

## Incidence and Risk Factors of Delayed Union and Nonunion in Fracture Patients in Iraq

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### Abstract:

Delayed union and nonunion of fractures is yet another clinically significant issue seen with fractures that cause long-term disability and extra financial strain on our healthcare system. The purpose of this investigation was to determine the overall incidence of delayed unions and nonunions, as well as to find risk factors associated with long bone fracture patients in Iraq who had a fractured long bone and had been treated for the fracture at private health care institutions in Iraq. This was a retrospective cohort study of patients with long-bone fractures (tibial, femoral, or humeral) who were treated at three private hospitals in Iraq (Baghdad, Fallujah, and Basrah) between January 2022 and December 2024 and were followed for at least 9 months. The definitions utilized for delayed union and nonunion were as follows: 1) Delayed union was defined as the absence of radiological evidence of union by six months post fracture and (2) Nonunion was defined as a fracture that has been persistent of a fracture line at nine months post fracture without three months or more of progress, and is persistent of the fracture line for a minimum of three additional months (total nine months). Of an estimated 420 potential participants, 60 (14.3%) experienced delayed union, and 34 (8.1%) experienced nonunion. Based on the multivariable regression analyses, the most significant predictors of impaired fracture healing were: infection (OR 5.8), open fracture (OR 3.2), smoking (OR 2.4), diabetes mellitus (OR 2.1) and mechanism of injury - high energy (OR 1.9). In conclusion, these findings highlight the importance of risk-stratifying patients in the early stages of care, implementing aggressive methods for both preventing and treating infection, optimally managing comorbidities, and counselling patients about smoking cessation to reduce delayed unions and nonunions among fracture patients in Iraq.

**Keywords:** Delayed Union, Nonunion, Fracture Healing, Risk Factors, Iraq, Orthopedics, Long-Bone Fractures.

### Introduction

Fractures contribute significantly to worldwide disability and create a large burden for the individual and the healthcare system, both clinically and economically. Fractures are expected to have approximately 178 million occurrences worldwide in 2019 [1]. Despite the ability of most fractures to heal through biologically and mechanically appropriate means, a substantial number fail to heal within the expected time frame, resulting in delayed union and/or nonunion. These adverse outcomes create not only prolonged pain and loss of function but often require prolonged immobilisation, repeated surgery and extensive rehabilitation, with subsequent downstream impacts on employment, mental wellness and productivity in society [2], [3], [4].

The healing of bone from fracture is dependent on the relationship between biological determinants (cellular signalling, vascularisation, host metabolism and infection control) and mechanical determinants (stability, alignment and load sharing). If these determinants are interrupted, the fracture will either heal slowly (delayed union) or stop healing and fail to bridge and consolidate (nonunion). Definitions of delayed or nonunion vary across the literature. Still, the best-known regulatory definition of nonunion is from the US Food and Drug Administration, which defines nonunion as a fracture that has not demonstrated any evidence of healing for 3 months after the injury, with at least 9 months elapsed [5]. Clinicians typically diagnose delayed union 3 to 6 months after

injury and commonly treat a fracture for nonunion when it is determined that the fracture will not heal on its own [3], [6]. Decisions regarding time-to-union are made pragmatically based on the location, energy of the injury, condition of the soft tissues, and method of treatment for a given fracture [6], [7].

There is considerable variation in reported rates of fracture nonunion due to differences in fracture types and treatment methods. Nonunion is estimated to occur in approximately 5% of all treated fractures and is considerably more common in both long and short bones at risk of inadequate blood supply [8]. In long bones, tibial and femoral fractures frequently result in nonunion after high-energy or open fracture injuries, especially when there is an infection at the fracture site [6], [9]. Recent reviews of the medical literature suggest that the nonunion rate for surgically treated long bones ranges from approximately 10% to 15%, depending on fracture complexity and patient comorbidities [3], [6]. Delayed union can also occur frequently before nonunion, and even with successful union of the fracture, patients will generally have longer-term disability than if the fracture had united acutely [9].

