

Impact of Topical Heparin on Improved Healing Outcomes of Skin Graft Donor Site

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ARTICLE INFORMATION	ABSTRACT
Article Type: Original Article How to Cite: Khalid S, Khan H, Kiani JA, Warraich ARA. Impact of Topical Heparin on Improved Healing Outcomes of Skin Graft Donor Site. <i>Journal of Precision Medicine and Health Research</i>. 2026;3(1):1-9. Article ID: 45 DOI: https://doi.org/10.68279/wap6b507 Article Link: https://jpmhr.com/index.php/jpmhr/article/view/45 Declarations: See end of article. OPEN ACCESS This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0).	Background: Split-thickness skin graft harvesting creates a secondary donor-site wound that may cause postoperative pain, delayed epithelialization, and additional morbidity. Topical heparin has been proposed as an adjunct to promote wound recovery. Objective: To compare healing and postoperative morbidity outcomes between topical heparin-treated and conventionally dressed split-thickness skin graft donor sites. Methods: This within-participant controlled interventional study was conducted at the Department of Burn and Reconstructive Surgery, Holy Family Hospital, Rawalpindi. Forty adults undergoing split-thickness skin grafting contributed two donor sites each, yielding 40 paired comparisons and 80 donor sites. One site received topical heparin from postoperative days 2–5, while the other received conventional dressing. Pain, analgesic requirement, healing time, and edema resolution were assessed. Continuous paired outcomes were analyzed using paired comparisons. Results: Mean pain scores were 2.82 ± 0.23 with heparin and 3.99 ± 0.28 with conventional dressing, a mean difference of -1.17 points. Mean analgesic requirements were 1575.0 ± 378.76 mg and 2292.5 ± 462.09 mg, respectively. Mean healing time was 14.15 ± 1.95 versus 19.60 ± 2.08 days, a difference of -5.45 days, while edema resolved at 4.93 ± 0.89 versus 6.94 ± 1.15 days. Conclusion: Topical heparin-treated donor sites showed shorter mean healing and edema-resolution times and lower postoperative pain and analgesic requirements than conventionally treated sites. Keywords: Skin Transplantation; Heparin; Wound Healing; Pain Management; Burn Patients; Donor Site.

Introduction

Split-thickness skin grafting (STSG) remains a widely used and practical reconstructive technique for covering acute and chronic soft-tissue defects when primary closure is not feasible. Despite advances in reconstructive surgery and flap-based wound coverage, STSG continues to offer a relatively simple, reliable, and accessible option for wound reconstruction (1,2). However, harvesting a split-thickness graft creates an additional wound at the donor site, effectively adding a second area that must undergo epithelial regeneration and wound healing (3,4). Although donor-site wounds usually heal spontaneously, they may be associated with considerable postoperative morbidity, including pain, delayed epithelialization, pruritus, pigmentation changes, scarring, and cosmetic dissatisfaction, all of which can adversely affect patient recovery and comfort (5).

Management of the skin graft donor site is therefore an important component of postoperative care. Conventional donor-site management commonly relies on protective dressings intended to maintain an appropriate wound environment, absorb exudate, reduce contamination, and support spontaneous epithelialization. Different dressing materials and wound-care approaches have been evaluated, but substantial variation remains in clinical practice regarding the optimal method for accelerating donor-site healing while minimizing pain and other complications (6,7). Pharmacologically active topical agents have consequently received increasing attention because they may provide additional biological effects beyond those achieved through physical wound coverage alone. Evidence from other acute wound and burn-care settings has similarly demonstrated continued interest in interventions that can promote epithelialization, control local inflammation, and reduce wound-related morbidity (8).

Heparin is a highly sulfated glycosaminoglycan traditionally recognized for its anticoagulant activity, although its biological functions extend beyond coagulation and have led to increasing interest in its potential application in tissue repair and wound management (9). Experimental and translational evidence suggests that heparin can interact with several proteins involved in cellular proliferation, angiogenesis, and extracellular-matrix regulation. In wound environments where proteolytic activity may reduce the availability of endogenous growth factors, heparin may bind and stabilize growth-promoting molecules and thereby prolong their biological activity (10,11). Heparinized collagen-chitosan wound constructs have demonstrated favorable effects on early wound-healing processes, including increased expression of vascular endothelial growth factor and epidermal growth factor, supporting a plausible role for heparin-containing approaches in tissue regeneration (12). Similarly, concomitant administration of heparin with basic fibroblast growth factor has been investigated for skin graft donor-site healing, with findings suggesting that heparin may enhance the stability and biological action of growth factors involved in tissue repair (13).

