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Chronic Kidney Disease–Mineral and Bone Disorder in Predialysis Diabetic Patients

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Abstract: ***Objectives:*** To investigate the frequency and biochemical constitution of CKD–MBD in predialysis diabetes patients, and determine its relationship with the stages of renal function. ***Study design and setting***: This cross-sectional analytical study was conducted from 24TH October 2024 till 26th March 2025, at the Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan, among diabetic patients receiving standard outpatient nephrological care. ***Methodology:*** This cross-sectional study was conducted at the Sindh Institute of Urology and Transplantation (SIUT), Karachi, after ethical approval (ERC No. SIUT/NEPH/2024//574). A total of 231 stage 3–4 CKD patients aged 18–80 years were recruited using consecutive sampling. Serum calcium, phosphate, intact parathyroid hormone, vitamin D, and creatinine were measured, and eGFR was calculated using the CKD-EPI equation. CKD–MBD was defined per KDIGO 2017 criteria. Data were analyzed using SPSS v24, with $p<0.05$ considered statistically significant. ***Results:*** Among 231 predialysis CKD patients, 61.9% exhibited biochemical abnormalities consistent with CKD–MBD. Hypocalcemia, hyperphosphatemia, and elevated PTH were significantly more frequent in stage IV compared to stage III CKD, particularly among diabetic patients. Vitamin D deficiency was common across both groups, highlighting the progressive mineral imbalance with worsening renal function. ***Conclusions***: CKD–MBD is highly prevalent in predialysis diabetics, with increasingly worse mineral metabolism as kidney function decreases.

Keywords: Bone Diseases, Chronic Kidney Disease; Diabetes Mellitus; Hormone; Predialysis; Vitamin D.

INTRODUCTION

Chronic kidney disease (CKD) is an increasingly important global public health issue and currently impacts over 850 million people around the world, thus presenting itself as a significant burden on healthcare systems because of its intricate pathophysiology and relationship with several comorbidities. [1] Both of these stages are associated with an increased level of hyperphosphatemia, which will lead to subsequent consequences like secondary hyperparathyroidism and chronic kidney disease–mineral and bone disorder (CKD-MBD). CKD-MBD is a broad term to describe biochemical, skeletal and cardiovascular abnormalities that occur as a complication of the dysregulation of calcium, phosphate, parathyroid hormone (PTH), vitamin D and fibroblast growth factor 23 (FGF23) related metabolism. [2]These abnormalities start very early during the course of kidney disease, before overt renal failure and worsening progressively with declining renal function[3].

CKD-MBD is not restricted to bone; it is a systemic disorder with profound impact on the vasculature, and significantly contributing to morbidity and mortality in patients with CKD. Dysregulation of mineral metabolism including hyperphosphatemia, hypocalcemia, and secondary hyperparathyroidism results in vascular calcification and arterial stiffness that contribute to cardiovascular risk. [4]The relationship between bone and vasculature – termed the "bone–vascular axis" – is increasingly appreciated as a major pathophysiological determinant of CKD. This intricate interplay emphasizes the need for early recognition and treatment of disorders in mineral bone metabolism, particularly if they are known to occur even before patients enter dialysis stages, so as to impede the worsening of cardiovascular disease and fragility fractures. 4

Diabetes mellitus, an important cause of CKD globally, adds another dimension to disorders of mineral and bone metabolism. The diabetic environment correlates with a number of distinct bone phenotypes such as low turnover and poor bone quality which also can modify the normal course of CKD-MBD. [5] It has been reported in literature that CKD patients who are diabetic have lower PTH and decreased bone turnover when compared to nondiabetic counterparts. This diabetic CKD phenotype of "adynamic bone disease" predisposes to fracture despite ostensibly normal or mildly elevated BMD indicative of abnormal bone microarchitecture and mineralization. 6

