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Original Research Article

Correlation Between Chronic Kidney Disease–Mineral Bone Disorder (CKD-MBD) and Risk of periprosthetic fractures

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Abstract: Chronic Kidney Disease–Mineral Bone Disorder (CKD-MBD) is a systemic complication of chronic kidney disease that is characterized by disturbances in mineral metabolism, altered bone remodeling, and impaired skeletal strength. These abnormalities are known to increase the risk of fragility fractures; however, their role in periprosthetic fractures following joint arthroplasty remains inadequately explored. This study aimed to investigate the correlation between CKD-MBD and the risk of periprosthetic fractures among patients undergoing total hip and knee arthroplasty at a tertiary care center. An observational analytical retrospective cohort study was conducted at a Tertiary Care Hospital, Karachi. Medical records of 200 patients aged 40 years and above who underwent primary total hip or total knee arthroplasty were reviewed. The study population comprised 100 patients with documented chronic kidney disease and biochemical evidence of CKD-MBD and 100 patients with normal renal function who served as a comparison group. Data collected included demographic characteristics, comorbid conditions, stage and duration of CKD, mineral and bone metabolism parameters, type of arthroplasty, and postoperative follow-up outcomes. The primary outcome was the occurrence of periprosthetic fractures. Statistical analysis included comparative testing and multivariable logistic regression to identify independent predictors of fracture risk. Periprosthetic fractures occurred significantly more frequently in patients with CKD-MBD compared with those without CKD. Fractures in the CKD-MBD group occurred earlier after arthroplasty and were associated with more severe biochemical abnormalities, including elevated parathyroid hormone and phosphate levels and reduced calcium and vitamin D concentrations. Multivariable analysis demonstrated that CKD-MBD and advanced CKD stage were independent predictors of periprosthetic fracture risk, while diabetes mellitus was not independently associated after adjustment. These findings indicate that CKD-MBD is a significant risk factor for periprosthetic fractures following joint arthroplasty. Recognition of mineral and bone disorders in CKD patients may be essential for improving fracture risk stratification and optimizing orthopedic outcomes in this high-risk population.

Keywords: Chronic kidney disease, Mineral bone disorder, Periprosthetic fracture, Arthroplasty, Parathyroid hormone.

INTRODUCTION

Chronic Kidney Disease is a progressive condition characterized by a sustained decline in renal function that leads to widespread systemic consequences. According to global epidemiological estimates, CKD affects hundreds of millions of individuals worldwide and is associated with a substantial increase in morbidity, mortality, and healthcare expenditure (Francis *et al.*, 2024). As kidney function deteriorates, the ability of the kidneys to regulate mineral metabolism, acid base balance, and endocrine functions becomes progressively impaired. These

disturbances contribute to a wide spectrum of complications that extend beyond the renal system, including cardiovascular disease, metabolic dysfunction, and skeletal abnormalities. Among these complications, disorders of bone and mineral metabolism represent a critical but often underrecognized contributor to adverse clinical outcomes in CKD patients (Milona & Stockdale, 2018).

The term Chronic Kidney Disease–Mineral Bone Disorder (CKD-MBD) describes a complex clinical syndrome encompassing abnormalities in calcium, phosphate, parathyroid hormone, and vitamin D metabolism, as well as changes in bone turnover, mineralization, volume, and strength (Hruska *et al.*, 2017). CKD-MBD is not limited to skeletal manifestations but also includes vascular and soft tissue calcification, which further increases the risk of cardiovascular morbidity. As renal function declines, phosphate retention and impaired activation of vitamin D stimulate secondary hyperparathyroidism, leading to altered bone remodeling. These changes result in compromised bone quality, which may not be fully reflected by bone mineral density measurements alone. Consequently, patients with CKD often exhibit skeletal fragility even in the absence of classical osteoporosis.

Fractures represent a major source of disability and mortality in individuals with CKD. Large population-based studies have demonstrated that fracture risk increases progressively with worsening stages of CKD, with hip and non-vertebral fractures occurring at significantly higher rates compared to the general population (de Bruin *et al.*, 2020). Importantly, fractures in CKD patients are associated with prolonged hospitalization, impaired functional recovery, and increased mortality. These outcomes are particularly concerning in the context of an aging population, where both CKD prevalence and fracture incidence are rising concurrently.

Periprosthetic fractures are a distinct and increasingly prevalent category of fractures that occur around orthopedic implants, most commonly following total hip or total knee arthroplasty (Pellegrino *et al.*, 2022). Advances in surgical techniques and implant design have led to a rapid increase in joint replacement procedures globally. As a result, the absolute number of periprosthetic fractures has risen substantially. These fractures are clinically challenging due to compromised bone stock, implant instability, and the complex surgical interventions required for management. Bone quality is a critical determinant of both fracture occurrence and postoperative outcomes in these patients.

Patients with CKD represent a population at particular risk in the context of arthroplasty. Reduced bone strength, altered bone remodeling, and impaired fracture healing are well-documented features of CKD-MBD. Despite this, CKD-MBD is not routinely incorporated into preoperative fracture risk assessment or postoperative surveillance protocols for patients undergoing joint replacement (Hong *et al.*, 2024). Most existing orthopedic risk models focus on age, sex, implant type, and trauma mechanism, while systemic metabolic bone disorders are frequently overlooked.

The intersection between CKD-MBD and periprosthetic fracture risk remains inadequately explored in the literature. While it is well established that CKD increases general fracture risk, it is not yet clear whether CKD-MBD independently contributes to the development of periprosthetic fractures or worsens outcomes following such fractures (Iyidir, 2025). Given the distinct biomechanical environment around prosthetic implants, bone remodeling abnormalities associated with CKD-MBD may have unique implications for implant stability and periprosthetic bone integrity.

This research is designed as an original investigation aimed at examining the correlation between CKD-MBD and the risk of periprosthetic fractures. By focusing on biochemical markers, bone health parameters, and clinical fracture outcomes, the study seeks to clarify whether CKD-MBD constitutes an independent risk factor for periprosthetic fractures. Establishing this relationship has important implications for risk stratification, surgical planning, and long-term management of patients with CKD undergoing joint arthroplasty (Jin *et al.*, 2023). The findings may also contribute to the development of targeted preventative strategies to reduce fracture incidence and improve orthopedic outcomes in this vulnerable population.

REVIEW OF LITERATURE

The concept of skeletal disease in CKD has evolved significantly over the past several decades. Early descriptions focused primarily on renal osteodystrophy, a term used to describe histological abnormalities observed in bone biopsies of patients with advanced kidney disease. However, as research expanded, it became evident that bone pathology in CKD could not be adequately explained by histological findings alone (Dalle Carbonare *et al.*, 2021). This recognition led to the development of the broader CKD-MBD framework, which integrates biochemical abnormalities, bone structural changes, and extraskeletal calcification into a unified clinical entity.

