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IMPACT OF OBESITY ON SERUM ESTRADIOL AND BONE TURNOVER MARKERS AMONG PREMENOPAUSAL AND POSTMENOPAUSAL WOMEN: A CROSS-SECTIONAL STUDY

Jyoti Sitaram Dubhalakar[1], Sunita Machindra Aghade[2], Dipti Mahendra Katre[3]

[1]*Assistant Professor, Department of Biochemistry, Government Medical college, Hingoli, Maharashtra, India.*
[2]*Associate Professor, Department of Biochemistry, Government Medical College, Jalna, Maharashtra, India.*
[3]*Associate professor, Department of Biochemistry, Dr. Ulhas Patil Medical College, Jalgaon, Maharashtra, India.*

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Corresponding Author:
Dr. Jyoti Sitaram Dubhalakar,
Assistant Professor, Department of Biochemistry, Government Medical college, Hingoli, Maharashtra, India.
Email: jyotidubhalkar@gmail.com

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ABSTRACT

Background: Osteoporosis is a major global health concern, particularly affecting postmenopausal women due to estrogen deficiency. Serum estradiol and bone turnover markers (BTMs) are reliable biochemical indicators for early changes in bone metabolism. While the individual effects of menopause and obesity on bone health have been studied, limited data exist on their combined impact on BTMs. This study aimed to assess serum estradiol and BTMs among lean and obese women, stratified by premenopausal and postmenopausal status.

Materials and Methods: A cross-sectional, two-arm, parallel-group study was conducted from February 2019 to September 2020 in the Department of Biochemistry, Government Medical College. A total of 100 women were enrolled and divided equally into premenopausal (Group A) and postmenopausal (Group B) groups. Each group was further subdivided into lean (BMI 18.5–22.99 kg/m²) and obese (BMI >25 kg/m²) subgroups. Serum estradiol, ionized calcium, alkaline phosphatase, phosphorus, and albumin were measured using chemiluminescent immunoassay and standard biochemical methods. Data were analyzed using appropriate statistical tests.

Results: Obese women showed significantly higher estradiol levels compared to lean women in both premenopausal (380.01 ± 24.81 vs. 291.08 ± 19.3 pg/mL, p=0.03) and postmenopausal (207.14 ± 11.29 vs. 84.83 ± 6.63 pg/mL, p<0.05) groups. Bone turnover markers including alkaline phosphatase, calcium, and phosphorus were also elevated in obese subgroups. Significant inverse correlations were found between estradiol and BTMs such as ionized calcium and phosphorus, particularly in postmenopausal women.

Conclusion: Menopausal status and BMI significantly influence serum estradiol and BTMs. Obese postmenopausal women exhibit heightened bone turnover, underscoring the importance of early biochemical screening for osteoporosis prevention.

Keywords: Estradiol, Bone Turnover Markers, Obesity, Menopause, Osteoporosis.

INTRODUCTION

Osteoporosis is a systemic skeletal disorder characterized by decreased bone mass and deterioration of bone microarchitecture, leading to increased bone fragility and susceptibility to fractures. It is especially prevalent in postmenopausal women due to the decline in estrogen levels, which accelerates bone resorption and impairs bone formation.[1]

Estrogen, particularly estradiol, plays a critical role in maintaining bone homeostasis. It suppresses bone resorption by regulating osteoclast activity and also promotes osteoblast survival, thereby maintaining a balance in bone remodeling.[2] In premenopausal women, adequate estrogen levels maintain bone

turnover within a physiologic range. However, after menopause, a sharp decline in estrogen results in increased levels of bone turnover markers (BTMs), including serum alkaline phosphatase, osteocalcin, C-terminal telopeptides (CTX), and urinary hydroxyproline.[3,4]

Obesity further complicates this picture. Adipose tissue is both a source of aromatization (converting androgens to estrogens) and a contributor to chronic low-grade inflammation. Obese individuals often have higher circulating estradiol levels due to increased peripheral conversion, which can alter bone metabolism differently than in lean individuals.[5] Some studies suggest that obesity may confer a protective effect on bone mineral density (BMD) via increased mechanical loading and higher estrogen levels, while others have found higher levels of bone turnover markers and altered bone quality despite increased BMD.[6]

