

SYSTEMATIC REVIEW

Navigating the neglected transition: menopause care disparities in Pakistan and South Asia across a multidimensional framework of risk, stigma, and therapeutic innovation

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Abstract

Menopause is a universal physiological transition yet one of the most inequitably managed health events globally. In Pakistan and South Asia, women entering menopause face structural healthcare gaps, cultural barriers to care-seeking, provider knowledge deficits, and limited policy attention. With a mean age at natural menopause of approximately 47 years, Pakistani women experience a prolonged postmenopausal period that may amplify cardiovascular, skeletal, and metabolic risks; however, formal menopause care remains available to only a minority of symptomatic women. This narrative review was conducted according to the Scale for the Assessment of Narrative Review Articles (SANRA) framework. Literature searches were performed in PubMed, EMBASE, Scopus, and Google Scholar from 1990 through March 2025. Thirty-five references meeting predefined inclusion criteria were included. The review synthesizes evidence across six domains: vasomotor symptom epidemiology, menopausal hormone therapy (MHT) controversies, cardiovascular risk, osteoporosis burden, sociocultural barriers, and non-hormonal and digital therapeutic approaches. Vasomotor symptom prevalence in South Asian women is comparable to Western estimates of 50 to 74 percent, yet treatment uptake remains low. Postmenopausal osteoporosis affects 20 to 49 percent of Pakistani women, with a substantial burden of osteoporotic fractures. Pakistan also reports a comparatively elevated age-standardized ischemic heart disease mortality-to-prevalence ratio among women, although this finding requires cautious interpretation given heterogeneity in regional datasets. MHT prescribing is influenced by persistent concerns following the Women's Health Initiative findings, despite evidence supporting its safety when initiated within the appropriate timing window. Fezolinetant and investigational elinzanetant represent emerging non-hormonal options; however, equitable access in LMICs remains unresolved. Pakistan's Lady Health Worker network and digital platforms such as DoctHERS represent potential pathways for community outreach. Addressing this gap requires coordinated action across policy, clinical training, community engagement, and digital health infrastructure.

Keywords: Menopause, vasomotor symptoms, Pakistan, South Asia, hormone therapy, osteoporosis, cardiovascular disease, fezolinetant, telemedicine, low- and middle-income countries.

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Introduction

By 2030, more than one billion women worldwide will be postmenopausal, with the majority living in low- and middle-income countries (LMICs), where clinical, cultural, and structural conditions for managing this transition remain underdeveloped [1]. Pakistan, the world's fifth most populous country, exemplifies this gap. The country has a rapidly expanding population of women experiencing midlife biological changes in the context of limited systematic clinical support, earlier mean age at menopause, increased skeletal risk, higher cardiovascular mortality among women, and cultural barriers that discourage care-seeking throughout this stage of life.

Existing reviews of menopause in LMICs either consider South Asia as a homogeneous epidemiological entity without Pakistan-specific granularity or address isolated dimensions of the problem. This narrative review, conducted in accordance with the Scale for the Assessment of Narrative Review Articles (SANRA) framework, provides an integrated, evidence-based analysis across six domains: vasomotor symptom epidemiology; menopausal hormone therapy (MHT) controversies; cardiovascular risk; osteoporosis burden; sociocultural barriers; and emerging non-hormonal and digital therapeutic approaches.

Methods

This narrative review was conducted and reported in accordance with the Scale for the Assessment of Narrative Review Articles (SANRA), a validated six-item quality framework for narrative reviews that evaluates justification of the review, literature search, referencing, scientific reasoning, and appropriate presentation of data [2]. No systematic review registration was undertaken because this was a narrative review; however, the search strategy and selection process are described transparently below to support reproducibility.

PubMed, EMBASE, Scopus, and Google Scholar were searched from 1990 through March 2025. Primary search terms included menopause, perimenopause, vasomotor symptoms, hot flushes, hormone therapy, menopausal hormone therapy, osteoporosis, cardiovascular disease, South Asia, Pakistan, India, Bangladesh, fezolinetant, elinzanetant, neurokinin receptor antagonists, telemedicine, digital health, Lady Health Workers, cultural barriers, and low- and middle-income countries. Boolean operators (AND, OR) were used to construct targeted search strings. In addition, reference lists of retrieved articles and grey literature sources, including position statements from the North American Menopause Society (NAMS), the Asia-Pacific Menopause Federation (APMF), and WHO, were hand-searched.

