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A CLINICAL OUTCOME OF VACUUM ASSISTED DRESSING AND CONVENTIONAL SALINE DRESSINGS IN MANAGEMENT OF CHRONIC NON- HEALING ULCERS – A RANDOMIZED CONTROLLED STUDY

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A B S T R A C T

Background: Chronic non-healing ulcers frequently lead to hospital admissions in surgical wards. Despite identifying the underlying cause, such ulcers pose treatment challenges due to factors like diabetes mellitus and infection. The present study aimed to investigate the clinical outcomes of vacuum-assisted wound dressing compared to conventional saline dressing in non-healing ulcers.

Materials & Methods: This hospital-based randomized controlled study was conducted among patients aged over 18 years with non-healing ulcers persisting for more than three weeks, admitted to the inpatient services of the Department of General Surgery,Karpaga vinayaka institute of medical science Chengalpettu over an 18-month period. Patients with complete necrosis, bleeding disorders, malignant ulcers, abdominal wounds, and electrical burns were excluded. Patients were allocated into two groups based on intervention: Group A received vacuum-assisted dressing, while Group B received conventional saline dressing. Patients were evaluated for wound healing rate, granulation tissue formation, culture reports, and total duration of hospital stay.

Results: A total of 66 patients were included, with a mean age of 54.63 ± 9.36 years, comprising an equal distribution of male and female participants. There were no significant differences in demographic details between the groups ($p > 0.05$). The study revealed a significantly higher wound healing rate in patients of Group A compared to those in Group B ($p < 0.05$). Similarly, pus culture sterilization and shorter hospital stays were significantly better in Group A compared to Group B ($p < 0.05$).

Conclusion: Vacuum-assisted dressing led to reduced overall hospital stays, improved pus culture sterilization, and exhibited better wound healing rates and granulation tissue formation compared to conventional dressing for non-healing ulcers.

Keywords: Dressing, Vacuum-Assisted, Conventional, Complication, Ulcer, Wound Closure.

INTRODUCTION

Chronic non healing ulcer common reason for admission in surgical ward.[1,2]Non healing ulcers are difficult to treat even if the etiology is made out, because of coexisting factors like diabetes mellitus, infection.[3,4]Chronic non healing ulcer patient's majority of cases experience prolonged phase of pain, prolonged treatment requiring longer duration of stay in hospitals, morbidity and require major reconstructive surgery, amputation.[5] Looking from patient's point of view, management protocol for chronic wounds is mostly painful and uncomfortable imposing a social stigma and financial burden to the family & society. Vacuum assisted closure dressing which is now termed under negative pressure assisted wound therapy is a significant discovery in management of non-healing wounds.[5]Negative pressure wound therapy as delivered by vacuum assisted closure causes the tissue at wound bed to be stretched and drawn into the open pores of the granu foam used, fluid from the extravascular space is removed, improved circulation, increased bacterial clearance, and

cell mitosis is stimulated leading to proliferation of granulation tissue contributing towards hastening of wound closure.

It is commonly recognized that the ―use of negative pressure to produce a suction force allows surgical wounds to drain and speeds up the healing process.[6,7]If extravascular surplus fluid is not sufficiently removed from a wound during surgery, the fluid components will obstruct ulcer healing both chemically and physically. The surrounding tissue may not be mechanically impacted much by a hidden drain.‖[8,9]A revolutionary idea has been developed in the application process, whereby the suction is topically applied over the wound's surface to promote quicker healing on the nonhealing wound.
Topical negative pressure, or vacuum, is applied in VAC therapy to ―remove blood and serous fluid, slough, and controlled debridement. It also lowers infection rates (a closed, sealed system creates a hypoxic environment that draws out bacteria and debris, reducing the colony count) and increases localized blood flow, which supplies oxygen and nutrients to the wound to promote granulation and speed up the healing of the wound surface area.‖[10]

There has not been extensively reported studies on use of NPWT in the India. Only few Indian studies have provided intuition into the usage of NPWT in Indian setting.[2]This study will provide high quality evidence of faster and improved wound healing, reduced duration of hospital stays, decreased need of repeated surgical debridement. Present study aimed to assess the clinical outcome of vacuum assisted wound dressing and conventional saline dressing in nonhealing ulcers

AIMS & OBJECTIVES
Aim:
To study the clinical outcome of vacuum assisted wound dressing and conventional saline dressing in nonhealing ulcers
Objectives:
Primary:
To study the clinical outcome of using vacuum assisted dressing and conventional saline dressing technique in chronic nonhealing ulcers
Secondary:
To find out the occurrence of wound related complications
To find out the difference in duration of hospital stay

MATERIAL & METHOD
Setting: Patients attending department of general surgery at Karpaga vinayaka institute of medical science , Chengalpettu in inpatient setting, above 18 years
Study Design: Hospital Based randomized controlled Study.
Inclusion criteria
1. Patients above age of 18 years both sexes presenting with nonhealing ulcer
>3weeks) admitted in inpatient services, department of general surgery, AVMC&H.
Exclusion criteria:
1. Wounds exhibiting complete necrosis of tissue requiring amputation at time of admission to hospital
2. Patients with bleeding disorders
3. Patients with malignant ulcer
4. Patients with untreated osteomyelitis / unstable fractures within vicinity of the wound
5. Abdominal wounds
6. Electrical burns
Study duration: 18 months Sample size and calculation:
with the help of following formula:
Thus sample size according to this formula is 33 (Minimum Per Group) Total 66 (Minimum in two groups).
The sample size was calculated based on previously published study was calculated with expected difference in rate of wound healing as 0.5 and the standard deviation of 0.71. the level of significance is taken as 5% and 80% respectively.
Sampling Technique: Simple Random Sampling Method.
Study design: Hospital based randomized controlled study
Study procedure:
GROUP A: patients receiving vacuum assisted dressing
GROUP B: patients receiving conventional saline dressings
After correction from the IRC&IEC, random sampling of patients admitted as in patient services during the study period mentioned, fulfilling the inclusion and exclusion criteria as listed were recruited for the study, after obtaining informed written consent under the guidance of the guide and co-guide
 The nature, purpose and their roles in the study was explained in detail, including the information that their non-participation in the study would not affect the quality of their treatment that they are to receive and that they are free to

exit the study at any time. After assuring that their responses would remain confidential, an informed written consent for the same shall be obtained from all participants‖

 Data were collected using a pre-tested semi-structured proforma to collect sociodemographic details about the patients participating in the study.

