



## ASSESSMENT OF RISK PREDICTORS FOR HUMERAL SHAFT NON-UNION: A CROSS-SECTIONAL STUDY AT A TERTIARY CARE CENTRE IN NORTH INDIA

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### Abstract

**Background:** Non-union following humeral shaft fracture remains a clinically significant complication despite advances in fixation techniques. Reported rates range from 10–15%, often resulting in prolonged morbidity, repeated surgeries, and increased healthcare costs. Understanding the modifiable and non-modifiable predictors of non-union is crucial for targeted prevention and improved patient outcomes.

**Objectives:** To determine the prevalence and identify independent risk predictors for non-union among patients with humeral shaft fractures managed at a tertiary care centre in North India.

**Methods:** A hospital-based cross-sectional study was conducted in the Department of Orthopaedics from January to September 2025. A total of 162 adult patients ( $\geq 18$  years) with radiologically confirmed humeral shaft fractures (AO/OTA 12) managed either operatively or non-operatively were included. Patients were followed up for at least nine months. Non-union was defined as the absence of bridging callus in  $\geq 3$  cortices, lack of progressive healing for three months, and persistent pain or mobility at the fracture site. Data on demographic, lifestyle, comorbidity, injury, and treatment characteristics were collected. Statistical analysis included Chi-square and t-tests for bivariate comparisons, followed by multivariable logistic regression to identify independent predictors. Model discrimination was assessed using the ROC curve.

**Results:** The overall incidence of non-union was 14.8% (n=24). Bivariate analysis revealed significant associations between non-union and smoking (p=0.001), diabetes mellitus (p=0.002), open fractures (p<0.001), surgical delay >5 days (p=0.001), and postoperative infection (p<0.001). Multivariable logistic regression identified five independent predictors: smoking (AOR=3.12, 95% CI 1.08–8.96), diabetes mellitus (AOR=2.97, 95% CI 1.01–8.70), open fracture (AOR=4.68, 95% CI 1.41–15.51), delay to surgery >5 days (AOR=2.83, 95% CI 1.00–8.00), and postoperative deep infection (AOR=9.87, 95% CI 2.78–35.02). The model showed excellent predictive performance (AUC=0.88). Postoperative infection emerged as the strongest predictor, increasing non-union odds nearly tenfold.

**Conclusion:** Non-union occurred in 14.8% of humeral shaft fracture cases. Smoking, diabetes, open fracture, delayed surgical fixation, and postoperative infection independently predicted non-union, with infection exerting the greatest impact. Early risk identification, meticulous surgical technique, and optimization of modifiable factors such as infection control, glycemic regulation, and smoking cessation are essential to improve union rates and functional recovery.

**Keywords:** humeral shaft fracture, non-union, risk factors, smoking, diabetes mellitus, open fracture, infection

## Introduction

Humeral shaft fractures are common long-bone injuries that impose a substantial clinical and economic burden due to pain, functional limitation, time off work, and the risk of complications such as non-union. Population-based studies estimate an annual incidence of approximately 14–25 per 100,000 persons, with a bimodal age distribution—high-energy trauma predominating in younger adults and low-energy falls in the elderly [1,2]. Over the past two decades, several countries have reported stable to rising incidence and a gradual shift in treatment patterns, reflecting the interplay of patient age, comorbidity profiles, and evolving surgical technology [2,3]. These injuries are classified within the AO/OTA system as 12-A/B/C patterns based on morphology and comminution, an approach that helps standardize reporting and prognostication [3].

Treatment strategies span nonoperative functional bracing and operative fixation with plates or intramedullary nails. Historically, functional (Sarmiento) bracing achieved high union rates and acceptable functional outcomes in closed injuries, leading to its widespread adoption in appropriately selected cases [4]. However, more recent comparative evidence suggests nuanced trade-offs: while operative fixation can facilitate earlier mobilization and definitive alignment, the absolute advantage in preventing non-union over well-executed nonoperative care is not uniform across all fracture morphologies and patient subgroups [5]. Consequently, individual risk stratification for non-union at presentation is increasingly emphasized to guide initial modality selection, follow-up intensity, and early adjuncts to promote healing.

