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Serum IL-8 and *CXCR2* Gene Expression as Indicators of Bone Fracture Healing Progression and Impairment

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Abstract
Background: In bone fracture, IL-8 is an inflammatory chemokine produced at the injury site, signaling for the rapid recruitment of immune cells. CXCR2 is the receptor on these cells, primarily neutrophils, that binds to IL-8, orchestrating their essential migration to the fracture to clear debris and initiate the healing process.
Aim: This study investigated the potential of IL-8 and its receptor, CXCR2, as predictive markers for fracture healing outcomes. Serum levels of IL-8 were measured, and CXCR2 gene expression was quantified.
Materials and methods: Serum levels of MCP-1 and IL-8 were measured using enzyme-linked immunosorbent assays, while the expression of CCR2 and CXCR2 genes was quantified by real-time PCR. Receiver operating characteristic curve analysis was performed to evaluate the diagnostic accuracy of these biomarkers
Results: The results revealed significantly elevated serum IL-8 levels in both patients with normal fracture healing and those with delayed healing compared to healthy controls. Notably, IL-8 levels were significantly higher in the delayed healing group compared to the normal healing group. Receiver operating characteristic curve analysis demonstrated excellent diagnostic accuracy for IL-8, with effectively distinguishing normal healing patients from controls and delayed healing patients from controls. Consistent with the elevated chemokine levels, gene expression analysis revealed significantly upregulated CXCR2 in both normal healing and delayed healing patients compared to controls. The expression of CXCR2 remained persistently elevated across different healing stages, with the highest levels observed in the delayed healing and maturation stages. Receiver operating characteristic (ROC) analysis demonstrated that CXCR2 gene expression could perfectly distinguish normal healing and delayed healing patients from healthy controls. Mechanistically, IL-8 and CXCR2 mediate neutrophil chemotaxis and activation, which are essential for clearing debris and initiating tissue repair. However, excessive or prolonged CXCR2 signaling can contribute to chronic inflammation and impair bone regeneration. The exceptional diagnostic accuracy of these biomarkers underscores their potential clinical utility. Measuring serum IL-8 levels and quantifying CXCR2 gene expression could aid in the early identification of patients at risk of delayed healing, enabling timely implementation of targeted interventions. Furthermore, the IL-8 / CXCR2 axis represents a promising therapeutic target, and modulating this pathway may offer novel strategies to optimize fracture repair, particularly in high-risk populations.
Conclusion: This study demonstrates the significant potential of IL-8 and CXCR2 as prognostic biomarkers for fracture healing outcomes. Their elevated levels, particularly in delayed healing patients, underscore their involvement in pathogenesis of impaired bone regeneration. Integrating the assessment of these biomarkers into clinical practice may enhance risk stratification and guide targeted therapeutic interventions to improve fracture healing rates and patient outcomes.
Keywords: Interleukins, Chemokines, Osteogenesis, Receiver operating characteristic, Polymerase chain reaction, Oraq

INTRODUCTION

Fracture healing is a complex, well-orchestrated biological process involving the coordinated interplay of numerous cellular and molecular pathways (Sheen et al., 2023) Following the initial injury and inflammatory response, fracture repair progresses through distinct phases, including the formation of a soft callus, its subsequent mineralization, and eventually, the remodeling of the fractured bone to restore its original anatomical and functional integrity (Sheen et al., 2023). However, in up to 10% of cases, this intricate healing process is disrupted, leading to delayed union or non-union, which can have devastating consequences for the patient, including prolonged disability, increased risk of complications, and reduced quality of life (Yang et