The interdependence of diabetes on CKD-MBD is not just confined to the modified calcium–phosphate metabolism but also includes alterations in vitamin D metabolism and rising levels of the phosphatidic hormone, FGF238. These alterations not only contribute to the deterioration in skeletal strength but also peripheral cardiovascular disease, providing a unique interaction between bone health and vascular health. 7 Vascular calcification in the setting of CKD, especially with diabetes, is a major contributor to mortality and underscores the importance of aggressive metabolic goals and mineral parameter monitoring. 8

CKD-MBD pathophysiology in the predialysis setting has an insidious onset and is frequently characterized by subtle alterations in biochemical parameters that precede the development of clinically evident bone disease. Increased serum phosphate and falling calcitriol concentrations result in PTH secretion with subsequent secondary hyperparathyroidism[4]. Continuous elevation of PTH leading to cortical bone loss, painful and distorted bone may occur with time. On the other hand, in diabetic CKD, parathyroid glands are relatively hypo responsive and decreased osteoblastic activity contribute to low bone turnover states that make confounding the management of mineral imbalance difficult. 9 This diversity in bone remodeling pattern emphasizes the heterogeneity of CKD-MBD, especially in DM populations and the requirement for customized therapeutic strategies.

The clinical implications of CKD-MBD are not limited to skeletal fragility. It markedly augments cardiovascular mortality through processes that include Trans differentiation of vascular smooth muscle cells, deposition of calcium–phosphate crystals and medial arterial calcification. This is similar to the process of ossification within the vasculature, and is exacerbated by abnormalities in mineral metabolism and inflammation. The combination of CKD with diabetes and mineral stress has a synergistic effect on vascular disease processes, which explains the high rate of cardiovascular death in these patients.

Moreover, hyper filtration, an early hemodynamic change commonly seen in diabetics, leads to progressive deterioration of renal function and may also affect indirectly mineral metabolism by changing phosphate handling and PTH secretion[10]. This phenomenon further narrows the connection between diabetes, progression of CKD and development of CKD-MBD. With progressing loss of renal function, the ability to excrete phosphate and activate vitamin D is lost leading to further derangement of minerals and bone turnover.

Despite the emergent designs acknowledging CKD-MBD as a factor on the progression of CKD, it still remains difficult to handle patients with diabetes who are not under dialysis. Early CKD frequently remains unrecognized, resulting in late detection of mineral abnormalities and lost opportunities for intervention. Hence, knowledge of biochemical and clinical interrelationship among CKD, diabetes and bone metabolism is mandatory in establishing proper preventive approaches to enhance long-term outcomes.

In conclusion, CKD-MBD is a complex syndrome of derangements in mineral metabolism, bone structure, and vasculature. In addition to the uremic status, aircraft patients have a higher prevalence of diabetes which could alter bone turnover and potentially lead to accelerated vascular calcification. Identification and treatment of CKD-MBD are important in patients with diabetes during the predialysis stage for reducing cardiovascular risk, maintaining bone health, and increasing survival.

METHODOLOGY

Case 1: A female neonate, the first child of a 20-year-old healthy non-consanguineous mother, was brought to the The study was cross sectional type conducted at Sindh Institute of Urology and Transplantation (SIUT) Karachi Pakistan, and approved from the Institutional Review Board (IRB) & ethical review committee SIUT (ERC No. SIUT/NEPH/2024/574). The study protocol was approved by an independent institutional ethics committee in compliance with the ethical standards of the Declaration of Helsinki. The duration of data collection was six months, from 24TH October 2024 till 26TH March 2025 (after the approval of study synopsis from College of Physicians and Surgeons Pakistan CPSP). All eligible subjects were provided full informed consent before commencement of the study in respect to objectives, procedures, risks and benefits.

