

Estimate the Influence of CK-MM and CRP Level in Lower Extremity Bone Fracture Patients: A Cross-Sectional Study

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ABSTRACT

Background: C-reactive protein (CRP) and creatine kinase-MM (CK-MM) are laboratory biomarkers associated with inflammation and muscle injury. Their patterns in patients with lower extremity fractures may provide information about associated tissue damage.

Objective: To assess CRP and CK-MM findings among adults with lower extremity bone fractures.

Methods: This cross-sectional comparative study included 105 adults aged 20–70 years with lower extremity fractures following road traffic accidents, falls, or slipping. Blood samples were collected at Zia Darman Clinical Laboratory, Mardan, Khyber Pakhtunkhwa, Pakistan, from January 1 to April 30, 2025. CRP was assessed qualitatively using latex agglutination, while CK-MM was measured spectrophotometrically using a Micro-Lab 200. Data were analyzed using SPSS version 25.0. Categorical variables were compared using the chi-square test, with $p < 0.05$ considered statistically significant.

Results: Of 105 patients, 76 (72.4%) were male and 29 (27.6%) female. Fractures involved the hip joint in 37 (35.2%) patients, femur in 35 (33.3%), and tibia in 33 (31.4%). Combined CRP and CK-MM positivity was reported in 68 (64.8%) patients. Positivity rates were 22/37 (59.5%) for hip joint fractures, 21/35 (60.0%) for femoral fractures, and 25/33 (75.8%) for tibial fractures. Differences across fracture sites were not statistically significant ($\chi^2 = 2.34$, $df = 2$, $p = 0.312$). Elevated CK-MM was observed in 24 (22.9%) patients.

Conclusion: CRP and CK-MM positivity was observed among patients with lower extremity fractures, with the highest proportion in tibial fractures. However, differences between fracture sites were not statistically significant. Further controlled studies with standardized sampling are needed to clarify their clinical significance.

Keywords: C-reactive protein; creatine kinase-MM; bone fracture; lower extremity; inflammation; biomarkers

INTRODUCTION

Bone fracture refers to a breakdown in the continuity of skeletal bone. The human skeleton is divided into the appendicular skeleton (126 bones) and the axial skeleton (80 bones). The appendicular skeleton comprises the upper extremity (64 bones) and the lower extremity (62 bones). The axial skeleton includes the skull, vertebral column, and thoracic cage. Fractures may be simple or compound. In accidental conditions, surrounding muscle tissue may also be damaged, leading to inflammation. In response, the liver produces C-reactive protein (CRP), and muscle cells release creatine kinase-MM (CK-MM) enzyme¹. We hypothesized that both CRP and CK-MM levels would be elevated in patients with lower extremity bone fractures, and that the magnitude of elevation would vary by fracture site and severity. CRP is a non-specific indicator of inflammation and may serve as a primary defense function of the human body. The liver secretes CRP into the blood during infection and injury as a result of inflammation². It is synthesized in response to the acute phase of bacterial or fungal infection and may serve as a proxy measurement for general wellness. Structurally, CRP is a symmetrical ring molecule consisting of five non-covalently associated protomers. Each protomer has two calcium ions responsible for the specific binding of phosphocholine.

Phosphocholine is a common constituent of many bacterial and most living cell membranes, such as the phosphocholine residues of C-polysaccharide of *Streptococcus pneumoniae*³. The protein was designated "C-reactive" because of this reaction⁴.

Serum CRP levels have been measured by rate nephelometry, with a detection limit of 6–10 mg/L. A commercially available high-sensitivity CRP (hs-CRP) test is a latex particle-enhanced immunoturbidimetric assay with a detection limit of approximately 0.15 mg/L. It has been used extensively to detect cardiovascular disease, monitor cardiac treatment, and predict future cardiovascular outcomes. The critical range of CRP levels in cardiovascular disease patients is 1–10 mg/L. The baseline level in perfectly healthy persons may be < 0.15 mg/L, particularly in Asian populations⁴. Low-grade inflammation, as estimated by hs-CRP level, has been shown to interfere with bone metabolism and affect the risk of nontraumatic fractures⁵.

