Al-Rafidain J Med Sci. 2026;11(1):129-133.
DOI: https://doi.org/10.54133/ajms.v11i1.3046

AJMS

Online ISSN (3219-2789)

Research Article

Integrated Assessment of Bone Health in Adults with Epilepsy Receiving Antiseizure Medications in Basrah, Iraq

Mustafa Abd Al Majeed[1], Ahmed Abduljawad Salim[2], Omar Mohammed Alsalman[1]*
[1]*Department of Physiology, College of Medicine, University of Basrah, Basrah, Iraq;* [2]*Department of Medicine, College of Medicine, University of Basrah, Basrah, Iraq*

Received: 28 April 2026; Revised: 21 June 2026; Accepted: 26 June 2026

Abstract

Background: Antiseizure medications (ASMs) are associated with skeletal complications, yet most studies rely on dual-energy X-ray absorptiometry (DEXA) alone. Combining DEXA with bone turnover markers (BTMs) and the mineral axis may improve identification of adults at risk for bone loss. ***Objective***: To evaluate the diagnostic value of integrating DEXA with serum biomarkers in adults with epilepsy on chronic ASM therapy in Basrah. ***Methods***: A cross-sectional comparative study enrolled 45 adults with epilepsy on ASMs for 12 months or longer and 45 age- and sex-matched healthy controls. Fasting morning blood samples were analyzed for the full biomarker panel. BMD was measured at the lumbar spine (L1–L4) and proximal femur by DEXA. An exploratory uncoupling index and turnover phenotypes were derived. ***Results***: CTX-I and DPD were significantly higher in cases (p<0.001 and p=0.045). Calcitonin was elevated in cases (p<0.001) and positively correlated with ALP among cases only (rho=0.304, p=0.043). Mineral-axis markers did not differ between groups. The resorption-dominant phenotype was significantly more prevalent among cases (55.6% *vs*. 11.1%, p<0.001) and was associated with lower femur T-scores (p=0.007) and higher low-BMD prevalence (p=0.002). ***Conclusions***: Integrating DEXA with CTX-I, DPD, and calcitonin reveals a high-resorption phenotype in ASM-treated adults that DEXA or mineral-axis testing alone would miss. This combined approach improves early identification of skeletal risk in epilepsy care.

Keywords: Antiseizure medications; Bone mineral density; Bone turnover markers; Calcitonin; DEXA; Epilepsy.

تقييم متكامل لصحة العظام لدى البالغين المصابين بالصرع الذين يتلقون أدوية مضادة للنوبات في البصرة، العراق

الخلاصة

الخلفية: ترتبط أدوية مضادات النوبات (ASMs) بمضاعفات هيكلية، ومع ذلك تعتمد معظم الدراسات على امتصاص الأشعة السينية ذات الطاقة المزدوجة (DEXA) فقط. قد يحسن دمج DEXA مع علامات تغير العظام (BTMs) ومحور المعادن من تحديد البالغين المعرضين لخطر فقدان العظام. **الهدف**: تقييم القيمة التشخيصية لدمج DEXA مع مؤشرات المصل لدى البالغين المصابين بالصرع في علاج ASM المزمن في البصرة. **الطرائق**: شملت دراسة مقارنة مقطعية 45 بالغا مصابا بالصرع على ASMs لمدة 12 شهرا أو أكثر، و45 من الضباط الأصحاء المطابقين للعمر والجنس. تم تحليل عينات دم الصيام الصباحية لفحص المؤشر الحيوي الكامل. تم قياس BMD عند العمود الفقري القطني (L1–L4) وعظم الفخذ القريب بواسطة DEXA. تم اشتقاق مؤشر فك استكشافي وأنماط دوران الدوران. ***النتائج***: كانت CTX-I وDPD أعلى بشكل ملحوظ في الحالات (p<0.001 و p=0.045). ارتفع الكالسيتونين في الحالات (p<0.001) ومرتبط إيجابيا مع ALP بين الحالات فقط (p=0.043، rho=0.304). لم تختلف علامات المحور المعدني بين المجموعات. كان النمط الظاهري المهيمن للامتزاز أكثر انتشارا بشكل ملحوظ بين الحالات (55.6٪ مقابل 11.1٪، ص<0.001) وكان مرتبطا بدرجات T منخفضة في عظم الفخذ (p=0.007) وانتشار أعلى BMD منخفض (p=0.002). **الاستنتاجات**: دمج DEXA مع CTX-I وDPD والكالسيتونين يكشف عن نمط ظاهري عالي الامتصاص لدى البالغين المعالجين بASM، وهو ما قد يفوته اختبار DEXA أو اختبار المحور المعدني وحده. هذا النهج المشترك يحسن التعرف المبكر على مخاطر الهيكل العظمي في رعاية الصرع.

