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Menopause and hormone replacement therapy: from diagnosis to follow-up.

Menopause and hormone replacement: from diagnosis to follow-up

Menopausia and hormonal replacement: from diagnosis to follow-up

Maria Antônia Pulu Campos da Cruz1
Rafaela Miriam Cardoso1
Rebecca Gomes Magalhães da Silva1
Maria Clara dos Santos Rodrigues1
Thais Santana de Oliveira 2

1-Student of Biomedicine at the Higher Education Institute of Brasília – IESB
2-Master's Professor of Biomedicine at the Higher Education Institute of Brasília - IESB

SUMMARY

Introduction: Menopause is a physiological event with multisystemic impact that requires Rigorous clinical monitoring. This study aimed to analyze, through an integrative literature review, the physiological aspects of menopause, the relevance of hormone replacement therapy (HRT), and the indispensable role of laboratory tests in safe diagnosis and monitoring. Methodology: The research involved a structured search in the PubMed, Google Scholar, and SciELO databases for articles published between 2020 and 2025, using descriptors combined with Boolean connectors, resulting in a final sample of 12 articles after rigorous screening. Results: The findings highlight Anti-Müllerian Hormone (AMH) as a superior and early biomarker of ovarian reserve in the face of severe FSH fluctuations.

It has been shown that HRT is highly effective in symptomatic relief and metabolic preservation, provided it is initiated within the ten-year "window of opportunity" and preferably administered transdermally in combination with micronized progesterone, mitigating vascular and thromboembolic risks. Final Considerations: Menopause constitutes a critical window for the primary prevention of chronic diseases, with laboratory monitoring being the fundamental pillar for the safety and individualization of treatment. In this scenario, the biomedical professional plays an indispensable role in ensuring the excellence and analytical accuracy of the reports, enabling an assertive therapeutic approach focused on promoting healthy female aging.

Descriptors: *Menopause, Hormone Replacement Therapy, Biomarkers, FSH, Estradiol.*

1 INTRODUCTION

Menopause is a physiological event that marks the end of reproductive life and, given the With increasing female longevity, it represents a period in which women will live, on average, a third longer. of their life (Gatenby; Simpson, 2024). In this context, the implementation of a follow-up Rigorous laboratory testing and individualized therapeutic strategies are essential to mitigate the Systemic impacts of estrogen deprivation. Measures such as continuous hormone monitoring, The assessment of the metabolic profile and the safe indication of hormone replacement therapy can... significantly reduce the risks of chronic diseases. In addition to promoting physiological balance, These practices improve quality of life and reduce complications and damage caused by... comorbidities associated with menopause (Flores; Pal; Manson, 2021).

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From a clinical perspective, this natural stage of the female life cycle is marked by definitive interruption of menstruation and cessation of ovarian function, resulting from failure. The progressive shrinking of follicles and the consequent reduction in estrogen and progesterone levels. This The process, which generally occurs between the ages of 45 and 55, is associated with an increase. compensatory increase in serum concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) (Faubion et al., 2022). These hormonal changes cause a variety of manifestations, symptoms such as hot flashes, night sweats, mood swings, insomnia, genitourinary syndrome Menopause (MGS) and loss of bone mineral density. In addition to the immediate symptoms, the Hypoestrogenism promotes the development of osteoporosis and metabolic dysfunctions. cardiovascular, making menopause a critical public health issue (Gatenby; Simpson, 2024).

Although the diagnosis has established clinical criteria, laboratory evaluation plays an essential role both in confirming the transition to menopause and in differential diagnosis. Hormonal tests, such as FSH and estradiol (E2) levels, are widely used to confirm the menopausal state, the condition being characterized by A significant elevation of FSH associated with estradiol levels below the reference limit for the reproductive phase (Moolhuijsen; Visser, 2020). More recently, the anti-Müllerian hormone (AMH) has emerged as a promising and highly accurate marker of ovarian reserve. While directly reflecting the number of antral follicles, AMH allows for an estimation of the remaining time until... menopause, assisting in clinical planning (Gunasheela et al., 2021).

