LMJ LINK MEDICAL JOURNAL OF HEALTH AND COMMUNITY RESEARCH

Crossref DOI: https://doi.org/10.61919/xrpzj971

Original Article

Clinical Efficacy of Rifampicin Nanoparticle Local Delivery in Post-Surgical Wound Infections Caused by Resistant Bacteria

Bushra Rasool[1], Hijab Zahra[1], Aramish Iqbal[2], Muhammad Azhar[3], Sana Ahmed[4], Rafia Arshad[5]

[1] MPhil, Department of Microbiology and Molecular Genetics, Bahauddin Zakariya University, Multan, Pakistan.
[2] PGR, HFH, Rawalpindi, Pakistan.
[3] Professor of Surgery, Wah Medical College, National University of Medical Sciences (NUMS), Wah Cantonment, Pakistan.
[4] Lecturer Inorganic Chemistry, Department of Chemistry, Faculty of Basic Sciences, Sardar Bahadur Khan Women University, Quetta, Pakistan.
[5] Final Year MBBS, Baqai Medical University, Karachi, Pakistan. ORCID: https://orcid.org/0009-0004-3824-7057

***Corresponding author: Rafia Arshad, rafia718arshad@gmail.com**

ABSTRACT

Background: Post-surgical wound infections caused by resistant bacteria remain difficult to manage because conventional antimicrobial strategies may provide inadequate local drug exposure, delayed bacterial clearance, frequent dressing requirements, and prolonged wound healing. Nanoparticle-based local antibiotic delivery may improve wound-site drug retention while reducing treatment burden. Objective: To evaluate the clinical efficacy and local tolerability of rifampicin nanoparticle dressing in adults with culture-confirmed resistant post-surgical wound infections. Methods: A parallel-group randomized controlled trial was conducted in a tertiary care surgical unit in Central Punjab, Pakistan, from September 2025 to January 2026. Seventy-two adults aged 18–65 years were randomized equally to receive either localized rifampicin nanoparticle dressing or conventional antimicrobial dressing for four weeks. Primary outcomes were percentage wound area reduction and quantitative bacterial load. Secondary outcomes included dressing frequency, pain, comfort score, and local adverse effects. Results: Sixty-three participants completed follow-up and were included in the final post-intervention analysis. The rifampicin nanoparticle group showed greater wound area reduction than controls (68.5 ± 12.4% vs 49.2 ± 11.8%; $p<0.001$) and lower bacterial load (2.1 ± 0.6 vs 3.4 ± 0.7 log CFU/ml; $p<0.001$). The intervention group also had fewer dressing changes, lower pain scores, and higher comfort scores, while local adverse effects were comparable between groups. Conclusion: Localized rifampicin nanoparticle delivery significantly improved wound healing, bacterial clearance, and patient-centered outcomes in resistant post-surgical wound infections, supporting its potential as an adjunctive wound-care strategy. Keywords: Antibacterial Agents; Drug Delivery Systems; Nanoparticles; Postoperative Wound Infection; Rifampicin; Randomized Controlled Trial; Wound Healing.

"Cite this Article" | **Received**: 12 August 2025; **Accepted**: 12 December 2025; **Published**: 31 December 2025.
Author Contributions: Concept: BR and HZ; Design: AI and MA; Data Collection: SA and RA; Analysis: MA; Drafting: BR, HZ, and RA. **Ethical Approval**: Bahauddin Zakariya University, Multan, Pakistan. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest; **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

INTRODUCTION

Post-surgical wound infections remain a major cause of delayed recovery, prolonged hospitalization, increased treatment cost, and preventable morbidity in surgical practice. Although improvements in aseptic technique, perioperative prophylaxis, and wound-care protocols have reduced infection risk, surgical site infections continue to occur across diverse clinical settings and are increasingly complicated by antimicrobial resistance (1). Resistant organisms, including multidrug-resistant Staphylococcus aureus and resistant Gram-negative bacteria, can persist within wound tissue, delay granulation and epithelialization, and increase the risk of recurrent infection or systemic spread. These challenges are particularly important in patients with culture-confirmed infected wounds in whom standard antimicrobial approaches may provide incomplete bacterial clearance and suboptimal healing outcomes (2,3).

Conventional management of infected post-surgical wounds generally combines local wound care with systemic antibiotics selected according to clinical assessment and microbiological sensitivity. However, systemic antimicrobial therapy may fail to maintain sufficiently high and sustained drug concentrations

at the wound bed, especially in poorly vascularized, necrotic, or biofilm-associated tissue. This limitation can reduce antimicrobial efficacy while increasing systemic exposure, adverse effects, drug interactions, and selection pressure for further resistance. Localized antimicrobial delivery has therefore emerged as a clinically relevant strategy because it offers the potential to concentrate therapy directly at the infected site while limiting unnecessary systemic drug burden (4,5).