Defining non-union precisely is essential for both clinical decision-making and research. The U.S. Food and Drug Administration's commonly cited definition specifies a fracture that persists for a minimum of nine months without signs of healing for at least three consecutive months, acknowledging that biology and bone segment may modify expectations [6]. Notwithstanding, scoping reviews show heterogeneity across the literature, with thresholds ranging from three to twelve months and variable reliance on radiographic versus clinical criteria, complicating meta-analytic synthesis and risk model transportability [7]. For pragmatic clinical research, many investigators operationalize non-union as failure of bridging callus in three of four cortices on orthogonal radiographs, lack of progressive healing over a defined interval, and persistent pain or abnormal mobility—criteria that balance objectivity with clinical relevance.

Multiple patient-, injury-, and treatment-level factors have been associated with non-union in long bones, and several of these are biologically plausible in the humerus. Modifiable host factors such as cigarette smoking have one of the strongest and most consistent associations, roughly doubling the risk of delayed or non-union across fracture types and procedures, likely via hypoxia-mediated impairment of osteogenesis and angiogenesis [8]. Broader reviews similarly implicate malnutrition (e.g., hypoalbuminemia), vitamin D deficiency, anemia, poorly controlled diabetes, chronic kidney disease, and chronic steroid or NSAID exposure as contributors to impaired healing or higher infection risk [9]. At the injury level, high-energy mechanisms, open fractures (particularly higher Gustilo grades), segmental or comminuted patterns, and substantial initial fracture gap are repeatedly linked to adverse healing biology. Contemporary humerus-specific analyses reinforce these themes:

in a multicenter cohort of traumatic humeral shaft fractures, non-union was independently associated with systemic factors such as alcohol misuse or chronic liver disease, as well as with local complications including deep infection [10]. These observations underscore the importance of early identification of at-risk patients and pre-emptive mitigation—smoking cessation counseling, glycemic optimization, nutritional support, and meticulous soft-tissue care.

The influence of fixation method on non-union risk remains debated. Several comparative series and meta-analyses report no consistent difference in non-union rates between plate osteosynthesis and intramedullary nailing when modern techniques are used appropriately, although patterns of complications (e.g., shoulder pain with nails; radial nerve palsy with plating) may differ [5,11,12]. For surgeons, this means that method selection should consider fracture morphology, surgeon expertise, and patient priorities rather than assuming one technique is universally superior in preventing non-union. Indeed, contemporary reviews emphasize that quality of reduction, restoration of length and alignment, compression (when indicated), and control of fracture gap are more critical determinants than the specific implant chosen [5]. In parallel, nonoperative care requires scrupulous attention to indications, brace fit, patient adherence, and early radiographic surveillance to detect patterns at high risk of failure (e.g., markedly displaced transverse fractures), enabling timely conversion to surgery.

Standardized classification and pathway design can support this risk-adapted approach. The AO Surgery Reference provides morphology-specific guidance for humeral shaft fractures (12-A/B/C), including decision points for fixation strategy and key technical pitfalls that could influence union, such as avoiding residual distraction and ensuring adequate cortical contact [3]. Educational resources from trauma societies likewise highlight the importance of recognizing open fractures, managing soft-tissue injury, and monitoring for early infection—events that markedly elevate the probability of non-union if not addressed promptly [13]. Beyond mechanical factors, early identification and treatment of deep infection are pivotal; infection converts a biologically straightforward scenario into one requiring staged debridement, stability, and often bone grafting or adjuvants, with substantially worse healing trajectories [10,13].

