A Dissertation on

"A COMPARATIVE STUDY OF TOPICAL PLATELET DERIVED GROWTH FACTOR (RH-PDGF) VERSUS HYDROGEL VERSUS NORMAL SALINE DRESSING FOR TREATING DIABETIC FOOT ULCERS"

Dissertation submitted

In partial fulfilment of the regulations

For the award of the degree of

M.S.DEGREE BRANCH-I

GENERAL SURGERY

Of

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

E.S.I.C.MEDICAL COLLEGE & PGIMSR,

K.K.NAGAR, CHENNAI-78

APRIL-2020

DECLARATION BY THE CANDIDATE

I Solemnly declare that this dissertation entitled "**A COMPARATIVE STUDY OF TOPICAL PLATELET DERIVED GROWTH FACTOR (RH-PDGF) VERSUS HYDROGEL VERSUS NORMAL SALINE DRESSING FOR TREATING DIABETIC FOOT ULCERS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.BHANUMATI GIRIDHARAN,** Department of General Surgery, ESIC-Medical College & PGIMSR, K.K.Nagar, Chennai-78.

This dissertation is being submitted to TamilNadu Dr.M.G.R Medical University, Chennai, towards partial fulfilment of requirements of the degree of M.S.[General Surgery] examination to be held in April 2020.

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This is to certify that the dissertation entitled "**A COMPARATIVE STUDY OF TOPICAL PLATELET DERIVED GROWTH FACTOR (RH-PDGF) VERSUS HYDROGEL VERSUS NORMAL SALINE DRESSING FOR TREATING DIABETIC FOOT ULCERS"** is a bonafide research work done by **Dr. DINESH.M**, Post graduate resident in M.S.(General Surgery),ESIC Medical College & PGIMSR,K.K.Nagar, Chennai-78 under direct guidance an supervision of Dr.BHANUMATI GIRIDHARAN. M.S, ASSOCIATE PROFESSOR, Dept of General Surgery, ESIC MEDICAL COLLEGE &PGIMSR, K.K. NAGAR, CHENNAI-78 in partial fulfilment of the requirements for the degree of M.S. General Surgery of The Tamilnadu Dr. M.G.R. Medical University, Chennai. I forward this to The Tamilnadu Dr. M.G.R. Medical University, Chennai, Tamilnadu.

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ACKNOWLEDGEMENT

I avail this opportunity to express my gratitude to my beloved teacher, Guide and Mentor**, Dr. Bhanumati Giridharan,** Associate Professor of Surgery for her constant guidance ,support and interest in my academic progress. The work and time spent in this study has given me a clear vision in approaching a clinical study and documentation of observations made. Throughout the study she has been my driving force in pursuing and completing the study in meticulous manner.

I would also like to thank Prof. **Dr. P.N.Shanmugasundaram** M.S, HOD , Co-guide for his blessings and moral support in all my professional duties I carry out.

I would like to convey my gratitude to our respected Dean **Dr.Sowmya sampath** M.D, for providing me unflinching encouragement and support.

Sincere thanks Prof.Uday S Kumbhar, **Dr.Madhusudhan, Dr.Vishwanathan, Dr.Murugesan ,Dr.Muthuraj, Dr.Prabhakar, Dr.Poornima, Dr.Pankaj Surana, Dr.Vijayalakshmi, Dr.Balasubramaniam, Dr.Vasanth, Dr.Arunraj, Dr.Lohitsai**, who all have helped me tread this difficult path holding my hands in times of need and in various ways have enriched me with their knowledge and rich experience.

Many thanks in particular to the Chairman and Members of the Institutional Ethical committee for approving our study and for their valuable suggestions. I thank our Biostatistician **Dr. Aruna B.Patil** MSc.Ph.D., (Statistics), Asst. Professor in Department of Community Medicine, ESIC Medical College and PGIMSR, Chennai -78, for her passionate guidance and enlightening knowledge with which we were able to commute sample size and Data analysis.

I also express my sincere thanks and gratitude to my colleagues**,** **Dr.Dhanasekaran.P** & **Dr.Amudhan** and my Juniors Dr.Naveenkumar, Dr.Keerthana, who all had been a source of constant support throughout my course.

I extend my warm regards to my dad, mom, sister, Dr.Chandhini who were my emotional support all the time.

My heartfelt thanks go to each and every patient who agreed to be a part of this study and also my apologies to them in case of any inconvenience caused.

CERTIFICATE OF APPROVAL

To

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KK Nagar, Chennai-78.

Dear Dr.Dinesh.M

The Institutional Ethics Committee of ESIC Medical College & PGIMSR reviewed and discussed your application for approval of the proposal entitled "**A comparative study of Topical Platelet Derived Growth factor(rh-PDGF) vs Hydro gel vs Normal Saline Dressing for treating diabetic foot ulcers**", No. 03/2018.

The following members of the Ethics Committee were present in the meeting held on 21.03.2018 conducted at ESIC Medical College & PGIMSR, KK Nagar, Chennai-78.

S.No.	ETHICS COMMITTEE MEMBERS
1.	Prof. A.V. Srinivasan, Chairperson
2.	Prof. V. Rajalakshmi, Registrar, ESIC Medical College & PGIMSR, Member Secretary
3.	Prof. Usha Kothandaraman, Medical Superintendent, ESIC Medical College & PGIMSR, EC Member
4.	Prof. S. Seethalakshmi, Vice Principal, ESIC Medical College & PGIMSR, EC Member
5.	Prof. Sowmya Sampath, Prof. & HOD, Department of Paediatrics, ESIC Medical College & PGIMSR, EC Member
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7.	Dr. A. Sundaram, Dept. of Medicine [Diabetologist], EC Member
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9.	Dr. S. Dhanalakshmi, Dept. of OBG, EC Member
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11.	Dr. Rajkumar Williams, Dept. of Surgery, EC Member
12.	Prof. C. Rajendiran, Department of General Medicine, EC Member
13.	Dr. Napinai, Clinical Psychologist, EC Member
14.	Dr. C.V. Aravindan, Scientist, EC Member
15	Shri. K M Venugopal, Advocate, EC Member

The proposal is approved to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and significant adverse effects occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

[DR. A.V. SRINIVASAN]
CHAIRPERSON
ETHICAL COMMITTEE

PLAGIARISM CHECK

URKUND

Urkund Analysis Result

Analysed Document:	0_palgiarism check.docx (D57427115)
Submitted:	10/22/2019 11:09:00 AM
Submitted By:	nidmahal@gmail.com
Significance:	20 %

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Instances where selected sources appear:

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CONTENTS

INTRODUCTION

Diabetes Mellitus:

- It is a serious and complex disease affecting almost all the vital organs in the body.
- About 347 million in the world are diagnosed with DM.
- The Incidence will raise and has been predicted to double by the year 2030.
- It is known to have many complications and one of the most distressing is Diabetic Foot Ulcers.

Diabetic Foot Ulcers:

- Lower Extremity ulcers are serious complications of DM which account for more than 60% of all non-traumatic lower leg amputations.
- 15% of Diabetic patients will develop foot ulcer during their life time.
- 6-40% of them may require an amputation.

RISK FACTORS:

- Male sex
- DM more than 10 years duration
- Peripheral neuropathy
- Deformity of Foot
- Peripheral Arterial Disease
- Smoking
- H/O Previous ulcer or Amputation

Classification of ulcers:

- Wagner-Classification system
- University of Texas Wound Classification

WAGNER-CLASSIFICATION SYSTEM

					
Grade 0 No open Lesion	Grade 1 Superficial Lesion	Grade 2 Deep Ulcer	Grade 3 Abscess/ Osteomyelitis	Grade 4 Partial Foot Gangrene	Grade 5 Whole Foot Gangrene

Wound Dressings:

- Wound dressings have been used since the time of antiquity.
- Lister introduced antiseptic dressings by soaking lint and gauze in carbolic acid.
- Wound healing is most successful in a moist, clean, and warm environment.

It is important to note that not all dressings can provide all the aforementioned characteristics**.**

Dressing is done

- To keep ulcer moist
- To keep surrounding skin dry
- To reduce pain
- To soothe tissue
- To protect the wound**.**

Factors that affect wound healing:

Local factors:

- Mechanical injury
- Infection
- Ischemia with low oxygen tension
- Ionizing radiation
- Foreign bodies

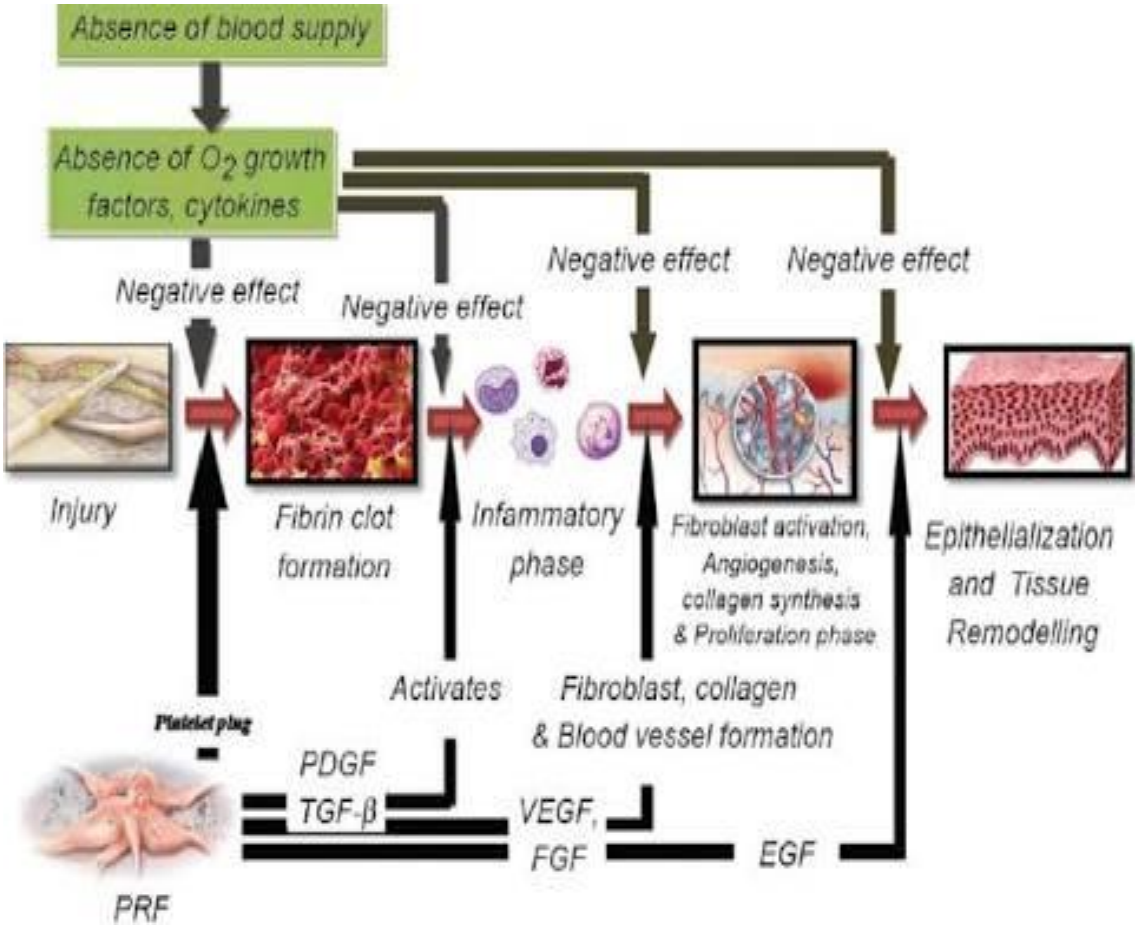
Regional Factors:

- Arterial & Venous insufficiency
- Neuropathy

Systemic Factors:

- Inflammation
- Poor nutrition
- Immunosuppression
- Smoking
- Connective tissue disorders

Pathophysiology of Wound Healing:



Growth Factors:

Growth factors are substances that are naturally produced in the body. They promote growth of new cells and help in healing of wounds. Treatment of diabetic foot ulcers with growth factors may improve and promote the healing of ulcers.

The non-recombinant growth factors investigated were:

- Autologous growth factors
- Allogeneic platelet derived growth factor
- Transforming growth factor
- Arginine-glycine-aspartic acid (RGD) peptide

The recombinant growth factors were:

- Recombinant human platelet-derived growth factor.
- Recombinant human epidermal growth factors.
- Recombinant human basic fibroblast growth factors.
- Recombinant human vascular endothelial growth factor
- Recombinant human lactoferrin and
- Recombinant human acidic fibroblast growth factor.

In this study we have compared Topical Platelet Derived Growth factor (rh-PDGF) and Hydrogel and Normal Saline Dressing for treating diabetic foot ulcers.

This clinical trial has been conducted in ESIC Medical College & PGIMSR, K.K Nagar, Chennai-78, with diabetic foot patients admitted as in-patients in the department of surgery. Ethical committee approval was obtained priorly as per protocol. Study includes ---- patients of diabetic foot. Results has been analysed in both statistical point of views and brought out in a simple understandable format for the readers. Discussion of this study has been done with the review of literature and appropriate references.

AIM OF THE STUDY

The Primary aim of the study was to Evaluate efficacy of rhPDGF, Hydrogel and Normal Saline dressing In Diabetic Foot Ulcers.

The secondary objectives were to correlate the efficacy of each method in terms of:

- Ulcer Healing time
- Length of hospital stay
- Abstinence from work
- Need of secondary intervention

MATERIALS AND METHODS

The study was conducted as a clinical trial at ESIC Medical College & PGIMSR, Chennai -78 during a period of 18 months.

SAMPLE AND SAMPLE SIZE DEFINITIONS:

POPULATION:

The Patients diagnosed to have Diabetic foot ulcer attending the Surgery out Patient Department (OPD) of ESIC Medical College & PGIMSR.

INCLUSION CRITERIA:

All the patients presenting with Diabetic Foot Ulcers

1. Between Age: 20-80 yrs
2. Blood Glucose levels: FBS >110, PPBS >200, HbA1c >7.5
3. Grade 1 and 2(Wagner's classification)
4. Size of Ulcer less than 15 cm in Greatest Dimension
5. Able to understand the merits and demerits of both the procedures and provide consent

EXCLUSION CRITERIA:

1. Critically ill patients
2. Pregnancy
3. Chronic Venous/ Arterial Insufficiency Ulcer
4. Malignant ulcer
5. Patients with severe Anaemia(<7 gm/dl)
6. H/o immunosuppressive therapy within previous 6 months
7. Peripheral Vascular Disease

SAMPLE:

With the above mentioned inclusion and exclusion criteria, the appropriate sample was drawn from the population.

SAMPLE SIZE CALCULATION:

Proportion in group I	**0.93**
Proportion in group II	0.50
Estimated risk difference (in healing size of wound)	0.43
Power (1- beta) %	90
Alpha error (%)	5
1 or 2 sided	2
Required sample size for each arm	21=25

The required sample size is 21 patients per group by using formula.

But after consideration the lost to follow up, the sample size is 25 patients per group to test the proportion difference between three groups for healing size of wound. The nMaster (2.0) software was used to calculate the sample size**.**

SAMPLING METHOD:

Total 75 patients with Diabetic foot ulcer attending Surgical Out patient Department were enrolled in this study. Every alternate consenting patient presenting to us were allocated to Group A, Group B, Group C respectively.

MATERIALS & METHODS:

- Out of 75,
- 25 will be treated in the form of standard care with Hydrogel dressing.
- 25 will take treatment in the form of standard care with rh-PDGF.
- 25 will be treated with standard care and Normal Saline dressing once a day.

In all the groups the foot Ulcer was classified as per the Wagner's grading.

WAGNER'S GRADING:

0-Intact skin

1-Superficial ulcer of skin or subcutaneous tissue

2-Ulcers extend into tendon, bone, capsule

3-Deep ulcer with Osteomyelitis /abscess

4-Gangrene of Toes/forefoot

5-Midfoot/Hind foot gangrene

MANAGEMENT:

- History, Clinical Examination will be recorded
- A complete Haemogram, Fasting and Post prandial Blood sugar, Renal Function test will be taken.

- X-Ray foot will be taken to rule out Osteomyelitis.
- Doppler study for Vasculopathy.
- Neurological Examination by Tuning fork(Large fibres), Hot/cold objects(Small fibres) and Ankle Reflexes for Neuropathy.

STANDARD CARE:

- Glycaemic control.
- Adequate control of infection.
- Debridement.

The initial area measurement will be calculated by impression of ulcer floor on a sheet of cellophane paper and transferring to graph paper then it is measured by Measuring Tape. Follow up also will be the same at first week, 4^{th} week and 10^{th} week for size assessment.

FOLLOWING WILL BE ASSESSED:

- Change in size of Ulcer at 1^{st}, 4^{th}, 10^{th} week
- Number of Days in Hospital Bed
- Number of Days Absent from Work Due to Disease
- Needed Secondary Intervention like Debridement, SSG, FLAP COVER etc,.

DRESSING TECHNIQUE:

FOR NORMAL SALINE DRESSING:

The ulcer will be cleaned with Normal Saline and saline soaked gauze piece will be kept over the ulcer which will be covered with pad and roller bandage.

FOR HYDROGEL DRESSING:

The ulcer will be cleaned with Hydrogel and saline soaked gauze piece will be kept over the ulcer which will be covered with pad and roller bandage.

FOR RH-PDGF DRESSING:

The infected ulcer will be cleaned with normal saline. Commercially available rh-PDGF-BB gel(0.01%) will be applied on the gauze piece and put on the ulcer. It will then covered with pad and roller bandage.

The amount of rh-PDGF (Becaplermin gel) per application is calculated by the ulcer size, as

(length in cm × width in cm)/0.4.

Rate of contraction of wound after 07 days of treatment=

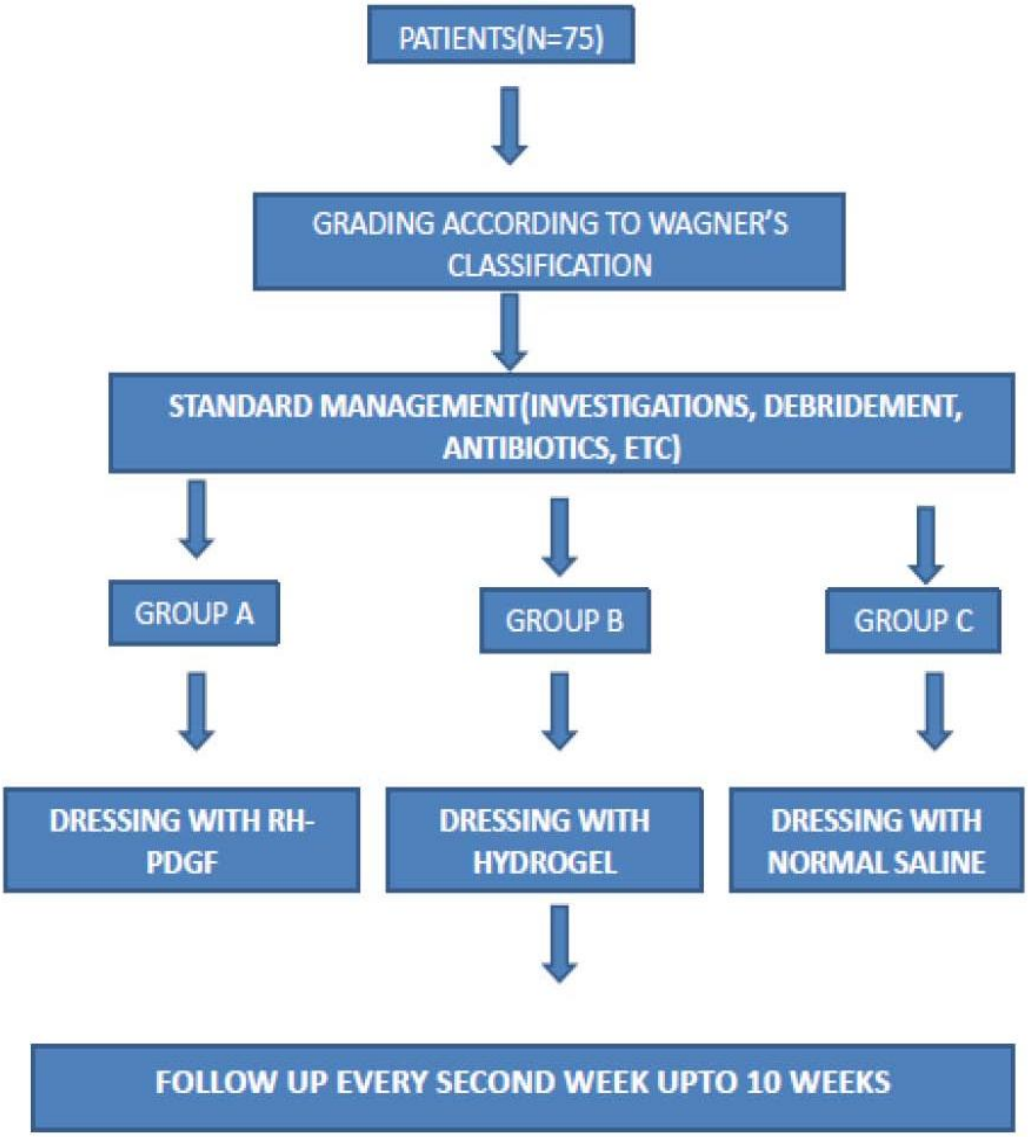
$$\frac{\textbf{(Initial – Final area)}}{\textbf{`Initial area}} \textbf{ x 100}$$

Statistical Analysis Plan:

The data will be analysed by using the following tests. To investigate the significance between proportion of two groups for the various parameters, Student's unpaired t-test will be used. The quantitative data will be represented by descriptive statistics. The categorical findings will be presented by tables & graphs.