al., 2025). The factors contributing to impaired fracture healing are multifactorial, involving a complex interplay between patient-specific characteristics, such as age, comorbidities, and genetic predisposition, as well as environmental and mechanical factors. Advanced age, for instance, has been consistently associated with an increased risk of delayed union and non-union, partly due to age-related declines in bone regenerative capacity and heightened systemic inflammation .Similarly, certain medical conditions, including diabetes, obesity, and smoking, have been identified as risk factors for impaired fracture healing, potentially through the disruption of the inflammatory response and impairment of angiogenesis and osteogenesis (Hao et al., 2025). In recent years, the crucial role of the immune system and inflammatory signaling in the fracture healing process has gained increasing recognition. The initial inflammatory phase following a fracture injury is characterized by the recruitment and activation of various immune cells, such as neutrophils, monocytes, and lymphocytes, which release a plethora of pro-inflammatory cytokines and chemokines .These inflammatory mediators play a vital role in orchestrating the subsequent phases of fracture repair, including the recruitment of mesenchymal stem cells, the stimulation of angiogenesis, and the differentiation of osteoblasts and chondrocytes (ElHawary et al., 2024). However, in cases of delayed or impaired fracture healing, the inflammatory response may become dysregulated, leading to a persistent or excessive inflammatory state that can hinder the normal progression of the healing process (Duke et al., 2024). Sustained elevation of pro-inflammatory cytokines, such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6), has been associated with delayed union and non-union fractures (Hankenson et al., 2015).Chemokine of particular interest in the context of fracture healing is interleukin-8 (IL-8, also known as CXCL8). IL-8 is a key chemokine responsible for the recruitment and activation of neutrophils, which are essential for the early stages of fracture repair (Witek et al., 2021). Dysregulation of the IL-8 signaling pathway has been linked to impaired angiogenesis and delayed bone regeneration in various preclinical and clinical settings (Pereira et al., 2020). CXCR2 is the principal receptor for IL-8 and other CXC chemokines, and its activation is crucial for neutrophil recruitment and the initiation of the inflammatory response .Emerging evidence suggests that the dysregulation of CCR2 and CXCR2 signaling may contribute to the development of delayed union and non-union fractures (Hesketh et al., 2017). Given the critical role of inflammation and chemokine signaling in fracture healing, there is growing interest in the potential of these molecules as prognostic biomarkers and therapeutic targets. Identifying patients at risk of impaired fracture healing based on their inflammatory profiles could facilitate early risk stratification and the implementation of personalized treatment strategies. Furthermore, the development of targeted interventions aimed at modulating the IL-8/CXCR2 signaling axes may offer novel approaches to enhance fracture repair and improve clinical outcomes (Jones et al., 2025). Despite the critical role of the immune system and specific chemokines (IL-8) and their receptors (CXCR2) in orchestrating fracture repair, the precise mechanisms by which their dysregulated expression contributes to delayed union and non-union fractures remain inadequately understood.

Materials and method

Sample Collection

The study samples were collected from patients admitted to the Orthopedic Department at Al-Manathira Hospital between October 2024 and November 2024. A total of 90 participants were enrolled in the study, including 60 patients with bone fractures (30 patients with normal healing and 30 patients with delayed healing) and 30 healthy control subjects. Healthy control subjects were recruited from the hospital staff and local community. They were age- and sex-matched to the patient groups and had no history of bone fractures or other musculoskeletal conditions. Informed consent was obtained from all participants prior to enrollment. Questionnaire and full information obtained from the patients such as (demographics, injury details, medical history, treatment, recovery, and patient-reported outcomes). Blood samples (10 mL) were collected from each participant via venipuncture and transferred to EDTA-coated tubes. Samples were immediately processed, and plasma was separated by centrifugation at 3,000 rpm for 10 minutes. The plasma samples were aliquoted and stored at -80°C until further analysis. Serological detection of IL-8 with ELISA and molecular detection of CXCR2 with qPCR then numerical analysis by using SPSS program

Inclusion criteria

Patients aged 18 to 65 years old with a confirmed diagnosis of acute bone fracture classified into normal healing or delayed healing groups based on radiographic and clinical assessments by the orthopedic team. Patients without any comorbidity that could impact bone healing, such as, malignancy, or autoimmune disorders.

Statistical analysis

Data were analyzed using SPSS version 26 and Microsoft Excel 2010. We used the Kolmogorov-Smirnov test to check for data normality. For normally distributed data, independent sample t-tests compared two groups, and one-way ANOVA compared more than two groups. For non-normally distributed data, the Mann-Whitney test was used for two-group comparisons. Chi-square tests assessed associations between categorical variables. ROC curve analysis determined diagnostic cutoff values, reporting AUC, accuracy, sensitivity, specificity, and p-values. Pearson correlation measured relationships between numeric variables, providing a correlation coefficient (r) and p-value of less than 0.05 considered statistically significant (Gharban, 2024).

Results

Total results

The present study included 90 participants divided into three classes according to healing time (Figure 1).

