IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 9 Ser.7 (September. 2021), PP 06-28
www.iosrjournals.org

A comparative Study of collagen granule dressing versus conventional dressing in diabetic foot ulcers

Kilambi Srinivas[1], S Sree sai rekha[2] Hima soumya madasu[3] Kotla Balaraju[1]
[1]*Department of General surgery, St. Teresa's general hospital, Hyderabad,INDIA*
[2]*Department of plastic surgery, Osmania General Hospital, Hyderabad, INDIA*
[3]*Department of General Surgery, Osmania General Hospital, Hyderabad, INDIA*
**Corresponding author: Dr Hima soumya madasu*
Department of General surgery, Osmania General Hospital, Hyderabad, INDIA

Abstract
Background: *Diabetic Foot Ulcers remain a major health care problem and is challenging to the health care professionals who attend them.These create a major cause of morbidity,mortality and/or disability being the commonest cause for lower limb amputation.In recent times, biological dressings are becoming popular and gaining importance but none of them have become gold standard for treating diabetic foot ulcers.Collagen dressings have many advantages when compared to conventional dressings in terms of ease of application and being natural. We compared the Collagen granule dressing with conventional dressing in treating diabetic foot in terms of number of time taken for healing,number of dressings required,duration of antibiotic therapy,number of surgical debridements that are needed and follow up time.*
Methods: *A prospective study was conducted on 60 patients comparing Collagen granule dressing with conventional dressing in the treatment of diabetic foot ulcers among the patients who got admitted with diabetic foot in the Department of General Surgery at ST. Teresa s hospital , Hyderabad (November 2016 to June 2018).*
Results: *The patients in both the groups were analyzed using Chi-square test,Mann Whitney U test, and results were formulated.*
Collagen granule dressing group needed lesser number of dressings with mean number of number of dressings of 18.30 when compared to conventional dressing group which had mean of 34.80.Collagen granule dressing gave better results in terms of duration of antibiotic therapy,number of surgical debridements and time taken for healing with mean of 4.70 days,0.63 debridements and 23.93 days when compared to means of conventional dressing group which were 8.00 days,1.13 debridements and 54.08 days respectively.All the above proved statistical significance.
Conclusions: *Collagen granule dressing consumes significantly lesser number of dressings with less duration of antibiotic therapy and significantly fewer number of surgical debridements and less time for healing.The concept of collagen granule dressing for diabetic foot ulcers is safe,provides better healing with less number of dressings and fewer surgical debridements which indirectly reflects on lesser follow up time.*
Keywords: *Diabetic Foot Ulcer, Collagen granule dressing, Conventional dressing*

Date of Submission: 29-08-2021 Date of Acceptance: 13-09-2021

I. Introduction

India is commonly referred to as the diabetic capital of the world.It is home to the largest population of Type-2 Diabetic patients in the world which was estimated at 50 million patients.Thus,it is needless to say that India faces a huge challenge.According to the World Health Organization(WHO) and other government sources,5% of the Indian population is plaqued with Diabetes.In fact,the number of Type-2 diabetic patients in India are higher than present in any other country.The future too looks bleak with the diabetic patients in India expected to grow at a rate of 58% to 87 Million people in 2030[1].With the number of deaths rising due to diabetes and its complications,it is[2] quite clear that we have to understand the consequences of this dangerous disease.

Diabetes,in short,is a metabolic disorderof multiple aetiology in which there is an insufficient amount of insulin production and secretion by the pancreas.This is termed as Type-1 diabetes.The inadequate response of insulin is commonly referred to as Type-2 diabetes.Out of the two kinds,the later one is more common in India.The risk factors for Type-2 diabetes are classified into Non-modifiable and Modifiable risk factors[2].Non modifiable risk factors being Age over 45 years,Race/Ethnicity,Family history of diabetes,History of Gestational

diabetes,Gene-environment interactions while Modifiable risk factors include physical inactivity(sedentary life style),high body weight(BMI),high blood pressure,high cholesterol levels,unhealthy diet,smoking.

The interaction between hyperglycemia or other metabolic consequences of insulin deficiency and other poorly defined independent genetic or environmental factors in a patient with diabetes leads to various short term complications like hypoglycemia,Diabetic ketoacidosisNon ketotic hyperosmolar diabetic coma,lactic acidosis and long term complications that include both macro vascular and micro vascular complications.

Macrovascular[3] complications affect the larger blood vessels such as those supplying blood to the heart,brain and legs leading to Coronary artery disease,Stroke,Peripheral Vascular disease causing disability and death in patients with diabetes.Microvascular[3] complications are the diseases resulting from the thickening of the vessel membranes in the capillaries and arterioles in response to conditions of chronic hyperglycemia (Microangiopathy).Microangiopathy affects eye,kidneys,peripheral nerves resulting in Diabetic Retinopathy,Nephropathy,Neuropathy and Dermopathy that includes Diabetic foot ulcers in it.

Diabetic foot ulcer is any infection involving the foot in a person with diabetes originating in a chronic or acute injury to the soft tissues of the foot,with evidence of pre-existing neuropathy and/or ischemia[4].Diabetic foot is queit dread of disability because of a)Long stretches of hospitalization b)Mounting impossible expenses and c)Ever dangling end result of amputation.Diabetes causes more than 70% of lower limb amputations.Diabetes causes more amputations than land mines even in war zones.Foot ulceration,sepsis,and amputation are feared complication of diabetes.Lower limb amputation causes disability to the patient that results in increased burden to the family causing psychological stress.

Diabetic foot ulcer management is important in surgical practice as the patients with diabetic foot contributes to majority of surgical inpatient and outpatient load.Wound dressings represent a part of the management of diabetic foot ulceration.Ideally,dressings should alleviate symptoms,provide wound protection and encourage healing.No single dressing fulfills all the requirements of a diabetic patient with an infected foot ulcer.However,each category of dressings has particular characteristics that aid selection.

Nonadhesive dressings are simple,inexpensive and well tolerated.Foam and alginate dressings are highly absorbent and effective for heavily exuding wounds.Hydrogels facilitate autolysis and may be beneficial in managing ulcers containing necrotic tissue.Dressings containing inidine and silver may aid in managing wound infection.Ointments and solutions like metronidazole based preparations,iodine containing soultions are also used.Collagen dressing(biological dressing) aids in increased collagen formation with greater reduction in inflammatory cells.

In choosing a dressing for an infected diabetic foot ulcer,several factors have to be taken into account.Infected wounds tend to have heavy exudate that needs to be controlled to prevent maceration of surrounding tissue.There may be considerable odour associated with infection that may be unpleasant and distressing for the patient and family.A dressing must be comfortable and acceptable for the patient and should help alleviate or,at the very least,not worsen pain,especially at dressing changes.Ideally, the dressing should also aid in the management of infection itself.These dressings must also accommodate practical issues such as allowing observation of the wound and providing mechanical protection and conformability,of course the dressings must also be cost effective.

In recent years,several new treatment strategies have been developed to stimulate wound healing in diabetic foot ulcers.These are the topical growth factors,extra cellular matrix products,bioengineered human skin,hyperbaric oxygen therapy,granulocytes macrophage colony stimulating factors and collagen granules[5].

Collagen is a main structural component of connective tissue.There is a growing body of knowledge about the biochemical aspects of collagen and its role in wound healing. Collagen is available as spherical hydrophilic particles of collagen which are of 0.1 to 0.3 mm in diameter.It is available in 5,10,15 ml packets[5].

There is no single ideal dressing for treatment of diabetic foot ulcers.The newer forms have to compared with the standard dressing forms of dressing.Hence there is need to compare different types of dressings in treatment of diabetic foot ulcer as diabetic foot ulcer is the single most important predictor to decide on the need for amputation.

II. Methods

Study Design:

This is a prospective comparative study conducted on 60 patients in two groups.

Study period

From November 2016 to June 2018.

Settings:

Department of General Surgery at ST.Teresa's general hospital,Hyderabad, Telangana

Source of data:

60 patients - 30 in each group admitted in the Department of General Surgery at Department of General Surgery at ST.Teresa's general hospital,Hyderabad, Telangana

Method of collection of data:

A prospective comparative study was conducted on 60 patients comparing collagen granules with conventional dressing for treatment of diabetic foot ulcers in the Department of General Surgery atST.Teresa's general hospital,Hyderabad, from November 2016 to June 2018. 60 patients who got admitted with foot ulcers who were known diabetics were selected for the study. Following admission after taking detailed history about the duration of ulcer,history of trauma and smoking,whether persistence of ulcer is on one foot or both feet,duration of diabetes and thorough clinical examination of ulcer(size,edge,presence of slough and discharge) patients were randomly selected to two groups. In Group A, the ulcer is washed with normal saline and cleansed following which medicated collagen granules are sprinkled over the ulcer to form a single layer over the floor of the ulcer.Then aseptic dressing is done followed by bandaging of the ulcer as shown in Figure below.