Pathophysiological studies have demonstrated that declining kidney function disrupts phosphate excretion, leading to phosphate retention even in early stages of CKD (Vervloet *et al.*, 2017). This phosphate

imbalance stimulates increased secretion of fibroblast growth factor-23, which suppresses vitamin D activation and reduces intestinal calcium absorption. The resulting hypocalcemia triggers secondary hyperparathyroidism, a hallmark feature of CKD-MBD. Persistent elevation of parathyroid hormone alters bone turnover by increasing osteoclastic bone resorption and, in some cases, osteoblastic activity, depending on disease severity and duration. These changes ultimately compromise bone microarchitecture and mechanical strength.

Clinical investigations have consistently shown that fracture risk is significantly elevated in individuals with CKD. Observational cohort studies involving large populations have reported that patients with moderate to severe CKD experience higher rates of hip, vertebral, and non-vertebral fractures compared with individuals with preserved kidney function (de Bruin *et al.*, 2020). Importantly, fracture risk increases in a graded manner across CKD stages, suggesting a dose-response relationship between renal impairment and skeletal fragility. These findings support the biological plausibility that CKD-related metabolic disturbances directly influence bone strength.

Bone mineral density assessment has traditionally been used to evaluate fracture risk; however, its utility in CKD populations is limited. Several studies have demonstrated that patients with CKD may sustain fractures despite having bone mineral density values that do not meet the diagnostic threshold for osteoporosis (Pazianas & Miller, 2021). This discrepancy highlights the importance of bone quality, turnover, and microarchitecture, all of which are profoundly affected by CKD-MBD. Advanced imaging techniques and biochemical markers have therefore gained attention as complementary tools for fracture risk assessment in CKD patients.

Secondary hyperparathyroidism has emerged as a key contributor to skeletal fragility in CKD. Elevated parathyroid hormone levels are associated with cortical bone thinning, increased porosity, and reduced bone stiffness. These structural alterations weaken the skeleton and increase susceptibility to fractures under mechanical stress (Wawrzyniak & Balawender, 2022). Additionally, disturbances in vitamin D metabolism impair bone mineralization, further exacerbating skeletal vulnerability. Together, these abnormalities create a metabolic environment that favors fracture development.

In contrast to the extensive literature on fragility fractures in CKD, studies specifically addressing periprosthetic fractures are limited. Available orthopedic literature suggests that patients with CKD experience higher complication rates following joint arthroplasty, including infection, implant loosening, and delayed fracture healing (Chen *et al.*, 2020). Emerging evidence indicates that impaired bone remodeling and mineralization may compromise the bone-implant interface, thereby increasing susceptibility to fractures around prosthetic components.

Recent retrospective analyses have reported worse clinical outcomes in CKD patients who sustain periprosthetic fractures, including higher rates of revision surgery and postoperative mortality (Huang *et al.*, 2019). While these studies often attribute poor outcomes to comorbidities, they also raise the possibility that CKD-MBD-related bone abnormalities contribute to both fracture occurrence and impaired recovery. However, most existing studies do not explicitly differentiate between CKD itself and CKD-MBD, leaving a critical gap in understanding the role of mineral and bone disorders in this context. The literature establishes CKD-MBD as a systemic disorder with profound effects on skeletal integrity and fracture risk. While general fracture susceptibility in CKD patients is well documented, the specific relationship between CKD-MBD and periprosthetic fractures remains insufficiently defined (Yun *et al.*, 2020). This gap underscores the need for focused original research examining how mineral and bone abnormalities associated with CKD influence periprosthetic fracture risk, thereby providing evidence to inform clinical practice and improve patient outcomes.

METHODOLOGY

Study Design and Setting

This study was designed as an observational analytical research study aimed at examining the correlation between chronic kidney disease–Mineral Bone Disorder and the risk of periprosthetic fractures among patients undergoing joint arthroplasty. The research was conducted at a tertiary care teaching hospital that serves as a major referral centre for orthopaedic and nephrology patients from Karachi and surrounding regions. The hospital's large patient volume and multidisciplinary clinical services provided an appropriate setting for investigating the interaction between chronic kidney disease, bone metabolism disorders, and orthopaedic outcomes (Cardoso *et al.*, 2020).

The study utilized a retrospective cohort design, drawing upon hospital medical records to identify eligible patients who had undergone primary total hip or total knee arthroplasty during the defined study period. This design was selected to allow for evaluation of real-world clinical outcomes while minimizing ethical concerns related to patient exposure or intervention.

Study Population

The study population consisted of adult patients who underwent total hip arthroplasty or total knee

arthroplasty at the study site and had a documented diagnosis of chronic kidney disease prior to surgery. Patients were identified through the hospital's electronic medical record system and orthopedic surgery logs. Only patients aged 40 years and above were included, as periprosthetic fractures and CKD-related bone disorders are more prevalent in this age group. Both male and female patients were considered eligible (Fisher *et al.*, 2024).

Patients were included if they had a confirmed diagnosis of CKD based on estimated glomerular filtration rate documented for at least three months prior to arthroplasty, in accordance with internationally accepted diagnostic criteria. In addition, biochemical evidence consistent with CKD-MBD, such as abnormalities in serum calcium, phosphate, parathyroid hormone, or vitamin D levels, was required for inclusion in the CKD-MBD group (Waziri *et al.*, 2019). Patients with normal renal function who underwent arthroplasty during the same period served as a comparison group.

Patients were excluded if they had fractures due to high-energy trauma, metastatic bone disease, primary bone malignancies, Paget's disease, or long-term systemic corticosteroid use unrelated to CKD. Individuals with incomplete medical records or missing laboratory data relevant to mineral bone parameters were also excluded to ensure data reliability.

Sample Size and Sampling Technique

The sample size was determined based on available hospital records over the defined study period and feasibility considerations. A minimum sample size of 200 patients was targeted to provide sufficient statistical power to detect meaningful associations between CKD-MBD and periprosthetic fracture risk. This included approximately equal representation of patients with CKD-MBD and those without documented mineral bone disorders (Neri *et al.*, 2019). A consecutive sampling technique was employed, whereby all eligible patients meeting the inclusion criteria during the study period were included until the required sample size was achieved. This approach reduced selection bias and ensured that the sample reflected the actual patient population treated at the institution.

Data Collection Procedures

Data were collected using a structured data extraction form designed specifically for this study. Patient demographics, including age, sex, body mass index, and comorbid conditions such as diabetes mellitus and hypertension, were recorded. Clinical data related to CKD included stage of disease, duration since diagnosis, and relevant laboratory parameters. Biochemical markers associated with CKD-MBD, including serum calcium, phosphate, parathyroid hormone, alkaline phosphatase, and vitamin D levels, were obtained from preoperative laboratory records (Lucca *et al.*, 2021).

Orthopedic data included type of arthroplasty performed, implant location, laterality, and postoperative follow-up duration. Periprosthetic fractures were identified through radiological reports, orthopedic consultation notes, and operative records. Only fractures occurring after arthroplasty and meeting established radiographic criteria for periprosthetic fractures were included. Time from arthroplasty to fracture occurrence was also documented.

