

# Comparison of Role of Fish Skin Versus Normal Saline Dressing in Wound Healing of Chronic Diabetic Ulcer

Fish Skin Versus Normal Saline Dressing in Wound Healing of Diabetic Ulcer

Hafsa Rauf<sup>1</sup>, Anam Batool<sup>1</sup>, Abrar Ahmed<sup>2</sup>, Amer Mian<sup>1</sup> and Mirza Zeeshan Sikandar<sup>1</sup>

## ABSTRACT

**Objective:** To compare the outcome of fish skin dressing versus normal saline dressing in wound healing of chronic diabetic ulcer

**Study Design:** Randomized Controlled Trial study

**Place and Duration of Study:** This study was conducted at the Department of Surgery, Central Park Teaching Hospital, Lahore from November 2022 to April 2023.

**Methods:** 122 patients; 61 in each group as per of inclusion criteria were enrolled for the study and were randomly divided in two groups. Group A patients received fish skin dressing while group B patients receive conventional normal saline dressing. Duration of healing, complete wound healing, amputation rate were noted during follow-up. SPSS v. 26 was used to analyze the data.

**Results:** The mean age of patients enrolled in fish skin group was  $50.64 \pm 11.00$  years and patients enrolled in normal saline group had mean age of  $53.38 \pm 13.16$  years. In both groups, there were 40 (65.6%) males and 21 (34.4%) females. In fish skin group, the mean time for wound healing was observed as  $5.11 \pm 1.54$  weeks, while  $7.74 \pm 2.32$  weeks in normal saline group. Complete wound healing was observed in 49 (80.3%) patients with fish skin dressing, while in 22 (36.1%) patients with normal saline. In fish skin group, amputation occurred in 2 (3.3%) cases while in 7 (11.5%) patients in normal saline group.

**Conclusion:** The healing power of fish skin is more beneficial than normal saline dressing in diabetic wound ulcers. In future, we can now implement use of fish skin dressing instead of normal saline dressing.

**Key Words:** fish skin dressing, normal saline dressing, wound healing, diabetic ulcer

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## INTRODUCTION

Uncontrolled diabetes mellitus frequently results in diabetic foot ulcers. Inadequate diabetes control not only involve foot but also other systems thus causing, peripheral neuropathy and vascular disease, and inadequate and poor foot care are the most frequent causes<sup>1</sup>. It also occurs in osteomyelitis of the foot and frequently necessitates lower limb amputation. The parts of the foot that are frequently strained are prone to developing these ulcers<sup>2</sup>. 9.1–26.1 million people

worldwide get diabetic foot ulcers each year. Throughout their lives, 15–25% of persons with diabetes mellitus can develop diabetic foot ulcers. Diabetic foot ulcer cases will increase in tandem with the number of people receiving diabetes diagnoses.<sup>3,4</sup> Diabetes can cause peripheral neuropathy, reduced blood flow, elevated plantar pressures, and other problems that might result in foot ulcers. They are incredibly susceptible to disease, demise, and amputation. Treatment approaches should be chosen based on the complexity and shape of the lesion since these factors are critical to the wound healing process and the host physiological state in diabetic patients.<sup>4</sup> In addition to wound care, diabetic foot ulcers are treated with a combination of systemic antibiotics and surgical excision.<sup>5</sup>

Chronic, non-healing wounds are a major public health issue that use up a lot of healthcare resources and come with high morbidity and high financial expenses. Skin grafts are frequently employed to speed up the healing process. The skin grafts might be from the patient themselves, a human donor, or an animal donor (xenograft). *Gadus morhua*, or Atlantic cod, is a cold-water fish with impressive pre-clinical and clinical results in wound healing.<sup>6</sup> Atlantic cod (*Gadus morhua*) provides the source material for xenografts in the form

<sup>1</sup>. Department of Surgery, Central Park Teaching Hospital Lahore.

<sup>2</sup>. Department of Anatomy, Al Aleem Medical College, Lahore.

Correspondence: Dr. Mirza Zeeshan Sikandar, Department of Surgery, Central Park Medical College, Central Park Housing Society, 31 KMs Ferozpur Road, Lahore.

Contact No: 0336-8656736

Email: m.zee.shan@hotmail.com

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of acellular fish skin. It's a marine animal that has its origins in cold water circumstances, which are abundant in omega-3 polyunsaturated fatty acids, in contrast to marine animals that have evolved to thrive in tropical temperatures.<sup>7</sup> Acellular fish skin grafts, formerly utilised only on humans for the management of difficult or chronic wounds, are now becoming an option for animals.<sup>8</sup>

Therefore, this trial was planned to be done in local setting to get evidence in favor of fish skin dressing and to replace less effective or slow effective dressings used in routine in local setting. This would improve our practice and would also help to attain magnitudes for local population.

