Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(4):1217-26

# Efficacy and safety of antibiotic-loaded nanohydroxyapatite beads in the management of chronic osteomyelitis

**Ali Can Cicek, Mehmet Fatih Aksay**

*Ağrı İbrahim Cecen University Medicine Faculty, Ağrı Education and Research Hospital, Department of Orthopedics, Ağrı, Türkiye*

Received 22 May 2025; Accepted 23 July 2025
Available online 30 November 2025 with doi: 10.5455/medscience.2025.05.134



**Abstract**

The research investigated the effectiveness and security of antibiotic-impregnated nanohydroxyapatite beads (nHA-ATB) as a treatment for chronic osteomyelitis through a retrospective study. The study included 42 patients who received surgical debridement and nHA-ATB beads with gentamicin, vancomycin or fosfomycin for refractory chronic osteomyelitis. The assessment included demographics, Cierny-Mader classification, microbiological profiles, therapeutic drug monitoring, inflammatory markers, radiographic parameters, and quality of life (SF-36) over 48 weeks. The patient population consisted of 61.9% males with an average age of 48±14 years who mainly had lower extremity infections (76.2%). The success rate achieved 88.1% at the 48-week mark. The success of treatment depended on the extent of anatomic spread and host condition and particular comorbidities. Gentamicin and vancomycin produced better results than fosfomycin in treatment outcomes ($p=0.042$). The strong relationship between material resorption rates (90.5%) and bone healing outcomes (71.4%) was demonstrated through a correlation coefficient of $r=0.85$ ($p<0.001$). The inflammatory markers returned to normal in 83.3% of patients who also showed major improvements across all SF-36 domains. The high local antibiotic concentrations did not result in any systemic toxicity. The nHA-ATB beads demonstrated both safety and effectiveness in treating chronic osteomyelitis through their targeted antimicrobial action and bone regenerative properties. The dual delivery system of antibiotics with host bone integration provides better benefits than conventional antibiotic delivery methods. Further research should include multicenter randomized controlled trials with extended follow-up to determine the comparative efficacy of this treatment against standard intravenous antibiotic therapies for different patient groups.

**Keywords:** Chronic osteomyelitis, nanohydroxyapatite, localized antibiotic delivery, bone regeneration

## Introduction

The management of chronic osteomyelitis proves to be an enduring infectious condition that impacts various age groups because of its difficult pathophysiology. The inflammatory bone condition shows various symptoms that make both medical diagnosis and treatment option selection challenging. Standard therapeutic methods combining long-term antibiotic use and surgical debridement often yield unsatisfactory results. Frequent relapses prompt the need for new therapeutic approaches [1].

The management of chronic osteomyelitis needs a structured multi-stage approach which combines infection control with bone reconstruction. The initial treatment of early-stage chronic osteomyelitis requires complete removal of infected bone tissue together with thorough removal of necrotic tissue. After surgical debridement infection control is achieved through local filling materials that contain appropriate antibiotics to deliver sustained antimicrobial concentrations directly at the infection site. The systematic approach enables the simultaneous treatment of both infection and bone defects which leads to better treatment outcomes with reduced systemic complications [1-5].

The limitations of systemic antibiotic therapy in treating chronic osteomyelitis can be overcome through local antibiotic delivery systems especially for patients with compromised vascular supply [2]. The antibiotic-impregnated nanohydroxyapatite beads (nHA-ATB) serve as an innovative delivery system which provides targeted antimicrobial therapy while promoting bone tissue regeneration. The biocompatible delivery system provides sustained antibiotic concentrations at the infection site while decreasing systemic exposure. This leads to better therapeutic outcomes, lower adverse effects, and improved patient

**CITATION**
Cicek AC, Aksay MF. Efficacy and Safety of Antibiotic-Loaded Nanohydroxyapatite Beads in the Management of Chronic Osteomyelitis. Med Science. 2025;14(4):1217-26.

**Corresponding Author:** Ali Can Cicek, Ağrı İbrahim Cecen University Medicine Faculty, Ağrı, Türkiye
Email: alicancicek36@gmail.com

DOI: 10.5455/medscience.2025.05.134

compliance [3].

The main benefit of nHA-ATB beads emerges from their dual capability to fight infections and act as osteoconductive materials. Nanohydroxyapatite demonstrates high biocompatibility and tissue integration properties due to its structural similarity with natural bone minerals. This characteristic enables both infection elimination and bone healing promotion [4]. The biomimetic nature of nHA-ATB distinguishes it from PMMA beads. While nHA-ATB integrates with tissue, PMMA beads require removal and do not contribute to bone growth. The nanoscale dimensions of hydroxyapatite particles create additional surface space that boosts both antibiotic release rates and cell-to-material interactions [5].

Research has shown that using local antibiotic delivery systems with various carriers leads to both effective infection management and bone defect treatment [6]. The controlled delivery mechanism of antibiotics from nHA-ATB beads maintains prolonged antimicrobial effects, reducing the occurrence of reinfection [7]. The method maintains therapeutic antibiotic levels at the infection site while minimizing systemic drug exposure. This approach reduces toxicity risks and improves treatment outcomes. The localized therapy method enhances treatment compliance through reduced frequency of administration compared to oral or intravenous antibiotics [8].

The theoretical advantages of nHA-ATB beads for treating chronic osteomyelitis need additional clinical evidence for validation. The existing literature includes research with limited participant numbers and short observation durations which restrict the assessment of extended results and material breakdown patterns and life quality assessments. The lack of comparative studies between nHA-ATB and standard therapeutic approaches hinders the evaluation of their relative effectiveness and cost-effectiveness. The purpose of this research is to evaluate nHA-ATB beads for chronic osteomyelitis treatment through clinical assessment of their safety profile and quality of life impacts on patients. Our extensive evaluation will establish if this unique delivery system offers better treatment options than conventional methods.

## Material and Methods

The retrospective cohort study took place at İbrahim Çeçen University Medical Center from January 2020 through December 2023 with ethical approval from the institutional committee (approval number: ICU-2020-034). All procedures followed the Declaration of Helsinki and ICH guidelines for good clinical practice and participants signed written informed consent.

