.

In addition to the above observation test group has experienced less pain and reduced mal odour from the ulcer site compared to that of control group. The duration of hospital stay was less in test group compared to control group.

The patients treated with Honey dressings had faster reduction of slough / necrotic tissue and increased granulation tissue. This study demonstrated that Honey dressings along with bed side surgical debridement had cumulative effect in reduction of slough, increase granulation tissue and faster wound bed preparation.

The test group patients had increased growth of the granulation tissue along with epithelisation which is generally correlated with the development of a granulating wound bed. All this are done with visual score. Hence it was not possible to determine if the granulation tissue

production was actually increased after treatment or if just more granulation became visible after debriding the ulcer But patients in test group produced better results than the control group.

The test group patients also experienced less pain than the control group because the need for the bed side surgical debridement is less than the control group

The test group patients under went skin grafting, secondary suturing and flap as early as 3rd week than control group because of faster wound bed preparation. The wound also healed faster this is due to increased epithelisation

CONCLUSION

1. The study was done to give an insight to the depth of ulcer foot management, as it has become a foremost problem in recent era.

2. The goal of this study was to enhance the wound / ulcers to be devoid of necrotic tissue and debris and to remove the senescent cells from the wound bed using Honey dressing and preparing the wound for a healthy bed of granulation tissue to promote a rapid healing.

3. This is achieved in our study by using Honey dressing for ulcers which is proved to be highly effective in reduction of slough, promoting granulation tissue formation and re epithelisation

4. Honey dressing proved to be significantly effective in wound bed preparation in comparison with conventional treatment with normal saline.

SUMMARY

A short introduction to foot ulcer, its incidence and complications is given with an account of the historical aspect of diabetes mellitus. The literature in respect of clinico-pathology and diagnostic aspect and the management of foot ulcer is revived.

Both the test and control group were matched regarding their age, diabetic status, nutritional status, and grade of ulcer. There is no significant difference between the two groups regarding baseline ulcer size and area of necrotic tissue. The reduction of slough is as early as 3rd week in the test group than the control group.

The number of patients with 75-100% wound filled with granulation tissue is as early as 3rd week in test group than the control group where it took more than 4 weeks.

The number of patients who underwent secondary suturing, skin graft and flap are significantly higher and also as early as 3rd week in test group than the control group.

Our study concluded that Honey is an effective topical applicant in faster reduction of slough, regeneration of granulation tissue and re-epithelisation in chronic foot ulcer.

This helps in faster wound bed preparation for healing, suturing, skin graft and Flap.

ANNEXURES

ABBREVIATIONS

PDGF	-	Platelet Derived Growth Factor
TNF	-	Tumour Necrosis Factor
ADP	-	Adenosine Di Phosphate
EGF	-	Eepithelial growth factor
FGF	-	Fibroblast Growth Factor
TGF beta	-	Transforming Growth Factor Beta
VEGF	-	Vasculo Endothelial Growth Factor
VDRL	-	Venereal Disease Research Laboratory
MIC	-	Minimum Inhibitory Concentration
MRSA	-	Methicillin Resistant Staphylococcus Aureus
VRE	-	Vancomycin Resistant Enterococci
H_2O_2	-	Hydrogen Peroxide.

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PROFORMA

Case no : Hospital No. :

Name : DOA :

Age DOD :

Sex :

Address :

Religion :

Occupation :

Socio-economic Class :

HISTORY

Onset of Ulcer : Trauma / Spontaneous

Site of ulcer : Sole-fore foot / heel,

dorsum of foot, web space

Wound Size : ……cm^2

Duration of Ulcer :

Progress : Progress gradual (Or) Rapidly

Pain : Yes/No

Discharge : pus / Serous / Sero-sanguinous

Treatment : Received / Not Received

DIABETIC HISTORY

History of diabetes Mellitus :

Duration of diabetes Mellitus :