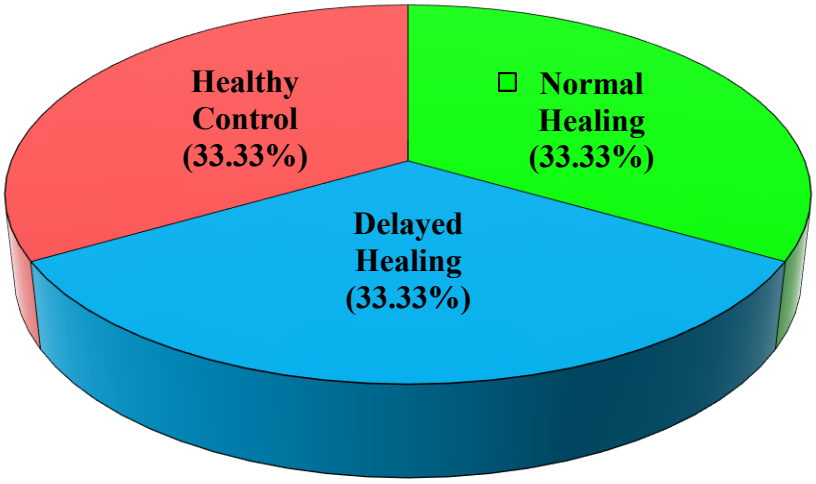


Figure (1): Subject groups according to healing time

Interleukin-8 (IL-8) level in patients and healthy controls

The comparison of Interleukin-8 (IL-8) level between patients and control groups has been carried out and the results were demonstrated (Table 1, Figure 2).

Table (1): Interleukin-8 (IL-8) level in patients and healthy control

Groups		Interleukin-8 (IL-8) level
Normal healing	Mean ± SE	464.32 ± 5.11^{A}
	Range	400.00-508.36
Delayed healing	Mean ± SE	575.07 ± 5.35^{B}
	Range	505.11-623.81
Control	Mean ± SE	160.60 ± 3.11^{C}
	Range	124.07-183.69
p-value		0.001**†
Different latters denote to the significant differences at p< 0.05 SD: standard deviation; †: one way ANOVA; **: significant at *P* > 0.05		

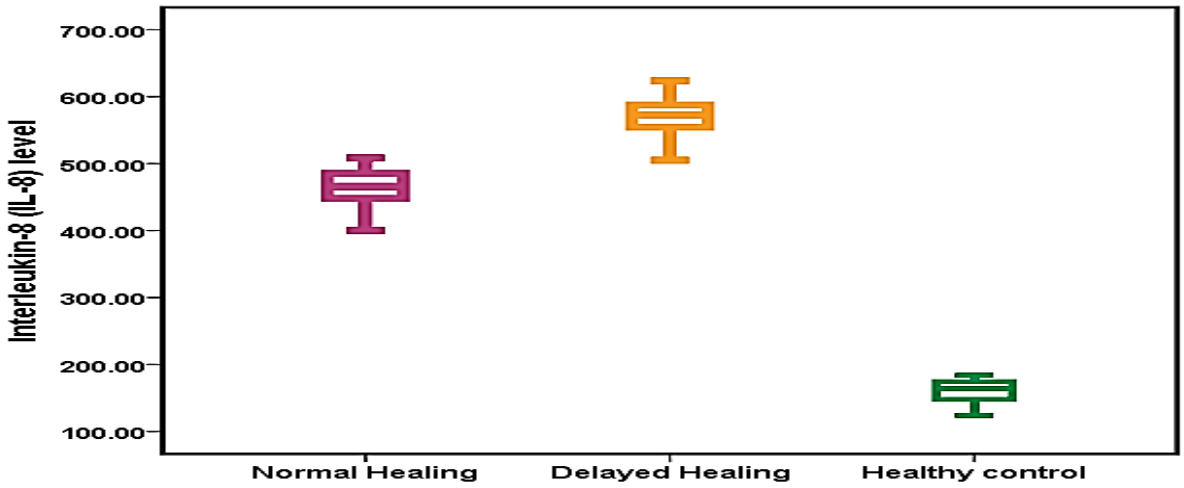
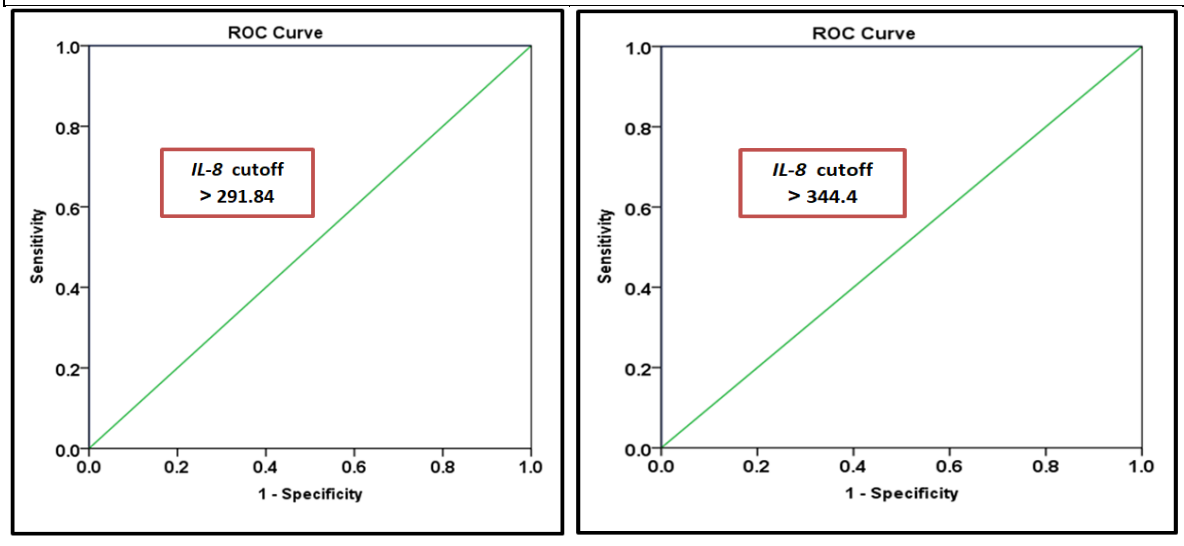