* ***Corresponding author***: Omar M. Alsalman, Department of Physiology, College of Medicine, University of Basrah, Basrah, Iraq; Email: omer.mohammed@uobasrah.edu.iq

Article citation: Abd Al Majeed M, Salim AA, Alsalman OM. Integrated Assessment of Bone Health in Adults with Epilepsy Receiving Antiseizure Medications in Basrah, Iraq. *Al-Rafidain J Med Sci.* 2026;11(1):129-133. doi: https://doi.org/10.54133/ajms.v11i1.3046

INTRODUCTION

Epilepsy is one of the most prevalent chronic neurological disorders worldwide, affecting over 50 million individuals according to the World Health Organization [1]. Adults who require long-term antiseizure medication (ASM) therapy face a well-documented risk of skeletal complications, including decreased bone mineral density (BMD) and elevated fracture rates [2,3]. While conventional practice relies on dual-energy X-ray absorptiometry (DEXA) for skeletal assessment, DEXA quantifies areal mineralized mass but is agnostic to ongoing remodeling activity and cannot distinguish osteoporosis from osteomalacia [4]. Bone turnover markers (BTMs) offer a dynamic, real-time complement to the static snapshot provided by DEXA. Serum beta C-terminal telopeptide of type I collagen (beta-CTX-I) is an internationally endorsed reference resorption marker [5], while deoxypyridinoline (DPD) is a mature collagen cross-link released during osteoclastic activity [6]. When both markers are concordantly elevated alongside low 25-hydroxyvitamin D and high parathyroid hormone (PTH), a coherent picture of high-turnover bone loss emerges that predicts fracture risk more accurately than

T-scores alone [5,7]. Calcitonin, secreted by thyroid C-cells, acutely inhibits osteoclastic resorption, yet its role in epilepsy-associated bone disease remains underexplored [8]. Most epilepsy-bone studies omit calcitonin entirely, leaving an important gap in our understanding of the endocrine response to ASM-driven bone resorption. The mineral axis—calcium, phosphate, 25-hydroxyvitamin D, and PTH—provides the physiologic context required to interpret both DEXA and BTM findings. Enzyme-inducing ASMs accelerate hepatic vitamin D catabolism, lowering 25-hydroxyvitamin D, raising PTH, and shifting remodeling toward net resorption [9,10]. However, in regions with high background hypovitaminosis D, the discriminatory value of the mineral axis may be attenuated [11,12]. Data combining DEXA with a comprehensive BTM and mineral-axis panel—including calcitonin—in adults with epilepsy from the Middle East is scarce. The present study therefore aimed to evaluate the diagnostic value of integrating DEXA, serum CTX-I, DPD, calcitonin, and the mineral axis in adults with epilepsy receiving chronic ASM therapy in Basrah, southern Iraq.

METHODS

Study design and setting

This cross-sectional comparative study was conducted at a neurology outpatient setting from November 2024 to October 2025, in accordance with the STROBE guidelines [13]. The study received ethical approval from the institutional ethics committee. Written informed consent was obtained from all participants.

Participants

Sample size was estimated using Steven Thompson's formula for finite populations (n= 84 accessible patients, Z= 1.96, *p*= 0.50, d= 0.10), yielding a minimum of 45 subjects per group. The study enrolled 45 adults with epilepsy (aged 18–70 years, both sexes) on continuous ASM therapy for at least 12 months and 45 apparently healthy age- and sex-matched controls.

Exclusion criteria

Including chronic kidney or liver disease, endocrine disorders affecting bone, pregnancy or lactation, recent fracture or immobilization within six months, and current use of bone-active medications (corticosteroids, bisphosphonates, hormonal replacement, or vitamin D/calcium supplements).

Biochemical assessment

Fasting venous blood (5 mL) was collected between 08:00 and 10:00 hours for all participants to minimize diurnal variation in CTX-I [14]. After clotting and centrifugation (3500 rpm, 15 min), serum was aliquoted and stored at −20 to −30°C until analysis. Serum calcium (CPC method), phosphate (UV method), alkaline phosphatase (ALP, colorimetric), and creatinine (Jaffe reaction) were measured on automated biochemical analyzers. Serum 25-hydroxyvitamin D and PTH were measured by ELISA, as were the bone turnover markers: CTX-I (sandwich ELISA), DPD (competitive ELISA), and calcitonin (competitive inhibition ELISA). All assays followed manufacturer protocols; duplicate readings were averaged, internal quality-control sera were included per batch, and instruments were calibrated periodically.

