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Unveiling The Burden of Bone Mineral Density in Chronic Kidney Disease Patients on Hemodialysis: Insights into Risk Factors

Kishalay Mahajan[1*], Pratik Tripathi[2], Gaurav Khandelwal[3], Shaurya Mehta[4], Ankur Baidya[5]

[1,2,3,4]Department of Nephrology, National Institute of Medical Sciences and Research, Jaipur, India
[5]Department of Community Medicine, Uttar Pradesh University of Medical Sciences, Lucknow, India

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***Corresponding author**:
Dr. Kishalay Mahajan
Email: bappa.mahajan@gmail.com

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is a growing global health burden, often complicated by mineral and bone disorders (CKD-MBD) that significantly increase fracture risk. This study aims to establish the proportion of CKD-MBD among hemodialysis patient and to establish correlation between intact PTH (iPTH) and bone mineral density in dialysis patients.

Methods: A cross-sectional study was conducted at the National Institute of Medical Sciences, Jaipur, involving 100 adult CKD patients on maintenance hemodialysis between August 2024 and January 2025. BMD was assessed using Dual-Energy X-ray Absorptiometry (DEXA) at the lumbar spine and femoral neck. Clinical, anthropometric, and laboratory data including intact parathyroid hormone (iPTH), alkaline phosphatase (ALP), vitamin D, and hemoglobin were collected. Fracture risk was analyzed using Pearson correlation and multivariate logistic regression.

Results: Among the 100 patients, mean age was 44.6 ± 14.1 years. The multivariate logistic regression analysis identified age >45 years, presence of diabetes, and moderate iPTH levels as significant independent predictors of high fracture risk in chronic kidney disease (CKD) patients. Serum albumin positively correlated with BMD at the radius-ulna site.

Conclusion: This study highlights elevated iPTH and ALP levels, older age, and diabetes as key predictors of low BMD and high fracture risk in CKD patients on hemodialysis. Routine BMD assessment and monitoring of CKD-MBD parameters are essential for timely intervention. These findings emphasize the need for integrated bone health management strategies in this CKD on hemodialysis patients.

Keywords: Hemodialysis, Bone -Mineral density, Parathyroid hormone

INTRODUCTION

Chronic kidney disease (CKD) has emerged as a significant global public health challenge. CKD is the 12th leading cause of death and 17th cause of disability worldwide.[1] CKD leads to poor outcomes like End Stage Renal Disease (ESRD), Cardio Vascular Disease (CVD) and Premature Death.[2]

In chronic kidney disease (CKD), disturbances in mineral metabolism give rise to a condition known as chronic kidney disease-mineral and bone disorder (CKD-MBD). Individuals with CKD frequently exhibit increased bone

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turnover along with a reduction in bone mineral density[3] A variety of pathophysiological factors contribute to these changes, including: secondary hyperparathyroidism[4], hyperphosphatemia[5], diminished vitamin D synthesis[6], hypocalcemia[5], and older age. Patients with end-stage renal disease (ESRD) are disproportionately vulnerable to fractures compared to the general population.[7,8]

During the progression of chronic kidney disease (CKD), serum calcium levels often decline due to phosphate accumulation, impaired calcitriol (active vitamin D) synthesis by the kidneys, reduced intestinal absorption of calcium.and skeletal resistance to the calcemic action of Parathyroid hormone (PTH), but the levels of free calcium remain within the normal range in most patients as a result of compensatory hyperparathyroidism. In Chronic kidney disease response to a decrease in ionized calcium mediated by the calcium sensing receptor is likely the most potent stimulus for PTH release. Phosphate (PO4) also causes PTH release ultimately leading to secondary hyperparathyroidism. Bone mineral density (BMD) serves as a crucial indicator for assessing bone mass and mineral content [9]. According to the International Society for Clinical Densitometry (ISCD), BMD should be measured using Dual-Energy X-ray Absorptiometry (DEXA), commonly targeting the postero-anterior lumbar spine (L1-L4) and the hip region, including the femoral neck or total proximal femur.[10]

DEXA scan findings are typically expressed as BMD (g/cm^2), Z-score, or T-score the latter indicating how many standard deviations an individual's bone density deviates from the average of a healthy young adult reference population.