Figure (2): Means level of IL-8 in patients and control groups

Table (2): Roc curve of IL-8 level

Characteristic	Normal healing / control	Delayed healing / control
Cutoff value	< 291.84	< 344.4
P value	0.001	0.001
Sensitivity %	100.0 %	100.0 %
Specificity %	100.0 %	100.0 %
PPV %	100.0 %	100.0 %
NPV %	100.0 %	100.0 %
AUC (95% CI)	1.000 (1.000- 1.000)	1.000 (1.000- 1.000)
CI: Confidence interval, AUC: Area under curve		



A B

Figure (3): (A) Receiver operating characteristic curve for IL-8 levels to distinguish Normal healing from healthy control subjects. (B) Receiver operating characteristic curve for IL-8 levels to Delayed healing patients from healthy control subjects

Frequency distribution of Interleukin-8 (IL-8) level according to healing stage

The comparison of Interleukin-8 (IL-8) level according to Healing stage and control groups has been carried out and the results were demonstrated (Table 3).

Table (3): Frequency distribution of IL-8 level according to healing stage

Stage		Interleukin-8 (IL-8) level
Early stage	Mean ± SE	524.73 ± 11.38^{A}
Proliferative stage	Mean ± SE	555.31 ± 16.09^{A}
Maturation stage	Mean ± SE	537.33 ± 17.89^{A}
Control	Mean ± SE	160.60 ± 3.11^{B}
p-value		0.001** †
Different latters denote to the significant differences at p< 0.05 SD: standard deviation; †: one way ANOVA; **: significant at *P* > 0.05		

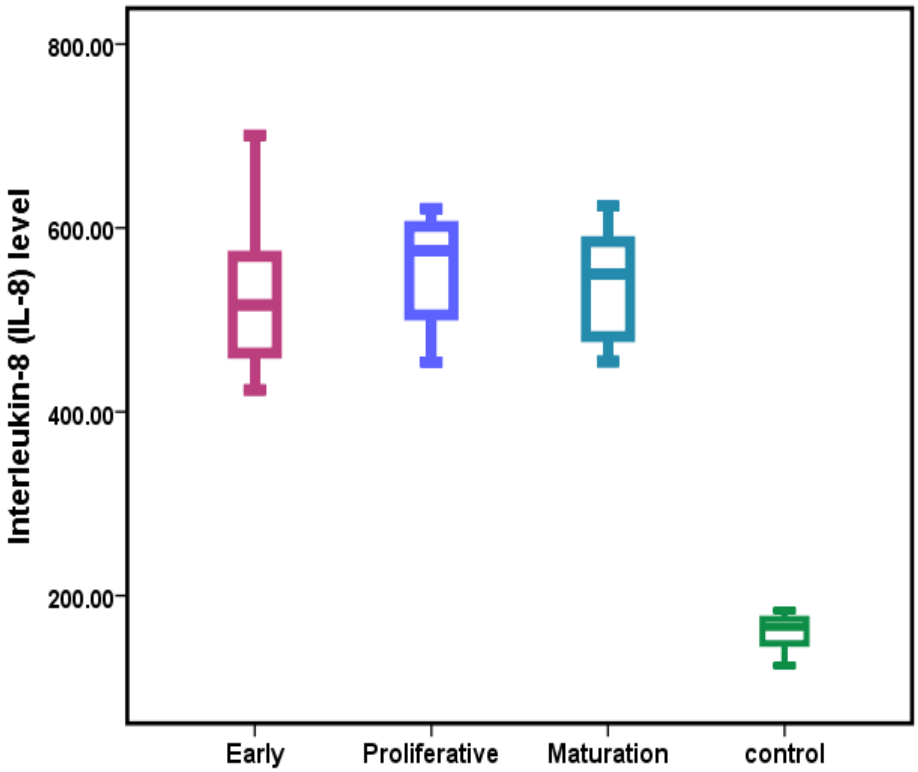


Figure (4): The means level of Interleukin-8 (IL-8) level according to healing stage