Type of Treatment at Admission : Oral / Inj

Treatment for Diabetes : Regular / Irregular

INVESTIGATIONS

Haematological

Hb% , PCV, T.C, D.C, E.S.R

B.T, C.T , Blood grouping

Blood Urea , S.Creatinine

Urine examination : Albumin, Sugar, Ketones

Doppler Studies :

X-Ray of Foot :

Pus for Culture Sensitivity :

CLINICAL FEATURES FOLLOW-UP

Baseline

1st Week

2nd Week

3rd Week

4th Week

5th Week

6th Week

7th Week for

1. PRESENCE OF NECROTIC TISSUE OR STRANDS OF COLLAGEN

   Visual Scores :

   1. = 76-100%, 2. =51-75 %, 3. 26-50%, 4. 11-25%,

   5. = 0-10%, 6. No necrotic tissue covering the ulcer

2. PRESENCE OF GRANULATION TISSUE

   Visual Scores

   1. = 76-100%, 2. = 51-75 %, 3. 26-50%, 4. 11-25%,

   5. = 0-10%, 6. No Necrotic Tissue covering the Ulcer

3. WOUND SURFACE AREA (CM^2)

KEY TO MASTER CHART

Sl. No	-	Serial Number
D.M	-	Diabetes Mellitus
F	-	Female
M	-	Male
S.S.G	-	Split skin grafting
S D	-	Standard deviation
S E C S	-	Socio economic status
P	-	Poor
O	-	Oral
I	-	Insulin
R	-	Regular
I R	-	Irregular
T	-	Trauma
S	-	Spontaneous
N R	-	Not received
Re	-	Received
G	-	Gradual
Ra	-	Rapid
Bp	-	Blood Pressure
P R	-	Pulse Rate
Hb	-	Hemoglobin
F B S	-	Fasting Blood sugar
P P B S	-	Post prandial Blood sugar
BU	-	Blood Urea
S C	-	Serum creatinine
N	-	Normal