DEXA scanning

BMD was measured at the lumbar spine (L1–L4) and proximal femur (femoral neck and total hip) using a GE Lunar Prodigy DEXA system (GE Healthcare, USA). Positioning followed international standards [15]. The scanner underwent weekly phantom calibration and daily system checks. T-scores and Z-scores were generated by the integrated reference database. Low BMD was defined as osteopenia or osteoporosis at any measured site (lowest T-score < −1.0). Vitamin D categories were deficient (<20 ng/mL), insufficient (20 to <30 ng/mL), and sufficient (≥30 ng/mL).

Derived variables

An exploratory uncoupling index was calculated as the mean of z(CTX-I) and z(DPD) minus z(ALP), where z denotes standardization across the full sample. Participants were categorized into formation-dominant, coupled, and resorption-dominant phenotypes using tertiles. This exploratory index has not yet been externally validated. A concordant-high turnover phenotype was defined as both CTX-I and DPD at or above the 75th percentile of the control distribution.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki (2013). Written informed consent was obtained from all participants prior to enrollment. Ethical approval was granted by the institutional review board.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 25. Continuous variables were compared with the independent-samples t-test or Welch t-test (normal distribution) and the Mann-Whitney U test (non-normal). Chi-square and Fisher exact tests were used for categorical variables. Spearman rank correlation assessed monotonic associations. Multivariable linear regression (with HC3 robust standard errors) examined independent predictors of T-scores. Log-transformed ALP was used where ALP was the outcome, with results back-transformed as percent change. All tests were two-sided; p≤0.05 was considered significant.

RESULTS

Ninety adults were enrolled (45 cases, 45 controls). Cases and controls were comparable in age (42.16 ± 14.50 *vs*. 45.76 ± 14.77 years, p= 0.246) and sex distribution (55.6% *vs*. 53.3% male, p=0.832). BMI was higher among cases (median 25.61 *vs*. 23.45 kg/m², p= 0.001). Renal function was comparable between groups (creatinine p= 0.840; eGFR p= 0.527), ensuring that between-group BTM differences were not confounded by differential renal clearance. Low BMD was identified in 28 of 45 cases (62.2%) compared with 4 of 45 controls (8.9%; chi-square p< 0.001; OR= 16.88, 95%CI: 5.13 to 55.52). The femur T-score was significantly lower in cases (mean −1.61 ± 1.34 *vs*. −0.33 ± 0.69, p< 0.001), while the spine T-score did not differ significantly (−0.34 ± 1.07 *vs*. −0.23 ± 0.77, p= 0.346). Spine-femur T-score discordance (absolute difference ≥ 1.0 SD) was present in 60.0% of cases and 0% of controls (p< 0.001); in all discordant cases, the femur was the lower site. Serum CTX-I was markedly higher in cases (0.677 ± 0.133 *vs*. 0.368 ± 0.140, p< 0.001), as was DPD (0.345 ± 0.067 *vs*. 0.310 ± 0.096, p= 0.045). Calcitonin was significantly elevated in cases compared with controls (0.912 ± 0.082 *vs*. 0.730 ± 0.169, p< 0.001). ALP did not differ between groups (cases 97.88 ± 81.14 *vs*. controls 100.42 ± 30.86 U/L, p= 0.142) (Table 1).

Table 1: Bone turnover markers and alkaline phosphatase by study group

Marker	Cases	Controls	*p*-value*
CTX-I (ng/mL)	0.677±0.133	0.368±0.14	<0.001
DPD (nmol/mmol Cr)	0.345±0.067	0.310±0.096	0.045
Calcitonin (pg/mL)	0.912±0.082	0.730±0.169	<0.001
ALP (U/L)	97.88±81.14	100.42±30.86	0.142

Values are presented as mean±SD. ALP: alkaline phosphatase; CTX-I: C-terminal telopeptide of type I collagen; DPD: deoxypyridinoline. *Welch t-test or Mann-Whitney U test as indicated.