Clinical interest in heparin has also extended to the management of burn-related injuries. Although evidence from nebulized heparin in inhalation injury represents a different route of administration and clinical indication, it illustrates the broader therapeutic investigation of heparin in patients with burn injuries (14). More directly relevant evidence has emerged from studies evaluating topical heparin in cutaneous burns. A systematic review and meta-analysis of randomized controlled studies reported that topical heparin was associated with improvements in clinically relevant burn-wound outcomes, including reductions in pain and local wound complications, without evidence of a corresponding increase in major systemic complications within the included studies (15). Clinical comparisons of conventional therapy with topical heparin in second-degree burns have also reported shorter wound-healing periods and reduced analgesic requirements among patients receiving heparin treatment (16). These findings provide clinical support for the hypothesis that topical heparin may influence both wound repair and pain-related outcomes, although evidence derived from burn wounds cannot automatically be extrapolated to STSG donor sites because the underlying wound characteristics and treatment context differ.

Evidence specifically addressing skin graft donor-site wounds is more limited but increasingly relevant. Clinical investigation of topical heparin at STSG donor sites has demonstrated earlier wound improvement, including reductions in wound surface area and edema during the early postoperative period, together with favorable healing outcomes compared with conventional management (3). Another prospective study evaluating heparin in donor-site care reported shorter healing time and improved scar-related outcomes in treated areas compared with conventional treatment (17). Related evidence from patients with second-degree burns has likewise shown clinically meaningful reductions in pain and healing duration with heparin-containing dressings compared with conventional dressings (18). Collectively, these studies support the biological and clinical plausibility of topical heparin as an adjunct to wound care, but the available literature remains heterogeneous with respect to wound type, treatment regimen, dose, outcome assessment, and follow-up.

Despite this emerging evidence, topical heparin has not been routinely incorporated into skin graft donor-site management in many local clinical settings, where conventional dressings remain the predominant approach. Direct evidence comparing topical heparin with conventional donor-site care within the same patient population remains relatively limited, particularly in local surgical practice. Because donor-site pain, analgesic use, edema, and delayed epithelialization contribute to postoperative morbidity, an intervention capable of improving these outcomes could have practical value in reconstructive and burn surgery. A within-patient comparison, in which treated and conventionally managed donor sites are evaluated in the same individual, may also help reduce variability related to patient-level biological characteristics, although the resulting paired nature of the observations must be considered in the analysis.

Therefore, the present study aimed to compare topical heparin with conventional dressing treatment for split-thickness skin graft donor sites in adult patients requiring skin grafting. Specifically, the study evaluated differences between heparin-treated and conventionally treated donor sites in wound-healing time, postoperative pain intensity, analgesic requirement, and edema resolution. The study sought to determine whether topical heparin was associated with more favorable donor-site healing and postoperative morbidity outcomes than conventional dressing management.

Materials and Methods

This within-patient, controlled interventional study was conducted in the Department of Burn and Reconstructive Surgery, Holy Family Hospital, Rawalpindi, over a six-month period. The study was designed to compare the healing outcomes of topical heparin treatment with conventional donor-site dressing in patients undergoing split-thickness skin grafting, with each participant contributing both an intervention donor site and a control donor site. Ethical approval was obtained from the institutional ethics review board before initiation of data collection. All eligible participants were informed preoperatively about the objectives of the study, the proposed treatment procedures, potential benefits, and anticipated postoperative care, and both verbal and written informed consent were obtained before enrollment.

The target population comprised adult patients of either sex, aged 18–65 years, who required split-thickness skin grafting. Patients were eligible if their hemoglobin concentration was >10 g/dL, platelet count was between 150 and 400×10^9 /L and activated partial thromboplastin time was within the reported normal range of 33–41 seconds. Patients with known bleeding disorders, including hemophilia or thrombocytopenia, a family history of bleeding diathesis, documented hypersensitivity to heparin, diabetes mellitus, hypertension, other multiple medical comorbidities, or an immunocompromised state were excluded. Participants were recruited through non-probability consecutive sampling from patients presenting for skin grafting during the study period.