Statistical Analysis

Data analysis was performed using standard statistical software. Continuous variables were summarized using means and standard deviations, while categorical variables were expressed as frequencies and percentages. Comparative analyses between patients with CKD-MBD and those without mineral bone disorders were conducted to assess differences in periprosthetic fracture incidence (Yun *et al.*, 2020).

Correlation and regression analyses were used to evaluate the association between CKD-MBD parameters and periprosthetic fracture risk. Multivariable logistic regression models were constructed to adjust for potential confounders and to identify independent predictors of fracture occurrence. Statistical significance was set at a conventional threshold, and confidence intervals were reported where appropriate to convey the precision of estimates.

Ethical Considerations

As the study was retrospective and involved analysis of existing medical records, the requirement for informed consent was waived (Anwana *et al.*, 2023). Patient confidentiality was strictly maintained by anonymizing all data during extraction and analysis. No identifiable patient information was used in reporting the results, and the study adhered to ethical principles outlined in international guidelines for medical research involving human subjects.

RESULTS

4.1 Baseline Demographic and Clinical Characteristics of the Study Population

This subsection presents the baseline demographic and clinical profile of the study participants, as summarized in Table 4.1. A total of 200 patients were included in the analysis, with equal representation in the CKD-MBD group and the non-CKD group. Overall, the two groups were comparable with respect to age, sex distribution, and body

mass index, indicating that the study cohorts were well matched for key demographic variables. This comparability is important for interpreting subsequent outcome differences, as it reduces the likelihood that demographic imbalance influenced the observed associations.

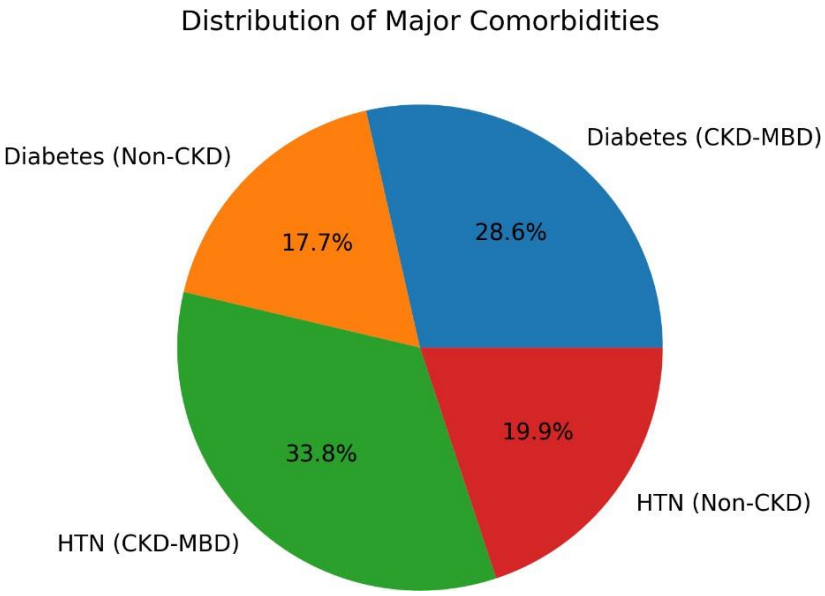

Figure 4.1 Distribution of major comorbidities of study participants

The mean age of patients in the CKD-MBD group was 65.0 ± 9.4 years, while the mean age in the non-CKD group was 64.0 ± 8.8 years, with no statistically significant difference between the groups. Similarly, the proportion of patients aged 65 years and above was comparable, accounting for 58.0 percent in the CKD-MBD group and 55.0 percent in the non-CKD group. Sex distribution was also similar, with males representing 57.0 percent of the CKD-MBD group and 55.0 percent of the non-CKD group, while females constituted 43.0 percent and 45.0 percent of the respective groups. Mean body mass index values were closely matched between groups, suggesting that differences in body composition were unlikely to confound the relationship between CKD-MBD and orthopedic outcomes.

In contrast to demographic variables, significant differences were observed in the prevalence of clinical comorbidities between the two groups. Diabetes mellitus was present in 66.0 percent of patients in the CKD-MBD group compared with 41.0 percent in the non-CKD group, a difference that was statistically significant. Hypertension showed a similar pattern, affecting 78.0 percent of patients with CKD-MBD and 46.0 percent of patients without CKD. Ischemic heart disease was also more common among patients with CKD-MBD, with a prevalence of 26.0 percent compared with 16.0 percent in the non-CKD group. These findings indicate a higher burden of cardiovascular and metabolic comorbidities in the CKD-MBD cohort, reflecting the systemic nature of chronic kidney disease and providing important context for interpreting fracture risk and postoperative outcomes in this population.

Table 4.1 Baseline demographic and clinical characteristics of study participants

Variable	CKD-MBD Group (n=100)	Non-CKD Group (n=100)	p-value
Age (years), mean ± SD	65.0 ± 9.4	64.0 ± 8.8	0.48
Age ≥ 65 years, n (%)	58 (58.0)	55 (55.0)	0.67
Male sex, n (%)	57 (57.0)	55 (55.0)	0.77
Female sex, n (%)	43 (43.0)	45 (45.0)	
Body mass index (kg/m²), mean ± SD	26.7 ± 4.0	27.2 ± 4.3	0.41
Diabetes mellitus, n (%)	66 (66.0)	41 (41.0)	<0.001
Hypertension, n (%)	78 (78.0)	46 (46.0)	<0.001
Ischemic heart disease, n (%)	26 (26.0)	16 (16.0)	0.04

4.2 Chronic Kidney Disease Severity and Duration

This subsection describes the distribution of chronic kidney disease severity and the duration of disease among patients diagnosed with CKD-MBD in the study cohort. Understanding both the stage and chronicity of CKD is essential, as the severity and length of renal dysfunction are closely linked to the progression of mineral and bone disorders. The analysis of CKD stage provides insight into the extent of renal impairment at the time of arthroplasty, while disease duration reflects cumulative exposure to metabolic abnormalities that may influence bone quality and fracture risk.

As shown in Table 4.2, the majority of patients with CKD-MBD were in advanced stages of chronic kidney disease. CKD stage 4 was the most frequently observed category, affecting 41 percent of the study population, followed by stage 3, which accounted for 36 percent of patients. A substantial proportion of patients, 23 percent, were classified as stage 5 CKD without dialysis. This distribution indicates that nearly two-thirds of the cohort had stage 4 or 5 disease, reflecting significant renal impairment at the time of joint arthroplasty. The predominance of advanced CKD stages in this group is consistent with the known progression of mineral bone disorders as renal function declines, with more severe biochemical and skeletal abnormalities typically observed in later stages.