 Patients based on convenience sampling were divided into group A& group B

 Pre-operatively in both the groups detailed history was taken and routine investigations like Hb, TC, DC, ESR, RBS, HBA1C, Hiv, Hbsag, Chest Xray PA, Ecg, Lft, Rft, Pus C/S was done.

 Wound preparation were done by removing the dressing from the wound and discarded. A culture swab for microbiology culture was taken before the wound irrigation with normal saline.

 Surgical debridement was done and adequate haemostasis was achieved.

 Sterile, ―open-cell foam dressing was gently placed into the wound cavity. the site was then sealed with an adhesive drape ensuring that the drapes covered the foam 41and the fenestrated tube inside. Drapes should be placed till three to five centimeters of surrounding healthy tissue. Controlled pressure was uniformly applied to all tissues on the inner surface of the wound using centralized vacuum pump. The pressure could be delivered either continuous or intermittent type, ranging from 50 to 125 mm hg. The foam dressing would get compressed in response to the negative pressure. The pressure was applied continuously for the first 48 hours and then changed to continuous therapy‖

 After 5 days the vac was removed and the wound healing rate will be assessed; culture swab for microbiology was taken

 Conventional saline dressing daily was done in control group – daily debridement of slough was done if present. wound was washed with betadiene and normal saline. wound was dressed with moist saline gauze and covered with layers of gauze sealed with a roller bandage Data were tabulated, analysed based on statistical tests.

Results obtained and conclusions was drawn Clinical trial registration: done

Data collection procedure:

This is randomized control study in which patient were studied in two groups from in patient setting Routine hematological investigations was done at time of admission.

Post procedure comparison between the two groups shall be done for the clinical outcome

• Rate of wound healing at the end of treatment – dimension of the wound

"Before the start of VAC therapy, after initial debridement, the wound is photographed with a ruler placed beside the wound. A double layer of polyethylene sheets was held firmly in place over the wound, and an outline of the wound was traced using a permanent marker. The layer in direct contact with the wound is discarded"

• Number of days of hospital stay

• Pus c&s before & after the procedure in both groups

• Fall in hemoglobin

• Split skin graft

• Amputation

Outcome Tabulations

a. Age /sex distribution of wound

b. Location of wound

c. Outcome of treatment: SSG / discharge / amputation (vacuum dressing and saline dressing group)

d. Organism grown in culture before and after vacuum dressing and saline dressing 4344

e. Hospital stay: duration (vacuum dressing and saline dressing group)

Outcome variables:

Result at the end of treatment – wound healing pattern and rate (measure the wound dimension before & after using wound pattern print on graph paper wound bed

Granulation tissue formation - Number of days of hospital stay C&s before & after vac

STATISTICAL ANALYSIS

―The continuous variables' values were represented as Mean ± Standard deviation (SD) for both research groups, whereas the data on categorical variables were expressed as n(% of instances). Fisher's exact probability test or the Chi-Square test were used to determine the significance of the difference in the categorical variable distribution between the two study groups. To determine the statistical significance of the differencein the average of continuous variables between the two research groups, the independentsample t test or unpaired t test was employed. The t test was used to the research variables only after the underlying assumption of normality had been verified. The proper non-parametric tests were employed when normality was absent.

RESULTS

A total of 66 patients included with mean age of 54.63±9.36yrs, with 50% male and female in study. The mean age between the groups was comparable with no significant

Table 1: Comparison of baseline parameters between the groups

	Vacuum assisted dressing		Conventional dressing		p-value
	Mean	SD	Mean	SD	
Age (yr)	54.42	9.77	54.85	9.08	0.96

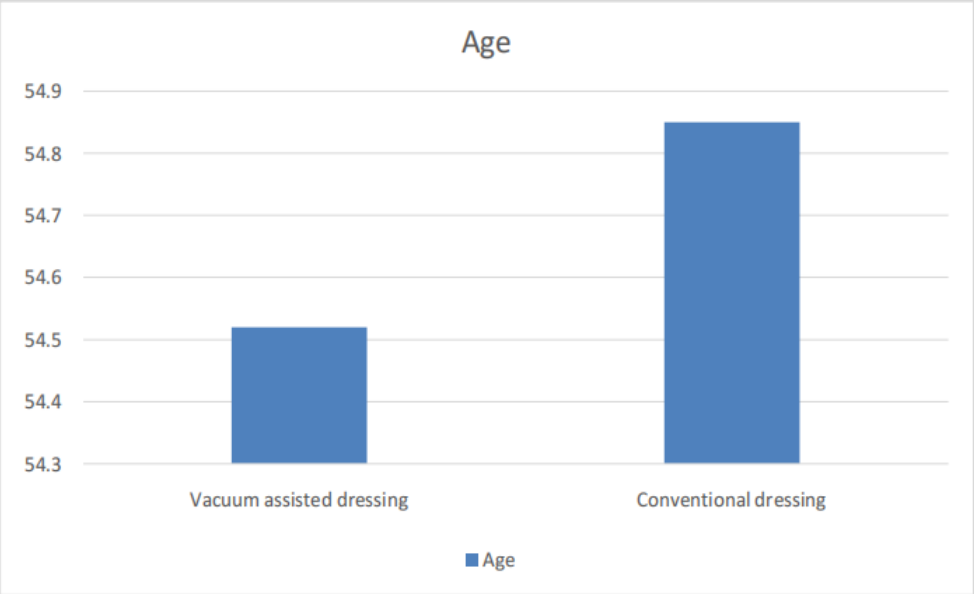

FIGURE 1 : Comparison of baseline parameters between the groups

Table 2: Comparison of physical parameters between the groups

	Vacuum assisted dressing		Conventional dressing		p-value
	Mean	SD	Mean	SD	
Height (cm)	161.9	7.2	158.1	6.8	0.66
Weight (kg)	70.2	11.7	66.3	12.3	0.74