The required sample size was calculated using the OpenEpi sample-size calculator with a 95% confidence level and 80% statistical power. The calculation was based on previously reported differences in donor-site pain scores and healing time between conventional treatment and topical heparin treatment. The assumed mean pain scores were 3.0 ± 0.89 for donor sites managed without heparin and 2.0 ± 0.82 for heparin-treated donor sites, while the corresponding mean healing times were 20 ± 4 days and 14 ± 1 days, respectively (3). On this basis, 40 patients were enrolled. Because each patient contributed two separate donor sites, the study included 40 paired donor-site comparisons, representing 80 donor sites in total.

During the operative procedure, two split-thickness skin grafts of approximately 10×6 cm were harvested from the anterior thigh of each participant using either a Humby knife or a dermatome. Following graft harvesting, both donor sites were photographed and irrigated with normal saline. Initial donor-site coverage consisted of chlorhexidine-impregnated gauze and sterile cotton secured with roll gauze. The two donor sites in each participant were then allocated to the intervention and control conditions. One site was assigned to topical heparin treatment as Group A, while the other site was managed with conventional dressing as Group B, thereby allowing each participant to serve as their own control and reducing between-patient variability in biological and clinical characteristics.

For the intervention donor site, topical heparin was administered daily from the second through the fifth postoperative day. The heparin preparation consisted of 1 mL containing 5,000 IU of heparin diluted with 19 mL of normal saline to produce a total volume of 20 mL at a concentration of 250 IU/mL. The reported dosing regimen was 5,000 IU per 1% of total body surface area. The diluted heparin solution was applied through the donor-site dressing. The control donor site received conventional dressing consisting of chlorhexidine-impregnated paraffin gauze, surgical gauze, and crepe bandage without topical heparin.

Both intervention and control donor-site dressings were opened, and the wounds were photographed on the fifth postoperative day. The wound appearance was compared with the baseline condition documented immediately after graft harvesting. Topical heparin administration was discontinued after the day-5 assessment, and both donor sites were subsequently redressed. Further clinical assessments were performed on postoperative days 14, 28, and 56 during inpatient care or outpatient follow-up, as applicable. Serial wound photographs were used alongside clinical examination to document the progression of donor-site healing.

The principal clinical outcomes were donor-site pain, analgesic requirement, wound-healing time, degree of epithelialization, wound-size reduction, and resolution of surrounding edema. Postoperative pain was assessed during the first five postoperative days using a 0–10 Numeric Rating Scale, with higher scores indicating greater pain intensity. The type, strength, and amount of analgesic medication required for postoperative pain control were also recorded. Donor-site healing was evaluated clinically through epithelialization, reduction in wound size, and resolution of surrounding edema. Assessment of wound healing was performed by the principal investigator and was confirmed by senior faculty members in plastic surgery.

Data were entered and analyzed using IBM SPSS Statistics version 23.0. Continuous variables, including age, body weight, pain score, analgesic requirement, healing time, and edema-resolution time, were summarized as mean $\pm$ standard deviation where appropriate. Categorical variables, including sex, educational level, socioeconomic status, and donor-site characteristics, were summarized as frequencies and percentages. Because the intervention and control donor sites originated from the same participant, comparisons of continuous outcomes between Group A and Group B were treated as paired observations. Paired-samples t-tests were used to compare

mean pain scores, analgesic requirements, healing time, and other continuous paired outcomes when parametric assumptions were satisfied. Statistical significance was defined as a two-sided p-value ≤ 0.05 .

Potential effect modification was explored according to age, sex, donor-site location, educational level, and socioeconomic status. These variables were examined in relation to the principal outcomes to determine whether the observed treatment differences varied across clinically relevant participant subgroups. All subgroup analyses were interpreted as secondary analyses in relation to the primary within-patient comparison between the heparin-treated and conventionally treated donor sites.

Results

A total of 40 participants contributed 80 split-thickness skin graft donor sites, providing 40 within-participant intervention–control site pairs. The mean age of the study population was 38.5 ± 8.8 years, and the mean body weight was 69.6 ± 7.56 kg.

Across the principal clinical outcomes, the heparin-treated donor sites showed lower mean values than the conventionally treated control sites. The mean postoperative pain score was 2.82 ± 0.23 in the heparin-treated sites compared with 3.99 ± 0.28 in the control sites, corresponding to an absolute mean difference of -1.17 points on the 0–10 Numeric Rating Scale. Mean total analgesic requirement was 1575.0 ± 378.76 mg in the heparin-treated sites and 2292.5 ± 462.09 mg in the control sites, giving an absolute mean difference of -717.5 mg.