Rifampicin is a potent bactericidal agent with recognized activity against biofilm-associated bacterial populations, making it a biologically plausible candidate for targeted wound infection therapy. Its ability to penetrate biofilms is especially relevant in post-surgical wounds, where bacterial persistence within extracellular matrices can reduce responsiveness to conventional treatment. Despite these advantages, systemic rifampicin use is constrained by hepatotoxicity, clinically important drug interactions, and the risk of rapid resistance when used inappropriately or as functional monotherapy. These limitations support the need for delivery systems that preserve rifampicin's local antimicrobial activity while reducing systemic exposure and improving controlled release at the wound surface (6,7).

Nanoparticle-based drug delivery systems offer several advantages for infected wound management, including improved drug stability, sustained release, enhanced tissue penetration, and the ability to maintain higher local antimicrobial concentrations for prolonged periods. When rifampicin is incorporated into nanoparticle carriers, the formulation may theoretically improve bacterial eradication, reduce dressing burden, and support a more favorable wound-healing environment through prolonged local drug availability. Previous experimental and early clinical work on antimicrobial nanocarriers has suggested potential benefit in resistant and biofilm-associated infections, but robust clinical evidence remains limited, particularly for rifampicin nanoparticle delivery in culture-confirmed resistant post-surgical wound infections (8).

The key evidence gap is the lack of controlled human data evaluating whether localized rifampicin nanoparticle therapy improves clinically meaningful wound outcomes beyond conventional antimicrobial dressings. Existing literature has often emphasized laboratory antimicrobial activity, biofilm disruption, or general nanomedicine applications, while fewer studies have assessed practical clinical endpoints such as percentage wound-area reduction, quantitative bacterial-load reduction, dressing frequency, patient-reported pain, comfort, and local tolerability in a randomized setting. Addressing these outcomes is important because effective wound therapy should not only reduce bacterial burden but also accelerate healing, reduce patient discomfort, minimize repeated dressing manipulation, and remain safe for routine clinical use (9,10).

On this basis, the present randomized controlled trial was designed to evaluate adult patients with culture-confirmed resistant post-surgical wound infections who received either localized rifampicin nanoparticle dressing or conventional antimicrobial dressing over a four-week intervention period. The primary objective was to determine whether localized rifampicin nanoparticle delivery produced greater wound-area reduction and bacterial-load reduction compared with standard antimicrobial wound care. Secondary objectives were to compare dressing frequency, pain intensity, patient comfort, and local adverse effects between treatment groups. The study hypothesis was that localized rifampicin nanoparticle delivery would provide superior wound healing and bacterial clearance while improving patient-centered outcomes compared with conventional antimicrobial dressings.

MATERIALS AND METHODS

A parallel-group randomized controlled trial was conducted to evaluate the clinical efficacy and local tolerability of rifampicin nanoparticle delivery in patients with resistant post-surgical wound infections. The study was carried out in a tertiary care surgical unit in Central Punjab, Pakistan, over a five-month period from September 2025 to January 2026. Each enrolled participant received a four-week intervention and follow-up assessment. The randomized design was selected to compare localized rifampicin nanoparticle dressing with conventional antimicrobial wound dressing under controlled

clinical conditions while minimizing selection bias and allowing direct evaluation of treatment-related differences in wound healing, bacterial clearance, dressing burden, pain, comfort, and local adverse effects.

Adult patients aged 18–65 years were eligible if they presented with clinically infected post-surgical wounds and had microbiological confirmation of antibiotic-resistant bacterial infection on culture and sensitivity testing. Resistant infection was operationally defined as growth of a bacterial pathogen showing resistance to at least one first-line antimicrobial agent used for post-surgical wound infection management. Eligible patients were required to have delayed wound healing with an assessable wound surface area suitable for serial planimetric measurement. Patients were excluded if they had immunocompromised status, uncontrolled diabetes mellitus, hepatic dysfunction, known hypersensitivity to rifampicin, or concurrent participation in another investigational therapy, because these factors could independently influence wound healing, antimicrobial response, drug safety, or outcome interpretation (11).