Given these physiological changes, hormone replacement therapy (HRT) constitutes the primary therapeutic resource for managing symptoms and preventing resulting complications of estrogen deficiency. Studies show that therapy, when initiated in the so-called "window" "Opportunity," in younger women and those nearing the onset of menopause, may reduce Cardiovascular events and prevent bone loss (Nelson et al., 2023). HRT can be administered via different routes (oral, transdermal, or vaginal), and the regimens vary according to the The anatomical and clinical needs of each patient may include estrogen alone or a combination of both. combination of estrogen and progesterone (Flores; Pal; Manson, 2021).

However, to ensure the patient's safety, the treatment must be rigorously followed. Individualized and monitored, since there are described risks of venous thromboembolism and of metabolic dysfunctions. In this scenario, continuous laboratory monitoring becomes indispensable. In addition to the hormonal profile, complementary tests, such as the lipid profile and the Fasting blood glucose levels are fundamental for screening for metabolic changes and resistance to... Insulin. Simultaneously, bone densitometry (DXA) and liver function tests are evaluated.

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Thyroid monitoring ensures accurate risk stratification, allowing for safe control of side effects.
systemic effects during hormonal intervention (Lee; Hanevik, 2022).

In this context, the aim of this work was to analyze, through an integrative review of literature, the physiological aspects of menopause and the relevance of hormone replacement therapy, addressing the indispensable role of laboratory tests in the diagnosis of ovarian failure both in clinical follow-up and in the safe monitoring of women's health during menopause.

2 METHODOLOGY

This study consisted of an integrative literature review, with the aim of gathering...
scientific evidence on the physiological aspects of menopause and the importance of therapy Hormone replacement therapy (HRT), highlighting the indispensable role of laboratory tests in diagnosis of ovarian failure and monitoring of women's health. To ensure a
The organized approach to the research followed essential methodological steps, such as: Formulating the guiding question, defining the inclusion and exclusion criteria, and selecting articles in scientific databases and the analysis of the most relevant information for the synthesis of knowledge.

The literature review took place from August 2025 to May 2026, with a search Structured using the PubMed, Google Scholar, and SciELO databases, without language restrictions. selecting articles published between 2020 and 2025. The following descriptors were used, obtained Based on a search in the Health Sciences Descriptors (DeCS): "Menopause", "Hormone Replacement Therapy", "Biomarkers", "FSH", "Estradiol" and "Laboratory Monitoring", combined using the Boolean connectors AND/OR. The following structured searches were performed: "Menopause" AND "Hormone Replacement Therapy", "FSH" AND "Estradiol", "Menopause" AND "Biomarkers", "Hormone Replacement Therapy" AND "Laboratory Monitoring".

The inclusion criteria adopted were: articles published in the last five years (2020 to 2020). 2025), available in full and free of charge, that addressed the laboratory diagnosis of menopause, the indication for HRT, and the monitoring of hormonal, metabolic, and biomarkers. safety. Studies that provided relevant information on the interpretation were prioritized. clinical aspects of tests (such as FSH, estradiol, and AMH) and the prevention of cardiovascular risks and of osteoporosis during treatment.

The exclusion criteria considered were: duplicate studies or studies without access to the text. Complete for reading and analysis; studies conducted exclusively with animal models; and articles. that did not present clear methodological criteria or that did not have a direct relationship with the

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Laboratory monitoring during menopause.

3 RESULTS

Based on a structured search conducted in the Google Scholar, PubMed and databases SciELO identified 752 studies in the initial sample. In a first screening, 282 articles were found. 102 were excluded due to duplication and 180 due to non-compliant publication formats. adhering to the inclusion criteria, such as editorials, letters to the editor, conference abstracts and book chapters. After screening titles and abstracts, a further 425 were excluded. work due to divergent populations (145), experimental studies with animals (20) and to deviation from the proposed theme (260). Thus, 45 articles were selected for the eligibility stage. After a full reading, 33 were discarded for not meeting the objectives or for lack of... laboratory correlation. In this way, a final sample of 12 articles was consolidated to compose the corpus of analysis for this review (Figure 1).

Figure 1 - Article selection flowchart, 2026.

(Source: prepared by the author, 2026)

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To systematize the findings and facilitate the understanding of the data extracted from the final sample, The information from each study was organized descriptively. Table 1 presents the...
A summary of the 12 articles that make up this review, detailing the authorship, year of publication, and title. from the study and the main results and conclusions. The extraction of this data prioritized the evidence. related to laboratory diagnosis (such as the use of FSH, estradiol, and AMH), and current guidelines. for Hormone Replacement Therapy (HRT) and its impact on metabolic monitoring and cardiovascular disease in patients.