Mean healing time was 14.15 ± 1.95 days for the heparin-treated donor sites compared with 19.60 ± 2.08 days for the control sites, corresponding to a mean difference of -5.45 days. Edema resolution occurred at a mean of 4.93 ± 0.89 days in the heparin-treated sites and 6.94 ± 1.15 days in the control sites, representing an absolute mean difference of -2.01 days.

Table 1. Characteristics of the study participants

Characteristic	Overall
Participants, n	40
Donor sites, n	80
Age, years, mean $\pm$ SD	38.5 ± 8.8
Weight, kg, mean $\pm$ SD	69.6 ± 7.56

Table 1 footnote: Each participant contributed two donor sites, yielding 40 paired intervention–control comparisons. Sex, educational-level, and socioeconomic-status frequencies require reconciliation against the original patient-level dataset before publication.

Table 2. Clinical outcomes at heparin-treated and conventionally treated donor sites

Outcome	Heparin-treated site (Group A), Mean $\pm$ SD	Control site (Group B), Mean $\pm$ SD	Mean difference (A – B)
Pain score, NRS (0–10)	2.82 ± 0.23	3.99 ± 0.28	-1.17
Total analgesic requirement, mg	1575.0 ± 378.76	2292.5 ± 462.09	-717.5
Healing time, days	14.15 ± 1.95	19.60 ± 2.08	-5.45
Edema resolution, days	4.93 ± 0.89	6.94 ± 1.15	-2.01

Table 2 footnote: NRS, Numeric Rating Scale. Group A and Group B represent paired donor sites from the same 40 participants. Mean differences were calculated as the heparin-treated value minus the control value from the reported group means. Valid paired 95% confidence intervals, p-values, and paired effect sizes require the within-participant differences or participant-level data.

These values are directly reported in the manuscript, except the differences, which are validly derived by subtraction. Pasted text

Table 3. Reported outcome measures according to participant sex

Outcome	Male, n	Male, Mean $\pm$ SD	Female, n	Female, Mean $\pm$ SD
Pain score	57	3.42 ± 0.68	23	3.39 ± 0.53
Analgesic requirement, mg	57	1945.61 ± 588.00	23	1904.35 ± 468.54
Healing time, days	57	17.05 ± 3.47	23	16.43 ± 3.24

Table 3 footnote: Values reproduce the manuscript's reported site-level stratification. The denominators represent 80 donor-site observations rather than 40 unique participants and therefore should not be interpreted as numbers of male and female participants. Inferential p-values have not been retained because donor sites within the same participant are not independent.

The source table reports $p=0.17$, 0.354 , and 0.618 , respectively, but its denominators again total 80 rather than 40 participants. Pasted text

Table 4. Reported outcome measures according to donor-site laterality

Outcome	Right, n	Right, Mean $\pm$ SD	Left, n	Left, Mean $\pm$ SD
Pain score	40	3.44 ± 0.67	40	3.39 ± 0.62
Analgesic requirement, mg	40	1917.0 ± 505.30	40	1950.0 ± 604.26
Healing time, days	40	16.93 ± 3.44	40	16.83 ± 3.40

Table 4 footnote: Right and left donor-site observations arise from the same study population. The original independent comparisons are not retained as final inferential analyses because the study contains repeated observations within participants.

Source values are reported in the original Table 5. Pasted text

Table 5. Reported outcome measures according to age category

Outcome	18–40 years, n	18–40 years, Mean $\pm$ SD	41–65 years, n	41–65 years, Mean $\pm$ SD
Pain score	44	3.42 ± 0.63	36	3.41 ± 0.66
Analgesic requirement, mg	44	1938.64 ± 537.53	36	1927.78 ± 580.45
Healing time, days	44	16.39 ± 3.49	36	17.47 ± 3.23

Table 5 footnote: The reported denominators total 80 donor-site observations rather than 40 unique participants. These descriptive values should therefore not be interpreted as participant counts. Formal treatment-by-age interaction analysis requires the participant-level paired dataset.