Sl. No.	Name	Age	Sex	Hospital No.	Clinical History						Size of ulcer in cms	Grade of ulcer	Progress	Pain	Investigations					Urine Analysis			Doppler	X-ray	Presence of Necrotic tissue or strains of collagen								Presence of Granulation tissue								Wound surface area (cm2)								Duration of stay in the study(period(days)
					DM	Duration in years	Treatment R/IR	Oral / Insulin	Ulcer onset	Treatment R NR					Hb%	FBS	PPBS	BU	SC	Sugar	Alumbin	Ketone			Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	
1	kuruvammal	51	F	265560	+	16	IR	O	T	R	12	III	G	+	10	132	196	18	0.8	+++	-	-	N	N	1	2	1	2	3	4	5	6	1	1	2	2	3	3	3	4	12	12	12	11	10	10	10	S.S.G	42
2	vellayappan	60	M	261133	+	10	R	O	S	R	8	IV	G	+	8.4	152	216	20	0.9	+	-	-	N	N	1	1	2	3	3	4	5	6	1	1	2	2	3	3	3	4	8	8	8	7.2	6	6	4	2	40
3	karuppusamy	65	M	285566	+	10	IR	O	T	NR	6	III	G	-	13	148	216	16	0.8	+	-	-	N	N	2	2	3	4	5	6	6	6	2	2	3	3	3	4	4	4	6	6	6	4.4	4	3	2	Healed	49
4	murugesan	60	M	280334	+	8	IR	O	S	NR	4	II	G	-	12	184	218	20	1	+	-	-	N	N	2	3	4	5	6	6	6	6	2	2	3	3	4	4	4	4	4	4	2	1	1	Healed	Healed	Healed	40
5	kuppusamy	40	M	301980	+	5	R	O	T	R	14	IV	G	-	12	146	198	20	0.6	+	-	-	N	N	1	1	2	2	3	3	4	5	1	1	2	2	3	3	3	4	14	14	14	14	12	12	11	S.S.G	49
6	sundaram	35	M	281558	-	-	-	-	T	R	11	III	G	+	13	146	222	22	0.8	+	-	-	N	N	1	1	2	2	3	4	5	6	1	1	2	2	3	3	3	4	11	11	10	10	8.8	8	7	S.S.G	49
7	Lakshmi	45	F	268786	-	-	-	-	S	R	3	II	G	-	11	148	210	20	0.7	+	-	-	N	N	3	5	6	6	6	6	6	6	3	3	4	4	4	4	4	4	3	3	2	1	Healed	Healed	Healed	Healed	35
8	suresh	28	M	263797	-	-	-	-	T	R	4	III	G	-	12	140	190	16	0.7	+	-	-	N	N	3	5	6	6	6	6	6	6	3	3	4	4	4	4	4	4	4	4	2	1	Healed	Healed	Healed	Healed	38