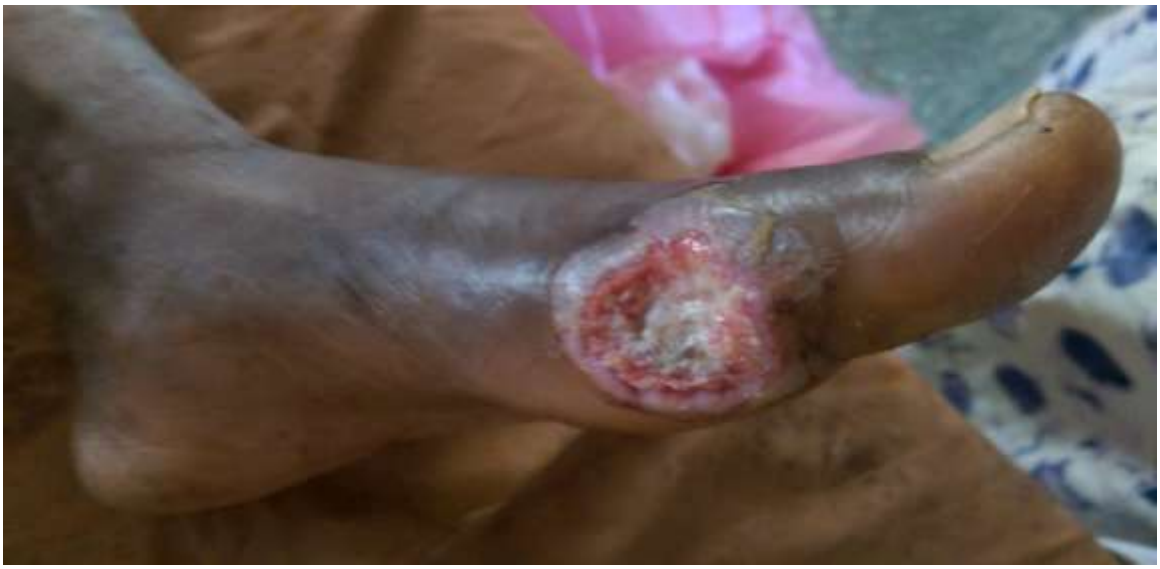


Fig 15 – Showing non healing ulcer over left great toe

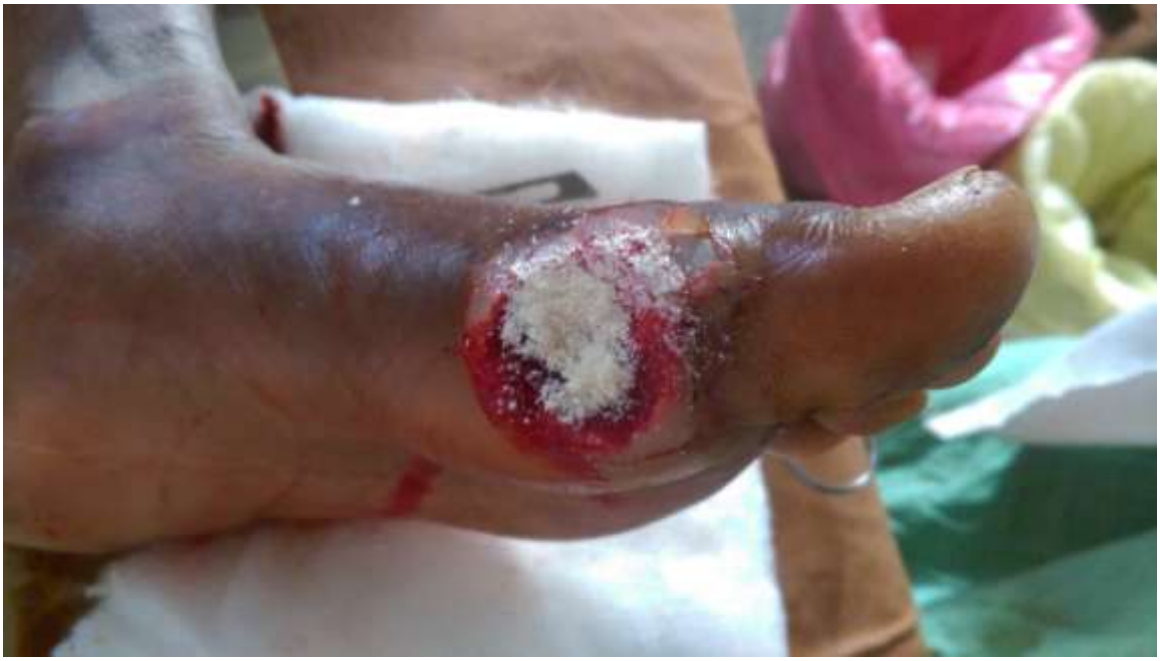


Fig 16 – Shows collagen granules application over the ulcer

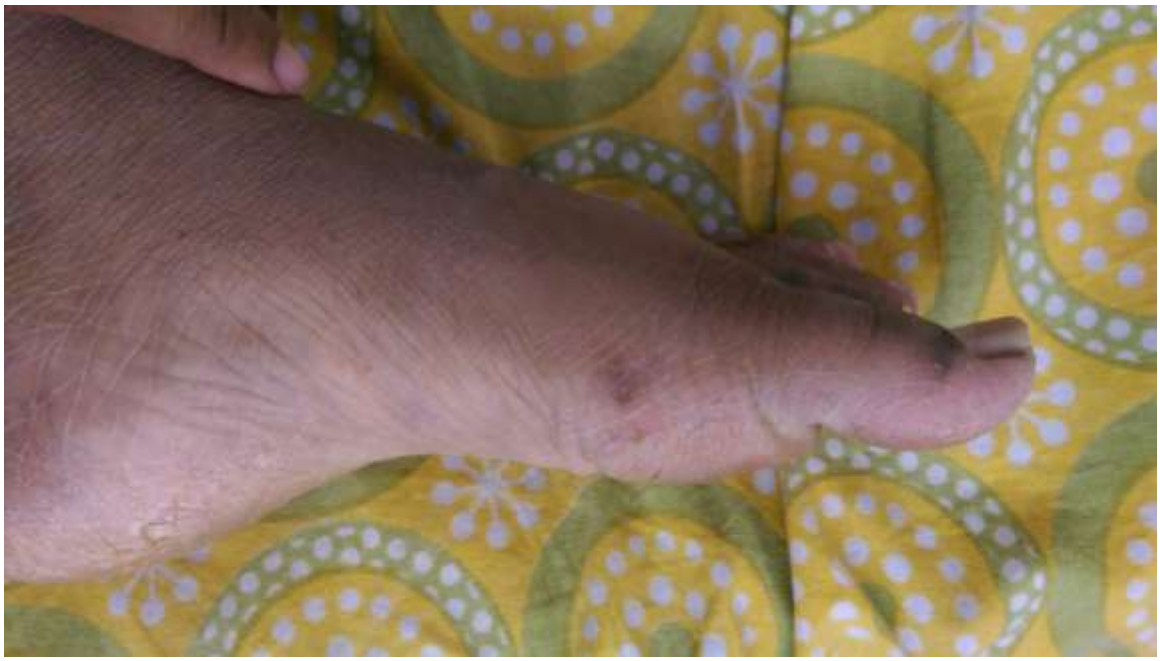


Fig 17 – Shows healed ulcer after two weeks of dressing with collagen granules.

In Group B, the ulcer is washed with normal saline and povodine iodine following which povodine iodine soaked gauze is placed over the floor of the ulcer.Then aseptic dressing applied and bandaging is done.After taking detailed history and thorough examination of the patients,blood investigations like complete haemogram,BT,CT,HIV,HBsAg,blood sugars(fasting and post prandial),HbA1c,blood urea and serum creatinine[other relevant investigations if required].Specific investigations like swab or pus(if infected ulcer or abscess) for culture and sensitivity,X ray of the affected foot and Arterial Doppler study of the affected lower limb is done.

All the patients were started on empirical antibiotics at admission which were later changed according to culture and sensitivity report.Dressing of the ulcer was done on regular basis or on alternate day depending on the size of the ulcer,presence of slough,discharge and soakage of the dressing.Based on regular assessment of the ulcer, surgical debridement or disarticulation or amputation were done in patients who required surgical interventions.Patients were followed up on day 1,3,7,14,21,28 days or even more days in events of any adverse effects related to medication or aggravation of symptoms or complications.All the patients were followed up till the development of complete healthy granulation tissue,which was considered as the end.

In both the groups,number of dressings,durations of antibiotic therapy,healing time,number of surgical debridements needed and whether follow up was completed or not were compared.After the ulcer is healthy,the ulcer is assessed whether it is completely epithelized or whether split skin graft is needed to cover the defect.If SSG is requied for the closure of defect of the ulcer the same has been carried out at our department.
The ulcer is classified based on Wagner-Meggitt classification.

WAGNER-MEGGITT CLASSIFICATION OF DIABETIC FOOT:
Grade 0 - No open lesion.
Grade 1 – Superficial lesion.
Grade 2 – Deep ulcer
Grade 3 – Abscess or Osteomyelitis
Grade 4 – Partial foot gangrene.
Grade 5 – Whole foot gangrene.

All the patients who were included in our study with diabetic foot ulcers were been classified as described above.Patients with Grade 0 were not included as there is no open ulcer or wound.The patients with Grade 1 and 2 were admitted and evaluated along with regular dressings and debridement if needed.Patients with Grade 3 who had abscess underwent drainage of the abscess with debridement and patients with osteomyelitis of the involved underwent bone curettage or disarticulation.Grade 4 patients with partial foot gangrene had to undergo disarticulation or amputation.Amputation was done for Grade 5 patients with whole foot gangrene.All the ulcers of Grade 1,2 and 3 following drainage of the abscess with debridement were followed up till the formation of healthy granulation tissue and then SSG was done for the ulcers leaving a wide defect.

Healing ulcer is the ulcer with granulation tissue that is:
1)Red/Pink in colour
2)Shiny
3)Moist
4)Granular appearance
The cost effectiveness between the two groups was studied depending on the cost of material that was used for dressing in each method, indirectly with number of dressings needed. The duration of antibiotic therapy,requirement for any of the surgical intervention(debridement or disarticulation or amputation or SSG) for each patient was studied in a defined group.

Inclusion Criteria:
1)Age group less than 60 years
2)Diabetic foot ulcers
3)Patient's willing to give consent for my study

Exclusion Criteria:
1)Hypersensitivity to Collagen
2)Age group more than 60 years
3)Concurrent illnesses that may interefere with healing like immune compromised state,carcinomas,connective tissue disorders,patients on cytotoxic drugs and severe anaemia.
4)Patient's who did not give consent for my study

Method of Statistical Analysis:
Statistical Package for Social Sciences (SPSS) for Windows Version 22.0 Released 2013.Armonk, NY:IBM Corp.,will be used to perform statistical analyses.

Descriptive Statistics:
Descriptive analysis of all the explanatory outcome parameters will be done using Mean and Standard Deviation.

Inferential Statistics:
Chi Square Test was used to compare the study characteristics, the swab culture at admission including study characteristics between Group A and Group B during post follow up time period between Group A and Group B.
Mann Whitney Test was used to compare the mean Glycemic profile parameters at admission,Post op diabetic ulcer characteristics between Group A and B. The level of significance was set at $p<0.05$.

Statistical software: The Statistical software namely SPSS Windows Version 22.0 Released 2013 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Sample size estimation
Prospective study from November 2016 to June 2018 involving 60 cases which were randomly selected from the pateints who got admitted with diabetic foot ulcers and with no concurrent illness that affects wound healing.30 cases in each group with diabetic foot ulcer were selected randomly by using computer based system.

Group A:Collagen granule dressing group
Comprised of 30 pts for whom dressing was done using collagen granules.

Group B:Conventional dressing group
Comprised of 30 pts for whom dressing was done using conventional method.
The number of patients is kept constant in each group to allow for better comparison.

III. Results

In the study comparing collagen granules with conventional method for dressing of diabetic foot ulcers conducted in our hospital , a total of 60 patients were recruited.30 in each were included randomly among the Collagen Granule Dressing Group and Conventional Dressing Group. Observations and analysis were done under the following divisions.