Inclusion criteria: peer-reviewed original studies, systematic reviews, meta-analyses, and evidence-based position statements addressing menopause-related outcomes in South Asian or LMIC populations, or providing globally applicable clinical evidence relevant to the scope of this review. Exclusion criteria: conference abstracts without peer-reviewed full text, case reports including fewer than five subjects, and non-English publications without available translation. No formal quality assessment tool was applied, consistent with standard narrative review methodology; however, preference was given to systematic reviews, meta-analyses, and position statements over single-center studies when synthesizing clinical recommendations. A total of 35 references meeting these criteria are cited. This review involved no primary data collection and no human subjects research; therefore, institutional review board approval was not applicable.

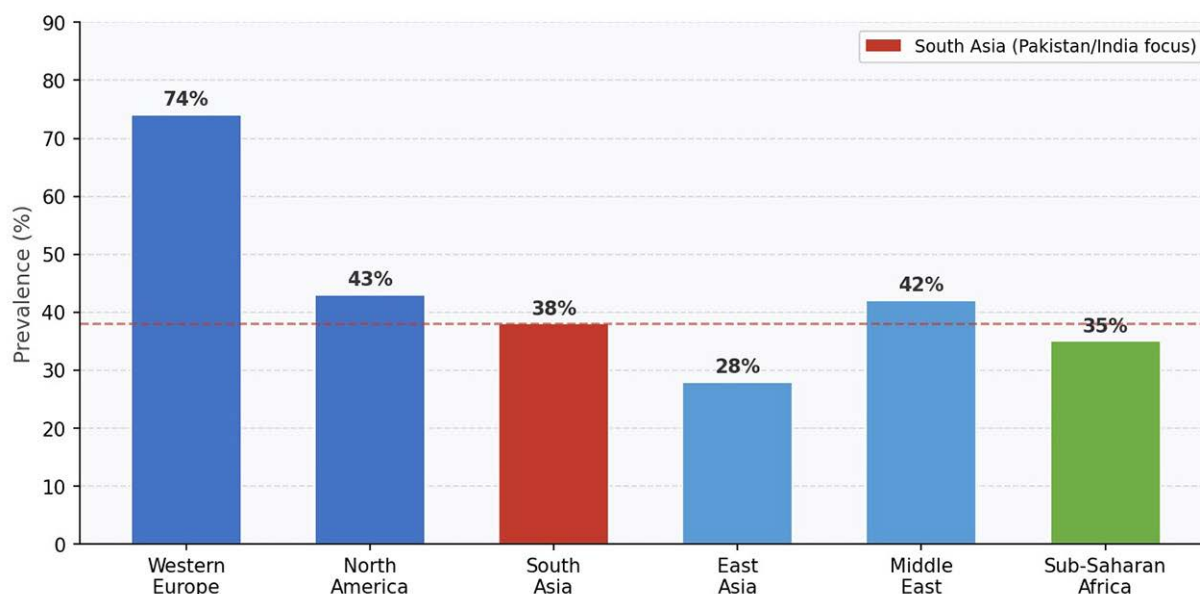
Vasomotor symptoms: comparable burden, insufficient response

Hot flushes and night sweats, collectively termed vasomotor symptoms (VMS), affect 70 to 80 percent of women undergoing natural menopause globally, with moderate-to-severe intensity in approximately 25 percent [3]. Their median duration is seven to ten years. The physiological basis lies in estrogen withdrawal disrupting hypothalamic thermoregulation through overstimulation of kisspeptin/neurokinin B/dynorphin (KNDy) neurons in the hypothalamic infundibular nucleus, a mechanism now targeted directly by the neurokinin-3 receptor antagonists.

A systematic review of 43 studies including 31,945 women found that VMS prevalence in South Asia was comparable to that reported in Western populations when studies used random sampling methods and validated questionnaires [4]. A global meta-analysis of 321 studies involving 482,067 women confirmed that prevalence among Asian women ranged from 22 to 63 percent, with substantial overlap with estimates

from North American and European populations [5]. In Pakistan, women more commonly report somatic symptoms, including lethargy, palpitations, and joint aches, rather than the classical heat-and-sweat profile, a pattern attributed to limited culturally specific terminology for describing vasomotor complaints [6]. A global cross-sectional survey demonstrated that moderate-to-severe VMS is associated with significant impairment in work productivity and daily activities [7].