There was no significant difference in the demographic details between the groups. ($p>0.05$)

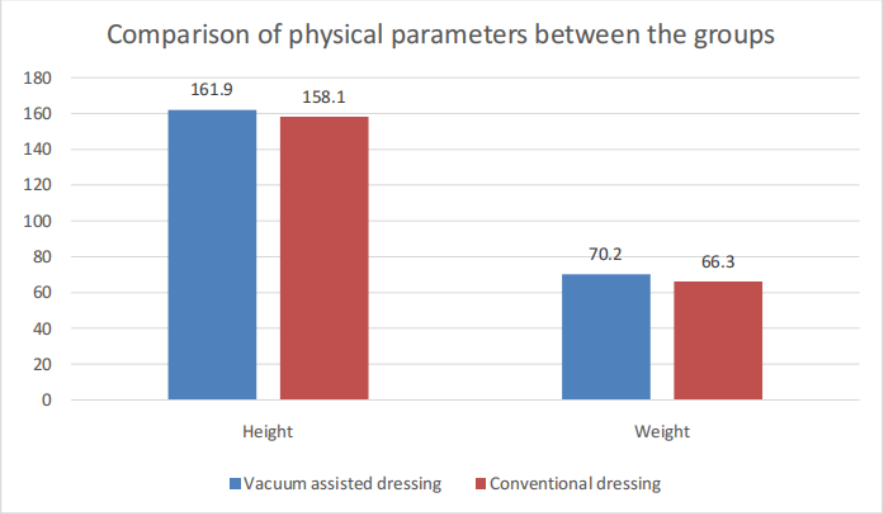

FIGURE 2 : Comparison of physical parameters between the group

Table 3: Comparison of vital parameters between the groups

	Vacuum assisted dressing		Conventional dressing		p-value
	Mean	SD	Mean	SD	
PR (bpm)	75.3	3.4	74.8	4.6	0.98
RR (permin)	15.2	1.3	14.9	1.0	0.64
SBP (mmHg)	109.7	14.7	114.2	10.0	0.51
DBP (mmHg)	76.7	11.4	78.5	10.0	0.69

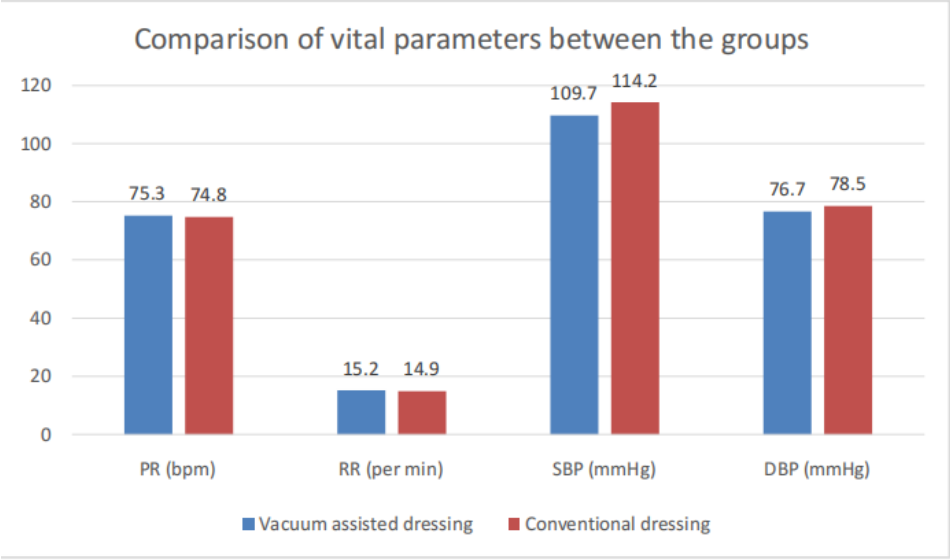

Figure 3: Comparison of vital parameters between the groups

Table 4: Comparison of blood parameters between the groups					
	Vacuum assisted dressing		Conventional dressing		p-value
	Mean	SD	Mean	SD	
Hemoglobin (g/dL)	11.9	2.2	12.4	2.0	0.74
Total Count (cumm)	13510.9	1568.3	15084.8	3789.2	0.12
ESR (mm/hr)	14.6	2.3	18.8	2.8	0.11

The mean level of hemoglobin, total blood cell count and ESR were comparable between two groups.