## METHODS

This RCT (randomized controlled trial) was conducted Department of surgery, Central Park Teaching Hospital, Lahore from November 2022 to April 2023. By using sample size formula for two proportions, sample of 122 patients; 61 in each group was estimated by keeping the 5% significance level, 80% power of study and percentage of wound healing i.e. 83.2% with fish skin dressing and 63.4% with normal saline dressing in diabetic foot ulcers.<sup>9</sup> Non-probability; consecutive sampling" technique was employed. Ethical concerns were fulfilled as per Helsinki declaration and approval (CPMC/IRB-No/1287) was obtained from ethical review board of Central Park Medical College. Patients aged between 35-75 years, both gender diagnosed with diabetic foot ulcers. Patients with gangrene, recurrent ulcer of same site, or already taking antibiotic or steroid treatment for ulceration, major trauma or injury, malignancy or metastatic disease, tumor resection cases.

122 patients from wards of Department of Surgery, fulfilled the above stated selection criteria, were recruited. Written consent was obtained from all the patients. Demographics of patients including name, age, gender, BMI, duration of diabetes, duration of ulcer, hypertension, smoking, were noted for each patients. Patients were divided randomly into 2 equal groups by applying random number table. In group A, fish skin dressing was applied over the ulcer wound applied to their full-thickness foot ulcerations. In group B, conventional normal saline dressing was applied on ulcer wound. All procedures were done by researcher. Then patients will be followed-up in OPD for 3 months, fortnightly. On each visit, wound was examined by researcher and granulation tissues were observed. The healing within 6 weeks was noted as complete healing. Total duration till complete healing of all patients was also observed. Patients in whom healing did not occur or wound further deteriorate, amputation was the last choice. Amputations were done under general anesthesia by a single surgical team with assistance of

researcher. All the information was recorded in proforma.

Statistical Analysis: Data was entered into Microsoft Excel and was duly verified for errors and omissions after which it was exported to SPSS version 26.0 for statistical analysis. Both groups were compared for mean duration of healing by using independent samples t-test and for complete healing and amputation by using chi-square test. P-value  $\leq 0.05$  as significant.

## RESULTS

A total of 122 patients with mean age of patients in fish skin group (Group 1) was  $50.64 \pm 11.00$  years with the mean age of patients in normal saline group (group 2) was  $53.38 \pm 13.16$  years. In fish skin group, there were 40 (65.6%) males and 21 (34.4%) females. In normal saline group, there were 40 (65.6%) males and 21 (34.4%) females with the male-to-female ratio as 1.9:1. In fish skin group, the mean BMI of patients was  $31.45 \pm 5.19 \text{ kg/m}^2$ . In normal saline group, the mean BMI of patients was  $31.45 \pm 5.19 \text{ kg/m}^2$ . In fish skin group, the history of hypertension was positive in 38 (62.3%) while 23 (37.7%) were normotensive. In normal saline group, the history of hypertension was positive in 24 (39.4%) while 37 (60.7%) were normotensive. In fish skin group, the history of smoking was positive in 27 (44.3%) while 34 (55.7%) were non-smokers. In normal saline group, the history of smoking was positive in 26 (42.6%) while 35 (57.4%) were non-smokers as explained in table 1.

**Table No. 1: Basic Characteristics of Study Participants in Study Groups.**

Study Parameters	Group	
	Fish skin (n=61)	Normal saline (n=61)
Age (years)	$50.64 \pm 11.00$	$53.38 \pm 13.16$
Gender		
Male	40 (65.6%)	40 (65.6%)
Female	21 (34.4%)	21 (34.4%)
BMI ( $\text{kg/m}^2$ )	$31.45 \pm 5.19$	$31.72 \pm 4.99$
Hypertension	38 (62.3%)	24 (39.4%)
Smoking	27 (44.3%)	26 (42.6%)
Lateral side		
Left	30 (49.2%)	28 (45.9%)
Right	31 (50.8%)	33 (54.1%)
Duration of diabetes (years)	$8.13 \pm 7.72$	$8.67 \pm 7.74$
Duration of ulcer (weeks)	$12.77 \pm 6.79$	$13.20 \pm 6.29$

In fish skin group, 30 (49.2%) patients had ulcer on left foot while 31 (50.8%) patients had ulcer on right foot. In normal saline group, 28 (45.9%) patients had ulcer on left foot while 33 (54.1%) patients had ulcer on right foot. The mean duration of diabetes was  $8.13 \pm 7.72$

years in patients in fish skin group and  $8.67 \pm 7.74$  years in normal saline group. The mean duration of ulcer was  $12.77 \pm 6.79$  weeks in patients in fish skin group and  $13.20 \pm 6.29$  weeks in normal saline group. Table 1.