In the reported site-level stratified summaries, mean pain scores were 3.42 ± 0.68 among observations classified as male and 3.39 ± 0.53 among those classified as female. Corresponding mean analgesic requirements were 1945.61 ± 588.00 mg and 1904.35 ± 468.54 mg, while mean healing times were 17.05 ± 3.47 and 16.43 ± 3.24 days, respectively. Descriptive differences according to donor-site laterality were small: mean pain scores were 3.44 ± 0.67 for right-sided and 3.39 ± 0.62 for left-sided donor sites, while mean healing times were 16.93 ± 3.44 and 16.83 ± 3.40 days, respectively.

Across the reported age categories, mean pain scores were similar between observations from participants aged 18–40 years and those aged 41–65 years (3.42 ± 0.63 versus 3.41 ± 0.66). Mean analgesic requirements were 1938.64 ± 537.53 mg and 1927.78 ± 580.45 mg, respectively, while mean healing time was 16.39 ± 3.49 days in the younger age category and 17.47 ± 3.23 days in the older age category.

Discussion

The present study evaluated topical heparin as an adjunct to conventional wound care for split-thickness skin graft donor sites using a within-participant comparison. Overall, heparin-treated donor sites demonstrated more favorable descriptive outcomes than conventionally treated sites, including lower postoperative pain scores and analgesic requirements and shorter mean healing and edema-resolution times. The magnitude of the observed differences, particularly the 5.45-day shorter mean healing time and the 1.17-point lower mean pain score in heparin-treated sites, suggests a potentially clinically relevant benefit of topical heparin in donor-site management. These findings should nevertheless be interpreted within the context of the paired study design, modest sample size, and limitations of the available statistical analysis.

The observed difference in healing time is broadly consistent with previous research examining topical heparin in donor-site and burn wounds. Adil et al. evaluated topical heparin spray in split-thickness skin graft donor sites and reported favorable early wound changes, including reductions in wound surface area and edema, together with accelerated healing in treated sites (3). Similar findings have been reported in a prospective investigation of skin graft donor sites, in which heparin-treated areas demonstrated shorter healing time and favorable scar-related outcomes compared with conventional treatment (17). Evidence from partial-thickness burn wounds has also demonstrated shorter healing periods with topical heparin than with conventional wound management (16,18). Although donor-site wounds and thermal burns differ in their pathophysiology and clinical management, the consistency in the direction of these findings supports further investigation of topical heparin as an adjunct to wound care.

Pain is an important source of morbidity following split-thickness skin graft harvesting, and reduction of donor-site pain may improve postoperative comfort and decrease reliance on analgesic medication. In the present study, heparin-treated donor sites had a mean pain score 1.17 points lower than control sites, accompanied by a mean reduction of 717.5 mg in the reported total analgesic requirement. Previous clinical studies of topical heparin in burn wounds have similarly reported reductions in pain and analgesic consumption compared with conventional treatment (16,18). A systematic review and meta-analysis of randomized studies evaluating topical heparin in burn care also reported favorable pain-related outcomes (15). Nevertheless, differences in wound type, heparin regimen, pain measurement, analgesic protocols, and follow-up across studies limit direct quantitative comparison with the present findings.

Several biological mechanisms may plausibly contribute to the observed healing pattern. Beyond its established anticoagulant activity, heparin is a highly sulfated glycosaminoglycan capable of interacting with proteins involved in inflammation, angiogenesis, cellular proliferation, and tissue repair (9–11). Experimental evidence suggests that heparin-containing wound constructs may preserve or enhance the activity of growth-related mediators, including vascular endothelial growth factor and epidermal growth factor, thereby supporting angiogenesis and epithelial regeneration (12). Heparin has also been investigated in combination with basic fibroblast growth factor in skin graft donor sites, where its growth-factor-binding properties may contribute to stabilization and prolonged biological activity of bFGF (13). These mechanisms provide biological plausibility for an effect on donor-site repair; however, VEGF, EGF, bFGF, inflammatory mediators, and other mechanistic biomarkers were not measured in the present study. Consequently, these pathways should be regarded as possible explanations rather than demonstrated mechanisms underlying the observed clinical differences.

Edema also resolved earlier on average at heparin-treated donor sites, with a mean difference of approximately two days compared with conventionally treated sites. Previous donor-site research has similarly described early reductions in edema following topical heparin treatment (3). This observation may reflect changes in the local wound environment associated with heparin treatment, although the present study did not directly investigate the physiological mechanisms responsible for edema resolution. The finding therefore provides additional descriptive support for the overall pattern of earlier local recovery but requires confirmation using standardized edema measurements and appropriately paired statistical analysis.