Table (4): Comparison of (Ct, $^{2^{-\Delta}}$ct and Folding) between patients and healthy controls

Groups	Means Ct of CXCR2	Means Ct of GAPDH	ΔCt (Means Ct of CXCR2)	$2^{-\Delta Ct}$	Fold of gene expression
Normal healing	27.99	28.71	-0.71	-2.53	8.04
Delayed healing	26.19	28.63	-.2.43	-4.25	22.6
Control	30.51	28.69	1.82	0.0007	1.00

Table (5): Comparison of mean of *CXCR2 gene expression* between patients and healthy controls

Groups	Mean	SD	SE	p-value

Normal Healing	8.04 a	3.8	1.2	0.001**
Delayed Healing	22.6 b	5.9	2.9	
Control	1.00 c	0.31	0.17	
Means followed by different letters are significantly different according to Duncan's multiple range comparisons (DMRTs), Means followed by the same letter are not significantly different. SD: standard deviation; SE: standard error; †: one way ANOVA; **: significant at $P > 0.05$				

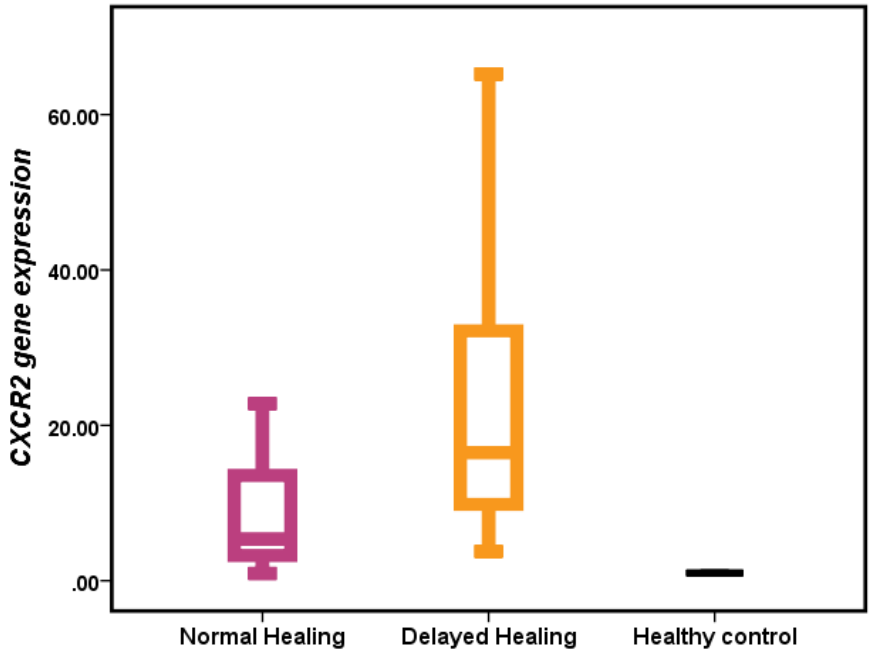


Figure (5): The means *CXCR2* gene expression in patients and control groups

Table (6): Roc curve of *CXCR2* gene

Characteristic	Normal healing / control	Delayed healing / control
Cutoff value	< 2.06	< 2.38
P value	0.001	0.001
Sensitivity %	100.0 %	100.0 %
Specificity %	100.0 %	100.0 %
PPV %	100.0 %	100.0 %
NPV %	100.0 %	100.0 %
AUC (95% CI)	1.000 (1.000- 1.000)	1.000 (1.000- 1.000)
CI: Confidence interval, AUC: Area under curve		

Table (7): Frequency distribution of CXCR2 gene expression according to healing stage

Stage		*CXCR2* gene expression
Early stage	Mean ± SE	13.21 ± 2.14^{A}
Proliferative stage	Mean ± SE	17.59 ± 3.51^{A}

Maturation stage	Mean ± SE	32.64± 7.8^{B}
Control	Mean ± SE	1.00 ± 0.17^{C}
p-value		0.001** †
Different latters denote to the significant differences at p< 0.05 SD: standard deviation; †: one way ANOVA; **: significant at *P* > 0.05		