Table 1 - Summary of articles included in the review.

Author(s)	Year Title GATENBY; 2024		Results
SIMPSON		Menopause: Physiology, definitions, and symptoms	The mechanisms of follicular depletion are primary causes of the drop in estradiol and inhibin, resulting in elevated FSH, which is the definitive laboratory marker for the diagnosis and classification of menopausal transition stages.
KAN *et al.*	2024	The impact of female sex hormones on cardiovascular disease: from mechanisms to hormone therapy	The direct impact of estrogen deprivation on endothelial health positions menopausal hormonal fluctuations as an independent cardiovascular risk factor requiring rigorous clinical monitoring for disease prevention.
OLIVEIRA *et al.*	2024	Brazilian Health Guidelines Cardiovascular Menopause and in Menopause – 2024	The neutrality of HRT on blood pressure and the reinforcement of its cardiovascular safety in Brazilian women, provided it is started early and accompanied by rigorous control of metabolic risk factors during menopause.
PASCHOU *et al.*	2024	Menopausal Hormone Therapy in Women with Type 2 Diabetes Mellitus: An Updated Review	The metabolic benefits of HRT, such as improved insulin sensitivity and glycemic control, offer an important adjunctive strategy for managing and reducing the risk of type 2 diabetes in postmenopausal women.
CHO *et al.*	2023	Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long?	A reassessment of HRT is needed in modern cardiology, highlighting that current formulations and lower doses offer greater vascular safety, provided that eligibility criteria and the time of initiation after the last menstrual period are respected.
KAWAKITA *et al.*	2023	Associations of LH and FSH with reproductive hormones depend	The significant correlation between androgen levels and variations in LH and FSH during menopause demonstrates that the behavior of these...

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		on each stage of the menopausal transition.	Gonadotropin levels vary at each stage of the transition and require careful laboratory interpretation.
NELSON *et al.*	2023	Anti-Müllerian hormone for the diagnosis and prediction of menopause: a systematic review	The high diagnostic accuracy of AMH in predicting the age of definitive menopause serves as a strategic tool for both reproductive planning and the anticipation of preventive care related to ovarian failure.
FAUBION *et al.*	2022	The 2022 hormone therapy position statement of The North American Menopause Society	Hormone Replacement Therapy (HRT) is established as the gold standard for relieving vasomotor symptoms and preventing bone loss, presenting a largely favorable risk-benefit profile for healthy women under 60 years of age.
VIGNESWARAN; HAMODA	2022	Hormone replacement therapy – Current recommendations	The importance of individualized therapy in menopause, with emphasis on choosing the transdermal route of administration to mitigate the risk of venous thrombosis and on periodic reassessment of doses, according to clinical evolution and the patient's needs.
FLOWERS; PAL; MANSON	2021	Hormone Therapy in Menopause: Concepts, Controversies, and Approach to Treatment	The "window of opportunity" is a determining factor for the safety of HRT, where early initiation of treatment reduces cardiovascular risks, especially when using transdermal estrogen and micronized progesterone to avoid thromboembolic events.
SANTORO *et al.*	2021	Menopause Transition: Signs, Symptoms, and Management Options	Menopause is characterized by marked hormonal fluctuations that impact quality of life, requiring clinical management that integrates pharmacological therapies, lifestyle support, and monitoring of biological and psychosocial symptoms.
MOOLHUIJSEN; VISSER	2020	Anti-Müllerian Hormone and Ovarian Reserve: Update on Assessing Ovarian Function	Anti-Müllerian hormone (AMH) is the most reliable biomarker of ovarian reserve because it shows stability during the menstrual cycle and a progressive decline years before the rise in FSH, allowing for the early identification of reproductive aging.

(Source: prepared by the author, 2026)

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4. DISCUSSION

The menopausal transition is a complex biological process, initiated by the gradual depletion of hormones. of the ovarian follicles, which triggers a cascade of significant endocrine changes.
As described by Gatenby and Simpson (2024), this follicular failure results in drastic hair loss. of inhibin B and estradiol, disrupting the negative feedback mechanism in the pituitary gland. This disruption Early hormonal changes are not only a marker of infertility, but also the trigger for the disease. Dysregulation of the hypothalamic-pituitary-ovarian axis. This scenario underlies all the manifestations. Systemic changes observed during menopause require a rigorous analysis of ovarian physiology. remaining.

