Section: Biochemistry

Original Research Article

CORRELATION BETWEEN SERUM ESTRADIOL AND BONE TURNOVER MARKERS IN PREMENOPAUSAL AND POSTMENOPAUSAL WOMEN: PREDICTIVE INSIGHTS FOR EARLY OSTEOPOROSIS DETECTION

Jyoti Sitaram Dubhalakar[1], Mayuri Madhukarrao Palmate[2], Panjab Vithal Shelke[3], Reshakiran Janardhan Shendye[4]

[1]Assistant Professor, Department of Biochemistry, Government Medical College, Hingoli, India.
[2]Assistant Professor, Department of biochemistry, MIMSR medical College Latur, Maharashtra, India
[3]Assistant Professor, Department of Medicine, Government Medical College, Hingoli, India.
[4]Professor, Government Medical College, Sambhaji Nagar. India.

Received : 05/07/2025
Received in revised form : 21/08/2025
Accepted : 11/09/2025

Keywords:
Estradiol, Bone turnover markers, Osteoporosis, Postmenopausal women, Obesity.

Corresponding Author:
Dr. Jyoti Sitaram Dubhalakar,
Email: jyotidubhalkar@gmail.com

DOI: 10.47009/jamp.2025.7.5.65

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (5); 326-329

ABSTRACT

Background: Osteoporosis is a major public health concern, particularly among postmenopausal women due to the decline in estrogen levels. Estradiol plays a central role in bone homeostasis, and its reduction is closely linked to increased bone turnover and decreased bone mineral density (BMD). Biochemical bone turnover markers (BTMs) respond more rapidly to metabolic changes than BMD and may offer early diagnostic potential. This study aimed to evaluate the correlation between serum estradiol and BTMs in lean and obese premenopausal and postmenopausal women to assess their predictive value in early osteoporosis risk. **Materials and Methods:** A cross-sectional, two-arm comparative study was conducted over 18 months at a tertiary care center, involving 100 women equally divided into premenopausal and postmenopausal groups. Each group was further stratified into lean (BMI 18.5–22.99 kg/m²) and obese (BMI >25 kg/m²) subgroups. Serum estradiol, ionized calcium, alkaline phosphatase (ALP), phosphorus, and albumin were measured using chemiluminescent immunoassay and standard biochemical methods. Correlations between estradiol and BTMs were analyzed using Pearson's correlation coefficient. **Result:** Serum estradiol levels were significantly higher in obese women across both groups. An inverse correlation was observed between estradiol and ALP, calcium, and phosphorus, which was more pronounced in postmenopausal women (e.g., estradiol and calcium: r = –0.533, p = 0.015). The correlation was also significant in lean premenopausal women (e.g., estradiol and calcium: r = –0.475, p = 0.032), indicating early hormonal influence on bone turnover. **Conclusion:** Estradiol levels are inversely correlated with bone turnover markers in both premenopausal and postmenopausal women, more strongly in the latter. Combined measurement of estradiol and BTMs may aid in the early detection and prevention of osteoporosis, particularly in high-risk groups.

INTRODUCTION

Osteoporosis is a progressive systemic skeletal disorder characterized by reduced bone mass and deterioration of bone microarchitecture, leading to increased bone fragility and fracture risk. It is widely prevalent in postmenopausal women due to estrogen deficiency, but also occurs in premenopausal women with contributing risk factors like low body mass index (BMI), lifestyle, and hormonal imbalances.[1] Estradiol, the principal estrogen in premenopausal women, plays a pivotal role in maintaining bone health by balancing bone formation and resorption. It promotes osteoblast survival while inhibiting osteoclast activity. A decline in estradiol levels after menopause disrupts this balance, accelerating bone turnover and enhancing resorption over formation.[2] This hormonal change correlates strongly with increased levels of bone turnover markers (BTMs) such as osteocalcin, alkaline phosphatase (ALP), and C-terminal telopeptide of type I collagen (CTX).[3] Several studies have highlighted that even modest reductions in estradiol can significantly influence BTMs and bone mineral density (BMD). Sypniewska

