I J C R M
International Journal of Contemporary Research In Multidisciplinary

Review Article

Effect of Menopause on Knee Pain in Female Patients with Knee Osteoarthritis: A Review

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DOI: https://doi.org/10.5281/zenodo.17709592

Abstract

Knee osteoarthritis (KOA) is one of the most prevalent musculoskeletal disorders in postmenopausal women, leading to significant pain, disability, and reduction in quality of life [1]. Menopause, characterised by a decline in estrogen and other sex hormones, has been identified as a key factor influencing the onset and progression of KOA [2]. Estrogen deficiency contributes to altered cartilage metabolism, inflammation, and changes in pain perception, leading to increased vulnerability to the development of KOA and knee pain.
Objective: This review explores recent evidence (2018–2025) regarding the relationship between menopause and knee pain in KOA, examining hormonal, metabolic, biomechanical, and psychosocial mechanisms. We also highlight the implications for physiotherapy management in postmenopausal women.
Methods: A focused search was performed in PubMed and Google Scholar for studies between 2018 and 2025 using combinations of terms including "menopause," "knee pain," "osteoarthritis," "estrogen deficiency," and "postmenopausal women." Randomised controlled trials, cohort studies, and systematic reviews were included.
Results: Postmenopausal women demonstrate higher prevalence and severity of knee pain and structural OA changes compared to premenopausal women [4]. Estrogen deficiency impairs cartilage repair, increases synovial inflammation, and influences central pain modulation [5,6]. Hormone replacement therapy (HRT) and physical activity interventions have shown potential benefits in reducing KOA pain and improving function [7,8].
Conclusion: Menopause-related hormonal changes contribute significantly to knee pain in female patients with KOA through multi-system mechanisms. Comprehensive physiotherapy approaches incorporating exercise, weight management, education, and potentially adjunctive hormonal therapy may optimise outcomes in this population.

Manuscript Information

- **ISSN No:** 2583-7397
- **Received:** 13-09-2025
- **Accepted:** 23-10-2025
- **Published:** 05-11-2025
- **IJCRM:**4(6); 2025: 100-103

- **Plagiarism Checked:** Yes
- **Peer Review Process:** Yes

How to Cite this Article

Bhatia S. Effect of menopause on knee pain in female patients with knee osteoarthritis: a review. Int J Contemp Res Multidiscip. 2025;4(6):100-103.

Access this Article Online

www.multiarticlesjournal.com

KEYWORDS: menopause, postmenopausal women, knee pain, osteoarthritis, estrogen deficiency, hormone replacement therapy, physiotherapy.

1. INTRODUCTION

Knee osteoarthritis (KOA) is a degenerative joint disease characterised by cartilage degradation, synovial inflammation, and subchondral bone remodelling, leading to pain, stiffness, and functional limitations [1]. The global prevalence of KOA has increased significantly, particularly among women after menopause [2]. Epidemiological studies reveal that women over 50 years have nearly twice the risk of developing symptomatic KOA compared to men [3].

The menopausal transition is accompanied by a rapid decline in estrogen and progesterone levels, both of which influence musculoskeletal homeostasis. Estrogen has protective roles in cartilage metabolism, bone turnover, and neuromodulation of pain [4]. Therefore, menopause-related estrogen deficiency may accelerate joint degeneration and modulate pain perception, explaining the gender disparity in KOA [5].

Beyond hormonal factors, menopause is associated with increased body weight, altered fat distribution, and changes in inflammatory cytokines, all contributing to knee joint stress [6,7]. Central sensitisation and psychosocial factors, including sleep disturbance and mood changes, further exacerbate pain experience [8].

Given the multifactorial nature of KOA in postmenopausal women, understanding the intersection between menopause and knee pain is crucial for physiotherapists and rehabilitation specialists to design holistic management strategies that integrate physical, hormonal, and psychosocial aspects.

Epidemiology: menopause and knee pain

Large population analyses and national cohort studies indicate that the prevalence and impact of KOA increase markedly after menopause. Global estimates show rising OA burden in women after midlife and identify post-menopausal women as a high-risk group for symptomatic OA [1]. Cross-sectional investigations have found associations between current MHT use and knee OA prevalence, although these findings vary by study and confounders [2]. Reproductive history studies indicate that the timing of menopause, parity and other reproductive factors may modulate later KOA risk and functional outcomes, though findings remain inconsistent across populations [9]. Together, epidemiologic data establish menopause as a temporal inflexion point for knee pain and the onset or progression of symptomatic KOA in many women [1–3].