The level of significance will be considered significant at $p < 0.05$. The SPSS (version 21.0) software will be used to analyse the data.

FLOW CHART – 1.1



REVIEW OF LITERATURE

Diabetes mellitus (a rise in the sugar (glucose) levels in the blood) is a serious health issue affects millions of people around the world.

Success in treating DM has improved the life expectancy of patients.

However the increased prevalence of DM, coupled with the extended time people now live with the disease, has led to increased numbers of DM-related complications, such as neuropathy (nerve damage) and peripheral arterial disease (PAD).

Both PAD and neuropathy are risk factors for the development of chronic foot ulceration in people with DM. [65,66]

PAD and neuropathy can occur separately (ischaemic foot and neuropathic foot, respectively), or in combination (in the neuro-ischaemic foot).

DIABETIC FOOT ULCERS:

Foot ulcers in people with diabetes mellitus are a common and serious global health issue.

An ulcer forms as a result of damage to the epidermis (skin) and subsequent loss of underlying tissue.

Specifically, the International Consensus on the Diabetic Foot defines a foot ulcer as a wound “that extends through the full thickness of the skin below the level of the ankle”(Apelqvist 2000a).

This is irrespective of duration (although some definitions of chronic ulceration require a duration of six weeks or more), and the ulcer can extend to muscle, tendon and bone.

Risk factors for foot ulcers include:

- Male sex,
- DM more than 10 years duration,
- Peripheral neuropathy,
- Abnormal structure of foot,
- Peripheral arterial disease,
- Smoking,
- History of previous ulcer or amputation
- Poor glycaemic control.

Chronic distal sensorimotor symmetrical neuropathy is the most common, affecting around 28% of people with diabetes.

It can lead to ulceration through the following route(s) (Tesfaye1996):

- Sympathetic autonomic neuropathy leads to decreased sweating causing anhidrotic (dry) skin which is prone to cracks and fissures causing a break in the dermal barrier.
- Motor neuropathy causes wasting of the small, intrinsic muscles of the foot by de-enervation. As the muscles waste they cause retraction of the toes and lead to a subsequent deformity.

The abnormal foot shape can promote ulcer development due to an increase in plantar pressures (Murray 1996).

- Sensory neuropathy results in impaired sensation, making the patient unaware of potentially dangerous foreign bodies and injuries.

BURDEN OF DIABETIC FOOT ULCER:

Diabetic foot ulcers can seriously impact on an individual's quality of life and as many as 85% of foot-related amputations are preceded by ulceration.[65]

Patients with diabetes have a 10 to 20-fold higher risk of losing a lower limb or part of a lower limb due to non-traumatic amputation than those without diabetes (Morris 1998;Wrobel 2001).

Diabetic foot ulcers represent a major use of health resources, incurring costs not only for dressings applied, but also staff costs, tests and investigations. Hospital admissions add to the costs.

GRADING OF DIABETIC FOOT ULCERS:

Foot ulcers in people with DM can be graded for severity using a number of systems.

The Wagner wound classification system was one of the first described and has. Historically been widely used although it is now rarely used in clinical practice (Wagner 1981).

The system assesses:

- Ulcer depth
- Presence of osteomyelitis (bone infection) or ischemia
- Infection

GRADING:

Grade 0 (pre- or post-ulcerative lesion)

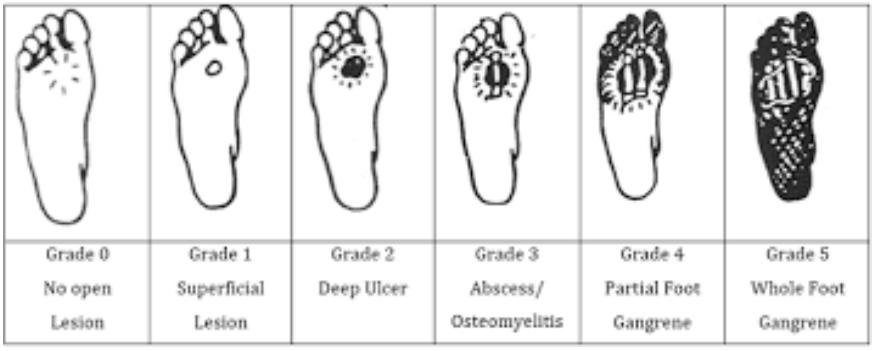
Grade 1(partial/full-thickness ulcer)

Grade 2 (probing to tendon or capsule)

Grade 3 (deep with osteitis (bone inflammation)

Grade 4(partial foot gangrene)

Grade 5(whole foot gangrene).



Newer grading systems:

PEDIS system (Schaper 2004),

The University of Texas Wound Classification System and

SINBAD(Ince 2008; Oyibo 2001) been developed.

TREATMENT MODALITIES FOR DIABETIC FOOT:

Broadly, the treatment of diabetic foot ulcers includes pressure relief by resting the foot or wearing special footwear, the removal of dead cellular material from the surface of the wound (debridement or desloughing), infection control and the use of wound dressings.

Other general strategies in the treatment of diabetic foot ulcers include: patient education optimisation of blood glucose control; correction (where possible) of arterial insufficiency; and surgical interventions (debridement,

drainage of pus, revascularisation, amputation). Wound dressings are used extensively in the care of these ulcers.

There are many different types of dressings available, from basic wound contact dressings to more advanced gels, films, and specialist dressings that may be saturated with ingredients that exhibit antimicrobial activity.

TYPES OF DRESSINGS:

Dressing materials can include natural, modified and synthetic polymers, as well as their mixtures or combinations, processed in the form of films, foams, hydrocolloids and hydrogels may be employed as medicated systems, through the delivery of therapeutic substances (drugs, growth factors, peptides, stem cells).

1. Basic wound contact dressings

- Low-adherence dressings and wound contact materials:

It consists of cotton pads that are placed directly in contact with the wound. These can be non-medicated (e.g. paraffin gauze dressing), or medicated (e.g. containing povidone iodine or chlorhexidine).

- Absorbent dressing:

They are applied directly to the wound, and may be used as secondary absorbent layers in the management of heavily exuding wounds. Eg. Primapore Mepore and absorbent cotton gauze .

2. Advanced wound dressings

- Alginate dressings:

Are highly absorbent, available as calcium alginate or calcium sodium alginate, which can be combined with collagen. Alginates form gel when in contact with the wound surface. Bonding the alginate to a secondary viscose pad increases absorbency.

Eg., Cura-sorb , SeaSorb

- Films -permeable film and membrane dressings:

They are permeable to water vapour and oxygen, but not to water or micro-organisms.

Eg., Tegaderm and Opsite

- Soft polymer dressings:

They are composed of a soft silicone polymer held in a non-adherent layer and are moderately absorbent. Eg. Mepitel and Urgotul.

- Hydrocolloid dressings:

They are occlusive and usually composed of a hydrocolloid matrix bonded onto a vapour-permeable film or foam backing. Forms a gel in contact to wound to provide a moist environment for the wound. eg Granuflex® (ConvaTec) and NU DERM® (Systagenix).

- Foam dressings:

It contain hydrophilic polyurethane foam and are designed to absorb wound exudate and maintain a moist wound surface. Eg.Allevyn® ,Biatain® and Tegaderm® .

- Capillary-action dressings:

They consist of an absorbent core of hydrophilic fibres held between two low-adherent contact layers.

eg: Advadraw® and Vacutx® (Protex).

- Odour-absorbent dressings:

It contain charcoal and are used to absorb wound odour.

eg CarboFLEX®

3. Anti-microbial dressings:

- Iodine-impregnated dressings:

It release free iodine when exposed to wound exudate. The free iodine act as a wound antiseptic.

Eg. Iodoflex® and Iodozyme®

- Silver-impregnated dressings

They are used to treat infected wounds.eg .Acticoat® and Urgosorb Silver®

- Other antimicrobial dressings

Eg. chlorhexidine gauze dressing and dressing im-pregnated with the anti-microbial polyhexamethylene biguanide (PHMB).

Dressing	Advantages	Disadvantages
Low-adherence	Simple	Minimal absorbency
	Hypoallergenic	
	Inexpensive	
Hydrocolloids	Absorbent	Concerns about use for infected wounds
	Can be left for several days	May cause maceration
	Aid autolysis	Unpleasant odor
Hydrogels	Absorbent	Concerns about use for infected wounds
	Aid autolysis	May cause maceration
	Donate liquid	
Foams	Thermal insulation	Can adhere to wound
	Good absorbency	Occasional dermatitis with adhesive
	Confirm to contours	
Alginates	Highly absorbent	May need wetting before removal
	Bacteriostatic	
	Hemostatic	
	Useful in cavities	
Iodine preparations	Antiseptic	Iodine allergy
	Moderately absorbent	Discolors wounds
		Avoid in case of thyroid disease or pregnancy
Silver-impregnated	Antiseptic	Cost
	Absorbent	No proven advantage

IDEAL DRESSING:

Several attributes of an ideal wound dressing have been described (BNF 2010) including:

- The ability of the dressing to absorb and contain exudates without leakage.
- Lack of particulate contaminants left in the wound by the dressing.
- Thermal insulation.
- Permeability to water and bacteria.
- Avoidance of wound trauma on dressing removal.
- Frequency with which the dressing needs to be changed.
- Provision of pain relief and comfort.

However, no existing dressing fulfils all the ideal requirements and the choice of the correct dressing depends on the wound type and stage, injury extension, patient condition etc.

ROLE OF HYDROGEL DRESSINGS

- INTRASITE Gel is an amorphous hydrogel.
- Partially hydrated hydrogel formulation contains: 65% glycerol, 17.5% water and 17.5% polyacrylamide.
- Re-hydrates necrotic tissue.
- Facilitating autolytic debridement.
- It can also be used to provide the optimum moist wound management environment during the later stages of wound closure.
- It is non-adherent and does not harm viable tissue or the skin surrounding the wound.

- This makes INTRASITE Gel ideal for every stage in the wound management process.

A moist environment is thought to provide optimal conditions for the cells involved in the healing process as well as allowing autolytic debridement, which is an important part of the healing pathway (Cardinal 2009).

Different wound dressings vary in their level of absorbency so that a very wet wound can be treated with an absorbent dressing (such as a foam dressing) to draw excess moisture away from the wound to avoid skin damage, whilst a drier wound can be treated with a more occlusive dressing to maintain a moist environment.

Hydrogel dressings consist of cross-linked insoluble polymers (i.e. Starch or carboxymethylcellulose) and up to 96% water. These dressings are designed to absorb wound exudate, or rehydrate a wound, depending on the wound moisture levels. They are supplied in flat sheets, as an amorphous hydrogel, or as beads.

Eg. ActiformCool® (Activa) and Aquaflo® (Covidien).

When hydrogel material is formed into a fixed structure via cross-linking of the polymers it is considered a hydrogel sheet dressing.

RECOMBINANT HUMAN PLATELET DERIVED GROWTH FACTOR DRESSINGS:

- Rh-PDGF gel (Regranex) was first approved by the US Food and Drug Administration (FDA) in 1997 for treatment of diabetic foot ulcers.
- Rh-PDGF gel is recombinant platelet-derived growth factor (PDGF)-BB produced by insertion of the gene into yeast *Saccharomyces cerevisiae*.
- Rh-PDGF gel has been shown to promote wound healing in a number of studies.
- PDGF induces chemotaxis of cells, including neutrophils, macrophages, and fibroblasts to the wound and promotes fibroblast and collagen production.
- Furthermore, PDGF signals for collagen remodelling and crosslinking.

STUDIES COMPARING THE EFFICACY OF VARIOUS TOPICAL AGENTS:

1) In a study conducted by Jo C Dumville et al which be included five studies (446 participants).

Meta analysis of three studies (COMPARISION 3) comparing hydrogel dressings with basic wound contact dressings found significantly greater healing with hydrogel: risk ratio (RR) 1.80, 95% confidence interval (CI) 1.27 to 2.56.

The three pooled studies were

Comparison 1: hydrogel dressing compared with larval therapy (one trial; 140 participants)

Comparison 2: hydrogel dressing compared with platelet-derived growth factor (one trial; 104 participants)

Comparison 3: hydrogel dressing compared with basic wound contact dressing (three trials; 198 participants)

2) In a study conducted by Adrienne M. Gilligan, et al to determine the long-term cost effectiveness of becaplermin gel plus good wound care (BGWC) vs. good wound care (GWC) alone in terms of wound healing and risk of amputation in patients with diabetic foot ulcers (DFUs) it was found that patients treated with BGWC had substantially more closed-wound weeks compared with GWC(16.1 vs. 12.5 weeks, respectively).

More patients receiving BGWC had healed wounds at 1 year compared with those receivingGWC (48.1% vs. 38.3%).

Risk of amputation was lower in the BGWC cohort.

3) According to the overview put forward by Lihua Wu1 et all to summarize data from systematic reviews of randomised controlled trial evidence on the effectiveness of dressings for healing foot ulcers in people with diabetes mellitus (DM) says that

Only four of the comparisons informed by direct data found evidence of a difference in ulcer healing between dressings, but these results were classed as low quality evidence.

There was no clear evidence that any of the 'advanced' wound dressings types were any better than basic wound contact dressings for healing foot ulcers.

4) In the study conducted by Christine Ma,at al sought to compare the efficacy of topical platelet derived growth factor (test group) to placebo (control group) in treating diabetic foot ulcers.

All subjects had a short leg walking cast with a window fashioned in the cast over the site of the ulcer.

Result: Topical platelet derived growth factor does not appear to

Significantly improve healing of Wagner grade I diabetic foot ulcers that are treated by offloading with a short leg walking cast.

Excellent healing rates may be achieved with casting alone.

5) The study conducted by Xiao-hong Zhao, et al compared rhPDGF treatment in the context of standard of care (SOC) to placebo or SOC alone.

In the absence of study heterogeneity, a fixed-effects model was performed, and the combined odds ratio (OR) indicated a significantly greater complete healing rate in patients treated with rh PDGF compared to placebo or SOC alone.

6) In the study Growth factors for diabetic foot ulcers: Mixed treatment comparison analysis of randomized clinical trials conducted by Kannan Sridharan1 et al concluded that rhEGF, rhPDGF and autologous PRP significantly improved the healing rate when used as adjuvants to standard of care, of which rhEGF may perform better than other growth factors.

7) Shyam S. Jaiswal et al studied the Efficacy of topical recombinant human platelet derived growth factor on wound healing in patients with chronic diabetic lower limb ulcers.

This study did not show any statistically significant improvement in ulcer healing rates after the use of topically applied rhPDGF.

STATISTICAL ANALYSIS

The data were analysed using SPSS (Statistical Package for Social Science) software. The data collected were scored and analysed, Continuous variables were presented as means with Standard Deviation (SD) and categorical variables were presented as frequency and percentages. ANOVA test was used for testing the significance of all the mean and standard deviation in groups. Chi-square test was used to compare proportions. P value <= 0.05 was considered as statistically Significant in all statistical results.

STUDY DEMOGRAPHY:

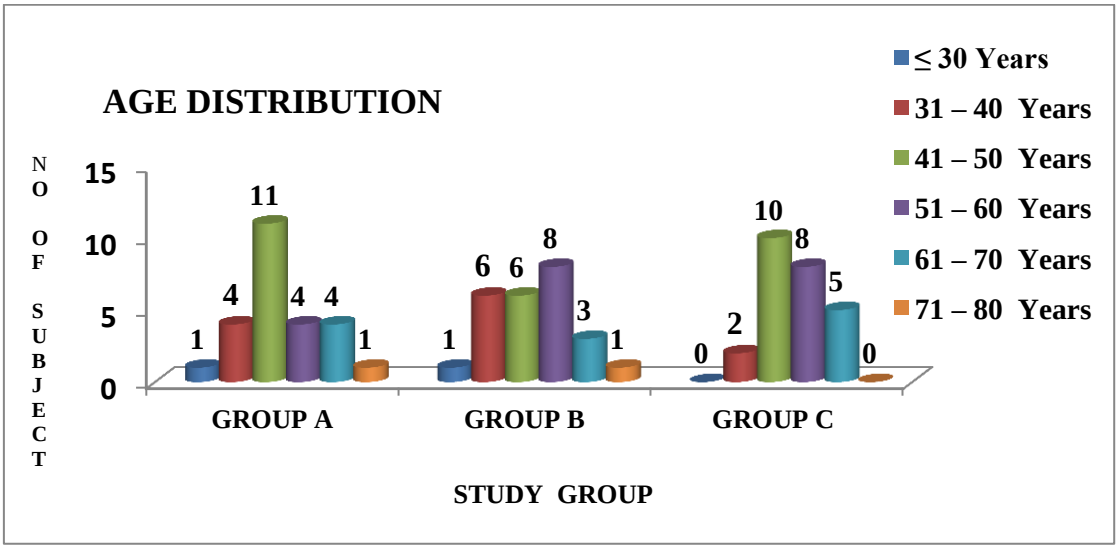
This clinical trial has been conducted in ESIC Medical College & PGIMSR, K.K.Nagar, Chennai-78, with diabetic foot patient attending the Surgical OPD. Ethical committee approval was obtained properly as per protocol. Study has includes 75 patients of Diabetic foot ulcers.