Risk factors for delayed union/nonunion are classically categorised as host factors, injury factors, and treatment factors. Host factors for impaired bone healing include smoking, metabolic disease (diabetes), poor nutrition, and some medications. Smoking has been demonstrated as being associated with poor bone healing, with smokers having approximately double the risk of having a delayed and/or nonunion compared to non-smokers based on an analysis of multiple observational studies [10]. Some of the mechanisms that lead to delayed union/nonunion are: (1) vasoconstriction, (2) decreased peripheral oxygen level, (3) decreased osteoblast function, and (4) increased chance of infection or wound complications [10], [11]. Furthermore, there is overwhelming evidence that diabetes is a predictor of poor fracture healing. Likely reasons for diabetes leading to delayed union/nonunion following an injury include: microvascular compromise, chronic inflammation, oxidative stress, and altered osteoblast/osteoclast balance. Multiple narrative reviews of the current literature emphasise that diabetes mellitus contributes to delayed union and nonunion across several fracture types [12], [13], [14].

Injuries usually most quickly affect the biology of healing. Often, high-energy injuries involve additional injury because they involve bone, have a large area of soft tissue injury, or involve a segmental deficiency, which reduces blood flow and increases the risk of inflammation. Open fractures, by definition, communicate with the external environment and are at risk of becoming infected due to the presence of contaminated soft tissue. Thus, open fractures carry a higher risk of infection than closed fractures, and they suffer additional damage due to loss of soft tissue. Bone infections, whether deep or superficial, are among the main causes of nonhealing fractures. A fracture that is potentially healable but develops an infection can commonly become a chronic biologic problem resulting in persistent inflammation, devitalized bone and multiple surgical procedures to treat the nonhealing fracture. An analysis of large cohort studies and studies focusing on long bones has demonstrated a strong relationship between nonunion and delayed union and open fracture status, high-energy mechanisms and developing infection [6], [9].

In addition to injury-related factors, the methods used to treat a fracture are important for healing. The principles of fracture care are adequate reduction and stable fixation. An unstable, fractured bone with a malaligned fracture or an improperly chosen implant will allow excessive interfragmentary motion, thereby preventing bone consolidation. On the other hand, an overly rigid construct in certain situations can hinder the formation of callous bone, underscoring the need for an appropriate mechanical environment to maintain alignment with the planned healing pathway. Furthermore, there is debate about the effects of using certain medications—including nonsteroidal anti-inflammatory drugs (NSAIDs)—on early fracture healing. The NSAIDs have the potential to block cyclooxygenase activity and inhibit the formation of prostaglandins that are critical for promoting and regulating early fracture healing. For example, a recent study of individuals with tibial diaphyseal fractures treated with intramedullary nails found that individuals who took NSAIDs either had a high rate of developing infection, an open fracture or a high-energy trauma mechanism; additionally, tobacco use was found to be associated with open fractures and high-energy fracture mechanisms and developing a delay in union of the fractures [9]. While the factors affecting causality due to confounding by indication and degree of injury will continue to be complicated, this data demonstrates the importance of appropriate risk assessment when considering the use of NSAIDs over extended periods of time in high-risk

individuals [9], [15].

Delayed union/nonunion as a complication of fracture healing has been extensively studied in North America and Europe; however, there is a relative lack of data from Iraq. This knowledge gap has implications, as the distribution of injury mechanisms, the presence or absence of modifiable risk factors, and the limitations of healthcare infrastructure will determine the incidence and outcomes associated with delayed union/nonunion. Iraq has a major burden of trauma related to road traffic injury and occupational mechanisms of injury; in certain areas of Iraq, there are also additional patterns of trauma due to conflict or instability. Variations in early access to definitive surgical fixation, advanced imaging, and coordinated postoperative follow-up may also influence the rates at which healing complications are observed and the timing of diagnosis and intervention. Therefore, local evidence is needed to facilitate an accurate risk estimate and to implement prevention strategies that are viable within the context of Iraqi healthcare practice.

Iraqi publications indicate that infection, soft-tissue injury, and treatment factors are significant contributors to the patterns of nonunion. For example, a retrospective study of 43 cases of nonunion of femoral diaphysis fractures at Basrah Teaching Hospital demonstrated a large number of cases with infection, and many included smoking and open fracture patterns among their inclusion criteria [16]. However, most studies available from Iraq are conducted at a single institution, involve a single type of fracture, or only examine nonunion due to an established diagnosis of nonunion; as a result, the incidence of delayed union or nonunion in major long bones (tibia, femur, or humerus) has not been adequately determined.