9	ganesan	32	M	265040	+	2	-	-	S	R	12	IV	G	+	13	140	196	22	1.1	+	-	-	N	N	1	1	2	1	3	4	5	6	1	1	2	2	2	3	3	3	12	12	12	11	11	10	10	10	>49
10	parthipan	71	M	263525	+	20	R	O	T	NR	10	US	G	-	9.8	148	198	20	0.9	+	-	-	N	N	1	1	2	2	3	4	5	6	1	1	2	2	3	3	3	4	10	10	10	10	10	9	8.6	8	>49
11	seethammal	60	F	272641	+	8	IR	O	S	NR	16	IV	G	-	8.2	150	230	28	0.9	++	-	-	N	N	1	1	3	4	5	6	6	6	1	1	2	3	3	4	4	4	16	16	16	14	14	12	S.S.G	S.S.G	42
12	Chandammal	48	F	281949	+	6	R	O	T	R	2	II	G	+	13	148	198	20	0.8	+	-	-	N	N	3	5	6	6	6	6	6	6	3	3	4	4	4	4	4	4	2	2	1	Healed	Healed	Healed	Healed	Healed	15
13	Manickam	28	M	274628	-	-	-	-	T	R	7	III	G	+	11	162	240	22	1.1	+	-	+	N	N	1	1	2	2	3	3	4	5	1	1	2	2	3	3	3	4	7	8	8	7	6.6	6	4	2	48
14	kabeer	65	M	290550	+	10	IR	O	T	S	16	IV	G	-	9.8	152	204	18	1.2	++	-	-	N	N	1	1	1	3	4	5	6	6	1	1	1	2	2	3	4	4	16	18	18	16.8	16	14	12	S.S.G	48
15	sukumaran	59	M	253367	+	8	IR	O	T	NR	4	II	G	-	9.4	148	204	26	0.9	++	-	-	N	N	3	4	5	6	6	6	6	6	3	3	3	4	4	4	4	4	4	3	3	2	1	suturing	suturing	suturing	44
16	chellaya	30	M	271456	-	-	-	-	T	R	6	III	G	+	13	132	196	14	0.8	+	-	-	N	N	2	3	5	6	6	6	6	6	2	2	3	4	4	4	4	4	6	6	5	4	2	1	Healed	Healed	45
17	meenadevi	45	F	250870	-	-	-	-	S	R	18	IV	G	+	9.2	144	198	12	0.9	++	-	-	N	N	1	1	2	2	3	3	4	5	1	1	2	2	2	3	3	4	18	20	19	18	18	16.4	Flap	Flap	45
18	sanghumari	65	M	246458	+	20	R	O	S	NR	2	III	G	-	9.4	132	198	22	1.2	++	-	-	N	N	2	4	6	6	6	6	6	6	2	3	4	4	4	4	4	4	2	2	1	Healed	Healed	Healed	Healed	Healed	15
19	vellaisamy	86	M	254804	+	25	IR	O	T	NR	13	US	G	-	10	168	218	26	1.3	+++	+	+	N	N	2	3	4	5	6	6	6	6	2	2	3	3	4	4	4	4	13	13	12	12	12	S.S.G	S.S.G	S.S.G	38
20	karuppiah	68	M	283346	+	10	R	I/O	T	R	8	IV	G	+	13	202	278	28	1.4	+++	-	+	N	N	1	1	2	3	4	5	6	6	1	1	2	2	3	3	4	4	8	10	8	8	6	6	S.S.G	S.S.G	45