AGE DISTRIBUTION:

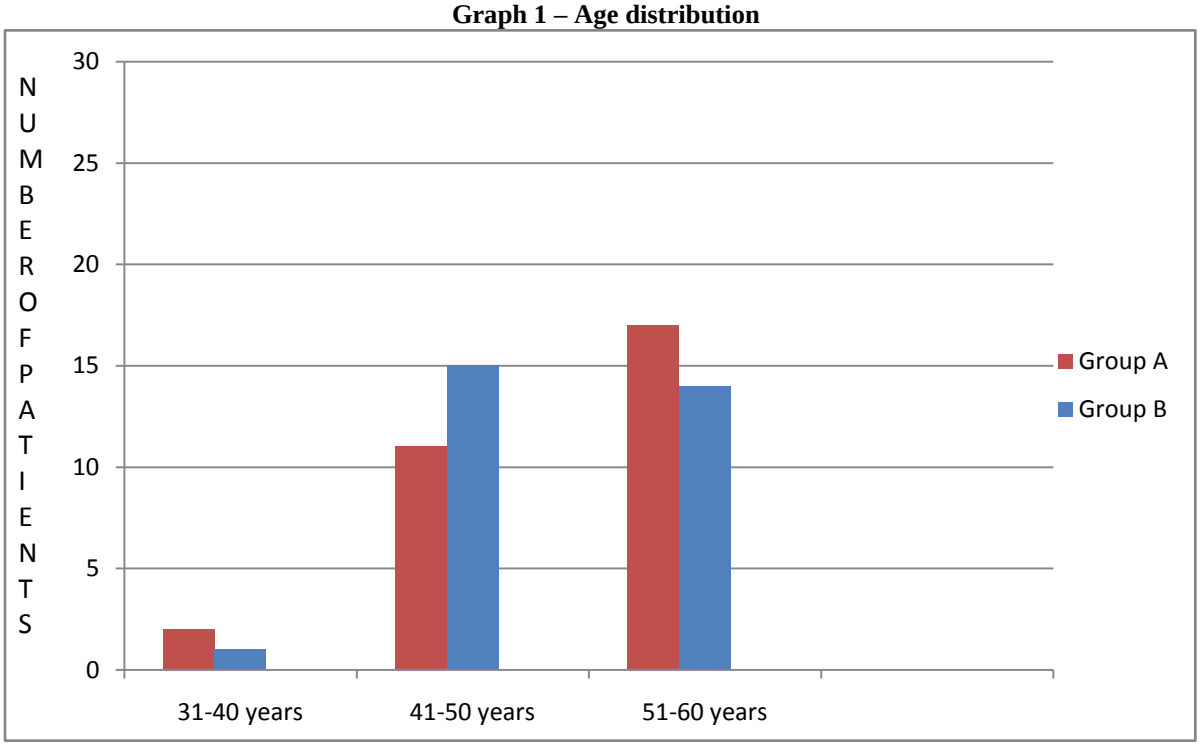
Table 8 – Age distribution of patients in collagen group and conventional group

Age(in years)	Collagen Granules Dressing Group(A)	Conventional Dressing Group(B)	Total
31-40	2(3.33%)	1(1.66%)	3(5%)
41-50	11(18.33%)	15(25%)	26(43.33%)
51-60	17(28.33%)	14(23.33%)	31(51.66%)
Total	30(50%)	30(50%)	60(100%)
Mean±SD	51.5±6.5	50.6±5.4	

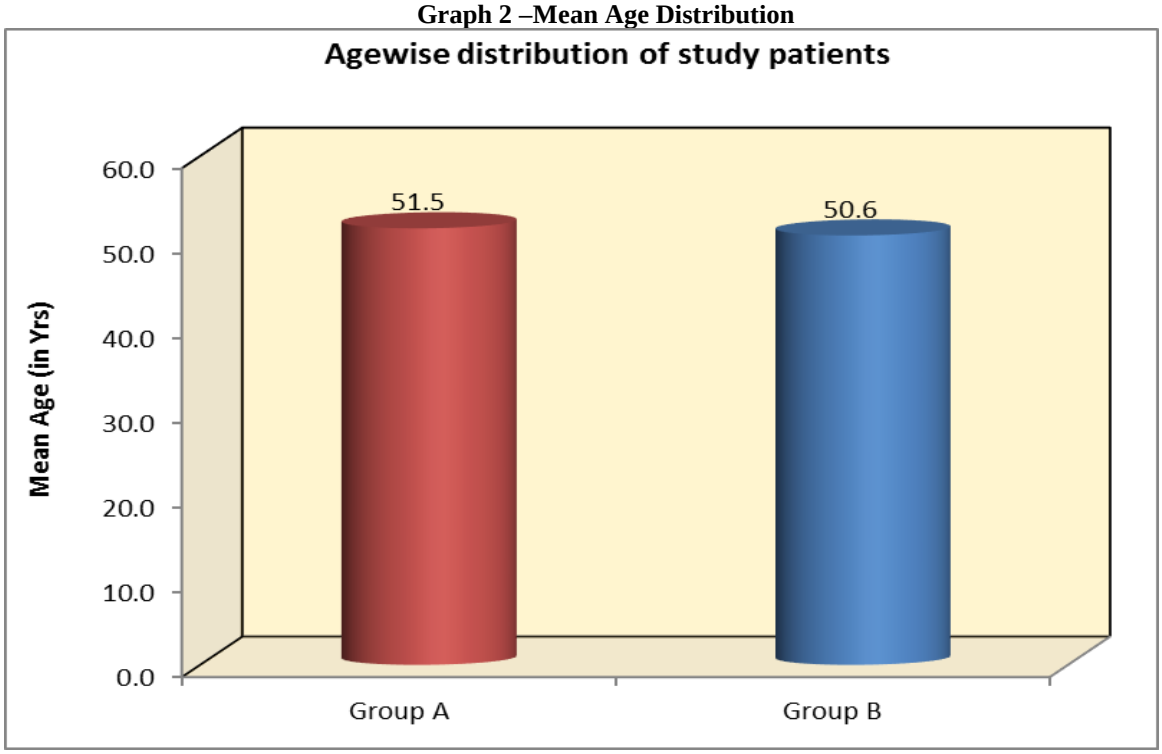
P=0.59,Not statistically significant,Mann Whitney U Test

Out of the total 60 patients,majority of the patients i.e 31 patients fall under the age group of 51-60 years with a percentage of 51.66%, there were 26 patients with a percentage of 43.33% between 41-50 years age group and 3 patients in the age group of 31-40 years with a percentage of 5%.The mean age and standard deviation in Collagen granule dressing group was 51.5±6.5 and in Conventional dressing group was 50.6±5.4 as shown in the Table-.The above data can be graphically represented as follows.

Graph 1 – Age distribution



Graph 2 –Mean Age Distribution



GENDER :
This table illustrates that out of 17(28.33%) female population 9 were in Collagen Granule Dressing Group(A) and 8 in Conventional Dressing Group(B). Out of 43(71.66%) males, 21 were in Collagen Granule Dressing group(A) and 22 in Conventional Dressing Group(B).

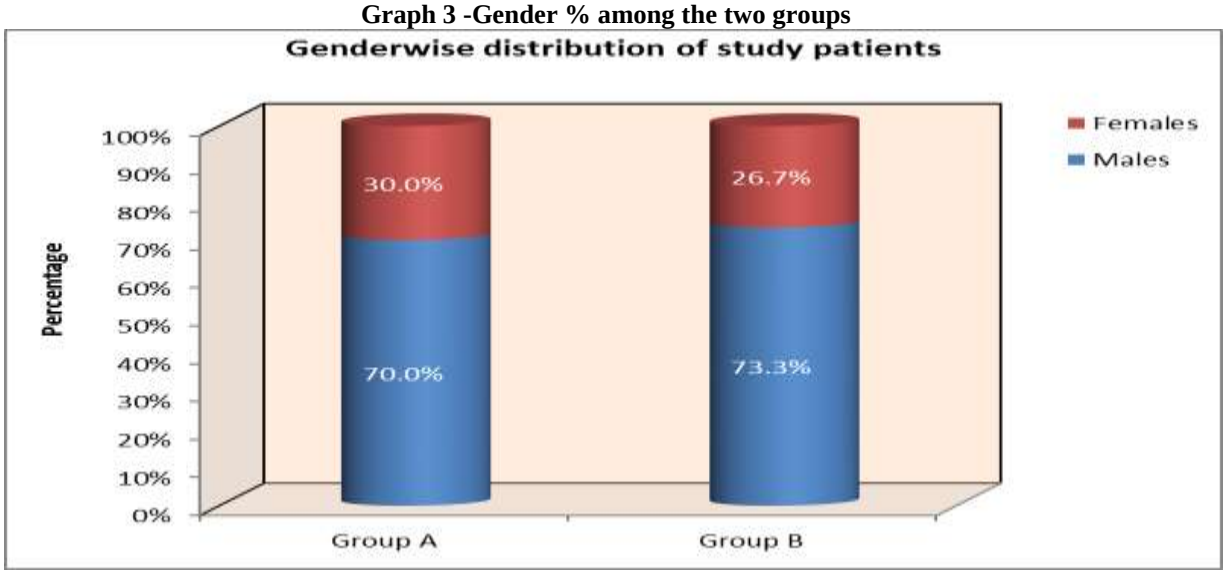
Table 9 - Gender distribution of two groups in our study

Gender	Collagen Granule Dressing Group(A)	Conventional Dressing Group(B)	Total
Female	9(15%)	8(13.33%)	17(28.33%)
Male	21(35%)	22(36.66%)	43(71.66%)
Total	30(50%)	30(50%)	60(100%)

P=0.77, Not Significant, Chi-Square Test

The following graph shows that among the total 60 patient population , male sex were predominant with 43 patients (71.66%) in total. Out of which 21 were in Collagen Granule Dressing Group(A) and 22 patients in Coventional Dressing Group(B).

Graph 3 -Gender % among the two groups



This is a graphical representation to show that among the male population in our study. In both the groups males outnumbered the females.

Table 10 – Age and Gender distribution among the two groups in our study

Age and Gender Distribution among study patients in 02 groups						
		Group A		Group B		
Variables	Category	Mean	SD	Mean	SD	P-Value
Age (in yrs)	Mean & SD	51.5	6.5	50.6	5.4	0.59[a]
	Range	38 -60		40 - 60		
Gender	Males	21	70.0%	22	73.3%	0.77[b]
	Females	9	30.0%	8	26.7%	

a-Mann Whitney U Test
b-Chi Square Test

Study characteristics of different variables in our study:

The different variables that have been considered in our study were Socioeconomic status,History of trauma for the ulcer formation,duration of ulcer,the foot affected,duration of diabetes,history of smoking,whether the foot affected was either Neuropathic or Neuro Ischemic foot,Wagner-Meggitt classification of the ulcer and family history of diabetes.

Socio economic status:
Socio economic status categorized into lower,middle and Higher classes wherein the majority of the patients included in our study fall under Lower class followed by Middle class with a p value of 0.09 measured by Chi Square Test that is statistically not significant.