AGE DISTRIBUTION:

TABLE-5.1

AGE GROUP	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
≤ 30 Years	1	4.00	1	4.00	0	0
31 – 40 Years	4	16.00	6	24.00	2	8.00
41 – 50 Years	11	44.00	6	24.00	10	40.00
51 – 60 Years	4	16.00	8	32.00	8	32.00
61 – 70 Years	4	16.00	3	12.00	5	20.00
71 – 80 Years	1	4.00	1	4.00	0	0
Total	**25**	**100**	**25**	**100**	**35**	**100**
Mean	**49.40**		**50.80**		**52.56**	
SD	**11.62**		**10.50**		**8.52**	
ANOVA	**0.59**					
p-value	**0.56**					
Significant	**Not Significant**					

FIGURE-5.1



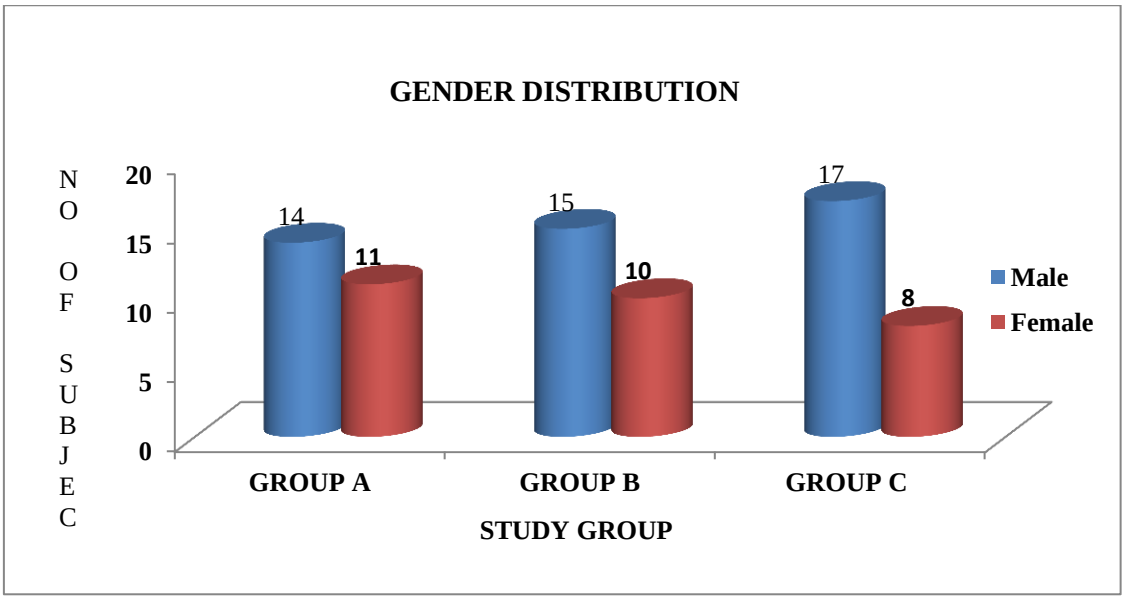
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant. In simple words both the groups were comparable.

GENDER DISTRIBUTION:

TABLE-5.2

Gender	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Male	14	56.00	15	60.00	17	68.00
Female	11	44.00	10	40.00	8	32.00
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**0.79**					
p-value	**0.68**					
Significant	**Not Significant**					

FIGURE-5.2



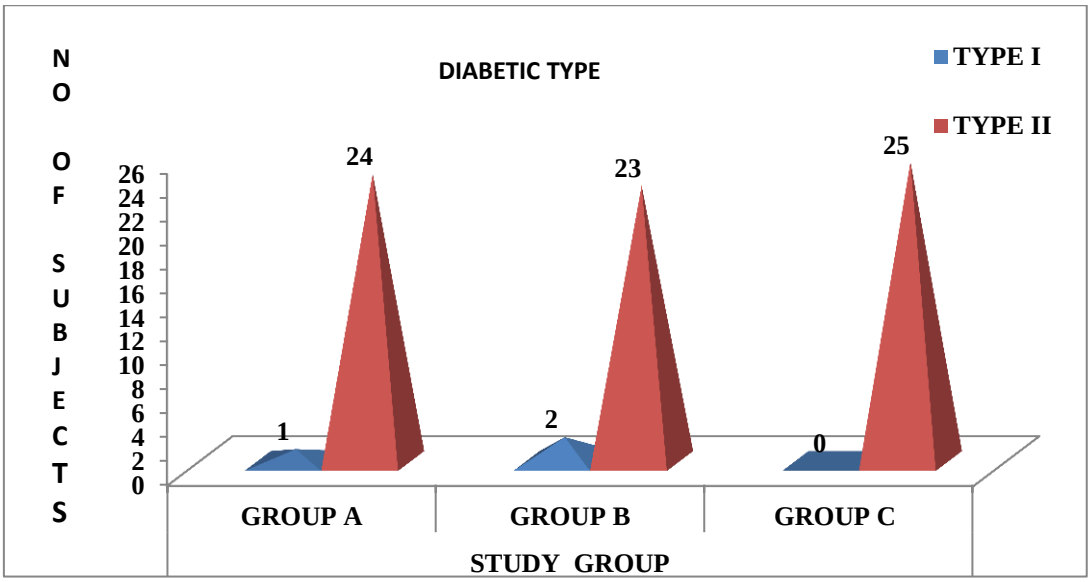
By conventional criteria the difference between the groups were comparable because the p value is **>0.05** and so it is statistically not significant. Hence both the groups were comparable.

DIABETIC TYPE DISTRIBUTION:

TABLE-5.3

TYPE	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
TYPE I	1	4.00	2	8.00	0	0
TYPE II	24	96.00	23	92.00	25	100
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**2.08**					
p-value	**0.35**					
Significant	**Not Significant**					

FIGURE-5.3



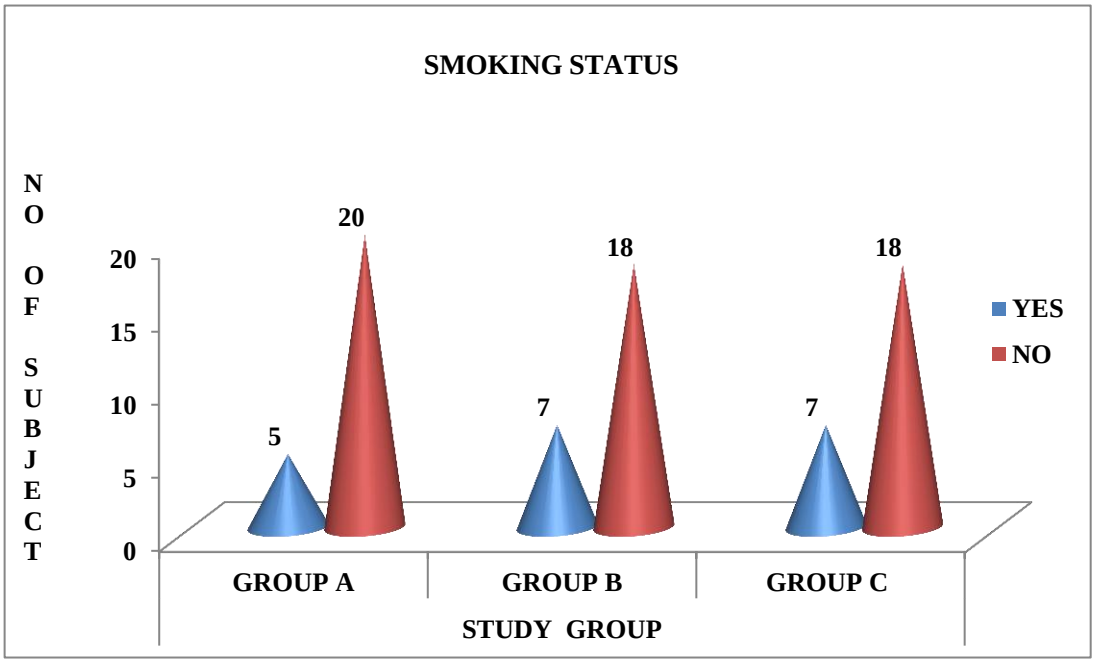
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

SMOKING STATUS

TABLE-5.4

SMOKING	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Yes	5	20.00	7	28.00	7	28.00
No	20	80.00	18	72.00	18	72.00
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**0.56**					
p-value	**0.75**					
Significant	**Not Significant**					

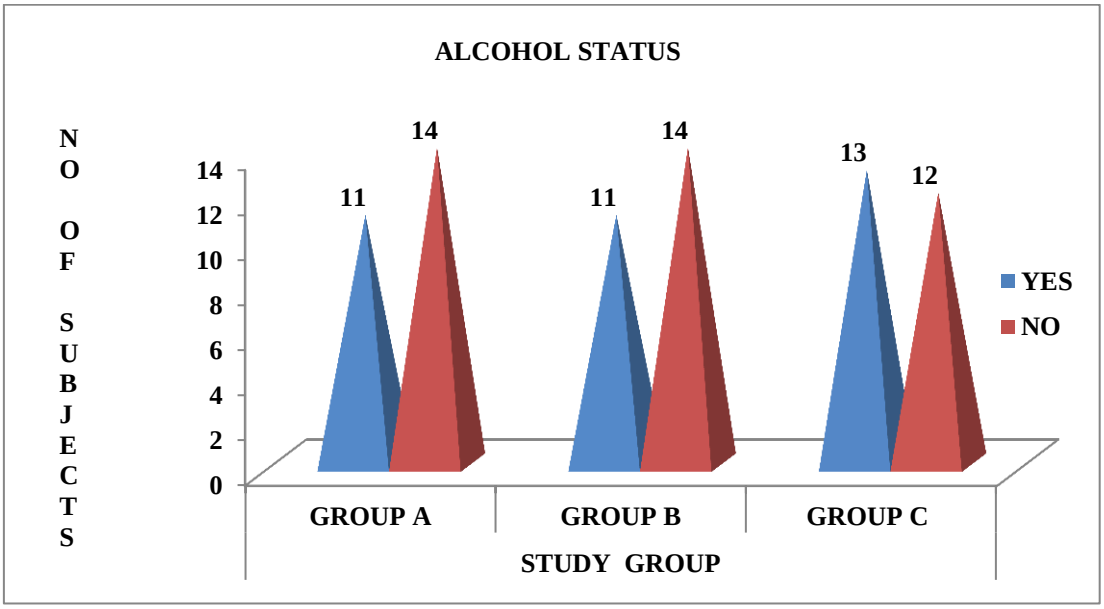
FIGURE-5.4



ALCOHOL STATUS

TABLE -5.5

ALCOHOL	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
YES	11	44.00	11	44.00	13	52.00
NO	14	56.00	14	56.00	12	48.00
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**2.08**					
p-value	**0.35**					
Significant	**Not Significant**					



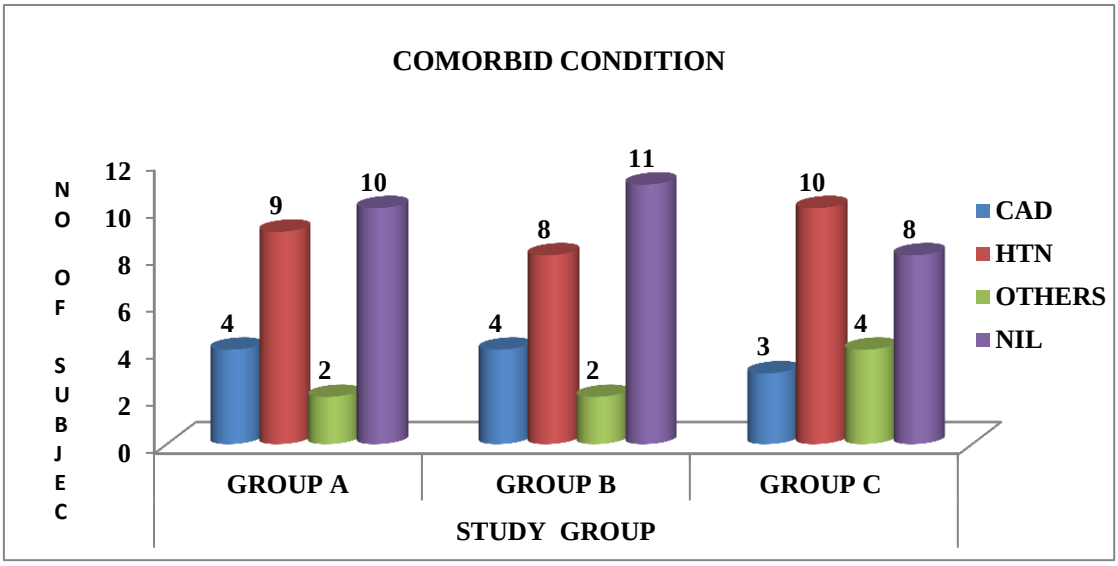
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant. In simple words both the groups were comparable.

COMORBID CONDITION:

TABLE-5.6

Comorbid	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
CAD	4	16	4	16	3	12
HTN	9	36	8	32	10	40
OTHERS	2	08	2	8	4	16
NIL	10	40	11	44	8	32
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**1.89**					
p-value	**0.93**					
Significant	**Not Significant**					

FIGURE-5.6

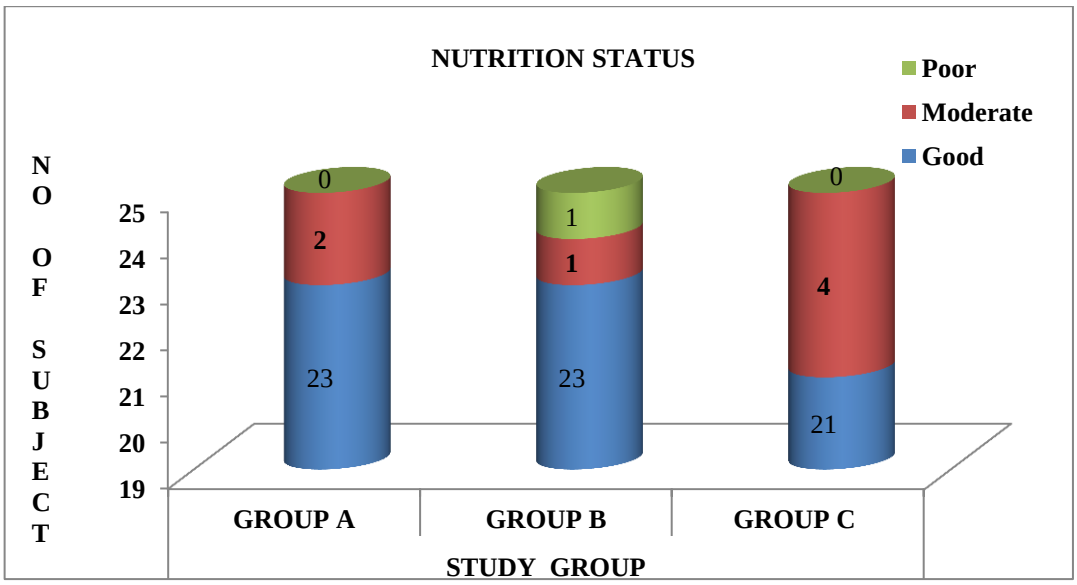


Nutrition Status:

TABLE 5.7

Nutrition	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Good	23	92	23	92	21	84
Moderate	2	8	1	4	4	16
Poor	0	0	1	4	0	0
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**4.12**					
p-value	**0.39**					
Significant	**Not Significant**					

FIGURE – 5.7

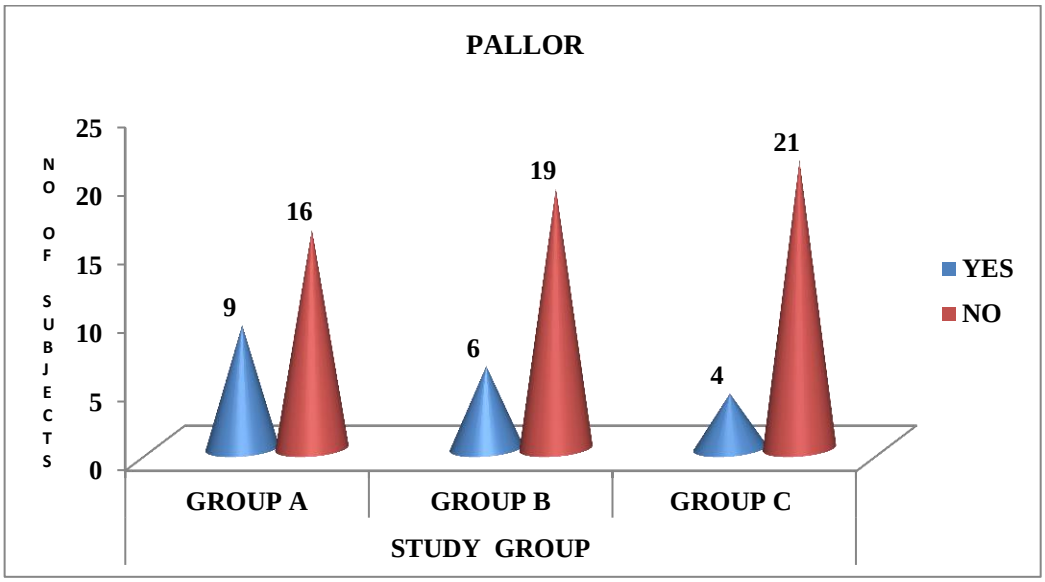


By conventional criteria the difference between the groups were comparable due to the p value is **>0.05** and so it is statistically not significant.

TABLE-5.8

Comorbid	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
YES	9	36	6	24	4	16
NO	16	64	19	76	21	84
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**2.68**					
p-value	**0.26**					
Significant	**Not Significant**					

FIGURE-5.8



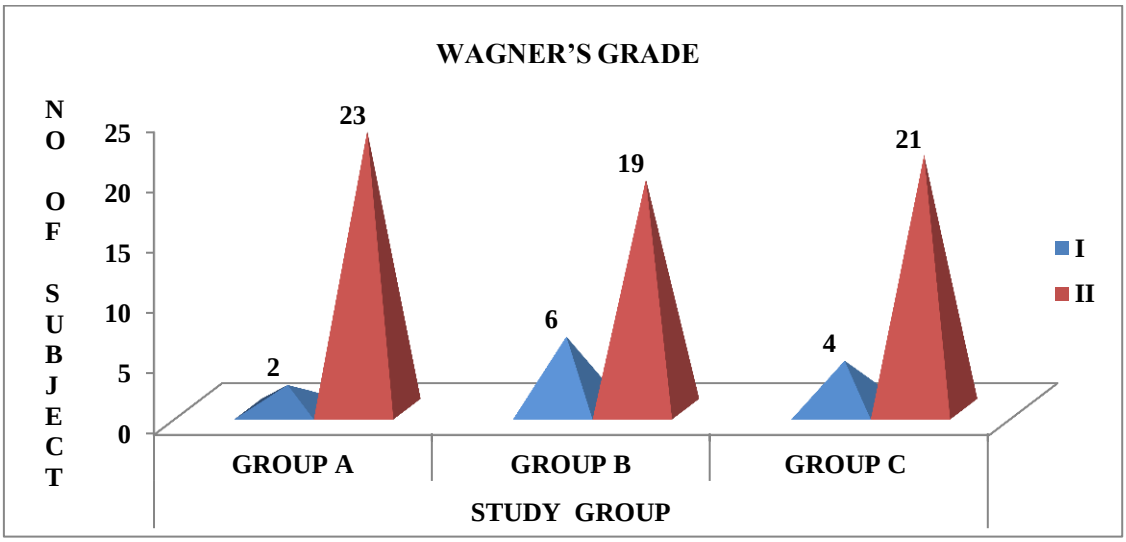
By conventional method the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant. In simple words both the groups were comparable.