The 2017 KDIGO guidelines for chronic kidney disease-Mineral and Bone Disorder (CKD-MBD) recommend BMD evaluation in CKD patients who exhibit signs of CKD-MBD or possess risk factors for osteoporosis [11].

A meta-analysis involving CKD populations demonstrated a strong association between reduced BMD and an elevated risk of fractures [12], highlighting the clinical value of early BMD assessment and fracture prevention strategies.

Early identification of low BMD is particularly vital for patients awaiting kidney transplantation, as managing bone health becomes increasingly 14complex after transplantation [13]. This study aims to establish the proportion of CKD-MBD among hemodialysis patient and to establish correlation between intact PTH (iPTH) and bone mineral density in dialysis patients.

MATERIALS AND METHODS

This cross-sectional study was conducted between August 2024 and January 2025 at the dialysis centre of National Institute of Medical Sciences, Jaipur. A total of 100 patients were included.

Sample Size calculation using the formula $n= z^2pq/d^2$ where n is sample size, z is 1.96 at 95% confidence interval, p is prevalence of high fracture risk from previous study (85%) [14], q is 1-p and d are allowable error (7%). The calculated sample size was 99.9 which was rounded to 100.

Inclusion criteria: All chronic kidney patients on dialysis were included in the study.

Exclusion criteria: Patients having (1) Diagnosis of primary hyperparathyroidism is established by the presence of elevated serum calcium with unsuppressed iPTH levels; (2) Patients with conditions associated with malabsorption of vitamin D, such as inflammatory bowel disease, chronic pancreatitis, or a history of gastric or small bowel resections; (3) Those patients taking any medication (s) that could adversely affect bone metabolism and thus contribute to a decreased BMD by causing vitamin D deficiency like (rifampicin, ketoconazole, phenytoin, valproic acid, corticosteroid) etc; and (4) Patients with secondary osteoporosis, prolonged glucocorticoid intake (defined as use of prednisolone in a dosage of more than 5 mg/d for at least 3 months), or significant hepatic or thyroid dysfunction as measured from liver function tests and thyroid profile.

Out of 130 patients considered for inclusion, 100 patients were included in the study and 30 patients were excluded from the study based on the eligibility criteria.

After obtaining informed consent, data were collected from patients. Variables included age, gender, body mass index (BMI), and duration of dialysis, tobacco consumption, smoker means those who has smoking history, comorbidities, history of fractures, previous kidney transplantation, prior haemodialysis (HD) treatment, menopausal status, and current medications.

Laboratory and biochemical parameters such as serum 25-hydroxyvitamin D, albumin, calcium, phosphate, alkaline phosphatase (ALP), intact parathyroid hormone (iPTH), and haemoglobin were measured from venous blood samples collected during the patients' routine monthly follow-up visits. All samples were immediately transported to the laboratory and analyzed on the same day.

Patient with BMD T score < -1.0 is defined as high fracture risk (Osteoporosis and Osteopenia) while Patient with BMD T score ≥ -1.0 is defined as low fracture risk (normal bone density).[15,16]

Table 1: Biochemical parameters in Stage V CKD on Dialysis

Parameter	Low	Medium*	High
Calcium(mg/dl)	<8.4	8.4-9.5	>10.2
Phosphorus(mg/dl)	<3.5	3.5-5.5	>5.5
Uric acid(mg/dl)	<4	4-7	>7
Serum Albumin(g/dl)	<3.5	3.5-5.0	>5
Vitamin D 25(OH)D (ng/ml)	<20	30-50	>100
iPTH(pg/ml)	<150	150-300	>300
ALP(U/L)	<40	40-120	>120-250

*Target/Acceptable Range

Bone mineral density (BMD), bone mineral content (BMC), and corresponding T-scores were evaluated at the hip and lumbar spine using dual-energy X-ray absorptiometry (DEXA). For the lumbar spine, BMD was determined by averaging measurements from vertebrae L1 to L4. T-scores and Z-scores were computed based on normative data stratified by age and sex, as provided by the DEXA equipment manufacturer, ensuring accurate benchmarking against reference populations.

Ethical approval: Ethical approval was obtained from Institutional Ethics Committee [NIMSUR/IEC/2024/629, Proposal no. IEC/P-322/2024. Patient confidentiality was strictly maintained.