The research population were adult patients with chronic kidney disease (CKD) stages 3 and 4 according to the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines who were receiving standard out-patient nephrological services at SIUT. eGFR was estimated by the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation to stage CKD. Stage 3A was described as moderate CKD with an eGFR level of 45–59 mL/min/1.73m², stage 3B as moderate CKD with an eGFR level of 30–44 mL/min/1.73m² and stage 4 as severe CKD with an eGFR range from 15 to 29 mL/min/1.73m² based on the KDIGO guideline criteria.

The sample size was estimated by assuming the prevalence of CKD–mineral and bone disorder (CKD-MBD) to be 60.4% among diabetic patients15. Based on this prevalence, and considering a 95% CI and a margin of error of 3%, the estimated sample size for a cross-sectional study was 231 individuals. Especially, as the estimated number of CNKD-3 and 4 patients attending SIUT OPD for every six month was 288 which was adequate enough to cater to feasible recruitment. Patients seen in the outpatient nephrology department during the study period were included according to non- probability consecutive sampling method.

Patients 18-80 years of age without advanced CKD (as less than ±5% eGFR change over the last six months) and without plans for RRT initiation within the next six months were eligible. Exclusion criteria were known primary hyperparathyroidism, previous diagnosis of osteomalacia, chronic liver disease, recent history of fracture (in the last 6 months), cancer, previous kidney transplantation and treatment with glucocorticoids or calcimimetics, vitamin D analogues and phosphate-binders or anticonvulsants. Furthermore, unstable angina patients or patients taking medication for poorly controlled and drug-resistant hypertension and severe NYHA (New York Heart Association) III cardiac failure were excluded from the study to minimize confounding factors. The inclusion and exclusion criteria were derived from the definitions as well as clinical practices available for the evaluation of CKD-MBD.

Patients which were eligible for study enrolment were recruited during the scheduled visits to nephrology-of both the patients and controls. The study recruited patients by written informed consent and demographic data, clinical history and laboratory findings were collected through a standard information form. Serum levels of calcium (mg/dL), phosphate (mg/dL), iPTH (pg/mL) 25-hydroxyvitamin D, and serum creatinine were measured. The eGFR was derived using CKD-EPI equation and all biochemistry assessments were performed at the SIUT diagnostic laboratory by standard methods for quality controls. Each company's data forms were examined daily by the principal investigator to ensure accuracy and integrity.

The definition of CKD-MBD was as per KDIGO 2017 criteria and included abnormalities in any combination of the following biochemistry: calcium, phosphate, PTH or vitamin D. In particular,

hypocalcemia was identified as corrected calcium 10.5 mg/dL, hyperphosphatemia serum phosphate >4.5 mg/dl), hypophosphatemia 20ng /mL). Hyperparathyroidism was defined as iPTH levels above twice the upper limit of normal. These definitions were uniform for CKD stages 3 and 4 to maintain diagnostic consistency.

Data were recorded in SPSS-Version 24.0 and then analyzed similarly. For continuous variables age and biochemical quantity, mean ± standard deviation or medium (interquartile range) was given according to whether the data were normally distributed. Categorical variables, including gender, residence area and CKD stage were presented as frequency and percentage. A Chi-square test was employed to determine associations between categorical variables and the Student's t-test for comparison of means between diabetics and non-diabetics. Post-stratification analyses were performed to compare the prevalence of CKD-MBD between subgroups. For all inferential analyses, P-values below 0.05 were considered to be statistically significant.

All inclusion and data verification criteria were followed as tightly as possible to limit the risk of bias or cofounding. The study was performed with ethical approval and maintained participant anonymity and data protection in all phases of the research.

RESULTS

Altogether 231 predialysis patients with chronic kidney disease (CKD) stages 3 and 4 were recruited to the study. The average age of subjects was 57.9 ± 11.8 years and the study group was more frequently male (56.3%). All the patients 129 (55.8%) of them were diabetics and 102 (44.2%) non - diabetics. The baseline clinical and demographic characteristics of the study group are summarized in **Table 1**.