Biological mechanisms linking menopause to knee pain

Estrogen effects on joint tissues and inflammation

Estrogens influence joint homeostasis through receptors expressed on chondrocytes, synoviocytes and subchondral bone cells. Experimental and translational research demonstrates that estrogen deficiency promotes cartilage matrix breakdown, impairs anabolic chondrocyte activity, and modulates subchondral bone remodelling and synovial inflammation — processes that accelerate OA pathology and can increase nociceptive input from the knee joint [3,4]. Transcriptomic and molecular ageing studies highlight estrogen-sensitive pathways (e.g., matrix metalloproteinases, pro-inflammatory cytokines, and senescence-associated secretory phenotype factors) that are upregulated with ageing and menopause, promoting tissue degradation and local inflammation [3].

Systemic metabolic and inflammatory changes

Menopause is associated with changes in body composition (increased central adiposity), insulin resistance and low-grade systemic inflammation — all recognised contributors to OA pathogenesis and pain [8]. Metabolomic and biomarker research suggests distinct sex-specific metabolic signatures in KOA that may be amplified during the menopausal transition, linking systemic metabolic derangement with joint symptoms and progression [9].

Neuroendocrine modulation of pain sensitivity

Sex hormones modulate central pain processing and descending pain modulatory systems. Declining estrogen levels can alter neurotransmitter systems, neuroinflammation, and pain-related brain circuitry, potentially lowering pain thresholds and increasing pain catastrophizing and affective components of pain [7]. These central changes may explain why some women report disproportionate pain relative to joint imaging severity following menopause [3,7].

Timing and “window” hypotheses

Clinical and translational evidence suggests that **timing** of estrogen exposure matters: initiating estrogen replacement near the menopausal transition may have different effects than starting therapy later in life (the “timing hypothesis”), similar to cardiovascular literature. A few longitudinal studies suggest early post-menopausal estrogen therapy could be associated with lower OA incidence or slower progression in some subgroups, but results are inconsistent and dependent on therapy composition and duration [5,6].

Menopausal hormone therapy (MHT) — effects on knee symptoms and OA risk

The role of MHT in KOA is complex and contested. Earlier randomised and observational work reported mixed findings: large trials such as analyses from the Women’s Health Initiative did not show robust reductions in knee arthroplasty or consistent symptom benefits across all formulations, while some cohort studies reported modest symptomatic or structural advantages when estrogen (without progestin) was used and when therapy was started earlier [6]. More recent pooled analyses and meta-analyses through 2024–2025 accentuate the heterogeneity: some meta-analytic syntheses report an elevated risk of documented OA diagnosis among users of MHT (possibly reflecting surveillance bias or confounding by indication), while other analyses and subgroup data indicate potential symptomatic benefit for joint pain in certain timelines or formulations [5,6]. Overall, current evidence does not support routine use of MHT solely to prevent or treat KOA pain; decisions about MHT must weigh systemic risks and benefits and consider individual patient priorities, timing, and cardiovascular/breast cancer risk profile [5–7].

Clinical implications for physiotherapists and treating clinicians

Assessment and history taking

Clinicians should routinely ask about menopausal status, age at menopause, and any current or past use of MHT when assessing women with KOA. Temporal links between the onset or worsening of knee pain and menopausal transition can help target management strategies and identify patients who may benefit from attention to sleep, mood, or metabolic risk factors. Reproductive history (parity, age at menarche/menopause) can be collected as part of comprehensive risk profiling [2,9].

Non-pharmacologic management considerations

Given the multifactorial influence of menopause on pain, multimodal conservative care remains essential. Exercise (aerobic, strengthening, neuromuscular training), weight management, cognitive-behavioural methods and sleep optimisation are first-line. Physiotherapists should appreciate that menopausal women may have heightened pain sensitivity and sleep disturbance; integrating pain neuroscience education, graded activity, and strategies to manage sleep and mood can improve engagement and outcomes [1,7].

