Comparison of Preoperative Serum Albumin Levels in Patients With and Without Early Infection Following Intramedullary Nailing of Femur Fractures

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Abstract:

Introduction: Early postoperative infection following intramedullary fixation of femur fractures is a significant complication in orthopedic surgery, associated with increased morbidity, prolonged hospital stay, and higher healthcare costs. Patient nutritional status and preoperative biological markers, particularly serum albumin levels, play a crucial role in immune response and tissue healing. Therefore, this study aimed to compare preoperative serum albumin levels between patients with and without early infection following intramedullary fixation of the femur.

Methods: This case-control study was conducted at Shohada Hospital, Tabriz, in 2024. A total of 70 patients (35 in the infection group and 35 in the non-infection group) were enrolled. Preoperative serum albumin levels were measured, and patients were systematically monitored for signs of infection for up to four weeks postoperatively. Quantitative variables were compared using the independent-samples t-test, while qualitative variables were analyzed using the Chi-square test.

Results: The mean preoperative serum albumin level was significantly lower in patients who developed early infection compared to those without infection. Specifically, the mean ± standard deviation of serum albumin was 2.98 ± 0.41 g/dL in the infection group and 3.78 ± 0.36 g/dL in the non-infection group ($P < 0.001$).

Conclusion: The findings of this study demonstrate a statistically significant association between lower preoperative serum albumin levels and an increased risk of early infection following intramedullary femur fixation. These results suggest that preoperative nutritional assessment, particularly through simple and accessible markers such as serum albumin, can serve as a valuable auxiliary tool in identifying high-risk patients and guiding informed clinical decision-making.

Keywords: Serum albumin, Early infection, Femur surgery, Intramedullary femoral fixation

Introduction

Postoperative orthopedic infections, particularly those involving internal metal hardware, remain among the most daunting clinical challenges, imposing substantial increases in patient morbidity, length of hospital stay, and healthcare expenditures.[1]

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Received: 00/00/2026
Accepted: 00/00/2026

Please Cite this Article as:
Al-Yasin V, Neshat Ghalibaf M, Maroufi M. Comparison of Preoperative Serum Albumin Levels in Patients With and Without Early Infection Following Intramedullary Nailing of Femur Fractures. Iranian Journal of Surgery. 2026; 34 (3): ?-?. doi:

Despite notable refinements in surgical techniques and preventive strategies, early infection after femoral intramedullary fixation continues to occur, carrying severe long-term functional implications for affected patients.[2]

Early implant-associated infections typically manifest within the initial postoperative weeks and generally stem from a multifaceted interplay among microbial burden, intraoperative conditions, and host immune defenses.[3] Such infections may lead to hardware loosening, recurrent debridement, implant exchange or hardware removal, and ultimately protracted functional impairment.[4] Identifying modifiable and measurable preoperative risk determinants is therefore pivotal to averting implant-related infections and enhancing clinical decision-making.[5] In this context, evaluating the patient's overall physiological status and baseline biological profile prior to surgery warrants heightened attention.[6]

In recent years, patient nutritional status has gained widespread recognition as a major determinant of postoperative outcomes.[7] Malnutrition compromises host immunity, impairs tissue repair, and heightens susceptibility to infection, negatively impacting recovery following major surgical interventions.[8]

Serum albumin serves as a practical, widely accessible parameter for evaluating baseline nutritional and inflammatory status and has been extensively investigated across diverse clinical settings.[9] Depressed serum albumin concentrations often mirror malnutrition, ongoing systemic inflammation, or chronic underlying conditions.[10] Beyond its classical role in preserving plasma oncotic pressure, albumin is actively involved in ligand transport, inflammatory modulation, free-radical scavenging, and immune regulation.[11] Consequently, diminished serum albumin may undermine host resilience against postoperative infectious challenges.[12]

A growing body of literature indicates that preoperative hypoalbuminemia correlates with an elevated incidence of postoperative adverse events, including surgical site infections and delayed wound healing.[13] This association is particularly prominent in orthopedic procedures characterized by extensive soft-tissue trauma and metallic hardware implantation.[14] In femoral surgery, internal hardware provides a conducive substrate for microbial colonization and biofilm formation.[15] Under such circumstances, compromised host defenses allow opportunistic pathogens to establish early infection.[16]