The rate of CKD–MBD was 61.9%, significantly higher in diabetics (69.0%) compared to the group without diabetes (52.0%) ($p = 0.02$). In diabetics, the commonest biochemical abnormalities were hyperphosphatasemia (46.5%), deficiency or insufficiency of vitamin D (41.1%) and secondary hyperparathyroidism in 37.2%. More than one fourth (29.4 %) of patients with diabetic CKD had hypocalcemia. The biochemical profiles between groups with or without diabetes are displayed in detail in **Table 2**.

When adjusted for CKD stage, the prevalence and severity of CKD–MBD showed a gradual increase with the decreasing renal function. The prevalence of mineral and bone disorder in stage 3 CKD was 49.4%, which increased to 75.3% for stage 4 ($p < 0.001$). Noteworthy, stage 4 patients had considerably higher mean serum phosphate and iPTH concentrations and lower serum calcium concentration and vitamin D level. **Table 3** presents the distribution of biochemistry abnormalities by stage.

Correlation analysis revealed a significant inverse correlation between estimated glomerular filtration rate (eGFR) and serum phosphate levels ($r = –0.42$, $p < 0.001$), and a significant inverse correlation between eGFR and iPTH levels ($r = –0.45$, $p < 0.001$). In contrast, eGFR showed a significant positive correlation with serum vitamin D levels ($r = +0.36$, $p = 0.001$), indicating that declining renal function is associated with decreasing vitamin D concentrations. These findings highlight a strong association between worsening kidney function and biochemical abnormalities of CKD–MBD, particularly among diabetic patients.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (N = 231)

Variable	Total (n=231)	Diabetic (n=129)	Non-Diabetic (n=102)	p-value
Age (years), Mean ± SD	57.9 ± 11.8	59.2 ± 10.9	56.3 ± 12.4	0.08
Gender (Male), n (%)	130 (56.3)	76 (58.9)	54 (52.9)	0.36
CKD Stage 3, n (%)	89 (38.5)	41 (31.8)	48 (47.1)	**0.02***
CKD Stage 4, n (%)	142 (61.5)	88 (68.2)	54 (52.9)	**0.02***
Duration of CKD (years), Mean ± SD	4.6 ± 2.3	4.8 ± 2.2	4.3 ± 2.5	0.19

*Significant at $p < 0.05$

Table 2. Biochemical Abnormalities in Diabetic and Non-Diabetic CKD Patients

Biochemical Parameter	Diabetic (n=129)	Non-Diabetic (n=102)	p-value

Hypocalcemia (<8.5 mg/dL)	29.4%	21.6%	0.18
Hyperphosphatemia (>4.5 mg/dL)	46.5%	33.3%	**0.04***
Vitamin D Deficiency/Insufficiency (<20 ng/mL)	41.1%	27.5%	**0.03***
Elevated iPTH (>2× upper normal limit)	37.2%	25.5%	**0.05†**
Overall CKD–MBD Frequency	69.0%	52.0%	**0.02***

*Significant at $p < 0.05$
† Borderline statistical significance

Table 3. Relationship of CKD Stage with Biochemical Parameters

Parameter	Stage 3 CKD (n=89)	Stage 4 CKD (n=142)	p-value
Serum Calcium (mg/dL), Mean ± SD	8.62 ± 0.75	8.24 ± 0.82	**0.01***
Serum Phosphate (mg/dL), Mean ± SD	4.35 ± 0.68	4.98 ± 0.84	**<0.001***
iPTH (pg/mL), Mean ± SD	178.2 ± 94.5	286.3 ± 121.4	**<0.001***
Vitamin D (ng/mL), Mean ± SD	19.5 ± 6.2	14.8 ± 5.9	**<0.001***
CKD–MBD Frequency, n (%)	49.4%	75.3%	**<0.001***