A recent systematic review and meta-analysis including 48 studies found that CRP/hs-CRP-related exposures were associated with hip fracture (pooled ratio estimate 1.39, 95% CI 1.17–1.67) and vertebral fracture (2.16, 95% CI 1.47–3.18) (6). In the population-based Bruneck Study ($n = 919$), the adjusted relative risk of nontraumatic fracture in the highest versus lowest tertile group for hs-CRP was 9.4 (95% CI, 3.6–24.8; $P < .001$)⁵.



Data from the Study of Women's Health Across the Nation (SWAN) demonstrated that fracture risk increases with increasing CRP, particularly above a threshold of 3 mg/L⁶. More recent evidence from the prospective STRAMBO study in older men suggests that while higher hs-CRP concentrations are associated with faster cortical bone loss, they are not independently associated with fracture risk⁸.

Creatine kinase is a compact molecule of approximately 82 kDa normally found in the cytosol and mitochondria of cells where energy demands are high.

CK is made up of two peptide chains of about 42 kDa: The M subunit (muscle) and the B subunit (brain). These two polypeptides combine to form three different isoenzymes: CK-MB (cardiac muscle), CK-BB (brain), and CK-MM (all skeletal muscles)⁹. CK-MM is the predominant isoenzyme in skeletal muscle, where it is found in the myofibril bound to the M-line structure of the sarcomere¹⁰. The physiological role of CK is associated with adenosine triphosphate (ATP) generation for contractile or transport systems¹¹. CK is released into blood following damage to muscle tissue, resulting in elevated serum/plasma CK activity¹².

Normal serum CK-MM values in the general population range from 35–175 U/L, though values as high as 16,000 U/L have been noted due to asymptomatic cases, minor injury, and genetic factors. When CK-MM levels are found to be between 10,000–200,000 U/L, this warns of myocyte damage or membrane disruption resulting in the release of intracellular mechanisms into the blood. Serum concentrations of CK begin to increase within 2–12 hours after the onset of muscle injury, reach a maximum at 24–72 hours, and drop at 3–5 days as the muscle injury subsides¹³. Analysis of CK isoforms in serum can provide an earlier indicator of skeletal muscle damage than total CK or perception of soreness and may be useful in tracking the time course of skeletal muscle damage and repair¹⁴.

The levels of CRP and CK-MM determine their correlation with risk factors such as inflammation, muscle degeneration, and skeletal bone damage. Generally, serum CRP levels are elevated during inflammation, while CK-MM levels increase due to connective tissue damage¹⁵. In patients with closed tibial shaft fractures, serum creatine phosphokinase (CPK) activity has been shown to increase significantly after fracture ($p < 0.001$), with high-energy and slowly healing fractures demonstrating significantly higher levels than low-energy and normally healing fractures, suggesting that CPK determinations could be used to assess the severity of trauma and possibly prognosis¹⁶. Additionally, studies on plasma myosin heavy chain fragments have shown that these contractile protein markers peak at 24 hours after injury or surgery, providing supplementary information for the assessment of tissue damage in patients with musculoskeletal injuries¹⁷.

The primary objective of this study was to estimate the influence of CK-MM and CRP levels in cross-sectional blood samples from adult patients with lower extremity bone fractures resulting from any cause. Specifically, we aimed to determine the prevalence of elevated CRP and CK-MM levels in this population, to compare biomarker positivity rates across different fracture types (hip joint, femur, and tibia), and to assess the potential clinical utility of these markers in fracture management.