Statistical Analysis: All the statistical analysis was done using SPSS Version 20.0. Analysis of generated data was done by using descriptive statistics such as range, mean, and standard deviation were used to describe continuous variables while numbers and percentages were used to present discreet variables. Pearson's correlation coefficient was used to assess the inter-relationship between various laboratory markers. Univariate and multivariate logistic regression were applied.

RESULTS

Among the study group of 100 patients, 65% were male while female was 35%. The mean age of our participants was 44.6 years (SD = 14.1) with a frequency of 54% for ≤45 years age group and 46% for >45 years age group.

Among the participants, 49% had hypertension and 49% had Diabetes mellitus. Around 48% had history of fractures while on dialysis. Table 2 provides an overview of the patients' initial demographic, clinical, and biochemical characteristics.

Number of patients with BMD T score ≤-2.5 were 18 labelled as High fracture risk (Osteoporosis). Patients with BMD T score < -1.0 to > -2.5 were 30 labelled High fracture risk (Osteopenia). Patients with BMD T score ≥ -1.0 were 52 labelled as Low fracture risk.

This table 3 examines the relationships between demographic variables, chronic diseases, lifestyle habits, and the risk of fractures, with the goal of identifying significant predictors that may guide preventative strategies in clinical settings. A statistically significant association was observed between age and fracture risk (p = 0.02). Participants over 45 years of age had a higher fracture risk (60.9%), whereas those under 45 had a lower risk (37.0%). Diabetes was significantly associated with fracture risk (p = 0.004). Diabetic individuals had a markedly higher fracture risk (60.7%) compared to non-diabetics (31.8%).

Pearson correlation analysis conducted between total bone mineral density (BMD) and intact parathyroid hormone (iPTH) levels in a sample of 100 individuals (N = 100) revealed a weak negative correlation (r = -0.19) which was not statistically significant (p = 0.062).

Table 2: Clinical and laboratory parameters of the participants

Variables	Frequency (%)	Mean ± SD
Age		
≤45 years	54 (54.0)	44.6 ± 14.1
>45 years	46 (46.0)	
Gender		
Male	65 (65.0)	
Female	35 (35.0)	
BMI		
Underweight (16-<18.5)	11 (11.0)	
Normal (18.5-24.9)	33 (33.0)	
Overweight (25-29.9)	17 (17.0)	
Obese (>30)	39 (39.0)	
Diabetes (Yes)	49 (49.0)	
HTN (Yes)	49 (49.0)	
CVD (Yes)	21 (21.0)	
Smoker (Yes)	43 (43.0)	
Tobacco consumption (Yes)	45 (45.0)	
History of Fracture (Yes)	48 (48.0)	
Hemoglobin(Hb)		8.4 ± 1.1
Calcium		8.8 ± 1.8
Phosphate		5.2 ± 1.9
Uric acid		7.1 ± 1.8
Vit D		27.9 ± 14.8
iPTH		358.1 ±281.3
ALP		142.6 ± 66.8

Table 3: Association of chronic diseases and lifestyle habits with fracture risk

Variables	Fracture risk		*p*-value
	Low (BMD ≥-1.0)	High (BMD < -1.0)	
Age			
≤45	34 (63.0)	20 (37.0)	***0.02****
>45	18 (39.1)	28 (60.9)	
Gender			
Male	33 (50.8)	32 (49.2)	0.73
Female	19 (54.3)	16 (45.7)	
BMI			
Underweight	5 (45.5)	6 (54.5)	
Normal	14 (42.4)	19 (57.6)	0.42
Overweight	11 (64.7)	6 (35.3)	
Obese	22 (56.4)	17 (43.6)	
Diabetes			
Yes	22 (39.3)	34 (60.7)	***0.004****
No	20 (68.2)	14 (31.8)	
HTN			
Yes	27 (55.1)	22 (44.9)	0.54
No	25 (49.0)	26 (51.0)	
CVD			
Yes	9 (42.9)	12 (57.1)	0.34
No	43 (54.4)	36 (45.6)	
Smoker			
Yes	21 (48.8)	22 (51.2)	0.58
No	31 (54.4)	26 (45.6)	
Tobacco consumption			
Yes	27 (60.0)	18 (40.0)	0.15
No	25 (45.5)	30 (54.5)	
Fracture			
Yes	26 (54.2)	22 (45.8)	0.67
No	26 (50.0)	26 (50.0)	