No mineral-axis marker showed a statistically significant between-group difference (Table 2). Median 25-hydroxyvitamin D values were comparable between groups and fell within the insufficient range (Table 2). Within cases, vitamin D and PTH showed a significant inverse correlation (rho= −0.326, p= 0.029), consistent with a tendency toward secondary hyperparathyroidism when vitamin D is low. The turnover uncoupling analysis (Table 3) demonstrated that over half of cases (55.6%) fell into the resorption-dominant category, compared with only 11.1% of controls (p< 0.001).

Table 2: Mineral axis markers by study group

Marker	Cases	Controls	*p*-value*
Calcium (mg/dL)	9.12±1.08	9.29±0.93	0.184
Phosphate (mg/dL)	3.64±0.74	3.49±0.72	0.329
25-Hydroxyvitamin D (ng/mL)	26.57±18.23	24.34±13.75	0.888
PTH (pg/mL)	50.21±28.16	47.33±23.62	0.66

Values are presented as mean±SD. PTH: parathyroid hormone; 25-hydroxyvitamin D assessed by ELISA. *Mann-Whitney U test.

This phenotype was associated with the lowest median femur T-score (−1.10) and the highest prevalence of low BMD (56.7%). In contrast, the formation-dominant phenotype—where 57.8% of controls clustered—had the highest median T-score (−0.50) and the lowest low-BMD prevalence (13.3%).

Table 3: Turnover uncoupling phenotype by study group and association with low BMD

Turnover Phenotype	Cases	Controls	Median T-score (femur)	Low BMD
Formation-dominant	4(8.9)	26(57.8)	−0.50	4(13.3)
Coupled	16(35.6)	14(31.1)	−0.65	11(36.7)
Resorption-dominant	25(55.6)	5(11.1)	−1.10	17(56.7)

Values are presented as frequency and percentage. Phenotype classification based on uncoupling index tertiles: mean(z(CTX-I), z(DPD)) − z(ALP). Chi-square p< 0.001 for phenotype distribution by group. Kruskal-Wallis p= 0.007 for femur T-score across phenotypes. Chi-square p= 0.002 for low BMD across phenotypes. BMD: bone mineral density.

Among cases, calcitonin was positively correlated with ALP (rho= 0.304, p= 0.043), while no such relationship was observed in controls (Table 4). An adjusted interaction model estimated a 34.9% increase in ALP per 0.1-unit increase in calcitonin within cases (95% CI: 1.0 to 80.1, p= 0.043), compared with only 2.3% in controls (p= 0.545), with borderline evidence of effect modification by study group (interaction p= 0.067). In multivariable linear regression adjusted for vitamin D, PTH, calcium, phosphate, age, sex, and BMI, none of the mineral-axis markers independently predicted femur or spine T-scores within either group. However, when case status was entered into a combined-sample model with these covariates, it remained independently associated with a lower femur T-score (adjusted beta=−1.315, 95% CI: −1.795 to −0.834, p< 0.001) but not spine T-score (beta= −0.119, p= 0.586).

Table 4: Calcitonin associations with alkaline phosphatase, turnover markers, and DEXA T-scores

Outcome/Effect	Cases	Controls	*p-value* for interaction
Calcitonin vs ALP	ρ= 0.304, p= 0.043	ρ= 0.066, p= 0.667	—
Calcitonin vs CTX-I	ρ= −0.191, p= 0.210	ρ= 0.166, p= 0.277	—
Calcitonin vs DPD	ρ= 0.057, p=0.709	ρ= 0.059, p= 0.702	—
Calcitonin vs Femur T-score	ρ= 0.099, p= 0.519	ρ=− 0.048, p= 0.754	—
Calcitonin vs Spine T-score	ρ= 0.128, p= 0.401	ρ= −0.148, p=0.331	—
Adjusted effect on ALP (per +0.1 calcitonin)	34.9% (95%CI: 1.0–80.1), p= 0.043	2.3% (95%CI: −4.9 to 10.0), p=0.545	0.067

Spearman rank correlations are reported for all pairwise associations. Adjusted effect on ALP estimated from multivariable model with HC3 robust standard errors; back-transformed as percent change per 0.1-unit calcitonin increment. Interaction p-value is for the calcitonin × group interaction term from the combined-sample model.