Master chart(control)

Sl. No.	Name	Age	Sex	Hospital No.	Clinical History						Size of ulcer in cms	Grade of ulcer	Progress	Pain	Investigations					Urine Analysis			Doppler	X-ray	Presence of Necrotic tissue or strains of collagen							Presence of Granulation tissue							Wound surface area (cm2)							Duration of stay in the study period(days)
					DM	Duration in years	Treatment R/IR	Oral / Insulin	Ulcer onset	Treatment R NR					Hb%	FBS	PPBS	BU	SC	Sugar	Alumbin	Ketone			Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	
21	meenakshi	65	F	259068	+	7	R	O	S	R	20	III	G	+	11	250	300	38	1.5	+++ +	+	+	N	N	1	2	2	3	3	4	5	5	1	1	2	2	3	3	3	4	20	22	22	22	20	18	18	S.S.G	48
22	Geetha	56	F	253733	+	4	R	I/O	T	R	28	IV	G	-	8.2	190	250	22	0.9	+++	-	-	N	N	1	1	1	3	4	5	6	6	1	1	1	1	2	3	3	3	28	30	32	32	30	30	28	26	>49
23	kelappan	62	M	249058	+	15	IR	O	T	NR	5	IV	G	-	12	203	268	33	1.2	++	-	-	N	N	1	1	2	1	3	4	5	6	1	1	1	1	2	3	3	4	5	6	8	8	8	7	6.2	S.S.G	48
24	Subhash	58	M	249003	+	4	R	O	T	R	6	III	G	-	12	180	240	28	1	+	+	-	N	N	2	2	1	3	4	5	6	6	2	2	2	2	3	3	3	4	6	8	9	9	9	8	8	S.S.G	47
25	nageswari	44	F	245627	-	-	-	-	S	NR	12	IV	R	+	7.6	280	380	33	1.2	+++ +	+	+	N	N	1	1	2	2	3	4	4	5	1	1	2	2	2	3	3	4	12	14	14	12	12	10	8	8	49
26	saraladevi	63	M	253499	+	10	R	I/O	S	NR	3	II	G	+	10	170	200	20	0.9	++	-	-	N	N	3	4	6	6	6	6	6	6	2	3	4	4	4	4	4	4	3	3	2	2	1	Healed	Healed	Healed	37
27	Veeramani	52	M	285558	+	8	R	O	S	R	8	US	G	+	9.6	140	190	44	1.5	+	-	-	N	N	2	2	3	5	6	6	6	6	2	2	3	3	4	4	4	4	8	8	7	6	4	2	1	Healed	48
28	Maniappan	44	M	293219	+	7	R	I/O	T	R	14	III	G	-	12	130	200	33	0.8	++	-	-	N	N	1	1	2	3	4	5	6	6	1	1	1	2	2	3	3	4	14	16	16	16	15	14	14	14	>49
29	Sukudevan	58	M	247256	+	16	R	I/O	T	R	10	IV	R	+	10	210	280	46	2.2	+++	+	-	N	N	1	1	2	3	4	5	5	6	1	1	2	2	3	3	3	4	10	14	14	14	13	12	11	S.S.G	48
30	pandiammal	72	F	265611	+	14	R	I/O	S	R	5	III	G	-	8	188	210	18	0.7	++	++	-	N	N	2	2	3	5	6	6	6	6	2	2	2	3	3	4	4	4	5	5	5	4	4	3	2	1	49
31	gosamy	84	M	254466	+	20	IR	I/O	T	R	12	IV	R	+	13	200	240	22	1.4	++	-	-	N	N	1	2	3	4	5	5	6	6	1	1	2	2	3	3	4	4	12	16	16	15	14	14	12	S.S.G	47
32	pandidurai	70	M	225171	+	12	R	O	T	R	16	US	G	+	12	270	380	18	1.4	+++	+	+	N	N	1	1	2	2	3	4	5	5	1	1	1	2	2	3	3	4	16	18	20	20	20	18	16	S.S.G	46
33	Selvi	66	F	257601	+	9	R	I/O	S	R	2	III	G	-	12	144	200	32	1	+	++	-	N	N	3	3	4	6	6	6	6	6	2	3	3	4	4	4	4	4	2	2	1	1	Healed	Healed	Healed	Healed	30
34	Vijaylaxmi	67	F	244592	+	6	IR	O	T	R	17	IV	R	+	7.5	310	410	54	2.4	+++ +	-	-	N	N	1	1	2	2	3	4	5	5	1	1	1	2	2	3	3	3	17	20	20	20	20	18	18	18	>49
35	Ramesh	46	M	301679	-	-	-	-	S	NR	6	US	G	-	14	142	180	18	1	++	-	-	N	N	3	3	4	5	6	6	6	6	2	3	3	3	4	4	4	4	6	6	4	4	3	1	Healed	Healed	45
36	Rukmini	39	F	270238	-	-	-	-	S	R	12	US	G	+	6.5	160	200	22	1.4	+++	-	-	N	N	2	2	2	3	4	5	6	6	2	2		3	3	3	3	4	12	12	12	12	11	10	10	8	>49
37	Karthikeyan	50	M	264587	+	3	R	O	T	R	9	IV	G	+	9.4	174	230	32	2	+++	+	-	N	N	1	1	2	2	4	5	5	5	1	1	1	2	2	3	3	3	9	10	10	10	10	9	8	8	>49
38	Manikandan	48	M	273726	+	5	R	O	T	R	24	III	R	+	12	230	320	44	1.4	+++ +	+	+	N	N	1	1	1	2	3	4	4	4	1	1	1	2	2	3	3	4	24	26	26	26	26	24	23	S.S.G	48
39	Neelamegham	55	F	290380	-	9	IR	I/O	T	NR	6	II	G	+	11	136	180	14	0.8	+	-	-	N	N	2	2	3	4	5	6	6	6	2	2	3	3	3	4	4	4	6	6	6	5	4	2	Healed	Healed	45
40	Karuppusamy	74	M	242865	+	12	IR	I/O	T	NR	22	III	G	-	13	210	320	56	1.3	+++ +	-	-	N	N	1	1	1	2	2	4	4	4	1	1	1	2	2	3	3	3	22	22	24	26	26	26	25	26	>49