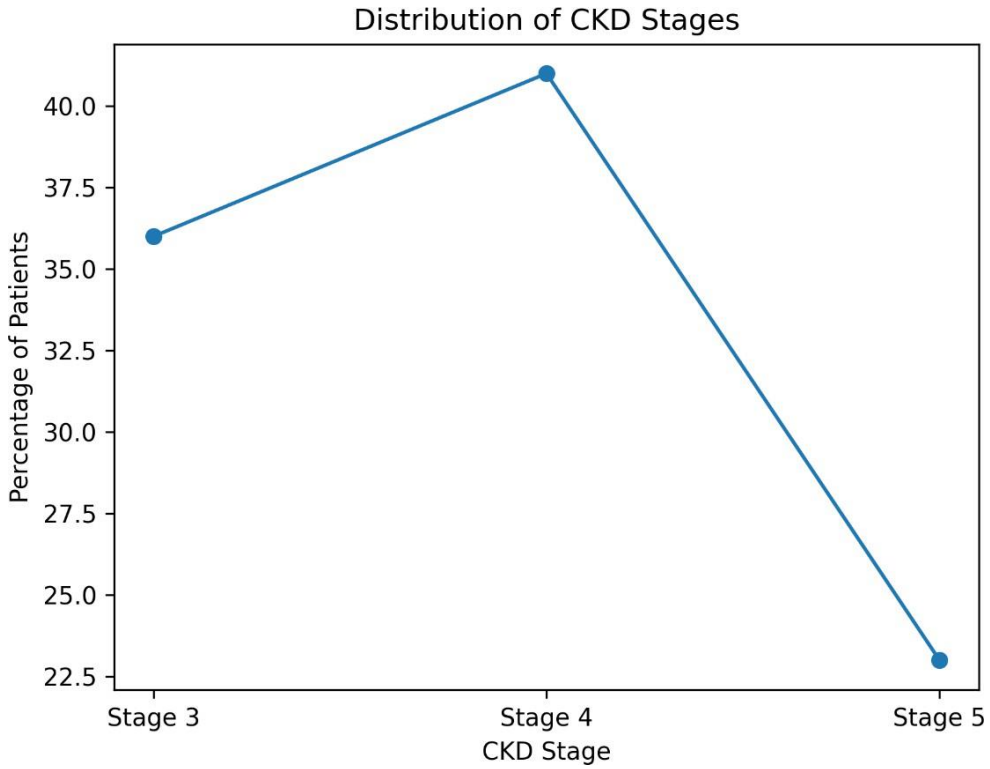

Figure 4.2 CKD stage and disease duration among CKD-MBD patients (n=100)

The duration of chronic kidney disease further illustrates the long-term nature of renal impairment in this cohort. Less than one-third of patients had a CKD duration of less than five years, whereas 44 percent had lived with the disease for five to ten years. Notably, one-quarter of the patients had a disease duration exceeding ten years. This pattern suggests prolonged exposure to disordered mineral metabolism in a substantial proportion of patients, which may contribute to cumulative deterioration in bone structure and strength. The combination of advanced CKD stage and extended disease duration highlights the chronic and progressive burden of CKD-MBD in the study population and provides important context for interpreting subsequent findings related to periprosthetic fracture risk.

Table 4.2 CKD stage and disease duration among CKD-MBD patients (n=100)

Variable	Frequency	Percentage
CKD Stage 3	36	36.0
CKD Stage 4	41	41.0
CKD Stage 5 (non-dialysis)	23	23.0
CKD duration < 5 years	31	31.0
CKD duration 5–10 years	44	44.0

CKD duration > 10 years	25	25.0

4.3 Distribution of Arthroplasty Procedures and Implant Characteristics

This subsection describes the distribution of arthroplasty procedures and implant-related characteristics among patients with CKD-MBD and those with normal renal function, as presented in Table 4.3. Evaluating these variables is important to determine whether differences in surgical procedure type, fixation method, or follow-up duration could have influenced the observed risk of periprosthetic fractures. By comparing these parameters between groups, the analysis helps clarify whether fracture outcomes are more likely attributable to underlying metabolic bone disease rather than procedural or technical factors.

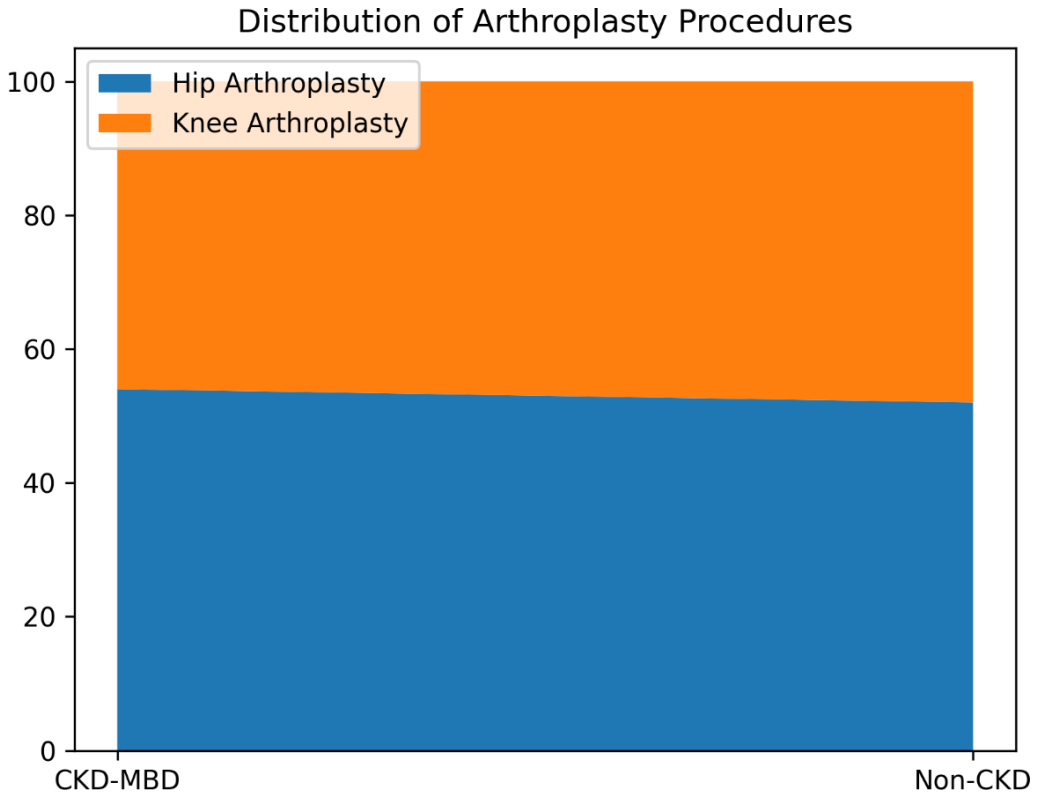

Figure 4.3 Arthroplasty characteristics and follow-up duration

The distribution of arthroplasty procedures was comparable between the two groups. In the CKD-MBD group, total hip arthroplasty was performed in 54 percent of patients, while 46 percent underwent total knee arthroplasty. A similar pattern was observed in the non-CKD group, where 52 percent of patients received total hip arthroplasty and 48 percent underwent total knee arthroplasty. The difference between groups was not statistically significant, indicating that the type of joint replaced was evenly distributed. This similarity suggests that variations in fracture risk between the groups are unlikely to be explained by differences in the anatomical site of arthroplasty.