This study recruited adult patients who were at least 18 years old with chronic osteomyelitis that failed to respond to standard treatment methods. The study defined chronic osteomyelitis nonresponsiveness to standard treatments through four specific criteria: (1) The infection persisted or recurred after receiving intravenous antibiotics for at least six weeks, (2) The infection failed to resolve with oral antibiotics used for more than twelve weeks, (3) The infection did not respond to surgical debridement alone without local antibiotic delivery, and (4) The patients maintained elevated inflammatory markers (ESR >30 mm/hr, CRP >10 mg/L) after finishing standard treatment protocols. The established criteria selected only cases that showed proven treatment resistance for inclusion in the study. The diagnosis included at least six weeks of clinical symptoms coupled with radiological results from MRI, CT, or three-phase bone scan and at least one of the following: sinus tract drainage, abscess formation, intraoperative purulence, histopathological confirmation, or positive microbiological cultures. The complete Cierny-Mader classification system was utilized for patient documentation where we recorded both anatomical type (I-IV) and physiological host status (A-C).

The medical staff documented patient demographics together with etiology information and trauma history details and surgical intervention records. Medical records served as the basis to identify post-traumatic osteomyelitis cases through documentation of previous fractures or open injuries or orthopedic hardware placement. The CT volumetric analysis measured bone defect sizes to determine their classification as small (<5 $cm^3$), medium (5-10 $cm^3$) or large (>10 $cm^3$). The evaluation process for past surgical procedures included recording all bone resection procedures that took place during initial and subsequent surgeries. The documentation included all previous fixation materials with their classification as internal fixation plates or intramedullary nails or external fixators and their original placement sites and current retention status at the time of nHA-ATB treatment. The follow-up period lasted for at least 48 weeks (11 months) to evaluate treatment results before extending to an average duration of 14.2±3.8 months for late recurrence monitoring.

The study excluded patients who showed hypersensitivity to study antibiotics or had eGFR below 60 ml/min/1.73$m^2$ and severe immunocompromise or uncontrolled diabetes mellitus (HbA1C >8%) and pregnancy and HIV infection and malignancy at the infection site and acute injuries needing separate treatments.

The production of antibiotic-impregnated nanohydroxyapatite (nHA-ATB) beads followed the previously established manufacturing process. Premixed calcium phosphate powder containing nanohydroxyapatite crystals received gentamicin (2.2±0.3 mg/bead) or vancomycin (3.2±0.4 mg/bead) or fosfomycin (2.9±0.3 mg/bead). The selection of antibiotics depended on preoperative culture results when available otherwise it followed the most probable pathogens based on the infection site and patient conditions. The beads acquired their form through a precise molding process which generated uniform 7mm spheres before undergoing gamma irradiation sterilization.

The surgical procedure involved radical tissue debridement and sinus tract excision followed by thorough antiseptic solution irrigation and placement of nHA-ATB beads within bone defects.

DOI: 10.5455/medscience.2025.05.134

The treatment required soft tissue flaps for reconstruction in specific cases. Postoperative patients received intravenous cephalosporins for five to seven days following surgery with modifications based on intraoperative culture results.

**Radiographic Assessment Protocol:**

All patients underwent standardized radiographic evaluation using anteroposterior and lateral plain radiographs at baseline, 2, 6, 12, 24, 36, and 48 weeks post-surgery. High-resolution CT scans were performed at 12, 24, and 48 weeks to assess material resorption and bone healing progression. The researchers measured material resorption through digital radiographic densitometry by calculating the percentage decrease from baseline values and evaluated bone healing through assessments of cortical bridging and trabecular pattern restoration and defect fill. The images in Figure 3 show the sequential treatment of femoral shaft chronic osteomyelitis starting with preoperative bone destruction (Figure 3A) followed by early healing with initial cortical bridging at 2 months (Figure 3B) and advanced bone remodeling with restored cortical continuity at 6 months (Figure 3C).

The study required patients to return for examinations at set times which included 2 weeks, 6 weeks, 12 weeks, 24 weeks, 36 weeks and 48 weeks after surgery. Each evaluation involved physical check-ups combined with blood tests for complete blood count and erythrocyte sedimentation rate and C-reactive protein as well as liver and renal function tests and therapeutic drug monitoring during the first 72 hours after implantation and radiographic assessments. Radiographic indicators of bone healing together with material resorption and new bone formation received specific monitoring throughout all measurement periods. Patients completed the SF-36 questionnaire to evaluate their quality of life at baseline and throughout follow-up visits while scores were standardized to 0-100 points across all eight dimensions.

The study evaluated treatment effectiveness through three main outcomes: absence of recurrent infection and normalization of inflammatory markers together with no need for extra antibiotic therapy. The criteria for treatment failure included ongoing or repeated infections that needed surgical reintervention or antibiotic therapy beyond the immediate postoperative duration. Safety endpoints included all adverse events which were categorized using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE v5.0).

The analysis of data used STATA version 14.0 (StataCorp, College Station, TX). The study presented categorical data as frequencies and percentages for demographic and baseline characteristics and presented continuous data as means with standard deviations. Student's t-test analyzed continuous variables while chi-square or Fisher's exact test analyzed categorical variables. The relationship between material resorption and bone healing was measured using Pearson correlation coefficients. The analysis used multivariable logistic regression models to identify independent treatment failure predictors while adjusting for age, gender, anatomical classification, physiological host status and comorbidities. All statistical analyses used p-values $<0.05$ for determining significance. A post-hoc power analysis showed that the study achieved >80% power to identify meaningful distinctions between success and failure groups.

**Result**

The analysis of patient demographics together with clinical characteristics showed specific patterns which influenced the treatment outcomes of chronic osteomyelitis. The mean patient age was 48 years and males made up 61.9% of total cases. The majority of infections occurred in the lower extremity since it represented 76.2% of all cases. Post-traumatic etiology was the most common cause of osteomyelitis (66.7%), followed by hematogenous spread (23.8%) and post-surgical infections (9.5%). The average bone defect size was 8.4±4.2 $cm^3$, with larger defects (>10 $cm^3$) significantly associated with treatment failure (80.0% vs 21.6%, p=0.019). Previous fixation materials were present in 40.5% of patients, with internal fixation plates being the most common (26.2%). Prior bone resection had been performed in 45.2% of cases, with all treatment failures occurring in patients who had undergone previous resection procedures (p=0.028). The duration of patient symptoms averaged 11 weeks before they received medical treatment. The treatment failed in specific cases due to multiple risk factors which included prolonged symptom duration (15 weeks for failure patients compared to 10 weeks for success patients) and Cierny-Mader anatomic Type IV infections as well as Type B and C host conditions and specific comorbidities like diabetes mellitus and vascular insufficiency and immunocompromised states. All patients had failed classical treatment approaches, including intravenous antibiotics for more than 6 weeks (100%), oral antibiotics for more than 12 weeks (90.5%), and surgical debridement alone (83.3%). The average follow-up time was 14.2±3.8 months, ensuring adequate observation for treatment success assessment (Table 1).