WAGNER'S GRADE

TABLE-5.9

WAGENERS GRADE	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
I	2	4	6	24	4	16
II	23	96	19	76	21	84
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**2.38**					
p-value	**0.30**					
Significant	**Not Significant**					

FIGURE-5.9



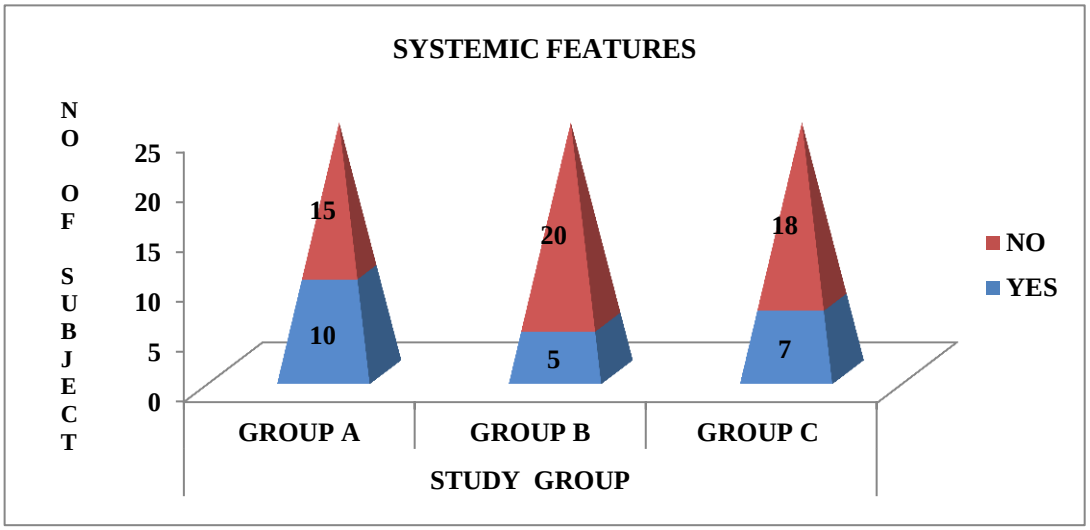
By conventional method the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

SYSTEMIC FEATURES

TABLE-5.10

SYSTEMIC FEATURES	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
YES	10	40	5	20	7	28
NO	15	60	20	80	18	72
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**2.44**					
p-value	**0.30**					
Significant	**Not Significant**					

FIGURE-5.10



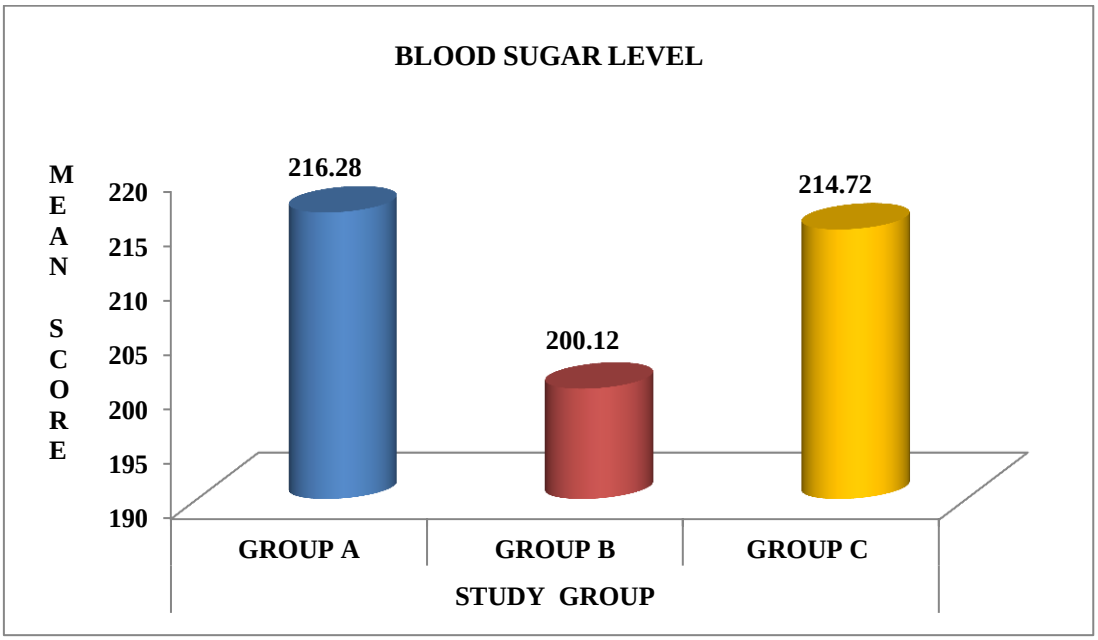
By conventional criteria the difference between the groups were comparable because the p value is **>0.05** and so it is statistically not significant.

BLOOD SUGAR LEVEL

TABLE-5.11

BLOOD SUGAR	STUDY GROUP		
	GROUP A (N=25)	GROUP B (N=25)	GROUP C (N=25)
Mean	216.28	200.12	214.72
SD	58.41	57.29	52.13
Anova Value	**0.63**		
p-value	**0.53**		
Significant	**Not Significant**		

FIGURE-5.11



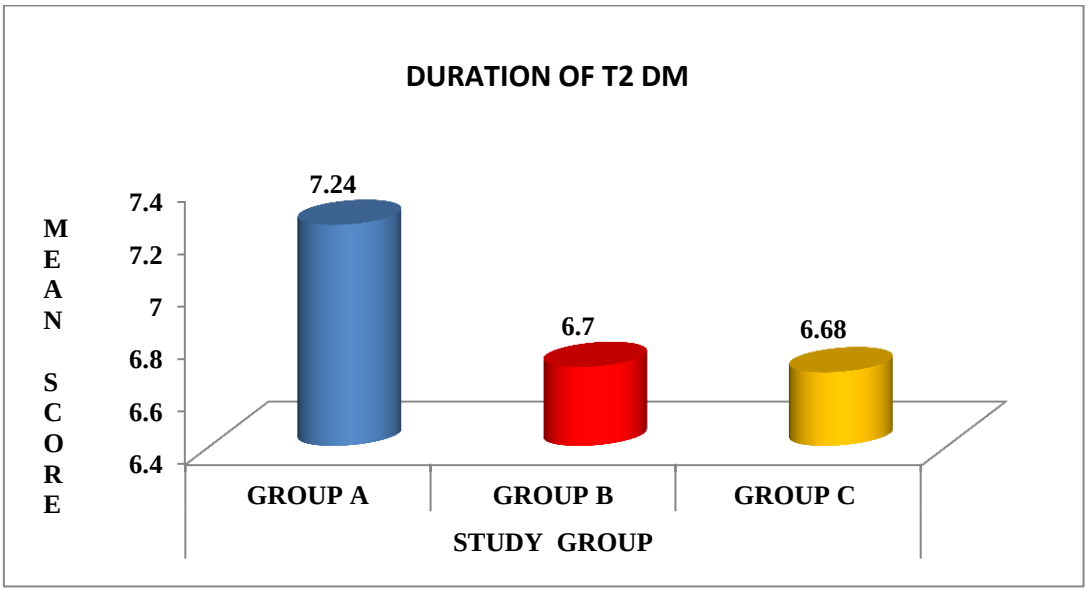
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

DURATION OF T2 DM

TABLE-5.12

DURATION	STUDY GROUP		
	GROUP A (N=25)	GROUP B (N=25)	GROUP C (N=25)
Mean	7.24	6.70	6.68
sd	6.11	4.66	4.60
Anova Value	**0.09**		
p-value	**0.91**		
Significant	**Not Significant**		

FIGURE-5.12



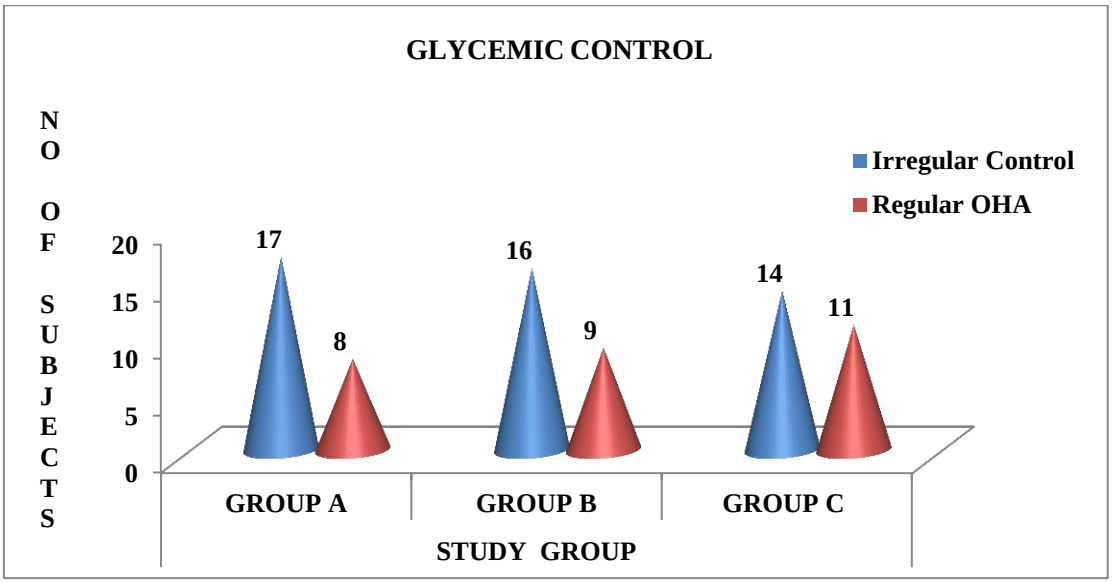
By conventional criteria the difference between the groups were comparable due to the p value is **>0.05** and so it is statistically not significant.

GLYCEMIC CONTROL

TABLE-5.13

GLYCEMIC CONTROL	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Irregular Control	17	68	16	64	14	56
Regular OHA	8	32	9	36	11	44
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**0.80**					
p-value	**0.67**					
Significant	**Not Significant**					

FIGURE-5.13



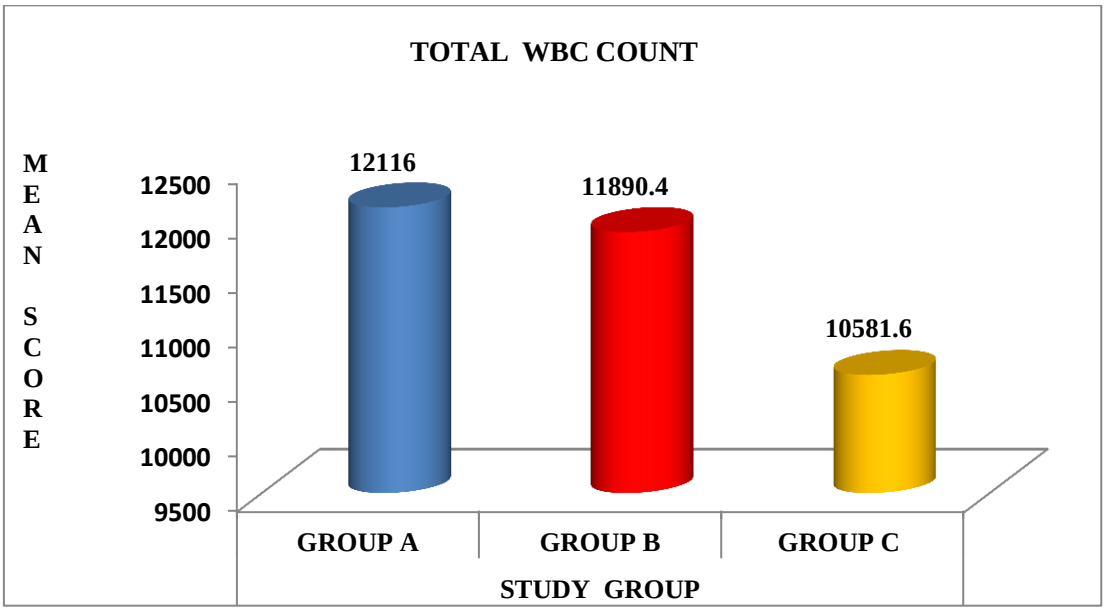
By conventional method the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

TOTAL WBC COUNT

TABLE-5.14

	STUDY GROUP		
	GROUP A (N=25)	**GROUP B (N=25)**	**GROUP C (N=25)**
Mean	12116.00	11890.40	10581.60
sd	4399.50	4744.86	3101.65
Anova value	**1.00**		
p-value	**0.37**		
Significant	**Not Significant**		

FIGURE 5.14



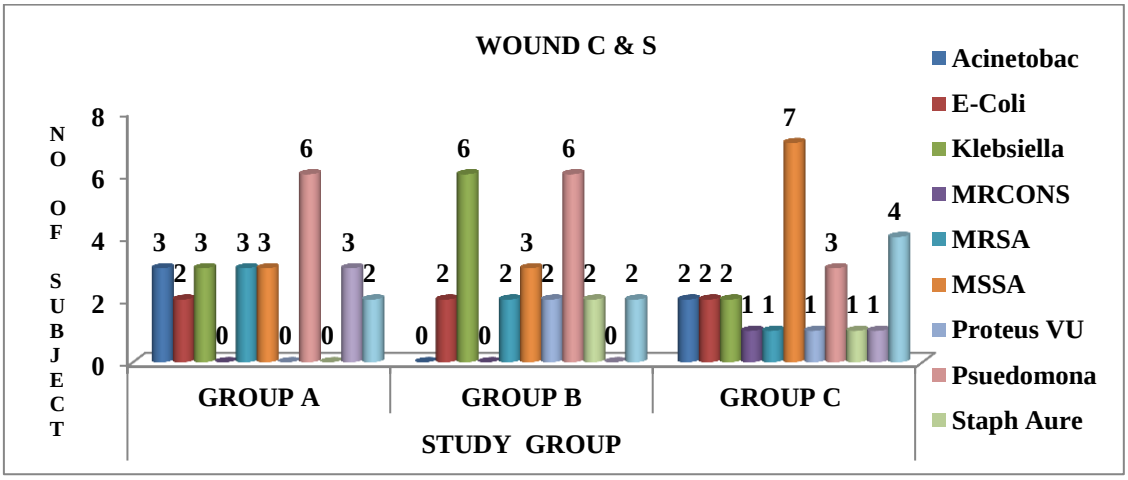
By conventional method the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

WOUND C & S

TABLE-5.15

WOUNDS	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Acinetobacter	3	12	0	0	2	8
E-Coli	2	8	2	8	2	8
Klebsiella	3	12	6	24	2	8
MRCONS	0	0	0	0	1	4
MRSA	3	12	2	8	1	4
MSSA	3	12	3	12	7	28
Proteus Vulgaris	0	0	2	8	1	4
Pseudomonas	6	24	6	24	3	12
Staph Aureus	0	0	2	8	1	4
Sterile	3	12	0	0	1	4
Strep Pyogenes	2	8	2	8	4	16
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**20.33**					
p-value	**0.44**					
Significant	**Not Significant**					

FIGURE-5.15



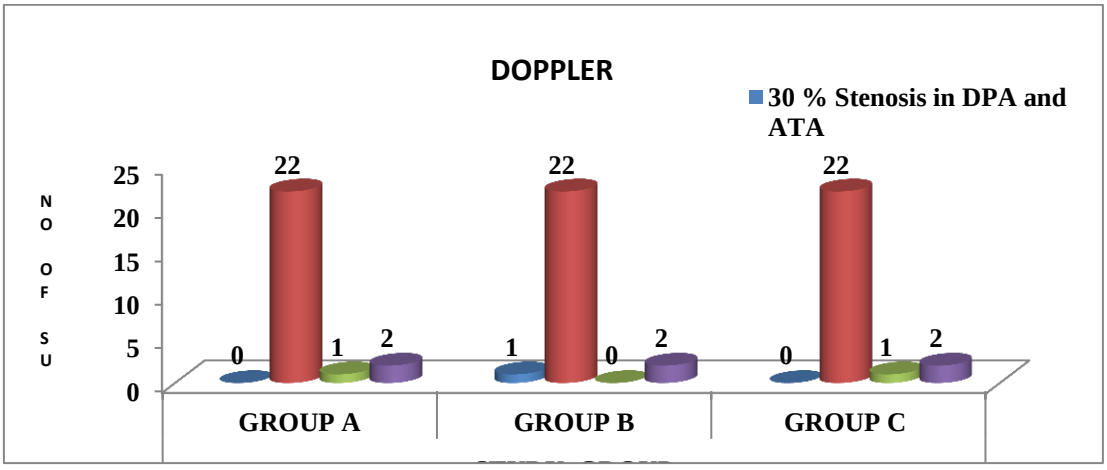
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant. In simple words both the groups were comparable.

DOPPLER

TABLE-5.16

DOPPLER	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
30 % Stenosis in DPA and ATA	0	0	1	4	0	0
NAD	22	88	22	88	22	88
Non-Significant Luminal Narrowing	1	4	0	0	1	4
Normal Study	2	8	2	8	2	8
Total	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**3.00**					
p-value	**0.81**					
Significant	**Not Significant**					

FIGURE-5.16



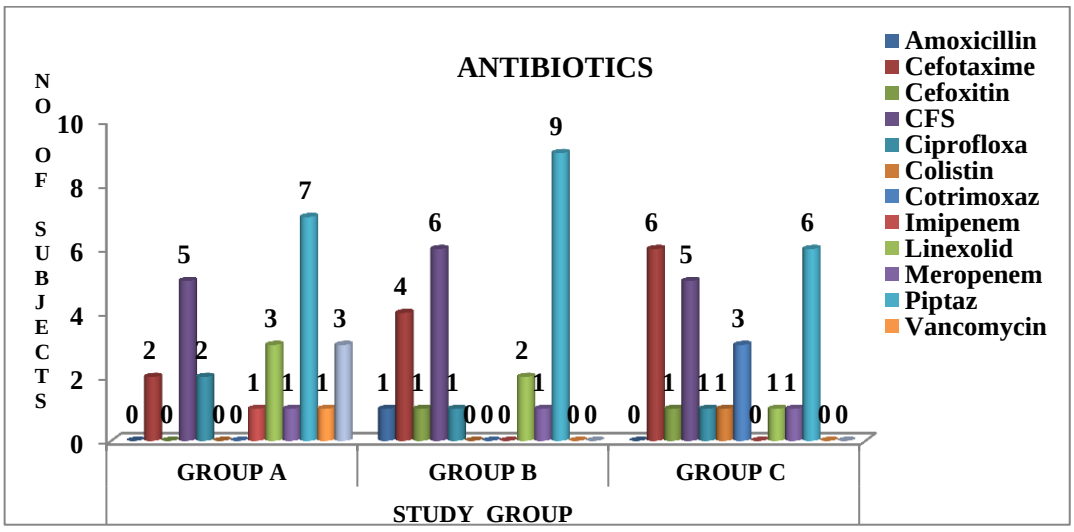
By conventional method the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

Antibiotics

TABLE-5.17

Antibiotics	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Amoxicillin	0	0	1	4	0	0
Cefotaxime	2	8	4	16	6	24
Cefoxitin	0	0	1	4	1	4
CFS	5	20	6	24	5	20
Ciprofloxa	2	8	1	4	1	4
Colistin	0	0	0	0	1	4
Cotrimoxaz	0	0	0	0	3	12
Imipenem	1	4	0	0	0	0
Linexolid	3	12	2	8	1	4
Meropenem	1	4	1	4	1	4
Piptaz	7	28	9	36	6	24
Vancomycin	1	4	0	0	0	0
Nil	3	12	0	0	0	0
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**25.26**					
p-value	**0.39**					
Significant	**Not Significant**					

FIGURE-5.17



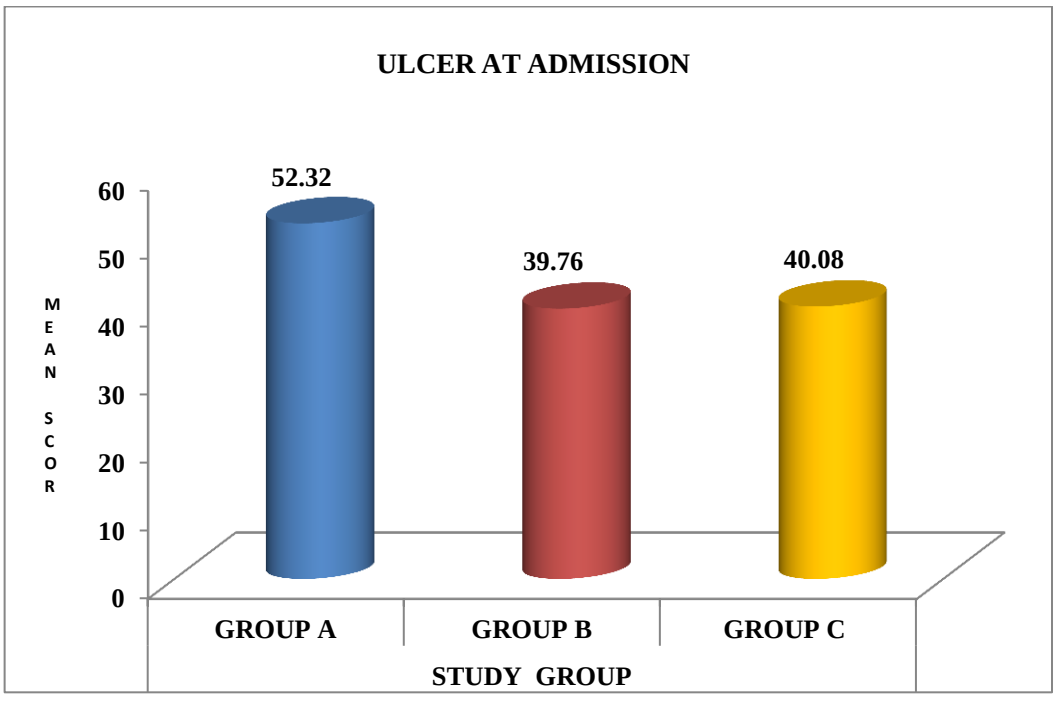
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant.