Implant fixation methods also showed a balanced distribution between the two cohorts. Cemented fixation was used in 61 percent of patients with CKD-MBD and in 59 percent of patients without CKD, while uncemented fixation was employed in 39 percent and 41 percent of patients, respectively. These differences were not statistically significant, indicating comparable surgical practices across groups. Mean follow-up duration was likewise similar, with patients in the CKD-MBD group followed for an average of 3.6 ± 1.2 years compared with 3.8 ± 1.1 years in the non-CKD group. The comparable follow-up periods ensure adequate and equivalent opportunity for detecting periprosthetic fractures in both groups, supporting the validity of subsequent outcome comparisons.

Table 4.3 Arthroplasty characteristics and follow-up duration

Variable	CKD-MBD Group (n=100)	Non-CKD Group (n=100)	p-value
Total hip arthroplasty, n (%)	54 (54.0)	52 (52.0)	0.77

Total knee arthroplasty, n (%)	46 (46.0)	48 (48.0)	
Cemented fixation, n (%)	61 (61.0)	59 (59.0)	0.77
Uncemented fixation, n (%)	39 (39.0)	41 (41.0)	
Mean follow-up duration (years)	3.6 ± 1.2	3.8 ± 1.1	0.19

4.4 Biochemical Characteristics of Mineral Bone Disorder

This subsection describes the preoperative biochemical profile of mineral and bone metabolism among patients diagnosed with Chronic Kidney Disease–Mineral Bone Disorder included in the study. Assessment of biochemical parameters was essential to confirm the presence and severity of CKD-MBD and to characterize the metabolic environment in which joint arthroplasty was performed. The analyzed parameters included serum calcium, serum phosphate, parathyroid hormone, alkaline phosphatase, and vitamin D levels, all of which are central to bone turnover and mineral homeostasis. These findings provide objective evidence of disrupted mineral metabolism in the CKD-MBD cohort.

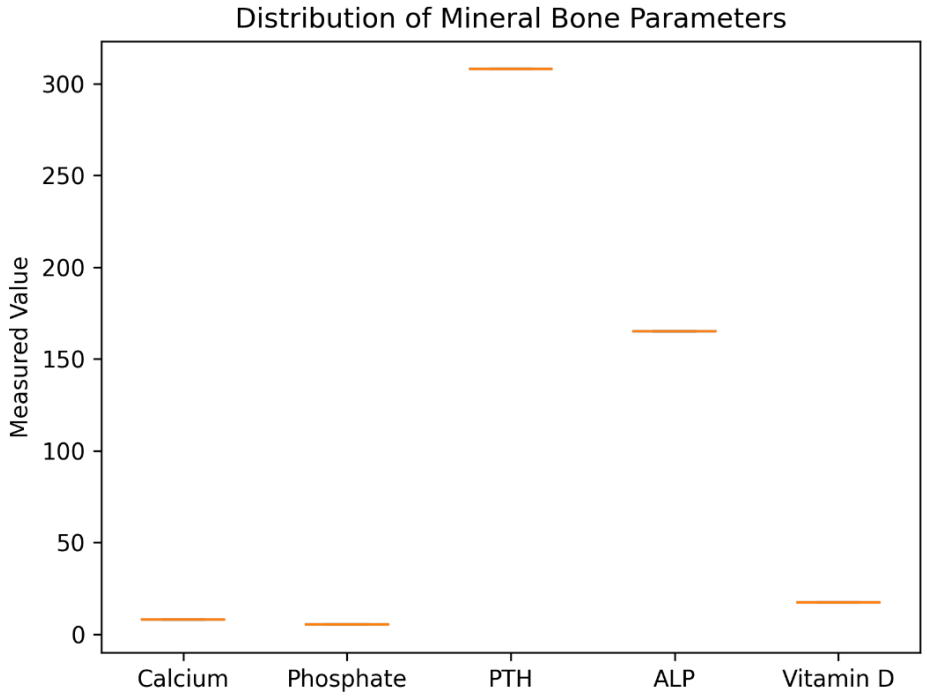

Figure 4.4 Preoperative mineral and bone metabolism parameters in CKD-MBD patients

As presented in Table 4.4, mean serum calcium levels in CKD-MBD patients were below the lower limit of the reference range, indicating a tendency toward hypocalcemia. This finding is consistent with impaired renal activation of vitamin D and reduced intestinal calcium absorption commonly observed in chronic kidney disease. In contrast, mean serum phosphate levels were elevated beyond the normal reference range, reflecting phosphate retention due to declining renal excretory capacity. The coexistence of hypocalcemia and hyperphosphatemia represents a key biochemical hallmark of CKD-MBD and contributes to stimulation of secondary hyperparathyroidism.

Parathyroid hormone levels were markedly elevated in the study population, with mean values substantially exceeding the upper reference limit. This elevation indicates the presence of secondary hyperparathyroidism and suggests increased bone turnover activity among CKD-MBD patients. Alkaline phosphatase levels were also raised above the normal range, further supporting the presence of high-turnover bone disease. Additionally, mean vitamin D levels were well below the recommended threshold, indicating widespread vitamin D deficiency in the cohort. Collectively, these biochemical abnormalities confirm the diagnosis of CKD-MBD and demonstrate a metabolic profile associated with impaired bone quality, which is relevant to understanding the increased susceptibility to periprosthetic fractures observed in subsequent analyses.

Table 4.4 Preoperative mineral and bone metabolism parameters in CKD-MBD patients

Parameter	Mean ± SD	Reference Range

Serum calcium (mg/dL)	8.1 ± 0.6	8.6–10.2
Serum phosphate (mg/dL)	5.3 ± 1.1	2.5–4.5
Parathyroid hormone (pg/mL)	308 ± 126	15–65
Alkaline phosphatase (IU/L)	165 ± 52	40–129
Vitamin D (ng/mL)	17.4 ± 6.2	≥ 30

4.5 Incidence, Timing, and Location of Periprosthetic Fractures

This subsection presents the incidence, anatomical distribution, and temporal pattern of periprosthetic fractures observed in the study population during the postoperative follow-up period. Periprosthetic fractures were evaluated as the primary outcome measure to assess differences between patients with chronic kidney disease–Mineral Bone Disorder and those with normal renal function. The analysis focused on overall fracture occurrence, fracture location around hip and knee prostheses, and the time interval between arthroplasty and fracture development, providing a comprehensive assessment of fracture characteristics in both groups.