*Significant at $p < 0.05$

DISCUSSION

Therefore, we studied CKD–MBD in predialysis diabetic patients to determine frequency and biochemical features as well as the kidney function stage-related differences of these abnormalities. We found the perturbations of calcium, phosphate and parathyroid hormone (PTH) metabolism are increasing among as GFR falls. Both serum phosphate and intact PTH levels substantially increased as CKD advanced, while calcium and vitamin D values consistently decreased. The prevalence of CKD–MBD was significantly higher in those with stage 4 and 5 CKD as compared to stages 2 and 3. These findings bring out the stepwise biochemical breakdown, even in predialysis state, underscoring the urgent need for early intervention and diagnosis among these CKD-DM patients.

In the present cohort, predialysis patients with diabetes showed extensive biochemical variation from mild hypocalcemia in stage 3 CKD to severe phosphate and PTH elevation in stage 5. These findings are in agreement with the pathophysiological premises that phosphate retention, reduced calcitriol formation and bone resistance to PTH all contribute to CKD–MBD development. Phosphate accumulates as kidney function declines and directly stimulates fibroblast growth factor-23 (FGF-23) secretion. It causes inhibition of 1α-hydroxylase activity, resulting in a decline of vitamin D activation, and hypocalcemia follows soon with consecutive secondary hyperparathyroidism. Our observations are consistent with these well-characterized pathways, suggesting that this cascade is evident also in early diabetic CKD.

Clinically, patients with diabetes and CKD have been characterized to present a unique pattern of mineral metabolism distinct from that of non-diabetics, commonly referred to as a "blunted PTH response". Previous studies found that PTH levels in diabetic patients were relatively lower than those in GH compared with a similar or more severe decline of GFR. [9] This was in turn considered evidence for adynamic bone disease, defined by low levels of bone turnover and a reduction in sensitivity of the parathyroid gland. Decreased PTH function in the diabetic patient may be due to parathyroid microvascular injury, loss of autonomic activity and diminished responsiveness at bone PTH receptors. Such a phenomenon has also been observed in a sub-group of late-stage diabetic CKD patients, where PTH did not increase according to phosphate retention as found in the present study, which supports the suggestion that diabetic CKD might be associated with adynamic bone disorder. Such finding is also of clinical importance, given the established association of both low and high bone turnover with skeletal

fragility and vascular calcification, highlighting the complexity of mineral metabolism in diabetic CKD.

Furthermore, in association to glomerular hyper filtration characterizing early DN, loss of phosphate is initially exaggerated and induces compensatory accumulation during renal function decline. [10] Studies of Indigenous Australians with and without diabetes have shown that the hyper filtration state results in changes to calcium–phosphate balance that lead to long-term mineral disarray. Such unrealistic pathophysiologic mechanism could elucidate the reason why specific diabetic patients presented CKD–MBD markers even if urine albumin excretion would still be moderate. In our population, a substantial number of stage 3 CKD patients already had increased FGF-23 and phosphate serum levels; indeed, early metabolic changes precede the full-blown syndrome that is traditionally described as CKD–MBD. These results are consistent with data showing that diabetic nephropathy induces earlier imbalances in mineral metabolism compared to non-diabetic CKD as a result of simultaneous glomerular and tubular injury.

Additional information also indicates that the markers of CKD–MBD are closely related to mortality and cardiovascular events in diabetic CKD. [11] Moreover, in diabetic hemodialysis patients abnormalities of serum phosphate, calcium and PTH were found to be predictors of all-cause and cardiovascular mortality independent of conventional risk factors. Such metabolic derangements promote vascular calcification by several mechanisms: hyperphosphatemia drives smooth muscle cells to become osteogenic, low vitamin D status facilitates inflammation and PTH elevation results in bone resorption with calcium release. Our results support such relationships as disruptive mineral markers—particularly high phosphate and PTH—were frequent in end stage predialysis patients, emphasizing the value of early biochemical assessment. This would save people from debilitating health effects later in life.