METHODOLOGY

A cross-sectional comparative study was conducted from 1 January to 30 April 2025 at Zia Darman Clinical Laboratory, Mardan, Khyber Pakhtunkhwa, Pakistan, to assess C-reactive protein (CRP) and creatine kinase-MM (CK-MM) findings in adults with lower extremity fractures. Eligible participants were aged 20–70 years and had fractures resulting from road traffic

accidents, falls, or slipping. Newborns and children were excluded, as were patients with pre-existing inflammatory conditions, active infections, malignancies, chronic kidney or liver disease, or muscle disorders. Patients taking medications potentially affecting CRP or CK-MM measurements, including statins, corticosteroids, and non-steroidal anti-inflammatory drugs, were also excluded. The calculated minimum sample size was 97 participants, based on the single-proportion formula, ($n = Z^2 p(1-p)/d^2$), with a 95% confidence level ($(Z=1.96)$), an assumed prevalence of 50%, and a margin of error of 5%. The final sample comprised 105 patients. The sampling technique was not specified in the study records.

Approximately 2 mL of venous blood was collected from the forearm using standard venipuncture procedures and transferred into serum separator tubes. Following clot formation at room temperature, samples were centrifuged at 3,000 rpm for 10 minutes, and the serum was separated. Analyses were performed within two hours of collection or after storage at 2–8 °C for up to 24 hours. CK activity was measured using a commercial enzymatic assay on a Micro-Lab 200 spectrophotometer at 340 nm and 37 °C.

The method involved coupled enzymatic reactions, with NADPH formation monitored through changes in absorbance per minute to determine enzyme activity. CRP was assessed qualitatively using latex agglutination by mixing 50 µL of serum with latex reagent and rotating the reaction slide for two minutes. Visible agglutination indicated a positive result. Where performed, semi-quantitative assessment used serial two-fold dilutions in 0.9% saline, with a stated detection threshold of 6 mg/L. Laboratory quality control included appropriate control materials, with a reported coefficient of variation below 5% for CK measurements. Patient investigation reports were transcribed onto a standardized data collection form. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean $\pm$ standard deviation or median (interquartile range), as appropriate, while categorical variables were presented as frequencies and percentages. Associations between categorical variables were evaluated using the chi-square test or Fisher's exact test, where appropriate. Statistical significance was set at $p < 0.05$, and missing observations were handled using complete-case analysis.

Ethical approval was granted by the Institutional Review Board/Ethics Committee of the Institute of Health Sciences, Mardan, affiliated with Abdul Wali Khan University Mardan (Approval No. IHS/EC/2025/012; 10 January 2025). Written informed consent was obtained from participants. Confidentiality was maintained, and the study was conducted in accordance with the Declaration of Helsinki. Reporting followed the STROBE guidelines for cross-sectional studies, with the completed checklist provided as supplementary material.

RESULTS

Influence of CK-MM and CRP Levels in Lower Extremity Bone Fracture Patients: Demographic Characteristics

A total of 105 adult patients with lower extremity bone fractures were included in this cross-sectional study to estimate the influence of CK-MM and CRP levels. Among the 105 patients, 76 (72.4%) were male and 29 (27.6%) were female, indicating a male predominance in the fracture population.

The mean age of the study population was 45.2 ± 12.8 years (range: 20–70 years). The median time from injury to sample collection was 36 hours (IQR: 18–60 hours).

Table 1. Baseline demographic and clinical characteristics of study population (n = 105)

Characteristic	Category	Number of Patients (n)	Percentage (%)
Gender	Male	76	72.4%
	Female	29	27.6%
Age Group (years)	20–30	18	17.1%
	31–40	24	22.9%
	41–50	28	26.7%
	51–60	21	20.0%
	61–70	14	13.3%
	> 70	19	18.1%
Fracture Type	Hip Joint	37	35.2%
	Femur	35	33.3%
	Tibia	33	31.4%
Fracture Cause	Road Traffic Accident	58	55.2%
	Sudden Slipping/Fall	39	37.1%
	Other Causes	8	7.6%
Time from Injury to Sampling	< 24 hours	42	40.0%
	24–72 hours	45	42.9%
	> 72 hours	18	17.1%

Note: Data presented as frequency (n) and percentage (%).