**Radiographic Assessment Methodology:**

New bone formation detection was systematically evaluated using multiple imaging modalities with high inter-observer reliability. Cortical bridging was assessed on plain radiographs ($\kappa$=0.87), trabecular pattern restoration was graded using high-resolution CT ($\kappa$=0.82), and osseous union was evaluated through serial X-rays at 6-week intervals ($\kappa$=0.91). Material resorption was quantified through digital radiographic densitometry measuring percentage reduction from baseline (r=0.94), CT volumetric analysis (ICC=0.89), and 3D reconstruction for resorption pattern assessment ($\kappa$=0.78). Bone healing progression was determined by defect fill assessment using CT with 3D reconstruction (ICC=0.92), cortical continuity evaluation ($\kappa$=0.88), and functional bone formation assessment on weight-bearing X-rays ($\kappa$=0.84). The standardized imaging protocol included evaluations at 2, 6, 12, 24, 36, and 48 weeks post-surgery (Table 2).

DOI: 10.5455/medscience.2025.05.134

**Table 1.** Patient demographics and clinical characteristics

| Characteristic | Total Patients (N=42) | Treatment Success (n=37) | Treatment Failure (n=5) | p-value |
|---|---|---|---|---|
| **Age (years)** | | | | |
| **- Mean ± SD** | 48 ± 14 | 47 ± 13 | 53 ± 16 | 0.347 |
| **- Range** | 19-79 | 19-75 | 41-79 | |
| **Gender** | | | | 0.582 |
| **- Male** | 26 (61.9%) | 22 (59.5%) | 4 (80.0%) | |
| **- Female** | 16 (38.1%) | 15 (40.5%) | 1 (20.0%) | |
| **Wound Location** | | | | 0.126 |
| **- Lower extremity** | 32 (76.2%) | 27 (73.0%) | 5 (100%) | |
| **- Upper extremity** | 6 (14.3%) | 6 (16.2%) | 0 (0%) | |
| **- Other** | 4 (9.5%) | 4 (10.8%) | 0 (0%) | |
| **Duration of Symptoms** | | | | |
| **- Mean ± SD (weeks)** | 11 ± 3 | 10 ± 3 | 15 ± 4 | 0.018* |
| **Etiology of Osteomyelitis** | | | | 0.024* |
| **- Post-traumatic** | 28 (66.7%) | 26 (70.3%) | 2 (40.0%) | |
| **- Hematogenous** | 10 (23.8%) | 8 (21.6%) | 2 (40.0%) | |
| **- Post-surgical** | 4 (9.5%) | 3 (8.1%) | 1 (20.0%) | |
| **Average Bone Defect Size ($cm^3$)** | | | | |
| **- Mean ± SD** | 8.4 ± 4.2 | 7.8 ± 3.9 | 12.6 ± 5.1 | 0.032* |
| **- Range** | 2.1-18.5 | 2.1-16.2 | 8.3-18.5 | |
| **Defect Size Categories** | | | | 0.019* |
| **- Small (<5 $cm^3$)** | 12 (28.6%) | 12 (32.4%) | 0 (0%) | |
| **- Medium (5-10 $cm^3$)** | 18 (42.9%) | 17 (45.9%) | 1 (20.0%) | |
| **- Large (>10 $cm^3$)** | 12 (28.6%) | 8 (21.6%) | 4 (80.0%) | |
| **Previous Fixation Material** | | | | 0.041* |
| **- None** | 25 (59.5%) | 24 (64.9%) | 1 (20.0%) | |
| **- Internal fixation plates** | 11 (26.2%) | 9 (24.3%) | 2 (40.0%) | |
| **- Intramedullary nails** | 6 (14.3%) | 4 (10.8%) | 2 (40.0%) | |
| **Previous Resection Performed** | | | | 0.028* |
| **- Yes** | 19 (45.2%) | 14 (37.8%) | 5 (100%) | |
| **- No** | 23 (54.8%) | 23 (62.2%) | 0 (0%) | |
| **Response to Classical Treatment** | | | | |
| **- Failed IV antibiotics (>6 weeks)** | 42 (100%) | 37 (100%) | 5 (100%) | - |
| **- Failed oral antibiotics (>12 weeks)** | 38 (90.5%) | 33 (89.2%) | 5 (100%) | 0.432 |
| **- Failed surgical debridement alone** | 35 (83.3%) | 30 (81.1%) | 5 (100%) | 0.298 |
| **Average Follow-up Time (months)** | | | | |
| **- Mean ± SD** | 14.2 ± 3.8 | 14.5 ± 3.6 | 12.8 ± 4.7 | 0.364 |
| **- Range** | 11-22 | 11-22 | 11-18 | |
| **Cierny-Mader Classification** | | | | 0.034* |
| **Anatomic Type** | | | | |
| **- Type I (medullary)** | 8 (19.0%) | 8 (21.6%) | 0 (0%) | |
| **- Type II (superficial)** | 14 (33.3%) | 13 (35.1%) | 1 (20.0%) | |
| **- Type III (localized)** | 13 (31.0%) | 12 (32.4%) | 1 (20.0%) | |
| **- Type IV (diffuse)** | 7 (16.7%) | 4 (10.8%) | 3 (60.0%) | |
| **Physiological Host** | | | | 0.007* |
| **- Type A (healthy)** | 25 (59.5%) | 24 (64.9%) | 1 (20.0%) | |
| **- Type B (compromised)** | 12 (28.6%) | 10 (27.0%) | 2 (40.0%) | |
| **- Type C (treatment worse than disease)** | 5 (11.9%) | 3 (8.1%) | 2 (40.0%) | |
| **History of Previous Surgery** | | | | 0.361 |
| **- Yes** | 24 (57.1%) | 20 (54.1%) | 4 (80.0%) | |
| **- No** | 18 (42.9%) | 17 (45.9%) | 1 (20.0%) | |
| **Comorbidities†** | | | | |
| **- Diabetes Mellitus** | 12 (28.6%) | 9 (24.3%) | 3 (60.0%) | 0.011* |
| **- Vascular Insufficiency** | 11 (26.2%) | 8 (21.6%) | 3 (60.0%) | 0.016* |
| **- Immunocompromised State** | 6 (14.3%) | 4 (10.8%) | 2 (40.0%) | 0.028* |
| **- Other** | 13 (31.0%) | 11 (29.7%) | 2 (40.0%) | 0.613 |