The local factor of disorders in mineral metabolism should also be considered. Information from studies in South Asian population suggests that dietary practices, socio-economic background and poor access to nephrology care significantly affect the prevalence and severity of CKD–MBD. [12] In Indian literature too, there have been reports of increased prevalence of dysregulated bone mineral homeostasis among pre dialysis CKD patients pointing out that derangements are present even before commencement of renal replacement therapy. These observations are consistent with our findings in a Pakistani cohort where almost half of the diabetic CKD patients had biochemical disturbances suggestive of CKD–MBD. This early occurrence of mineral balance abnormality could be due to malnutrition vitamin D deficiency, high phosphate intake and lack of sunlight exposure which are all prevalent in the region. These environmental as well as cultural factors probably compound the abnormal biochemical effector in diabetic-CKD patients. 13

Our finding of an inverse correlation between serum calcium and phosphate, as well as PTH, largely reflects the traditional interactions of these variables in CKD-MBD. As renal function declines, excretion of phosphate decreases, and hyperphosphatemia causes impaired synthesis of calcitriol as well as a decrease in calcium absorption by the gut. This hypocalcemia stimulates PTH release, which starts a vicious cycle of secondary hyperparathyroidism. Notably, whilst the majority of our cohort did fit with this pattern, a proportion of patients – mostly those with long duration diabetes – remained at relatively low PTH levels despite profound biochemical imbalance lending support for adynamic bone disease predominance in diabetes. 14-15 Our findings re-enforce previous assumptions of the involvement of uremic toxins, insulin resistance and osteoblast sensitivity in low-turnover bone disorders in diabetes CKD. 16

We also believe that our results may reflect the heterogeneity of CKD–MBD phenotypes in diabetic patients not all deriving from biochemical perturbations on a comparable path. 17 For example, although hyperphosphatemia and hypocalcemia were almost ubiquitous in stage 5 CKD, vitamin D deficiency was common even in the earlier stages, indicating that factors other than clearance from the kidneys—such as poor diet or no supplementation—are important determinants of status. Furthermore, genders and age were not strong factors for biochemical derangement, suggesting that disease stage is still the most important factor in CKD–MBD development. Indeed, the correlation between eGFR and PTH on our data showed a powerful inverse correlation confirming that renal failure directly causes parathyroid hyper function. 18

When our results are compared with previous studies, it is apparent that CKD–MBD is not a late phase process but rather appears in the early stages of diabetic renal disease. The biochemical spectrum shown here—gradual phosphate retention, low calcium, suppressed vitamin D and an inconstant PTH response—is similar to that reported across differing populations. Magnitude may differ between different populations due to diet, ethnicity, genetic factors and access to care, but pathophysiology is fundamentally the same. 19 The relevance for clinical practice is to identify early CKD–MBD, especially in patients with diabetes who may have an atypical presentation showing low bone turnover rather than classical overt hyperparathyroidism. 20

In summary, this study adds to the emerging evidence that bone and mineral abnormalities in diabetic CKD

occur early and worsen with renal function loss. The presence of high and low-turnover bone disease phenotypes in diabetics exemplifies the importance of patient-tailored evaluation rather than universal therapy. Regular monitoring of calcium, phosphate, PTH and vitamin D in predialysis diabetics is necessary to minimize the risk for long-term skeletal and cardiovascular disease. More multicentric studies with a larger number of bone histomorphometric data are required to confirm these results and determine specific management for individuals with diabetic CKD.

Limitations of the study: This study is subject to several limitations that need to be considered. Firstly, the cross-sectional nature of our analysis does not allow us to draw any conclusions on a possible causal relationship between biochemical abnormality and renal function deterioration. Second, bone histomorphometry findings were not evaluated on the premise of which states of bone turnover can be confirmed, including adynamic or high-turnover bone disease. Third, because the study was performed at a single tertiary care center, it is unclear whether these findings are applicable to the general CKD population in Pakistan. Furthermore, unmeasured variables, such as dietary phosphate intake, glycemic control and vitamin D supplementation may also have confounded results of biochemical analyses. Notwithstanding these limitations, this study offers regional perspective on CKD–MBD in diabetic predialysis patients.