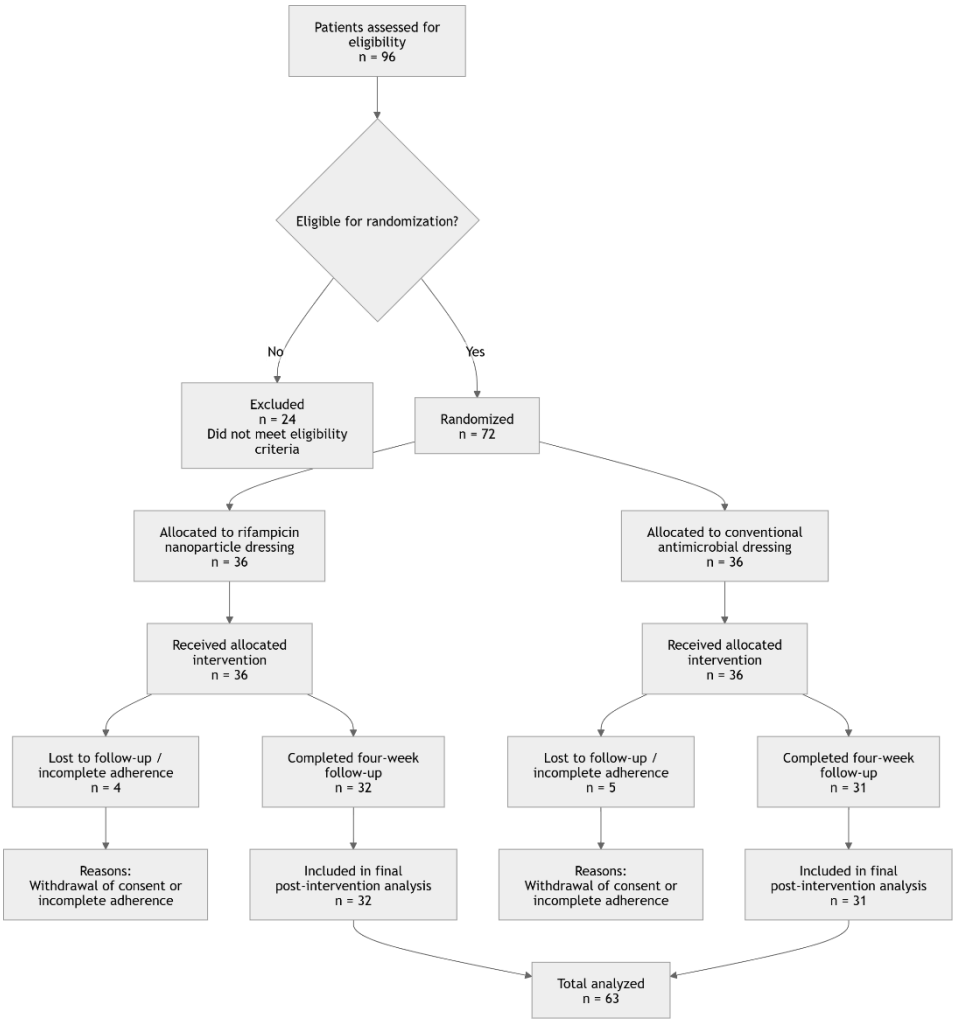

Figure 1 CONSORT Flowchart

Patients were screened consecutively from the surgical unit during the recruitment period. Clinical eligibility was assessed through wound examination, review of surgical and medical history, and laboratory confirmation of resistant bacterial growth. Written informed consent was obtained before randomization. A total of 72 eligible participants were enrolled and allocated in a 1:1 ratio to either the intervention group or the control group. Randomization was performed using a computer-generated random sequence, and allocation concealment was maintained using sequentially numbered, sealed, opaque envelopes prepared by an independent researcher who was not involved in participant assessment or treatment delivery. Because of the visible nature of the dressing interventions, participant

blinding was not feasible; however, outcome assessors and data analysts were blinded to group allocation to reduce assessment and analytical bias.

Participants assigned to the intervention group received localized rifampicin nanoparticle formulation applied directly to the wound bed after standard wound preparation. Before application, wounds underwent debridement when clinically indicated and irrigation with sterile normal saline to remove debris, exudate, and nonviable material. The rifampicin nanoparticle dressing was then placed over the wound surface and covered with sterile gauze according to the intervention protocol. Participants assigned to the control group received conventional antimicrobial wound care using standard antimicrobial dressings, including silver-based or povidone-iodine dressings according to institutional protocol. Both groups received routine supportive care, including analgesia and systemic antibiotics guided by culture sensitivity when clinically indicated, to ensure ethical management of active infection.

The primary outcome variables were wound healing progression and bacterial load reduction after four weeks of treatment. Wound healing progression was defined as the percentage reduction in wound surface area from baseline to week four, measured using planimetric wound assessment. Wound area was recorded in square centimeters at baseline and at the end of the intervention period, and percentage reduction was calculated using the baseline and post-intervention wound area values. Bacterial load was assessed using quantitative culture analysis and expressed as log CFU/ml. Baseline bacterial burden and post-intervention bacterial burden were compared to determine the magnitude of bacterial clearance. These two outcomes were selected as co-primary measures because they represent both clinical tissue recovery and microbiological infection control.

Secondary outcomes included dressing frequency, pain intensity, patient comfort, and local adverse effects. Dressing frequency was recorded as the number of dressing changes per week during the intervention period. Pain was assessed using the Visual Analog Scale, with higher scores indicating greater pain intensity. Patient comfort was assessed using a standardized Likert-type comfort score, with higher scores indicating better comfort during wound management. Local adverse effects were documented throughout follow-up and included erythema, irritation, allergic reaction, or other localized intolerance at the wound site. Adherence to the assigned dressing protocol was monitored through daily clinical logs, and deviations from the intervention schedule were recorded.