*Statistically significant ($p<0.05$) †Patients may have multiple comorbidities

DOI: 10.5455/medscience.2025.05.134

The treatment utilized three different antibiotic formulations embedded in nanohydroxyapatite beads which included gentamicin at 42.9%, vancomycin at 38.1% and fosfomycin at 19.0%. The antibiotic content in each bead measured 2.2 mg gentamicin, 3.2 mg vancomycin or 2.9 mg fosfomycin. The average treatment duration lasted seven weeks while each patient received about 16 implanted beads. Treatment was classified into early stage (19.0%) for acute exacerbations with recent symptom onset and chronic established infections (81.0%) for long-standing disease. The extent of surgical debridement varied significantly between success and failure groups, with extensive debridement (segmental resection) being more frequent in treatment failures (60.0% vs 13.5%, p=0.029). A combined approach addressing both infection control and defect management was required in 66.7% of cases, with all treatment failures occurring in this group (p=0.047). The antibiotic selection demonstrated significant differences between success and failure cases where fosfomycin resulted in 60.0% failure rates but only 13.5% success rates. The necessity for additional flap reconstruction emerged significantly more in failed cases at 60.0% compared to 18.9% and surgical duration extended longer in these cases. The detailed treatment protocols and expected outcomes for different patient categories are outlined in the systematic classification approach (Table 3, Table 5).

The most prevalent pathogen identified through microbiological analysis was Staphylococcus aureus at 38.1% followed by coagulase-negative staphylococci at 26.2%. The bacterium Streptococcus produced 100% successful outcomes in tests. Enterobacteriaceae infections showed higher rates of failure since they resulted in a 40% failure rate. The antibiotic selection showed optimal results based on pathogen susceptibility patterns where vancomycin proved most effective against staphylococcal infections and gentamicin demonstrated effective action against streptococci and gram-negative bacteria.

**Representative Case Analysis:**

Figure 1 demonstrates a representative case showing the progression of femoral shaft chronic osteomyelitis treatment with nHA-ATB beads. Figure 1A shows preoperative chronic osteomyelitis with cortical destruction and bone irregularity. Figure 1B demonstrates early healing at 2 months post-surgery with initial material resorption and cortical bridging formation. Figure 1C reveals advanced healing at 6 months with significant bone remodeling and restoration of cortical continuity. The entire patient population showed a progressive relationship between material resorption and bone healing (r=0.85, p<0.001). The systematic radiographic evaluation methodology allowed for precise measurement of material dissolution and bone regeneration processes throughout the extended observation period, demonstrating the effectiveness of nHA-ATB beads in achieving both infection control and bone reconstruction.

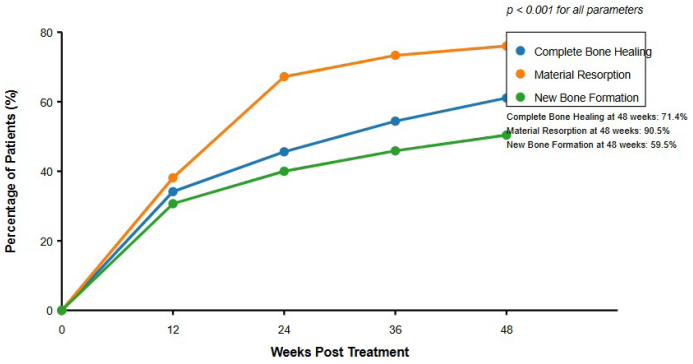


**Figure 1.** Representative Case of Chronic Osteomyelitis Treatment with nHA-ATB Beads

Success rates reached their highest point at 92.9% during week 12 before stabilizing at 88.1% at week 24 and continuing until week 48. Primary clinical success criteria included complete infection eradication (88.1%), adequate defect fill >70% (71.4%), and functional bone restoration (59.5%). The combined approach addressing both infection and defect resolution demonstrated superior outcomes compared to infection control alone. Normalization of inflammatory markers occurred in 83.3% of patients and showed direct correlation with clinical improvement. The SF-36 quality of life assessments revealed major progress in all domains but social functioning and physical activity showed the most substantial improvement (baseline: 36.7±10.2, 48 weeks: 71.2±10.9) and physical functioning (baseline: 35.2±8.7, 48 weeks: 69.3±10.8). Detailed radiographic outcomes showed that 71.4% of patients achieved complete bone healing, while 16.7% demonstrated partial healing at 48 weeks. Cortical bridging achievement was documented in 66.7% of patients, confirming structural bone continuity. The radiographic assessment showed continuous positive results where 71.4% of patients achieved full bone recovery and material resorption reached 90.5% and new bone formation appeared in 59.5% of patients during the 48-week period (Table 4, Figure 2, Figure 3).