History of trauma:
The formation of ulcer was either spontaneous(non-traumatic) or traumatic.Among the patients in Group A, cause of ulcer formation is non-traumatic in 17(56.7%) patients and traumatic in 13(43.3%) cases.In Group B,majority were non-traumatic ulcer 18(60%) cases and 12(40%) were traumatic ulcers.p value was 0.79 which is statistically not significant was assessed by using Chi Square Test.

Duration of ulcer:
The duration of ulcer is categorized as < 1 month,1-6 months,6 months-1 year,1-3years and >3 years.Majority of the patients were suffering with ulcer formation for a duaration of <1 month with 30% in Group A and 40% in Group B.The p value was 0.44 that was calculated with Chi Square Test which is statistically insignificant.

Foot affected:
Right foot was affected more commonly affected in Group A(40%) and left foot in Group B (50%).Both feet were affected for few patients with 30% in Collagen Granule Dressing Group(Group A) and 13.3% in Conventional Dressing Group(Group B).p value was 0.18 which is not significant statistically and is measured by Chi Square Test.

Duration of diabetes:
Duration of diabetes was classified into diabetes with a duration of <1 year,1-5 years,6-10 years and >10 years in our study.Many patients with diabetes for a duration of 1-5 years in our study had to get admitted with ulcer formation with 60% in Collagen Granule Dressing Group(Group A) and 56.7% in Conventional Dressing Group(Group B) that is statistically tested by using Chi Square Test that resulted a significant p value of 0.04.

History of smoking:
More than half of the patients in Group A were smokers in our study where as in Group B number of smokers were comparable to smokers.p value was 0.44 which was measured by Chi square Test and is not statistically significant.

Neuropathic foot:
Group A patients(76.7%) have suffered from Neuropathy more than the patients in Group B(33.3%) which was assessed by using Chi Square Test that gave a p value of 0.001 which is statistically significant.

Neuroischemic foot:
Majority of the patients in both groups didn't have NeuroIschemic Foot which was statistically tested by chi Square test that gave a p value of 0.07 that is statistically not significant.

Wagner-meggitt classification of ulcer in our study:
Among the patients in Collagen Granule Dressing Group(Group A) many patients had ulcers of Grade-2 and 3.And in patients of Conventional Dressing Group(Group B) majority were graded with Grade-2 ulcer.Statistically analyzed by Chi Square Test with a p value of 0.15 that is statistically not significant.

FAMILY HISTORY OF DIABETES:
Majority of the cases in Group A(73.3%) had a positive family history of diabetes whereas in Group B 63.3% did not have a positive family history.This was statistically analyzed by Chi Square Test with a p value of 0.004 that is statistically significant.

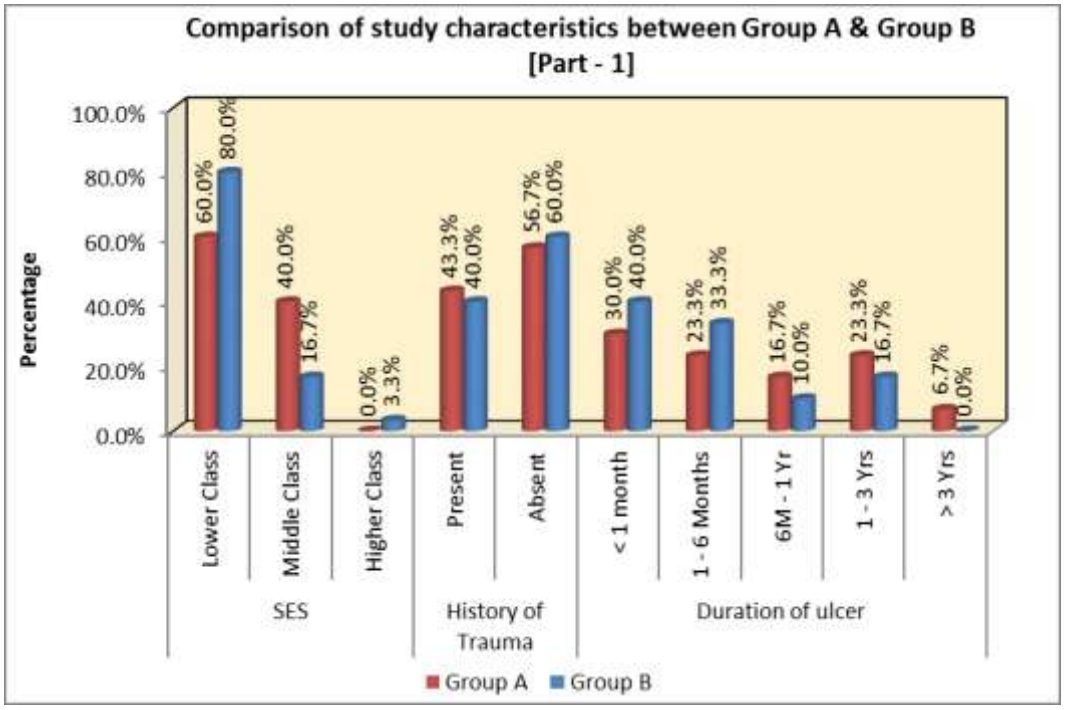
The following table shows the above described study characteristics and variables that were considered in our study.Overall,there was a statistically significant p value for Duration of diabetes,Neuropathic foot and family history of diabetes which were respectively 0.04,0.001 and 0.004.All these variables were statistically analyzed by using Chi Square Test.

Table 11 – Comparison of study characteristics between the two groups in our study

Comparison of study characteristics between Group A & Group B using Chi Square Test							
		Group A		Group B			
Variables	Category	n	%	n	%	χ^2 Value	P-Value
SES	Lower Class	18	60.0%	24	80.0%	4.739	0.09
	Middle Class	12	40.0%	5	16.7%		
	Higher Class	0	0.0%	1	3.3%		
History of Trauma	Present	13	43.3%	12	40.0%	0.069	0.79
	Absent	17	56.7%	18	60.0%		
Duration of ulcer	< 1 month	9	30.0%	12	40.0%	3.791	0.44
	1 - 6 Months	7	23.3%	10	33.3%		
	6M - 1 Yr	5	16.7%	3	10.0%		
	1 - 3 Yrs	7	23.3%	5	16.7%		
	> 3 Yrs	2	6.7%	0	0.0%		
Foot Affected	Left	9	30.0%	15	50.0%	3.467	0.18
	Right	12	40.0%	11	36.7%		
	Both	9	30.0%	4	13.3%		
Duration of Diabetes	< 1 yr	2	6.7%	9	30.0%	8.083	0.04*
	1 - 5 Yrs	18	60.0%	17	56.7%		
	6 - 10 yrs	8	26.7%	2	6.7%		
	> 10 yrs	2	6.7%	2	6.7%		
History of Smoking	Present	17	56.7%	14	46.7%	0.601	0.44
	Absent	13	43.3%	16	53.3%		
Neuropathic Foot	Yes	23	76.7%	10	33.3%	11.380	0.001*
	No	7	23.3%	20	66.7%		
Neuroischemic foot	Yes	10	33.3%	4	13.3%	3.354	0.07
	No	20	66.7%	26	86.7%		
Wagner Meggit grading of ulcer	Grade 1	8	26.7%	10	33.3%	6.722	0.15
	Grade 2	9	30.0%	15	50.0%		
	Grade 3	9	30.0%	3	10.0%		
	Grade 4	2	6.7%	0	0.0%		
	Grade 5	2	6.7%	2	6.7%		
Family history of Diabetes	Present	22	73.3%	11	36.7%	8.148	0.004*
	Absent	8	26.7%	19	63.3%		

***-Statistically Significant**

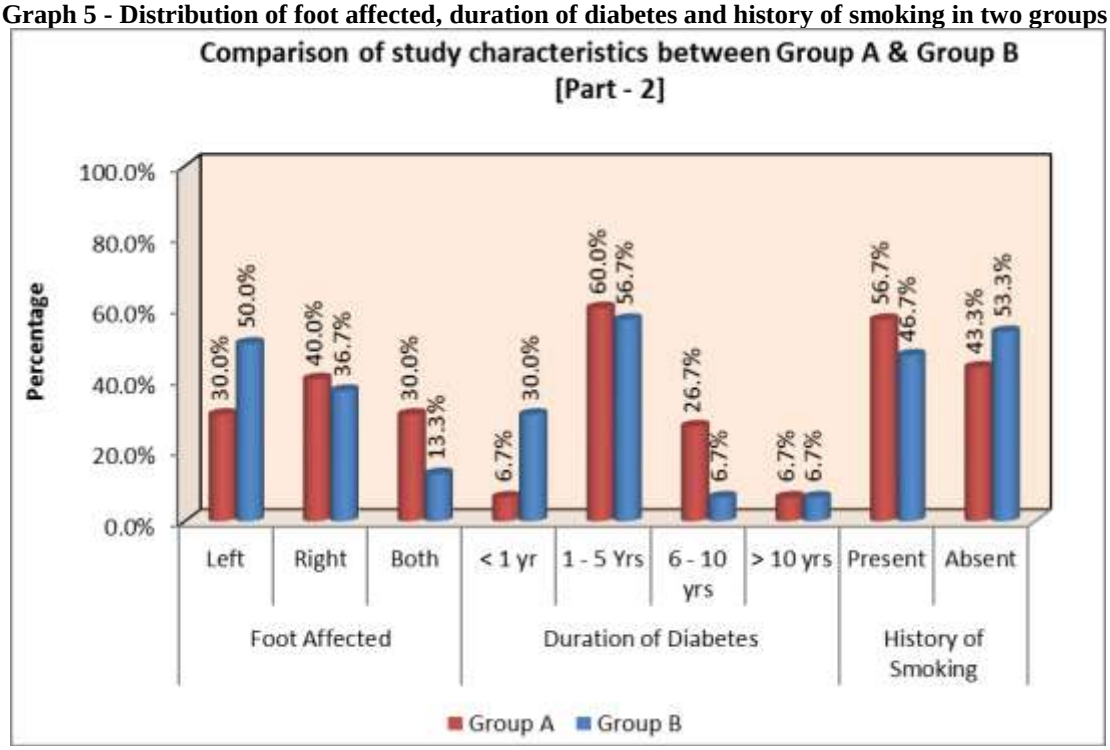
Graph 4 - Distribution of Socio economic status, cause and duration of ulcer both groups



The above graph shows the Socio economic Status-Lower class,Middle class and Higher class,History of trauma-Present(Traumatic ulcer) and Absent(Non-traumatic) and the duration of ulcer-<1 month,1-6 months,6 months-1 year,1-3 years and >3 years in both the groups in our study.