Figure 1. Prevalence of Vasomotor Symptoms (VMS) by Region in Peri- and Postmenopausal Women.



Menopausal hormone therapy (MHT): evidence and access

MHT remains the most effective treatment for VMS and is the first-line recommendation of major international guidelines for appropriately selected women [8]. Its benefits include reduction of VMS, prevention of postmenopausal bone loss, improvement of genitourinary symptoms, and potential benefits on mood disturbances [9]. The 2002 Women's Health Initiative (WHI) trial generated persistent physician concerns that continue to influence MHT use in LMICs, where subsequent evidence from age- and time-since-menopause-specific analyses has disseminated slowly. Importantly, the WHI enrolled women with a mean age of 63 years, most of whom were more than ten years postmenopausal and had pre-existing cardiometabolic risk factors; extrapolating these findings to younger, recently menopausal women is not supported by current evidence.

The "Timing Hypothesis", endorsed by multiple international bodies, establishes that women initiating MHT within ten years of their final menstrual period or before age 60 have a more favorable cardiovascular risk-benefit profile [10]. A meta-analysis of randomized controlled trials confirmed a reduced risk of coronary heart disease among early initiators [10]. Transdermal estradiol formulations are preferred when cardiometabolic or thrombotic risk is a concern, as they avoid the hepatic first-pass metabolism associated with the prothrombotic effects of oral conjugated equine estrogen [11]. It is important to note that combined estrogen-progestogen therapy is associated with a modest increase in breast cancer risk with prolonged use; therefore, regimen selection and duration should be individualized after a thorough benefit-risk discussion.

A study of MHT prescribing practices among Pakistani obstetricians and gynecologists published in 2023 identified knowledge gaps and cultural hesitancy as primary drivers of conservative prescribing. MHT was offered mainly for hot flushes and vaginal dryness and was rarely prescribed for osteoporosis prevention or metabolic indications [12]. The APMF 2024 Consensus Statement supports MHT use in symptomatic women within the appropriate age and risk window and specifically identifies premature ovarian insufficiency (POI) and early menopause as conditions requiring MHT at least until the average age of natural menopause [11]. No national menopause guideline currently exists in Pakistan.

Cardiovascular risk after menopause in Pakistan

Estrogen withdrawal initiates a cascade of adverse cardiometabolic changes, including accelerated visceral adiposity, atherogenic dyslipidemia, impaired insulin sensitivity, vascular endothelial dysfunction, and arterial stiffening [13]. In the South Asian context, Pakistan has a comparatively elevated age-standardized ischemic heart disease (IHD) mortality-to-prevalence ratio among women relative to men, as reported in a cross-country analysis by Khalid et al. [14]. The authors noted that these findings should be interpreted cautiously given heterogeneity in national disease registries, differences in data quality across South Asian datasets, and the ecological nature of country-level comparisons; nonetheless, the results are consistent with data from Pakistan's tertiary cardiac hospital network [15].