Substantial evidence suggests that patients presenting with reduced preoperative serum albumin levels are particularly vulnerable to implant-associated infections.[17] Nevertheless, most previous investigations have addressed albumin merely as a secondary parameter or as a postoperative sequela.[18] Evaluating baseline serum albumin levels prior to surgical intervention creates an opportunity to stratify patients by infectious risk beforehand.[19] Such a proactive approach establishes a clinical foundation for timely, targeted preventive measures prior to implant placement.[20]

Because early infection after femoral intramedullary fixation develops within a short post-injury window, it typically reflects an unfavorable baseline biological milieu at the time of surgery.[21] In this setting, serum albumin—acting as an integrated marker of nutritional adequacy and systemic inflammation—represents a pertinent indicator for assessing host susceptibility.[22] From a practical standpoint, preoperative identification of vulnerable individuals allows clinicians to optimize nutritional support, tailor perioperative antibiotic prophylaxis, and implement closer postoperative surveillance.[23] These targeted interventions can help curtail the incidence of early infection and optimize surgical outcomes.[24]

Despite the clinical relevance of this issue, available evidence regarding the correlation between preoperative serum albumin levels and early infection following femoral intramedullary nailing remains limited and inconsistent.[25] Furthermore, variations across study populations, dietary patterns, and institutional management protocols constrain the generalizability of earlier reports.[26] Conducting regional investigations is essential to elucidate this relationship within specific clinical environments. Such local data are indispensable for designing risk-adapted preventive protocols in orthopedic practice. Therefore, the present study was conducted to

compare preoperative serum albumin levels between patients with and without early infection following intramedullary fixation of femur fractures.

Methods

Study Design

This investigation was structured as a case-control study. The case cohort comprised patients diagnosed with early infection following femoral Küntscher (intramedullary) nailing, whereas the control cohort consisted of uninfected patients undergoing the same procedure. The source population encompassed trauma patients indicated for femoral intramedullary nailing who received surgical management at Shohada Hospital, Tabriz, during 2024.

Eligibility Criteria – Infection Cohort

Inclusion criteria for the case group were trauma patients with isolated femoral fractures who underwent femoral intramedullary nailing within 72 hours of injury and subsequently developed early postoperative infection during initial follow-up. Exclusion criteria comprised polytrauma, concurrent fractures in other skeletal regions, preexisting active infection prior to surgery, known immunocompromising conditions, chronic corticosteroid therapy, chronic renal or hepatic failure, active malignancies, and incomplete clinical documentation.

Eligibility Criteria – Non-Infection Cohort

Inclusion criteria for the control group included trauma patients with isolated femoral fractures who underwent femoral intramedullary nailing within 72 hours post-injury and demonstrated no clinical or laboratory evidence of infection throughout the follow-up period. Exclusion criteria mirrored those of the case cohort, ruling out polytrauma, systemic conditions affecting immunological or nutritional competence, prior surgical site infection, and missing clinical data.

Matching Process

To mitigate confounding, individual matching was performed between the case and control cohorts. Participants were matched for age, sex, fracture pattern, timing of surgery (≤72 hours post-injury), hardware type, surgical technique, and baseline clinical status. This rigorous matching strategy was applied to ensure that observed discrepancies between groups could be predominantly attributed to baseline preoperative serum albumin levels.

Sampling Strategy

Over the one-year study window, all consecutive eligible trauma patients who developed early infection following femoral intramedullary nailing were enrolled via total population (census) sampling. For each infected patient, a matched uninfected control was selected and allocated to the control cohort. Ultimately, the sample size was established at 35 patients per group, totaling 70 participants.

Study Protocol

Upon identification of eligible candidates, peripheral venous blood samples were drawn upon hospital admission, prior to any therapeutic intervention or extensive fluid resuscitation. Samples were transferred under standardized conditions to the hospital central laboratory, where serum albumin concentrations were determined via the bromocresol green (BCG) colorimetric assay. Identical reagent kits were utilized across all specimens to eliminate inter-assay variability. All assays were executed by designated laboratory personnel, with automated equipment calibrated daily.