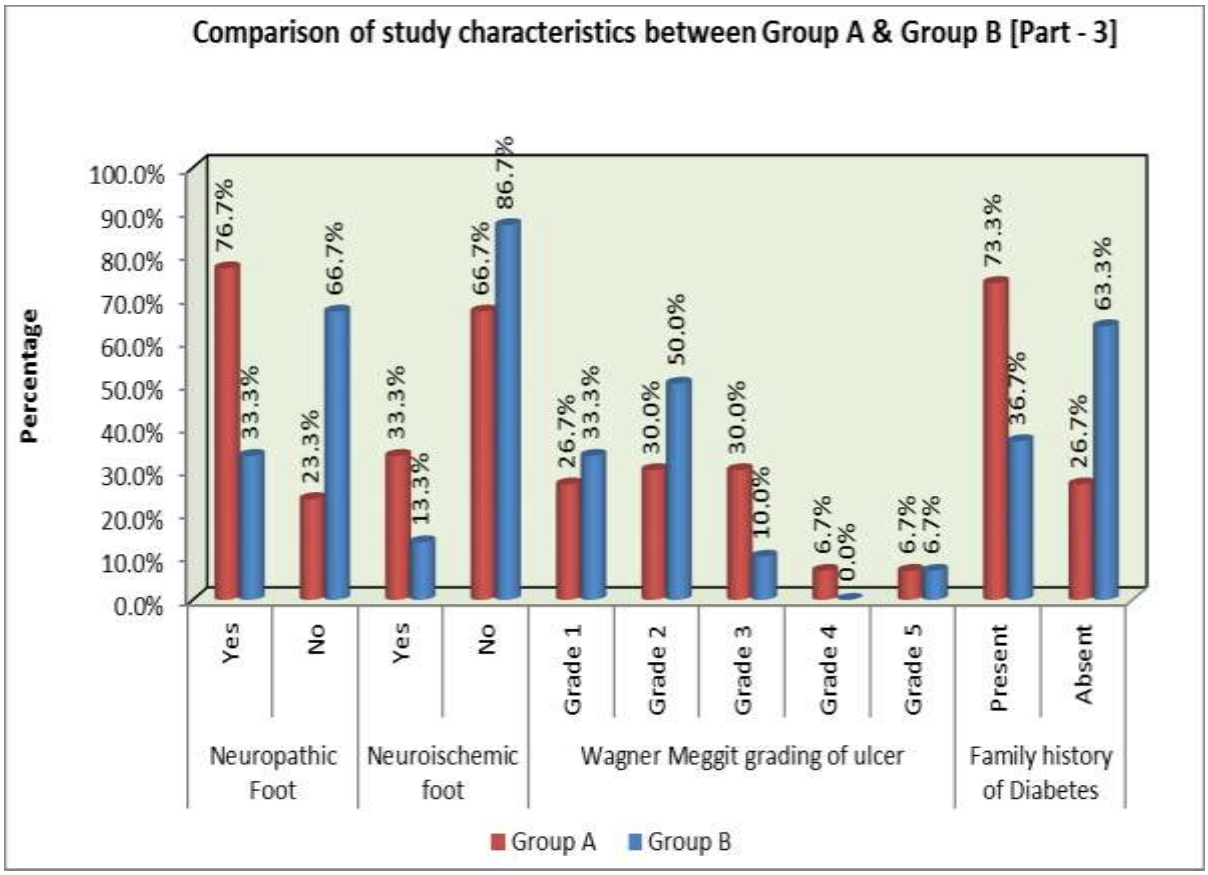
The following graph below shows the foot affected-left foot,right foot or whether both the feet were involved,duration of diabetes-<1 year,1-5 years,6-10 years and >10 years and the history of smoking and compares these variables in the Collagen Granule Dressing Group(Group A) and Conventional Dressing Group(Group B) in our study.The following graph also shows the percentages of these variables in both the groups that were included in our study.

Graph 5 - Distribution of foot affected, duration of diabetes and history of smoking in two groups



The following graph shows and compares different variables in both the groups such as the patients who got admitted with diabetic foot ulcer had Neuropathic or NeuroIschemic Foot,Grading of ulcer that was done using Wagner-Meggitt classification and Family history of diabetes.Majority of the patients in Collagen Granule Dressing Group had Neuropathic foot with Wagner's Grade-2 and 3 who had a positive family history of diabetes.In Conventional Dressing Group major population had NeuroIschemic Foot with Wagner's Grade-2 ulcer and also positive family history of diabetes.These variables have been compared and show with percentages in both the groups which were statistically analyzed by using Chi Square Test.

Graph 6 - Distribution of Neuropathic and Neuro Ischemic foot,Grading of ulcer and family history of diabetes



GLYCEMIC PROFILE:

Following admission of the patients in both groups, Fasting Blood Sugar(FBS),Post Prandial Blood Sugar(PPBS) and HbA1c were sent as a part of the laboratory work up to know the diabetic status of each individual whether the sugars are controlled or uncontrolled.

The mean FBS in Group A was 168.70±47.57 and Group B was 148.90±41.03 with a mean difference of 19.80 and a p value of 0.09 that is statistically not significant and measured using Mann Whitney Test.

The mean PPBS in Group A was 261.20±80.88 and Group B was 242.20±65.81 with a mean difference of 19.00 and p value of 0.37 that is statistically not significant which was analyzed by Mann Whitney Test.

The glycosylated haemoglobin value (HbA1c) is statistically analyzed by using Mann Whitney Test with mean values of 9.33±2.04 in Collagen granule dressing group and 8.74±1.92 in conventional dressing group.Mean difference between the two groups was 0.59 and p value of 0.24 which is statistically not significant.

The table below shows the Glycemic profile parameters-FBS ,PPBS and HbA1c in both Collagen granule dressing group and Conventional dressing group with their means,mean difference and p values.

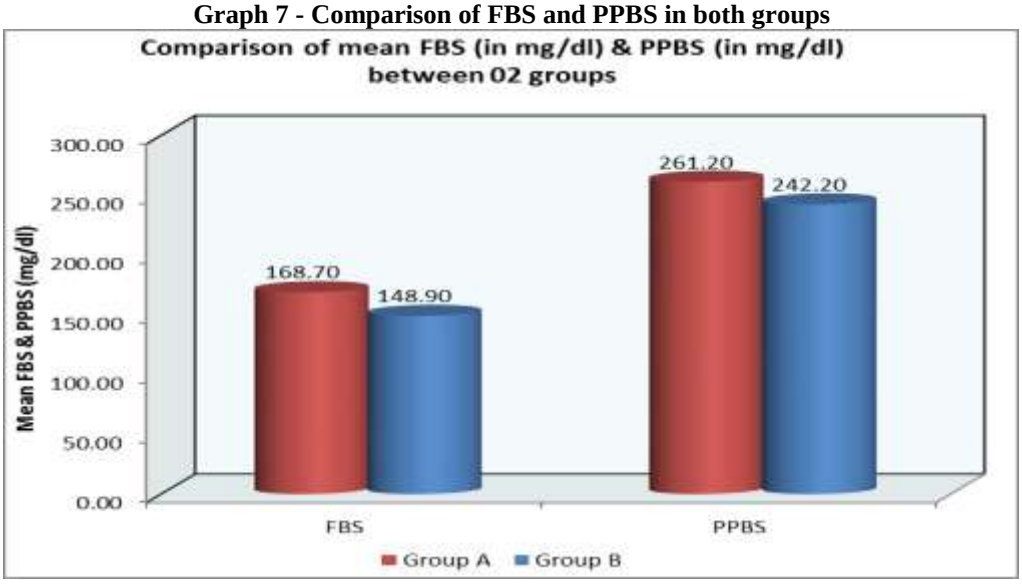
Table 12 - Comparison of mean glycemic profile parameters at admission in both groups included in our study

Comparison of mean Glycemic profile parameters at admission between Group A & B using Mann Whitney Test						
Variables	Group	N	Mean	SD	Mean Diff	P-Value
FBS	Group A	30	168.70	47.57	19.80	0.09
	Group B	30	148.90	41.03		
PPBS	Group A	30	261.20	80.88	19.00	0.37
	Group B	30	242.20	65.81		
HbA1c	Group A	30	9.33	2.04	0.59	0.24
	Group B	30	8.74	1.92		

P values = 0.09,0.37,0.24 Statistically not significant;Mann Whitney U test

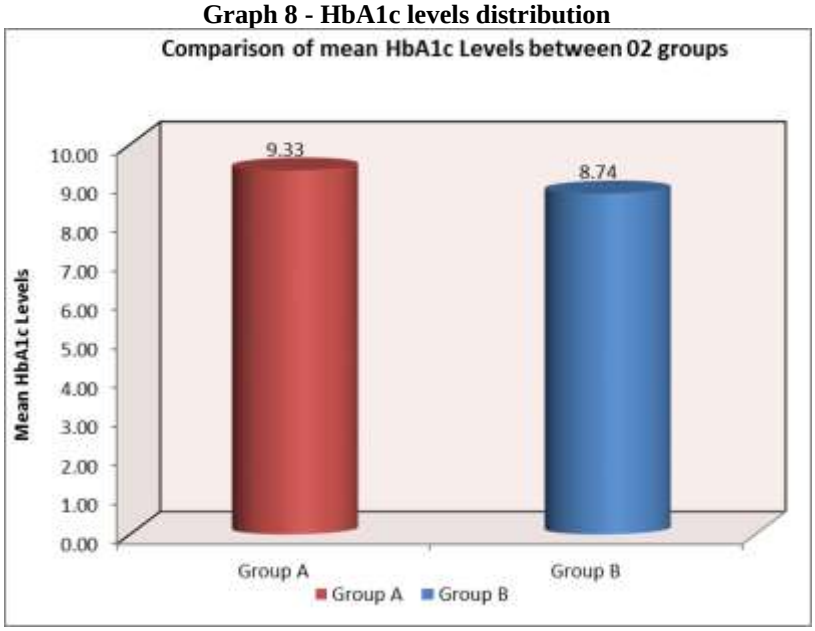
The following graph shows the comparison of mean values of FBS, PPBS in Group A and Group B.The mean value of FBS in Group A was 168.70 mg/dl and 148.90 mg/dl in Group B.The means of PBBS in mg/dl for Group A and Group B respectively were 261.20 and 242.20.HbA1c mean value was 9.33 in Collagen granule dressing group and 8.74 in Conventional dressing group.

Graph 7 - Comparison of FBS and PPBS in both groups



The following graph shows the mean HbA1c values in both groups.HbA1c mean value was 9.33 in Collagen granule dressing group and 8.74 in Conventional dressing group. The p value was statistically not significant.