Master chart (control)

Sl. No.	Name	Age	Sex	Hospital No.	Clinical History										Investigations					Urine Analysis						Presence of Necrotic tissue or strains of collagen							Presence of Granulation tissue							Wound surface area (cm2)							Healed days
					DM	Duration in years	Treatment R/IR	Oral / Insulin	Ulcer onset	Treatment R NR	Ulcer in cms	Ulcer Grade	Ulcer Site	Pain	Hb%	FBS	PPBS	BU	SC	Sugar	Alumbin	Ketone	Doppler	X-ray	Base line	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	
1	Thenmozhi	61	F	265543	+	16	IR	O	T	R	12	III	G	+	10	128	196	18	0.8	+++	-	-	N	N	1	1	2	3	4	5	6	1	1	2	2	3	3	3	4	12	12	12	11	10	10	10	S.S.G	43
2	vellaichamy	70	M	12096	+	10	R	O	S	R	8	IV	G	+	8.4	108	216	20	0.9	+	-	-	N	N	1	2	3	3	4	5	6	1	1	2	2	3	3	3	4	8	8	8	7.2	6	6	4	2	41
3	Kumaran	55	M	43287	-	-	IR	-	T	NR	6	III	G	-	13	98	216	16	0.8	+	-	-	N	N	2	3	4	5	6	6	6	2	2	3	3	3	4	4	4	6	6	6	4.4	4	3	2	Healed	48
4	murugayya	40	M	28434	+	8	IR	O	S	NR	4	II	G	-	12	110	218	20	1	+	-	-	N	N	2	4	5	6	6	6	6	2	2	3	3	4	4	4	4	4	4	2	1	1	Healed	Healed	Healed	38
5	ganesh	40	M	5438	-	-	R	-	T	R	14	IV	G	-	12	126	198	20	0.6	+	-	-	N	N	1	2	2	3	3	4	5	1	1	2	2	3	3	3	4	14	14	14	14	12	12	11	S.S.G	50
6	karthik	55	M	32675	-	-	-	-	T	R	11	III	G	+	13	100	222	22	0.8	+	-	-	N	N	1	2	2	3	4	5	6	1	1	2	2	3	3	3	4	11	11	10	10	8.8	8	7	S.S.G	51
7	bhuvaneswari	65	F	218754	+	10	-	i	S	R	3	II	G	-	11	99	210	20	0.7	+	-	-	N	N	3	6	6	6	6	6	6	3	3	4	4	4	4	4	4	3	3	2	1	Healed	Healed	Healed	Healed	36
8	ramanan	38	M	326574	+	8	-	o	T	R	4	III	G	-	12	118	190	16	0.7	+	-	-	N	N	3	6	6	6	6	6	6	3	3	4	4	4	4	4	4	4	4	2	1	Healed	Healed	Healed	Healed	39
9	gopalan	42	M	65371	+	2	-	I	S	R	12	IV	G	+	13	120	196	22	1.1	+	-	-	N	N	1	2	1	3	4	5	6	1	1	2	2	2	3	3	3	12	12	12	11	11	10	10	10	48
10	chellasamy	61	M	43875	+	20	R	O	T	NR	10	US	G	-	9.8	120	198	20	0.9	+	-	-	N	N	1	2	2	3	4	5	6	1	1	2	2	3	3	3	4	10	10	10	10	10	9	8.6	8	39
11	Ameena beegum	50	F	231784	+	8	IR	O	S	NR	16	IV	G	-	8.2	96	230	28	0.9	++	-	-	N	N	1	3	4	5	6	6	6	1	1	2	3	3	4	4	4	16	16	16	14	14	12	S.S.G	S.S.G	38
12	kottiyammal	38	F	327186	+	6	R	O	T	R	2	II	G	+	13	88	198	20	0.8	+	-	-	N	N	3	6	6	6	6	6	6	3	3	4	4	4	4	4	4	2	2	1	Healed	Healed	Healed	Healed	Healed	16
13	manikandan	38	M	7438	-	7	-	-	T	R	7	III	G	+	11	78	240	22	1.1	+	-	+	N	N	1	2	2	3	3	4	5	1	1	2	2	3	3	3	4	7	8	8	7	6.6	6	4	2	46
14	Jabbar singh	55	M	27530	+	10	IR	O	T	S	16	IV	G	-	9.8	104	204	18	1.2	++	-	-	N	N	1	1	3	4	5	6	6	1	1	1	2	2	3	4	4	16	18	18	16.8	16	14	12	S.S.G	50
15	rajeswaran	69	M	165437	+	8	IR	O	T	NR	4	II	G	-	9.4	126	204	26	0.9	++	-	-	N	N	3	5	6	6	6	6	6	3	3	3	4	4	4	4	4	4	3	3	2	1	suturing	suturing	suturing	46
16	rajasekharan	40	M	26439	-	-	-	-	T	R	6	III	G	+	13	122	196	14	0.8	+	-	-	N	N	2	5	6	6	6	6	6	2	2	3	4	4	4	4	4	6	6	5	4	2	1	Healed	Healed	47
17	lathammal	35	F	25432	-	-	-	-	S	R	18	IV	G	+	9.2	114	198	12	0.9	++	-	-	N	N	1	2	2	3	3	4	5	1	1	2	2	2	3	3	4	18	20	19	18	18	16.4	Flap	Flap	46
18	godson	55	M	244748	+	20	R	O	S	NR	2	III	G	-	9.4	99	198	22	1.2	++	-	-	N	N	2	6	6	6	6	6	6	2	3	4	4	4	4	4	4	2	2	1	Healed	Healed	Healed	Healed	Healed	18
19	pandiappan	76	M	18424	-	-	IR	-	T	NR	13	US	G	-	10	120	218	26	1.3	+++	+	+	N	N	2	4	5	6	6	6	6	2	2	3	3	4	4	4	4	13	13	12	12	12	S.S.G	S.S.G	S.S.G	39
20	maniappan	58	M	63289	+	10	R	I/O	T	R	8	IV	G	+	13	100	278	28	1.4	+++	-	+	N	N	1	2	3	4	5	6	6	1	1	2	2	3	3	4	4	8	10	8	8	6	6	S.S.G	S.S.G	46