BMI-Body Mass Index, CVD-Cardio Vascular Disease

Table 4: Association of laboratory characteristics with fracture risk

Variables	Fracture risk		*p*-value
	Low (BMD ≥-1.0)	High (BMD < -1.0)	
Calcium			
Low	18 (45.0)	22 (55.0)	
Normal	14 (60.9)	9 (39.1)	0.46
High	20 (54.1)	17 (45.9)	
Phosphate			
Low	4 (44.4)	5 (55.6)	
Normal	27 (45.0)	33 (55.0)	0.11
High	21 (67.7)	10 (32.3)	
Uric acid			
Low	7 (87.5)	1 (12.5)	0.11
Normal	22 (48.9)	23 (51.1)	
High	23 (48.9)	24 (51.1)	
Vit D			
Low	16 (55.2)	13 (44.8)	
Normal	28 (49.1)	29 (50.9)	0.8
High	8 (57.1)	6 (42.9)	
iPTH			
Low	31 (67.4)	15 (32.6)	
Normal	4 (66.7)	2 (33.3)	**0.006***
High	17 (35.4)	31 (64.6)	
ALP			
Normal	21 (67.7)	10 (32.3)	**0.035***
High	31 (44.9)	38 (55.1)	

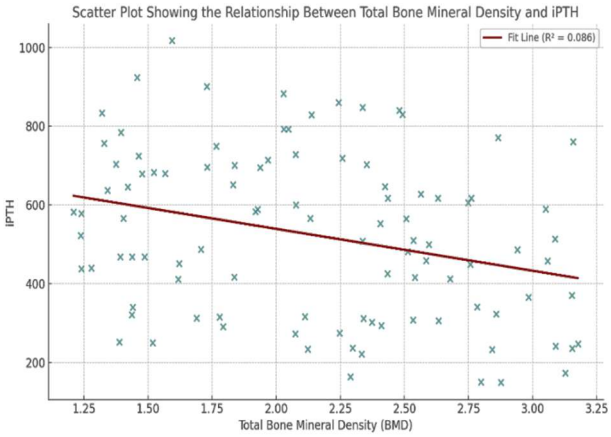

Figure 1: A scatter plot showing relationship between total bone mineral density (BMD) and intact parathyroid hormone (iPTH) levels

This is a scatter plot depicting the relationship between total bone mineral density (BMD) and intact parathyroid hormone (iPTH) levels revealed a weak negative correlation (R 2 =0.086). Although a declining trend of iPTH with increasing BMD was observed, the strength of association was minimal, suggesting that iPTH alone may not substantially influence BMD variations in the population.

Table 5: Factors associated with High Risk of Fracture" in CKD patients

Factors of High Risk of Fracture	Univariate OR (95% CI)	P value	Multivariate AOR (95% CI)	P value
Age				
≤45 years	Reference	-	Reference	-
>45 years	0.40 (0.17-0.92)	0.031	0.351 (0.137-0.900)	0.029
Diabetes				
Yes	4.05 (1.65-9.94)	0.002	3.942 (1.509-10.300)	0.005
No	Reference	-	Reference	-
iPTH				
Normal	Reference	-	Reference	-
Medium	0.19 (0.07-0.54)	0.002	0.186 (0.068-0.506)	0.001
High	0.23 (0.04-1.51)	0.127	0.229 (0.034-1.528)	0.128
ALP				
Normal	Reference	-	Reference	-
Elevated	0.51 (0.20-1.30)	0.159	0.466 (0.169-1.288)	0.141

Table 6: Correlation coefficients between biochemical and anthropometric variables with BMD at different skeletal sites (Radius-Ulna, Lumbar Spine, and Femoral Neck)

