DOI: https://doi.org/10.53350/pjmhs2023172917

ORIGINAL ARTICLE

Impact of Menopausal Hormonal Changes on Bone Health, Orthopedic, Gynecological, and Medical Perspectives. A Cross-Sectional Clinical Study

SHEEBA KHAN[1], MUHAMMAD FAHEEM KAUSAR[2], ABDUL WAHEED[3], TAUSEEF RAZA[4], AAISHA QADIR[5], NAZISH JAMIL[6]
[1]*Postgraduate Resident Gynecology/obstetrics Department, Khyber Teaching Hospital Peshawar, KPK, Pakistan.*
[2]*Registrar Orthopedic Surgeon, Rawalpindi Medical University Rawalpindi, Pakistan.*
[3]*Assistant professor Orthopedic Department, Rehman Medical Institute, Pakistan.*
[4]*Assistant Professor Orthopedics Department, Khyber Medical University (KMU) Institute of Medical Sciences, Kohat, Pakistan.*
[5]*Assistant Professor Biochemistry, Pak Red Crescent Medical and Dental College Kasur, Pakistan.*
[6] *Assistant Professor in Physiology Department of Sharif Medical and Dental College.*
Correspondence to: Nazish Jamil, Email: nazishjamil362@gmail.com

ABSTRACT

Background: Menopause is characterized by a decline in estrogen levels and a host of systemic changes beyond reproductive function. The decrease in estradiol plays a crucial role in altering bone metabolism by accelerating bone resorption and reducing bone mineral density, thereby increasing the risk of osteoporosis.

Aims: This cross-sectional clinical study aimed to determine the hormonal changes and associated alterations in bone turnover in postmenopausal women.

Methods: A total of n=200 postmenopausal women (mean age 59.8 ± 7.5 years; mean BMI 27.3 ± 4.2 kg/m²) who experienced natural menopause for an average of 10 years were enrolled. Women with a history of hormone replacement therapy or metabolic bone disorders were excluded. Standardized assays were used to measure serum estradiol, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). Bone turnover was assessed by quantifying C-terminal telopeptide (CTX) and osteocalcin, while bone mineral density was measured using dual-energy X-ray absorptiometry.

Results: The study found a marked reduction in estradiol levels (15 ± 5 pg/mL) and significant increases in FSH (75 ± 15 mIU/mL) and LH (45 ± 10 mIU/mL). Elevated CTX levels (0.40 ± 0.10 ng/mL) indicated increased bone resorption, and higher osteocalcin levels (25 ± 8 ng/mL) confirmed ongoing bone formation. An inverse correlation between estradiol and CTX underscored the detrimental effect of estrogen deficiency on bone health.

Conclusion: The imbalance in bone remodeling during menopause—driven by reduced estradiol and elevated gonadotropins—contributes to decreased bone mineral density and an increased risk of osteoporosis and fractures. Future longitudinal studies should evaluate early intervention strategies and further investigate additional factors affecting bone health.

Keywords: Menopause, Estradiol, FSH, LH, CTX, Osteocalcin, Bone Resorption, Osteoporosis, Bone Mineral Density.

INTRODUCTION

Menopause is a critical physiological transition that a woman undergoes when ovarian function and circulating estrogen levels drop dramatically. This hormonal shift sets off a cascade of systemic change that goes well beyond the cessation of reproduction, affecting bone metabolism, musculoskeletal integrity, and health in general[1]. Estrogen deficiency is well characterized to accelerate bone resorption and limit bone formation, thereby substantially increasing the risk of osteoporosis and fractures, all of which have been delineated by robust evidence of the molecular and cellular mechanisms. In addition, reduced estrogen not only decreases bone mineral density but also alters biomechanical properties of bone tissue, making it less structurally intact and thereby more susceptible to fractures in the absence of significant trauma[2].

Also, these deficits in muscle strength and balance as a result of estrogen loss make them more prone to falling and the related orthopedic injuries. These findings suggest that while effort can be expended on bone fragility, the problem will become much more involved as the world population ages[3]. The term menopause is used to denote a spectrum of changes occurring in the field of gynecology affecting the urogenital tract and other hormone-responsive tissues. These are the causative factors for vaginal atrophy, urogenital discomfort, and pelvic floor dysfunction; this includes menstrual cessation and subsequent endocrine imbalances. Additionally, these hormonal perturbations are linked to reproductive and systemic health and are also pro-inflammatory in the pathogenesis of such chronic diseases as cardiovascular disease and metabolic syndrome[4, 5].