Graph 8 - HbA1c levels distribution



SWAB FOR CULTURE AND SENSITIVITY:

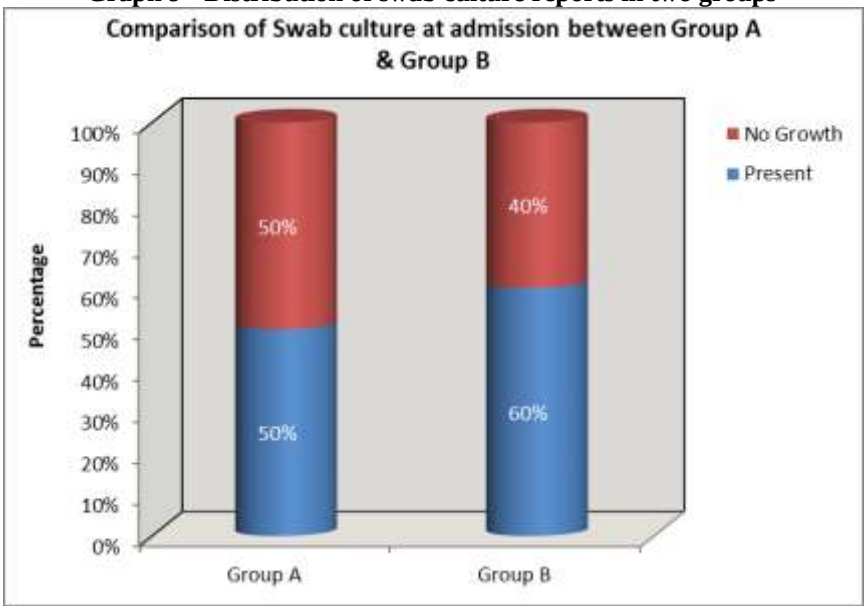
Swab or pus from the floor of the ulcer was taken and was sent for culture and sensitivity in all the patients included in our study.Swab taken for culture revealed positive report in 15 patients(50%) of Group A and 18 patients(60%) of Group B whereas the report showed no growth in 15 cases(50%) in Group A and 12 cases(40%) in Group B.These values were statistically tested by using Chi Square Test and gave a p value of 0.44 that is statistically not significant.

The following table shows the above results in both the groups of our study.

Table 13 - Comparison of swab culture at admission between Groups A and B

Comparison of Swab culture at admission between Group A & Group B using Chi Square Test							
		Group A		Group B			
Variables	Category	n	%	n	%	χ^2 Value	P-Value
Swab culture at	Present	15	50%	18	60%	0.606	0.44
Admission	No Growth	15	50%	12	40%		

Graph 9 - Distribution of swab culture reports in two groups



The above graph shows the results of swab for culture sensitivity in Collagen granule dressing group and Conventional dressing group in our study.50% of the cases in Group A had positive report and 50% had no growth.Among the patients in Group B 60% of the cases had positive report while 40% had no growth.

NUMBER OF DRESSINGS:

The patients who got admitted in our department had foot ulcers which required dressings.Dressing for the ulcer was done on alternate days or earlier if there is any soakage of the dressing.The number of dressings in each group were compared in our study.

The table below illustrates the mean and standard deviation in each group.The mean number of dressings in Group A was 18.30±6.22 and mean in Group B was 34.80±10.87.The mean difference between two groups was -16.50.This variable is compared by using Mann Whitney Test and showed a p value of <0.001 that is statistically significant. Following

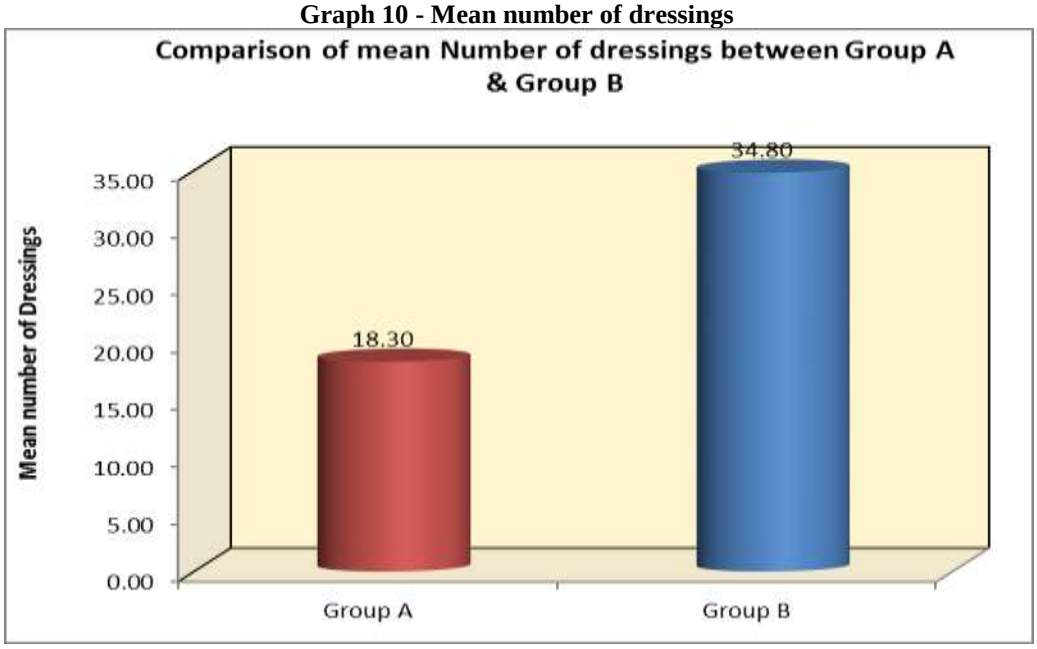
Comparison of mean number of dressings in Group A and Group B using Mann Whitney U Test

Variables	Group	N	Mean	SD	Mean Diff	P-Value
Number of dressings	Group A	30	18.30	6.22	-16.50	<0.001*
	Group B	30	34.80	10.87		

P <0.001;Statistically significant, Mann Whitney Test

The following graph shows the mean number of dressings in Collagen granule dressing group and Conventional dressing group.

Graph 10 - Mean number of dressings



Duration of antibiotic therapy:

Depending on the clinical examination of the ulcer-presence of slough or pus, cellulitis of surrounding tissue and total leukocyte count empirical antibiotic was started and later was changed according to culture and sensitivity report.The duration of antibiotics was calculated in number of days-0,3,5,7,10,14 or 21 days.

The mean duration of antibiotic therapy in Collagen granule dressing group was 4.70±5.00 and in Conventional dressing group was 8.00±5.12.The mean difference between the groups was calculated using Mann Whitney Test the value was -3.30.The same test was used to calculate p value which was 0.005 that is statistically significant. The mean and standard deviation in each group is shown in the following table:

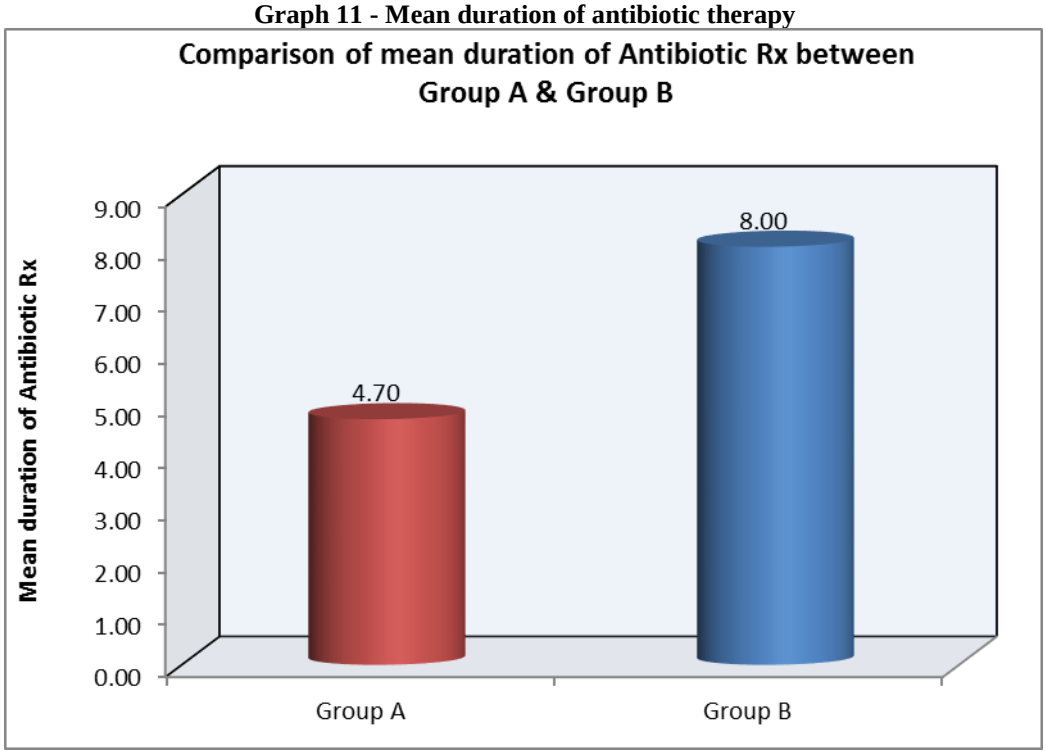
Table 15 - Comparison of mean duration of antibiotic therapy in two groups in our study

Comparison of mean duration of antibiotic therapy in Group A and Group B						
Varaibles	**Group**	**N**	**Mean**	**SD**	**Mean Diff**	**P- Value**
Duration of Antibiotic Rx	Group A	30	4.7	5	-3.3	0.005*
	Group B	30	8	5.12		

P=0.005,Statistically significant, Mann Whitney Test

The following graph shows the mean duration of antibiotic therapy in Collagen granule dressing group and Conventional dressing group.

Graph 11 - Mean duration of antibiotic therapy



NUMBER OF SURGICAL DEBRIDEMENTS:

Based on the clinical examination of the ulcer-presence of slough or necrotic tissue debridement of the ulcer was done.the number of surgical debridements were compared in both the groups in our study.The table drawn below shows the mean number of surgical debridemnts that were required in Group A and Group B and were compared between the two groups.The mean number of surgical debridements in Group A were 0.63±0.77 and in Group B were 1.13±0.82.The mean difference was -0.50.The p value was assessed by using Mann Whitney test and gave a result of 0.02 that is statistically significant.