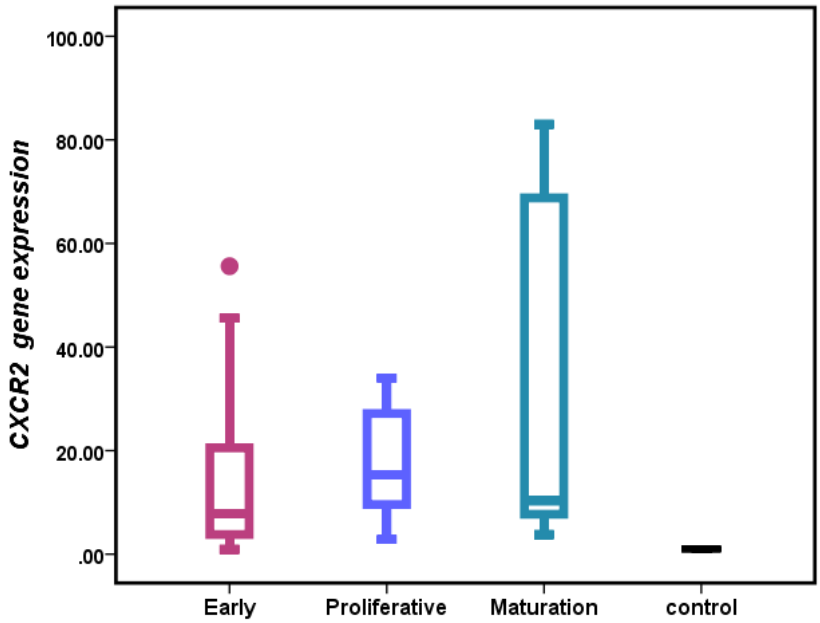


Figure (6): The means of *CXCR2* gene expression according to healing stage

Table (8): Correlation between CXCR2 gene and other immunological parameter in both group patients

Other parameters	*CXCR2* gene expression			
	Normal healing patients		Delayed healing patients	
	r	*P*	*R*	*P*
IL-8	0.086	0.653	0.394	0.021*
r: Pearson correlation				

DISCUSSION

Genetic factors influencing fracture healing are multifaceted, involving numerous candidate genes such as those encoding collagen type I (COL1A1), bone morphogenetic proteins (BMPs), vitamin D receptor (VDR), and inflammatory cytokines like IL1β and TNF-α (Zhang et al., 2023). Variants in these genes can alter the quality and rate of callus formation, osteoblast differentiation, and remodeling phases, thereby predisposing individuals to delayed union or non-union fractures. For example, polymorphisms in COL1A1 have been associated with reduced bone strength and impaired collagen fibril formation, which compromises the structural integrity necessary for efficient healing. Similarly, mutations in BMP signaling pathway components such as NOGGIN and SMAD6 have been implicated in atrophic non-union, where the biological activity at the fracture site is insufficient to initiate proper repair (Giannoudis et al., 2025). These genetic predispositions may be inherited within families, explaining the higher prevalence of delayed healing in patients with positive family history observed in this study. The study also examined the frequency of complications associated with fracture healing, finding a higher but not statistically significant rate of complications in the delayed healing