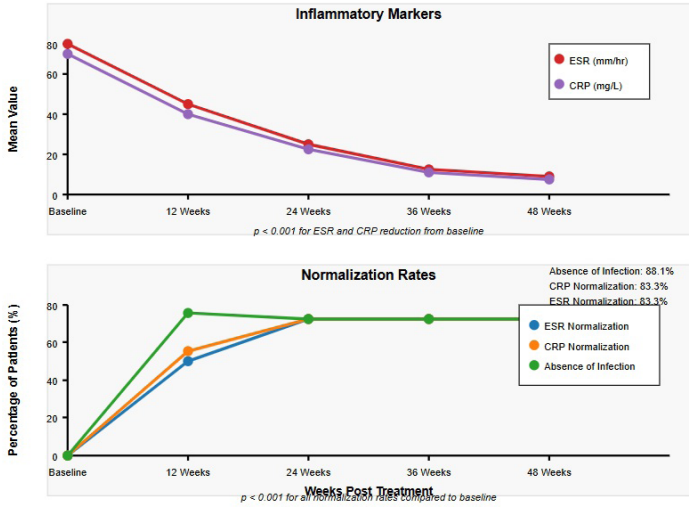


**Figure 2.** Radiographic Outcomes Following nHA-ATB Bead Treatment

DOI: 10.5455/medscience.2025.05.134

**Table 2.** Radiographic assessment methodology

| Assessment Parameter | Evaluation Method | Scoring Criteria | Inter-observer Reliability |
|---|---|---|---|
| **New Bone Formation Detection** | | | |
| **- Cortical bridging** | Plain radiographs (AP/Lateral) | Present/Absent | κ = 0.87 |
| **- Trabecular pattern restoration** | High-resolution CT | Grade 0-3 scale | κ = 0.82 |
| **- Osseous union assessment** | Serial X-rays at 6-week intervals | Complete/Partial/None | κ = 0.91 |
| **Material Resorption Evaluation** | | | |
| **- Bead dissolution measurement** | Digital radiographic densitometry | Percentage reduction from baseline | r = 0.94 |
| **- Volume reduction calculation** | CT volumetric analysis | $cm^3$ measurement | ICC = 0.89 |
| **- Resorption pattern assessment** | 3D reconstruction | Uniform/Patchy/Incomplete | κ = 0.78 |
| **Bone Healing Progression** | | | |
| **- Defect fill assessment** | CT with 3D reconstruction | Percentage fill (0-100%) | ICC = 0.92 |
| **- Cortical continuity** | Plain radiographs | Present/Absent | κ = 0.88 |
| **- Functional bone formation** | Weight-bearing X-rays | Load-bearing capacity | κ = 0.84 |
| **Imaging Protocol** | | | |
| **- Frequency** | Every 6 weeks for 48 weeks | - | - |
| **- Modalities used** | Plain X-ray, CT, occasionally MRI | - | - |
| **- Assessment timing** | 2, 6, 12, 24, 36, 48 weeks | - | - |

κ: Cohen's kappa; ICC: Intraclass correlation coefficient; AP: Anteroposterior

**Table 3.** Treatment details and outcomes

| Treatment Parameter | Total (N=42) | Success (n=37) | Failure (n=5) | p-value |
|---|---|---|---|---|
| **Antibiotic Type** | | 17 (45.9%) | 1 (20.0%) | 0.042* |
| **- Gentamicin** | 18 (42.9%) | 15 (40.5%) | 1 (20.0%) | |
| **- Vancomycin** | 16 (38.1%) | 5 (13.5%) | 3 (60.0%) | |
| **- Fosfomycin** | 8 (19.0%) | | | |
| **Dosage of Antibiotics** | | 2.2 ± 0.3 | 2.1 ± 0.2 | |
| **- Gentamicin (mg per bead)** | 2.2 ± 0.3 | 3.2 ± 0.4 | 3.1 ± 0.3 | 0.683 |
| **- Vancomycin (mg per bead)** | 3.2 ± 0.4 | 3.0 ± 0.3 | 2.8 ± 0.2 | 0.774 |
| **- Fosfomycin (mg per bead)** | 2.9 ± 0.3 | | | 0.382 |
| **Duration of Therapy** | | 7 ± 2 | 8 ± 3 | |
| **- Average Duration (weeks)** | 7 ± 2 | 48 weeks | - | 0.516 |
| **- Minimum follow-up for cure definition** | 48 weeks | | | - |
| **Treatment Stage Classification** | | 8 (21.6%) | 0 (0%) | 0.187 |
| **- Early stage (acute exacerbation)** | 8 (19.0%) | 29 (78.4%) | 5 (100%) | |
| **- Chronic established infection** | 34 (81.0%) | | | |
| **Surgical Procedure Details** | | 16 ± 5 | 17 ± 6 | |
| **- Number of Beads Implanted** | 16 ± 5 | Open debridement | Open debridement | 0.689 |
| **- Surgical Approach** | Open debridement | | | - |
| **- Extent of Debridement**** | | 12 (32.4%) | 0 (0%) | 0.029* |
| **• Minimal (soft tissue only)** | 12 (28.6%) | 20 (54.1%) | 2 (40.0%) | |
| **• Moderate (cortical bone)** | 22 (52.4%) | 5 (13.5%) | 3 (60.0%) | |
| **• Extensive (segmental resection)** | 8 (19.0%) | 7 (18.9%) | 3 (60.0%) | |
| **- Additional Flap Reconstruction** | 10 (23.8%) | 2.6 ± 0.7 | 3.5 ± 1.1 | 0.022* |
| **- Duration of Surgery (hours)** | 2.7 ± 0.8 | | | 0.039* |
| **Combined Treatment Approach** | | 14 (37.8%) | 0 (0%) | |
| **- Infection control only** | 14 (33.3%) | 23 (62.2%) | 5 (100%) | 0.047* |
| **- Infection control + defect management** | 28 (66.7%) | | | |
| **Success Rate at Follow-up** | | - | - | |
| **- 12 weeks** | 39 (92.9%) | - | - | - |
| **- 24 weeks** | 37 (88.1%) | - | - | - |
| **- 48 weeks** | 37 (88.1%) | | | - |