Data collection was performed at baseline and after completion of the four-week intervention. Baseline variables included age, sex, wound surface area, and bacterial load. Outcome data were collected using standardized assessment procedures to maintain consistency across participants. Wound measurements were performed using the same planimetric approach at each assessment point, and microbiological sampling was conducted using quantitative culture methods. Clinical staff documented dressing applications, dressing changes, patient-reported symptoms, and local adverse events. Data entries were reviewed for completeness and consistency before statistical analysis, and participant records were coded to preserve confidentiality.

Potential sources of bias and confounding were addressed through random allocation, concealed assignment, blinded outcome assessment, blinded data analysis, standardized eligibility criteria, and consistent timing of baseline and post-intervention assessments. Exclusion of patients with uncontrolled diabetes mellitus, hepatic dysfunction, immunocompromised status, or rifampicin hypersensitivity reduced the influence of major biological and safety-related confounders. Supportive care was provided according to clinical need in both groups, and culture-guided systemic antibiotic use was incorporated into routine management to avoid withholding necessary treatment. Protocol adherence was monitored prospectively to identify incomplete adherence and loss to follow-up.

The sample size was set at 72 participants, with 36 participants allocated to each study arm, based on expected clinically meaningful differences in wound healing outcomes observed in comparable localized antimicrobial intervention studies. This sample size was selected to provide adequate power for

detecting between-group differences in the primary outcomes while allowing for participant withdrawal and incomplete adherence during follow-up. During the study, participants lost to follow-up or with incomplete dressing adherence were documented, and the final post-intervention outcome dataset included participants with complete four-week assessments.

Statistical analysis was performed using standard statistical software. Continuous variables were summarized as mean ± standard deviation, and categorical variables were summarized as frequency and percentage. Normality of continuous data was assessed using the Shapiro–Wilk test. Baseline comparability between treatment groups was evaluated using independent-samples t-tests for continuous variables and appropriate categorical tests for frequency data. Between-group comparisons of post-intervention wound reduction, bacterial load, dressing frequency, pain score, and comfort score were conducted using independent-samples t-tests. Within-group baseline-to-post-intervention changes in wound area and bacterial load were assessed using paired-samples t-tests. Repeated-measures analysis of variance was applied to evaluate time effects, group effects, and time-by-group interaction effects across the intervention period. Pearson correlation analysis was used to examine the relationship between bacterial load reduction and wound area reduction. A p-value of less than 0.05 was considered statistically significant.

Ethical conduct was maintained throughout the study. Participants were enrolled only after informed consent, and all clinical interventions were delivered within a wound-care framework that allowed appropriate supportive treatment when medically indicated. Patient confidentiality was maintained through coded data handling, and access to identifiable information was restricted to authorized study personnel. Data integrity was supported through standardized measurement procedures, prospective clinical logs, blinded analysis, consistent outcome definitions, and review of records for completeness before final statistical evaluation.

RESULTS

A total of 96 patients with suspected post-surgical wound infection were screened during the study period. Of these, 72 patients fulfilled the eligibility criteria and were randomized equally into the rifampicin nanoparticle group and the conventional antimicrobial dressing group, with 36 participants allocated to each arm. During the four-week intervention period, 9 participants did not complete follow-up, including 4 from the intervention group and 5 from the control group. The final post-intervention analysis included 63 participants, comprising 32 in the rifampicin nanoparticle group and 31 in the control group. Losses to follow-up were due to withdrawal of consent and incomplete adherence to the dressing protocol.

Table 1. Participant Flow and Analysis Population

Study Stage	Total, n	Rifampicin Nanoparticle Group, n	Control Group, n	Percentage of Total Screened
Patients screened	96			100.0%
Randomized	72	36	36	75.0%
Lost to follow-up/incomplete adherence	9	4	5	9.4%
Included in final post-intervention analysis	63	32	31	65.6%
Completion rate among randomized participants	—	88.9%	86.1%	—

Baseline demographic and clinical characteristics were comparable between the two groups. The mean age was 44.2 ± 10.3 years in the rifampicin nanoparticle group and 45.1 ± 9.8 years in the control group, with no statistically significant difference between groups. Male participants represented 58.3% of the intervention group and 55.6% of the control group. Baseline wound area was similar between groups, measuring 12.6 ± 3.6 cm^2 in the intervention group and 13.0 ± 3.4 cm^2 in the control group. Baseline bacterial load was also comparable, with mean values of 5.8 ± 0.9 log CFU/ml and 6.0 ± 0.7 log CFU/ml, respectively.