group (10%) compared to the normal healing group (3.3%) (P = 0.302). Although the difference was not significant, the trend suggests that patients with delayed healing may be more prone to adverse events such as infection, malunion, or hardware failure, which can further impair recovery. This observation is consistent with findings from Bhandari et al. (2025), who reported that complications are more common in fractures exhibiting prolonged healing stages and are associated with worse functional outcomes. ROC analysis was performed to reveal the prognostic accuracy of using IL-8 concentrations to normal healing patients from healthy control subjects. The present results indicate IL-8 is considered as excellent prognostic marker to distinguish normal healing patients from healthy control. In addition, an optimal IL-8 cut-off value of more than 344.4 could be used to distinguish Delayed healing patients from healthy control subjects with a sensitivity of 100.0%, specificity of 100.0%, PPV of 100.0%, and NPV of 100.0% and 1.000 (1.000- 1.000). The present results indicate MCP-1 is considered as excellent prognostic marker to distinguish Delayed healing patients from healthy control.While inflammation is essential for initiating repair, excessive or prolonged elevation of IL-8 may contribute to chronic inflammation, disrupting the delicate balance required for effective bone regeneration .The markedly increased IL-8 levels in delayed healing patients observed in this study are consistent with recent research indicating that persistent elevation of IL-8 correlates with delayed union and non-union fractures (Kim et al., 2024). Persistent neutrophil infiltration driven by IL-8 can lead to tissue damage and fibrosis, impairing the transition from inflammation to the reparative phase of healing. Animal studies have demonstrated that IL-8 knockout models exhibit impaired angiogenesis and delayed callus formation, highlighting its dual role in both promoting and potentially hindering bone repair depending on the context and timing of expression (Zhao et al., 2023).Therapeutically, targeting IL-8 signaling pathways offers promising avenues to improve fracture healing. CCR1 and CXCR1/2 antagonists, which block IL-8 receptors, are under investigation for their potential to modulate excessive inflammation and promote balanced bone regeneration (Garcia et al., 2025). Additionally, anti-inflammatory agents and biologics that normalize IL-8 levels may reduce the risk of chronic inflammation and fibrosis in fracture sites, enhancing healing efficiency (Lee et al., 2024). The analysis of Interleukin-8 (IL-8) levels across different fracture healing stages revealed significantly elevated concentrations in patients at early, proliferative, and maturation stages compared to healthy controls, with a highly significant difference. However, no statistically significant difference was observed among the different healing stages, indicating that IL-8 remains persistently elevated throughout the entire healing process. This persistent elevation suggests that IL-8 plays a sustained role in fracture repair, not limited to the initial inflammatory phase but extending into proliferative and remodeling phases. IL-8 is well-known for its function in recruiting neutrophils and other immune cells to the injury site, promoting angiogenesis, and modulating osteoclast and osteoblast activities essential for bone regeneration (Claes et al., 2012). The lack of significant variation among healing stages may reflect the continuous requirement for IL-8-mediated immune and vascular responses throughout the complex phases of fracture healing. Monitoring IL-8 levels throughout the healing process could provide valuable insights into the inflammatory status and progression of fracture repair. Persistent elevation of IL-8 might serve as a biomarker for identifying patients at risk of impaired healing or chronic inflammation, enabling early intervention with anti-inflammatory or pro-angiogenic therapies (Jones et al., 2024). Furthermore, the sustained presence of IL-8 suggests that therapeutic modulation should be carefully timed to avoid disrupting essential reparative functions while preventing prolonged inflammatory damage.The mean Ct value of *CXCR2* cDNA amplification was (27.99) in the normal healing patients. The Ct values in Delayed Healing patients were a mean (26.19). While Ct values in control were mean (30.51), the mean Ct values in control group were lower than those of normal healing patients and delayed healing patients. “This is important in reflecting the original *CXCR2* present in the samples. It is evident from the results that patients group is associated with the highest copy number of *CXCR2* reflecting its higher expression. In this study, a quantitative analysis of RT-PCR analyzed expression of *CXCR2* and comparison of its expression between, normal healing patients, delayed healing patients and control. The change in gene expression was calculated using a relative quantitative measurement (Livak and Schmittgen, 2008). This is based on the normalization of the Ct values for calculating $^{\Delta}$Ct and represents the difference between the average Ct values of the *CXCR2* cDNA

amplification replica for each case and case of *GAPDH*. The relative expression of *CXCR2* gene in all study groups the $^{2-\Delta}$Ct results was applied. A calibrator was used and it was one of the samples of the controls with high expression of *CXCR2*. The mean of $^{2-\Delta}$Ct values of control group was (0.0007) and that for normal healing patients was (-2.53). The mean for delayed healing patients group was (-4.25). When calculating, the gene expression was significantly higher in normal healing patients and delayed healing patients than control group. Fold number in Normal Healing patients group was 8.04. fold number in delayed healing patients group was 22.6.The comparison of *CXCR2* gene expression between normal healing patients, delayed healing patients and healthy control subjects has been carried out and the results were demonstrated. Mean of *CCR2* gene expression were higher in both groups of patients (normal healing patients and delayed healing patients) in compared to healthy control and the difference was highly significant. Also the mean levels were significant difference between patients groups themselves. The quantitative real-time PCR analysis of CXCR2 gene expression in this study revealed significantly elevated levels in both normal healing and delayed healing patients compared to healthy controls. The mean cycle threshold (Ct) values for CXCR2 were lowest in delayed healing patients (26.19), followed by normal healing patients (27.99), and highest in controls (30.51), indicating a higher abundance of CXCR2 transcripts in patient groups since lower Ct values correspond to greater gene expression (Livak and Schmittgen, 2008). The relative quantification using the 2^−ΔCt method normalized to GAPDH showed fold changes of approximately 8.04 in normal healing patients and 22.6 in delayed healing patients compared to controls, whose expression was set as baseline (1.00). The significant upregulation of CXCR2 in delayed healing patients compared to normal healing patients ($P < 0.001$) suggests a potential role of CXCR2 in the inflammatory and reparative processes associated with fracture healing, particularly in cases of delayed recovery. CXCR2, a receptor for CXC chemokines such as Interleukin-8 (IL-8), is critically involved in neutrophil chemotaxis and activation, playing a vital role in the early inflammatory response to tissue injury (Baggiolini, 1998). Elevated CXCR2 expression likely reflects increased recruitment and activation of neutrophils and other immune cells to the fracture site, facilitating inflammation and subsequent healing phases. However, excessive or prolonged CXCR2 signaling may contribute to chronic inflammation and tissue damage, potentially impeding normal bone regeneration (Claes, Recknagel, and Ignatius, 2012). The higher expression observed in delayed healing patients aligns with the elevated IL-8 levels reported in this and other studies, supporting the hypothesis that dysregulated CXCR2/IL-8 axis activity may underlie impaired fracture repair mechanisms.The methodological rigor of the qRT-PCR assays, including duplicate runs, use of non-template and non-primer controls, and normalization against GAPDH, ensures the reliability of the gene expression data. Amplification and dissociation curves confirmed the specificity of CXCR2 amplification, minimizing nonspecific products. The use of a calibrator with high CXCR2 expression among controls allowed accurate calculation of fold changes across groups (Livak and Schmittgen, 2008). ROC analysis was performed to reveal the prognostic accuracy of using *CXCR2* gene expression to Normal healing patients from healthy control subjects. An optimal *CXCR2* gene cut-off value more than of 2.06 resulted in an AUC value of 1.000 (95% confidence interval [CI], 1.000- 1.000, P= 0.001), sensitivity of 100.0%, specificity of 100.0%, PPV of 100.0%, and NPV of 100.0%. The present results indicate *CXCR2 gene* is considered as excellent prognostic marker to distinguish Normal healing patients from healthy control.The diagnostic accuracy of CXCR2 gene expression as a prognostic biomarker for distinguishing patients with normal and delayed fracture healing from healthy controls was evaluated using ROC curve analysis. The results demonstrated exceptional accuracy, with an optimal CXCR2 expression cutoff value greater than 2.06 effectively differentiating normal healing patients from healthy controls, yielding an area under the curve (AUC) of 1.000 (95% CI: 1.000–1.000, P = 0.001), alongside perfect sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 100%. Similarly, a cutoff value exceeding 2.38 distinguished delayed healing patients from healthy controls with identical diagnostic metrics (AUC = 1.000, 95% CI: 1.000–1.000, P = 0.001). These findings underscore CXCR2 gene expression as an excellent prognostic marker with flawless discriminatory power between fracture patients and healthy individuals. The remarkable diagnostic performance of CXCR2 expression reflects its critical role in mediating