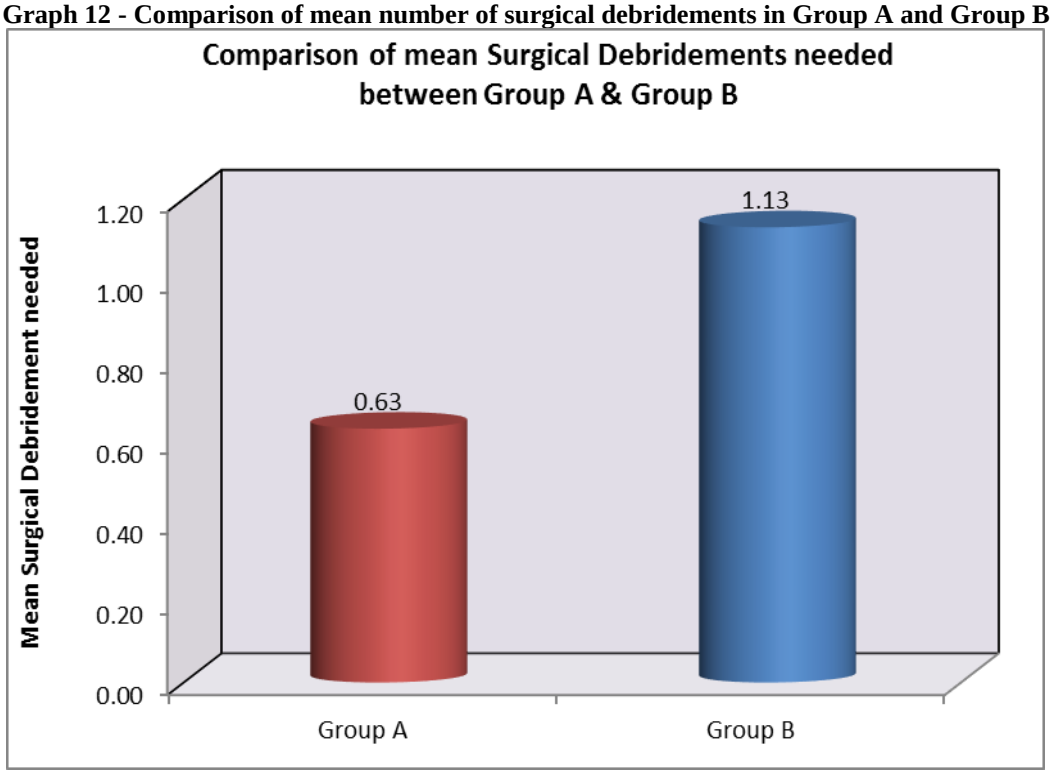
Table 16 - Comparison of mean number of surgical debridements in Group A and Group B

Comparison of mean number of surgical debridements in Group A and Group B						
Variables	**Group**	**N**	**Mean**	**SD**	**Mean Diff**	**P- Value**
Surgical Debridements	Group A	30	0.63	0.77	-0.5	0.02*
	Group B	30	1.13	0.82		

P=0.02, Statistically significant, Mann Whitney Test

The following graph shows the mean number of surgical debridements between Collagen granule dressing group and Conventional dressing group.

Graph 12 - Comparison of mean number of surgical debridements in Group A and Group B



TIME TAKEN FOR HEALING:

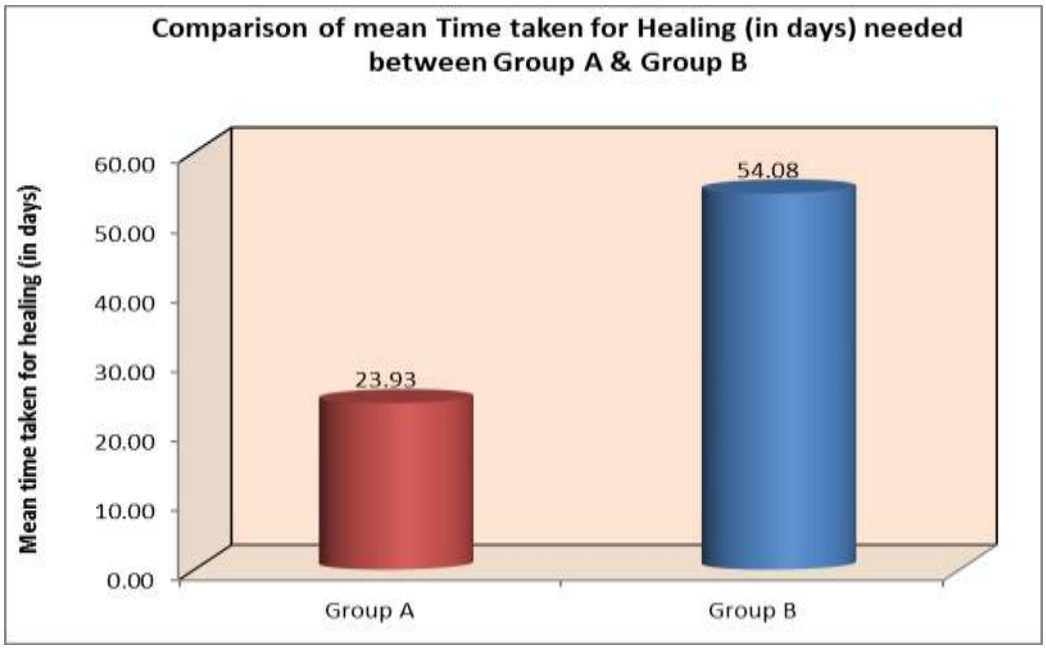
The time for healing of ulcer was measured in days.The healing time was measured in each individual and mean number of days for healing was calculated in both the groups.

The table given below compares the mean number of days required for healing of the ulcer in Group A and group B.The mean time taken for ulcer healing in Group A was 23.93±12.93 days and in Group B was 54.08±25.52.The mean difference between two groups was -30.15 and p value was <0.001 that is statistically significant which was analyzed by using Mann Whitney Test.

Table 17 - Comparison mean time taken for healing(in days) in two groups in our study

Comparison of mean time taken for healing (in days) in Group A and Group B						
Variables	**Group**	**N**	**Mean**	**SD**	**Mean Diff**	**P- Value**
Time taken for healing(Days)	Group A	30	23.93	12.93	-30.15	<0.001*
	Group B	26	54.08	25.52		

P <0.001, statistically significant, Mann Whitney test



Graph 13 - Mean time taken for wound healing

Follow up time:

The follow up time for both groups was categorized as regular,irregular and lost for follow up.Majority of the cases were followed up regularly.

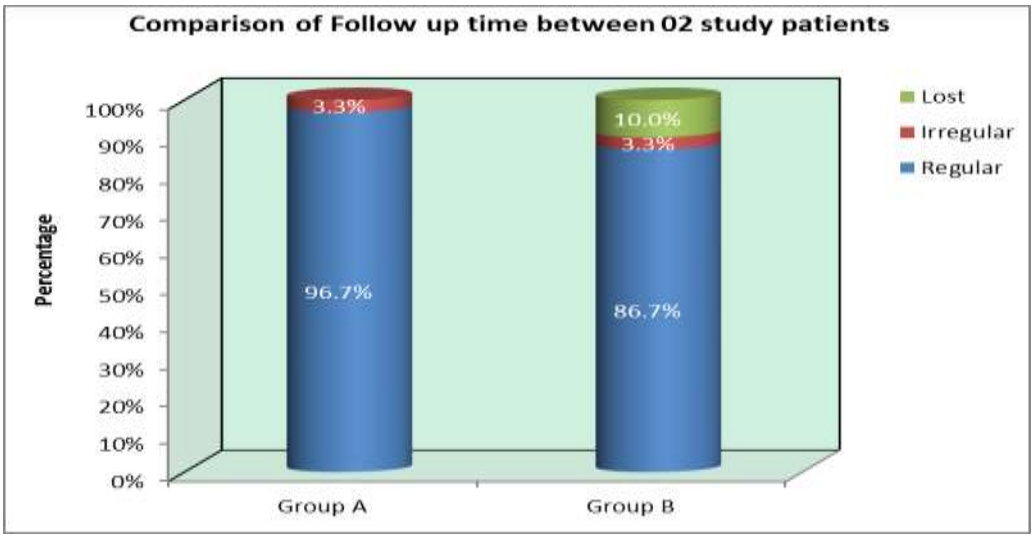
The following table illustrates the follow up time in Collagen granule dressing group and Conventional dressing group.29 patients in Group A were followed up regularly while 26 patients in Group B were regular for follow up.1 patient was irregular in Group A and Group B also.3 patients among group B were lost for follow up.Statistical analysis was done using Chi Square Test which gave a p value of 0.21 that is statistically not significant.

Table 18 - Comparison of follow up in both groups in our study

Comparison of study characteristics between Group A & Group B during Post Follow-up time period using Chi Square Test							
		Group A		Group B			
Variables	Category	n	%	n	%	χ^2 Value	P-Value
Follow up time	Regular	29	96.7%	26	86.7%	3.164	0.21
	Irregular	1	3.3%	1	3.3%		
	Lost	0	0.0%	3	10.0%		

P=0.21, Statistically not significant, Chi Square Test

The graph shown below compares the follow up time in Collagen granule dressing group and Conventional dressing group.96.7% cases were regular for follow up in Group A and 86.75% cases in Group B.3.3% were irregular in both the groups and 10% in Group B was lost for follow up.



Graph 14 - Follow up distribution

Requirement for ssg and amputation:

Patients with gangrene of foot required amputation and ulcer that did not heal with secondary intention or having large defect was advised SSG.

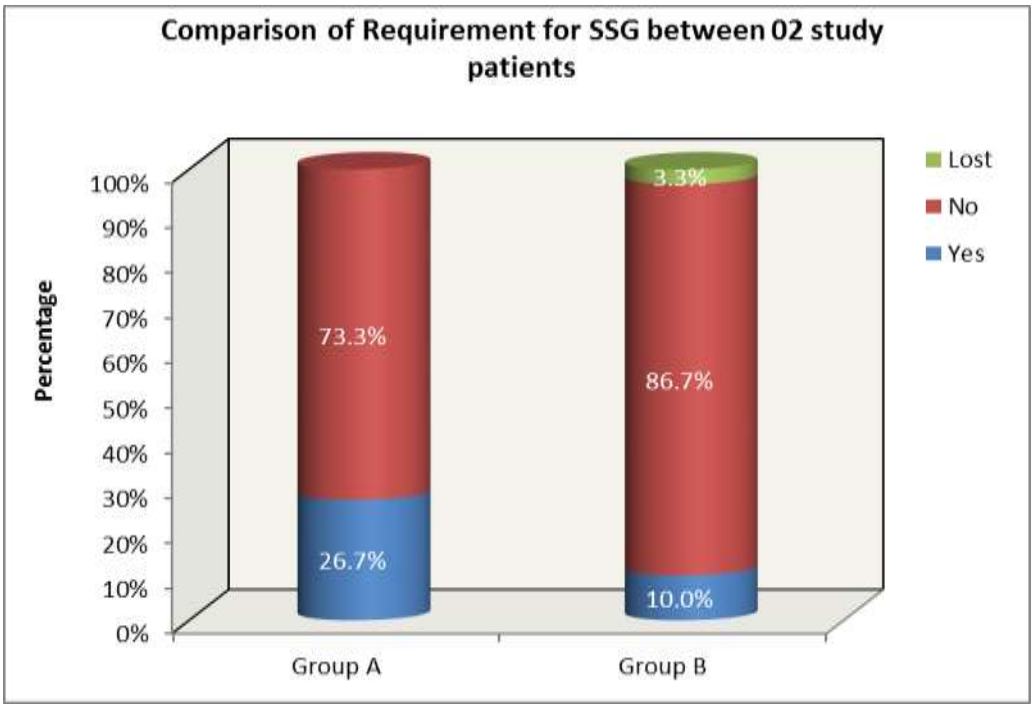
The following table showed that 8 patients in Group A required SSG and 4 patients required amputation.Among patients in Group B, 3 patients required SSG whereas 2 patients needed amputation.1 patient in Group b was lost for follow up.P value was calculated using Chi Square Test which was 0.43 that is statistically not significant.