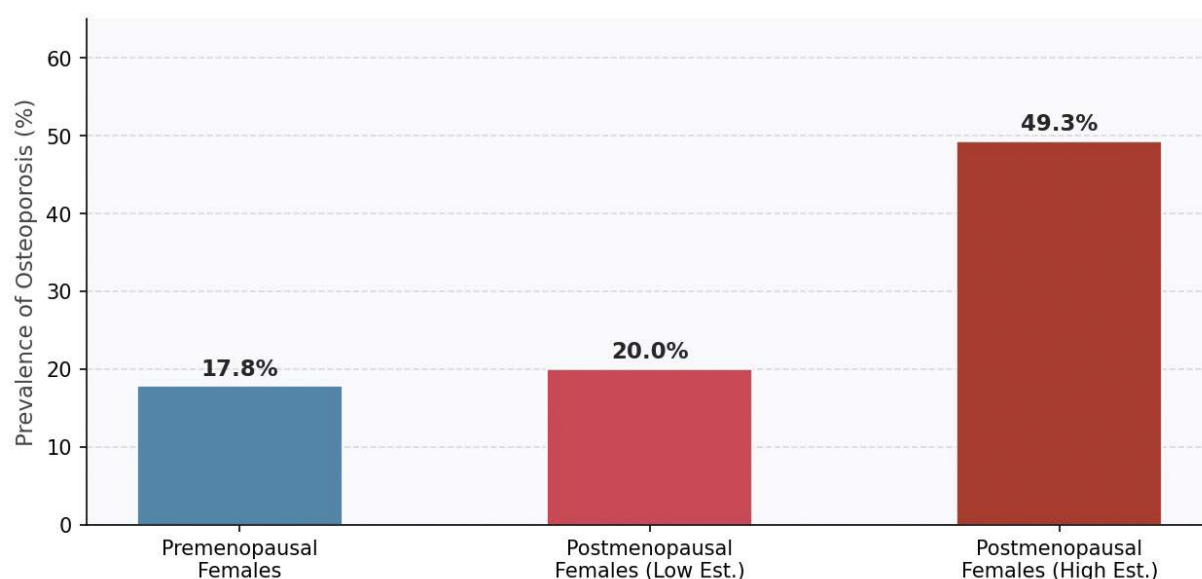
These patterns reflect delayed care-seeking and atypical symptom presentation among women, both of which are amplified by the cultural barriers described in later sections. A meta-analysis of randomized controlled trials confirmed that the cardiovascular benefit of MHT is dependent on the timing of initiation [10]. The menopausal consultation therefore represents an opportunity for cardiovascular risk assessment, incorporating blood pressure measurement, fasting lipid profile, and glycemic evaluation, rather than serving solely as a symptom-relief encounter.

Osteoporosis and fragility fracture

The Global Burden of Disease 2021 analysis confirmed that low bone mineral density contributed to 219,552 deaths and 7.76 million disability-adjusted life years (DALYs) among postmenopausal women globally, with South Asia bearing the greatest absolute burden [16]. In Pakistan, hospital-based studies have documented osteoporosis in 20 to 49.3 percent of postmenopausal women and osteopenia in 34 to 72.9 percent [17]. An analysis from Faisalabad estimated 9.91 million current osteoporotic fractures in Pakistan, with projections reaching 12.91 million by 2050 [18].

Contributing factors include widespread vitamin D deficiency associated with limited sun exposure related to veiling practices, inadequate dietary calcium intake, high parity, early menopause, and low physical activity [19]. Dual-energy X-ray absorptiometry (DEXA), the diagnostic gold standard, is available only in a limited number of tertiary hospitals and remains prohibitively expensive for many Pakistani women. The FRAX fracture risk assessment tool, which estimates fracture probability using clinical risk factors without requiring DEXA, represents a feasible screening strategy at the primary care level but has not yet been incorporated into any Pakistani care protocol [17]. A national survey found that awareness of osteoporosis as a menopause-related complication was absent among a substantial proportion of Pakistani women surveyed [20].

Figure 2. Osteoporosis Prevalence in Pakistani Women by Menopausal Status (Range from Published Studies).