ULCER AT ADMISSION

TABLE-5.18

ULCER SIZE (Cm^2)	STUDY GROUP		
	GROUP A (N=25)	GROUP B (N=25)	GROUP C (N=25)
Mean	52.32	39.76	40.08
sd	32.17	29.06	23.74
ANOVA VALUE	**1.57**		
p-value	**0.21**		
Significant	**Not Significant**		

FIGURE-5.18

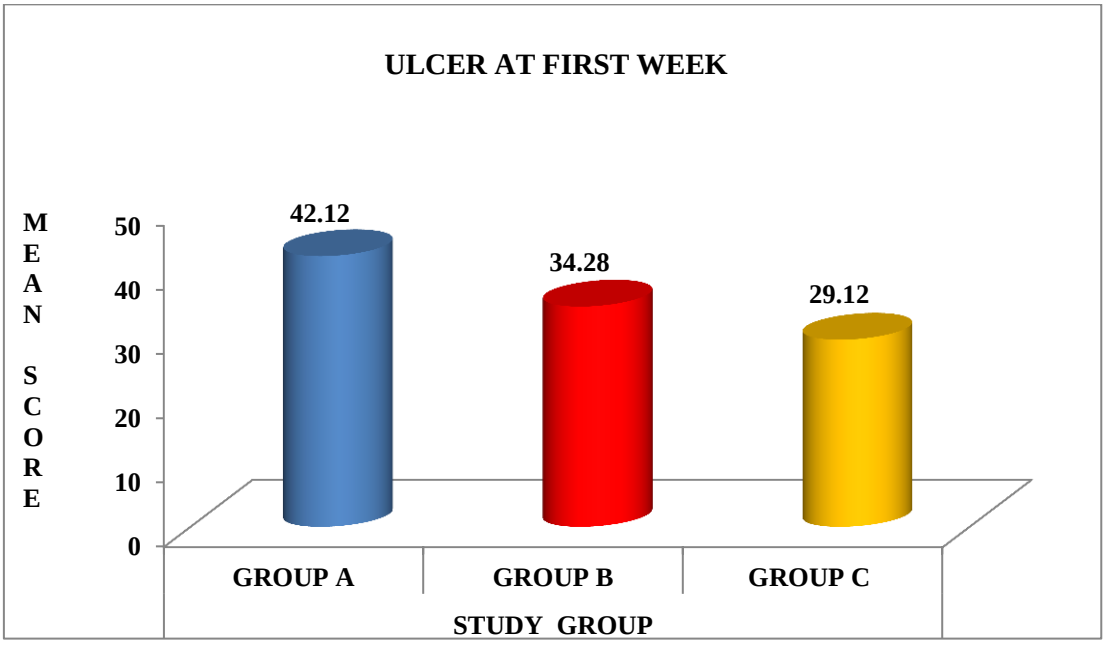


ULCER AT FIRST WEEK

TABLE-5.19

ULCER SIZE (Cm^2)	STUDY GROUP		
	GROUP A (N=25)	GROUP B (N=25)	GROUP C (N=25)
Mean	42.12	34.28	29.12
SD	31.49	23.63	16.49
ANOVA VALUE	**1.76**		
p-value	**0.18**		
Significant	**Not Significant**		

FIGURE-5.19



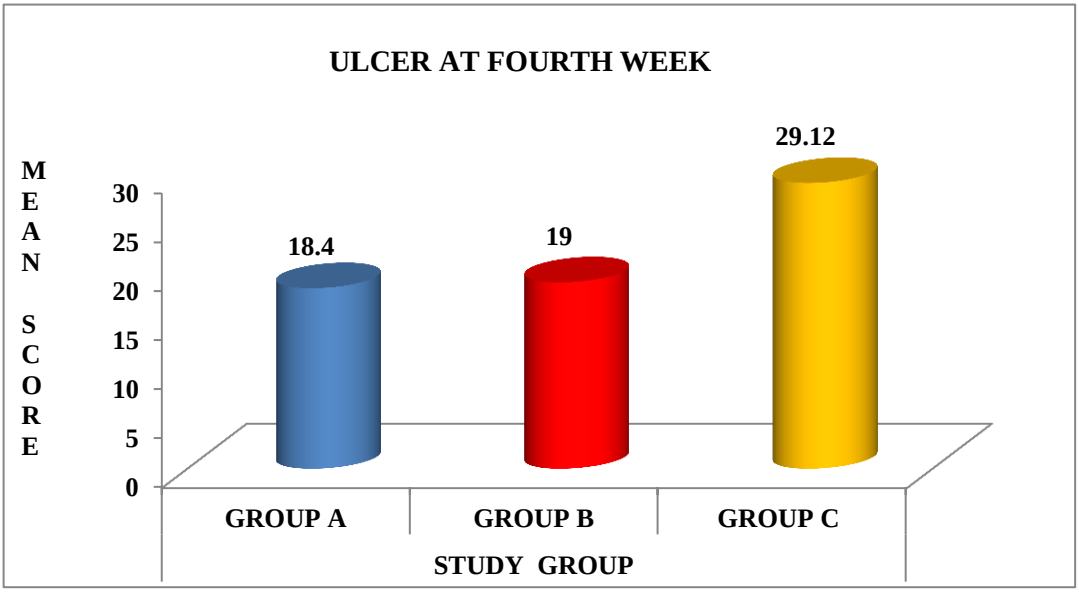
By conventional criteria the difference between the groups were comparable since the p value is **>0.05** and so it is statistically not significant. In other words both the groups were comparable.

ULCER AT FOURTH WEEK

TABLE-5.20

ULCER SIZE (Cm^2)	STUDY GROUP		
	GROUP A (N=24)	GROUP B (N=25)	GROUP C (N=25)
Mean	18.40	19.00	29.12
SD	13.56	12.60	23.41
ANOVA VALUE	**3.06**		
p-value	**0.03**		
Significant	**Significant**		

FIGURE-5.20



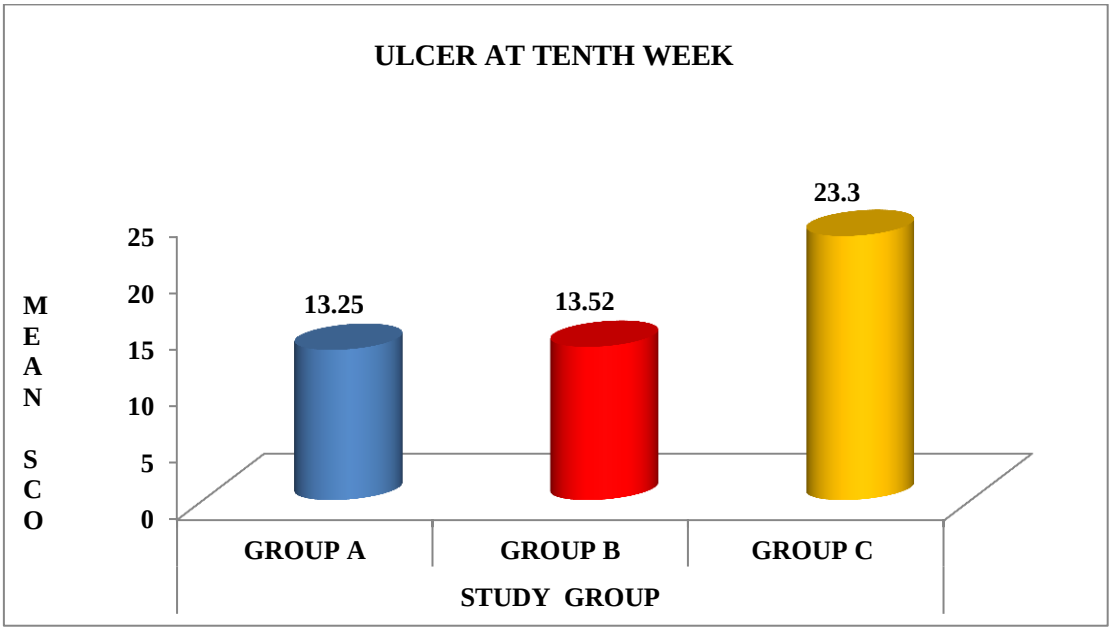
By conventional criteria the difference between the groups were comparable since the p value is **<0.05** and so it is statistically significant.

ULCER AT TENTH WEEK

TABLE-5.21

ULCER SIZE (Cm^2)	STUDY GROUP		
	GROUP A (N=20)	GROUP B (N=20)	GROUP C (N=21)
Mean	13.25	13.52	23.30
SD	8.42	7.12	17.32
ANOVA VALUE	**3.28**		
p-value	**0.05**		
Significant	**Significant**		

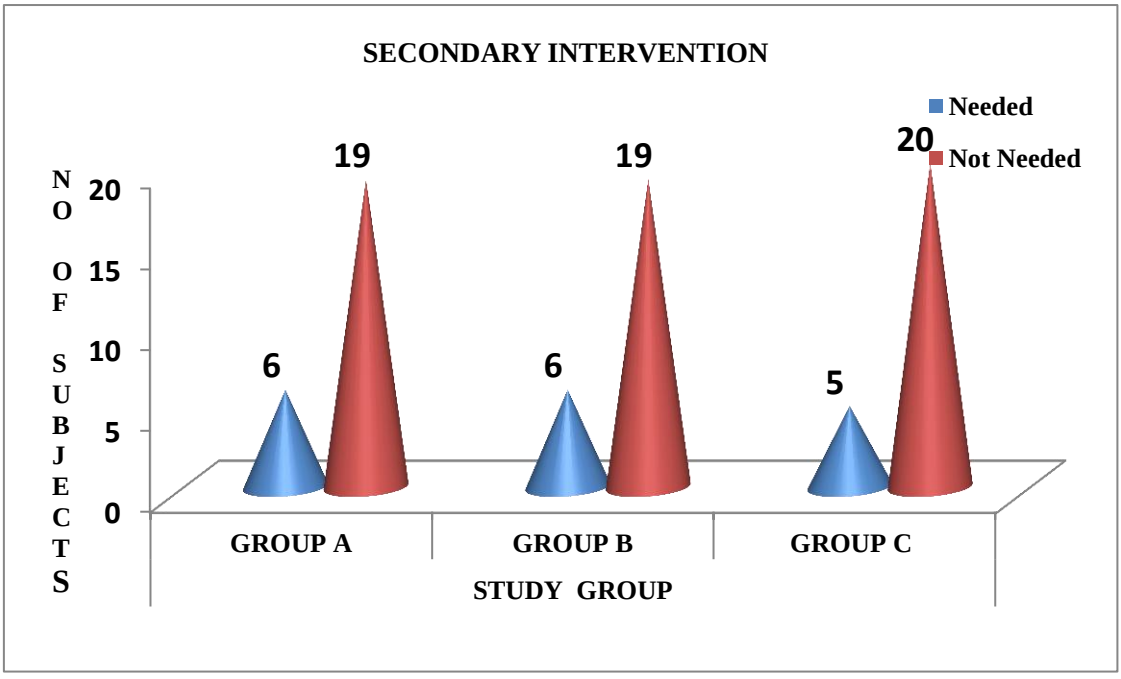
FIGURE 5.21



SECONDARY INTERVENTION

TABLE-5.22

INTERVENTION	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Needed	6	24	6	24	5	20
Not Needed	19	76	19	76	20	80
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**0.15**					
p-value	**0.93**					
Significant	**Not Significant**					

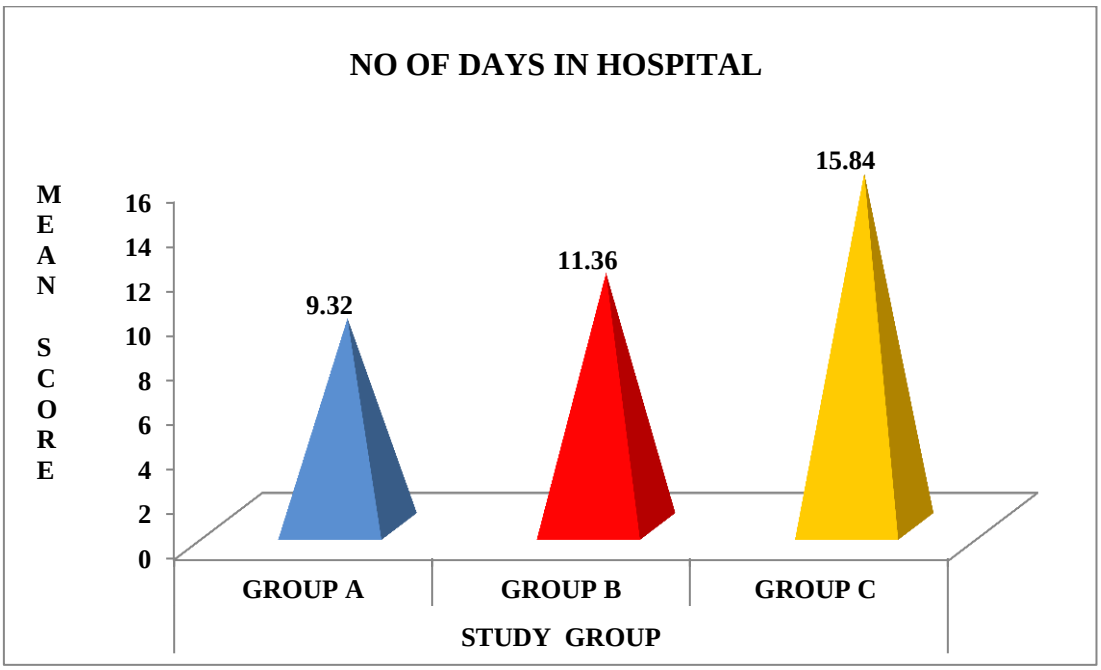


NO OF DAYS IN HOSPITAL

TABLE-5.23

	STUDY GROUP		
	GROUP A (N=24)	**GROUP B (N=25)**	**GROUP C (N=25)**
Mean	9.32	11.36	15.84
sd	5.80	10.10	10.51
ANOVA VALUE	**3.12**		
p-value	**0.05**		
Significant	**Significant**		

FIGURE-5.23

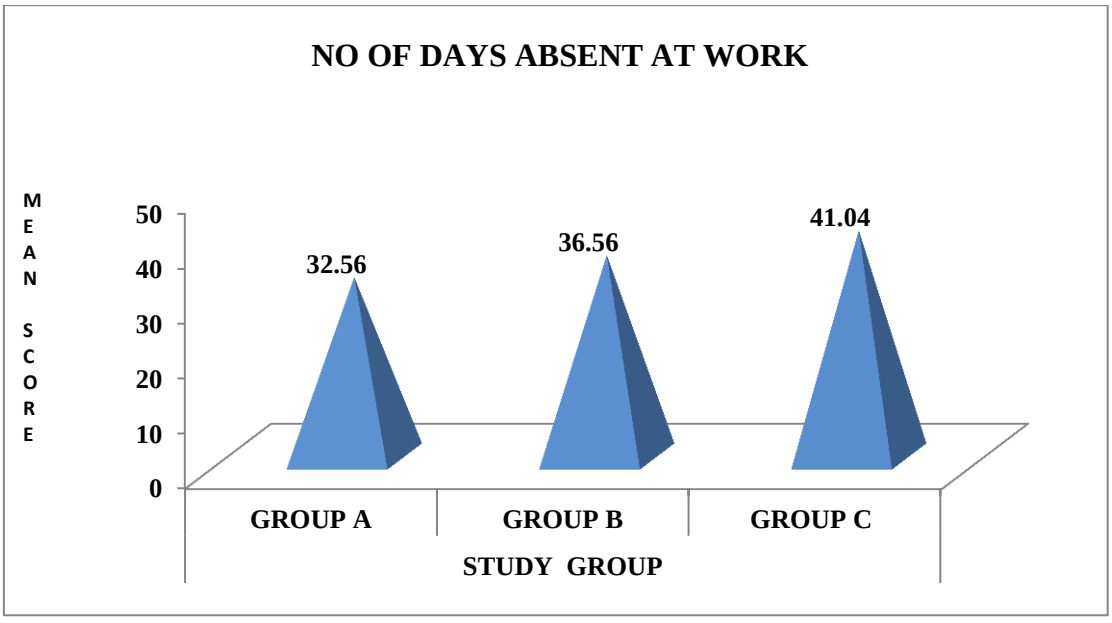


NO OF DAYS ABSENT FROM WORK:

TABLE-5.24

	STUDY GROUP		
	GROUP A (N=24)	**GROUP B (N=25)**	**GROUP C (N=25)**
Mean	32.56	36.56	41.04
sd	27.72	30.40	35.36
ANOVA VALUE	**3.49**		
p-value	**0.05**		
Significant	**Significant**		

FIGURE-5.24

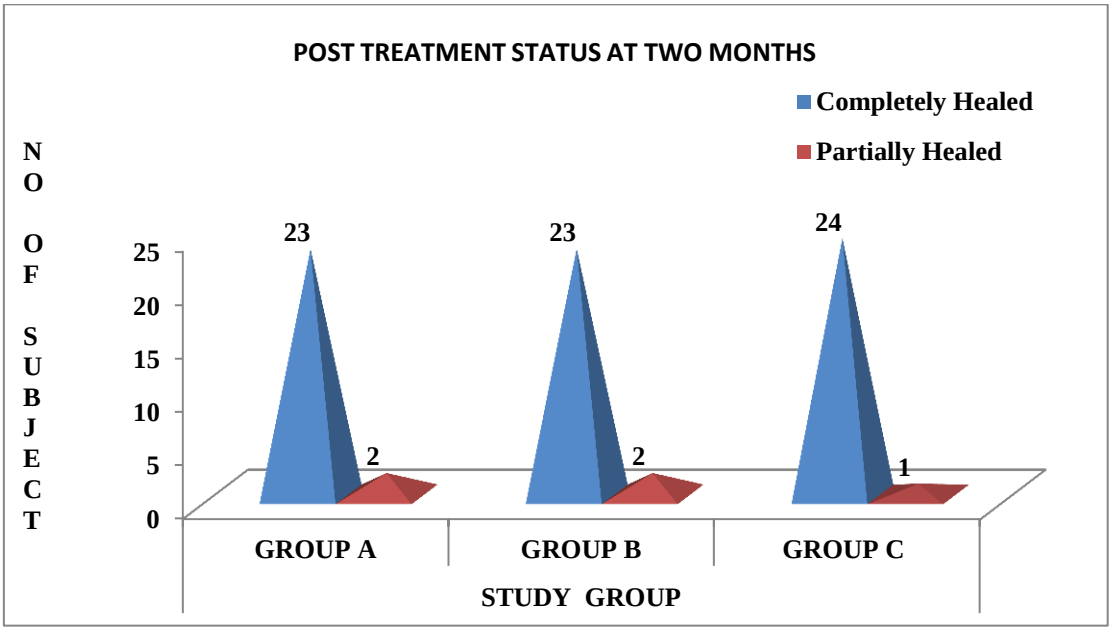


POST TREATMENT STATUS:

TABLE-5.25

	STUDY GROUP					
	GROUP A		GROUP B		GROUP C	
	N	%	N	%	N	%
Completely Healed	23	92	23	92	24	96
Partially Healed	2	8	2	8	1	4
TOTAL	**25**	**100**	**25**	**100**	**25**	**100**
Chi square Value	**0.43**					
p-value	**0.81**					
Significant	**Not Significant**					

FIGURE-5.25



DISCUSSION

Diabetic Foot Ulcers:

Overall, one out of four diabetic patients runs the risk of developing foot ulceration in his lifetime.[66] Foot ulcers result from the composite interaction of three major entities: ischemia, neuropathy, and infection.[63,64,66]

Ischemia is ascribed to peripheral arterial disease, which is exceedingly frequent in diabetes, and leads to poor nutrient supply to peripheral tissue.[64,67] Neuropathy deprives patients of protective sensation, so that trauma (such as induced by stepping on a sharp object or, simply, due to ill-fitting shoes) may be unrecognized, leading to continuing tissue destruction.[63,64,66]

Moreover, it leads to various foot deformities, resulting in abnormal focal pressure distribution on the plantar aspect of the foot.[63,64,66] Accordingly, some plantar sites have very high pressures and can easily develop ulcers.[63,64,66] Ultimately, more than half of chronic foot ulcers become infected.[65] Infection is usually polymicrobial, with a combination of Gram-positive cocci, Gram-negative bacteria, and anaerobes, and may rapidly lead to necrosis.[64] A clinically useful classification is into two categories: neuroischemic and neuropathic foot ulcers.[64,68] In the former, neuropathy and ischemia coexist. The ulcer is usually located on the margins of the foot, has irregular shape and is typically painful, although peripheral neuropathy in some patients reduces or obviates pain. The foot is not warm, but may be cold and pulseless.[64,68]

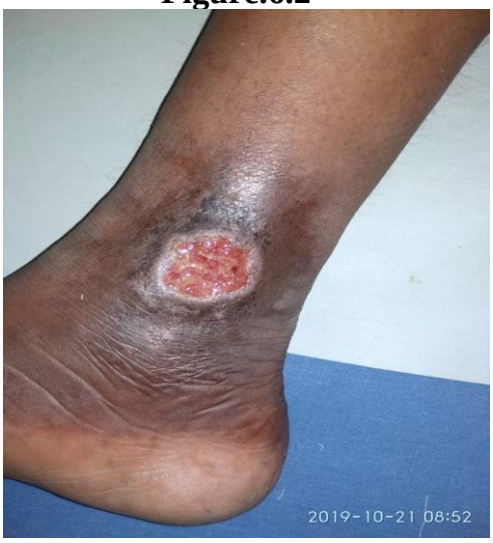
The latter is most commonly found in high-pressure areas, notably prominent metatarsal heads and apices of toes.[64,68] It is usually painless, surrounded by heavy callus formation and may be somewhat circular with a raised rim. The foot is warm, with intact pulses, while sensation is diminished.[63,64,68]

This distinction is of vital importance, because treatment differs according to etiology.[64,68]

Figure.6.1

Non healing Ulcer with minimal Granulation and more slough

Figure.6.2



Healing ulcer with sloping edges

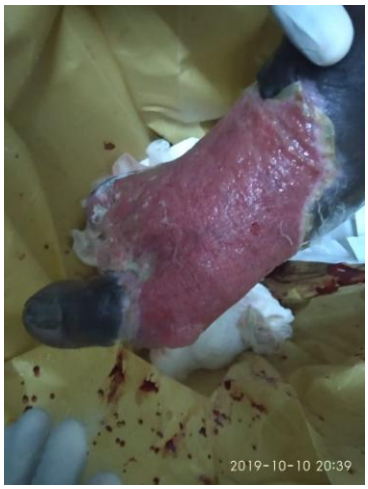


Figure 6.3 Healing Ulcer with no slough, well granulation.

Treatment of Diabetic Foot Ulcers:

Treatment of diabetic foot ulcers needs to address the three major causal factors: ischemia, neuropathy, and infection.

In the neuro-ischemic foot, it is imperative to diagnose ischemia immediately and to restore normal blood flow to the limb. This can be achieved either surgically (bypass graft surgery) or intravascularly (percutaneous transluminal angioplasty) as required (al, 2003).

In the neuropathic foot, the ulcerated area needs to be off-loaded with casts and cushioning in soles. Off-loading is combined with surgical debridement, which has been documented to promote granulation and wound closure. In both neuroischemic and neuropathic ulcers, a high index of suspicion for the diagnosis of infection is necessary to enable timely institution of antibiotics, choosing initially broad-spectrum agents and, subsequently, guided by appropriate cultures. These are usually swab cultures, although some authorities prefer deep tissue specimens.

Advances in these treatment modalities have led to improvement in healing rates. However, a significant number of ulcers (as high as 49%) still may fail to heal, indicating the need for further improvement.

Growth Factors in promoting wound healing:

Growth factors have been shown to be omnipresent throughout the healing process[40]. They act by binding to specific receptors in the plasma membranes of target cells, thereby activating signal transduction mechanisms[40].

At the cellular level, growth factors mediate macrophage migration, neovascularization, collagen synthesis, fibroblast proliferation, as well as final re-epithelialization[47]. Importantly, each growth factor acts on several cell lines, and this interaction enhances healing[40]. The need to improve the aforementioned cellular functions has led to the on going exploration of several growth factors[40]. The rationale for this investigation is that while the restoration of a normal healing cascade may be elusive, any improvement in healing rates obtained with growth factors would be useful[40].

The main growth factors involved in healing are: PDGF, fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), insulin-like growth factors (IGF_1, IGF_2), epidermal growth factor (EGF), and transforming growth factor β (TGF-β)[40]. To date, only PDGF has been approved by the US Food and Drug Administration and European authorities.[47]

Other growth factors include granulocyte-colony stimulating factor (GCSF) and nerve growth factor (NGF)[47].

Initially, GCSF yielded very good results in infected diabetic foot ulcers without severe ischemia, but these were not replicated in the following studies, so that its clinical utility is rather questionable[47]. Experience with the other growth factors remains very limited.[47]

PDGF: a protagonist in healing

Platelet-derived growth factor is mainly secreted by the platelets' α-granule, but it is also produced by other cells involved in early wound healing, ie, macrophages, endothelial cells, fibroblasts, and keratinocytes[47].

PDGF is a powerful chemoattractant and mitogen, exerting its action on fibroblasts, smooth muscle cells, and endothelial cells[47]. It also induces production of fibronectin and hyaluronic acid. There is a synergistic effect between PDGF and EGF, as well as TGF-β, and so PDGF has a pivotal role at all stages of wound healing.[47]

PDGF is a dimer consisting of A and/or B chains, held together by a disulfide bond. Three isomers (AA, BB, and AB) have been isolated. The most common and potent isomer is the BB isomer.[47]

Therefore, this isomer is the one used in the management of foot ulcers.[47]

At present, recombinant PDGF is produced by DNA technology via incorporation of the gene for the β-chain of human PDGF into the yeast *Saccharomyces cerevisiae*. The resultant homodimeric protein, becaplermin, has a biological activity similar to the endogenous PDGF-BB.[47]

A gel form of 100 μg/g becaplermin (Regranex® gel; Ortho-McNeil Pharmaceutical, Inc, Titusville, NJ, USA) has been approved by the US Food and Drug Administration for the treatment of diabetic neuropathic ulcers with adequate peripheral circulation.[47]

Efficacy of becaplermin gel in neuropathic diabetic foot ulcers:

The efficacy of becaplermin gel in the management of neuropathic ulcers has been documented by a number of randomized controlled trials, reviewed in more detail elsewhere.[47]

In these, 922 patients were studied in total[12,23,33,36]. Steed conducted the first randomized, double-blind placebo-controlled trial.[36] He enrolled 118 patients, randomized to topical application of 30 μg/g becaplermin (N = 61) or placebo (N = 57). At the end of the study, 48% (29/61) of ulcers healed in the becaplermin group vs. 25% (14/57) in the placebo group (p = 0.01).[36] There was also a non-significant trend (p = 0.09) for a greater median reduction in wound area in the becaplermin group (98.8%) as compared with the placebo group (82.1%).

Wieman and colleagues (1998) conducted a phase III randomized double-blind placebo-controlled trial on the efficacy and safety of becaplermin gel 30 μg/g (N = 132) vs. becaplermin gel 100 μg/g (N = 123) vs. placebo (N = 127)[23]. This work showed that becaplermin gel 100 μg/g added to standard wound care significantly increased healing rates and decreased time to complete healing.[23] Healing rates were 49.5% (61/123) in patients receiving becaplermin gel 100 μg/g, 36.3% (48/132) in those receiving becaplermin gel

30 μg/g, and 34.6% (44/127) in those receiving placebo. There was a significant difference (p = 0.007) between high-dose becaplermin and placebo.[23]

D'Hemercourt and colleagues (1998) compared three treatment regimens, ie, good wound care alone (N = 68), topical carboxymethylcellulose gel (N = 70), and becaplermin gel 100 μg/g added to standard wound care (N = 34). This study was statistically underpowered. However, becaplermin-treated patients did achieve a slightly higher healing rate (44.1%) in comparison with carboxymethylcellulose-treated patients (35.7%) and those receiving standard wound care alone (22%).[33]

A multi-center phase IIIB open-label study examined the efficacy and safety of becaplermin gel 100 μg/g in 134 patients (Embil et al 2000). It was shown that as high as 57.5% of ulcers managed to heal with a mean time to wound closure of 63 days and a 21% six-month recurrence rate.

Smiell and colleagues (1999) carried out a combined analysis based on all 922 patients recruited in the aforementioned studies.[23,33,36]

This analysis provided evidence for a significant beneficial effect of becaplermin on healing. Indeed, becaplermin gel 100 μg/g significantly (p = 0.0007) increased the likelihood of complete wound healing in comparison with placebo by 39% (50% vs. 36%, respectively). The drug also significantly (p = 0.01) decreased the time to heal as compared with placebo by 30% (14.1 weeks vs. 20.1 weeks, respectively).[12]

In all studies, inclusion criteria were: a) chronic foot ulcer of duration ≥8 weeks); b) adequate arterial perfusion as documented by Ankle-Brachial Pressure Index >0.70 and/or transcutaneous partial pressure of oxygen ≥30 mmHg; c) absence of infection.[47]

Safety of becaplermin gel in neuropathic diabetic foot ulcers:

In all clinical trials, the safety profile of becaplermin has consistently been found excellent, comparable with that of placebo.[47] The clinical safety of the drug has also been specifically examined by.[12] It was demonstrated that rash occurred in 2% of becaplermin-treated patients and in 1% of those receiving placebo. Similarly, cardiovascular, respiratory, musculoskeletal and central or peripheral nervous system disorders did not differ between becaplermin- and placebo-treated subjects. Moreover, there were no neutralizing antibodies against becaplermin.[12]

Cost-Effectiveness of becaplermin gel in neuropathic diabetic foot ulcers:

Several authors have examined the cost-effectiveness of becaplermin.[58,59,60,61,62] The drug has been shown to be cost-effective in Sweden[58], in four European countries (Sweden, Switzerland, UK, and France)[59] in the USA.[60] In the USA, the addition of becaplermin is associated with an initial higher cost, but this effectively reduces expenses resulting from more prolonged treatment, namely office visits and dressings, as well as complication rates.[61] Indeed, adding up to 20 weeks of becaplermin to best

medical care over 12 months resulted in 26 fewer ulcer-days per patient, equating to an avoided cost-effectiveness ratio of US$6 per ulcer-day.[62] A cost-effectiveness study of becaplermin in other parts of the world, including developing countries, is missing.[47]

A similar randomized prospective trial in India compared once-daily application of 0.01% recombinant human PDGF (Plermin, Dr. Reddy's Laboratories Inc, Hyderbad, India) to saline-moistened gauze dressing, both applied through a cast window.[9] Ten subjects were in each group. All wounds healed by the end of the study, but mean time to healing was shorter by 41.8% in the growth factor group (50 ± 23 days compared to 86 ± 31 days, $P = 0.02$). The divergence of these results from the findings in the current study may be related to the superior efficacy of the hydrogel vehicle for PDGF-BB compared to saline gauze. In support of this, one of the studies performed to secure US Food and Drug Administration approval of topical recombinant human PDGF in the United States compared saline-moistened gauze to placebo hydrogel for treatment of diabetic foot ulcers, which showed 22% healing for the gauze vs 36% for the hydrogel ($P = 0.078$, chi-square).[10]

Given the small number of subjects in the present study, it is possible the inherent efficacy of the topical PDGF was masked by the study being underpowered to detect the approximate 30%-35% greater healing in diabetic foot ulcers reported in previous and larger randomized trials.[10-12]

Moreover, there were 2 differences in the treatment groups that may have confounded the analysis by favourably influencing the control group; namely, higher ESR and longer duration of the wounds in the test group. Erythrocyte sedimentation rate was measured to detect previously undiagnosed bone infection, and in general, higher ESR is not associated with worse prognosis when osteomyelitis is absent, as was the case here. On the other hand, previous studies have shown that wound chronicity is a significant prognostic factor for healing.[13] This disparity could have overshadowed a modest positive effect of the topical PDGF on healing. It seems likely, however, that even if a positive effect with topical PDGF was missed, the magnitude of the effect, when casting is employed, is not as large as has been observed with less stringent off-loading.

This study has been done to Evaluate efficacy of PDGF, Hydrogel and Normal Saline dressing in Diabetic Foot Ulcers in terms of**:**

- Decrease in ulcer size
- Length of hospital stay
- Abstinence from work
- Need of secondary intervention

Study period over 18 months by enrolling a total of 75 patients.

Out of 75, 25 will be treated in the form of standard care with Hydrogel dressing, 25 will take treatment in the form of standard care with rh-PDGF, 25 will be treated with standard care and Normal Saline dressing once a day.

MANAGEMENT:

History, Clinical Examination will be recorded. A complete Haemogram, Fasting and Post prandial Blood sugar, Renal Function test will be taken. X-Ray foot will be taken to rule out Osteomyelitis. Doppler study for Vasculopathy.

Neurological Examination by Tuning fork (Large fibres), Hot/cold objects (Small fibres) and Ankle Reflexes for Neuropathy. Standard cares given were Glycaemic control, Adequate control of infection, Debridement.

And the following parameters will be assessed and entered in a preformed protocol:

Size of the ulcer at the time of admission, Size of the ulcer at the end of 1^{st} week, Size of the ulcer at the end of 4^{th} week, Size of the ulcer at the end of 10^{th} week, Need of secondary intervention , Number of days stay in hospital, Number of days absent from work, Post treatment status at the end of the study.

These parameters were entered in preformed protocol and analysed indicated that Dressings with rh-PDGF are associated with faster healing rate than Hydrogel dressings and normal saline dressing.

Significant difference were found in terms of ulcer size at 4th week, ulcer size at 10th week , no of days stay in hospital and no of days absent from work and also in terms of cost effectiveness in the treatment of diabetic foot patients.

There is no significant difference in change of ulcer size at the end of 1st week and whether need of secondary intervention and post treatment status.

AGE & GENDER DISTRIBUTION:

In the study group less than 30 years who had dressing with rh-PDGF was 1 (4%), dressing with Hydrogel was 1(4%) and dressing with normal saline was 0(0%).

While in age group 31-40 ,dressing with rh-PDGF was 4(16%), dressing with Hydrogel was 6(24%) and dressing with normal saline was 2(8%).

Age group 41-50, dressing with rh-PDGF was 11 (44%), dressing with Hydrogel was 6(24%) and dressing with normal saline was 10(40%).

Age group 51-60, dressing with rh-PDGF was 4(16%), dressing with Hydrogel was 8(32%) and dressing with normal saline was 8(32%).

Age group 61-70, dressing with rh-PDGF was 4(16%), dressing with Hydrogel was 3(12%) and dressing with normal saline was 5(20%).

Age group 71-80, dressing with rh-PDGF was 1 (4%), dressing with Hydrogel was 1(4%) and dressing with normal saline was 0(0%).

Among the group, males who had dressing with rh-PDGF was 14(56%), dressing with Hydrogel was 15(60%) and dressing with normal saline was 17(68%).

Females who had dressing with rh-PDGF were 11(44%), dressing with Hydrogel were 10(40%) and dressing with normal saline were 8(32%).

Since age and gender are not statistically significant ,it means that there is no difference between the groups. Also in simple terms the groups contain subjects with the same demographic characteristics.

WAGNERS GRADING:

WAGNER GRADE 1: Patients who had dressing with rh-PDGF were 2(4%), dressing with Hydrogel were 6(24%) and dressing with normal saline were 4(16%).

WAGNER GRADE 2: Patients who had dressing with rh-PDGF were 23(96%), dressing with Hydrogel were 19(76%) and dressing with normal saline were 21(84%).

Since p value >0.05 it is statistically not significant.

Since WAGNER'S GRADE are not statistically significant ,it means that there is no difference between the groups. Also in simple terms the groups contain subjects with the same demographic characteristics and comparable.

ULCER SIZE AT END OF 1ST WEEK:

In this study the size of the ulcer was assessed at the end of 1st week of treatment and recorded. Patients who had dressing with rh-PDGF whose mean 42.12(SD=31,49), dressing with Hydrogel whose mean 34.28(SD – 23.63) and dressing with normal saline whose mean 29.12(SD-16.49).

Since p value is 0.18 (>0.05), the test value is statistically not significant. Hence it is proposed that there is no difference in change of size of ulcer at the end of 1st week in all the three groups.

ULCER SIZE AT END OF 4th WEEK:

The size of the ulcer was again assessed at the end of 4th week of treatment and recorded. Patients who had dressing with rh-PDGF whose mean 18.40(SD=13.56), dressing with Hydrogel whose mean 19.00(SD – 12.60) and dressing with normal saline whose mean 29.12(SD-23.41).

Since p value is 0.03 (<0.05), the test value is statistically significant. Hence it is proposed that there is difference in change of size of ulcer at the end

of 4th week. i.e, who underwent rh-PDGF dressings has better rate of decrease in size when compared to Hydrogel and Normal saline.

ULCER SIZE AT END OF 10th WEEK:

The size of the ulcer was again assessed at the end of 10th week of treatment and recorded. Patients who had dressing with rh-PDGF whose mean 13.25(SD=8.42), dressing with Hydrogel whose mean 13.52(SD-7.12) and dressing with normal saline whose mean 23.30(SD-17.32).

Since p value is 0.05 (=0.05), the test value is statistically significant.

Hence it is proposed that there is difference in change of size of ulcer at the end of 10th week. i.e, who underwent rh-PDGF dressings has better rate of decrease in size when compared to Hydrogel and Normal saline.

NEED OF SECONDARY INTERVENTION:

In this study, while conducting comparison of Dressings whether any patients needed Secondary intervention like Split Skin Grafting, Flap cover/wound debridement/amputation at the end of 10th week was assessed.

Of those who need secondary intervention who had dressing with rh-PDGF were 6(24%), dressing with Hydrogel were 6(24%) and dressing with normal saline were 5(20%).

And those who do not need secondary intervention had dressing with rh-PDGF were 19(76%), dressing with Hydrogel were 19(76%) and dressing with normal saline were 20(80%).