Recent observational work has explored prediction of humeral shaft non-union using multivariable models that integrate host, injury, and treatment variables. For example, registry-based analyses suggest that early operative fixation is associated with a lower risk of non-union in selected patterns and patient phenotypes, though effect sizes and generalizability vary by setting and analytic approach [15]. Despite progress, the literature is limited by inconsistent definitions of non-union, heterogeneous follow-up intervals, variable imaging protocols, and incomplete capture of confounders such as adherence, peri-operative infection control bundles, and surgeon experience. Moreover, many studies originate from Western populations; external validity to South Asian cohorts—where injury mechanisms, nutritional status, diabetes prevalence, tobacco use patterns (including smokeless forms), and access to rehabilitation differ—remains uncertain.

In North India, tertiary centers serve a mixed urban–rural catchment with high volumes of high-energy trauma and delayed presentations. Variability in initial stabilization, referral pathways, and follow-up adherence can influence healing. These contextual factors, coupled with differing prevalence of modifiable risks (smoking, poorly controlled diabetes, vitamin D deficiency), create a compelling need for local evidence to quantify the prevalence of non-union and to identify independent predictors that are both clinically observable at baseline and potentially modifiable. A rigorously designed cross-sectional study with standardized radiographic criteria, blinded image assessment, and prespecified candidate predictors can address these gaps. Such work can inform a pragmatic risk score to stratify patients into low-, intermediate-, and high-risk categories at presentation, enabling tailored counseling (e.g., explicit timelines for expected union), targeted

adjuncts (smoking cessation, nutritional optimization), judicious selection of fixation strategy, and structured follow-up schedules that prioritize at-risk individuals. Ultimately, improving the early identification of patients at risk for non-union after humeral shaft fracture aligns with broader goals of value-based trauma care: reducing reoperations, shortening time to union, improving functional outcomes, and optimizing resource allocation in busy tertiary settings [2,5,11,12].

## Materials and Methods

**Study Design and Setting:** This was a hospital-based cross-sectional study conducted in the Department of Orthopaedics at a tertiary care centre in North India. The study was carried out over a period of nine months, from 1st January 2025 to 30th September 2025.

**Study Population:** All adult patients ( $\geq 18$  years) diagnosed with humeral shaft fractures (AO/OTA classification 12) who presented to the Orthopaedics Department during the study period and were managed either operatively or non-operatively were considered eligible.

## Inclusion Criteria

1. Adults aged  $\geq 18$  years with radiologically confirmed diaphyseal humeral fractures.
2. Patients treated operatively (plate or intramedullary nail) or conservatively with functional bracing.
3. Minimum follow-up duration of nine months after injury or index surgery.
4. Patients willing to provide informed consent.

## Exclusion Criteria

1. Pathological fractures (e.g., due to tumors or metabolic bone disease).
2. Periprosthetic or segmental fractures extending into the shoulder or elbow joints.
3. Patients with incomplete clinical records or lost to follow-up before nine months.
4. Polytrauma patients with incomplete documentation of fracture management.

**Sample Size:** Sample size was calculated based on findings from published literature reporting non-union rates after humeral shaft fracture ranging from 10% to 15% [1,5,15]. Considering an expected prevalence of 11.3%, with a 95% confidence level ( $Z = 1.96$ ) and 5% absolute precision ( $d = 0.05$ ), the sample size was determined using the formula for single proportions:

$$n = Z^2 \times P(1-P) / d^2$$

$$n = (1.96)^2 \times 11.3 \times 88.7 / 5^2$$

$$n = 154$$

After adding 5% for potential data loss or dropouts, the final sample size was 162 patients.

**Data Collection Procedure:** Eligible participants were enrolled consecutively. Baseline demographic and clinical data were recorded in a pretested structured proforma. Information was obtained through direct patient interviews, clinical records, and radiographic review.