Variable	Radius Ulna BMD (r)		Lumbar Spine BMD (r)		Femoral Neck BMD (r)	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value	Correlation Coefficient	P-value
Age	-0.233	0.020*	0.143	0.161	-0.197	0.050
Height	0.269	0.007**	0.230*	0.023	0.266	0.007
Weight	0.126	0.213	0.015	0.884	0.074	0.463
Serum Uric Acid	-0.054	0.594	-0.174	0.087	0.058	0.566
R_U T-Score	0.823	0.000**	0.019	0.856	0.336	0.001
L_S Z-Score	-0.059	0.567	1 (Self)		0.542	0.000
Femoral Neck Z-Score	0.319	0.001**	0.461**	0.000	0.420	0.000
Femoral Neck T-Score	0.500	0.000**	0.380**	0.000	0.492	0.000
L_S T-Score	0.052	0.608	0.930**	0.000	0.552	0.000
Total Protein	-0.135	0.461	-0.204	0.262	-0.143	0.437
Vitamin D	0.033	0.741	0.076	0.459	0.200	0.046
Serum Albumin	0.271	0.006**	0.139	0.171	0.043	0.674
BMI	-0.042	0.675	-0.130	0.201	-0.071	0.481
Serum Phosphate	0.165	0.101	0.170	0.093	0.162	0.108
Serum Calcium	0.051	0.611	-0.155	0.127	0.104	0.303

The iPTH level and ALP, are a key marker in CKD-related mineral and bone disorder (CKD-MBD), also emerged as a significant factor. Patients with medium iPTH levels had a significantly lower risk of fractures (AOR = 0.186, 95% CI: 0.068-0.506, p = 0.001) shown by Pearson correlation.

The multivariate logistic regression analysis identified age >45 years, presence of diabetes, and moderate iPTH levels as significant independent predictors of high fracture risk in chronic kidney disease (CKD) patients.

DISCUSSION

This study comprises 100 individuals with a mean age of 44.6 ± 14.1 years, indicating a relatively young to middle-aged population. Males constituted the majority (65%), which may reflect higher healthcare-seeking behaviour or higher prevalence of comorbidities such as CKD or lifestyle-related diseases in men, consistent with earlier findings.[17] Obesity (39%) was the most prevalent BMI category, followed by normal weight (33%). A substantial proportion also reported modifiable risk behaviours, including smoking (43%) and tobacco use (45%) similar to study done by JA Kanis, both known contributors to bone demineralization and cardiovascular morbidity.[18] Obesity, can also predispose to bone fragility due to poor bone quality, especially in the presence of diabetes or CKD.[19]

The observation that 49% of individuals have diabetes and an equal proportion has hypertension underscores the substantial burden of metabolic comorbidities within the studied population. Cardiovascular disease (CVD) was present in 21% of patients, underscoring the interconnection between CKD-MBD (mineral bone disorder) and vascular calcification. Diabetes was significantly associated with fracture risk (p = 0.004). Diabetic individuals had a markedly higher fracture risk (60.7%) compared to non-diabetics (31.8%). This finding supports existing literature by J Linde and S Moe.[20,21]

Biochemical Parameters like Hemoglobin (Hb) was reduced (8.4 ± 1.1 g/dL), consistent with CKD-associated anemia. Calcium and phosphate levels were relatively maintained (8.8 ± 1.8 mg/dL, 5.2 ± 1.9 mg/dL), though phosphate appears elevated, suggesting impaired renal clearance. Uric acid was mildly elevated (7.1 ± 1.8 mg/dL), which may be linked to CKD progression. Vitamin D deficiency was evident (27.9 ± 14.8 ng/mL), which is common in CKD and contributes to secondary hyperparathyroidism. Intact parathyroid hormone (iPTH) levels were markedly elevated (358.1 ± 281.3 pg/mL), indicating secondary hyperparathyroidism, a key contributor to renal osteodystrophy.[22] Alkaline phosphatase (ALP) was raised (142.6 ± 66.8 U/L), supporting high bone turnover, often due to elevated PTH.