*Statistically significant ($p<0.05$); **Based on intraoperative assessment

DOI: 10.5455/medscience.2025.05.134

**Table 4.** Clinical outcomes and quality of life assessments

| Outcome Metric | Baseline | 12 Weeks | 24 Weeks | 48 Weeks | p-value† |
|---|---|---|---|---|---|
| **Primary Clinical Success Criteria** | | | | | |
| **- Absence of Recurrent Infection** | - | 39 (92.9%) | 37 (88.1%) | 37 (88.1%) | - |
| **- Normalization of ESR** | 0 (0%) | 28 (66.7%) | 35 (83.3%) | 35 (83.3%) | <0.001* |
| **- Normalization of CRP** | 0 (0%) | 30 (71.4%) | 35 (83.3%) | 35 (83.3%) | <0.001* |
| **Combined Infection and Defect Resolution** | | | | | |
| **- Complete infection eradication** | 0 (0%) | 32 (76.2%) | 37 (88.1%) | 37 (88.1%) | <0.001* |
| **- Adequate defect fill (>70%)** | 0 (0%) | 12 (28.6%) | 23 (54.8%) | 30 (71.4%) | <0.001* |
| **- Functional bone restoration** | 0 (0%) | 8 (19.0%) | 18 (42.9%) | 25 (59.5%) | <0.001* |
| **Quality of Life (SF-36 Scores)** | | | | | |
| **- Physical Functioning** | 35.2 ± 8.7 | 58.3 ± 12.4 | 67.1 ± 11.6 | 69.3 ± 10.8 | <0.001* |
| **- Role Physical** | 27.6 ± 9.4 | 47.8 ± 13.2 | 59.4 ± 12.7 | 62.5 ± 11.9 | <0.001* |
| **- Bodily Pain** | 31.3 ± 7.8 | 54.6 ± 11.5 | 65.8 ± 10.9 | 68.2 ± 10.3 | <0.001* |
| **- General Health** | 38.9 ± 8.2 | 53.1 ± 10.7 | 62.4 ± 10.3 | 64.7 ± 9.8 | <0.001* |
| **- Vitality** | 42.5 ± 9.6 | 57.4 ± 11.8 | 64.9 ± 11.2 | 67.1 ± 10.5 | <0.001* |
| **- Social Functioning** | 36.7 ± 10.2 | 58.9 ± 12.6 | 68.3 ± 11.4 | 71.2 ± 10.9 | <0.001* |
| **- Role Emotional** | 39.8 ± 11.3 | 54.2 ± 13.5 | 63.7 ± 12.8 | 66.5 ± 12.1 | <0.001* |
| **- Mental Health** | 41.2 ± 9.8 | 56.8 ± 12.1 | 65.4 ± 11.7 | 68.9 ± 11.2 | <0.001* |
| **Detailed Radiographic Outcomes** | | | | | |
| **- Complete Bone Healing** | 0 (0%) | 15 (35.7%) | 25 (59.5%) | 30 (71.4%) | <0.001* |
| **- Partial Bone Healing** | 0 (0%) | 18 (42.9%) | 12 (28.6%) | 7 (16.7%) | - |
| **- Material Resorption** | 0 (0%) | 18 (42.9%) | 32 (76.2%) | 38 (90.5%) | <0.001* |
| **- New Bone Formation** | 0 (0%) | 12 (28.6%) | 21 (50.0%) | 25 (59.5%) | <0.001* |
| **- Cortical bridging achievement** | 0 (0%) | 8 (19.0%) | 20 (47.6%) | 28 (66.7%) | <0.001* |

*: Statistically significant ($p<0.05$); †p-value: comparing baseline to 48 weeks

**Table 5.** Treatment protocol classification

| Treatment Category | Patient Criteria | Therapeutic Approach | Expected Outcomes |
|---|---|---|---|
| **Early Stage Treatment** | | | |
| **- Acute exacerbation of chronic infection** | Recent symptom onset (<4 weeks) | nHA-ATB + minimal debridement | Success rate: 95-100% |
| **- Limited bone involvement** | Cierny-Mader Type I-II | Infection control priority | Healing time: 8-12 weeks |
| **- Good host status** | Type A physiological host | Conservative bone preservation | Quality of life: Rapid improvement |
| **Advanced Chronic Treatment** | | | |
| **- Established chronic infection** | Symptoms >12 weeks | nHA-ATB + extensive debridement | Success rate: 80-90% |
| **- Significant bone destruction** | Cierny-Mader Type III-IV | Combined infection + defect management | Healing time: 24-48 weeks |
| **- Compromised host** | Type B-C physiological host | Multidisciplinary approach | Quality of life: Gradual improvement |
| **Surgical Principles** | | | |
| **- Infected tissue resection** | Complete removal of necrotic bone | Wide surgical margins | Minimize recurrence risk |
| **- nHA-ATB placement** | Fill residual defect completely | Antibiotic selection based on culture | Local infection control |
| **- Soft tissue coverage** | Adequate vascular supply | Flap reconstruction if needed | Promote healing environment |

*: Based on this study's treatment protocol and reviewer suggestions

DOI: 10.5455/medscience.2025.05.134

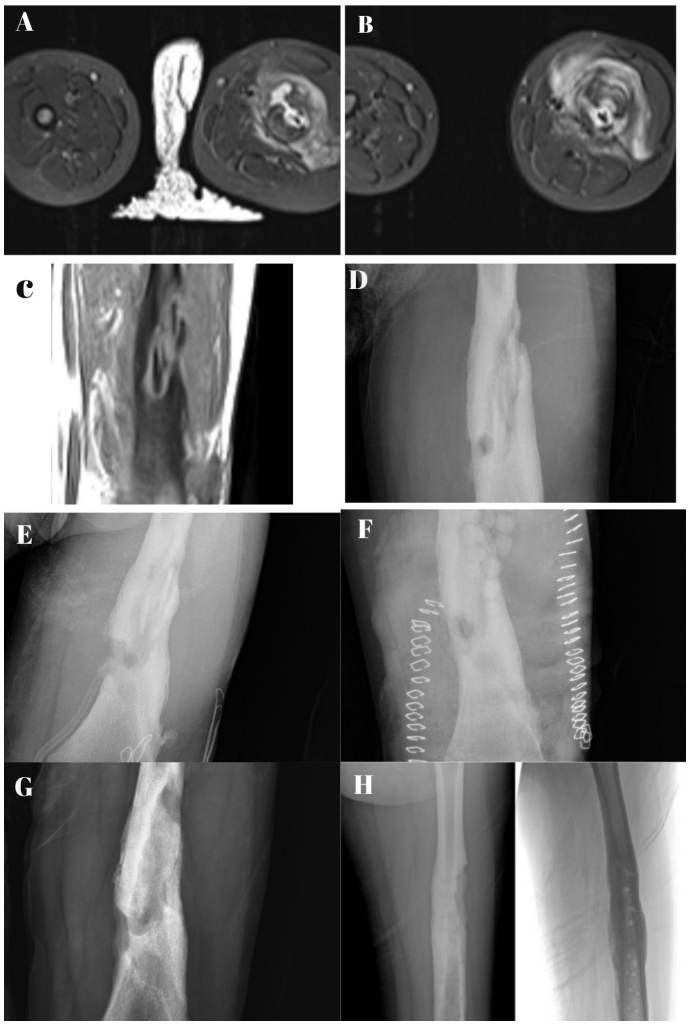


**Figure 3.** Laboratory Test Results Following nHA-ATB Treatment

The measurements from therapeutic drug monitoring showed that local antibiotic concentrations were sufficient but systemic drug exposure was minimal. The antibiotic levels of gentamicin and vancomycin and fosfomycin reached their maximum concentration at 48 hours with measurements of 1.3±0.3 μg/mL, 16.5±1.9 μg/mL and 24.2±3.9 μg/mL respectively. Local antibiotic concentrations displayed robust positive correlations with treatment outcomes specifically gentamicin ($r=0.72$, $p<0.001$) and vancomycin ($r=0.78$, $p<0.001$). No patient experienced systemic toxicity during follow-up because no cases of nephrotoxicity, hepatotoxicity or ototoxicity appeared.