Influence of CK-MM and CRP Levels in Lower Extremity Bone Fracture Patients: Distribution of Fractures

Figure 1 illustrates the distribution of lower extremity bone fractures by anatomical site to estimate the influence of CK-MM and CRP levels. Among the 105 patients, hip joint fractures were the most common (n = 37, 35.2%), followed by femur bone fractures (n = 35, 33.3%) and tibia bone fractures (n = 33, 31.4%).

Figure 1: Distribution of lower extremity bone fractures by type (n = 105).

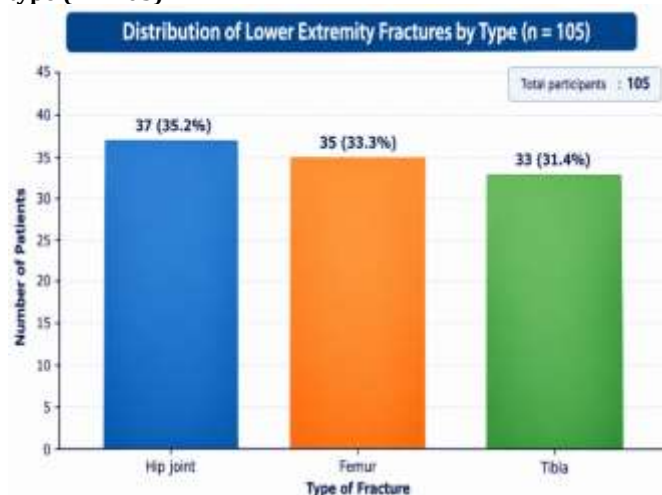


Table 2: Distribution of fracture types and biomarker positivity (Influence of CK-MM and CRP)

Fracture Type	Total Patients (n)	CRP/CK-MM Positive (n, %)	CRP/CK-MM Negative (n, %)
Hip Joint	37	22 (59.5%)	15 (40.5%)
Femur	35	21 (60.0%)	14 (40.0%)
Tibia	33	25 (75.8%)	8 (24.2%)
Total	105	68 (64.8%)	37 (35.2%)

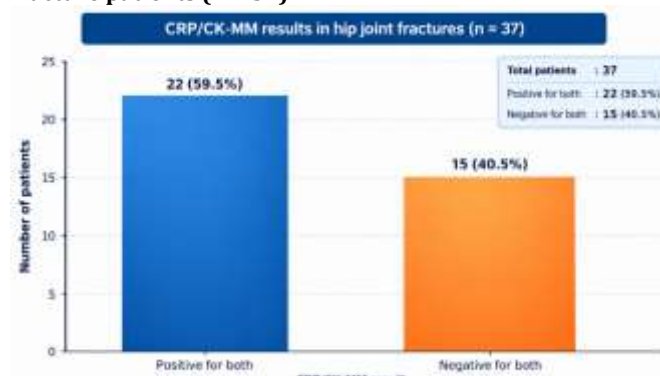
Abbreviations: CRP, C-reactive protein; CK-MM, creatine kinase-MM.

The overall positivity rate for combined CRP and CK-MM was 64.8% (68/105), demonstrating the influence of these markers in lower extremity bone fractures. The highest positivity rate was observed in tibia fractures (75.8%), followed by femur (60.0%) and hip joint (59.5%) fractures. However, the difference in positivity rates across fracture types was not statistically significant ($\chi^2 = 2.34$, $df = 2$, $p = 0.312$).

Influence of CK-MM and CRP Levels in Hip Joint Fracture Patients

Figure 2 shows the influence of CK-MM and CRP test results among hip joint fracture patients. Out of 37 hip joint fracture patients, 22 (59.5%) tested positive for both CRP and CK-MM, while 15 (40.5%) tested negative.

Figure 2: Influence of CRP and CK-MM test results in hip joint fracture patients (n = 37).