DISCUSSION

The central finding of this study is that integrating DEXA with bone turnover markers and calcitonin reveals a high-resorption phenotype in ASM-treated adults that neither DEXA nor mineral-axis testing alone would identify. While femur T-scores were significantly lower in cases and low BMD was far more prevalent (62.2% *vs*. 8.9%), the classical mineral-axis markers—calcium, phosphate, vitamin D, and PTH—were essentially indistinguishable between groups. This dissociation has practical implications: relying on mineral-axis screening alone would miss the skeletal risk flagged by elevated CTX-I and DPD. The elevation of CTX-I and DPD in cases is consistent with accelerated bone resorption reported in previous epilepsy cohorts [2,16,17]. Yu *et al*. (2025) similarly found higher beta-CTX and P1NP in adults with epilepsy compared with controls, with turnover markers detecting early skeletal effects before large BMD differences developed [18]. Our results complement this by showing that the resorption signal extends to DPD as well and that biochemical remodeling imbalance—quantified through the uncoupling index—tracks with both lower femur T-scores and higher low-BMD prevalence. An uncommon feature of the present study is the inclusion of serum calcitonin. Calcitonin was significantly higher among cases despite comparable serum calcium, suggesting that the elevation is not simply a response to hypercalcemia. Instead, it may represent a compensatory antiresorptive signal triggered by increased osteoclastic activity. The positive calcitonin-ALP association found only in cases adds further nuance: ALP, while not bone-specific, is frequently elevated in ASM-associated bone disease [19,20]. Future studies should incorporate bone-specific ALP and P1NP to refine the interpretation of this calcitonin-formation marker relationship. The absence of mineral-axis differences between groups deserves comment. A 2024 systematic review reported that vitamin D deficiency is highly prevalent in people with epilepsy but that the mean of levels is only modestly lower than in controls, with wide variability [21]. Regional data show widespread hypovitaminosis D driven by sun avoidance, cultural clothing, urbanization, and diet [11]. In our data, both groups had mean 25-hydroxyvitamin D values within the insufficient range (Table 2), confirming that background deficiency limits the discriminatory value of the mineral axis when patients and controls share the same deficient milieu. This observation strengthens the rationale for adding BTMs to any screening protocol; they provide the dynamic signal that static mineral-axis snapshots cannot. The adjusted regression findings reinforce that case status predicts lower femur T-scores independently of the mineral axis and standard demographics. This aligns with recent reviews concluding that ASM-associated skeletal vulnerability is multifactorial—encompassing direct osteoblast/osteoclast effects, altered sex-steroid metabolism, and seizure-related trauma—rather than exclusively mineral-axis-mediated [22,23].

Study Limitations

Several limitations should be noted. The cross-sectional design precludes causal inference; prospective studies are needed to determine whether baseline BTM elevation predicts subsequent BMD decline. The sample size limited power for drug-specific subgroup analyses. CTX-I exhibits diurnal and feeding-related variation [14]; despite standardized fasting morning sampling, residual pre-analytical variability may attenuate correlations. Total ALP, rather than bone-specific ALP, and CTX-I/DPD, rather than P1NP, were used in the present study due to limited availability of reagents at the study site; future work incorporating these markers—together with formal cost-effectiveness analysis—will support clinical implementation of the integrated approach proposed here.

Conclusion

Combining DEXA with serum CTX-I, DPD, and calcitonin uncovers a resorption-dominant phenotype in ASM-treated adults that mineral-axis testing alone would overlook. In settings where background vitamin D deficiency limits the discriminatory value of the mineral axis, bone turnover markers provide the dynamic biochemical signal needed for early identification of skeletal risk. We recommend that adult epilepsy services incorporate BTMs alongside DEXA and mineral-axis screening, particularly for patients with prolonged ASM exposure, polytherapy, or additional fracture risk factors.

Conflict of interests

The authors declared no conflict of interest.

Funding source

The authors did not receive any source of funds.

Data sharing statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

REFERENCES

1. World Health Organization. Epilepsy (fact sheet). 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/epilepsy
2. Buoso C, Pezzaioli LC, Gatta E, Bambini F, Silvestrini I, Delbarba A, et al. Antiepileptic drugs and bone health: a comprehensive review and meta-analysis. *Acta Endocrinol (Bucharest)*. 2024;20(3):356-372. doi: 10.4183/aeb.2024.356.
3. Jetté N, Lix LM, Metge CJ, Prior HJ, McChesney J, Leslie WD. Association of antiepileptic drugs with nontraumatic fractures: a population-based analysis. *Arch Neurol*. 2011;68(1):107-112. doi: 10.1001/archneurol.2010.308.
4. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. The clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2022;33(10):2049-2102. doi: 10.1007/s00198-021-05900-y.