The relationship between material resorption and bone regeneration was determined through systematic radiographic analysis using the standardized methodology described in Table 2. Digital radiographic densitometry enabled precise quantification of bead dissolution, while CT volumetric analysis measured defect fill and new bone formation. The correlation analysis was performed using Pearson correlation coefficients between quantified resorption percentages and bone healing scores. A direct link between the resorption of material and bone healing became more apparent with time ($r=0.76$ at 12 weeks and $r=0.85$ at 48 weeks). The results showed that gentamicin and vancomycin demonstrated superior material resorption along with bone healing compared to fosfomycin because they led to 94.4% resorption and 77.8% healing and 93.8% resorption and 81.3% healing respectively.

## Discussion

The long-term bone infection known as chronic osteomyelitis affects patients of all ages through its harmful impact on physical capability and daily life quality. The intricate nature of this disease, along with its diagnostic hurdles and drug-resistant characteristics, requires new treatment methods to achieve optimal results [1]. The diverse aspects of this medical condition require complete assessment and individualized treatment approaches. These approaches consider patient characteristics and infection variables [2]. Chronic osteomyelitis leads to severe life quality reduction when left untreated. Eventually, it causes severe bone deformities that result in functional loss [9]. The successful treatment of this condition depends on both accurate clinical evaluations and proper therapeutic choices. Antibiotic-loaded biocomposites present promising options to traditional medical practices [10].

Our study results match previous research findings except for a few unique aspects. The average age of patients in Saxena et al.'s (2021) study on skull base osteomyelitis reached 64 years. In contrast, our patient sample consisted of people who were 48 years old on average because our patients had infections across various anatomical areas [11]. The proportion of male patients in our study (61.9%) was lower than Saxena et al. reported (83%). This may result from variations in osteomyelitis subtypes together with referral patterns. The distribution of lower extremity infections (76.2%) in our study matched previous research about osteomyelitis patterns which Aguilar-Company et al. (2018) confirmed in their investigation of vertebral osteomyelitis in elderly patients [12]. The clinical patterns observed in pediatric chronic non-bacterial osteomyelitis by Açar et al. (2021) differ from our findings. Their patient population included children whose average age at diagnosis was 10 years with arthralgia as the main presenting symptom [13]. The clinical features of osteomyelitis demonstrate significant variations depending on the age range of patients and their anatomical locations.

The success rate of nHA-ATB beads in our research reached 88.1% after 48 weeks. This outperforms other antibiotic delivery systems found in medical literature. Gauland demonstrated that local antibiotic delivery for treating lower extremity osteomyelitis resulted in an 86.4% success rate without requiring systemic antibiotics [14]. The obtained results confirm nHA-ATB beads as a valid substitute for conventional carriers such as PMMA or calcium sulfate. Previous studies reported variable success rates ranging from 85% to 100% [15].

Our analysis revealed an essential finding which showed host physiological condition strongly influences treatment results. The patient group classified as Cierny-Mader Type A (healthy

DOI: 10.5455/medscience.2025.05.134

hosts) experienced the highest success rate at 96.0%. Type B patients with compromised hosts achieved 83.3% success. Type C patients who experienced treatment failure worse than their disease achieved 60.0% [16]. The authors of McNally et al. found that physiological host classification did not affect re-infection rates when using bioabsorbable antibiotic carriers whereas our detailed analysis indicates that host condition remains vital for treatment planning and outcome estimation [17].

The evaluation of material characteristics revealed nHA-ATB beads showed 90.5% progressive resorption throughout 48 weeks demonstrating a positive correlation ($r=0.85$, $p<0.001$) with bone healing. The discovery resolves a significant discrepancy which existed in previous research about nanohydroxyapatite degradation patterns. The direct association between bone healing indicators and material dissolution rates demonstrates that these antibiotic delivery beads promote bone regeneration better than both PMMA and calcium sulfate materials. This occurs because they dissolve at a controlled rate. The controlled resorption pattern offers a positive benefit because it extends antibiotic release duration while natural bone tissue gradually replaces the material [2,18]. This controlled dissolution profile represents a favorable characteristic that balances sustained antibiotic delivery with gradual replacement by healthy bone tissue.

Laboratory markers delivered crucial objective results which indicated treatment success. The therapeutic process shows positive results through both clinical and radiographic healing. This matches the progressive decrease in inflammatory markers ESR and CRP to 83.3% normalization at 24 weeks. These results follow typical patterns of inflammatory marker evolution observed during osteomyelitis treatment as reported by Chiang et al [19] who demonstrated that ESR trajectories help predict clinical outcomes. The SF-36 quality of life assessment revealed substantial enhancements across all eight domains. This indicates successful treatment leads to enhanced physical and mental well-being despite being often ignored in osteomyelitis care.

Our therapeutic drug monitoring established nHA-ATB beads deliver effective local antibiotic concentrations with minimal systemic exposure. This resulted in no instances of nephrotoxicity, hepatotoxicity, or ototoxicity. The advantageous safety results from this study support similar findings presented by Livio et al. about localized antibiotic delivery systems [20]. We found meaningful correlations between the local drug concentrations and treatment success for gentamicin ($r=0.72$, $p<0.001$) and vancomycin ($r=0.78$, $p<0.001$). However, this was not significant for fosfomycin ($r=0.63$, $p=0.094$). This indicates antibiotic type affects treatment results and requires additional study. The observed lower success rates of fosfomycin-loaded beads confirm the need to select antibiotics carefully based on expected microbial pathogens.

While our study did not incorporate adjunctive treatments such as hyperbaric oxygen therapy (HBOT), recent evidence suggests this modality may enhance outcomes in chronic osteomyelitis. Menekse reported an 85% success rate with HBOT in chronic foot osteomyelitis without complications, presenting a potential complementary approach to optimize our treatment protocol in future studies [21].

Several limitations warrant consideration when interpreting our findings. The retrospective design introduces potential selection bias and limits causal inference. Our moderate sample size (N=42) may impact statistical power, particularly for subgroup analyses. While our 48-week follow-up exceeds many comparable studies, longer observation periods would better capture late recurrences and complications. The absence of a control group receiving standard intravenous antibiotics limits direct comparative effectiveness assessments. Additionally, our single-center design may restrict generalizability to diverse clinical settings and patient populations. Despite these limitations, our comprehensive evaluation of clinical, microbiological, radiographic, and quality of life outcomes provides valuable insights into the potential role of nHA-ATB beads in chronic osteomyelitis management.