ISSN (O): 2687-5365; ISSN (P): 2753-6556

et al. found that women with estradiol levels <9 pg/ml exhibited significantly elevated bone resorption markers and reduced BMD, suggesting an early high-turnover state.[4] Another study by Gurban et al. showed a negative correlation between BTMs (like TRAP 5b and NTX) and lumbar spine BMD, with estradiol positively correlating with bone density.[5] Jamka et al. also demonstrated that estradiol level ≥25 pg/ml is associated with balanced bone formation and resorption processes. Interestingly, their data revealed that in women with normal estradiol, osteocalcin and CTX maintained a mutual positive correlation, reflecting homeostasis in bone turnover.[6]

Despite these advances, early prediction of osteoporosis before overt BMD loss remains a clinical challenge. BTMs, due to their dynamic nature, respond more quickly to metabolic changes than BMD, and may offer an early window for intervention.[7] Pardhe et al. emphasized that ALP and calcium levels correlate significantly with estradiol and age, and could serve as inexpensive tools in population screening.[8]

In the Indian context, early menopause, low dietary calcium, vitamin D deficiency, and low BMI contribute further to accelerated bone loss, even in the premenopausal phase. Therefore, understanding the correlation between serum estradiol and BTMs across menopausal transition and BMI categories can aid in early prediction of osteoporosis risk before radiologic changes occur.[9]

While several studies have independently evaluated hormone levels or bone markers, few have explored their correlation in stratified pre- and postmenopausal cohorts across BMI classifications. This study bridges that gap by investigating the relationship between serum estradiol and multiple BTMs (osteocalcin, ALP, CTX) and determining their predictive utility for osteoporosis across menopausal status and body habitus.

Such findings could enhance early diagnostic strategies, enable timely preventive care, and reduce the long-term burden of osteoporotic fractures, particularly in low-resource settings where DEXA scanning is not routinely accessible.

MATERIALS AND METHODS

This cross-sectional, observational, two-arm comparative study was conducted in the Department of Biochemistry at a Government Medical College (tertiary care center) between February 2019 and September 2020. The study aimed to evaluate the correlation between serum estradiol and bone turnover markers (BTMs) in lean and obese women, stratified by menopausal status, and assess their potential in predicting early osteoporosis. A total of 100 women were recruited from the gynecology outpatient department and among hospital health workers. Based on menopausal history, participants were divided into two equal groups: Group A (premenopausal, n = 50) and Group B (postmenopausal, n = 50). Each group was further stratified into lean (BMI 18.5–22.99 kg/m²) and obese (BMI >25 kg/m²) subgroups according to WHO guidelines.

The sample size was determined using the formula: $n = Z^2pq/d^2$, where Z = 1.96 at 95% confidence, p = 13.3% (prevalence of osteoporosis in Indian women as reported by Kadam et al.[10]), q = 1–p, and d = 7% precision. The calculated sample size was 90.4, rounded to 100 to accommodate for potential dropout and ensure adequate power for subgroup analysis. Participants were selected by non-probability convenient sampling. Inclusion criteria included women aged 35–65 years, with premenopausal women having regular cycles and postmenopausal women having at least 2 years since their last menstrual period. Exclusion criteria included history of osteoporosis, pregnancy, diabetes mellitus, chronic renal failure, hormone replacement therapy, or gynecological surgeries such as hysterectomy or myomectomy.

Anthropometric measurements including height, weight, BMI, waist and hip circumference, and waist-hip ratio (WHR) were recorded following standard protocols. Following informed consent, 5 mL fasting venous blood was collected under aseptic conditions. Serum was separated and analyzed for estradiol, ionized calcium, alkaline phosphatase (ALP), phosphorus, and albumin. Estradiol was measured using a chemiluminescent immunoassay (Access Sensitive Estradiol Assay, Beckman Coulter). Other parameters were estimated using standard biochemical methods in the central clinical laboratory. Correlation between estradiol and BTMs was assessed using Pearson's correlation coefficient (r) and statistical significance set at $p < 0.05$. Data were analyzed using MS office Excel 2021.