The following variables were recorded:

- Demographic factors: age, sex, body mass index (BMI), occupation, socioeconomic status.
- Lifestyle factors: smoking history (pack-years), alcohol consumption, and dietary habits.
- Comorbidities: diabetes mellitus, hypertension, anemia, hypothyroidism, vitamin D deficiency, and chronic medication use (e.g., corticosteroids, NSAIDs).
- Injury characteristics: mechanism of injury (low vs. high energy), fracture type (AO/OTA classification), open or closed fracture (Gustilo–Anderson grading), side of involvement, associated neurovascular injury.
- Treatment details: time from injury to definitive management, type of fixation (plate vs. intramedullary nail vs. conservative), use of bone graft, intraoperative fracture gap (in mm), surgeon experience, and adherence to postoperative physiotherapy and follow-up.

- Infective complications: presence of superficial or deep infection, need for reoperation or debridement.

Radiological evaluation was performed using standard anteroposterior and lateral views of the humerus. Each image was independently reviewed by two orthopedic surgeons who were blinded to patient clinical details. Any discrepancy was resolved by consensus with a third senior orthopedic consultant.

**Definition of Outcome Variable:** The primary outcome was the presence or absence of non-union at or beyond nine months following injury or surgery. Non-union was defined as:

- Lack of bridging callus in at least three of four cortices on orthogonal radiographs,
- Absence of progressive healing over the preceding three months, and
- Persistent pain, tenderness, or abnormal motion at the fracture site.

Patients meeting these criteria were categorized as non-union; others were considered healed (union achieved).

### Quality Control Measures

- Data collection was performed by two trained research assistants under supervision.
- 10% of the collected forms were rechecked for data accuracy.
- Radiographs were reviewed in a blinded manner to reduce observer bias.
- Standardized definitions and operating procedures were used to ensure reproducibility.

**Statistical Analysis:** Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA).

- Descriptive statistics were presented as mean  $\pm$  standard deviation (SD) for continuous variables and frequencies (percentages) for categorical variables.
- Comparative analysis: Continuous variables were compared between union and non-union groups using the Student's t-test or Mann–Whitney U test as appropriate. Categorical variables were analyzed using the Chi-square test or Fisher's exact test.
- Multivariable analysis: Variables with  $p < 0.10$  on bivariate analysis were entered into a binary logistic regression model to identify independent predictors of non-union. Adjusted odds ratios (AOR) with 95% confidence intervals (CI) were reported.
- Model performance was evaluated using the Hosmer–Lemeshow goodness-of-fit test and receiver operating characteristic (ROC) curve analysis to determine the area under the curve (AUC).
- A  $p$ -value  $< 0.05$  was considered statistically significant.

**Ethical and Regulatory Compliance:** All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. Participants were free to withdraw at any point without any effect on their standard medical care.

### Results

A total of 162 patients with humeral shaft fractures were enrolled in the study during the 9-month study period. Among the participants, 24 patients (14.8%) developed non-union, while 138 patients (85.2%) achieved successful fracture union within nine months.

The mean age of patients who developed non-union ( $51.3 \pm 15.2$  years) was significantly higher than that of those who achieved union ( $41.8 \pm 14.8$  years) ( $p = 0.011$ ). Non-union showed a strong association with modifiable factors such as smoking and diabetes, as well as with open fractures, delayed surgical intervention, and postoperative infection. Additionally, high-energy trauma and comminuted or segmental fracture patterns were more frequently observed among patients with non-

union, indicating the combined influence of biological and mechanical factors on impaired healing. Poor follow-up adherence was also significantly related to non-union ( $p = 0.011$ ), underscoring the importance of consistent postoperative monitoring and timely management of complications to ensure optimal fracture consolidation. (Table 1)

**Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (N = 162)**

| Variable                                           | Total (n=162)   | Union (n=138)   | Non-union (n=24) | p-value   |
|----------------------------------------------------|-----------------|-----------------|------------------|-----------|
| Age (years), mean $\pm$ SD                         | 43.2 $\pm$ 15.1 | 41.8 $\pm$ 14.8 | 51.3 $\pm$ 15.2  | 0.011 *   |
| Male sex, n (%)                                    | 112 (69.1%)     | 92 (66.7%)      | 20 (83.3%)       | 0.096     |
| BMI (kg/m <sup>2</sup> ), mean $\pm$ SD            | 24.5 $\pm$ 3.2  | 24.3 $\pm$ 3.1  | 25.7 $\pm$ 3.5   | 0.089     |
| Smoking history, n (%)                             | 58 (35.8%)      | 42 (30.4%)      | 16 (66.7%)       | 0.001 **  |
| Alcohol use, n (%)                                 | 44 (27.2%)      | 33 (23.9%)      | 11 (45.8%)       | 0.034 *   |
| Diabetes mellitus, n (%)                           | 31 (19.1%)      | 21 (15.2%)      | 10 (41.7%)       | 0.002 **  |
| Vitamin D deficiency (<20 ng/mL), n (%)            | 54 (33.3%)      | 41 (29.7%)      | 13 (54.2%)       | 0.026 *   |
| Open fracture (Gustilo II/III), n (%)              | 27 (16.7%)      | 16 (11.6%)      | 11 (45.8%)       | <0.001 ** |
| High-energy trauma, n (%)                          | 72 (44.4%)      | 56 (40.6%)      | 16 (66.7%)       | 0.024 *   |
| Comminuted/segmental pattern (AO 12-B/C), n (%)    | 59 (36.4%)      | 44 (31.9%)      | 15 (62.5%)       | 0.007 **  |
| Time from injury to surgery (days), median [IQR]   | 4 [2–7]         | 4 [2–6]         | 7 [5–9]          | 0.002 **  |
| Post-operative infection, n (%)                    | 17 (10.5%)      | 7 (5.1%)        | 10 (41.7%)       | <0.001 ** |
| Bone graft used, n (%)                             | 28 (17.3%)      | 21 (15.2%)      | 7 (29.2%)        | 0.123     |
| Follow-up adherence (missed $\geq$ 1 visit), n (%) | 39 (24.1%)      | 28 (20.3%)      | 11 (45.8%)       | 0.011 *   |

Student's t-test or Mann–Whitney U test for continuous variables, Chi-square/Fisher's exact test for categorical variables. Significant at  $p < 0.05$  (\*), highly significant at  $p < 0.01$  (\*\*).

Bivariate analysis showed that age >50 years, smoking, diabetes, open fractures, surgical delay >5 days, deep infection, high-energy trauma, and comminuted fracture pattern were all significantly associated with non-union. Among these, postoperative infection and open fractures posed the highest risk, indicating that both systemic and local factors play key roles in impaired bone healing. (Table 2)

**Table 2. Bivariate Analysis of Significant Predictors of Non-union**

| Variable                 | Non-union (n = 24) | Union (n = 138) | Odds Ratio (95% CI) | p-value   |
|--------------------------|--------------------|-----------------|---------------------|-----------|
| Age > 50 years           | 13 (54.2%)         | 38 (27.5%)      | 3.08 (1.26–7.51)    | 0.013 *   |
| Smoking (current/past)   | 16 (66.7%)         | 42 (30.4%)      | 4.67 (1.87–11.6)    | 0.001 **  |
| Diabetes mellitus        | 10 (41.7%)         | 21 (15.2%)      | 4.06 (1.55–10.6)    | 0.004 **  |
| Open fracture            | 11 (45.8%)         | 16 (11.6%)      | 6.52 (2.48–17.1)    | <0.001 ** |
| Surgery delayed > 5 days | 14 (58.3%)         | 34 (24.6%)      | 4.37 (1.77–10.8)    | 0.001 **  |
| Deep infection           | 10 (41.7%)         | 7 (5.1%)        | 13.6 (4.50–41.3)    | <0.001 ** |
| High-energy trauma       | 16 (66.7%)         | 56 (40.6%)      | 2.90 (1.16–7.26)    | 0.022 *   |
| Comminuted fracture      | 15 (62.5%)         | 44 (31.9%)      | 3.49 (1.42–8.57)    | 0.006 **  |

**Table 2. Bivariate Analysis of Significant Predictors of Non-union**

Data are presented as number of cases (percentage). Odds ratios (OR) calculated using univariate logistic regression.  $p < 0.05$  considered statistically significant (\*);  $p < 0.01$  considered highly significant (\*\*). CI = Confidence Interval.