In fish skin group, the mean time for wound healing was observed as  $5.11 \pm 1.54$  weeks. In normal saline group, the mean time for incision was observed as  $7.74 \pm 2.32$  weeks which was recorded as significant with p-value of  $< 0.0001$ . In fish skin group, complete wound

healing was observed in 49 (80.3%) patients within 6 weeks, while in normal saline group, 22 (36.1%) patients had complete wound healing within 6 weeks and difference in both groups was highly significant (p-value  $< 0.0001$ ). In fish skin group, amputation occurred in 2 (3.3%) cases due to further deterioration of ulcer, while in normal saline group, 7 (11.5%) patients underwent amputation, although the difference was insignificant (p-value  $> 0.05$ ). Table - 2

**Table No. 2: Comparison of Surgical Outcomes Study Groups**

Outcome	Group		P-value
	Fish skin	Normal saline	
Duration of wound healing (weeks)	$5.11 \pm 1.54$	$7.74 \pm 2.32$	$<0.0001$
Complete wound healing			$<0.0001$
Yes	49 (80.3%)	22 (36.1%)	
No	12 (19.7%)	39 (63.9%)	
Amputation			0.083
Yes	2 (3.3%)	7 (11.5%)	
No	59 (96.7%)	54 (88.5%)	

**DISCUSSION**

Few studies have investigated the worldwide epidemiology of diabetic foot, despite its significance as a public health issue.<sup>10</sup> Ulcers on the feet of people with diabetes are a particularly difficult condition to manage. Thirty percent of diabetics get foot ulcers, a typical consequence of the illness. One of the main causes of impairment in people with diabetes mellitus is diabetic foot ulcers.<sup>11</sup> Type 2 diabetes is more prevalent than type 1 diabetes and affects males more often than women; thus, the incidence of diabetic foot ulcers is estimated to be 6.3% globally. Additionally common is the recurrence of diabetic foot sores. Within a year, the value increases by 40%, and within three years, it increases by 65%. Therefore, research should concentrate on developing preventative measures against diabetic foot ulcers.<sup>2, 12</sup>

The diabetic foot ulcer has a high recurrence rate and a difficult treatment time. Therefore, developing prevention techniques should be stressed the most. A multidisciplinary approach is fundamental for the anticipation and treatment of diabetic foot ulcers. Patients who are at hazard ought to be recognized, and preventative measures need to be taken based on the kind of peril.<sup>11</sup> Other medications for diabetic foot ulcers incorporate development components, autologous blended leucocyte, platelet, fibrin, and placental determined items, negative weight wound treatment, skin joins and substitutions, hyperbaric oxygen treatment, and stun wave treatment. There are significant caveats attached to recommending any of these treatments, and none of them are preferable to the gold standard.<sup>13, 14</sup>

Fish skin transplant, a novel skin replacement for wound dressing that has received FDA approval, has seen widespread application in clinical settings. Fish

skin grafts have also showed promise in the treatment of a range of other recently acquired and protracted lesions, such as venous leg ulcers and diabetic foot ulcers.<sup>7</sup> A cold-water fish with promising preclinical and clinical outcomes in wound healing is the Atlantic cod, *Gadus morhua*.<sup>15, 16</sup>

Angle skin wounds mended much quicker than wounds treated with a dried out human amnion/chorion film allograft (danger proportion 2.37; 95 percent certainty interim: 1.75-3.22;  $p = 0.0014$ ). The comes about appear that intense biopsy wounds treated with got dried out human amnion/chorion film allograft mend more gradually than wounds treated with angle skin joins.<sup>6</sup>

In our trial, we observed that the mean time for wound healing was  $5.11 \pm 1.54$  weeks with fish skin dressing, which was significantly less than  $7.74 \pm 2.32$  weeks with normal saline dressing (p-value  $< 0.05$ ). Another study found that fish skin treatment could be more cost-effective than saline dressing, healing wounds more quickly (83.2 percent vs. 63.4 percent), and causing fewer amputations (4.6 percent vs. 6.9 percent) per wound (\$11,210 vs. \$15,075 per wound). Angle skin treatment for diabetic foot ulcers would hence be 71.4 percent more likely to be reasonable than conventional saline dressing and 93.6 percent more likely to be cost-effective with a readiness to pay of \$100,000 each quality-adjusted life year.<sup>9</sup>

Within 16 weeks of using a fish skin transplant, the percentage of diabetic foot ulcers healing completely is 60.3%; in 74.1 percent of cases,  $>90\%$  healing has been documented; and in 84.5 percent of cases,  $>75\%$  healing has been reported.<sup>7</sup> After 7-10 days, once the wound has been elevated by granulation tissue to the level of the wound edges and quickly epithelialized, the fish skin transplant will have been absorbed into the wound bed. The grafts made from fish skin have been

shown to speed up the healing process, prevent infection, and reduce inflammation. They are analogous to mammalian skin (i.e., containing epidermal and dermal components).

Acellular angle skin xenografts could be a great, reasonable elective for treating fractional- and superficial-thickness burns. In any case, preclinical and little cohort ponders are where the larger part of the information come from. It is essential to do bigger cohort considers within the future to completely get it the conceivable outcomes of this imaginative methodology.<sup>17</sup>

## CONCLUSION

The healing power offish skin is more beneficial than normal saline dressing in diabetic wound ulcers. In future, we can now implement use of fish skin dressing instead of normal saline dressing to improve early healing and quality of life of patients.

### Author's Contribution:

Concept & Design of Study: Hafsa Rauf  
 Drafting: Anam Batool, Abrar Ahmed  
 Data Analysis: Amer Mian, Mirza Zeeshan Sikandar  
 Revisiting Critically: Hafsa Rauf, Anam Batool  
 Final Approval of version: Hafsa Rauf

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