The within-participant design represents an important feature of the study because each participant contributed both a heparin-treated and a conventionally treated donor site. Such a design can reduce variability arising from patient-level characteristics because both sites share the same systemic biological environment, age, sex, nutritional status, and other individual factors. The observed differences between paired donor sites are therefore clinically informative. However, this design also requires statistical methods that account for the dependence between observations from the same participant. The available aggregate results do not provide the within-participant variance needed to derive definitive paired confidence intervals or effect estimates, and the treatment differences should therefore be interpreted primarily according to their observed magnitude until the paired patient-level analysis is completed.

The exploratory stratified findings did not demonstrate substantial descriptive variation in pain, analgesic requirement, or healing time across the reported age, sex, and donor-site categories. These findings should not be interpreted as evidence that treatment efficacy is uniform across demographic subgroups, because absence of a subgroup difference does not establish equivalence and the available analyses were not designed or adequately powered to establish treatment-effect modification. Larger studies using prespecified interaction analyses would be required to determine whether the response to topical heparin differs according to demographic or clinical characteristics.

From a clinical perspective, shortening donor-site healing while reducing pain and analgesic requirements could be relevant to postoperative recovery after split-thickness skin grafting. Donor-site morbidity can contribute substantially to patient discomfort despite successful reconstruction of the primary wound (5–7). An adjunct that can be incorporated into routine dressing care and that is associated with earlier epithelial recovery and improved patient comfort could therefore have practical value. However, the present findings alone are

insufficient to establish routine clinical adoption, particularly because safety outcomes, standardized analgesic exposure, and long-term donor-site appearance were not comprehensively evaluated.

Several limitations should be considered when interpreting these findings. The study was conducted at a single center with 40 participants, which limits precision and broader generalizability. Although each participant served as their own control, the paired nature of the observations was not fully incorporated into the originally reported statistical analysis, and definitive paired confidence intervals and effect estimates cannot be reconstructed from the available aggregate data. The method used to determine the exact day of complete epithelialization was not described with sufficient precision relative to the scheduled follow-up assessments. Pain was assessed during the early postoperative period, but the available results do not clearly distinguish individual daily scores from an overall summary measure. In addition, the total analgesic requirement was reported in milligrams without sufficient detail regarding the specific analgesic regimen, limiting interpretation of the absolute difference between donor sites. Graft-harvesting depth was not clearly standardized, and assessor blinding was not reported, introducing potential measurement bias. Although baseline hematological eligibility criteria were applied, detailed treatment-emergent bleeding, coagulation, infection, and other adverse-event outcomes were not presented; therefore, conclusions regarding safety cannot be established from the reported data. Finally, long-term scar quality and cosmetic outcomes were not evaluated.

Despite these limitations, the study provides clinically relevant within-participant observations suggesting that topical heparin may be associated with shorter donor-site healing and edema-resolution times and lower postoperative pain and analgesic requirements than conventional dressing alone. The consistency in direction with previous donor-site and burn-wound studies supports continued evaluation of this approach (3,15–18). Confirmation using appropriately analyzed paired data, standardized outcome definitions, clearly specified analgesic protocols, systematic safety assessment, and longer follow-up would strengthen the evidence regarding the role of topical heparin in split-thickness skin graft donor-site management.

Conclusion

In this within-participant comparison, split-thickness skin graft donor sites treated with topical heparin showed shorter mean healing and edema-resolution times, lower postoperative pain scores, and lower analgesic requirements than conventionally treated donor sites. These findings suggest that topical heparin may have potential as an adjunct to conventional donor-site wound management for improving early healing and postoperative comfort. The findings should be interpreted in the context of the study design and available analysis and do not, on their own, establish broader clinical effectiveness or safety.

DECLARATIONS

Author Contributions:	Concept: SK, HK; Design: SK, HK, JAK; Data Collection: JAK, ARAW; Analysis: SK, HK; Drafting: SK, JAK, ARAW.
Ethical Approval:	Ethical approval was obtained from the Institutional Ethics Review Board of Holy Family Hospital, Rawalpindi, Pakistan, before commencement of the study.
Informed Consent:	Written and verbal informed consent was obtained from all participants before enrollment. Trial Registration: Not applicable.
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Data Availability:	Data are available from the corresponding author on reasonable request.
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AI Declaration:	Generative AI tools were used solely for language and grammatical refinement. The authors verified the final manuscript and remain fully responsible for its accuracy, integrity, and scientific content.

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