Postoperative monitoring was performed through an active, structured follow-up regimen. Patients were thoroughly assessed for signs of infection during their inpatient stay, at hospital discharge, and during scheduled outpatient visits throughout the initial four weeks postoperatively. Evaluations comprised

wound inspections, monitoring of systemic signs, and review of inflammatory markers. Whenever infection was suspected, wound discharge was sampled for microbiological cultures, and the definitive diagnosis of infection was reached through consensus by the attending orthopedic and clinical care team.

Extracted data—including laboratory profiles, time to onset of symptoms, need for reoperation or supplementary interventions, and duration of hospital readmission—were systematically entered into standardized case report forms. To minimize observer bias, the investigator responsible for clinical data collection was blinded to the patients' baseline albumin levels throughout the follow-up period. Following data completion, entries were coded, imported into a central database, and verified for entry errors and discrepancies prior to formal statistical processing.

Statistical Analysis

Collected data were analyzed using SPSS software. The normality of continuous variables was assessed and confirmed via the Kolmogorov-Smirnov test. Quantitative variables were compared between groups using the independent-samples t-test, while qualitative categorical parameters were evaluated using the Chi-square test. For all statistical evaluations, a two-tailed P-value of less than 0.05 was defined as the threshold for statistical significance.

Ethical Considerations

The study protocol was reviewed and granted ethical clearance by the Research Ethics Committee of Tabriz University of Medical Sciences (ethical code: IR.TBZMED.REC.1404.008). All patient data were recorded and handled with strict confidentiality, and research ethics principles—including patient privacy protection and exclusive data usage for authorized scientific purposes—were stringently upheld.

Results

Comparison of baseline demographic and clinical characteristics revealed no statistically significant differences between the two groups regarding age (P = 0.671), sex distribution (P = 0.624), body mass index (P = 0.703), history of cigarette smoking (P = 0.598), and diabetes mellitus (P = 0.741). Furthermore, no significant differences were observed between the two groups in terms of trauma mechanism (P = 0.631), time to surgery (P = 0.639), and length of hospital stay (P = 0.468). These findings indicate appropriate baseline homogeneity between the study groups and minimize the confounding effect of potential variables on the association between preoperative serum albumin and the occurrence of early infection (Table 1).

Table 1Baseline demographic and clinical characteristics of patients in the two study groups

Variable	*Infection Group (N = 35)*	*Non-Infection Group (N = 35)*	*P-value*
Age (years), mean ± SD	*41.31 ± 15.84*	*40.76 ± 14.92*	*0.671*
Male sex, n (%)	*23 (65.71)*	*21 (60.00)*	*0.624*
Body mass index (kg/m²), mean ± SD	*24.98 ± 3.21*	*25.14 ± 3.08*	*0.703*
History of smoking, n (%)	*11 (31.43)*	*9 (25.71)*	*0.598*
Diabetes mellitus, n (%)	*6 (17.14)*	*5 (14.29)*	*0.741*
High-energy trauma mechanism, n (%)	*19 (54.29)*	*21 (60.00)*	*0.631*
Time to surgery (hours), mean ± SD	36.48 ± 14.67	34.92 ± 13.85	0.639
Length of stay (days), mean ± SD	7.41 ± 2.63	6.98 ± 2.44	0.468

The mean preoperative serum albumin level was significantly lower in patients who developed early infection compared to those without infection. Specifically, the mean ± standard deviation of serum albumin was reported as 2.98 ± 0.41 g/dL in the infection group and 3.78 ± 0.36 g/dL in the non-infection group. Comparison between the two groups using the independent-samples t-test demonstrated that this difference was statistically significant ($P < 0.001$); the mean difference between the two groups was estimated at 0.80 g/dL (95% confidence interval: 0.65 to 0.95). Moreover, the evaluation of the effect size for the mean difference revealed a very large clinical effect size (Cohen's d = 2.07 and eta-squared $\eta^2 = 0.51$), indicating that the occurrence of infection accounts for the majority of the variance in preoperative serum albumin levels (Figure 1).