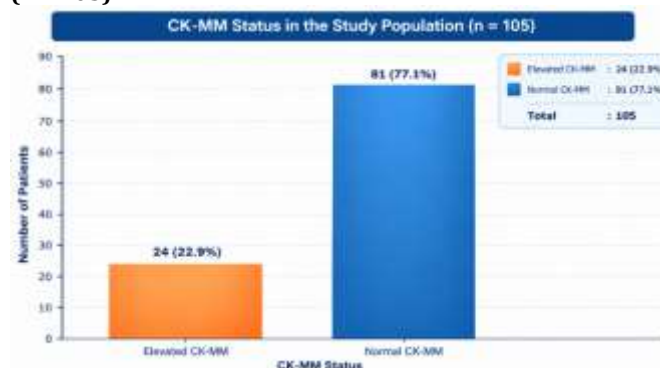


There was no statistically significant difference in CRP/CK-MM positivity between male and female hip joint fracture patients ($p = 0.782$).

Influence of CK-MM Levels in the Overall Study Population

Figure 3 presents the influence of CK-MM levels in the whole study population. Elevated CK-MM levels were observed in 24 patients (22.9%), whereas 81 patients (77.1%) had normal CK-MM levels.

Figure 3: Influence of CK-MM levels in the study population (n = 105).



The difference in CK-MM elevation between males and females

was not statistically significant ($\chi^2 = 0.71$, $df = 1$, $p = 0.399$).

Table 3: Distribution of CK-MM levels by fracture type (n = 105)

Fracture Type	Total Patients (n)	CK-MM Elevated (n, %)	CK-MM Normal (n, %)
Hip Joint	37	8 (21.6%)	29 (78.4%)
Femur	35	7 (20.0%)	28 (80.0%)
Tibia	33	9 (27.3%)	24 (72.7%)
Total	105	24 (22.9%)	81 (77.1%)

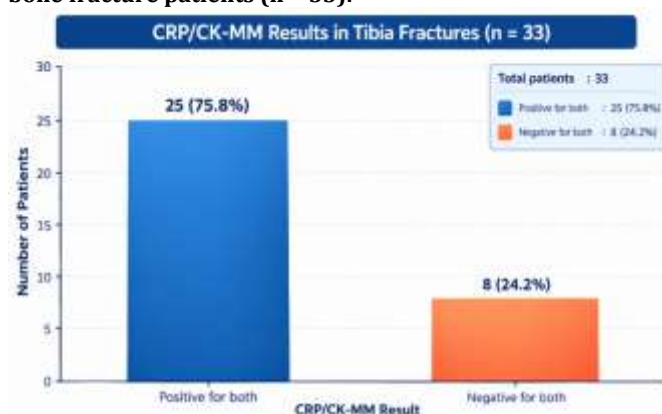
Abbreviation: CK-MM, creatine kinase-MM.

There was no statistically significant difference in CK-MM elevation across fracture types ($\chi^2 = 0.54$, $df = 2$, $p = 0.763$).

Influence of CK-MM and CRP Levels in Tibia Bone Fracture Patients

Figure 4 displays the influence of CRP and CK-MM test results among tibia bone fracture patients. Out of 33 tibia fracture patients, 25 (75.8%) tested positive for both CRP and CK-MM, while 8 (24.2%) tested negative.

Figure 4: Influence of CRP and CK-MM test results in tibia bone fracture patients (n = 33).



There was no statistically significant difference in CRP/CK-MM positivity between male and female tibia fracture patients ($p = 0.452$).

Influence of CK-MM and CRP Levels in Femur Bone Fracture Patients

Figure 5 displays the influence of CRP and CK-MM test results among femur bone fracture patients. Out of 35 femur fracture patients, 21 (60.0%) tested positive for both CRP and CK-MM, while 14 (40.0%) tested negative.