Since p value is 0.93(>0.05), the test value is statistically not significant.

Hence it is proposed that there is no difference in need of secondary intervention among the study groups. It means that there is no difference in study groups.

HOSPITAL STAY (NO. OF DAYS IN HOSPITAL):

In this study, the study groups were compared by number of days staying in hospital and analysed.

Patients who had dressing with rh-PDGF whose mean 9.32(SD=5.80), dressing with Hydrogel whose mean 11.36(SD-10.10) and dressing with normal saline whose mean 15.84(SD-10.51).

Here p value is 0.05(=0.05). So the study is statistically significant.

Hence it is proposed that there is difference in number of days staying in hospital. i.e, patients who underwent rh-PDGF dressings has less number of stay in hospital when compared to Hydrogel and Normal saline.

ABSTINENCE FROM WORK (NO. OF DAYS ABSENT FROM WORK):

In this study, the study groups were compared by number of days absent from work and analysed.

Patients who had dressing with rh-PDGF whose mean 32.56(SD=27.72), dressing with Hydrogel whose mean 36.56(SD-30.40) and dressing with normal saline whose mean 41.04(SD-35.36).

Here p value is 0.05(=0.05). So the study is statistically significant.

Hence it is proposed that there is difference in number of days absent from work. i.e, patients who underwent rh-PDGF dressings has less number of days absent from work and early return to work when compared to Hydrogel and Normal saline.

POST TREATMENT STATUS:

In this study, the study groups were compared by assessing the post treatment status at the end of the study and analysed.

Patients who had dressing with rh-PDGF were 23(92%), dressing with Hydrogel were 23(92 %) and dressing with normal saline were 24(96%) were completely healed.

Patients who had dressing with rh-PDGF were 2(8%), dressing with Hydrogel were 2(8 %) and dressing with normal saline were 1(4%) were partially healed.

Here p value is 0.81(>0.05). So the study is statistically not significant.

So it is proposed that there is no difference in healing status among the study groups at the end of the study.

This study observationally suggests that rh-PDGF dressing was better when compared with both Hydrogel & Normal saline dressing, while Hydrogel dressing was better when compared with Normal saline dressing in change of ulcer size at the end of 4^{th} and 10^{th} week and Number of days stay in hospital , return to work.

The present study emphasizes the cost effectiveness of the treatment and early return to work for the Diabetic foot ulcer patients.

SUMMARY

The present study to compare the efficacy of rh-PDGF dressing versus Hydrogel versus Normal saline dressing in Diabetic foot ulcer management was conducted at Department of General Surgery, ESIC Medical College & PGIMSR, Chenna-78 between APRIL 2018 and SEPTEMBER 2019. The population was selected based on specific inclusion and exclusion criteria. The total sample size was 75, out of which 25 belong to Group A(Dressing with rh-PDGF), 25 belong to Group B (Dressing with Hydrogel), 25 belong to Group C(Dressing with Normal saline).

The following details were analysed in this study.

- Change in size of Ulcer at 1^{st}, 4^{th}, 10^{th} week
- Number of Days in Hospital Bed
- Number of Days Absent from Work Due to Disease
- Needed Secondary Intervention like Debridement, SSG, FLAP COVER etc,.

Change in size of Ulcer:

Grade of ulcer:

Only WAGNER'S grade 1 and 2 were included.

As the grading increase more chance of amputation rate increases.

Size of ulcer at end of 1^{st} week: No significance while applying rh-PDGF dressing.

Size at 4th and 10th week:

There is significant rate of decrease in size at the end of 4th and 10th week while putting dressing with rh-PDGF when compared with Hydrogel and Normal saline dressing.

No. of Days in Hospital:

Group A patients when compared to Group B and Group C has significant minimum number of days stayed in hospital.

No. of days Absent from work:

Group A patients when compared to Group B and Group C has significant minimum number of days absent from work and early return to work.

Need of secondary intervention:

There is no significant difference among the study groups A,B & C for need of secondary intervention like SSG, Flap cover, Debridement etc,.

Improvement of ulcer / Recovery time:

The ulcer healing was assessed based on the ulcer size, granulation tissue, slough presence/absence.

CONCLUSION

Present study concludes that:

Management of diabetic foot ulcer with rh-PDGF dressing versus Hydrogel versus Normal saline dressing has:-

- Better ulcer healing and contraction rate
- Early recovery from the disease
- Early return to work
- Easily available in market and easy to use.
- Avoid cross contamination by long hospital stay.

Thus, Recombinant human Platelet Derived Growth Factor is a better topical agent in management of Diabetic foot ulcer patients.

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STUDY PROFORMA

DATE :

NAME :

AGE :

SEX :

ESIC NO :

IP NO :

ADDRESS :

DATE OF ADMISSION :

DATE OF DISCHARGE :

HISTORY :

CLINICAL EXAMINATION :

SIZE OF ULCER AT ADMISSION :

WAGNER'S GRADING :

DETAILS OF TREATMENT :

DURATION &DETAILS OF
T2DM TREATMENT :

NO OF DAYS IN HOSPITAL :

PATIENT UNDER GROUP A/B/C :

DETAILS OF SECONDARY INTERVENTION:

POST TREATMENT STATUS :

SIZE OF ULCER AT 10 WEEKS :

DAYS AFTER RETURN TO WORK :

INFORMED CONSENT

Informed consent for patients who are attending surgical OPD or casualty in ESIC MEDICAL COLLEGE &PGIMSR hospital, and whom we are inviting to participate in the research titled "**A comparative study of Topical Platelet Derived Growth factor(rh-PDGF) vs Hydro gel vs Normal Saline Dressing for treating diabetic foot ulcers"** at ESIC MEDICAL COLLEGE &PGIMSR, Chennai-78.

Dr. DINESH.M M.S(General surgery) post graduate is the principal investigator of this research under ESI-PGIMSR, Chennai.

Part I: Information Sheet

Introduction

We, **Dr. DINESH.M** 1st year General Surgery PG, Guided by Dr. BHANUMATI GIRIDHARAN Associate Professor Of General Surgery, are going to give you information and invite you to be a part of this research. Before you decide, you can talk to anyone of us you feel comfortable with about the research. This consent form may contain words that you do not understand. Please ask us to stop as we go through the information and we will take time to explain. If you have questions later, you can ask us.

Purpose of the research

We will be giving you treatment for diabetic foot ulcers by hydrogel dressing or platelet derived growth factor dressing or Normal Saline dressing based on the group you are allotted.

Type of Research

This research will involve your participation in a non-experimental manner, with assured privacy and confidentiality.

Right to Refuse or Withdraw

Your participation is strictly voluntary. Refusal to participate will not affect subsequent services to you

Procedures

Risks

Benefits

Confidentiality

All information you provide will be kept confidential. Your name will not be used in any way.

Whom to Contact

If you have any questions, you can ask them now or later. If you wish to ask questions later, you may contact:

Dr. DINESH.M 9626956889

This proposal has been reviewed and approved by Institute Ethical Committee, which is a committee whose task is to make sure that research participants are protected from any harm.

If you have any questions regarding any part of the study, feel free to ask.

Part II: CERTIFICATE OF CONSENT

I have read the information in the consent form (or it has been read to me.) I was free to ask any questions and they have been answered. I understand what is being requested of me as a participant in this study. I have been given satisfactory answers to my questions. I certify that I am more than 18 years of age. I freely consent to participate in the study called "**A comparative study of Topical Platelet Derived Growth factor(rh-PDGF) vs Hydro gel vs Normal Saline Dressing for treating diabetic foot ulcers"** at ESIC MEDICAL COLLEGE &PGIMSR, Chennai-78.

I have read and understood this consent form and the information provided to me.

I have been explained about the nature of the study.

My rights and responsibilities have been explained by the investigator

I agree to cooperate with the investigator.

Currently I am not participating in any research study.

I hereby give permission to the investigators to release the information obtained from me as a result of participation in the study to the regulatory authorities, government agency, ethical committee. I understand that they may inspect my original records.

My records will be kept confidential

I have decided to participate in the study.

As I was not able to read, the consent form has been read out to me by the investigator and all my questions have been answered and I give my consent with my free will.

_____

Name of Participant

_____ _____

Sign of Participant Name of Investigator (Signed)

ஒப்புதல் படிவம்

மருத்துவர் தினேஷ் தனது முதுநிலை அறுவைசிகிச்சை பட்டப்படிப்பு முழுமைபெறுவதர்காக நீரிழிவு நோய் கால் புண்ணிற்கு சிகிச்சை மற்றும் வளர்ச்சி மருந்துடன் மேற்கொள்ளும் ஆய்வினைப்பற்றி எனக்கு என் தாய்மொழியில் விளக்கப்பட்டது.

இந்த ஆய்வின் அனைத்து அம்சங்களும் விளக்கப்பட்டது. இதில் நான் என் முழு விருப்பத்துடன் கலந்து கொள்கிறேன். எனினும் எந்த நேரத்திலும், எந்த காரணமுமின்றி இந்த ஆய்விலிருந்து விலகிக்கொள்ள எனக்கு முழு உரிமையுள்ளது. இதனால் எனது நலனில் எந்த பாதிப்பும் ஏற்படாது என்று உருதியளிக்கப்படுகிறது. இந்த ஆய்வின் அறிக்கையில் என்னுடைய தனிப்பட்ட விவரங்கள் அனைத்தும் ரகசியமாய் பாதுகாக்கப்படும் என்று எனக்கு உறுதியளிக்கப்பட்டிருக்கிறது. மேற்கூறிய உறுதிமொழிகள் யாவும் பின்பற்றப்படும் பட்சத்தில் நான் இந்த ஆய்வுக்கட்டுரைக்கு என்னுடைய விவரங்களை அளிக்க முன்வருகிறேன். இதற்கு முழுமனதுடன் ஒப்புதலை தந்து இந்த ஆய்வறிக்கையில் பங்கேற்க்கிரேன்.

இப்படிக்கு,

(கையொப்பம்)

KEY TO MASTER – CHART

Group A	:	Dressing with rh – PDGF
Group B	:	Dressing with Hydrogel
Group C	:	Dressing with Normal Saline
Grade of Ulcer	:	WAGNER'S Grading.
NAD	:	No Abnormality Detected
TI	:	Type I Diabetes Mellitus
TII	:	Type II Diabetes Mellitus