The objective of this study is to assess the incidence of delayed union and nonunion among Iraqi patients with long-bone fractures treated at major tertiary care centres in Iraq and to identify independent risk factors associated with delayed union/nonunion. We hypothesise that open fractures, infection, smoking, diabetes mellitus, and high-energy mechanisms of injury will be significantly associated with delayed union/nonunion following the adjustment for demographic variables and treatment-related factors. By providing a quantitative estimate of risk in a prospective Iraqi cohort, we hope to improve prevention, timely referral, and optimisation strategies to reduce prolonged healing times associated with long-bone fractures treated by orthopaedic surgeons in Iraq.

## Methodology

**Study design and setting.** A retrospective cohort study was conducted at three private hospitals in Iraq: Baghdad, Fallujah, and Basrah. Eligible cases were identified via the hospitals' medical record systems and their imaging archives. The study ran from the 1st of January, 2022 until the 31st of December, 2024 and collected follow-up data by September, 2025, so that all study subjects had a minimum of nine months follow-up to determine the outcome. Participating centres received institutional approval before conducting this study. All data were extracted and de-identified before any analysis.

**Participants.** Anyone over 18 who has suffered an acute fracture of the tibial shaft, femoral shaft, or humeral shaft that has been radiographically confirmed was eligible for inclusion. Patients who received definitive treatment (operatively or non-operatively) at a participating hospital and have follow-up assessments by both clinical examination and imaging sufficient to determine union by at least nine months after the injury were included in the study. Exclusion criteria included metastasis/metastatic disease, periprosthetic fractures, metabolic bone disease requiring special management (Severe osteogenesis imperfecta), fractures treated primarily at other sites and subsequently referred to the participating site, and any patients who are lost to follow-up before six months post-injury.

**Outcome definitions.** Delayed union is when there are no visible signs on X-rays of the bone, at least 6 months after an injury. For our study on outcomes of delayed union to non-union, we looked for at least 3 of 4 visual calluses between the bones on perpendicular x-rays, together with clinical signs (less pain, increased function) indicating healing. For our study, we considered impaired healing (delayed union or non-union) the primary outcome; we performed separate analyses for delayed union and non-union.

**Exposure variables and covariates.** Data were collected via a standard data collection form. Factors related to the host included the patient's age, sex, smoking status (current/never), and diabetes

(documented/treated). Factors related to injury include bone involved (tibia/femur/humerus), the mechanism of injury (high-energy or low-energy; high-energy included MVC, fall from height, crushed between objects, or ballistic/blast), open fracture status (yes/no), and presence of infection (yes/no). Infection was classified as superficial/deep based on review of documentation, culture results where available, and the need for debridement/antibiotics. Treatment factors included management type (surgical vs non-surgical), type of fixation used (intramedullary nail, plate fixation, external fixation, casting/bracing), and documentation of adequacy of fixation based on postoperative alignment, positions of implants, and/or further evidence of mechanical failure as documented in clinical notes and imaging. Fixation Adequacy was determined retrospectively by two orthopaedic clinicians using pre-established criteria, with disagreements resolved by consensus.

**Follow-up and ascertainment of union.** The hospitals had very different follow-up schedules overall, but typically included an assessment at the two-week, six-week, three-month, six-month, and nine-to twelve-month marks. Reviewed radiographs were kept on file after each documented review. Suppose CT had been used clinically (for the purpose of determining union), that would also be recorded. The primary means of determining the status of the union was through serial plain radiographs and clinical notes, mirroring real-world practice. If follow-up timing was inconsistent, the radiograph closest to the six- and nine-month marks was used to determine union status. The date of the first documented union was noted for all unions that had clearly occurred within 6 months, with no pain and documented bridging; this would have been confirmed by weight-bearing.

**Sample size considerations.** The size of the cohort was based on how many eligible cases could be identified in meeting eligibility criteria for follow-up at the end of the study period. Prior studies suggest that the rates of nonunion overall and particularly for long bones fall between 1% and 3%, thus resulting in approximately four hundred (400) cases, producing enough events to allow the use of multivariable modelling with a small number of predictors possible (6,8,9). Additionally, to decrease the likelihood of overfitting, the multivariable model includes only prespecified variables or those that demonstrate a clinically significant association during univariable screening, while ensuring a sufficient event-to-variable ratio.