RESULTS

This study evaluated the correlation between serum estradiol and bone turnover markers (BTMs) in 100 women, equally divided into premenopausal (n = 50) and postmenopausal (n = 50) groups, with further stratification into lean and obese subgroups.

Table 1: Demographic Characteristics of Study Participants by Menopausal Status

Variable	Premenopausal (n = 50)	Postmenopausal (n = 50)	p-value
Age (years)	41.50 ± 3.15	58.90 ± 4.16	0.00001
Marital Status			
- Married	47 (94%)	49 (98%)	0.061
- Unmarried	3 (6%)	1 (2%)	
Diet Type			
- Vegetarian	21 (42%)	31 (62%)	0.0563

ISSN (O): 2687-5365; ISSN (P): 2753-6556

- Mixed	29 (58%)	19 (38%)	

As shown in [Table 1], the distribution of participants across age groups revealed that the 35–45 years category had the highest frequency (44%), comprising exclusively premenopausal women. The 55–65 years group accounted for 34%, largely representing postmenopausal women. The mean age of the total study population was 50.20 ± 9.48 years. The transitional age group of 45–55 years included both menopausal categories, while a small number (3%) were above 65 years.

Table 2: Correlation Between Serum Estradiol and Bone Turnover Markers in Premenopausal and Postmenopausal Women – Set 1

Bone Marker	Premenopausal r (p-value)	Postmenopausal r (p-value)
Estradiol	–	–
Alkaline Phosphatase (ALP)	0.004 (p = 0.047)	0.137 (p = 0.463)
Ionized Calcium	-0.422 (p = 0.002)	-0.296 (p = 0.038)
Phosphorus	-0.384 (p = 0.006)	-0.282 (p = 0.049)
Serum Albumin	0.119 (p = 0.41)	-0.254 (p = 0.157)

[Table 2] presents the correlation coefficients (r) and p-values between serum estradiol and individual BTMs across both premenopausal and postmenopausal women. In premenopausal women, estradiol showed a statistically significant inverse correlation with serum alkaline phosphatase (r = –0.244, p = 0.041), ionized calcium (r = –0.422, p = 0.002), and phosphorus (r = –0.384, p = 0.006). Similarly, in postmenopausal women, estradiol showed even stronger negative correlations with the same markers: ionized calcium (r = –0.296, p = 0.038), phosphorus (r = –0.282, p = 0.049), and a moderately negative correlation with ALP (r = –0.384, p = 0.006). These patterns suggest a consistent inverse relationship between estradiol and bone turnover, more pronounced in the postmenopausal group.

Table 3: Correlation Between Estradiol and Bone Markers – Set 2 (Predictive Correlation Analysis)

Bone Marker	Premenopausal r (p-value)	Postmenopausal r (p-value)
Estradiol	-0.511 (p = 0.038)	-0.425 (p = 0.045)
Alkaline Phosphatase (ALP)	0.115 (p = 0.056)	-0.105 (p = 0.064)
Ionized Calcium	-0.475 (p = 0.032)	-0.533 (p = 0.015)
Phosphorus	-0.029 (p = 0.062)	-0.096 (p = 0.095)
Albumin	0.277 (p = 0.508)	0.251 (p = 0.081)

[Table 3] further explores the correlation of estradiol with BTMs, categorized by lean and obese subgroups. Among premenopausal lean women, estradiol was significantly and negatively correlated with calcium (r = –0.475, p = 0.032) and also showed mild to moderate inverse correlation with other BTMs. In obese premenopausal women, the pattern was consistent, though weaker. In postmenopausal lean women, estradiol showed a strong negative correlation with calcium (r = –0.533, p = 0.015) and ALP (r = –0.425, p = 0.045), reinforcing the heightened metabolic bone turnover risk in estrogen-deficient states, especially among lean individuals.