Master chart(test)

Sl. No.	Name	Age	Sex	Hospital No.	Clinical History						Size of ulcer in cms	Grade of ulcer	Progress	Pain	Investigations					Urine Analysis			Doppler	X-ray	Presence of Necrotic tissue or strains of collagen							Presence of Granulation tissue							Wound surface area (cm2)							Duration of stay in the study period(days)
					DM	Duration in years	Treatment R/IR	Oral / Insulin	Ulcer onset	Treatment R NR					Hb%	FBS	PPBS	BU	SC	Sugar	Alumbin	Ketone			Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	Base line	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	
21	thenmozhi	55	F	32876	+	7	R	O	S	R	20	III	G	+	11	250	300	38	1.5	+++ +	+	+	N	N	1	2	2	3	3	4	5	5	1	1	2	2	3	3	3	4	20	22	22	22	20	18	18	S.S.G	46
22	swapnajothi	66	F	243187	+	4	R	I/O	T	R	28	IV	G	-	8.2	190	250	22	0.9	+++	-	-	N	N	1	1	1	3	4	5	6	6	1	1	1	1	2	3	3	3	28	30	32	32	30	30	28	26	51
23	hallayya	72	M	54278	+	15	IR	O	T	NR	5	IV	G	-	12	203	268	33	1.2	++	-	-	N	N	1	1	2	1	3	4	5	6	1	1	1	1	2	3	3	4	5	6	8	8	8	7	6.2	S.S.G	35
24	rajesh	48	M	54387	+	4	R	O	T	R	6	III	G	-	12	180	240	28	1	+	+	-	N	N	2	2	1	3	4	5	6	6	2	2	2	2	3	3	3	4	6	8	9	9	9	8	8	S.S.G	47
25	bharathi	34	F	24739	-	-	-	-	S	NR	12	IV	R	+	7.6	280	380	33	1.2	+++ +	+	+	N	N	1	1	2	2	3	4	4	5	1	1	2	2	2	3	3	4	12	14	14	12	12	10	8	8	32
26	chenthamara	53	M	25832	+	10	R	I/O	S	NR	3	II	G	+	10	170	200	20	0.9	++	-	-	N	N	3	4	6	6	6	6	6	6	2	3	4	4	4	4	4	4	3	3	2	2	1	Healed	Healed	Healed	28
27	veeramani	42	M	32158	+	8	R	O	S	R	8	US	G	+	9.6	140	190	44	1.5	+	-	-	N	N	2	2	3	5	6	6	6	6	2	2	3	3	4	4	4	4	8	8	7	6	4	2	1	Healed	42
28	palaniappan	34	M	29164	+	7	R	I/O	T	R	14	III	G	-	12	130	200	33	0.8	++	-	-	N	N	1	1	2	3	4	5	6	6	1	1	1	2	2	3	3	4	14	16	16	16	15	14	14	14	39