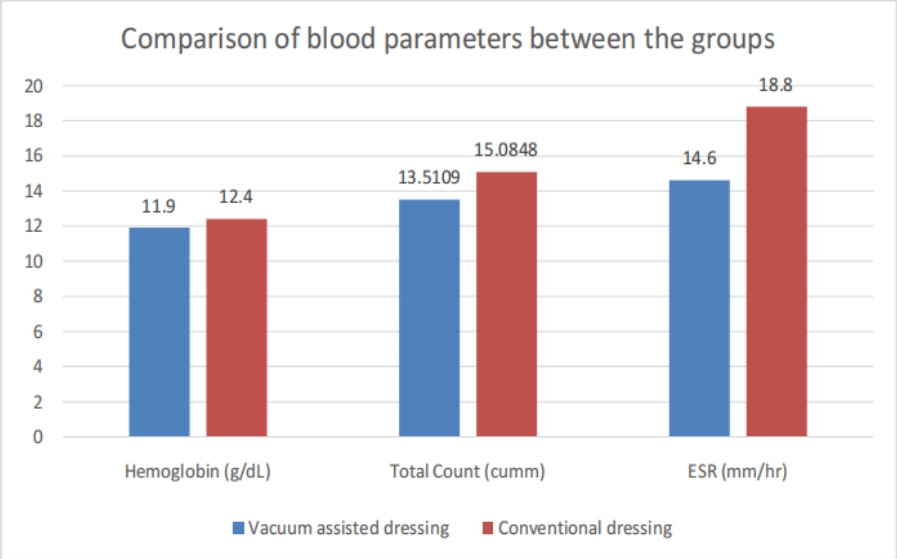

FIGURE 4 : Comparison of blood parameters between the group

Table 5: Comparison of serum creatinine and urea parameters between the groups					
	Vacuum assisted dressing		Conventional dressing		p-value
	Mean	SD	Mean	SD	
Creatinine (mg/dL)	.9	.2	.9	.1	0.99
Urea (mg/dL)	32.9	4.4	36.6	3.3	0.91

There is no significant difference in the mean level of serum creatinine and serum urea between the groups. ($p>0.05$)

		Vacuum assisted dressing		Conventional dressing		Chi-square (p-value)
		Count	N %	Count	N %	
C/S before	Absent	0	0.0%	3	9.1%	0.69
	Present	33	100.0%	30	90.9%	
C/S after	Absent	9	27.3%	8	24.2%	0.52
	Present	24	72.7%	25	75.8%	

There is no significant difference in the culture sensitivity positive between the groups, however the positive rate after treatment in vacuum assisted dressing was marginally lower than conventional dressing. (p>0.05)

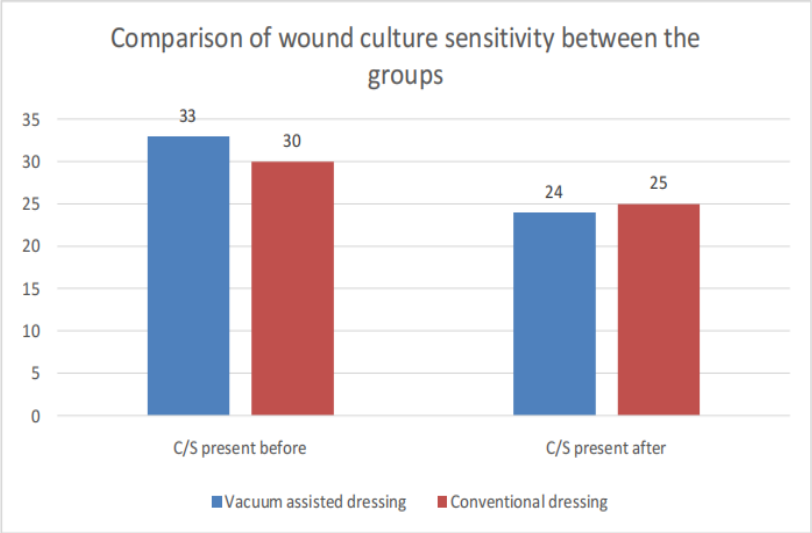

FIGURE 5 : Comparison of wound culture sensitivity between the groups

Table 6 le 10: Comparison of mean duration of hospital stay between the groups

	Vacuum assisted dressing		Conventional dressing		
	Mean	SD	Mean	SD	p-value
Hospital stay in days	19.5	6.0	28.7	9.1	0.01*

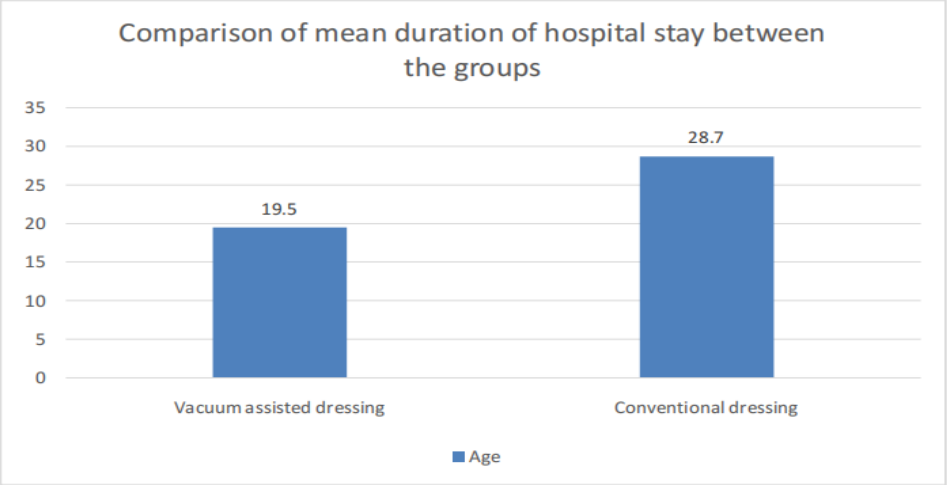

Figure 6 : Comparison of mean duration of hospital stay between the groups

There is significant shorter duration of hospital stay in vacuum assisted dressing group compared to the patients in conventional dressing group.