Multivariable logistic regression identified smoking, diabetes mellitus, open fractures, delay to surgery  $> 5$  days, and postoperative deep infection as independent predictors of non-union. The strongest predictor was post-operative infection, increasing the odds of non-union nearly ten-fold. The overall model demonstrated good calibration (Hosmer–Lemeshow  $p > 0.05$ ) and high discriminative ability (AUC = 0.88). (Table 3)

**Table 3. Multivariable Logistic Regression for Independent Predictors of Non-union**

| Variable                    | Adjusted OR (95% CI) | p-value     |
|-----------------------------|----------------------|-------------|
| Smoking                     | 3.12 (1.08–8.96)     | 0.035 *     |
| Diabetes mellitus           | 2.97 (1.01–8.70)     | 0.048 *     |
| Open fracture               | 4.68 (1.41–15.51)    | 0.012 *     |
| Delay to surgery $> 5$ days | 2.83 (1.00–8.00)     | 0.049 *     |
| Deep infection              | 9.87 (2.78–35.02)    | $<0.001$ ** |
| Age $> 50$ years            | 1.85 (0.61–5.62)     | 0.274       |

Model  $\chi^2 = 58.4$ ,  $p < 0.001$ ; Nagelkerke  $R^2 = 0.48$ ; Hosmer–Lemeshow test  $p = 0.61$ .

Area under ROC curve = 0.88 (95% CI 0.80–0.96), indicating excellent model discrimination.

The mean time to union was  $4.8 \pm 1.6$  months. Most fractures (52.2%) united between 4–6 months, while 29.7% healed within 3 months, and 18.1% required 7–9 months for complete union.

Receiver operating characteristic (ROC) analysis showed that infection was the strongest predictor of non-union (AUC = 0.84, 95% CI 0.74–0.94), followed by open fracture (AUC = 0.72) and smoking (AUC = 0.68). Surgical delay  $>5$  days (AUC = 0.67) and diabetes (AUC = 0.63) showed moderate predictive ability. The combined model achieved an overall AUC of 0.88, indicating excellent discriminative performance for predicting non-union risk. (Table 4)

**Table 4: ROC Curve Parameters for Predictive Model**

| Predictor        | AUC (95% CI)     | Optimal Cut-off | Sensitivity (%) | Specificity (%) |
|------------------|------------------|-----------------|-----------------|-----------------|
| Smoking          | 0.68 (0.56–0.80) | Yes/No          | 66.7            | 69.6            |
| Diabetes         | 0.63 (0.50–0.76) | Yes/No          | 41.7            | 84.8            |
| Open fracture    | 0.72 (0.60–0.83) | Yes/No          | 45.8            | 88.4            |
| Delay $> 5$ days | 0.67 (0.55–0.79) | $> 5$ days      | 58.3            | 75.4            |
| Infection        | 0.84 (0.74–0.94) | Present         | 41.7            | 94.9            |

Combined model AUC = 0.88 (0.80–0.96) — demonstrating excellent predictive accuracy.

## Discussion

In the present cross-sectional study conducted at a tertiary care centre in North India, the overall incidence of humeral shaft fracture non-union was 14.8%, which aligns well with the previously reported range of 10–15% in contemporary series [1,5,15]. This finding reaffirms that despite advancements in fixation technology and postoperative care, non-union of the humeral shaft remains a clinically significant complication. Identification of risk predictors at the time of presentation or during the early postoperative phase is therefore crucial to reduce the burden of delayed healing, functional impairment, and reoperation.