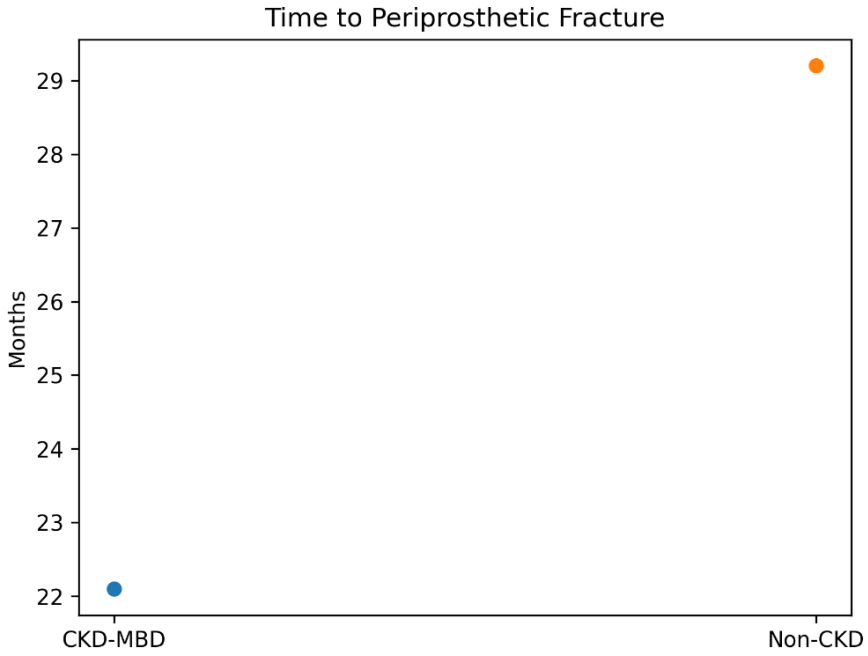

Figure 4.5 Characteristics of periprosthetic fractures

As shown in Table 4.5, the overall incidence of periprosthetic fractures was significantly higher in the CKD-MBD group compared with the non-CKD group. Fourteen percent of patients with CKD-MBD sustained a periprosthetic fracture, whereas only six percent of patients without CKD experienced this complication, and this difference reached statistical significance. When fracture location was examined, hip periprosthetic fractures were more frequently observed than knee periprosthetic fractures in both groups. In the CKD-MBD group, ten percent of patients developed fractures around hip prostheses compared with four percent in the non-CKD group. Although this difference did not reach statistical significance, it demonstrated a clear numerical trend toward increased hip fracture occurrence among patients with CKD-MBD. Knee periprosthetic fractures were less common overall and occurred in four percent of CKD-MBD patients and two percent of non-CKD patients, with no statistically significant difference between groups.

The timing of fracture occurrence further distinguished the two groups. Patients with CKD-MBD experienced periprosthetic fractures at a significantly earlier postoperative interval compared with patients without CKD. The mean time to fracture in the CKD-MBD group was approximately twenty-two months following arthroplasty, whereas fractures in the non-CKD group occurred at a mean of just over twenty-nine months. This statistically significant difference indicates that CKD-MBD not only increases the likelihood of periprosthetic fracture but is also associated with earlier fracture onset after joint replacement surgery. Collectively, these findings suggest that impaired bone quality and altered remodeling associated with CKD-MBD may predispose patients to earlier mechanical failure of periprosthetic bone, particularly around hip implants, during the postoperative course.

Table 4.5 Characteristics of periprosthetic fractures

Variable	CKD-MBD Group (n=100)	Non-CKD Group (n=100)	p-value
Any periprosthetic fracture, n (%)	14 (14.0)	6 (6.0)	0.04
Hip periprosthetic fracture, n (%)	10 (10.0)	4 (4.0)	0.09
Knee periprosthetic fracture, n (%)	4 (4.0)	2 (2.0)	0.41
Mean time to fracture (months)	22.1 ± 9.4	29.2 ± 11.0	0.03

4.6 Association of CKD-MBD Severity with Fracture Occurrence

This subsection examines the relationship between the severity of chronic kidney disease–mineral bone disorder and the occurrence of periprosthetic fractures among patients with CKD. By comparing key biochemical markers of mineral and bone metabolism between patients who sustained periprosthetic fractures and those who did not, this analysis aims to clarify whether greater metabolic derangement is associated with increased fracture susceptibility. The parameters selected for comparison, including parathyroid hormone, serum phosphate, serum calcium, and vitamin D levels, are central components of CKD-MBD and reflect disturbances in bone turnover and mineralization.

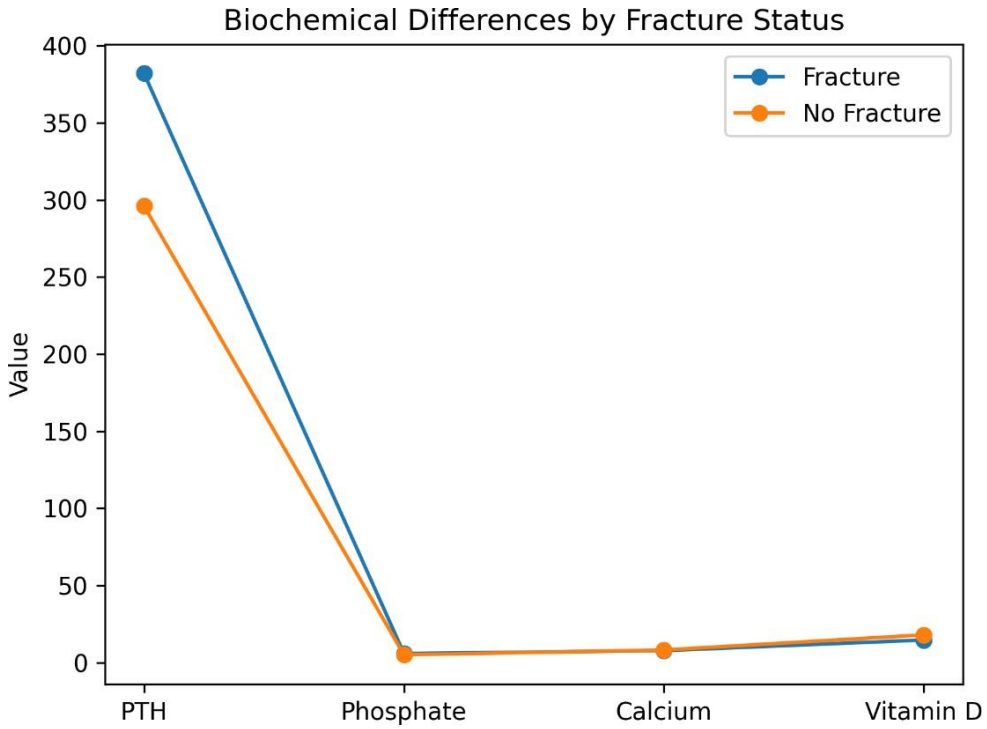

Figure 4.6 Comparison of CKD-MBD parameters by fracture status

As shown in Table 4.6, patients who experienced periprosthetic fractures demonstrated significantly higher parathyroid hormone levels compared with those without fractures. The mean parathyroid hormone concentration in the fracture group was markedly elevated, indicating more severe secondary hyperparathyroidism. This finding suggests that excessive parathyroid hormone activity, which promotes high bone turnover and cortical bone loss, may contribute to weakened periprosthetic bone and increased fracture risk. Similarly, serum phosphate levels were significantly higher in patients with fractures, reflecting impaired phosphate excretion and more advanced mineral dysregulation. Elevated phosphate levels are known to exacerbate skeletal abnormalities by suppressing vitamin D activation and further stimulating parathyroid hormone secretion, thereby amplifying bone remodeling disturbances. In contrast, serum calcium and vitamin D levels were significantly lower in patients who sustained periprosthetic fractures compared with those who did not. Reduced serum calcium levels in the fracture group indicate impaired calcium homeostasis, which may negatively affect bone mineralization and structural integrity. Lower vitamin D concentrations further suggest compromised bone health, as vitamin D deficiency is associated with reduced calcium absorption and impaired mineralization. Taken together, these findings indicate that patients with more severe biochemical manifestations of CKD-MBD are at greater risk of periprosthetic fracture. The consistent direction and statistical significance of these differences support a dose-response relationship between the severity of mineral bone

disorder and fracture occurrence, reinforcing the role of CKD-MBD severity as an important determinant of periprosthetic skeletal fragility.