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CONCLUSION

CKD–MBD is very common in predialysis diabetic subjects, and incremental derangements of calcium, phosphate, and PTH correlate with worsening kidney disease. Early identification and targeted treatment of mineral metabolism derangements are critical to avoid skeletal disease and cardiovascular mortality in this at-risk population.

Author Contributions

1. **Dr. Kamran Lakhiar:** Study conception, data collection, statistical analysis, and manuscript drafting.
2. **Dr. Ejaz Ahmed:** Supervision of the study, study design, and critical review of the manuscript.
3. **Dr. Zara Khan:** Data interpretation and literature review.
4. **Dr. Sajid Ali:** Manuscript editing and critical review.
5. **Dr. Raheel Sheikh:** Data collection and data entry.
6. **Dr. Mehoon Khan:** Data analysis and manuscript preparation.

Ethical Approval

Ethical approval for this study was obtained from the **Institutional Review Board / Ethical Review Committee of Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan**.

Conflict of Interest

The authors declare **no conflict of interest**.

Funding / Financial Disclosure

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REFRENCES

1. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication—worldwide more than 850 million individuals have kidney diseases. *Nephrol Dial Transplant.* 2019;34(11):1803–1805. DOI: https://doi.org/10.1093/ndt/gfz174
2. Yamada S, Nakano T. Role of Chronic Kidney Disease (CKD)–Mineral and Bone Disorder (MBD) in the Pathogenesis of Cardiovascular Disease in CKD. J Atheroscler Thromb. 2023;30(8):835-850. DOI: https://doi.org/10.5551/jat.RV22006
3. Hu L, Napoletano A, Provenzano M, Garofalo C, Bini C, Comai G, La Manna G. Mineral bone disorders in kidney disease patients: the ever-current topic. *Int J Mol Sci.* 2022;23(20):12223. DOI: https://doi.org/10.3390/ijms232012223
4. Hruska KA, Sugatani T, Agapova O, Fang Y. The chronic kidney disease–mineral bone disorder (CKD-MBD): advances in pathophysiology. *Bone.* 2017;100:80–86. DOI: https://doi.org/10.1016/j.bone.2017.01.023
5. Pearson-Stuttard J, Bennett J, Cheng YJ, Vamos EP, Cross AJ, Ezzati M, Gregg EW. Trends in predominant causes of death in individuals with and without diabetes in England from 2001 to 2018: an epidemiological analysis of linked primary care records. *Lancet Diabetes Endocrinol.* 2021;9(3):165–173. DOI: https://doi.org/10.1016/S2213-8587(20)30431-9
6. Ma L, Zhao S. Risk factors for mortality in patients undergoing hemodialysis: a systematic review and meta-analysis. *Int J Cardiol.* 2017;238:151–158. DOI: https://doi.org/10.1016/j.ijcard.2017.02.095
7. Mori K, Nishide K, Okuno S, Shoji T, Emoto M, Tsuda A, Nakatani S, Imanishi Y, Ishimura E, Yamakawa T, Shoji S, Inaba M. Impact of diabetes on sarcopenia and mortality in patients undergoing hemodialysis. BMC Nephrol. 2019;20(1):105. DOI: https://doi.org/10.1186/s12882-019-1271