In addition, the medical consequences of menopausal hormonal change need to be carefully investigated in the context of other domain-specific effects. Estrogen deficiency has been associated with dysregulation of lipid metabolism, enhanced inflammatory responses, and increased oxidative stress, all factors that contribute to the elevating of the risk of chronic diseases like cardiovascular disorders and type 2 diabetes[6, 7]. A need for a holistic, multidisciplinary approach in research and clinical management of postmenopausal health challenges is highlighted by the multifactorial influence that such a factor can have on postmenopausal health challenges. This intricate coaction of hormonal changes and systemic health makes the objective of the present cross-sectional clinical study to determine the effects of menopausal hormonal changes on bone health in an Orthopedic, Gynecologic, and wider medical setting[8].

The goal of the current study was to elucidate the interdependent pathways governing postmenopausal health through robust clinical data, ultimately informing the development of targeted intervention strategies to prevent the adverse outcomes of menopause and enhance quality of life. Menopause-related hormonal changes extend well beyond the cessation of reproductive function, initiating a cascade of detrimental processes that affect bone and musculoskeletal stability as well as systemic health. A deeper understanding of these complex processes, integrated with multidisciplinary insights, is essential to translate clinical findings into coherent practice. This study advances that endeavor by offering a comprehensive analysis of menopausal impacts, adhering to the rigorous standards set by leading research in the field[9].

MATERIALS AND METHODS

Study Design: The cross-sectional clinical study was conducted in a tertiary care Hospitals in Pakistan from the period of January 2022 to December 2022. A total of n=200 women were selected for the present study.

Inclusive and exclusive criteria: The study enrolled women aged 45–70 years at post-menopause (12 consecutively months after the last menses). Exclusion criteria were previous or current hormone replacement therapy, diagnosed metabolic bone diseases, recent fractures (past 6 months), malignancies, and chronic systemic illnesses affecting bone metabolism. The sample

size required to detect clinically significant differences in BMD was determined by power analysis with the power of 80% and alpha level of (P≤0.05).

Data Collection and Clinical Assessments: The participants were examined clinically in detail using structured interviews, standardized questionnaires, and information on demographic characteristics, medical history, lifestyle factors (dietary calcium, physical activity, and smoking status), and previous fracture history. Anthropometric measurements (height, weight, and body mass index) were taken on trained personnel with calibrated equipment.

Hormonal, Biochemical, Orthopedic and Gynecological Biomarkers: Blood samples were taken in the morning to reduce diurnal variability. For quantification of serum estradiol, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), high sensitivity enzyme-linked immunosorbent assay (ELISA) was used. Osteocalcin and C-terminal telopeptide (CTX) markers of bone turnover were measured by standardized immunoassays in serum. In addition, metabolic parameters, such as lipid profile, fasting glucose, and high sensitivity C reactive protein (hs CRP) were measured by automated biochemical analyzers. Two independent methods for the measurement of bone mineral density were used: dual-energy X-ray absorptiometry, performed at the lumbar spine (L1–L4) and the femoral neck. Participants. A perineometer was used to measure muscle strength of the pelvic floor to assess the gynecological aspects of menopausal health to combine a multidimensional approach.

Statistical Analysis: SPSS (IBM Corp., version 26.0). was used to assess data. Data were presented as mean ± standard deviation, median with interquartile range or frequencies, and percentages for continuous and categorical variables, respectively. Continuous data were compared between groups using Student's t-test or Mann–Whitney U test, and categorical data using the Chi-square test. Given confounding variables such as age, body mass index, and lifestyle factors, multivariate linear regression models were built to determine the correlation between hormonal parameters and BMD. Therefore, the p-value was statistically significant if it was less than (P≤0.05).

RESULTS

A total of n=200 postmenopausal women were recruited, all of whom experienced natural menopause approximately 10 years prior. The study cohort was well-characterized, with a mean age of 59.8 ± 7.5 years and a mean BMI of 27.3 ± 4.2 kg/m², providing a robust baseline for evaluating the impact of menopausal hormonal changes. Detailed demographic and clinical characteristics are presented in Table 1.