Table 2. Baseline Demographic and Clinical Characteristics of Randomized Participants

Variable	Total Sample (N=72)	Rifampicin Nanoparticle Group (n=36)	Control Group (n=36)	Mean Difference / Group Difference	p-value
Age, years	44.6 ± 10.0	44.2 ± 10.3	45.1 ± 9.8	-0.9 years	0.71
Male sex, n (%)	41 (56.9%)	21 (58.3%)	20 (55.6%)	+2.7 percentage points	0.81
Wound area, cm²	12.8 ± 3.5	12.6 ± 3.6	13.0 ± 3.4	-0.4 cm²	0.64
Bacterial load, log CFU/ml	5.9 ± 0.8	5.8 ± 0.9	6.0 ± 0.7	-0.2 log CFU/ml	0.52

After four weeks of treatment, the rifampicin nanoparticle group showed significantly greater wound healing than the control group. Mean wound area reduction reached 68.5 ± 12.4% in the intervention group compared with 49.2 ± 11.8% in the control group, yielding an absolute between-group difference of 19.3 percentage points with a 95% confidence interval of 13.2 to 25.4. Post-intervention bacterial load was also significantly lower in the rifampicin nanoparticle group, with a mean of 2.1 ± 0.6 log CFU/ml compared with 3.4 ± 0.7 log CFU/ml in the control group. The between-group difference was -1.3 log CFU/ml, with a 95% confidence interval from -1.6 to -0.9. Both primary outcomes showed strong statistical significance.

Table 3. Post-Intervention Primary Outcomes at Four Weeks

Primary Outcome	Rifampicin Nanoparticle Group (n=32)	Control Group (n=31)	Mean Difference (95% CI)	p-value
Wound area reduction, %	68.5 ± 12.4	49.2 ± 11.8	19.3 (13.2 to 25.4)	<0.001
Post-intervention bacterial load, log CFU/ml	2.1 ± 0.6	3.4 ± 0.7	-1.3 (-1.6 to -0.9)	<0.001

Within-group analysis showed statistically significant improvement in both treatment arms, although the magnitude of improvement was greater in the rifampicin nanoparticle group. In the intervention group, mean wound area decreased from 12.6 ± 3.6 cm² at baseline to 4.0 ± 2.1 cm² at week four, corresponding to an absolute reduction of 8.6 cm². In the control group, wound area decreased from 13.0 ± 3.4 cm² to 6.6 ± 2.8 cm², corresponding to an absolute reduction of 6.4 cm². Bacterial load declined from 5.8 ± 0.9 to 2.1 ± 0.6 log CFU/ml in the intervention group and from 6.0 ± 0.7 to 3.4 ± 0.7 log CFU/ml in the control group. Repeated-measures analysis demonstrated a significant time effect, group effect, and time-by-group interaction, indicating that wound area improved over time in both groups but with a significantly greater treatment response in the rifampicin nanoparticle group.

Table 4. Within-Group Pre–Post Changes and Repeated-Measures Analysis

Outcome	Group	Baseline	Week Four	Absolute Change	Within-Group p-value
Wound area, cm²	Rifampicin nanoparticle	12.6 ± 3.6	4.0 ± 2.1	-8.6 cm²	<0.001
Wound area, cm²	Control	13.0 ± 3.4	6.6 ± 2.8	-6.4 cm²	<0.001
Bacterial load, log CFU/ml	Rifampicin nanoparticle	5.8 ± 0.9	2.1 ± 0.6	-3.7 log CFU/ml	<0.001
Bacterial load, log CFU/ml	Control	6.0 ± 0.7	3.4 ± 0.7	-2.6 log CFU/ml	<0.001

Table 5. Repeated Measures ANOVA Parameters

Repeated-Measures Parameter	F-value	p-value
Time effect	182.4	<0.001
Group effect	36.7	<0.001
Time × group interaction	28.9	<0.001

Secondary outcomes also favored localized rifampicin nanoparticle delivery. The intervention group required fewer dressing changes, with a mean dressing frequency of 4.1 ± 0.9 per week compared with 6.3 ± 1.1 per week in the control group. This represented an absolute reduction of 2.2 dressing changes per week. Pain scores were lower in the rifampicin nanoparticle group, with a mean VAS score of 2.3 ± 1.0 compared with 4.1 ± 1.2 in the control group, giving a mean difference of -1.8 points.

Table 5. Secondary Outcomes and Correlation Analysis at Four Weeks

Outcome	Rifampicin Nanoparticle Group (n=32)	Control Group (n=31)	Between-Group Difference	p-value
Dressing frequency, per week	4.1 ± 0.9	6.3 ± 1.1	-2.2 per week	<0.001
Pain score, VAS	2.3 ± 1.0	4.1 ± 1.2	-1.8 points	<0.001
Comfort score	4.2 ± 0.6	3.1 ± 0.7	+1.1 points	<0.001
Local adverse effects, n (%)	3 (9.4%)	5 (16.1%)	-6.7 percentage points	0.41
Correlation between bacterial load and wound area reduction	r = -0.68	—	Strong negative correlation	<0.001