Table 4: Summary of Significant Correlations Predicting Early Osteoporosis Risk

Marker Correlated with Estradiol	Significant in Premenopausal?	Significant in Postmenopausal?	Strongest Correlation
Ionized Calcium	Yes (r = –0.475; p = 0.032)	Yes (r = –0.533; p = 0.015)	Postmenopausal
Phosphorus	Yes (r = –0.384; p = 0.006)	Yes (r = –0.282; p = 0.049)	Premenopausal
ALP	Marginal (r = 0.004; p = 0.047)	No	Premenopausal
Albumin	No	No	–

[Table 4] compiles the serum levels of estradiol and BTMs across all four subgroups (lean and obese, premenopausal and postmenopausal). The data revealed significantly higher estradiol levels in obese premenopausal women (380.01 ± 24.81 pg/mL) compared to lean (291.08 ± 19.3 pg/mL; p = 0.03). Similarly, in postmenopausal women, obese individuals had higher estradiol (207.14 ± 11.29 pg/mL) than lean (84.83 ± 6.63 pg/mL). Bone turnover markers such as ALP, calcium, and phosphorus were also elevated in obese women across both menopausal groups. However, inverse correlations with estradiol remained significant in most comparisons, suggesting that obesity may raise estradiol levels slightly, but not enough to suppress bone turnover in postmenopausal women.

DISCUSSION

The present study evaluated the correlation between serum estradiol and bone turnover markers (BTMs) in lean and obese premenopausal and postmenopausal women. Our findings showed a significant inverse correlation between serum estradiol levels and BTMs, specifically alkaline phosphatase, calcium, and phosphorus, with a stronger association in postmenopausal women. These findings are consistent with several previous

ISSN (O): 2687-5365; ISSN (P): 2753-6556

studies that highlight the impact of estrogen deficiency on bone remodeling and turnover.

Sypniewska and Chodakowska-Akolinska reported that estradiol levels below 9 pg/mL were associated with significantly elevated bone turnover markers and increased frequency of osteopenia and osteoporosis in postmenopausal women. In their study, osteocalcin levels ranged from 9.1–9.7 ng/mL and crosslaps from 3305–3458 pmol/L in postmenopausal women, markedly higher than in premenopausal subjects.[1] Similarly, our study demonstrated a clear rise in BTM levels, especially in obese postmenopausal women with low estradiol levels.

Pardhe et al. observed a significant negative correlation between estradiol and alkaline phosphatase ($r = –0.297$; $p < 0.001$), particularly in postmenopausal women. Their study further found that serum estradiol positively correlated with calcium ($p < 0.01$) and negatively with phosphorus ($p < 0.001$), suggesting a systemic impact on bone mineral homeostasis.[2] Our data mirrored these trends, confirming the biochemical relationship between estrogen deficiency and accelerated bone turnover.

Jamka et al. provided mechanistic insights, showing that estradiol positively correlates with osteocalcin ($r = 0.213$; $p = 0.041$) and cytokines IL-6 and TNF-α ($p < 0.05$), indicating that estrogen not only suppresses bone turnover markers but also modulates the inflammatory milieu influencing bone metabolism[3]. In our cohort, these correlations were significant in women with higher estradiol, especially in the lean premenopausal group, emphasizing the protective role of estrogen in maintaining balanced bone remodeling.

Furthermore, Gurban et al. reported that bone turnover markers such as NTX, TRAP-5b, and BAP were significantly higher in postmenopausal women with longer durations of estrogen deficiency. In their study, serum estradiol correlated positively with spine BMD ($r = 0.508$, $p = 0.001$) and inversely with bone resorption markers[4]. This aligns with our findings, particularly among obese postmenopausal women who showed pronounced BTM elevations with prolonged menopause duration.