S.No	Name	Age	sex	ESIC No	Address	DOA	DOD	History	DM	Smoking	ALCOHOL	Comorbid	Nutrition	Pallor	Wagner's grade	Systemic features	Blood sugar	Duration of T2DM	Glycemic Control	Total WBC Count	X ray	Wound C & S	Doppler	Antibiotics	Surgery	Dressing group	ULCER At Admsn	Size at 1 wk	Size at 4 weeks	Size at 10 weeks	Secondary intervention	NO of days in Hosp	No of days Absent from work	Post Treatment status (2mon)
1	Mahadevi	40	F	5150112660	Cuddalore	12/7/2018	12/11/2018	ulcer leg 10 days	T II	no	no	DM	well	no	I	no	180	5 yrs	Insulin inj and OHA	10400	NAD	MSSA	Normal study	piptaz	debridemen	B	6 *4 Rt Distal leg	5*4	3*3	NA	Wound debridement	4 days	1 month	Healed well
2	Nagammal	37	F	5114473853	Saidapet	4/3/2019	4/3/2019	ulcer foot with fever 10	T II	no	no	DM/SHTN	Fair	+	II	No	236	10 yrs	Insulin inj and OHA	12300	NAD	Klebsiella	Normal study	Ciprofloxacii	debridemen	A	10 *10 cm Rt foot	6*7	5*5	4*3	Nil	1 day	3weeks	Healed well
3	Jai Ganesh	40	M	5110180458	Vellore	5/31/2019	6/5/2019	Ulcer Rt foot 15 days	T II	Yes	Occasional	DM/BA	WELL	no	II	no	190	10 yrs	OHA	8600	NAD	rep pyogen	ficant luminal r	CFS	Debridemen	C	4 * 5 cm Rt foot	5*5	4*3	2*1	reat Toe disarticulatio	6 days	1 month	Healed well
4	Kali	54	M	5127529359	Chennai	3/26/2019	6/30/2019	Ulcer Rt foot 15 days	T II	No	Yes	DM	well	No	II	No	139	4 yrs	OHA	8900	NAD	E.coli	NAD	Meropenem	Debridemen	A	6*5	4*5	3*2	NA	NIl	5	2 weeks	Healed well
5	Saravanan	44	M	5115016751	Chennai	2/8/2019	2/15/2019	Swellin and ulcer rt dist	T II	No	Yes	DM	Good	No	I	No	164	2 yrs	OHA	7500	NAD	Sterile	n study	NIL	Debridemen	B	3 *3cm Rt leg	2*1 cm	1 * 1cm	NA	NIl	8 days	20 days	Healed well
6	Immanuel	62	M	5124617343	Chennai	3/6/2019	3/18/2019	Ulcer rt dorsum of foot	T II	No	Yes	DM	good	no	II	Fever	286	5yrs	Irregular OHA	15600	NAD	cinetobacte	NAD	otrimoxazol	Debridemen	A	10 * 10 cm rt foot	6*8 cm	5 *4 cm	3 * 3 cm	Nil	12 days	1 month	Doing well
7	Dhinakaran	54	M	5127826226	Chennai	1/25/2019	2/2/2019	Ulcer left foot 1 month	T II	Yes	yes	DM/CAD	Fair	No	I	No	190	3 yrs	OHA	11000	NAD	E.coli	Nad	Amoxicillin	Debridemen	C	6*7cm	5*5	4*3	NA	Nil	6 days	3 weeks	Helaed well
8	kumara chithra	40	F	5122489400	Cuddalore	3/26/2019	8/4/2019	ulcer foot with fever 10	T II	no	no	DM	fair	no	II	Fever	178	9yrs	OHA	17000	NAD	Klebsiella	NAD	cefotaxime	debridemen	B	10 * 10 cm rt foot	10*10cm	7*6	4*4	Nil	12 days	1 month	Doing well
9	Banumathy	59	F	5127513060	Chennai	3/26/2019	4/25/2019	ulcer foot with fever 2 d	T II	no	no	DM	Fair	yes	II	Fever	257	6yrs	Irregular OHA	16000	nad	MSSA	NAD	piptaz	debridemen	B	6*6 in left foot	5*4	4*4	3*2	nil	29 days	2 months	Healed well
10	kanniyammal	55	F	5116425380	Chennai	14/03/2019	18/03/2019	ulcer over Left foot* 3 d	T II	no	no	DM/SHTN	Fair	no	II	no	216	5 yrs	OHA	10000	nad	monas aue	nad	piptaz	debridemen	C	5*5 in left foot	5*5	4*3	2*1	nil	4 days	1 month	Healed well
11	Vasanthakumar	63	f	5116001585	Chennai	5/11/2019	10/11/2019	ulcer foot with fever 10	T II	no	no	dm	fair	yes	II	no	278	4yrs	OHA	12000	NAD	rep pyogen	nad	CFS	debridemen	B	4*4	4*3	3*3	1*2	NIL	5 DAYS	2 months	Healed well
12	UMA	43	F	5128537496	Chennai	12/3/2019	14/03/2019	ulcer foot with fever 10	T II	NO	no	DM	Fair	NO	II	Fever	147	4yrs	Insulin inj and OHA	11000	NAD	Klebsiella	NAD	cefotaxime	debridemen	A	4*4	4*3	2*2	NA	Nil	2 DAYS	25 DAYS	Healed well
13	BABU	62	M	51900817	Chennai	5/15/2019	31/05/2019	Ulcer rt dorsum of foot	T II	Yes	Yes	DM/HTN	Fair	NO	II	NO	169	15YRS	Insulin inj and OHA	16000	NAD	MRSA	NAD	LINEZOLID	debridemen	C	5*5	4*4	2*2	NA	NIL	15 DAYS	2 MONTHS	EALED WELL
14	JOSEPH	55	M	6380357229	Thanjavur	15/05/2019	31/05/2019	Ulcer Rt foot 15 days	T II	no	Occasional	DM/CAD	Fair	no	II	no	268	10yrs	oha	21000	nad	monas aue	nad	piptaz	debridemen	B	4*4	4*4	2*2	2*1	Nil	15 DAYS	2 months	Healed well
15	rajagopal	46	m	512981930	Chennai	15/05/2019	18/07/2019	ulcer Lt foot 1 month	T II	No	Yes	DM/CAD	Fair	yes	II	fever	357	6yrs	Insulin inj and OHA	16000	nad	mssa	nad	cfs	debridemen	A	10 * 10 cm rt foot	gangrene	6*6	5*5	, 4 th toes disarticula	35 days	3 months	Healed well
16	munuswamy	60	m	5124264822	Chennai	20/04/2019	30/04/2019	ulcer foot with fever 10	T II	no	no	DM/BA	fair	no	II	Fever	275	20	Insulin inj and OHA	22000	nad	monas aue	nad	piptaz	debridemen	C	10 * 10 cm rt foot	8*8	2*4	4*4	nil	20 days	2 months	EALED WELL
17	Shaji	52	male	5127765684	Chennai	28/03/2019	14/05/2019	ulcer Lt foot 1 month	T II	yes	Yes	DM/SHTN	fair	no	II	fever	367	10 yrs	OHA	14000	nad	MSSA	nad	CFS	debridemen	B	8*8	7*8	5*5 cm	4*4	t below knee amputa	2 months	2 months	EALED WELL
18	kannaiyan	67	male	5141900991	Chennai	20/04/2019	22/04/2019	ulcer foot with fever 10	T II	yes	no	DM/CAD	fair	no	II	Fever	267	10 yrs	oha	16000	nad	sterile	nad	cefotaxime	debridemen	A	4*4	2*2	na	na	Nil	2 DAYS	2 weeks	EALED WELL
19	arputharaj	49	male	5113824994	Chennai	4/22/2019	24/05/2019	ulcer Lt foot 1 month	T II	no	yes	DM/HTN	fair	no	II	nil	367	8yrs	Insulin inj and OHA	14000	nad	MSSA	nad	cfs	debridemen	C	10 * 14 cm lt foot	10*10cm	8*8	8*8	nil	30 days	2 months	EALED WELL
20	ranganathan	62	m	516119010	Chennai	19/06/2019	24/07/2019	Ulcer Rt foot 15 days	T II	Yes	yes	DM/CAD	fair	no	II	Fever	118	5yrs	OHA	6000	nad	monas aue	NAD	piptaz	debridemen	B	5*5	4*3	2*2	NA	Nil	43 DAYS	2 months	EALED WELL
21	varadhan	50	m	512581116	Chennai	31/07/2019	14/07/2019	ulcer Lt foot 1 month	T II	no	Occasional	DM/HTN	Fair	no	II	nil	228	6yrs	OHA	16000	NAD	MSSA	NAD	cefotaxime	debridemen	A	5*5	4*4	4*4	2*1	Nil	15 DAYS	1 month	EALED WELL
22	sankar	40	M	5124273021	kanchipuram	31/07/2019	3/8/2019	ulcer over Left foot* 3 d	T II	no	yes	DM/CAD	fair	no	II	nil	196	7yrs	Insulin inj and OHA	24000	NAD	rep pyogen	NAD	CFS	debridemen	C	5*5	4*3	5*5 cm	4*4	NIL	5 DAYS	2 months	healed well
23	stella	56	F	5115103083	kattupakam	3-Feb	5/3/2019	Ulcer rt dorsum of foot	T II	no	no	DM/HTN	fair	yes	II	Fever	207	9yrs	oha	19000	NAD	Klebsiella	NAD	cefotaxime	debridemen	B	6*6 in rt foot	5*4	3*3	2*1	NIL	3 DAYS	2 months	EALED WELL
24	saraswathy	50	F	5129179308	CHENNAI	5/15/2019	5/19/2019	ulcer over Left foot for 6	T II	NO	NO	DM/CAD	Fair	no	II	nil	256	6yrs	Insulin inj and OHA	10000	nad	monas aue	nad	piptaz	debridemen	A	5*6	5*6	5*5	5*2	nil	4 days	1 month	healed well
25	chitra	39	f	5122489400	Chennai	4/26/2019	5/8/2019	ulcer over left dorsal as	T II	no	no	DM	Fair	no	II	Fever	93	8YRS	OHA	6600	NAD	rep pyogen	NAD	CFS	debridemen	C	5*6	5*5	5*5	5*4	NIL	12 DAYS	3 WEEKS	healed well
26	USHA	49	F	512760658	HIRUVALLUR	3/25/2019	4/1/2019	ULCER OVER MEDIAL	T II	NO	no	DM	Fair	yes	II	NIL	156	5YRS	OHA	8900	NAD	monas aue	NAD	PIPTAZ	debridemen	B	4*5	4*5	4*5	4*4	NIL	6 DAYS	3 WEEKS	EALING WELL
27	MALAR	35	M	5123442783	CHENNAI	2/22/2019	3/5/2019	ULCER OVER LEFT F	TII	no	no	dm/shtn	Fair	no	II	nil	168	2yrs	oha	11600	nad	mssa	nad	CFS	debridemen	A	7*10	7*10	7*7	6*5	Nil	14 DAYS	MONTH 2 WEEK	EALED WELL
28	SANTHA	59	F	5122000548	CHENNAI	2/8/2019	2/18/2019	ULCER OVER RIGHT	TII	NO	NO	DM/SHTN	Fair	NO	II	nil	286	5YRS	OHA	9100	NAD	Klebsiella	NAD	cefotaxime	debridemen	C	5*7	5*7	5*5	5*4	NIL	10 DAYS	3 WEEKS	EALED WELL
29	ARAMESHWAR	48	F	5126109269	Chennai	5/18/2019	6/5/2019	ULCER OVER LEFT F	TII	NO	NO	DM	FAIR	NO	II	NIL	226	3YRS	OHA	15000	NAD	monas aue	NAD	PIPTAZ	debridemen	B	5*6	5*5	5*4	2*3	NIL	18 DAYS	1 MONTH	healed well
30	Somasundaram	66	M	5116386527	Chetpet	6/6/2019	6/12/2019	Ulcer over Left foot 2 wk	T II	No	yes	DM/SHTN	Moderate	+	II	No	212	25 yrs	OHA & Insulin	9500	NAD	cinetobacte	Nad	Ciprofloxacii	debridemen	A	5*6cm	4*5	4*3	2*3	nil	6 days	1 month	Healed well
31	Varadharajan	68	M	5113901682	Pallavaram	6/17/2019	6/24/2019	3*4cm ulcer over Rt foo	T II	No	yes	DM/SHTN	Well	no	I	No	164	10yrs	OHA	7200	NAD	Staph aureu	NAD	Cefoxitin	Dressing	C	3*4cm	3*4	3*2	2*2	Nil	7days	15 days	Healed
32	Raghu	48	M	5114123142	makrishnapur	8/3/2019	8/8/2019	Ulcer over left foot 2wee	T II	No	Occasional	M/hypothyro	well	no	II	No	200	1 1/2yrs	OHA	6500	NAD	Sterile	Nad	nil	debridemen	B	4*7cm	4*7	4*5	4*2	Nil	5days	3weeks	Healed
33	Robert	59	M	5123031176	Kundrathur	7/9/2019	8/20/2019	Ulcer left foot 1 year	T II	Yes	yes	DM	Moderate	No	II	Fever	189	10yrs	Insulin inj and OHA	9900	NAD	E coli	Nad	Meropenem	Debridemen	A	6*6	6*6	8*6	8*8	SSG	40 days	3 months	Healed
34	kumar	39	M	5115748104	Pattinpakkam	5/27/2019	6/1/2019	Ulcer rt lower leg 3wks	T II	yes	yes	M/CAD/SHT	Moderate	NO	II	No	234	3yrs	OHA	10000	NAD	MRSA	NAD	LINEZOLID	debridemen	C	4*8	4*8	4*5	4*3	Nil	7days	2weeks	Healed well
35	Murugesan	56	M	5128367141	Chennai	6/1/2019	6/17/2019	Ulcer lft foot 3wks	T II	Yes	no	DM/SHTN	Well	No	I	Fever	320	10 yrs	Irregular OHA	20000	NAD	monas aue	NAD	piptaz	debridemen	B	14*7	11*6	10*5	5*4	Nil	16days	1 1/2 month	Healed well
36	Senthil kumar	43	M	5112699866	Cuddalore	7/22/2019	7/27/2019	Ulcer lower leg 1 week	T II	Yes	no	DM	MOderate	no	II	no	230	2 years	OHA	10400	NAD	MSSA	Normal study	piptaz	debridemen	A	7*4cm	5*4	5*3	3*2	Nil	5 days	1 month	Helaed well
37	Selvaraj	57	M	5121409992	chennai	5/30/2018	6/26/2018	Ulcer over Rt Dorsum *	T II	Yes	Yes	DM/SHTN	Fair	+	II	No	187	10 yrs	Insulin inj and OHA	12300	NAD	Klebsiella	Normal study	Ciprofloxacii	debridemen	C	6*8 cm	6*6	4*3	2*1	Debridement	26 days	3 weeks	Partially healed
38	Mohan	32	M	5126845284	chennai	4/17/2018	5/11/2018	Ulcer left medial aspect	T I	Yes	Occasional	DM	WELL	no	II	Fever	190	6 months	OHA	8600	NAD	rep pyogen	NAD	CFS	Debridemen	B	15*8cm	10*10	8*9	10*8	SSG	24 days	2 months	Healed well
39	Selvam	62	M	5127443313	Chennai	5/18/2019	5/25/2019	Ulcer over left foot 2 mn	T II	No	Yes	DM	Good	No	II	No	164	6 yrs	OHA	7500	NAD	MRCONS	n study	Piptaz	Debridemen	A	6*6cm	6*4	4*5	3*3	Nil	8 days	3 weeks	Helaed well
40	Viswalingam	73	M	5123339228	Chennai	10/21/2018	10/25/2018	Ulcer over left foot* 6 m	T II	Yes	Yes	M/HTN/CA	Poor	+	II	Fever	232	15yrs	Irregular OHA	12100	NAD	oteus vulga	30% Stenosis in DPA and ATA	Piptaz	Debridemen	C	10*8cm	7*5	6*5	5*4	Debridement	6days	MONTH 2 WEEK	Healed well
41	Ramalingam	47	M	5122028479	Tambaram	10/25/2018	11/5/2018	Ulcer dorsum rt foot* 1v	T II	No	No	DM	Well	No	II	No	166	6 yrs	Insulin inj and OHA	7200	NAD	cinetobacte	NAD	Imipenem	debridemen	B	8*7cm	8*7	8*6	6*7	Debridement	10 days	3 months	Healed well
42	Vinoth	50	M	5126508989	Chennai	11/8/2018	11/19/2018	Ulcer left foot * 2 month	T II	Yes	yes	DM/SHTN	Fair	No	II	No	195	6 YRS	Insulin inj and OHA	9900	NAd	rep pyogen	NAD	otrimoxazol	Debridem	A	5*8cm	5*6	4*5	4*3	Nil	11 days	2 months	Healed well
43	Umaraj	39	M	5122041906	Chennai	11/25/2018	12/14/2018	Ulcer rt plantar * 2week	T II	No	No	DM	fair	no	I	NO	178	4 yrs	OHA	11000	NAD	Klebsiella	NAD	cefotaxime	debridemen	C	9*3	10*10cm	7*6	4*4	Nil	1 month	MONTH 2 WEEK	Healed well
44	Nagalingam	48	M	5125827810	Chennai	11/14/2018	11/19/2018	Ulcer Rt foot 15 days	T II	Yes	no	DM	Fair	+	II	Fever	257	3 yrs	Irregular OHA	16000	NAD	MSSA	ficant luminal r	piptaz	debridemen	B	15*5	15*8	12*7	10*8	SSG	1 month	1 month 2 weeks	Healed well
45	Gopi	44	M	5124625620	Chennai	11/17/2018	1/17/2019	Ulcer Rt foot 15 days	T II	Yes	yes	DM/SHTN	Fair	no	II	no	216	3 yrs	OHA	10000	NAD	monas aue	NAD	piptaz	debridemen	A	5*5 in left foot	5*5	5*6	8*5	Debridement	2 months	2 months 2wks	Healed well
46	Elumalai	50	M	5125567772	Chennai	11/14/2018	11/17/2018	Swellin and ulcer rt dist	T II	No	No	Dm	fair	No	II	No	231	5 yrs	OHA	9000	NAD	Klebsiella	NAD	CFS	debridemen	C	10*7 cm	8*6	4*5	4*3	y amputation of great	5 days	1 month 2 weeks	Helaed well
47	Gajendra lucas	80	M	5121213895	Chennai	6/5/2018	6/10/2018	Ulcer rt distal leg 3week	T II	NO	Yes	DM	Fair	NO	II	Fever	147	25 yrs	Insulin inj and OHA	11000	NAD	cinetobacte	NAD	LINEZOLID	debridemen	B	7*10cm	6*5	5*4	-	Nil	5 days	3weeks	Healed well
48	Andal Pillai	53	M	633450667	Nagerkoil	4/17/2019	4/24/2019	Ulcer rt dorsum of foot 2	T II	Yes	Yes	DM/HTN	Fair	NO	II	NO	169	3 yrs	OHA	8760	NAD	MSSA	NAD	Cefotaxime	debridemen	A	5*5	4*4	2*2	-	NIL	7 days	1 month	Helaed well
49	Krishnan	39	M	5121581245	chennai	4/3/2018	4/10/2018	Ulcer left heel * 2wks	T I	No	Occasional	DM	Fair	No	I	No	156	1 1/2 yrs	OHA	9070	NAD	monas aue	NAD	piptaz	debridemen	C	4*4	4*4	2*2	2*1	Nil	7 days	3 weeks	Partially healed
50	Christy	44	F	5123516641	Chennai	6/19/2019	6/22/2019	Ulcer in plantar lt foot *	T II	No	Yes	DM/SHTN	Fair	+	II	fever	225	4 yrs	Insulin inj and OHA	13200	NAD	MRSA	NAD	LINEZOLID	debridemen	B	13*5 cm	12*4	8*6	4*3	Nil	5 days	1 month 2 weeks	Partially healed
51	Manoranjitham	47	F	5121463439	Chennai	7/1/2019	7/16/2019	Ulcer rt Medial distal leg	T II	No	No	DM/BA	fair	+	II	No	176	2 yrs	Insulin inj and OHA	8800	NAD	monas aue	NAD	Piptaz	debridemen	A	7*8 cm	8*8	5*6	4*4	Nil	15 days	6 weeks	Healed well
52	Janaki	48	F	5128461087	Chennai	7/3/2019	7/7/2019	Ulcer rt dorsum foot*10	T II	No	NO	DM	fair	+	II	No	178	10 yrs	OHA	14000	Nad	MSSA	NAD	CFS	debridemen	C	4*8cm	7*8	5*5 cm	4*4	Debridement	5days	MONTH 2 WEEK	Healed well
53	Mangani	44	F	5117244107	Chennai	4/21/2019	4/23/2019	ulcer foot with fever 10	T II	no	no	DM/CAD	fair	no	II	No	156	4 yrs	OHA	7200	NAD	sterile	NAD	Nil	debridemen	B	4*4	2*2	NA	NA	Nil	1 day	7 days	Healed well
54	Malliga	52	F	5111270345	Vellore	9/12/2018	9/12/2018	ulcer Lt foot 1 week	T II	no	No	DM/HTN	fair	no	I	nil	167	5yrs	OHA	6700	NAD	MSSA	NAD	Cefixime	Debridem	A	06 * 4 cm lt foot	4*3	3*2	NA	Nil	1 day	1 month	Healed well
55	Geetha	29	F	5121785300	Chennai	9/14/2018	9/24/2018	Ulcer Rt foot 15 days	T I	NO	NO	DM/hypoth	Well	+	II	Nil	189	5yrs	Insulin inj and OHA	6000	NAD	monas aue	NAD	piptaz	debridemen	C	5*5	6*7	5*6	4*4	Debridement	11 days	2 months	Healed well
56	Vani	47	F	5121882200	Kanchipuram	6/26/2018	6/30/2018	ulcer Lt foot 2 wks	T II	No	No	DM/HTN	Fair	No	II	Nil	228	6yrs	OHA	16000	NAD	MRSA	NAD	Vancomycir	Debridemen	B	6*9 cm	6*8	5*5	3*2	Nil	5 days	2 weeks	Healed well
57	Dhanalakshmi	48	F	5124273021	kanchipuram	6/8/2018	6/12/2018	ulcer over Left foot* 3 d	T II	No	No	DM/BA	Well	No	I	Nil	196	5yrs	Insulin inj and OHA	13200	NAD	rep pyogen	NAD	CFS	debridemen	A	9*8	6*7	5*5 cm	2*2	NIL	5 days	10 days	Healed well
58	Farook nisha	56	F	5115103055	kattupakam	26-Feb	5/3/2019	Ulcer rt dorsum of foot	T II	no	no	DM/HTN	fair	yes	II	Fever	207	9yrs	OHA	19000	NAD	Klebsiella	NAD	cefotaxime	debridemen	C	6*6 in rt foot	5*4	3*3	2*1	NIL	6 days	3 week	Healed well
59	Lakshman	50	M	5129179351	CHENNAI	5/15/2019	5/19/2019	ulcer over Left foot for 6	T II	NO	NO	DM/CAD	Fair	no	II	Nil	256	6yrs	Insulin inj and OHA	10000	NAD	monas aue	NAD	Piptaz	debridemen	B	5*6	5*6	4*3	NA	Nil	5 days	15 days	Healed well
60	Daniel	49	M	5122489430	Chennai	4/26/2019	5/5/2019	ulcer over left dorsal as	T II	No	Yes	DM	Fair	no	II	Fever	290	8YRS	OHA	6600	NAD	rep pyogen	NAD	CFS	debridemen	A	5*6	5*5	4*3	2*1	NIL	10 days	1 month	Healed well
61	Raja	49	M	512760676	HIRUVALLUR	3/25/2019	3/31/2019	ULCER OVER MEDIAL	T II	NO	no	DM	Fair	yes	II	NIL	156	5YRS	OHA	8900	NAD	monas aue	NAD	PIPTAZ	debridemen	C	4*5	5*4	4*3	2*2	NIL	7 days	2 weeks	Healed well
62	Akhil maran	35	M	5123442756	CHENNAI	2/22/2019	30-02-2019	ULCER OVER LEFT F	TII	no	no	dm/shtn	Fair	no	II	nil	168	2yrs	OHA	11600	NAD	MSSA	NAD	CFS	debridemen	B	7*10	7*10	7*7	6*5	Nil	10 days	3 weeks	Healed well
63	SANTHANAM	59	M	5122000550	CHENNAI	2/8/2019	2/18/2019	ULCER OVER RIGHT	TII	NO	NO	DM/SHTN	Fair	NO	II	nil	286	5YRS	OHA	9100	NAD	Klebsiella	NAD	cefotaxime	debridemen	A	5*7	5*7	5*5	5*4	Debridement	10 days	1 month	Healed well
64	Ramesh	48	M	5126109278	Chennai	5/18/2019	6/5/2019	ULCER OVER LEFT F	TII	Yes	NO	DM	FAIR	NO	II	NIL	226	3YRS	OHA	15000	NAD	monas aue	NAD	PIPTAZ	debridemen	C	5*6	5*5	5*4	2*3	NIL	14 days	1 month	Healed well
65	Ramanathan	66	M	5116386563	Chetpet	6/6/2019	6/12/2019	Ulcer over Left foot 2 wk	T II	No	yes	DM/SHTN	Moderate	+	II	No	212	25 yrs	OHA & Insulin	9500	NAD	cinetobacte	NAD	Ciprofloxacii	debridemen	B	5*6cm	4*5	4*3	2*3	nil	7 days	1 month	Healed well
66	Velai kannu	65	M	5111760791	Pallavaram	6/17/2019	6/24/2019	3*4cm ulcer over Rt foo	T II	No	yes	DM/SHTN	Well	no	I	No	164	10yrs	OHA	7200	NAd	Staph aureu	NAD	Cefoxitin	Dressing	A	3*4cm	3*4	3*2	2*2	Nil	05 days	15days	Healed well
67	Bhavani	45	F	5117343934	Chennai	5/6/2019	5/18/2019	Ulcer left plantar	T II	No	No	DM	well	No	II	No	174	3 yrs	OHA	8900	NAD	oteus vulga	NAD	Piptaz	debridemen	C	4*7cm	4*7	4*5	3*3	Nil	13 days	2 months	Healed well
68	Navamani	27	F	5116344628	Chennai	7/21/2018	8/24/2018	Ulcer left foot 3months	T II	No	N	DM	Moderate	No	II	No	189	5yrs	Insulin inj and OHA	9900	NAD	E coli	Nad	Meropenem	debridemen	B	6*6	6*6	8*6	8*8	SSG	33 days	3 months	Healed well
69	Kaveri	56	F	5123323571	hiruvannamal	10/20/2018	10/26/2018	Ulcer lft foot 2wks	T II	NO	No	DM	Moderate	NO	I	No	184	10 yrs	Insulin inj and OHA	8380	NAD	MRSA	NAD	LINEZOLID	debridemen	A	5*7	4*5	4*3	2*2	Nil	6days	10 days	Healed well
70	Kamala	56	F	5116244543	Chennai	10/20/2018	10/29/2018	Ulcer left foot 1 wk	T II	Yes	Yes	DM/SHTn	Well	No	I	No	120	4 yrs	Regular OHA	6000	NAD	Staph aureu	NAD	cefotaxime	debridemen	C	5*4 cm	4*5	4*3	3*2	Nil	9 days	2 weeks	Healed well
71	Singaravelan	62	M	5127151512	Chengelpet	6/22/2018	6/26/2018	Ulcer left distal leg 1 wk	T II	No	Occasional	DM/SHTN	Fair	+	II	NO	206	10 yrs	Regular OHA	7900	NAD	E.coli	Nad	CFS	Debridemen	B	6*8	5*4	5*3	3*2	Nil	5 days	2 weeks	Healed well
72	Rajendran	58	M	5122445717	Chennai	6/18/2018	6/27/2018	Ulcer Rt foot 15 days	T II	No	Yes	DM/SHTN	Fair	No	II	No	176	6 yrs	Regular OHA	10000	NAD	oteus vulga	NAD	Colistin	Debridemen	A	8*7	6*6	5*4	3*3	Nil	10 days	3 weeks	Healed well
73	Suseela	62	F	5123657783	Chennai	5/23/2019	5/29/2019	Swellin and ulcer rt dist	T II	No	No	NO	Well	No	II	Fever	260	wly diagnos	started Insulin	16790	NAD	Klebsiella	Nad	CFS	Debridemen	C	6*7cm	5*5	4*2	NA	Nil	7 days	1 month	Healed well
74	Anusiya	43	F	5116765891	Vandavasi	8/20/2018	8/24/2018	Ulcer in Rt foot *6 days	T II	No	Yes	M/SHTN/B	Well	+	II	Fever	289	6 yrs	Irregular OHA	15600	NAD	MRSA	NAD	LINEZOLID	Debridemen	B	12*8 cm	12*6	11*6	8*5	SSG	6 + 7 days	1 month 2 weeks	Healed well
75	Ponni	51	F	5112748874	Chennai	4/3/2018	4/12/2018	Ulcer in distal leg lt *8d	T II	NO	NO	DM/BA	WEll	No	II	NO	198	6 yrs	Regular OHA	7800	NAD	E.coli	NAD	otrimoxazol	Debridemen	A	7*7	5*6	4*3	1*4	Nil	10 days	3 weeks	EALED WELL