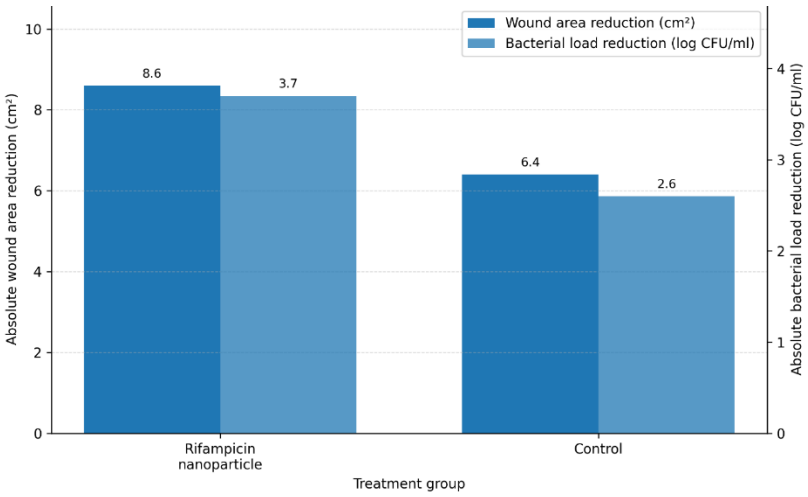

Figure 1. Integrated Clinical and Microbiological Improvement at Four Weeks

Patient comfort scores were higher in the intervention group, averaging 4.2 ± 0.6 compared with 3.1 ± 0.7 in the control group. Local adverse effects were reported in 3 participants in the intervention group and 5 participants in the control group, corresponding to rates of 9.4% and 16.1%, respectively; this difference was not statistically significant. Pearson correlation analysis showed a strong negative association between bacterial load and wound area reduction, with $r = -0.68$ and $p < 0.001$, indicating that lower bacterial burden was associated with greater wound healing.

The figure 1, integrated outcome profile shows a greater combined clinical and microbiological response in the rifampicin nanoparticle group than in the conventional dressing group. Mean wound area decreased by 8.6 cm² in the rifampicin nanoparticle group compared with 6.4 cm² in the control group, while bacterial load declined by 3.7 log CFU/ml versus 2.6 log CFU/ml, respectively. This dual improvement indicates that localized rifampicin nanoparticle delivery was associated with a larger absolute reduction in wound burden and a stronger microbiological response over the four-week treatment period, supporting the observed superiority of the intervention across both tissue-healing and infection-control endpoints.

Overall, localized rifampicin nanoparticle delivery produced greater improvement across both primary clinical and microbiological endpoints. The intervention group achieved a 19.3-percentage-point higher wound area reduction and a 1.3 log CFU/ml lower post-intervention bacterial load than the control group. Patient-centered outcomes also improved, with fewer dressing changes, lower pain intensity, and higher comfort scores, while local adverse effects remained uncommon and statistically comparable between groups.

DISCUSSION

The present randomized controlled trial demonstrated that localized rifampicin nanoparticle delivery produced superior clinical and microbiological improvement compared with conventional antimicrobial dressing in adults with resistant post-surgical wound infections. After four weeks of treatment, the intervention group achieved a greater mean wound area reduction than the control group, with a

difference of 19.3 percentage points, and showed a substantially lower post-intervention bacterial load, with a between-group difference of -1.3 log CFU/ml. These findings support the hypothesis that targeted local delivery of rifampicin through a nanoparticle-based system can enhance wound healing while improving bacterial clearance in infected surgical wounds. The simultaneous improvement in wound area and bacterial burden is clinically important because effective management of resistant wound infection requires both reduction of microbial load and restoration of tissue repair capacity, rather than improvement in either endpoint alone (12,13).

The stronger reduction in bacterial load observed in the rifampicin nanoparticle group is biologically plausible. Rifampicin has recognized antimicrobial activity against persistent and biofilm-associated bacterial populations, and localized nanoparticle delivery may help maintain higher antimicrobial concentrations at the wound bed for a longer period than conventional topical dressing approaches. In post-surgical wounds, impaired vascularity, necrotic tissue, exudate, and bacterial biofilm can reduce the effectiveness of systemic therapy and delay infection resolution. A local nanoparticle formulation may partly overcome these barriers by improving drug retention at the infected site, supporting sustained release, and increasing contact between the antimicrobial agent and the wound microenvironment. The observed decline in bacterial load from 5.8 ± 0.9 to 2.1 ± 0.6 log CFU/ml in the intervention group, compared with 6.0 ± 0.7 to 3.4 ± 0.7 log CFU/ml in the control group, suggests that the intervention provided a stronger microbiological effect during the four-week treatment period (14,15).