Figure 5: Influence of CRP and CK-MM test results in femur bone fracture patients (n = 35)

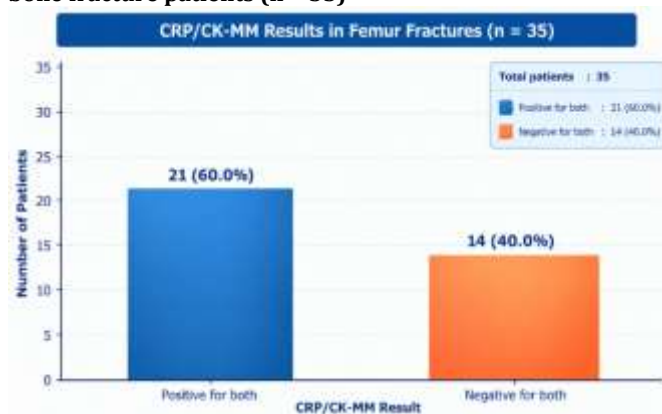


Table 4: Gender-wise distribution of CRP and CK-MM results

in femur bone fracture patients (n = 35)

Gender	Total Patients (n)	CRP/CK-MM Positive (n, %)	CRP/CK-MM Negative (n, %)
Male	24	15 (62.5%)	9 (37.5%)
Female	11	6 (54.5%)	5 (45.5%)
Total	35	21 (60.0%)	14 (40.0%)

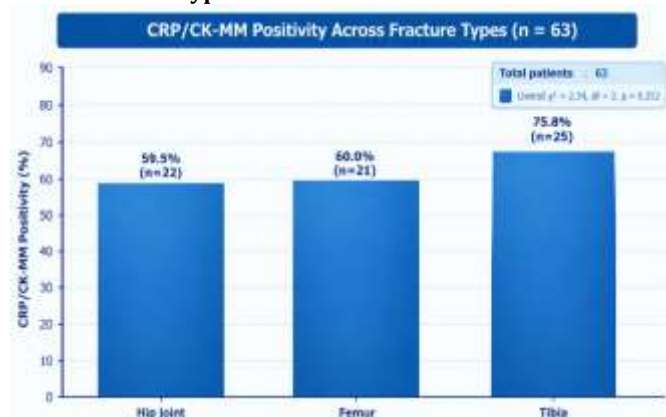
Abbreviations: CRP, C-reactive protein; CK-MM, creatine kinase-MM.

There was no statistically significant difference in CRP/CK-MM positivity between male and female femur fracture patients ($p = 0.654$).

Comparative Influence of CK-MM and CRP Positivity Across Fracture Types

Figure 6 presents a comparative analysis of the influence of CRP and CK-MM positivity rates across different lower extremity fracture types. The highest positivity rate was observed in tibia bone fracture patients (75.8%), followed by femur (60.0%) and hip joint (59.5%) fracture patients.

Figure 6: Comparative influence of CRP and CK-MM positivity across fracture types.



The difference in CRP/CK-MM positivity rates across fracture types was not statistically significant ($\chi^2 = 2.34$, $df = 2$, $p = 0.312$). The results demonstrate the influence of both CRP and CK-MM in a substantial proportion of patients with lower extremity bone fractures. The highest positivity rate was observed in tibia bone fracture patients (75.8%), followed by femur (60.0%) and hip joint (59.5%) fracture patients. Elevated CK-MM levels were found in 22.9% of the overall study population. These findings indicate that CK-MM and CRP levels are influenced by lower extremity bone fractures and associated tissue injury, though the response varies by fracture site and individual patient characteristics.

DISCUSSION

The results demonstrate the influence of both CRP and CK-MM tests in lower extremity bone fractures, including hip joint, femur, and tibia fractures, in the adult male and female population studied.

Our study shows that adult males constituted 72.4% and females 27.6% of the fracture population. Hip joint fractures were most common (37 patients), followed by femur (35) and tibia (33) fractures out of 105 patients among hip joint fracture patients, 59.5% were positive for both CRP and CK-MM, while 40.5% were negative. Our study shows that CK-MM was elevated in 22.9% of the population and normal in 77.1% among tibia fracture patients, 25 (75.8%) had positive results and 8 (24.2%) had negative results for both markers. This study shows that among femur fracture patients, 21 (60.0%) had positive results and 14

(40.0%) had negative results.