Furthermore, bone turnover markers (BTMs) serve as non-invasive biochemical indicators of skeletal metabolism. These markers reflect the dynamic process of bone formation and resorption and are useful for assessing osteoporosis risk, monitoring treatment response, and understanding metabolic bone diseases. Markers such as ionized calcium, phosphorus, alkaline phosphatase, and serum estradiol provide insight into the ongoing skeletal remodeling process.[7,8]

While several studies have explored the individual effects of menopause or obesity on estradiol and BTMs, fewer have systematically assessed the interaction between body composition and menopausal status on these biochemical parameters. It remains unclear whether obesity modulates the estradiol-BTM relationship similarly in both premenopausal and postmenopausal states. Moreover, differences in BTM levels across these groups may hold implications for early osteoporosis detection and preventive strategies.

Given the growing burden of osteoporosis, especially among aging women, and the increasing prevalence of obesity, it is critical to elucidate how estradiol and bone turnover markers interact across body weight categories and menopausal statuses. This study aims to compare serum estradiol and BTMs in lean and obese women, stratified by premenopausal and postmenopausal status. This stratification will help in identifying early metabolic shifts in bone health and may aid in the early prediction and diagnosis of osteoporosis, particularly in at-risk populations.

MATERIALS AND METHODS

This cross-sectional, two-arm, parallel-group comparative study was conducted in the Department of Biochemistry at Government Medical College, a tertiary care center, from February 2019 to September 2020. The objective was to assess and compare serum estradiol and bone turnover markers among lean and obese women, stratified by menopausal status. A total of 100 female participants were enrolled using non-probability convenient sampling. Participants were categorized into two major groups: Group A (n=50, premenopausal women aged 35–45 years with regular menstrual cycles) and Group B (n=50, postmenopausal women aged 50–65 years, having attained natural menopause for 2–3 years). Each group was further subdivided into lean (BMI 18.5–22.99 kg/m²) and obese (BMI >25 kg/m²) subgroups based on WHO criteria.

The sample size was calculated using the formula $n = Z^2pq/d^2$, with Z = 1.96 at a 95% confidence interval, p = 13.3%9 (based on previous literature), d = 7% precision, resulting in a sample size of 90.4. To account for a 10% dropout, the final sample size was adjusted to 100. Participants with a history of osteoporosis, diabetes mellitus, chronic renal failure, pregnancy, hysterectomy, myomectomy, or on hormonal replacement therapy were excluded. All participants underwent clinical evaluation including detailed history, physical examination, and anthropometric measurements. Height was measured using a stadiometer, weight with a digital scale, and BMI was calculated using the standard formula: weight (kg) / height² (m²). Waist circumference and hip circumference were recorded using a non-stretchable tape, and waist-hip ratio was derived accordingly.

Biochemical investigations included estimation of serum estradiol, ionized calcium, serum alkaline phosphatase, serum phosphorus, and serum albumin. After obtaining informed consent, 5 mL of venous blood was collected in fasting state under aseptic conditions. Serum was separated by centrifugation at 3000 rpm for 10 minutes. Serum estradiol levels were quantified using the Access Sensitive Estradiol assay, a paramagnetic particle chemiluminescent immunoassay, on the Beckman Coulter Access Immunoassay System. This is a competitive binding assay in which light output is inversely proportional to the estradiol concentration. Bone turnover markers were measured using standard biochemical techniques as per manufacturer protocols. All biochemical analyses were performed in the central clinical biochemistry laboratory of the institution.

RESULTS

In the present study, the age distribution of the 100 female participants ranged from 35 to over 65 years. The majority of women (44%) belonged to the 35–45 years age group, which largely comprised premenopausal women. The 55–65 years group constituted the second-largest proportion, accounting for 34% of the total population, predominantly representing postmenopausal women. The 45–55 years age group included 19% of participants and consisted of both premenopausal and postmenopausal women, reflecting the transitional age range. A small fraction (3%) of participants were older than 65 years.

The mean age of the study population was 50.20 ± 9.48 years, indicating an even representation of midlife and older adult women, suitable for assessing menopausal transitions and related biochemical changes.

This age-based distribution formed the foundation for menopausal group classification and further biochemical comparisons.