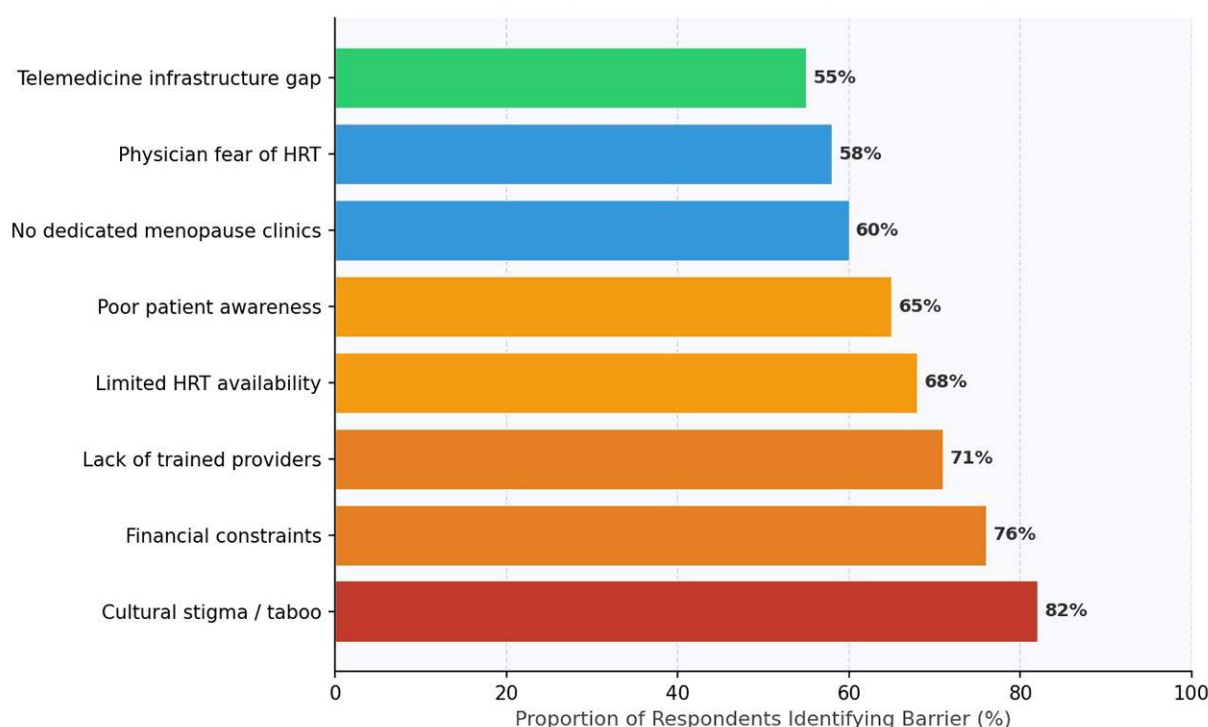
Source: Khan et al., 2018 (Ann Med Surg); Population-based studies, Pakistan

Cultural myths, stigma, and barriers to care

More than 80 percent of women with significant menopausal symptoms globally never seek formal medical attention; cultural stigma is among the most consistently identified contributing factors [21]. In Pakistan, menopause intersects with deeply embedded social taboos surrounding aging, female sexuality, and reproductive identity. Among South Asian women, including those living in diaspora settings, menopause has been described as shameful or embarrassing to discuss, even with female healthcare providers [22]. A grounded theory study of immigrant Muslim women in the United Kingdom found that misconceptions about MHT were a primary driver of treatment hesitancy; however, culturally responsive counseling resulted in significant symptom relief and retrospective recognition of delayed care [23].

Specific myths requiring targeted counter-messaging include the belief that MHT causes breast cancer, a misconception reinforced by distorted media interpretations of the WHI findings; that menopausal symptoms are spiritual in origin; and that discussing hormonal health with a male physician is culturally impermissible [24]. A cross-sectional study at Ziauddin University Hospital, Karachi, found that women from lower socioeconomic groups were significantly more likely to hold misconceptions, and 22 percent were unaware of any association between menopause and osteoporosis [24]. Pakistan's Lady Health Worker (LHW) program deploys more than 100,000 trained female health workers to rural and peri-urban households; expanding their mandate to include menopause literacy, basic symptom screening, and telehealth referral pathways is a structurally feasible and potentially cost-effective strategy.

Figure 3. Key Barriers to Menopause Healthcare in South Asia (Composite Data from Regional Surveys).



Non-hormonal therapies

Established pharmacological options

Given the widespread barriers to MHT use in Pakistan, non-hormonal therapies occupy a position of particular strategic importance. The NAMS 2023 Non-Hormone Therapy Position Statement stratifies interventions according to evidence level [25]. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have Level I evidence; escitalopram and venlafaxine are available as generic medications in Pakistan at low cost. Meta-analyses confirm a 40 to 60 percent reduction in VMS frequency with these agents, which is inferior to MHT but clinically meaningful for women with contraindications to hormone therapy [25]. Gabapentin demonstrates comparable efficacy, particularly among women with comorbid sleep disturbances, and is available as a generic medication; however, dose-limiting