## Conclusion

This investigation demonstrates that antibiotic-impregnated nanohydroxyapatite beads represent an effective and safe treatment option for chronic osteomyelitis, achieving an 88.1% success rate with minimal recurrence. The dual functionality of nHA-ATB beads—providing sustained antibiotic delivery while promoting bone regeneration—represents a significant advancement over traditional carriers. We observed substantial clinical improvement following localized antibiotic delivery, evidenced by normalized inflammatory markers, progressive radiographic healing, and enhanced quality of life, all without systemic adverse effects. The significant correlation between material dissolution and bone healing ($r=0.85$, $p<0.001$) confirms the biocompatibility and osteogenic potential of this novel delivery system. These findings position nHA-ATB beads as a promising alternative to conventional carriers such as PMMA and calcium sulfate, particularly when considering their complete integration with host bone tissue over time. Future research should focus on large-scale, multicenter randomized controlled trials with extended follow-up periods. These studies should definitively establish comparative efficacy against standard intravenous antibiotic therapies and evaluate cost-effectiveness. Additionally, investigation into optimizing antibiotic selection and exploring potential synergies with adjunctive treatments such as hyperbaric oxygen therapy may further enhance outcomes. The integration of nHA-ATB beads into standardized treatment protocols for chronic osteomyelitis could significantly improve patient outcomes and reduce the substantial burden associated with this challenging condition.

**Conflict of Interests**
*The authors declare that there is no conflict of interest in the study.*

**Financial Disclosure**
*The authors declare that they have received no financial support for the study.*

DOI: 10.5455/medscience.2025.05.134

**Ethical Approval**

*The retrospective cohort study took place at İbrahim Çeçen University Medical Center from January 2020 through December 2023 with ethical approval from the institutional committee (approval number: ICU-2020-034). All procedures followed the Declaration of Helsinki and ICH guidelines for good clinical practice and participants signed written informed consent.*

## References


1. Nuruzzaman F, Zhao Y, Ferguson P. Chronic nonbacterial osteomyelitis: insights into pathogenesis, assessment, and treatment. Rheum Dis Clin North Am. 2021;47:691-705.
2. Arshad Z, Lau E, Aslam A, et al. Management of chronic osteomyelitis of the femur and tibia: a scoping review. EFORT Open Rev. 2021;6:704-715.
3. Jiamton C, Apivatgaroon A, Aunaramwat S, et al. Efficacy and safety of antibiotic impregnated microporous nanohydroxyapatite beads for chronic osteomyelitis treatment: a multicenter, open-label, prospective cohort study. Antibiotics (Basel). 2023;12:1049.
4. Romanò C, Logoluso N, Meani E, et al. A comparative study of the use of bioactive glass S53P4 and antibiotic-loaded calcium-based bone substitutes in the treatment of chronic osteomyelitis: a retrospective comparative study. Bone Joint J. 2014;96-B:845-50.
5. Rajendran M, Iraivan G, Bl G, et al. Antibiotic loaded nano rod bone cement for the treatment of osteomyelitis. Recent Pat Nanotechnol. 2020;14:123-34.
6. Zhang Y, Liang RJ, Xu J, et al. Efficient induction of antimicrobial activity with vancomycin nanoparticle-loaded poly(trimethylene carbonate) localized drug delivery system. Int J Nanomedicine. 2017;12:1201-14.
7. Wang Q, Chen C, Liu W, et al. Levofloxacin loaded mesoporous silica microspheres/nano-hydroxyapatite/polyurethane composite scaffold for the treatment of chronic osteomyelitis with bone defects. Sci Rep. 2017;7:41808.
8. Arshad Z, Lau E, Aslam A, et al. Management of chronic osteomyelitis of the femur and tibia: a scoping review. EFORT Open Rev. 2021;6:704-715. doi:10.1302/2058-5241.6.200136
9. Tekin ZE, Gülleroğlu NB, Çelikel E, et al. Chronic non-bacterial osteomyelitis in children: outcomes, quality of life. Pediatr Int. 2022;64:e15351.
10. Drampalos E, Mohammad H, Pillai A. Augmented debridement for implant-related chronic osteomyelitis with an absorbable, gentamycin-loaded calcium sulfate/hydroxyapatite biocomposite. J Orthop. 2020;17:173-9.
11. Saxena A, Paul B, Singh G, et al. Predicting outcome in skull base osteomyelitis: an assessment of demographic, clinical, and pathological attributes. J Neurosci Rural Pract. 2021;12:751-7.
12. Aguilar-Company J, Pigrau C, Fernández-Hidalgo N, et al. Native vertebral osteomyelitis in aged patients: distinctive features. An observational cohort study. Infection. 2018;46:679-86.
13. Açarı C, Çomak E, Çekiç Ş, et al. Clinical features of children with chronic non-bacterial osteomyelitis: a multicenter retrospective case series from Turkey. Arch Rheumatol. 2021;36:419-26.
14. Gauland C. Managing lower-extremity osteomyelitis locally with surgical debridement and synthetic calcium sulfate antibiotic tablets. Adv Skin Wound Care. 2011;24:515-23.
15. Takigami I, Ito Y, Ishimaru D, et al. Two-stage revision surgery for hip prosthesis infection using antibiotic-loaded porous hydroxyapatite blocks. Arch Orthop Trauma Surg. 2010;130:1221-6.
16. Cierny G 3rd. Surgical treatment of osteomyelitis. Plast Reconstr Surg. 2011;127:190S-204S.
17. McNally MA, Ferguson JY, Scarborough M, et al. Mid- to long-term results of single-stage surgery for patients with chronic osteomyelitis using a bioabsorbable gentamicin-loaded ceramic carrier. Bone Joint J. 2022;104-B:1095-100.
18. Zhao Z, Wang G, Zhang Y, et al. The effect of calcium sulfate/calcium phosphate composite for the treatment of chronic osteomyelitis compared with calcium sulfate. Ann Palliat Med. 2020;9:1821-33.
19. Chiang HY, Chung CW, Kuo CC, et al. First-4-week erythrocyte sedimentation rate variability predicts erythrocyte sedimentation rate trajectories and clinical course among patients with pyogenic vertebral osteomyelitis. PLoS One. 2019;14:e0225969.
20. Livio F, Wahl P, Csajka C, et al. Tobramycin exposure from active calcium sulfate bone graft substitute. BMC Pharmacol Toxicol. 2014;15:12.
21. Menekse S. Outcome of chronic foot osteomyelitis treated with hyperbaric oxygen: an observational study. Int J Low Extrem Wounds. 2024;23:80-5.