The clinical healing pattern was consistent with the microbiological findings. Mean wound area decreased from 12.6 ± 3.6 cm^2 to 4.0 ± 2.1 cm^2 in the rifampicin nanoparticle group, whereas the control group decreased from 13.0 ± 3.4 cm^2 to 6.6 ± 2.8 cm^2. This larger absolute reduction in wound size indicates that improved bacterial control may have contributed to a more favorable healing environment. Persistent bacterial colonization and infection can prolong inflammation, impair granulation tissue formation, and delay epithelial migration. Therefore, the strong negative correlation between bacterial load and wound area reduction reinforces the clinical relationship between microbial clearance and tissue repair, showing that lower bacterial burden was associated with greater wound healing response. This relationship strengthens the interpretation that the intervention's benefit was not limited to surface-level wound contraction but was accompanied by meaningful infection control (16,17).

Secondary outcomes further support the practical value of localized rifampicin nanoparticle delivery. Participants in the intervention group required fewer dressing changes per week, reported lower pain scores, and had higher comfort scores than those receiving conventional antimicrobial dressings. The reduction in dressing frequency is clinically relevant because repeated dressing changes can disrupt newly formed tissue, increase patient discomfort, consume nursing time, and raise the risk of secondary contamination. The lower pain score in the intervention group may reflect reduced inflammatory activity, less frequent manipulation of the wound, and improved local wound conditions. Similarly, the higher comfort score suggests that the intervention may offer patient-centered advantages beyond microbiological efficacy. These outcomes are important in routine surgical care because successful wound therapy should reduce infection while also improving tolerability, adherence, and overall care efficiency (18,19).

The local safety findings were reassuring within the short follow-up period. Local adverse effects occurred in 9.4% of participants in the rifampicin nanoparticle group and 16.1% in the control group, with no statistically significant difference between groups. This suggests that the nanoparticle formulation was locally tolerated over four weeks of treatment. However, the modest sample size limits the ability to detect uncommon adverse events, and the study duration was not sufficient to assess late complications, recurrence of infection, scar quality, systemic rifampicin exposure, or emergence of rifampicin resistance. These safety considerations are particularly important for rifampicin because inappropriate or prolonged exposure can encourage resistance. Future evaluation should therefore

include longer monitoring, microbiological resistance profiling, and assessment of systemic absorption where clinically relevant (20).

The findings should be interpreted in light of the study's methodological limitations. Although randomization, allocation concealment, and blinded outcome assessment strengthened internal validity, participant blinding was not feasible because of the visible nature of the dressing intervention. This may have influenced subjective outcomes such as pain and comfort, although the primary outcomes included objective measures of wound area and bacterial load. The study was conducted in a single tertiary care setting, which may limit generalizability to other populations, surgical categories, microbial profiles, and healthcare systems. In addition, the control arm included conventional antimicrobial dressings according to institutional protocol, which may introduce variability if different dressing types were used. Systemic antibiotics were also permitted when clinically indicated, and differences in systemic antibiotic exposure could influence bacterial clearance and wound healing outcomes (21).

Despite these limitations, the study has several strengths. The randomized controlled design allowed direct comparison between localized rifampicin nanoparticle dressing and conventional antimicrobial wound care. Baseline demographic and clinical characteristics were comparable between groups, reducing the likelihood that observed differences were driven by initial imbalance. The use of quantitative wound area assessment and bacterial culture-based measurement provided objective endpoints, while inclusion of pain, comfort, dressing frequency, and local adverse effects allowed a broader assessment of clinical utility. The four-week treatment period was sufficient to detect early differences in wound healing and bacterial clearance, and the significant time-by-group interaction supports a stronger treatment trajectory in the rifampicin nanoparticle group (22).

Overall, the results indicate that localized rifampicin nanoparticle delivery may represent a promising adjunctive strategy for resistant post-surgical wound infections. The intervention was associated with greater wound area reduction, stronger bacterial-load decline, fewer dressing requirements, lower pain, and improved patient comfort compared with conventional antimicrobial dressing. These benefits suggest that nanoparticle-based local antibiotic delivery may address several limitations of standard wound infection management by improving antimicrobial exposure at the wound site while supporting clinically meaningful healing. Larger multicenter trials with standardized control protocols, longer follow-up, detailed systemic antibiotic reporting, resistance monitoring, and cost-effectiveness evaluation are needed to define its broader clinical role and determine whether these early benefits translate into durable improvements in infection recurrence, wound closure, and patient recovery (23).

CONCLUSION

Localized rifampicin nanoparticle delivery demonstrated superior clinical efficacy compared with conventional antimicrobial dressing in adults with resistant post-surgical wound infections. Over the four-week treatment period, the intervention produced greater wound area reduction, stronger bacterial-load decline, fewer dressing changes, lower pain scores, and improved patient comfort, while local adverse effects remained uncommon and statistically comparable between groups. These findings support localized rifampicin nanoparticle therapy as a promising adjunctive wound-care approach that may improve both infection control and tissue healing in resistant post-surgical infections; however, larger multicenter trials with longer follow-up are needed to confirm durability of response, recurrence prevention, long-term safety, resistance risk, and broader clinical applicability.