Table 7 able 11: Showing the outcome of treatment

		Frequency	Percent
Outcomeoftreatment	Amputation	4	6.1
	Discharge	24	36.4
	SSG	38	57.6
	Total	66	100.0

Among the participants, 36.4% discharged, 6.1% with amputation and 57.6% were SSG.

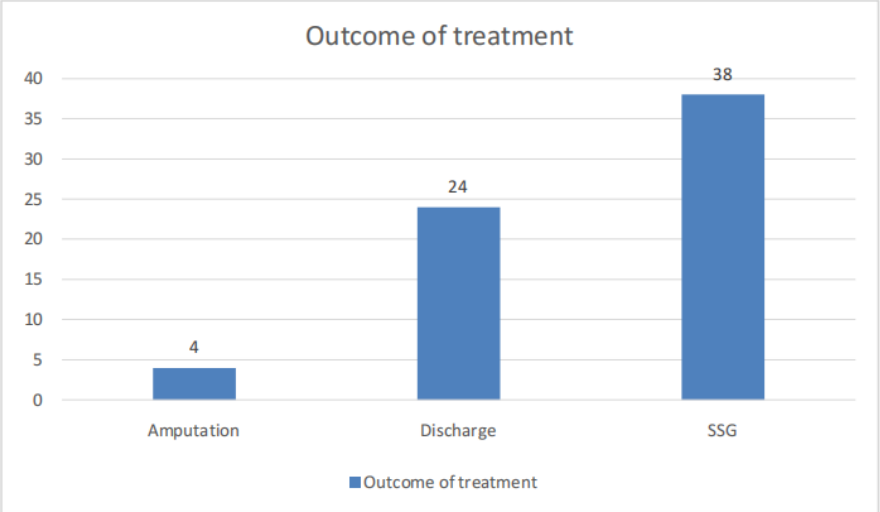

FIGURE 7 :Showing the outcome of treatment

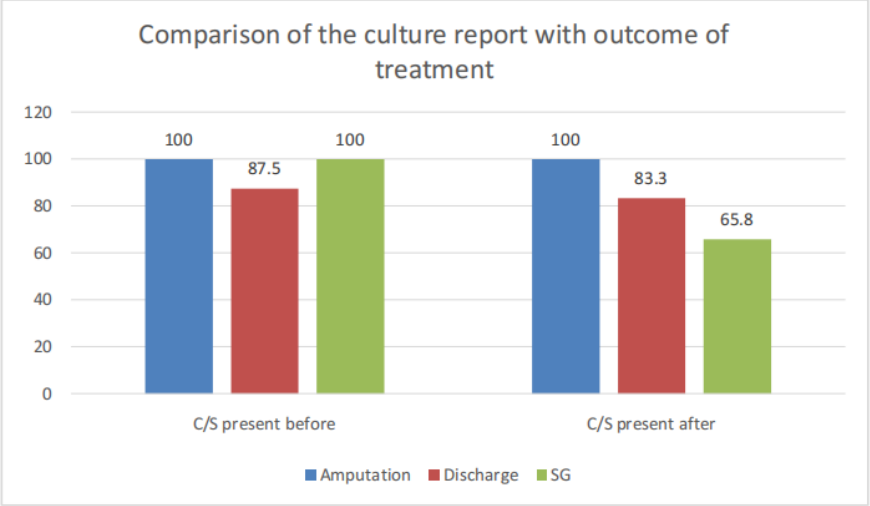

Figure 8: Comparison of the culture report with outcome of treatment

DISCUSSION

The practice of applying sub-atmospheric pressure to wounds is a relatively recent innovation, initially described by Fleischmann et al. in 1993. They were the first to report on the prolonged use of sub-atmospheric pressure to facilitate debridement and promote healing, following their successful application of this technique.Negative Pressure Wound Therapy (NPWT) using vacuum-assisted closure (VAC) offers distinct advantages in countries like India, where healthcare facilities face high patient loads and limited financial resources. With a significant portion of the population earning less than one US dollar per day and a modest allocation of the government budget to health, there is a pressing need for faster and cost-effective wound healing techniques. NPWT with VAC can potentially address these challenges by accelerating healing processes and reducing treatment costs, making it a valuable option for improving healthcare outcomes in resource-constrained settings like India.59—An adhesive drape covers an open-cell foam dressing that serves as the negative pressure. It is attached to a vacuum pump that generates and sustains a sub-atmospheric pressure for either intermittent or continuous treatment.A total of 66 patients included with mean age of 54.63±9.36yrs, with 50% male and female in study. there is no significant difference in mean demographic details, blood parameters between the groups. Reported studies from India by —Vaidhya et al.,60 Singh et al.,61 and Lone et.,48 al1 showed similar mean age of 56.5, 54.4 and 54.18 years respectively.

The study showed significant higher wound healing rate in group A patients compared to group B patients. ($p<0.05$) In similar to present study by Pragadheeswaran M et al., documented that the vacuum assisted closure was superior in term of wound healing and granulation tissue formation compared to conventional saline dressing,11 Another study by Muneer M et al., documented that the vacuum dressing is low cost and also reduced the healing time, hospital stay there by reducing the total cost incurred to the patients.The vacuum sealing technique is an effective option in the management of infected wounds.In concordance, another study by James SM et al., —found that VAC significantly reduced the time to complete wound healing, hasten granulation tissue formation and reduce the ulcer are compared to the conventional dressing.Additionally, this study showed that vacuum-assisted dressing is a more advantageous technique for promoting wound healing, especially in cases of chronic and non-healing ulcers.In study by Janmes SMD et al., stated that the VAC group required a notably shorter duration to achieve 75 percent to 100 percent granulation tissue coverage, with a higher rate of granulation tissue formation observed compared to the control group.Quicker recovery in Negative Pressure Wound Therapy (NPWT) is credited to both macrodeformation, such as stabilizing the wound environment, reducing swelling, promoting wound contraction, and microdeformation, like lowering bacterial presence, creating a conducive healing environment, and boosting cellular growth and blood vessel formation. These factors collectively contribute to improved granulation tissue formation.On culture sensitivity before treatment, majority were positive with E.coli, followed by MRSA, and Klebsilla. In the study conversion to negative growth was seen in 25.8% of the patients. Among the growths, 31.8% were commensals, 15.2% were E.coli, 10.6% were Diphtheroid infection. There is no significant difference in the culture sensitivity positive between the groups, however the positive rate after treatment in vacuum assisted dressing was marginally lower than conventional dressing. ($p>0.05$) Pseudomonas aeruginosa and Acinetobacter baumannii were the most often cultivated organisms in the NPWT group in an RCT by Ali M. Lone et al., whereas P. aeruginosa and Klebsiella were grown in the control group.Additionally, research conducted by Stannard et al., 64 and Blume et al., 65 demonstrated no discernible variance between Negative Pressure Wound Therapy (NPWT) and traditional dressings regarding infection rates or bacterial presence. Factors such as insufficient debridement, foam