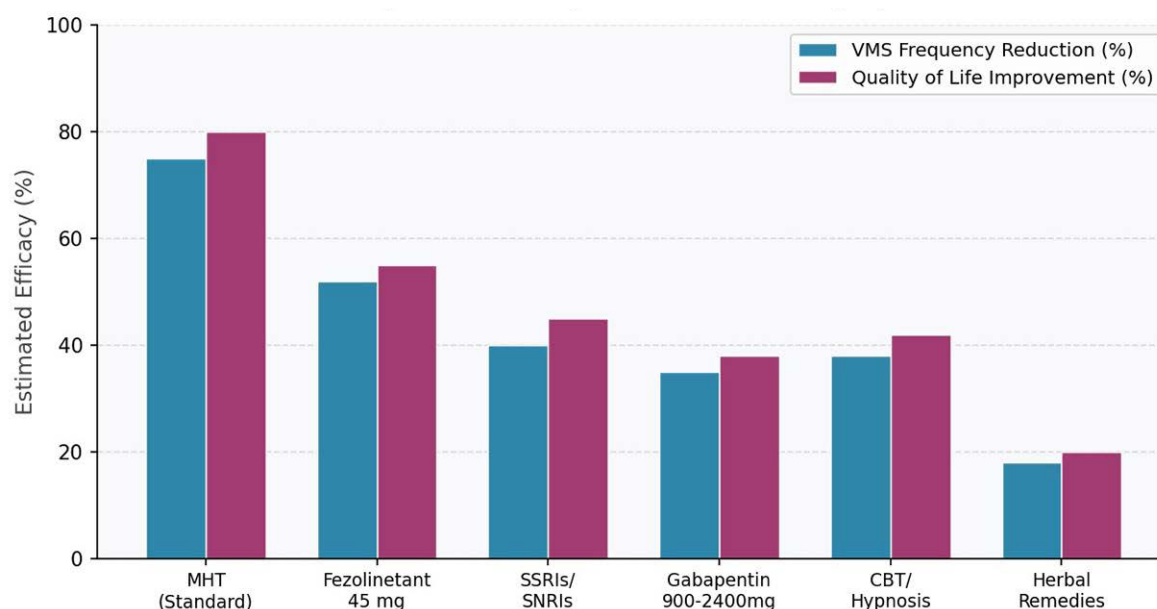
sedation at higher doses (900 to 2,400 mg daily) may restrict tolerability [25]. Cognitive behavioral therapy (CBT) and clinical hypnosis have Level I evidence and are scalable through digital delivery platforms [25].

Fezolinetant and elinzanetant: mechanistic advances

Fezolinetant (Veoza; Astellas Pharma, Tokyo, Japan), a selective neurokinin-3 (NK3) receptor antagonist, received US FDA approval in May 2023 at a dose of 45 mg once daily for the treatment of moderate-to-severe VMS [26]. The SKYLIGHT Phase 3 trials demonstrated statistically significant reductions in VMS frequency and severity from week four onward, with a favorable safety profile [26]. A 2024 network meta-analysis confirmed that fezolinetant 45 mg was statistically superior to all non-hormonal pharmacological comparators for reducing VMS frequency [27].

Elinzanetant (AstraZeneca, Cambridge, UK), a dual NK1/NK3 receptor antagonist, is currently under regulatory review and had not received FDA or EMA approval as of early 2025. It completed the OASIS Phase 3 program, demonstrating a 74 percent reduction in moderate-to-severe VMS at week 12 compared with placebo, with additional benefits on sleep and mood attributed to NK1 blockade [28]. Neither fezolinetant nor elinzanetant is currently registered or commercially available in Pakistan or other LMICs; current pricing in the United States may limit access without generic licensing or preferential procurement strategies. Advocacy for such pathways by South Asian medical societies represents an important global health equity objective.

Figure 4. Comparative Efficacy of Hormonal and Non-hormonal Therapies for Menopausal Vasomotor Symptoms.



Estimates based on NAMS 2023 Position Statement, Morga et al. 2024, and Lederman et al. 2023 (Lancet). MHT = Menopausal Hormone Therapy.