The reported non-union rate in our study corresponds closely to that of Ekholm et al., who found a 13% incidence in a large cohort of 401 humeral shaft fractures from Sweden [1]. Oliver et al. also reported a 15% non-union rate in their multicentre analysis of traumatic humeral fractures [15]. Similar figures were documented by van Bergen et al. in their systematic review of over 3,000 cases, emphasizing that non-union typically occurs in 10–15% of cases, depending on fixation method and host factors [5]. These congruent findings indicate that our results are consistent with global data despite population differences in nutrition, comorbidity prevalence, and healthcare access.

The slight variation between studies may stem from differences in inclusion criteria (e.g., open vs. closed fractures), definition of non-union, and duration of follow-up. Our study adopted a stringent definition—lack of bridging callus in  $\geq 3$  cortices at  $\geq 9$  months with clinical persistence of pain—consistent with the U.S. FDA definition [6] and contemporary orthopedic literature [7].

Among the host factors analyzed, smoking and diabetes mellitus emerged as independent predictors of non-union. Smokers in our study had nearly threefold higher odds of non-union compared to non-smokers (AOR 3.12, 95% CI 1.08–8.96). The detrimental effect of smoking on fracture healing has been extensively validated in meta-analyses. Pearson et al. reported that smokers had twice the risk of delayed or non-union across fracture types and an increased need for bone grafting [8]. The mechanism involves nicotine-induced vasoconstriction, hypoxia, and inhibition of osteoblast function, which together impair callus formation and angiogenesis [16].

Similarly, diabetes mellitus was associated with a threefold increased risk of non-union in our cohort. Hyperglycemia interferes with microvascular circulation, collagen cross-linking, and osteoblastic activity, leading to compromised callus maturation [17]. Loder et al. and subsequent studies have confirmed prolonged healing time and reduced mechanical strength of callus tissue in diabetics [18]. Our findings support incorporating diabetes screening and glycemic optimization into the early management plan for all fracture patients, especially those undergoing surgical fixation.

Vitamin D deficiency also showed a statistically significant association with delayed or failed union in univariate analysis, though it did not remain independent in multivariable modelling. Brinker et al. previously highlighted the high prevalence of hypovitaminosis D among patients with unexplained delayed union, recommending routine correction as a preventive measure [19]. The loss of significance in our regression model likely reflects partial confounding by comorbidities and lifestyle factors.

Open fractures were found to be a major independent risk predictor for non-union (AOR 4.68,  $p = 0.012$ ). This observation aligns with the findings of Ziran et al., who reported a strong relationship between open injury, soft-tissue compromise, and subsequent infection leading to biological failure of healing [20]. The degree of contamination, soft-tissue damage, and vascular compromise in open fractures can markedly impair the osteogenic microenvironment. Our data showed that 45.8% of non-union cases were open injuries, compared to 11.6% in the union group. This underscores the need for early and meticulous debridement, adequate stabilization, and antibiotic coverage to minimize infection and promote healing in such cases.



Fracture morphology also contributed to non-union risk. Comminuted and segmental patterns (AO 12-B/C) had a 3.5-fold higher risk of non-union on univariate analysis, consistent with studies by Gallusser et al. and AO Foundation guidelines emphasizing the importance of minimizing residual fracture gaps and achieving absolute stability in these complex configurations [14,21]. Although the variable lost significance after adjustment for infection and surgical delay, its contribution to mechanical instability and biological insufficiency remains clinically relevant.

Delay in surgery beyond five days emerged as another independent risk factor. Patients operated within five days of injury achieved a mean union time of  $4.3 \pm 1.2$  months, significantly shorter than  $5.7 \pm 1.8$  months in those with delayed fixation ( $p = 0.001$ ). Early stabilization promotes optimal biological response and prevents soft-tissue fibrosis or fracture gap widening that may occur with delayed intervention [22]. Conversely, logistical delays—such as late referrals or medical optimization—can compromise outcomes, especially in open or comminuted fractures.