retention, air leakage, inadequate sealing of underlying infections, and bleeding associated with NPWT can act as breeding grounds for infection or exacerbate existing infections. While some studies, including our own, indicate the positive impact of NPWT on wound microbiology, it is crucial not to view NPWT as a replacement for infection control measures.In study by Dsouza C et al., ―72.73 percent of ulcers in the VAC group showed no bacterial presence. Thus, Vacuum Assisted Closure therapy proved more effective than standard dressings for wound bed preparation in diabetic foot ulcers according to this study.In study by Anandi A et al., documented that patients with sterile pre-VAC cultures maintained sterility following VAC, while 90% of initially unsterile cultures became sterile after VAC. Moreover, the use of VAC dressings was associated with shorter hospital stays and improved outcomes, including reduced amputations and an increased number of patients eligible for skin grafts.There is significant shorter duration of hospital stay in vacuum assisted dressing group compared to the patients in conventional dressing group. ($p<0.05$) There was higher incidence of culture report positive in patients who had worst outcome as amputation compared to discharge and SSG.Sukur E et al., suggest that the ―VAC therapy system serves as an effective treatment modality for patients with complex diabetic foot ulcers (DFUs) who have undergone partial foot amputation previously. Another study by Vemulpalli SV et al., concluded that the ―negative pressure dressing group exhibited a higher rate of granulation tissue formation, better overall graft survival, and greater patient compliance compared to the traditional dressing group.Fleischmann et al. discovered that ―patients treated with vacuum-assisted closure (VAC) showed accelerated re-epithelialization rates and reduced need for repeat split-thickness skin grafts at the same site. VAC therapy proved superior in managing diverse chronic and complex wounds, achieving substantial reductions in wound volume, depth, and treatment duration. This approach promotes more effective healing outcomes compared to standard methods, with minimal incidence of serious complications noted. However, further rigorous studies involving larger sample sizes are necessary to comprehensively evaluate the efficacy of VAC therapy across various types of wounds.

―VAC therapy significantly reduces the time to achieve complete wound healing, accelerates granulation tissue formation, and diminishes ulcer area. Furthermore, the VAC therapy group did not experience a significant increase in bleeding or infection, as indicated by the study results.

SUMMARY

A total of 66 patients included with mean age of 54.63±9.36yrs, with 50% male and female in study. The mean age between the groups was comparable with no significant There was no significant difference in the demographic details between the groups. ($p>0.05$) The mean vital parameters between the group were comparable between the groups. The mean level of hemoglobin, total blood cell count and ESR were comparable between two groups. There is no significant difference in the mean level of serum creatinine and serum urea between the groups. ($p>0.05$) The study showed significant higher wound healing rate in group A patients compared to group B patients. ($p<0.05$) On culture sensitivity before treatment, majority were positive with E.coli, followed by MRSA, and Klebsilla. In the study conversion to negative growth was seen in 25.8% of the patients. Among the growths, 31.8% were commensals, 15.2% were E.coli, 10.6% were Diphtheroid infection.

There is ―no significant difference in the culture sensitivity positive between the groups, however the positive rate after treatment in vacuum assisted dressing was marginally lower than conventional dressing.‖ ($p>0.05$)

There is ―significant shorter duration of hospital stay in vacuum assisted dressing group compared to the patients in conventional dressing group.‖($p<0.05$)

There was higher incidence of culture report positive in patients who had worst outcome as amputation compared to discharge and SSG.

CONCLUSION

The vacuum-assisted dressing demonstrated reduced hospital stays, improved sterility in pus cultures, enhanced wound healing rates, and accelerated granulation tissue formation compared to conventional dressings for non-healing ulcers. Consequently, vacuumassisted dressing has emerged as a preferred and highly effective alternative for managing ulcers and wounds. It offers the added benefits of convenience, pain-free application, improved patient compliance, and reduced need for daily dressing changes.

REFERENCE

1. Meka M. Comparison of Conventional Normal Saline Dressing and Honey Dressing In the Management of Chronic Non-Healing Ulcers. J Med Sci Clin Res. 2017;5(03):19214–7.
2. Yadav S, Rawal G, Baxi M. Vacuum assisted closure technique: a short review. Pan Afr Med J. 2017;28:246–9.
3. Iqbal A, Jan A, Wajid MA, Tariq S. Management of Chronic Non-healing Wounds by Hirudotherapy. World J Plast Surg. 2017;6(1):9–17.
4. Suthar M, Gupta S, Bukhari S, Ponemone V. Treatment of chronic non-healing ulcers using autologous platelet rich plasma: a case series. J Biomed Sci. 2017;24(1):16.