Age greater than 45 years was found to be significantly associated with higher fracture risk(60.9%) with an (*AOR = 0.351*, 95% CI: 0.137-0.900, p = 0.029) whereas those under 45 had a lower risk (37.0%), the general trend in literature supports that increasing age is typically a risk factor due to decreased bone remodeling efficiency, cumulative comorbidities, reduced physical activity, increased fall risk, and hormonal changes (e.g., menopause in women) may contribute to a higher incidence of fractures in older adults.[23]

There was a significant negative correlation between age and Radius-Ulna BMD (r = -0.233, p = 0.020) and a borderline association with femoral neck BMD (p = 0.050). This aligns with previous study showing that increasing age is associated with reduced bone mass, particularly cortical bone, which is predominantly present in the forearm.[24]

Among the laboratory variables assessed, iPTH and alkaline phosphatase (ALP) were significantly associated with higher fracture risk, with p-values of 0.006 and 0.035, respectively. Elevated iPTH levels were predominantly observed in the high fracture risk group, suggesting that secondary hyperparathyroidism contributes significantly to bone demineralization in CKD patients. This is consistent with existing literature that highlights the role of iPTH in promoting bone resorption, leading to increased fracture susceptibility in CKD-related mineral and bone disorder (CKD-MBD).[22]

Moreover, a significant inverse correlation was observed between total BMD and iPTH levels (r = -0.19, p = 0.062), as depicted in the scatter plot. Although the correlation did not reach conventional statistical significance, the negative trend supports the hypothesis that higher iPTH levels may be linked to lower BMD values. This aligns with findings by Nickolas et al. (2008), who demonstrated that elevated PTH levels in CKD patients were associated with lower trabecular and cortical bone density and increased fracture rates.[22]

Serum Albumin was positively correlated with Radius-Ulna BMD (r = 0.271, p = 0.006), suggesting better nutritional status may contribute to improved cortical bone integrity. Hypoalbuminemia is a known marker of protein-energy wasting in CKD, which can adversely affect bone health.[25] Vitamin D had a positive but weak correlation with femoral neck BMD (r = 0.200, p = 0.046). Despite vitamin D's well-established role in calcium homeostasis and bone mineralization, its effects may be blunted in CKD due to altered metabolism and receptor sensitivity.[26] The Radius-Ulna T-score showed a very strong correlation with Radius-Ulna BMD (r = 0.823, p < 0.001), and Lumbar Spine T-score strongly correlated with both Lumbar Spine BMD (r = 0.930, p < 0.001) and Femoral Neck BMD (r = 0.552, p <0.001). This is expected as T- and Z-scores are derived from BMD values, but also underscores internal consistency and measurement reliability.

LIMITATIONS

This study has several limitations that should be acknowledged. Firstly, its cross-sectional design precludes the establishment of definitive cause-and-effect relationships between the variables studied. Secondly, as the research was conducted at a single clinical center, the findings may

not be fully generalizable to broader populations or different geographic regions. Thirdly, the relatively small sample size of 100 patients may limit the statistical power needed to detect more nuanced associations between variables. Fourthly, the exclusive reliance on Dual-Energy X-ray Absorptiometry (DEXA) for the diagnosis of osteoporosis may not capture the complete picture of bone health, especially in younger patients or those with other contributing conditions. Future longitudinal, multi-center studies with larger cohorts are warranted to validate these findings and to better understand the dynamic relationships between Bone Mineral Density (BMD) and various clinical and biochemical parameters.

Nevertheless, despite these limitations, the study provides valuable insights into BMD and its associations with biochemical markers in patients undergoing hemodialysis. The strength of this study lies in its meticulous data collection, robust statistical analysis, and comprehensive evaluation of potential confounders all of which contribute meaningfully to the current body of knowledge in this field.

CONCLUSION

On conclusion, our findings reinforce the role of elevated iPTH and ALP levels as key indicators of increased fracture risk in CKD patients, emphasizing the importance of regular monitoring and management of CKD-MBD parameters. Further large-scale prospective studies are warranted to validate these findings and to develop targeted interventions to reduce skeletal complications in CKD. These findings highlight the need for proactive strategies in the management of bone health among hemodialysis patients. This study lays the groundwork for further research aimed at enhancing fracture prevention and improving the quality of life in this vulnerable population.

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Author's Contribution: KM contributed to study conception, study design, data collection, data analysis and interpretation, and manuscript preparation. **PT and GK** contributed to study conception and study design. **SM** contributed to the study conception. **AB** contributed to data analysis and interpretation.

Availability of Data: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of Non-use of generative AI Tools: I hereby confirm that this work has been completed without the use of any Artificial intelligence (AI) tools. The ideas, analysis and writing are entirely my own and any sources consulted have been properly cited.

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