Telemedicine and digital health

Specialist gynecologists with expertise in menopause care are concentrated in a limited number of tertiary hospitals in Karachi, Lahore, Islamabad, and Peshawar, making access to care challenging for rural women who face substantial travel and financial burdens. Published systematic evidence supports telemedicine as a mechanism for expanding healthcare access in LMICs. A scoping review of telemedicine during the COVID-19 pandemic documented improved geographic reach and cost efficiency across South Asian settings, with infrastructure and regulatory barriers identified as the principal impediments [29]. A systematic umbrella review of 88 published reviews confirmed telemedicine as the most extensively studied digital health intervention in LMICs, with consistent evidence of improved healthcare delivery efficiency where specialist availability is limited [30].

In Pakistan, the Ministry of National Health Services has established a National Telemedicine Programme; private platforms including Oladoc, Marham, and DoctHERS have achieved meaningful penetration in urban and peri-urban markets. DoctHERS, which connects female patients with trained female physicians

through smartphone-based services, is of particular relevance to menopause care because it directly addresses cultural barriers related to access to male providers. According to publicly reported operational data from the platform, DoctHERS had facilitated more than 500,000 consultations by 2024.

To date, no peer-reviewed clinical study has evaluated telemedicine-delivered menopause care in Pakistani or South Asian populations; this represents a priority area for implementation research. None of the currently available Pakistani platforms includes a standardized menopause triage module or a validated Urdu-language symptom assessment tool. The following proposals are presented as evidence-informed opportunities requiring formal evaluation rather than established practice: integration of a structured menopause assessment and referral module into existing telehealth platforms; voice-based teleconsultation for women without smartphones; and SMS-delivered menopause health information in Urdu and regional languages [30].

Discussion

The evidence assembled in this review documents a substantial and multidimensional gap between the menopause-related health burden experienced by Pakistani and South Asian women and the clinical infrastructure available to address it. This gap reflects the combined effects of low policy priority, insufficient clinical training, entrenched cultural barriers, and inadequate diagnostic and therapeutic infrastructure.

Several methodological limitations of the available evidence should be acknowledged. The majority of Pakistani studies cited are hospital-based convenience samples from urban centers, principally Karachi, Lahore, and Hyderabad. Rural women, who constitute more than 60 percent of Pakistan's female population, are largely absent from the published evidence base. This geographic skew suggests that the burden estimates presented here may underestimate morbidity in the most underserved populations. Cross-country cardiovascular comparisons within South Asia are further constrained by heterogeneity in national disease registries and variable data quality and should therefore be interpreted with appropriate caution. As a narrative review, this work is subject to the inherent limitations of this methodology, including the potential for publication bias in the regional literature and the absence of formal quality assessment of included studies.

Research priorities arising from these gaps include nationally representative epidemiological studies of VMS prevalence and healthcare-seeking behavior in Pakistan; implementation trials of LHW-delivered menopause literacy programs; clinical evaluation of telemedicine-based menopause care in South Asian settings; and pharmacokinetic studies of fezolinetant and elinzanetant in South Asian women to determine whether data from Western trial populations can be extrapolated without qualification.

Policy-level actions supported by the evidence include the development of a national menopause health framework incorporating osteoporosis screening, cardiovascular risk reduction, and culturally adapted care; formal menopause training within medical curricula; expansion of the LHW program mandate to include menopause education and referral; a regulatory framework enabling teleconsultation-based prescribing; inclusion of oral bisphosphonates and generic SSRIs for menopausal indications in the national essential medicines list; and establishment of a South Asian menopause registry to generate the longitudinal outcome data currently lacking in the regional literature.

Conclusions

Pakistani women experience VMS at rates comparable to those reported in Western populations, face a substantial osteoporotic fracture burden, and have increased cardiovascular risk after menopause while navigating a cultural environment that may discourage care-seeking. Addressing these overlapping challenges requires coordinated action across policy, clinical training, community outreach, and digital health infrastructure. The emergence of novel non-hormonal therapies and the expansion of Pakistan's telemedicine sector represent important opportunities; translating these advances into equitable access for underserved South Asian women will require sustained institutional commitment. Future region-specific longitudinal research, including prospective cohort studies evaluating menopausal symptom trajectories, treatment uptake, and long-term cardiovascular and skeletal outcomes in Pakistani women, is essential to establish the evidence base needed for national policy reform.

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Conflict of interest statement

The author declares having no conflicts of interest.

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Ethics statement

This is a narrative review of published literature. No primary data collection, human subjects research, or clinical trial was conducted. Institutional review board approval is not applicable.

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