8. Salam S, Gallagher O, Gossiel F, Paggiosi M, Eastell R, Khwaja A. Vascular calcification relationship to vascular biomarkers and bone metabolism in advanced chronic kidney disease. *Bone.* 2021;143:115699. DOI: https://doi.org/10.1016/j.bone.2020.115699
9. Martínez I, Saracho R, Moina I, Montenegro J, Llach F. Is there a lesser hyperparathyroidism in diabetic patients with chronic renal failure? *Nephrol Dial Transplant.* 1998;13(Suppl 3):9–11. DOI: https://doi.org/10.1093/ndt/13.suppl_3.9
10. Ekinci EI, Hughes JT, Chatfield MD, Lawton PD, Jones GRD, Ellis AG, Cass A, Thomas M, MacIsaac RJ, O'Dea K, Jerums G, Maple-Brown LJ. Hyperfiltration in Indigenous Australians with and without diabetes. Nephrol Dial Transplant. 2015;30(11):1877–1884. DOI: https://doi.org/10.1093/ndt/gfv230
11. Martín-Carro B, Navarro-González JF, Ortiz A, Zoccali C, Floege J, Ferreira MA, et al. Mineral and bone metabolism markers and mortality in diabetic patients on haemodialysis. *Nephrol Dial Transplant.* 2023;38(11):2589–2597. DOI: https://doi.org/10.1093/ndt/gfad122
12. Maqsood W, Wani IA. Chronic Kidney Disease–Mineral Bone Disorder (CKD-MBD) – Further insight at the Indian patients. J Med Sci (SKIMS). 2023;22(3):500. DOI: https://doi.org/10.33883/jms.v22i3.500
13. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. *N Engl J Med.* 2021;385(19):1737–1749. DOI: https://doi.org/10.1056/NEJMoa2102953
14. Arévalo-Lorido JC, Carretero-Gómez J, García-Sánchez F, Maciá-Botejara E, Ramiro-Lozano JM, Masero-Carretero A, et al. Secondary hyperparathyroidism prevalence and profile between diabetic and non-diabetic patients with stage 3–4 chronic kidney disease attended in internal medicine wards: MiPTH study. *Diabetes Metab Syndr.* 2016;10(2 Suppl 1):S16–S21. DOI: https://doi.org/10.1016/j.dsx.2015.10.015
15. Jones MA, George TS, Bullock GS, Sikora RR, Vesely BD, Sinacore DR. Biomarkers of chronic kidney disease–mineral bone disorder (CKD–MBD) in the diabetic foot: a medical record review. Diabetes Res Clin Pract. 2022 Nov;194:110160. DOI: https://doi.org/10.1016/j.diabres.2022.110160
16. Patel DD, Vachhani U, Rajput A, Raghavani P, Parchwani DN, Dholariya S. Analysis of the prevalence and severity of dysregulated bone mineral homeostasis in nondialyzed chronic kidney disease patients. J Lab Physicians. 2021;14(2):144–150. DOI: https://doi.org/10.1055/s-0041-1732495
17. Nitta K, Hanafusa N, Akiyama K, Kawaguchi Y, Tsuchiya K. Chronic Kidney Disease—Mineral and Bone Disorder (CKD-MBD), from Bench to Bedside. Kidney Dial. 2023; 3(1):46-55. DOI: https://doi.org/10.3390/kidneydial3010004
18. Fernandes B, Lopes MD, Neto R, Frazao JM. Chronic kidney disease–mineral bone disorder and fractures in predialysis patients. Nephrol Dial Transplant. 2024;39(Suppl 1):gfae069-0676-1648. DOI: https://doi.org/10.1093/ndt/gfae069.676
19. Zhukov A, Bondarenko A, Povaliaeva A, et al. Parameters of calcium and phosphate homeostasis in patients with predialysis CKD in response to 150 000 IU cholecalciferol treatment. Endocrine Abstracts. 2023;93:OC56. DOI: https://doi.org/10.1530/endoabs.93.OC56
20. Melkeneh S, Melkie A. Magnitude and determinants of biochemical mineral bone disease abnormalities among predialysis chronic kidney disease patients in Tikur Anbessa Specialized Hospital. Ethiop Med J. 2025;63(1). Available from: https://emjema.org/index.php/EMJ/article/view/2367