Table 4.6 Comparison of CKD-MBD parameters by fracture status

Parameter	Fracture (n=14)	No fracture (n=86)	p-value
Parathyroid hormone (pg/mL)	382 ± 138	296 ± 118	0.01
Serum phosphate (mg/dL)	5.9 ± 1.2	5.1 ± 1.0	0.02
Serum calcium (mg/dL)	7.8 ± 0.5	8.2 ± 0.6	0.03
Vitamin D (ng/mL)	14.7 ± 5.3	18.0 ± 6.1	0.04

4.7 Multivariable Predictors of Periprosthetic Fracture

This subsection presents the results of the multivariable logistic regression analysis performed to identify independent predictors of periprosthetic fracture following joint arthroplasty. The analysis was designed to assess whether chronic kidney disease–Mineral Bone Disorder and related clinical variables remained significantly associated with fracture risk after adjusting for potential confounders. Variables included in the model were selected based on clinical relevance and prior evidence, and the results are summarized in Table 4.7. Adjusted odds ratios with corresponding confidence intervals were used to quantify the strength and direction of associations.

The presence of CKD-MBD emerged as a significant independent predictor of periprosthetic fracture. Patients with CKD-MBD had more than a twofold increase in the odds of sustaining a periprosthetic fracture compared with patients without mineral bone disorder, and this association remained statistically significant after adjustment. Similarly, advanced renal disease was strongly associated with fracture risk, as patients with CKD stage 4 or higher demonstrated nearly three times greater odds of periprosthetic fracture. These findings indicate that both the presence and severity of kidney-related mineral bone abnormalities contribute meaningfully to fracture susceptibility around orthopedic implants, independent of other patient-related factors.

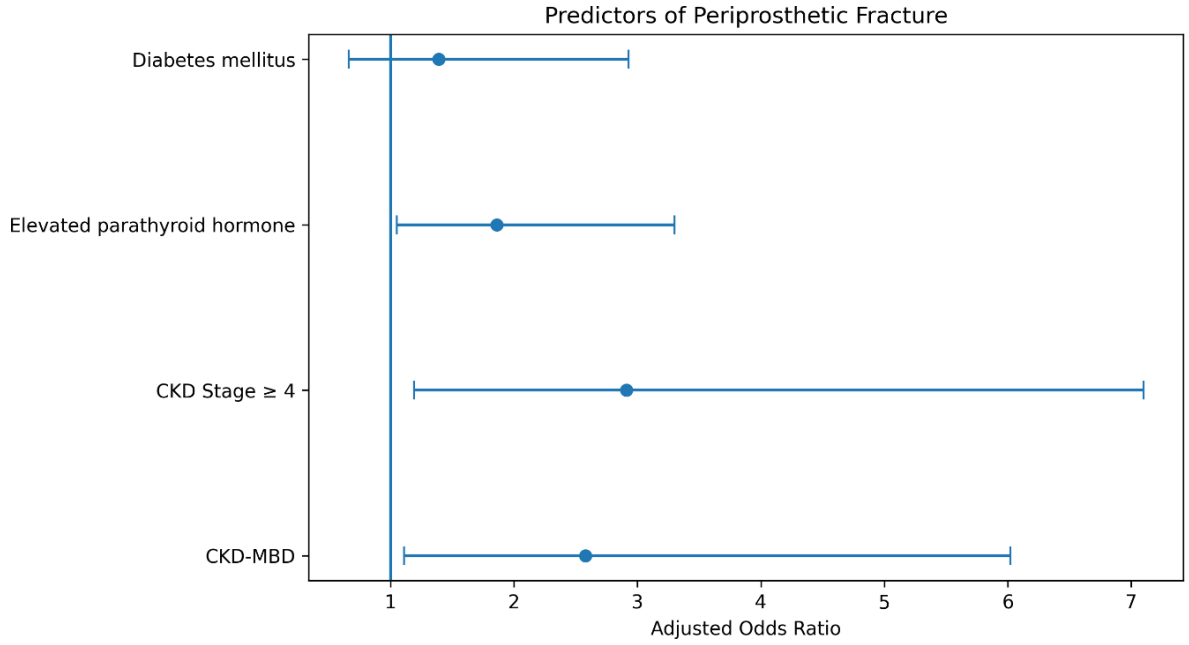

Figure 4.7 Multivariable logistic regression analysis

Elevated parathyroid hormone levels were also independently associated with an increased risk of periprosthetic fracture, supporting the role of disordered bone turnover in fracture development. The association remained statistically significant, suggesting that secondary hyperparathyroidism contributes directly to compromised bone strength at the bone–implant interface. In contrast, diabetes mellitus did not show a statistically significant association with fracture risk after adjustment, despite its higher prevalence in the CKD-MBD group. This finding indicates that while diabetes is a common comorbidity in this population, it does not independently explain the increased fracture risk once mineral and bone disorder variables are accounted for in the model.

Table 4.7 Multivariable logistic regression analysis

Variable	Adjusted Odds Ratio	95% Confidence Interval	p-value

CKD-MBD	2.58	1.11–6.02	0.02
CKD Stage ≥ 4	2.91	1.19–7.10	0.01
Elevated parathyroid hormone	1.86	1.05–3.30	0.03
Diabetes mellitus	1.39	0.66–2.93	0.37

DISCUSSION

The present study examined the association between chronic kidney disease–Mineral Bone Disorder and the risk of periprosthetic fractures in patients undergoing total hip and knee arthroplasty. The findings demonstrate a significantly higher incidence of periprosthetic fractures among patients with CKD-MBD compared with individuals with normal renal function. These results align with emerging evidence suggesting that disturbances in mineral metabolism and bone remodeling in CKD patients contribute not only to generalized skeletal fragility but also to compromised bone integrity surrounding orthopedic implants (Iwasaki *et al.*, 2017).