5. Agarwal P, Kukrele R, Sharma D. Vacuum assisted closure (VAC)/negative pressure wound therapy (NPWT) for difficult wounds: A review. J Clin Orthop Trauma. 2019;10(5):845–8.
6. Putnis S, Khan WS, Wong JM-L. Negative pressure wound therapy - a review of its uses in orthopaedic trauma. Open Orthop J. 2014;8:142–7.
7. Huang C, Leavitt T, Bayer LR, Orgill DP. Effect of negative pressure wound therapy on wound healing. Curr Probl Surg. 2014;51(7):301–31.
8. Schultz GS, Chin GA, Moldawer L, Diegelmann RF. Principles of wound healing. Mech Vasc Dis a Ref B Vasc Spec. 2011;423. 67
9. Guo S, Dipietro LA. Factors affecting wound healing. J Dent Res. 2010;89(3):219–29.
10. Nather A, Chionh SB, Han AYY, Chan PPL, Nambiar A. Effectiveness of vacuum-assisted closure (VAC) therapy in the healing of chronic diabetic foot ulcers. Ann Acad Med Singapore. 2010;39(5):353–8.
11. Pragadheeswaran M, Balan Y, Pyati AK, Ťoukalková M. A Comparative Study Between Vacuum Dressing and Normal Saline Dressing for Chronic Non-Healing Ulcers. Cureus. 2022;14(4):11–6.
12. Banwell PE, Musgrave M. Topical negative pressure therapy: mechanisms and indications. Int Wound J Rev. 2004;1(2):95–106.
13. Gonzalez AC de O, Costa TF, Andrade Z de A, Medrado ARAP. Wound healing - A literature review. An Bras Dermatol. 2016;91(5):614–20.
14. Fitridge R, Thompson M. Mechanisms of vascular disease: a reference book for vascular specialists. University of Adelaide Press; 2011. 1–12 p.
15. Bennett NT, Schultz GS. Growth factors and wound healing: Part II. Role in normal and chronic wound healing. Am J Surg. 1993;166(1):74–81.
16. Rumalla VK, Borah GL. Cytokines, growth factors, and plastic surgery. Plast Reconstr Surg. 2001;108(3):719–33.
17. Bennett NT, Schultz GS. Growth factors and wound healing: biochemical properties of growth factors and their receptors. Am J Surg. 1993;165(6):728–37.
18. Luster AD. Chemokines--chemotactic cytokines that mediate inflammation. N Engl J Med. 1998;338(7):436–45.
19. Gillitzer R, Goebeler M. Chemokines in cutaneous wound healing. J Leukoc Biol. 2001;69(4):513–21.
20. Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound Healing: A Cellular Perspective. Physiol Rev. 2019;99(1):665–706.
21. Duncan MR, Frazier KS, Abramson S, Williams S, Klapper H, Huang X, et al. Connective tissue growth factor mediates transforming growth factor beta-induced collagen synthesis: down-regulation by cAMP. FASEB J. 1999;13(13):1774–86.
22. Lebrun E, Tomic-Canic M, Kirsner RS. The role of surgical debridement in healing of diabetic foot ulcers. Wound repair Regen Off Publ Wound Heal Soc [and] Eur Tissue Repair Soc. 2010;18(5):433–8.
23. Karavan M, Olerud J, Bouldin E, Taylor L, Reiber GE. Evidence-based chronic ulcer care and lower limb outcomes among Pacific Northwest veterans. Wound Repair Regen. 2015;23(5):745–52.
24. Wu L, Norman G, Dumville JC, O'Meara S, Bell-Syer SEM. Dressings for treating foot ulcers in people with diabetes: an overview of systematic reviews. Cochrane database Syst Rev. 2015;2015(7):CD010471.
25. Bergin SM, Wraight P. Silver based wound dressings and topical agents for treating diabetic foot ulcers. Cochrane database Syst Rev. 2006;(1):CD005082. 68
26. Veves A, Falanga V, Armstrong DG, Sabolinski ML. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: a prospective randomized multicenter clinical trial. Diabetes Care. 2001;24(2):290–5.
27. Naughton G, Mansbridge J, Gentzkow G. A metabolically active human dermal replacement for the treatment of diabetic foot ulcers. Artif Organs. 1997;21(11):1203–10.
28. Marston WA, Hanft J, Norwood P, Pollak R. The efficacy and safety of Dermagraft in improving the healing of chronic diabetic foot ulcers: results of a prospective randomized trial. Diabetes Care. 2003;26(6):1701–5.
29. Liu R, Li L, Yang M, Boden G, Yang G. Systematic review of the effectiveness of hyperbaric oxygenation therapy in the management of chronic diabetic foot ulcers. Mayo Clin Proc. 2013;88(2):166–75.
30. Wang C, Schwaitzberg S, Berliner E, Zarin DA, Lau J. Hyperbaric oxygen for treating wounds: a systematic review of the literature. Arch Surg. 2003;138(3):272–9; discussion 280.
31. Roeckl-Wiedmann I, Bennett M, Kranke P. Systematic review of hyperbaric oxygen in the management of chronic wounds. Br J Surg. 2005;92(1):24–32.
32. Goldman RJ. Hyperbaric oxygen therapy for wound healing and limb salvage: a systematic review. PM R. 2009;1(5):471–89.
33. Stoekenbroek RM, Santema TB, Legemate DA, Ubbink DT, van den Brink A, 69Koelemay MJW. Hyperbaric oxygen for the treatment of diabetic foot ulcers: a systematic review. Eur J Vasc Endovasc Surg. 2014;47(6):647–55.
34. Kranke P, Bennett M, Roeckl-Wiedmann I, Debus S. Hyperbaric oxygen therapy for chronic wounds. Cochrane database Syst Rev. 2004;(2):CD004123.