REFERENCES

1. Kaiser P, Wächter J, Windbergs M. Therapy of infected wounds: overcoming clinical challenges by advanced drug delivery systems. Drug Deliv Transl Res. 2021;11(4):1545-1567.

2. Pormohammad A, Monych NK, Ghosh S, Turner DL, Turner RJ. Nanomaterials in wound healing and infection control. Antibiotics. 2021;10(5):473.

3. Quiñones-Vico MI, Ubago-Rodríguez A, Fernández-González A, Sanabria-de la Torre R, Sierra-Sánchez Á, Montero-Vilchez T, et al. Antibiotic nanoparticles-loaded wound dressings against Pseudomonas aeruginosa skin infection: a systematic review. 2024:7895-7926.

4. Cristea AG, Lisă EL, Iacob S, Dragostin I, Ştefan CS, Fulga I, et al. Antimicrobial smart dressings for combating antibiotic resistance in wound care. 2025;18(6):825.

5. Chirra B. Novel antimicrobials and drug delivery devices to treat multidrug resistant infections. 2022.

6. Ding X, Tang Q, Xu Z, Xu Y, Zhang H, Zheng D, et al. Challenges and innovations in treating chronic and acute wound infections: from basic science to clinical practice. 2022;10:tkac014.

7. Empitu MA, Kadariswantiningsih IN, Shakri NM. Pharmacological strategies for targeting biofilms in otorhinolaryngologic infections and overcoming antimicrobial resistance. Biofilm Res. 2025;22(6):95.

8. AlQurashi DM, AlQurashi TF, Alam RI, Shaikh S, Tarkistani MAM. Advanced nanoparticles in combating antibiotic resistance: current innovations and future directions. J Nanobiotechnology. 2025;6(2):9.

9. Ibne Shoukani H, Nisa S, Bibi Y, Ishfaq A, Ali A, Alharthi S, et al. Green synthesis of polyethylene glycol-coated, ciprofloxacin-loaded CuO nanoparticles and its antibacterial activity against Staphylococcus aureus. Sci Rep. 2024;14(1):21246.

10. Cetin FN, Mignon A, Van Vlierberghe S, Kolouchova K. Polymer- and lipid-based nanostructures serving wound healing applications: a review. Adv Healthc Mater. 2025;14(1):2402699.

11. Pathinathan K, Sial A, Khalil O, Ghahreman A, Diwan A. Strategies to prevent post-operative surgical site infection in spinal surgery: a narrative review. Eur Spine J. 2026:1-9.

12. Patil S, Asutkar S. Cutting-edge pharmacological innovations for enhanced post-surgical wound healing: integrating nanomedicine, targeted drug delivery, and natural therapeutics. J Pharm Pharmacother. 2025:0976500X251367992.

13. Wassif RK, Shamma RN, El-Hoffy NM, El-Kayal M. Recent advances in the local drug delivery systems for diabetic wound healing: a comprehensive review. AAPS PharmSciTech. 2025;26(6):177.

14. Caggiari G. New strategy in orthopaedics and in the reduction of spinal surgery infections. 2024.

15. Caporalini S, Azimi B, Zergat S, Ansari Chaharsoughi M, Maleki H, Batoni G, et al. Electrospinning enables opportunity for green and effective antibacterial coatings of medical devices. 2025;16(7):249.

16. Buriti BMAdB, Figueiredo PLB, Passos MF, da Silva JKR. Polymer-based wound dressings loaded with essential oil for the treatment of wounds: a review. Pharmaceutics. 2024;17(7):897.

17. Deng X. Drug-eluting biodegradable surgical suture for wound healing. Dunedin: University of Otago; 2024.

18. Hemmati J, Azizi M, Asghari B, Arabestani MR. Multidrug-resistant pathogens in burn wound, prevention, diagnosis, and therapeutic approaches: conventional antimicrobials and nanoparticles. Can J Infect Dis Med Microbiol. 2023;2023(1):8854311.

19. Yadav A, Yadav K. Nanomedicines in the treatment of methicillin-resistant Staphylococcus aureus. Adv Drug Deliv Pharmacother. 2026;2(1).

20. Wang X, Wu F, Liu J, Hong X, Dong S. Application and potential of local drug delivery systems for antibacterial treatment of periodontitis. Int J Mol Sci. 2026;27(7):2983.

21. Jampilek J, Kralova K. Advances in nanostructures for antimicrobial therapy. Molecules. 2022;15(7):2388.

22. Karnam S, Jindal AB, Agnihotri C, Singh BP, Paul AT. Topical nanotherapeutics for treating MRSA-associated skin and soft tissue infections. AAPS PharmSciTech. 2023;24(5):108.

23. Priya, Gaur PK, Kumar S. Nanocarrier-mediated dermal drug delivery system of antimicrobial agents for targeting skin and soft tissue infections. Adv Drug Deliv Rev. 2025;23(1):2-28.