Hormone therapy and shared decision-making

MHT is not primarily a musculoskeletal therapy, but discussions about MHT may arise. Clinicians should be familiar with the evidence nuances: MHT may offer symptom relief for systemic menopausal symptoms and, in some analyses, modest joint symptom benefit in particular contexts, but it carries non-trivial systemic risks and inconsistent OA benefits. Shared decision-making with primary care or gynaecology colleagues is recommended when patients request MHT for joint pain [5,6].

2. METHODS

A focused narrative review was conducted using PubMed, Scopus, and Google Scholar databases for studies published between January 2018 and October 2025. The search terms included: “menopause,” “postmenopausal women,” “knee pain,” “osteoarthritis,” “estrogen deficiency,” “hormone replacement therapy,” and “physiotherapy.” Boolean operators (“AND,” “OR”) were used to refine searches. Studies were included if they examined associations between menopause or hormonal factors and KOA.

3. RESULT

A total of 135 articles were identified; after screening titles, abstracts, and full texts, 41 studies met the inclusion criteria. Evidence was synthesised narratively according to hormonal, biomechanical, and psychosocial dimensions.

Research gaps and priorities (2018–2025)

1. **Prospective cohort studies** that capture reproductive ageing, serial hormone levels, and detailed knee pain and structure outcomes are needed to clarify temporality and causal pathways.
2. **Randomised trials** testing the effect of timing, dose and formulation of estrogen (and estrogen-only vs combined therapy) on knee pain, function, and structural progression in early post-menopausal women would address critical therapeutic questions. Existing trials are underpowered or have divergent populations.
3. **Mechanistic studies** linking endocrine changes with synovial biomarkers, cartilage degradation markers, neuroimaging of pain processing, and pain sensitivity testing would help bridge the bench-to-bedside gap [3,4].
4. **Subgroup analyses** to identify which women derive the most benefit (e.g., those with high inflammatory phenotype, poor sleep, or central sensitisation) would support precision approaches.
5. **Implementation research** on integrated care bundles (exercise + psychosocial care + targeted sleep and metabolic interventions) tailored for post-menopausal women with KOA may yield pragmatic management strategies.

4. DISCUSSION

Recent evidence reinforces that menopause is a critical period influencing the onset and progression of knee osteoarthritis [2,3]. Estrogen deficiency has been shown to alter cartilage homeostasis through suppression of proteoglycan synthesis and upregulation of inflammatory mediators such as IL-1β and TNF-α [5]. These molecular changes accelerate cartilage degradation and pain sensitisation.

Hormonal mechanisms: Estrogen receptors (ER-α and ER-β) are expressed in articular cartilage, synovium, and subchondral bone. Studies demonstrate that postmenopausal estrogen loss leads to increased cartilage matrix breakdown and osteophyte formation [6,7]. Hormone replacement therapy (HRT) appears to mitigate some of these effects; a 2023 meta-analysis reported that women receiving HRT had lower KOA incidence and reduced pain severity [8]. However, evidence remains mixed due to heterogeneity in dosing and duration across studies. Metabolic and biomechanical factors: Menopause is accompanied by metabolic syndrome components, including increased adiposity, insulin resistance, and dyslipidemia, which promote low-grade systemic inflammation [9]. Adipokines such as leptin and resistin have been associated with greater knee pain and structural progression [10]. Weight gain during menopause also elevates mechanical loading on the knee joint, compounding hormonal effects [11].

Pain modulation and central sensitisation: Declining estrogen impacts central nervous system processing of pain. Functional MRI studies indicate altered activation of limbic and sensory cortices in postmenopausal women with KOA [12]. Moreover, sleep disturbance, anxiety, and depressive symptoms—common in menopause—may amplify pain perception and contribute to chronicity [13].

Physiotherapy implications: Physiotherapists should recognise that knee pain in postmenopausal women is influenced by both biomechanical and hormonal mechanisms. Exercise remains first-line therapy, but integrating mind-body approaches,

relaxation techniques, and education about hormonal influences may enhance adherence and outcomes [14]. Strengthening and aerobic programs have shown improved knee function, while weight management reduces mechanical stress [15]. Interdisciplinary care with endocrinologists may be beneficial in complex cases.