These findings are consistent with previous literature indicating that CRP and CK-MM are suitable biomarkers for detecting bone and muscle tissue damage. Serum CK-MM levels are known to increase in response to skeletal and cardiac tissue injury, with elevations beginning within 2–12 hours of injury and peaking at 24–72 hours¹³. In a study by Yokoi et al., preoperative CK values in trauma patients were significantly higher than in non-trauma controls (254.9 ± 33.3 IU/L vs. 63.2 ± 7.4 IU/L, $P < 0.05$), with 28.9% of trauma patients having CK levels above 200 IU/L compared to only 2.2% of controls¹⁹. Similarly, a Chinese study of 175 trauma fracture patients found that CRP and CK levels were significantly higher in severe trauma patients compared to mild trauma patients at both day 1 and day 5 post-injury ($P < 0.05$)²⁰. Another study of 80 trauma fracture patients confirmed that PCT, CRP, CK, and CK-MB levels showed significant differences between mild and severe groups at 1 and 7 days' post-injury ($P < 0.05$)²¹.

CRP, produced by the liver in response to infection, inflammation, malignancy, and trauma, typically peaks at approximately 48 hours after the triggering event²². In patients with tibial shaft fractures, serum CPK activity has been shown to increase significantly after fracture, with higher levels observed in high-energy fractures¹⁶. Furthermore, studies have demonstrated that hs-CRP is a significant and independent risk predictor of nontraumatic fracture, suggesting a tight interplay between low-grade inflammation and bone turnover⁵. The SWAN study further confirmed that fracture risk increases with increasing CRP, only above the threshold of 3 mg/L, and that composite strength indices partially explain the increased fracture risk associated with inflammation⁷. A recent meta-analysis including 14 studies and 3,986 hip fracture patients found that both higher preoperative and postoperative CRP levels were correlated with higher risk of mortality following hip fracture surgery (preoperative MD: 0.67, 95% CI: 0.37–0.98, $P < 0.0001$; postoperative MD: 1.26, 95% CI: 0.87–1.65, $P < 0.00001$), suggesting the prognostic role of CRP²³.

However, the relatively low percentage of elevated CK-MM (22.9%) suggests that not all fractures are associated with significant muscle damage, or that sampling timing may influence detection. This is consistent with findings from studies on blunt trauma patients, where serum CRP levels on admission were like normal values, reaching peak values only after 3 days²⁴. Additionally, another study reported that CRP levels following accidental or surgical trauma should be assessed with caution, as early assessment of CRP or IL-6 was not useful for the diagnosis of sepsis in blunt trauma patients²⁵. More recent evidence from the STRAMBO study in older men indicates that while higher hs-CRP levels are associated with faster cortical bone loss at the distal tibia, they are not associated with fracture risk, suggesting that the relationship between inflammation and bone health is complex and may vary by population and fracture type⁸.

The diagnostic accuracy of these inflammatory markers in fracture-related infection has also been evaluated. A systematic review and meta-analysis by van den Kieboom et al. found that CRP had a pooled sensitivity of 77.0% and specificity of 67.9% for late fracture-related infection, while leucocyte count had 51.7% sensitivity and 67.1% specificity, and ESR had 45.1% sensitivity and 79.3% specificity. The authors concluded that serum inflammatory markers CRP, LC, and ESR are insufficiently accurate to diagnose late fracture-related infection but may be used as a suggestive sign in its diagnosis²⁶.

Studies on myosin heavy chain fragments have demonstrated that these contractile protein markers peak at 24 hours after injury or surgery, providing supplementary information for the assessment of tissue damage in patients with musculoskeletal

injuries¹⁷. The combination of total CK and CK-MM isoform has been considered a more sensitive marker than total CK alone for diagnosis of the stage of neuromuscular disease²⁷. Additionally, CK-MM isoform analysis in serum can provide an earlier indicator of skeletal muscle damage than total CK or perception of soreness¹⁴. In patients with tibial shaft fractures, high-energy and slowly healing fractures had significantly higher CPK levels than low-energy and normally healing fractures, suggesting that CPK determinations could be used to assess the severity of trauma and possibly prognosis¹⁶.