The most powerful predictor in our regression model was postoperative deep infection, which increased the odds of non-union nearly tenfold (AOR 9.87, 95% CI 2.78–35.02). This is consistent with the findings of Olson et al., who identified infection as the single strongest determinant of humeral non-union [15]. Infection interferes with bone healing by damaging local vascularity, introducing necrotic debris, and promoting osteolysis. Even when treated successfully, the prolonged inflammatory milieu can impede osteogenesis [20]. These findings highlight that infection prevention—through perioperative antibiotic prophylaxis, meticulous asepsis, and early wound monitoring—remains the most critical modifiable factor in preventing non-union.

Follow-up adherence also showed a significant relationship with union outcomes. Patients who missed scheduled visits had higher non-union rates (45.8% vs. 20.3%,  $p = 0.011$ ). Regular follow-up ensures early detection of complications such as fixation failure, infection, or displacement, allowing timely intervention before biological failure sets in. This finding is particularly relevant in the Indian context, where socioeconomic constraints and travel distance often limit compliance.

Although both plate osteosynthesis and intramedullary nailing were used in this study, the fixation method itself did not independently predict non-union. This corroborates findings from recent meta-analyses by Zhao et al. and van Bergen et al., which reported no significant difference in union rates between these techniques when performed by experienced surgeons [5,12]. Instead, mechanical stability and biological preservation were the critical determinants of success. Proper fracture reduction, adequate compression, and avoidance of distraction remain essential irrespective of implant type.

The final logistic regression model incorporating five independent predictors—smoking, diabetes, open fracture, surgical delay, and infection—demonstrated excellent discrimination (AUC = 0.88) and good calibration (Hosmer–Lemeshow  $p = 0.61$ ). This suggests that the model reliably differentiates between patients at high and low risk of non-union. Similar model performance (AUC 0.83–0.90) was reported in Western prediction models for long-bone non-union [15,22], supporting the generalizability of our findings.

In clinical practice, this model can aid orthopedic surgeons in risk stratification at presentation, guiding decisions on early bone grafting, aggressive infection control, and more frequent follow-up for high-risk individuals. For example, a diabetic smoker with an open fracture and surgical delay  $>5$  days should be closely monitored or managed proactively with bone graft augmentation or biological enhancers.

The strengths of this study include a well-defined cohort, standardized radiographic criteria, blinded image evaluation, and multivariable analysis adjusting for potential confounders. The inclusion of both operative and non-operative cases provides real-world applicability.

However, certain limitations must be acknowledged. First, the study's cross-sectional design precludes establishing temporal causation. Second, laboratory parameters such as serum calcium, inflammatory markers, or HbA1c were not uniformly available for all patients. Third, the study was conducted at a single tertiary centre, and results may not be directly generalizable to primary or rural

settings. Finally, longer follow-up beyond nine months might have detected late unions that were misclassified as non-union under strict criteria.

Despite these limitations, the study provides valuable insights into the determinants of humeral shaft non-union in an Indian tertiary care context, offering a basis for targeted preventive strategies and future multicentric prospective validation.

## Conclusion

This study found a 14.8% incidence of humeral shaft fracture non-union at a tertiary care centre in North India. The key independent predictors were smoking, diabetes mellitus, open fractures, surgical delay beyond five days, and postoperative infection, with infection being the strongest determinant. Both biological and mechanical factors were found to contribute to impaired healing. Addressing these modifiable risks through timely surgery, infection control, smoking cessation, and optimal glycemic management can significantly reduce non-union rates. Early identification of high-risk patients and adherence to standardized treatment protocols are essential for improving healing outcomes and preventing long-term disability.

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