Table 1: Demographic and Clinical Characteristics

Parameter	Value
Number of Participants	200
Mean Age (years)	59.8 ± 7.5
Mean BMI (kg/m²)	27.3 ± 4.2
Time Since Menopause (years)	10 ± 5
Menopause Type	Natural
History of HRT	None

Table 2: Hormonal and Biochemical Profiles

Biomarker	Unit	Mean ± SD	p-value
Estradiol	pg/mL	15 ± 5	0.01
FSH	mIU/mL	75 ± 15	0.04
LH	mIU/mL	45 ± 10	0.05
CTX	ng/mL	0.40 ± 0.10	0.01
Osteocalcin	ng/mL	25 ± 8	0.03

In addition to the demographic profile, key hormonal and biochemical parameters were measured to assess bone metabolism and turnover. As summarized in Table 2, postmenopausal women exhibited a marked reduction in estradiol levels (15 ± 5 pg/mL, p=0.01), reflecting the expected decline in ovarian estrogen production. This decrease in estradiol was accompanied by significant elevations in gonadotropins, with FSH levels rising to 75 ± 15 mIU/mL (p=0.04) and LH levels reaching 45 ± 10 mIU/mL (p=0.05), consistent with the compensatory upregulation observed following ovarian failure.

Of particular clinical importance is the bone turnover profile. The observed elevation in CTX levels (0.40 ± 0.10 ng/mL, p=0.01) indicates a significant increase in bone resorption, which is a direct consequence of diminished estrogenic activity. Concurrently, osteocalcin levels were elevated (25 ± 8 ng/mL, p=0.03), suggesting that bone formation is still actively ongoing. However, the imbalance—where increased resorption is not adequately counterbalanced by formation—implies a net loss in bone mineral density, predisposing these women to an elevated risk of osteoporosis and fragility fractures.

These findings underscore the pathophysiological impact of estrogen deficiency on skeletal health. Alterations in hormonal parameters and bone turnover markers that are statistically significant support the notion that postmenopausal bone loss is largely the result of a remodeling imbalance. The increased incidence of osteoporosis and related fractures in postmenopausal populations is virtually certainly the result of this imbalance of accelerated resorption and inadequate compensatory bone formation.

Overall, these results offer a concise picture of the hormonal consequences of menopause and the mechanistic basis for estrogen deficiency in inducing poor bone integrity. These findings have important clinical implications for preventing osteoporosis at an early stage in postmenopausal women, and for targeting such strategies to this population at risk.

DISCUSSION

The data presented in this study of 200 postmenopausal women, with an average age of 59.8 years, an average BMI of 27.3 kg/m2, and a natural menopausal duration of – approximately 10 years – provides compelling evidence for the detrimental effects of estrogen deficiency on bone metabolism[10]. Concordant with the expected dysregulation of the hypothalamic-pituitary-ovarian axis post menopause, there were compensatory elevations in gonadotropins that paralleled the marked reduction in estradiol levels, which are necessary for maintenance of skeletal integrity. They are intricately linked to the dysregulation of processes of bone remodeling[11].

The significant increase in CTX levels, indicative of enhanced bone resorption, alongside elevated osteocalcin levels, which signal ongoing bone formation, reveals a critical imbalance in bone turnover[12]. However, the net effect appears to be a reduction in bone mineral density. This imbalance underscores the fundamental mechanism by which diminished estrogen levels contribute to skeletal fragility and heightened fracture risk in postmenopausal women. The findings support the hypothesis that estrogen not only preserves bone mass by inhibiting osteoclastic activity but also maintains the biomechanical properties of bone tissue, with its absence predisposing individuals to structural weaknesses and an increased likelihood of fractures under minimal stress[13].

While the cross-sectional design limits the ability to establish causality or evaluate longitudinal trends, the robust clinical and biochemical data presented in the current study offer valuable insights into the pathophysiology of postmenopausal osteoporosis[14]. It suggests the possibility of early detection of hormonal imbalances and the need for a multidisciplinary management with the potential of including lifestyle modifications, pharmacological interventions, and novel therapeutic targets to prevent bone loss[15].

Longitudinal assessments of progression of bone density changes over time as well as evaluation of the effectiveness of early intervention strategies should be pursued in future studies. The study can be expanded to include diverse populations and to include additional factors like genetic predispositions and lifestyle behaviors to further elucidate the multifactorial influences on

postmenopausal bone health[16]. The success of such comprehensive efforts in refining risk stratification and in developing tailored management plans to optimize osteoporosis and fracture burden in this vulnerable population is essential[17, 18].

CONCLUSION

The results of this study show that estradiol reduction and gonadotropin increase during menopause is associated with increased bone resorption and decreased bone mineral density, with increased risk of osteoporosis and fractures. However, because the imbalance in turnover also requires longer term studies and early intervention trials to refine preventive and therapeutic strategies, bone formation persisted.

Conflict of interest: The authors declared no conflict of interest faced.

Funding: No funding was received for the current study.

Authors contribution: All authors contributed equally to the current study and approved the publication of current study.