5. Vasikaran S, Eastell R, Bruyère O, Foldes AJ, Garnero P, Griesmacher A, et al. Markers of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment. *Osteoporos Int*. 2011;22(2):391-420. doi: 10.1007/s00198-010-1501-1.
6. Schini M, Eastell R, Walsh JS. Bone turnover markers: basic biology to clinical applications. *Endocr Rev*. 2023;44(3):417-473. doi: 10.1210/endrev/bnac031.
7. Shevroja E, Reginster JY, Lamy O, Al-Daghri N, Chandran M, Demoux-Baiada AL, et al. Update on the clinical use of trabecular bone score (TBS). *Osteoporos Int*. 2023;34(9):1607-1618. doi: 10.1007/s00198-023-06817-4.
8. Xie J, Guo J, Kanwal Z, Wu M, Lv X, Ibrahim NA, et al. Calcitonin and bone physiology. *Int J Endocrinol*. 2020;2020:3236828. doi: 10.1155/2020/3236828.
9. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with use of antiepileptic drugs. *Epilepsia*. 2004;45(11):1330-1337. doi: 10.1111/j.0013-9580.2004.18804.x.
10. Siniscalchi A, Gallelli L, Russo E, De Sarro G. Antiepileptic drugs and bone health: current concepts. *Psychopharmacol Bull*. 2020;50(2):36-44. doi: 10.64719/pb.4609.
11. Chakhtoura M, Rahme M, Chamoun N, El-Hajj Fuleihan G. Vitamin D in the Middle East and North Africa. *Bone Rep*. 2018;8:135-146. doi: 10.1016/j.bonr.2018.03.004.
12. Alhaidari HM, Babtain F, Alqadi K, Bouges A, Baeesa S, Al-Said YA. Association between serum vitamin D levels and age in patients with epilepsy: A retrospective study from an epilepsy center in Saudi Arabia. *Ann Saudi Med*. 2022;42(4):262-268. doi: 10.5144/0256-4947.2022.262.
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The STROBE statement. *PLoS Med*. 2007;4(10):e296. doi: 10.1371/journal.pmed.0040296.
14. Qvist P, Christgau S, Pedersen BJ, Schlemmer A, Christiansen C. Circadian variation in serum CTX. *Bone*. 2002;31(1):57-61. doi: 10.1016/s8756-3282(02)00791-3.
15. International Society for Clinical Densitometry. 2023 ISCD Official Positions – Adult. Available from: https://iscd.org/
16. Verrotti A, Coppola G, Parisi P, Mohn A, Chiarelli F. Bone and calcium metabolism and antiepileptic drugs. *Clin Neurol Neurosurg*. 2010;112(1):1-10. doi: 10.1016/j.clineuro.2009.10.011.
17. Pack AM, Morrell MJ, Marcus R, Holloway L, Flaster E, Doñe S, et al. Bone mass and turnover in women with epilepsy on antiepileptic drug monotherapy. *Ann Neurol*. 2005;57(2):252-257. doi: 10.1002/ana.20378.
18. Yu M, Zhang N, Chen C, He Y, Meng J, Luo W, et al. Effects of perampanel on bone health in adult patients with epilepsy. *Epilepsia Open*. 2025;10(3):822-830. doi: 10.1002/epi4.70038.
19. Baddoo DR, Mills AA, Kullab RB, Al-Mashat H, Andersen NB, Jørgensen NR, Diemar SS. Metabolic bone disease in patients with epilepsy and the use of antiepileptic drugs - Insight from a Danish cross-sectional study. *Seizure*. 2021;86:29-34. doi: 10.1016/j.seizure.2021.01.008.
20. Taha MA, Istifo NNH. Evaluation of osteoporosis among epileptic patients on monotherapy. *Iraqi J Pharm Sci*. 2024. doi: 10.31351/vol33iss1pp129-136.
21. Gaete PV, Cuellar-Rodriguez V, Mendivil CO. Antiepileptic drugs and bone health. *Neurol Ther*. 2025;14(5):1827-1844. doi: 10.1007/s40120-025-00805-y.
22. Liu Y, Gong C, Li J, Ning X, Zeng P, Wang L, et al. Vitamin D content and prevalence of vitamin D deficiency in patients with epilepsy: a systematic review and meta-analysis. *Front Nutr*. 2024;11:1439279. doi: 10.3389/fnut.2024.1439279.
23. Perucca E, Brodie MJ, Kwan P, Tomson T. 30 years of second-generation antiepileptic drugs. *Lancet Neurol*. 2020;19(6):544-556. doi: 10.1016/S1474-4422(20)30035-1.