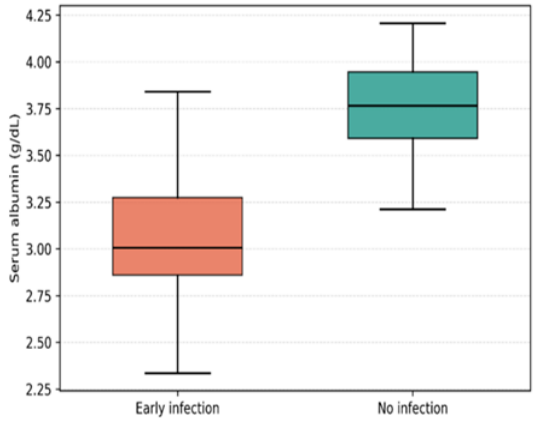


Figure 1. Comparison of preoperative serum albumin levels between patients with and without early infection following femoral Küntscher nail fixation.

Discussion

The aim of the present study was to compare preoperative serum albumin levels in patients with and without early infection following intramedullary femur fixation. The findings demonstrated that the mean preoperative serum albumin level in patients who developed early infection following intramedullary femoral fixation was significantly lower than in those who experienced no infectious complications after surgery. This discrepancy underscores the potential role of patient nutritional and metabolic status in the onset of early infections following orthopedic procedures.

Albumin is considered one of the most vital indicators of the body's nutritional status, and its reduction often reflects malnutrition, systemic inflammatory response, or a combination of both. In trauma patients or candidates for orthopedic surgery, depletion of protein reserves can lead to impaired collagen synthesis, soft tissue repair, and bone remodeling. These processes play a fundamental role in surgical wound healing, and any disruption within them can provide a favorable environment for the proliferation and growth of microorganisms. Numerous studies have indicated that preoperative hypoalbuminemia is associated with an increased incidence of surgical site infections and other postoperative complications.[13,14]

From an immunological perspective, reduced albumin levels are accompanied by a depression of both innate and adaptive immune functions. Albumin indirectly modulates neutrophil and macrophage activity as well as inflammatory responses, and its reduction can impair chemotaxis, phagocytosis, and the effective clearance of infectious agents. In patients with metallic implants, this immunological impairment assumes heightened importance because the presence of foreign material creates a conducive substrate for bacterial biofilm formation. Biofilms enhance the resistance of microorganisms to host immunity and antibiotic therapy, and in nutritionally compromised patients, the persistence of infection is far more likely.[15,16]

In addition to its immunological effects, albumin plays a crucial role in maintaining plasma oncotic pressure and body fluid balance. Decreased albumin can lead to fluid leakage into the interstitial space and tissue edema at the surgical site. Tissue edema is associated with reduced local blood supply and oxygenation, which is itself a key factor in delayed wound healing and heightened

susceptibility to infection. In major orthopedic surgeries such as intramedullary femur fixation, optimal tissue conditions are essential for preventing infection, and any impairment in perfusion can lead to adverse outcomes.[17,18]

The findings of this study align with previous research in the field of orthopedic surgery. Various studies have demonstrated that patients with low preoperative albumin levels experience higher rates of early and late infections, prolonged hospital stays, and an increased requirement for secondary surgical interventions. Nevertheless, many of these investigations have examined heterogeneous populations or diverse types of surgical procedures. The focus of the present study on patients undergoing intramedullary femur fixation and the investigation of early infections provides added value to the existing body of evidence, highlighting the role of albumin within the critical early postoperative window.[19,20]

From a clinical utility standpoint, the results of this study indicate that measuring preoperative serum albumin can serve as a simple, cost-effective, and accessible tool for identifying high-risk patients. Identifying these individuals prior to surgery enables targeted interventions such as nutritional optimization, metabolic conditioning, intensified infectious prophylaxis, and, in elective cases, appropriate surgical timing. Such an approach can play an important role in reducing the incidence of early infections and improving surgical outcomes.[21,22]

Despite these notable findings, the study has certain limitations. The case-control design and relatively modest sample size may limit the generalizability of the results, and the evaluation of other nutritional or inflammatory markers such as prealbumin or CRP was not feasible. Nonetheless, rigorous matching of the study groups and the focus on a specific biochemical variable represent strengths of this investigation, thereby reinforcing the validity of the findings.

Conclusion

The findings of this study demonstrate a statistically significant difference between lower preoperative serum albumin levels and an increased likelihood of early infection following intramedullary femur fixation surgery. These results suggest that the evaluation of patient nutritional status prior to surgery, particularly through simple and accessible markers such as serum albumin, can be considered as an auxiliary tool in identifying patients prone to complications and in making more informed clinical decisions.

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