Table 19 - Comparison of requirement of SSG and Amputation in two groups included in our study

Comparison of requirement of SSG and amputation in both groups in our study

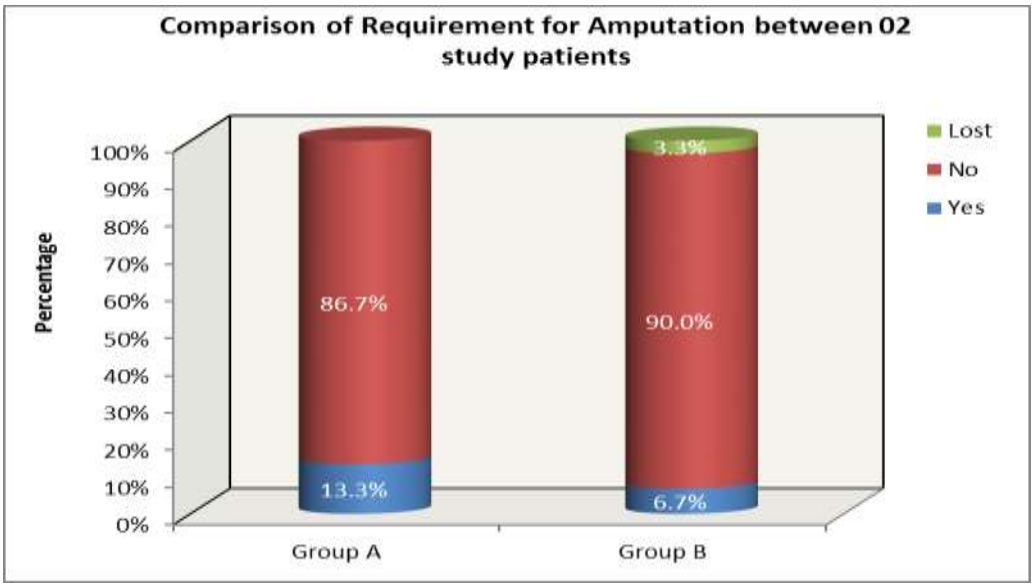
Variables	Category	Group A		Group B		χ^2 Value	P-Value
		n	%	n	%		
Requirement for SSG	Yes	8	26.7%	3	10.0%	3.606	0.17
	No	22	73.3%	26	86.7%		
	Lost	0	0.0%	1	3.3%		
Requirement for Amputation	Yes	4	13.3%	2	6.7%	1.686	0.43
	No	26	86.7%	27	90.0%		
	Lost	0	0.0%	1	3.3%		

P value of 0.17 and 0.43, Statistically Not significant, Chi Square Test



Graph 15 – Requirement for SSG

The above graph shows the requirement for SSG in both the groups.26.7% in Collagen granule dressing group and 10% in Conventional dressing group required SSG.3.3% in Group B lost for follow up.



Graph 16 – Requirement for Amputation

The graph drawn above shows the requirement for amputation in each group.13.3% in Group A and 6.7% in Group B needed amputation.3.3% in Group B was lost for follow up.

Overall significant p values were noted in the number of dressings required,duration of antibiotic therapy,number of surgical debridements needed and mean time taken for healing whereas p values were not statistically significant for follow up time,requirement for SSG and Amputation in both the groups

IV. Discussion

In the present study the two groups of dressings for diabetic foot ulcers which were, the collagen granule dressing group and conventional dressing group were compared. The aim was to compare the two groups in terms of number of dressings required,duration of antibiotic therapy,number of surgical debridements needed, the time taken for healing and follow up time.

AGE – Our study comprised of population with age group between 51-60 years in majority.The mean age in collagen granule dressing population was 51.5 years and in conventional dressing population it was 50.6 years.However age relation in comparison with duration of ulcer,duration of diabetes and amputations underwent was not attempted which could interfere with ulcer healing and bias.

GENDER – Our present study had a male predominance with 71.66% in total and 28.33% of female population.The same gender predominance was observed in both the groups.However this gender ratio was not significant in our study since patients were selected randomly and it had no effect with outcomes.

NUMBER OF DRESSINGS REQUIRED - As depicted in the present study the mean number of dressings in collagen granule dressing group 18.30 was lesser when compared to conventional dressing group where the mean number of dressings required were 34.80. Similar study was done by S Shanmugam et al[88] where they have seen that collagen granule dressing required lesser number of dressing when compared to conventional dressings where the dressings were done until the ulcer had completely healed.This factor will have an indirect effect on the overall cost and length of hospital stay which however were not compared in our present study.

This had a strong statistical significance showing that the mean number of dressings were lesser in collagen granule dressing group in comparison with conventional dressing group.

DURATION OF ANTIBIOTIC THERAPY – Polymicrobial[89] aetiology of diabetic foot ulcers have been reported world wide.However it is not uncommon to have single organism.Researchers have shown the predominance of both gram positive and gram negative organisms in diabetic foot infections.Various other studies have also shown a higher incidence of Pseudomonas infection,E. coli,Staph aureus species[89].The pattern of microbial infection is inconsistent in patients with diabetic foot and hence evaluation of the microbes and their antibiotic sensitivity is necessary for the selection of antibiotics for the management of patients with diabetic foot ulcers.

In a study conducted by Kavitha et al[90] the choice of wound care in diabetic foot ulcer including the duration of antibiotic therapy and parenteral,oral or topical antibiotics have been studied and reported an average time of 1-2 weeks of antibiotic therapy.Many other researchers have studied this in different types of dressings.Collagen and other biological dressings which were used for dressings in patients with diabetic foot required lesser duration of antibiotic therapy.

Our present study shows that collagen granule dressing group required lesser duration of antibiotic therapy when compared with conventional dressing group. The mean duration of antibiotic therapy in collagen granule dressing group was 4.70 days while the mean duration of antibiotic therapy in conventional dressing group was 8 days which was almost double the duration that was required for collagen granules dressing group.

This comparison had a strong statistical significance explaining that collagen granules help to reduce infection in diabetic foot ulcers requiring shorter duration of antibiotic therapy when compared to conventional dressing group.

NUMBER OF SURGICAL DEBRIDEMENTS – Debridement of the necrotic and non-viable tissue needs to be considered as the first and most important step that leads to wound closure and reduce the chances of amputation, as wound healing is reduced in the presence of necrotic tissue,non-viable tissue,debris or critical colonization by bacteria. Lawrence et al have studied role of debridement along with different kinds of dressings and described that newer dressings when combined with few debridements can achieve better results.

The Infectious Disease Society of America(IDSA) and Wound Healing Society recommends sharp debridement[91] over topical debriding agents.Sharp debridement has been found to be more effective in several clinical trials, though overall data that is available is limited.

Our study compared number of surgical debridements between Collagen granule dressing group and Conventional dressing group and proved statistically significant outcome. The mean number of surgical debridements in collagen group was 0.63 and in conventional group was 1.13.

TIME TAKEN FOR HEALING – In our present study we observed that the mean healing time taken for healing was less in patients for whom dressing was done using collagen granules when compared to patients who had dressings with conventional dressing.The mean time taken for healing in Group A was 23.93 and in Group B was 54.08 and gave a p value that was statistically significant.

Collagen plays a relevant role in cutaneous tissue repair and is a valid option when used as a bioactive advanced dressing for chronic non healing wounds like diabetic foot ulcers.In a study by Harish Rao et al[92] the healing time was significantly lower in the patients receiving collagen dressing (4.63±1.18 weeks) when compared to conventional dressing (7.79±1.19 weeks).The result of this study for time taken for healing can be compared to our present study wherein we have statistically significant difference between the two groups.

In a study conducted by Veves[93], 276 patients with diabetic foot ulcer, after 12 weeks of treatment, 51 (37.0%) Promogran'-a collagen/oxidized regenerated cellulose dressing-treated patients had complete wound closure when compared to 39 (28.3%) patients of control group (moistened gauze), but this difference was not statistically significant (P=0.12). In this study, author found an overall benefit of collagen on the rate of wound healing compared with moistened gauze.

Omkar Singh[94] study reveals that regarding Collagen Dressing Versus Conventional Dressings in 120 patients with chronic wounds of varied aetiologies,the appearance of healthy granulation tissue occurred earlier over collagen-dressed wounds than over conventionally treated wounds (P=0.03).

FOLLOW UP – Majority of the patients in both the groups were followed up regularly though it gave a p value that was not statistically significant (p=0.21).

In several studies like Donaghue VM et al[95] Blume P et al[96] the percentage of patients patients lost for follow up were studied and there were none those were lost for follow up in those studies.In our present study 10% of patients in Group B were lost for follow up that was comparable to studies conducted by Gotrrup et al[97] where 13% of the cases were lost for follow up in their study.

REQUIREMENT FOR SSG AND AMPUTATION:

Though the requirement for SSG and amputation were not included in objectives of our study these variables were compared out of interest and requirement for our patients who were included in the study.We found that Wagner's grade 3,4 and 5 ulcers needed the above surgeries in many who underwent either SSG or Amputation.

In a study by Harish Rao et al[92] the requirement of SSG use was also significantly lower in collagen dressing patients (64.47%) as compared to conventional dressing patients which was (100 %).In our present study there were no statistically significant values pertaining to the need for SSG or Amputation.

Acknowledgements

To start with-"Dear God I want to take a minute not to ask for anything but to thank you for everything I have".

It gives me immense pleasure to express my heartfelt gratitude and sincere thanks to my beloved teacher and my guide , Dr.Kilambi Srinivas Professor and Head of the Department in the Department of General surgery, ST.Teresa general hospitalfor being an inspiration and for providing all the guidance and emotional support during the course of my study,without whose towering presence this study would not have been possible.

I would also like to express my sincere gratitude to Dr. S sri sairekha, Dr. Hima Soumya madasu, who were instrumental in guiding me in this topic by providing valuable tips from time to time which helped me complete my work.I am also thankful to who also played a significant role in my literature and final stages of my work.

My sincere thanks to the staff and technicians of the department of sugery for helping me carry out the required work.I am grateful to all my friends and colleagues for their untiring support.

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