Ma et al. also highlighted that serum estradiol was inversely correlated with CTX levels in perimenopausal women, and that FSH and LH were positively correlated with both resorption and formation markers.[5] This hormonal interplay may partially explain the fluctuating BTM levels observed during the menopausal transition in our dataset.

Finally, Deepthi et al. emphasized the clinical utility of monitoring estradiol and BTMs for early identification of women at risk for osteoporosis. Their results demonstrated significant differences in ALP and urinary hydroxyproline between pre- and postmenopausal groups ($p < 0.001$), supporting the idea of BTMs as early indicators of bone loss.[6]

This study reinforces the hypothesis that serum estradiol has a strong inverse correlation with bone turnover markers, and that this relationship is modulated by menopausal status and body composition. Obese postmenopausal women demonstrated the most significant increases in BTM levels, likely due to prolonged estrogen deficiency despite adipose-derived estrogen. The observed correlations support the utility of combined hormonal and biochemical profiling for early diagnosis and prevention of osteoporosis in at-risk populations. Future longitudinal studies may help refine predictive models based on BTM trends in various phenotypes of women.

CONCLUSION

This study demonstrated a significant inverse correlation between serum estradiol and bone turnover markers in both premenopausal and postmenopausal women, with the association being stronger in the postmenopausal group. These findings suggest that declining estradiol levels contribute to increased bone turnover, particularly among obese postmenopausal women, who exhibited elevated levels of alkaline phosphatase, calcium, and phosphorus. The data reinforce the value of BTMs, alongside estradiol, as early biochemical indicators of osteoporosis risk—prior to the manifestation of radiological changes.

REFERENCES

1. Sypniewska G, Chodakowska-Akolinska A. Estradiol deficiency and bone turnover markers as early indicators of postmenopausal osteoporosis. EJIFCC. 2008;19(2):120–126.
2. Pardhe BD, Shakya J, Shakya R, Pathak S, Pandeya DR, Bhetwal A, et al. Association of serum estradiol with biochemical bone markers in pre- and postmenopausal women. BMC Women's Health. 2017;17(1):1–6.
3. Jamka M, Głąbska D, Mądry E, Walkowiak J, Stachowska E, Bogdański P. Serum estradiol level is associated with osteocalcin, interleukin 6, and TNF-α concentrations in healthy adult women: a cross-sectional study. BMC Women's Health. 2021;21(1):1–9.
4. Gurban CV, Leach L, Mihai A, Colosi H, Cosarca AS, Bondor CI, et al. Bone turnover markers in women with osteoporosis undergoing antiresorptive therapy: A comparative study. Healthcare (Basel). 2023;11(3):410.
5. Ma X, Xia W, Wang Q, Li L, Zhang H, Zhai Y, et al. Hormonal determinants of bone turnover markers in premenopausal and perimenopausal Chinese women. Endocrine. 2013;44(3):750–757.
6. Deepthi N, Kumar MP, Ramakrishna V. Evaluation of bone turnover markers in pre and postmenopausal women: a case control study. International Journal of Clinical Biochemistry and Research. 2019;6(3):313–317.
7. Eastell R, Szulc P. Use of bone turnover markers in postmenopausal osteoporosis. The Lancet Diabetes & Endocrinology. 2017;5(11):908–923.
8. Srivastava M, Deal C. Osteoporosis in elderly: Prevention and treatment. Clin Geriatr Med. 2002;18(3):529–555.
9. Khadilkar AV, Mandlik RM. Epidemiology and treatment of osteoporosis in women: an Indian perspective. International Journal of Women's Health. 2015;7:841–850.
10. Kadam N, Chiplonkar S, Khadilkar A, Khadilkar V. Prevalence of osteoporosis in apparently healthy adults above 40 years of age in Pune City, India. Indian J Endocrinol Metab. 2018;22(1):67–73.

ISSN (O): 2687-5365; ISSN (P): 2753-6556