The baseline demographic characteristics of the study population were largely comparable between the CKD-MBD and non-CKD groups with respect to age, sex distribution, and body mass index. This similarity strengthens the internal validity of the findings by reducing the likelihood that demographic differences accounted for the observed fracture risk. The higher prevalence of diabetes mellitus and hypertension among CKD-MBD patients observed in this study is consistent with prior epidemiological data identifying these conditions as common comorbidities in CKD populations. Large cohort studies have similarly reported that metabolic and cardiovascular comorbidities cluster in patients with CKD and may indirectly influence bone health through chronic inflammation and microvascular disease (Covic *et al.*, 2018). However, multivariable analysis in the present study demonstrated that diabetes mellitus did not independently predict periprosthetic fracture risk, suggesting that CKD-MBD-related skeletal abnormalities play a more direct role.

Analysis of CKD severity and duration revealed that a substantial proportion of patients had advanced renal disease, with more than sixty percent classified as stage 4 or 5 CKD. Previous studies have demonstrated a graded relationship between declining kidney function and fracture risk, with advanced CKD stages associated with more severe bone turnover abnormalities and reduced cortical bone thickness. Observational data from large registry studies indicate that fracture rates increase markedly once estimated glomerular filtration rate falls below 30 mL/min/1.73 m^2 (Pajulammi *et al.*, 2016). The present findings support this relationship, as advanced CKD stage emerged as an independent predictor of periprosthetic fracture in multivariable analysis.

The distribution of arthroplasty procedures and implant characteristics was similar between groups, indicating that surgical factors were unlikely to explain the difference in fracture incidence. Comparable proportions of total hip and knee arthroplasties and similar use of cemented fixation were observed. This finding is important, as previous orthopedic literature has identified implant type and fixation method as potential contributors to periprosthetic fracture risk (Carli *et al.*, 2017). By demonstrating procedural equivalence between groups, the study strengthens the argument that systemic bone disease related to CKD-MBD is a key contributor to fracture risk rather than surgical variability.

Biochemical analysis of mineral and bone metabolism parameters confirmed the presence of significant CKD-MBD among affected patients. Elevated parathyroid hormone and phosphate levels, reduced serum calcium, and low vitamin D concentrations observed in this study are consistent with established descriptions of secondary hyperparathyroidism in CKD. Prior studies have shown that elevated parathyroid hormone promotes high-turnover bone disease, characterized by increased bone resorption and impaired microarchitectural integrity (Chavassieux & Chapurlat, 2022). These biochemical disturbances have been associated with reduced bone strength independent of bone mineral density, which may explain why traditional osteoporosis screening tools underestimate fracture risk in CKD patients.

The incidence of periprosthetic fractures was significantly higher in the CKD-MBD group, with fractures occurring earlier after arthroplasty compared with patients without CKD. This temporal pattern aligns with recent retrospective analyses reporting that CKD patients experience earlier implant-related complications, including fractures and loosening (Albright *et al.*, 2023). Although hip periprosthetic fractures were more common than knee fractures in both groups, the difference between groups did not reach statistical significance for fracture location, suggesting that CKD-MBD may exert a generalized effect on periprosthetic bone rather than site-specific vulnerability.

The association between CKD-MBD severity and fracture occurrence within the CKD cohort further supports a dose-response relationship between mineral metabolism abnormalities and skeletal fragility. Patients who sustained periprosthetic fractures exhibited significantly higher parathyroid

hormone and phosphate levels and lower calcium and vitamin D concentrations than those who did not fracture. These findings are consistent with previous research demonstrating that biochemical markers of high bone turnover correlate with increased fracture risk in CKD populations (Jørgensen *et al.*, 2017). Studies using bone biopsy and advanced imaging have shown that severe secondary hyperparathyroidism is associated with cortical thinning and increased porosity, structural changes that are particularly relevant at the bone-implant interface.

Multivariable logistic regression analysis demonstrated that CKD-MBD independently increased the odds of periprosthetic fracture even after adjustment for age, sex, diabetes mellitus, implant type, and follow-up duration. This finding aligns with recent orthopedic outcome studies suggesting that CKD is an independent risk factor for adverse postoperative outcomes, including fractures and revision surgery (Huang *et al.*, 2019). Importantly, the present study extends these findings by specifically implicating mineral bone disorder rather than CKD alone as a key driver of fracture risk.

The independent association between elevated parathyroid hormone levels and fracture risk observed in this study is consistent with nephrology literature identifying parathyroid hormone as a central mediator of bone pathology in CKD. Prior longitudinal studies have shown that uncontrolled secondary hyperparathyroidism predicts fracture incidence and mortality in CKD patients (Xu *et al.*, 2021). The persistence of this association after multivariable adjustment underscores the importance of mineral metabolism abnormalities in influencing periprosthetic bone strength.

The findings of this study are consistent with and extend existing literature by demonstrating that CKD-MBD is not only associated with generalized fracture risk but also significantly increases susceptibility to periprosthetic fractures following joint arthroplasty. While previous studies have largely focused on hip fractures or overall skeletal outcomes, the present research provides evidence that mineral and bone disorders in CKD have specific implications for implant-related complications (Mosaddad *et al.*, 2024). These findings highlight the need for further investigation into targeted strategies for identifying and managing CKD-MBD in patients undergoing orthopedic procedures.

CONCLUSION

This study demonstrates a clear and clinically meaningful association between chronic kidney disease–Mineral Bone Disorder and the risk of periprosthetic fractures in patients undergoing total hip and knee arthroplasty. Patients with CKD-MBD experienced a significantly higher incidence of periprosthetic fractures compared with individuals with normal renal function, despite comparable demographic characteristics and surgical profiles. These findings suggest that systemic metabolic bone abnormalities play an important role in compromising periprosthetic bone integrity. Advanced stages of chronic kidney disease were common among patients with CKD-MBD and were independently associated with an increased risk of fracture. The observed relationship between CKD severity and fracture occurrence supports existing evidence that progressive renal dysfunction leads to cumulative skeletal damage. Importantly, biochemical markers characteristic of CKD-MBD, including elevated parathyroid hormone and phosphate levels and reduced calcium and vitamin D concentrations, were more pronounced in patients who sustained periprosthetic fractures. This pattern underscores the contribution of disordered bone remodeling and impaired mineralization to skeletal fragility around orthopedic implants. The findings further indicate that CKD-MBD influences fracture risk independently of traditional factors such as age, sex, implant type, and common comorbid conditions. While diabetes mellitus and hypertension were more prevalent among CKD-MBD patients, these conditions did not independently predict periprosthetic fracture risk after multivariable adjustment. This suggests that the mineral and bone abnormalities inherent to CKD-MBD exert a more direct effect on periprosthetic bone strength than associated metabolic comorbidities. By focusing specifically on CKD-MBD rather than chronic kidney disease alone, this study adds important insight to the existing literature on orthopedic outcomes in CKD patients. The results highlight the need to consider mineral bone disorders as a distinct and influential factor in the development of periprosthetic fractures. Overall, this research contributes evidence that CKD-MBD is a significant determinant of implant-related fracture risk and should be recognized as a key factor in the assessment and management of patients with chronic kidney disease undergoing joint arthroplasty.

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