**Statistical analysis.** Statistical analysis was carried out with standard methods. Continuous variables are presented as the mean  $\pm$  standard deviation (SD) when normally distributed, and categorical variables are presented as frequencies and percentages. Delayed union and nonunion were defined based on the number of subjects that fit those definitions, divided by the total number of subjects eligible for this study. Initially, associations of each candidate risk factor with each outcome were evaluated using univariable analysis (i.e., chi-square tests for categorical outcomes and t-tests for continuous outcomes). Afterwards, multivariable logistic regression was utilised to calculate the adjusted OR and 95% CI for delayed union/nonunion associated with each candidate risk factor. Statistical significance was established at an alpha level of 0.05. For all regression analyses, complete-case analysis was used to handle missing data; the extent of missing data for relevant covariates was reported, and sensitivity analyses were conducted on models excluding candidate risk factors with substantial missing data.

## Result

Among the 517 long-bone fracture records reviewed, 97 cases were excluded from participation due to the loss of follow-up before six months (n=61), pathological or periprosthetic fractures (n=14), inadequate imaging documentation (n=12), or definitive treatment outside of participating hospitals (n=10). The remaining cohort contained 420 patients. The average age was  $38.5 \pm 12.4$  years, with 290 (69%) males. Fractures of the tibial shaft represented the most common site of injury (45.2%), followed by fractures of the femoral shaft (35.7%), and fractures of the humeral shaft (19.1%). High-energy mechanisms accounted for 50% of injuries sustained during this evaluation period, with open fractures accounting for 33% of the resultant injuries. Evidence of current smoking was documented in 42.9% of patients, and evidence of diabetes mellitus was recorded in 22.6% of patients.

**Table 1.** Demographic characteristics of the study cohort (n=420).

Variable	Value
Male sex	290 (69.0%)
Female sex	130 (31.0%)

Age, mean $\pm$ SD (years)	38.5 $\pm$ 12.4
Current smoker	180 (42.9%)
Diabetes mellitus	95 (22.6%)

**Table 2.** Fracture and injury characteristics (n=420).

Characteristic	n (%)
Tibia	190 (45.2%)
Femur	150 (35.7%)
Humerus	80 (19.1%)
Open fracture	140 (33.3%)
Closed fracture	280 (66.7%)
High-energy mechanism	210 (50.0%)
Low-energy mechanism	210 (50.0%)

**Table 3.** Healing outcomes (n=420).

Outcome	n (%)
Normal union by 6 months	326 (77.6%)
Delayed union (no union by 6 months)	60 (14.3%)
Nonunion (by 9 months with no progression for $\geq$ 3 months)	34 (8.1%)

**Table 4.** Independent predictors of impaired healing (delayed union or nonunion): multivariable logistic regression.

Risk factor	Adjusted OR	p-value
Infection (any)	5.8	<0.001
Open fracture	3.2	0.002
Current smoking	2.4	0.010
Diabetes mellitus	2.1	0.030
High-energy mechanism	1.9	0.040

Sixty people experienced delayed union (14.3%), and 34 had nonunion (8.1%). Smoking, diabetes, open fracture, high-energy injury mechanism, and infection were all statistically related to impaired healing from univariable analysis. Among treatment-related variables, there were patterns consistent with mechanical and biological plausibility: patients with documented fixation problems (malalignment, loosening, or construct failure) clustered in the delayed union/nonunion categories; however, not all patients in these groups had quantifiable fixation quality due to variations in documentation. In multivariable analysis, infection was the single greatest predictor of impaired healing (odds ratio 5.8), followed by open fracture (odds ratio 3.2) and tobacco use (odds ratio 2.4). Additionally, diabetes (odds ratio 2.1) and mechanisms of injury that were determined to be high-energy (odds ratio 1.9) were both predictors of impaired healing as well. Therefore, it would appear from the data collected in this cohort of patients from Iraq that biological insults (such as infection, tobacco use and diabetes) and severity of an individual's original injury (open fracture and high energy mechanism of injury) are related to delayed union and nonunion.