The study has several limitations. The sample size was relatively small ($n = 105$), and the study duration was limited to four months. The cross-sectional design precludes assessment of temporal relationships between marker levels and clinical outcomes. Additionally, the qualitative CRP method used (latex agglutination) has lower sensitivity compared to hs-CRP assays²⁸. Furthermore, the study did not control confounding factors such as concomitant infections, pre-existing inflammatory conditions, or medications that could affect CRP and CK-MM levels. The timing of sample collection relative to fracture occurrence and surgical intervention (if any) was not standardized, which may have influenced the observed biomarker levels given the known kinetics of these markers¹³. Additionally, studies have shown that minimally invasive surgical techniques produce lower inflammatory marker secretion compared to traditional surgery, which was not accounted for in this study design²⁹.

Despite these limitations, the study provides valuable preliminary data on the influence of CRP and CK-MM as biomarkers in lower extremity fractures. The findings suggest that these markers may serve as adjunctive tools in the assessment of fracture severity and monitoring of healing, though larger prospective studies with standardized sampling protocols are needed to confirm these observations.

Recommendations

After bone fracture, laboratory tests should be correlated with physical examination, X-ray, MRI, and other required reports for optimal patient treatment.

Clinical history plays a most important role in ensuring better and successful survival of patients from dangerous complications.

Larger prospective studies with standardized timing of sample collection are needed to better characterize the temporal relationship between CRP and CK-MM levels and fracture outcomes.

More sensitive CRP assays (e.g., hs-CRP) should be considered for future studies to detect low-grade inflammation²⁸.

Future studies should account for surgical technique (minimally invasive vs. traditional) as a confounding factor for inflammatory marker levels²⁹.

Future studies should include a control group of patients with soft tissue injuries only or healthy volunteers to establish baseline biomarker levels.

CONCLUSION

Both CRP and CK-MM tests show cross-sectional influence during bone fracture and tissue injury in patients with lower extremity fractures.

CRP is an acute-phase protein present in normal serum that increases significantly after most forms of tissue injury, bacterial and viral infections, inflammation, and malignant neoplasia. During tissue necrosis and inflammation resulting from microbial infections, CRP concentration can rise by more than 300 mg/L within 12–24 hours²².

CK is a cellular enzyme with wide tissue distribution. Its physiological role is associated with adenosine triphosphate (ATP) generation for contractile or transport systems. Elevated

creatinine kinase values are observed in diseases of skeletal muscle¹¹.

Clinical diagnosis should not be made on a single test result; it should integrate clinical and other laboratory data.

From this cross-sectional study of CRP and CK-MM as inflammatory markers in lower extremity bone fractures, it is evident that these markers are not sufficient alone for definitive decision-making regarding fracture inflammation. Additional tests and investigations are required for a better and more successful approach to the study and management of lower extremity bone fractures.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board/Ethics Committee of the Institute of Health Sciences, Mardan, affiliated with Abdul Wali Khan University Mardan, KPK, Pakistan. Approval number: IHS/EC/2025/012. Approval date: 10 January 2025.

Data Availability

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

Author Contributions

Methodology: Majid, Seyab Khan.

Data Collection: Barkat Ali, Khizran Amjad.

Formal Analysis: Seyab Khan, Majid.

Writing – Original Draft: Majid, Barkat Ali.

Writing – Review & Editing: Seyab Khan, Khizran Amjad, Waseem Abbas.

Author Responsibility: All authors reviewed and approved the final manuscript, agree to be accountable for all aspects of the work, and ensure that questions related to the accuracy or integrity of any part of the research are appropriately investigated and resolved. Waseem Abbas is the corresponding author.

Informed Consent

Written informed consent was obtained from all subjects involved in the study.

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Conflict of Interest

No.

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Declaration of AI-Assisted Language Editing

The authors declare that no artificial intelligence tools were used in the preparation of this manuscript. All scientific content, data analysis, and writing are the original work of the authors.

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