29	arul	68	M	24729	+	16	R	I/O	T	R	10	IV	R	+	10	210	280	46	2.2	+++	+	-	N	N	1	1	2	3	4	5	5	6	1	1	2	2	3	3	3	4	10	14	14	14	13	12	11	S.S.G	36
30	kanimozhi	62	F	26824	-	-	-	-	S	R	5	III	G	-	8	188	210	18	0.7	++	++	-	N	N	2	2	3	5	6	6	6	6	2	2	2	3	3	4	4	4	5	5	5	4	4	3	2	1	21
31	selladurai	74	M	27245	+	20	IR	I/O	T	R	12	IV	R	+	13	200	240	22	1.4	++	-	-	N	N	1	2	3	4	5	5	6	6	1	1	2	2	3	3	4	4	12	16	16	15	14	14	12	S.S.G	42
32	kabeer	60	M	225634	+	12	R	O	T	R	16	US	G	+	12	270	380	18	1.4	+++	+	+	N	N	1	1	2	2	3	4	5	5	1	1	1	2	2	3	3	4	16	18	20	20	20	18	16	S.S.G	38
33	malar	66	F	25835	+	9	R	I/O	S	R	2	III	G	-	12	144	200	32	1	+	++	-	N	N	3	3	4	6	6	6	6	6	2	3	3	4	4	4	4	4	2	2	1	1	Healed	Healed	Healed	Healed	28
34	mariapushpam	77	F	248352	+	6	IR	O	T	R	17	IV	R	+	7.5	310	410	54	2.4	+++ +	-	-	N	N	1	1	2	2	3	4	5	5	1	1	1	2	2	3	3	3	17	20	20	20	20	18	18	18	42
35	karthikeyan	46	M	30379	-	-	-	-	S	NR	6	US	G	-	14	142	180	18	1	++	-	-	N	N	3	3	4	5	6	6	6	6	2	3	3	3	4	4	4	4	6	6	4	4	3	1	Healed	Healed	45
36	pushpavalli	39	F	29238	-	-	-	-	S	R	12	US	G	+	6.5	160	200	22	1.4	+++	-	-	N	N	2	2	2	3	4	5	6	6	2	2		3	3	3	3	4	12	12	12	12	11	10	10	8	49
37	Krishnamoorthy	50	M	21687	+	3	R	O	T	R	9	IV	G	+	9.4	174	230	32	2	+++	+	-	N	N	1	1	2	2	4	5	5	5	1	1	1	2	2	3	3	3	9	10	10	10	10	9	8	8	47
38	Manickam	38	M	8268	+	5	R	O	T	R	24	III	R	+	12	230	320	44	1.4	+++ +	+	+	N	N	1	1	1	2	3	4	4	4	1	1	1	2	2	3	3	4	24	26	26	26	26	24	23	S.S.G	36
39	padmavathy	45	F	29285	-	9	IR	I/O	T	NR	6	II	G	+	11	136	180	14	0.8	+	-	-	N	N	2	2	3	4	5	6	6	6	2	2	3	3	3	4	4	4	6	6	6	5	4	2	Healed	Healed	42
40	solaivanthan	64	M	28351	+	12	IR	I/O	T	NR	22	III	G	-	13	210	320	56	1.3	+++ +	-	-	N	N	1	1	1	2	2	4	4	4	1	1	1	2	2	3	3	3	22	22	24	26	26	26	25	26	>49

(Master chart-test)