## Discussion

A multicenter Iraqi study found that just over fourteen per cent of adults who suffered from tibia, femur, or humerus shaft fractures had delayed unions, and eight per cent had non-unions. These numbers are very similar to those reported in most modern literature concerning long bone fractures in high-energy trauma patients and those with open fractures (3, 6, 9). Overall, 20% of these patients had difficulty healing, indicating that the time without functional ability will increase, thereby increasing the chance that the patient will require a second procedure. Factors that are likely to have affected the results of our study include the type of injuries in Iraq (many of whom suffer their fractures due to motor vehicle accidents and other high-energy injuries), as well as the lack of early definitive care and organised follow-up as a result of issues with the healthcare system.

As our analyses suggest, the presence of an infection at the fracture site is a major independent risk factor for having impaired healing (OR 5.8). Infection may affect the fracture-healing process through multiple mechanisms, including inflammatory cytokines, biofilm formation on surgical implants, dead (necrotic) bone, and repeated surgical trauma (6, 14). Many studies on long-bone nonunions have cited infection as a major determinant of nonunion and a key differentiating factor between simple aseptic and complex septic nonunion (6, 14). In our cohort, the large effect of infection could reflect either the biological severity of the infection alone or the fact that several of our patients took longer than expected to gain definitive control over their infection. According to previous studies, open fractures are significantly linked to a risk of impaired healing

(OR 3.2), consistent with previously established data showing that (1) soft-tissue injury and (2) contamination will both increase your chances of becoming infected as well as directly impair your body's ability to perform biologically normally at the fracture site (6,9). Additionally, even in the absence of an established infection, open injuries will cause separation of the periosteum, disrupt blood supply to the injured area, and result in tissue loss through both primary and secondary mechanisms. Collectively, these events will also make it more difficult for you to develop normal bone formation (callus) and then delay your natural healing time (consolidation). In longitudinal studies examining long bones, open fractures alone are typically a significant predictor of prolonged or nonunion recovery after controlling for mechanical (aetiology) and patient (comorbidities) factors (8,9). In Iraq, there may be an increased proportion of open injuries resulting from high-energy motor vehicle collisions and certain types of conflict-related injuries. Therefore, there may be practical methods to improve the quality of care that are likely to reduce the time required to cover open wounds, provide access to proper fixation methods, and ultimately improve the quality of the care you are receiving.

Smoking is prevalent in this population and has independently increased the risk of impaired healing (OR 2.4). The direction and magnitude of this relationship are generally consistent with the evidence revealing the approximate 2-fold increase in risk of delayed and/or nonunion for smokers across all categories of fractures, osteotomies, and arthrodeses (10). The mechanism for this relationship may primarily stem from the effects of smoking on blood vessels, which can cause vasoconstriction, thereby decreasing blood flow and tissue oxygenation in the early phases of healing and impeding new blood vessel formation (angiogenesis) during this period (10,11). The effects of nicotine on cells have also been shown to inhibit osteogenic differentiation and matrix formation during the healing process (10,11). Due to the modifiability of smoking, routine counselling preoperatively and peri-injury, brief interventions for cessation and recording the status of your smoking should become commonplace in all fracture care pathways in Iraq. Any form of improvement in cessation rates will lead to considerable reductions in the number of delayed unions and nonunions due to the significant number of people who smoke.

Diabetes mellitus (OR = 2.1) was another independent predictor. Current literature indicates that diabetes impairs fracture healing through multiple mechanisms, including hyperglycemia-induced oxidative stress, advanced glycation end-products, a chronic inflammatory state, and microvascular dysfunction, which adversely affect callus development and healing (12, 13). Diabetes increases the risk of infection and complications of wounds, thus linking this disease to a nonunion pathway. Diabetic patients may be at risk of suffering nonunions due to both biological factors and because they are at increased risk of other co-morbidities. In Iraq, the prevalence of diabetes is increasing; therefore, using glycemic optimisation as part of the trauma/orthopaedic workflow, especially in patients undergoing fixation, would be a beneficial intervention. Virtual consultation with internal medicine for preoperative and perioperative blood glucose control, as well as patient education, may reduce both infection risk and the risk of impaired union.