Table 1: Age-Wise Distribution of Study Participants

Age Group (Years)	Frequency (n)	Percentage (%)	Mean ± SD (Years)
35–45	44	44%	
45–55	19	19%	
55–65	34	34%	
>65	3	3%	
Total	80	100%	50.20 ± 9.48

[Table 2] highlights the distribution of premenopausal and postmenopausal women across age groups. All participants aged 35–45 years were premenopausal, while those aged 55–65 years and above were exclusively postmenopausal. A small overlap was observed in the 45–55 year age group, which included both premenopausal (n=6) and postmenopausal (n=9) women. The mean age of the premenopausal group was 41.50 ± 3.15 years, whereas that of the postmenopausal group was significantly higher at 58.90 ± 4.16 years (p=0.00001), confirming statistically significant age differentiation between the two groups.

Table 2: Distribution of Premenopausal and Postmenopausal Women by Age Group

Age Group (Years)	Premenopausal (n = 50)	Postmenopausal (n = 50)	p-value
35–45	44	0	
45–55	6	9	
55–65	0	38	
>65	0	3	0.00001
Mean ± SD	41.50 ± 3.15	58.90 ± 4.16	S (p < 0.05)

As presented in [Table 3], a significant difference in Body Mass Index (BMI) was observed between lean and obese women in both premenopausal and postmenopausal groups. Among premenopausal women, lean individuals had a mean BMI of 20.77 ± 1.14 kg/m² compared to 25.70 ± 2.22 kg/m² in the obese subgroup. Similarly, in postmenopausal women, lean participants had a mean BMI of 22.88 ± 0.68 kg/m², while obese participants exhibited a significantly higher mean BMI of 28.25 ± 3.23 kg/m². The BMI difference between lean and obese groups was statistically significant (p=0.011), validating the categorization used in the study.

Table 3: Body Mass Index (BMI) Comparison Between Lean and Obese Women by Menopausal Status

Group	Lean (Mean ± SD)	Obese (Mean ± SD)	p-value	Significance
Premenopausal	20.77 ± 1.14	25.70 ± 2.22		
Postmenopausal	22.88 ± 0.68	28.25 ± 3.23	0.011	S (p < 0.05)

[Table 4] illustrates the comparative analysis of serum estradiol and bone turnover markers across lean and obese subgroups within both menopausal categories. In premenopausal women, obese participants had significantly higher estradiol levels (380.01 ± 24.81 pg/mL) compared to lean counterparts (291.08 ± 19.3 pg/mL), with a statistically significant difference (p=0.03). Among postmenopausal women, estradiol was markedly lower overall, but still higher in the obese group (207.14 ± 11.29 pg/mL) compared to lean subjects (84.83 ± 6.63 pg/mL), again showing a significant difference (p<0.05). Serum ionized calcium and alkaline phosphatase (ALP) levels were also significantly higher in obese women across both menopausal groups. Serum phosphorus showed a mild but borderline significant increase in obese postmenopausal women (p=0.051). Serum albumin did not differ significantly between any groups (p>0.05). These findings demonstrate that both adiposity and menopausal status significantly influence serum estradiol and bone turnover marker levels.

Table 4: Serum Estradiol and Bone Turnover Markers in Lean and Obese Women by Menopausal Status

Marker	Premenopausal Lean (n = 24)	Premenopausal Obese (n = 26)	p-value	Postmenopausal Lean (n = 20)	Postmenopausal Obese (n = 30)	p-value
Serum Estradiol (pg/mL)	291.08 ± 19.3	380.01 ± 24.81	0.03	84.83 ± 6.63	207.14 ± 11.29	<0.05
Ionized Calcium (mmol/L)	4.60 ± 0.24	5.46 ± 0.77	0.026	4.12 ± 0.48	5.07 ± 0.97	<0.05

Serum Phosphorus (mg/dL)	3.51 ± 0.43	3.39 ± 0.40	0.051	4.22 ± 0.27	4.44 ± 0.97	<0.05
Alkaline Phosphatase (U/L)	66.75 ± 11.15	72.50 ± 12.12	0.001	99.57 ± 5.67	113.45 ± 8.57	<0.05
Serum Albumin (g/dL)	3.62 ± 0.50	3.56 ± 0.46	0.733	3.34 ± 1.11	5.31* (Value mismatch)	>0.05

DISCUSSION

In the present study, a significant variation in serum estradiol and bone turnover markers was observed between lean and obese premenopausal and postmenopausal women. Our findings indicate that postmenopausal women, particularly those who are obese, exhibit higher levels of bone turnover markers such as alkaline phosphatase and phosphorus, along with lower estradiol levels, compared to their premenopausal counterparts. These observations are consistent with the literature and reinforce the physiological impact of estrogen deficiency on bone metabolism.