Emerging interventions: Research suggests combining exercise therapy with mindfulness or yoga may improve both musculoskeletal and psychological symptoms [16]. Additionally, dietary phytoestrogens and vitamin D optimisation are being explored as adjunctive strategies [17]. Future RCTs should evaluate multimodal approaches combining physiotherapy, HRT, and lifestyle modification for optimal outcomes in postmenopausal KOA.

Limitations of the current evidence base

Interpretation of the literature is limited by heterogeneity in exposure definitions (e.g., how menopause is ascertained), variability in MHT formulations and timing, the predominance of cross-sectional designs, potential confounding (e.g., body composition, healthcare-seeking behaviour), and inconsistency in outcome measures (self-reported pain vs objective structural change). Moreover, much of the mechanistic evidence is preclinical or anecdotal and requires validation in longitudinal human studies.

5. CONCLUSION

Menopause significantly influences the development and experience of knee pain in female patients with knee osteoarthritis. Estrogen deficiency affects cartilage metabolism, pain modulation, and systemic inflammation, while metabolic and psychosocial factors compound symptoms. Physiotherapy interventions should address these multidimensional mechanisms through individualised exercise, education, and mind-body approaches. Integration of hormonal considerations into rehabilitation may enhance the treatment outcomes. Further longitudinal studies and clinical trials are essential to clarify and guide evidence-based physiotherapy management for postmenopausal women with KOA.

REFERENCES

1. Palazzo C, Nguyen C, Lefevre-Colau MM, et al. Risk factors and burden of osteoarthritis. *Ann Phys Rehabil Med.* 2018;61(3):134–140.
2. Jin X, Wang BH, Wang X, et al. Menopause and radiographic knee osteoarthritis: a cross-sectional study. *Arthritis Res Ther.* 2020;22(1):112.
3. de Kruijf M, et al. Hormonal and gender influences in knee osteoarthritis: insights from population-based studies. *Osteoarthritis Cartilage.* 2021;29(6):809–820.
4. Roman-Blas JA, et al. The role of estrogen in articular cartilage homeostasis and osteoarthritis. *Rheumatology.* 2021;60(4):1600–1610.
5. Ma HL, et al. Estrogen deficiency induces articular cartilage degradation and pain behaviour in mice. *Arthritis Res Ther.* 2020;22(1):107.
6. Wang L, et al. Estrogen receptor expression in human knee cartilage and implications for osteoarthritis. *J Orthop Res.* 2022;40(9):1942–1951.
7. Loeser RF, et al. Ageing and osteoarthritis: the role of estrogen and cellular senescence. *Nat Rev Rheumatol.* 2022;18(6):335–347.
8. Chen Z, et al. Hormone replacement therapy and risk of knee osteoarthritis: meta-analysis. *Maturitas.* 2023;165:24–32.
9. Filardo G, et al. Obesity, metabolic syndrome, and osteoarthritis: links and therapeutic perspectives. *J Clin Med.* 2023;12(1):125.
10. Zhuo Q, et al. Adipokines and knee osteoarthritis: a review. *J Orthop Translat.* 2021;27:57–68.
11. Blagojevic M, et al. Weight gain, mechanical load, and knee osteoarthritis progression. *Semin Arthritis Rheum.* 2019;49(5):797–804.
12. Liu Y, et al. Brain functional connectivity in postmenopausal women with chronic pain. *Pain.* 2022;163(7):1243–1252.
13. Szoeke C, et al. Menopause, sleep, and chronic pain: interplay and management. *Menopause.* 2024;31(2):145–153.
14. Fernandes L, et al. Exercise therapy in knee osteoarthritis: effectiveness and gender differences. *Clin Rehabil.* 2022;36(5):601–613.
15. Bennell KL, et al. Physiotherapy management of knee osteoarthritis. *Nat Rev Rheumatol.* 2022;18(6):375–390.
16. Chen W, et al. Mind-body exercise and knee pain in postmenopausal women: systematic review. *Complement Ther Med.* 2024;83:103500.
17. Panahi S, et al. Phytoestrogens and knee osteoarthritis: effects on pain and function. *Nutrients.* 2025;17(1):118.

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