35. Gordillo GM, Sen CK. Revisiting the essential role of oxygen in wound healing. Am J Surg. 2003;186(3):259–63.
36. Frykberg RG, Franks PJ, Edmonds M, Brantley JN, Téot L, Wild T, et al. A Multinational, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen (TWO2) Therapy in the Treatment of Chronic Diabetic Foot Ulcers: The TWO2 Study. Diabetes Care. 2020;43(3):616–24.
37. Hunter P, Greco E, Cross K, Perry J. Topical Oxygen Therapy Shifts Microbiome Dynamics in Chronic Diabetic Foot Ulcers. Wounds a Compend Clin Res Pract. 2020;32(3):81–5.
38. Moretti B, Notarnicola A, Maggio G, Moretti L, Pascone M, Tafuri S, et al. The management of neuropathic ulcers of the foot in diabetes by shock wave therapy. BMC Musculoskelet Disord. 2009;10:54.
39. Saggini R, Figus A, Troccola A, Cocco V, Saggini A, Scuderi N. Extracorporeal shock wave therapy for management of chronic ulcers in the lower extremities. Ultrasound Med Biol. 2008;34(8):1261–71.
40. A N, Khan WS, J P. The evidence-based principles of negative pressure wound 70therapy in trauma & orthopedics. Open Orthop J. 2014;8:168–77.
41. Orgill DP, Manders EK, Sumpio BE, Lee RC, Attinger CE, Gurtner GC, et al. The mechanisms of action of vacuum assisted closure: more to learn. Surgery. 2009;146(1):40–51.
42. Morykwas MJ, Simpson J, Punger K, Argenta A, Kremers L, Argenta J. Vacuumassisted closure: state of basic research and physiologic foundation. Plast Reconstr Surg. 2006;117(7 Suppl):121S-126S.
43. Pendsey S, Abbas ZG. The step-by-step program for reducing diabetic foot problems: a model for the developing world. Curr Diab Rep. 2007;7(6):425–8.
44. Pendsey SP. Understanding diabetic foot. Int J Diabetes Dev Ctries. 2010;30(2):75–9.
45. Sinha K, Chauhan VD, Maheshwari R, Chauhan N, Rajan M, Agrawal A. Vacuum Assisted Closure Therapy versus Standard Wound Therapy for Open Musculoskeletal Injuries. Adv Orthop. 2013;2013:245940.
46. Ravari H, Modaghegh M-HS, Kazemzadeh GH, Johari HG, Vatanchi AM, Sangaki A, et al. Comparision of vacuum-asisted closure and moist wound dressing in the treatment of diabetic foot ulcers. J Cutan Aesthet Surg. 2013;6(1):17–20.
47. Lavery LA, Murdoch DP, Kim PJ, Fontaine J La, Thakral G, Davis KE. Negative Pressure Wound Therapy With Low Pressure and Gauze Dressings to Treat Diabetic Foot Wounds. J Diabetes Sci Technol. 2014;8(2):346–9. 71
48. Lone AM, Zaroo MI, Laway BA, Pala NA, Bashir SA, Rasool A. Vacuumassisted closure versus conventional dressings in the management of diabetic foot ulcers: a prospective case-control study. Diabet Foot Ankle. 2014;5:1–6.
49. Khan A, Singh S, Singh V, Khan S. Diabetic foot ulcer: a clinical study. Int Surg J. 2016;3(4):2098–103.
50. Amin N, Doupis J. Diabetic foot disease: From the evaluation of the ―foot at risk‖ to the novel diabetic ulcer treatment modalities. World J Diabetes. 2016;7(7):153– 64.
51. Dsouza C, Rouchelle ., Chirag ., Diaz E, Rao S. A randomized controlled trial comparing low cost vacuum assisted dressings and conventional dressing methods in the management of diabetic foot ulcers. Int Surg J. 2017;4(12):3858–65.
52. Sukur E, Akar A, Uyar AÇ, Cicekli O, Kochai A, Turker M, et al. Vacuumassisted closure versus moist dressings in the treatment of diabetic wound ulcers after partial foot amputation: A retrospective analysis in 65 patients. J Orthop Surg. 2018;26(3):230949901879976.
53. James SMD, Sureshkumar S, Elamurugan TP, Debasis N, Vijayakumar C, Palanivel C. Comparison of Vacuum-Assisted Closure Therapy and Conventional Dressing on Wound Healing in Patients with Diabetic Foot Ulcer: A Randomized Controlled Trial. Niger J Surg Off Publ Niger Surg Res Soc. 2019;25(1):14–20.
54. Vemulapalli SV, . S, K.S B, Pala TS. A Comparitive Study on Negative Pressure Dressing Versus Conventional Dressing in the Management of Diabetic Foot 7273 Ulcer. East African Sch J Med Sci. 2020;3(10):369–72.
55. Ramula M, Arivzhagan N. VAC (Vacuum assisted closure) in the management of chronic non-healing wounds: Institutional study. Int J Surg Sci. 2020;4(4):82–6.
56. Anandi A, Nedunchezhian CS, Karthikeyan R. A study of vacuum assisted closure in chronic non-healing diabetic ulcers. Int Arch Integr Med. 2020;7(3):47–52.
57. Kumar PG, Raja K, Haritha P, Saravanakumari AD, Shanthi D, Vasanthi S. Comparative study on microbiological and histopathological examination of diabetic wounds managed by conventional dressing and vacuum assisted closure therapy. Int Surg J. 2021;8(4):1195–9.
58. Subbiah MA, Nachiappan M, Raghuraman A, Maliq MA, Manikandan MS. A clinical study of management of chronic non-healing ulcer in diabetic patients using vacuum-assisted dressing. Int J Acad Med Pharm. 2023;5(5):1477–80