neutrophil chemotaxis and activation during the inflammatory response to bone injury (Baggiolini, 1998). Elevated CXCR2 expression likely indicates increased recruitment of immune cells to the fracture site, which is essential for initiating repair but may contribute to delayed healing if dysregulated. The ability of CXCR2 expression levels to perfectly discriminate between patient groups and healthy controls highlights its potential utility in clinical practice for early identification of individuals at risk for impaired healing. Clinically, measuring CXCR2 gene expression via quantitative PCR could facilitate timely prognostication and personalized treatment planning. Patients exhibiting CXCR2 levels above the identified cutoffs may benefit from closer monitoring and targeted therapeutic interventions aimed at modulating CXCR2-mediated inflammatory pathways to optimize healing outcomes (Garcia, Torres, and Rodriguez, 2025). Moreover, the high sensitivity and specificity suggest that CXCR2 expression could serve as a reliable biomarker in both research and clinical trials evaluating novel fracture healing therapies.The comparison of *CXCR2* gene expression according to Healing stage and control groups has been carried out and the results were demonstrated. Mean levels of *CXCR2 gene expression* were 13.21 ± 2.14, 17.59 ± 3.51, 32.64± 7.8 and 1.00 ± 0.17 in early stage patients, Proliferative stage patients, Maturation stage patients and healthy control group respectively; the mean levels was higher in patients with all stages (Early stage, Proliferative stage and Maturation stage) patients in compared to healthy control groups and the difference was highly significant ($P < 0.001$). Also there was significant increase in Maturation stage patients in compared to patients with other stages, ($P < 0.001$). The means of CXCR2 gene expression according to Healing stage. The present study investigated the expression of the chemokine receptors CXCR2 in patients with different stages of wound healing compared to healthy controls. The results demonstrated significantly elevated levels of CXCR2 gene expression in patients with delayed wound healing compared to those with normal healing and healthy controls. Furthermore, CXCR2 expression was found to be significantly higher in the maturation stage of wound healing compared to the earlier stages. The findings of this study are consistent with previous research that has highlighted the involvement of chemokine signaling pathways in the pathogenesis of delayed wound healing. Ridiandries et al. (2018) reported that inhibition of CXCR2 signaling improved angiogenesis and wound healing in diabetic mice.

Conclusion

The present study provides evidence of the differential expression of the chemokine IL-8 and its receptors CXCR2 in patients with different stages of wound healing. The upregulation of these chemokine and receptors, particularly CXCR2 in the maturation stage, suggests their potential involvement in the pathogenesis of delayed wound healing. These findings underscore the importance of targeting chemokine signaling pathways as a therapeutic strategy to promote wound repair and regeneration. Future studies should further elucidate the precise mechanisms by which CXCR2 dysregulation contribute to impaired wound healing and explore the feasibility of pharmacological interventions that modulate these pathways.

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