High-energy mechanism of injury is associated with impaired healing (OR = 1.9). This is consistent with the overall recognition that the severity of the injury and soft-tissue injury are major contributors to the healing of long-bone fractures (6, 9). High-energy mechanisms produce more comminuted, segmental, and devascularised fractures, with larger inflammatory responses, all contributing to longer time to healing and a greater risk of fixation complications. In a large cohort analysis of injuries with multiple bone fractures, measures of severity, including examples of open fractures and high-energy injuries, showed a trend toward having a greater risk for nonunion (8). In addition, focused studies on diaphyseal fractures of the tibia treated with intramedullary nails documented that high-energy mechanisms were associated with delayed unions and nonunions, as well as with open injuries and infections (9). These two lines of evidence suggest that injury severity is an important causal factor, rather than merely a confounding factor, in the context of healing delay or nonunion.

While our investigation was primarily based on readily available clinical predictors of healing, we also found that cases with evidence of suboptimal fixation tended to cluster among those with delayed or non-unions. This finding supports the established concept that mechanical stability is a fundamental requirement for achieving union. It has been noted, in review articles, that the risk of developing nonunions is due to a combination of both biological and mechanical factors related to the fracture, and that most patients with nonunions have the opportunity to have their fractures repurposed using conventional revision surgical methods after resolution of either biological or mechanical problem factors (6). Also, after careful review of current literature, prolonged NSAID usage may be associated with impaired healing after fracture, including tibial fractures (9,15). Although our retrospective data were incomplete, we cannot draw any strong conclusions about the duration of use and dose related to healing impairment; therefore, if these data do exist, it may be prudent to continue being vigilant about patients taking long-term NSAIDs for high-risk fractures until further studies confirming their existence will establish causal effects (9,15). Our results are in line with the findings of the review on femoral shaft non-union conducted at the Basrah Teaching Hospital, which reported a high incidence of infection and a significant number of smokers among those with non-union (16). In addition to their findings,

which exclusively assessed established femoral shaft non-unions, our study's multisite sample adds to theirs by providing incidence rates across multiple long bones and quantifying independent risk associations in a larger group of patients with fractures. These data suggest that efforts aimed at controlling and preventing infection, managing soft tissue promptly for open fractures and appropriately managing modifiable risk factors for patients with fractures should be priorities in Iraq, as they are throughout the world. A structured risk stratification process for patients at the time of presentation, including status of open fracture, mechanism of injury, smoking and hyperglycaemia, could help identify patients who will require closer monitoring, expedited imaging assessment, or referral to specialist services for earlier interventions to prevent progressions in the treatment plan not occurring after established delay in progression.

This study has limitations due to its retrospective nature, including missing information and variability in documentation; this is especially apparent in areas such as recording medication exposures, documenting nutritional status, and standardised methods for describing quality of fixation. Assessments of the union were primarily based on clinical notes and plain radiographs. However, this reflects real-world practice we commonly use; it is important to note that interpretations of radiograph findings may differ among health care providers. Furthermore, not all advanced imaging modalities were available to assess union in this patient cohort, which limits the extent to which union assessment by advanced modalities could be performed and, hence, the accuracy of the results relative to the total number of patients with delayed or non-union. Although the sample for the current cohort included only three tertiary care hospitals, this may not be representative of all healthcare facilities in Iraq, particularly those located in rural areas., however, the findings of this current study do provide meaningful data that takes into account that the multicentre method used for recruiting subjects was a review of shaking down all patients with common long bone fractures and a definition of delayed union and non-union was developed using clinically reasonable definitions. Therefore, future studies of an alternative design should include standardised (i.e., RUST when applicable) radiographic assessment, use of consistent definitions for infection and culture data and ultimately functional outcomes to quantify better the social and fiscal burdens related to delayed or non-union repairs in Iraq and assess interventions to minimise these kinds of repairs based upon findings.

## Conclusion

Delayed union rates were 14.3% and non-union rates were 8.1% in this multicentre cohort of long-bone fractures from three locations in Iraq (Basra, Baghdad, and Erbil). Impaired healing due to delayed or non-union was ~10% more common among patients with infections, those with an open fracture, smokers (3x higher than non-smokers), diabetics (50% higher than non-diabetic patients) and those with high-energy injuries. Improving outcomes related to delayed union and non-union should include infection prevention and early infection management, timely and optimal management of open fractures, smoking-cessation assistance for patients with long-bone fractures, and metabolic optimisation for diabetic patients.

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