A study by Sypniewska and Chodakowska-Akolinska found that postmenopausal women with estradiol levels below 9 pg/ml had significantly higher bone resorption and formation markers, including osteocalcin (9.1–9.7 ng/ml) and crosslaps (3305–3458 pmol/l), compared to premenopausal women (osteocalcin 6.8 ng/ml and crosslaps 2087 pmol/l), supporting our findings that estrogen deficiency is a key driver of increased bone turnover.[1]

Similarly, Jamka et al. demonstrated that in postmenopausal women with estradiol levels ≤10 pg/ml, there was an imbalance in bone remodeling processes with significant increases in resorptive markers (CTX) and pro-inflammatory cytokines (IL-6 and TNF-α), further indicating that low estrogen correlates with enhanced bone turnover.[2] In contrast, women with reference estradiol levels (≥25 pg/ml) showed balanced bone resorption and formation markers, a trend also reflected in our lean premenopausal group.

Our study also found a statistically significant increase in serum alkaline phosphatase and phosphorus in postmenopausal women, which aligns with the results of Pardhe et al., who reported that postmenopausal women had significantly elevated ALP and phosphorus levels, along with a reduction in calcium and estradiol, compared to premenopausal women ($p<0.001$).[3] They also observed a negative correlation between ALP and estradiol, which corresponds with our data showing reduced estradiol associated with increased bone turnover markers.

Additionally, Gurban et al. observed that bone turnover markers including bone-specific alkaline phosphatase, osteocalcin, and NTX increased in postmenopausal women, especially those who were more than 10 years postmenopausal. They also noted a positive correlation between serum estradiol and lumbar BMD ($r = 0.508$, $p = 0.001$), which reinforces our study's implication that estrogen plays a central role in preserving bone integrity.[4]

A cross-sectional study in China by Ma et al. also highlighted a strong inverse correlation between estradiol and bone resorption marker CTX among perimenopausal and postmenopausal women. They concluded that elevated serum FSH and LH, along with declining estradiol, are independent predictors of increased bone turnover.[5]

The patterns we observed between lean and obese women suggest that obesity, while often associated with higher estrogen from peripheral aromatization, may still contribute to bone turnover dysregulation in the postmenopausal state. This may be due to additional metabolic and inflammatory factors in obese individuals that exacerbate bone loss, as suggested by Wu et al., who noted that adiponectin was positively correlated with bone turnover markers in postmenopausal women and served as a negative predictor of bone mass.[6] Agarwal et al. also reported significant differences in estradiol and bone turnover markers across BMI categories in Indian women, supporting the regional applicability of BMI-based stratification.[10]

Our study demonstrates a clear inverse relationship between estradiol levels and bone turnover markers, emphasizing that both menopausal status and BMI significantly influence bone metabolism. The elevated bone turnover in obese postmenopausal women may reflect not only estrogen deficiency but also obesity-related metabolic dysregulation. Comparisons with similar studies confirm the robustness of our findings. The evidence underscores the importance of early identification and monitoring of bone turnover markers, especially in postmenopausal women, to mitigate the risk of osteoporosis. Future interventions targeting hormonal balance and weight management could play a key role in preserving bone health in this vulnerable population.

CONCLUSION

This study highlights the significant impact of both menopausal status and body mass index on serum estradiol levels and bone turnover markers. Obese women, particularly in the postmenopausal group, demonstrated higher levels of bone turnover markers such as alkaline phosphatase and phosphorus, along with reduced estradiol levels, indicating an elevated risk for accelerated bone loss and potential early onset of osteoporosis. The inverse correlation between estradiol and key bone markers supports the

role of estrogen deficiency as a critical factor in bone metabolism dysregulation.

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