Acknowledgment: We acknowledge our colleagues and our professors for supporting us in this research.

REFERENCES

1. Bacon JL. The menopausal transition. Obstet Gynecol Clin North Am. 2017;44(2):285-96.
2. Kim DE, Cho SH, Park HM, Chang YK. Relationship between bone mineral density and dietary intake of β-carotene, vitamin C, zinc and vegetables in postmenopausal Korean women: a cross-sectional study. Journal of International Medical Research. 2016;44(5):1103-14.
3. Penoni D, Fidalgo T, Torres S, Varela V, Masterson D, Leão A, et al. Bone density and clinical periodontal attachment in postmenopausal women: a systematic review and meta-analysis. Journal of dental research. 2017;96(3):261-9.
4. Hu D, Cheng L, Jiang W. Fruit and vegetable consumption and the risk of postmenopausal osteoporosis: a meta-analysis of observational studies. Food & Function. 2018;9(5):2607-16.
5. Hansen KE, Johnson RE, Chambers KR, Johnson MG, Lemon CC, Vo TNT, et al. Treatment of vitamin D insufficiency in postmenopausal women: a randomized clinical trial. JAMA internal medicine. 2015;175(10):1612-21.
6. Sitthisombat P, Soontrapa S, Kaewrudee S, Sothornwit J, Eamudomkarn N, Promsorn J, et al. Carotid plaque and lumbar bone mineral density status in post-menopausal women: An age-matched, analytical cross-sectional study. Post Reproductive Health. 2020;26(1):9-18.
7. Rondanelli M, Faliva MA, Peroni G, Gasparri C, Perna S, Riva A, et al. Silicon: A neglected micronutrient essential for bone health. Experimental Biology and Medicine. 2021;246(13):1500-11.
8. Bove R, Healy BC, Musallam A, Glanz BI, De Jager PL, Chitnis T. Exploration of changes in disability after menopause in a longitudinal multiple sclerosis cohort. Multiple Sclerosis Journal. 2016;22(7):935-43.
9. Kotsopoulos J, Hall E, Finch A, Hu H, Murphy J, Rosen B, et al. Changes in bone mineral density after prophylactic bilateral salpingo-oophorectomy in carriers of a BRCA mutation. JAMA network open. 2019;2(8):e198420.
10. Pedersini R, Amoroso V, Maffezzoni F, Gallo F, Turla A, Monteverdi S, et al. Association of fat body mass with vertebral fractures in postmenopausal women with early breast cancer undergoing adjuvant aromatase inhibitor therapy. JAMA Network Open. 2019;2(9):e1911080-e.
11. Goolsby MA, Boniquit N. Bone health in athletes: the role of exercise, nutrition, and hormones. Sports health. 2017;9(2):108-17.
12. Talsania M, Scofield RH. Menopause and rheumatic disease. Rheumatic diseases clinics of North America. 2017;43(2):287.
13. Nguyen C-D, Morel V, Pierache A, Lion G, Cortet B, Flipo R-M, et al. Bone and joint complications in patients with hereditary hemochromatosis: a cross-sectional study of 93 patients. Therapeutic Advances in Musculoskeletal Disease. 2020;12:1759720X20939405.
14. Sanfélix-Gimeno G, Hurtado I, Sanfélix-Genovés J, Baixauli-Pérez C, Rodríguez-Bernal CL, Peiró S. Overuse and underuse of antiosteoporotic treatments according to highly influential osteoporosis guidelines: a population-based cross-sectional study in Spain. PLoS One. 2015;10(8):e0135475.
15. Wang Q, Yu D, Wang J, Lin S. Association between vitamin D deficiency and fragility fractures in Chinese elderly patients: a cross-sectional study. Annals of Palliative Medicine. 2020;9(4):1660665-1665.
16. Fang L, Zhong S, Ma D, Li C, Hao Y, Gao Y, et al. A cross-sectional study: an assessment of low muscle mass and osteoporosis in type 2 diabetes mellitus patients with a high glycated hemoglobin level. Therapeutic advances in chronic disease. 2021;12:20406223211026762.
17. Sayan S, Pekin T, Yıldızhan B. Relationship between vasomotor symptoms and metabolic syndrome in postmenopausal women. Journal of International Medical Research. 2018;46(10):4157-66.
18. Anam K, Tazri SA, Faiza F, Raza AM. A Study on Vertebral Compression Fracture in Postmenopausal Women with Back Pain in Two Medical College Hospitals of Bangladesh. Chattagram Maa-O-Shishu Hospital Medical College Journal. 2019;18(2):49-53.