As a direct consequence of this failure, an elevation of FSH, a classic marker, is observed. for laboratory diagnosis when it exceeds the threshold of 30 IU/L. However, Santoro et al. (2021) warn that this hormone has severe limitations due to the luteal-out-of-body phenomenon. phase (LOOP), in which estradiol surges occur unpredictably. These fluctuations can masking the true diagnosis, generating conflicting results that do not reflect follicular exhaustion. Indeed. For this reason, the isolated interpretation of gonadotropins has been discouraged in favor of... markers with greater technical stability.

In this context, anti-Müllerian hormone (AMH) emerges as a superior biomarker. because it reflects non-cyclical follicular recruitment that is independent of gonadotropins. According to Moolhuijsen and Visser (2020), AMH production by granulosa cells of pre-antral follicles It allows for a direct assessment of functional ovarian reserve. Unlike FSH, AMH levels They do not undergo significant variations throughout the phases of the menstrual cycle, giving it a unparalleled diagnostic accuracy. This stability is fundamental for early and accurate characterization. To reliably measure reproductive decline in clinical practice.

The predictive ability of this marker is largely supported by a systematic review. Nelson et al. (2023) points to AMH as the most robust predictor of definitive menopause. The data indicate that their levels become undetectable about three to five years before the complete cessation of menstruation, which greatly anticipates the sustained increase in FSH. Such This feature allows the doctor to identify the end of the reproductive window with chronological precision. unprecedented. This makes it possible to implement preventive and therapeutic strategies. long before the damage from estrogen deprivation takes hold.

Despite the accuracy of AMH and FSH, the interpretation of these markers should not be done in isolation, as Kawakita et al. (2023) warn. The authors offer a counterpoint. It is important to note that the sensitivity of the pituitary gland to gonadotropins is influenced by the levels of

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androgens, a detail that neither Nelson et al. (2023) nor Moolhuijsen and Visser (2020) explored in depth. in their predictive analyses. For this group of researchers, the fluctuation of levels of Testosterone during transition alters the FSH response, requiring a more dynamic approach. Thus, Laboratory diagnosis becomes a piece of a puzzle that depends on the context. The individual androgenic profile of each patient.

This diagnostic complexity precedes the understanding of systemic risks, especially of vascular vulnerability described by Kan et al. (2024). While the previous authors focus on Ovarian failure: this study details the molecular mechanism by which the drop in estrogen occurs. This leaves the endothelium unprotected, increasing arterial stiffness through oxidative stress. The authors They clarify that hormonal loss is not only a reproductive event, but also a trigger for... Vascular dysfunction mediated by genomic and non-genomic receptors. This establishes... a direct link between the end of hormonal cyclicity and the exponential increase in the risk of events coronary.

When translating these risks into national clinical practice, the Guideline by Oliveira et al. (2024) This corroborates the severity of the vascular scenario and adds the variable of the woman's lipid profile. Brazilian. Unlike the purely pathophysiological analysis by Kan et al. (2024), the document Brazilian emphasizes that the climate transition in the country is intrinsically linked to the increase in visceral adiposity and metabolic syndrome. The guideline reinforces that the loss of estrogenic protection This requires rigorous and specific monitoring, adapted to the prevalent comorbidities in our population. population. This stance elevates the debate on physiology to a matter of public health urgency and of Continuous cardiometabolic monitoring.

Complementing the concern with vascular risk, Paschou et al. (2024) establish a critical relationship between menopause and glucose metabolism, which reinforces Oliveira's warning. et al. (2024). The research demonstrates that hormonal deprivation reduces the expression of transporters of glucose type 4 (GLUT4), predisposing women to insulin resistance and type 2 diabetes. The authors argue that early menopause should be considered a sentinel marker of Metabolic risk, something that transcends the simple management of hot flashes. Therefore, the integration of Fasting blood glucose and insulin levels in hormonal assessment become an inseparable step in prevention. irreversible cardiovascular damage.

Given the metabolic and vascular complexity described, Hormone Replacement Therapy (TRH) is consolidating itself as the intervention of choice to mitigate these risks. According to the According to the position of the North American Menopause Society (Faubion et al., 2022), this is the tool most effective for relieving vasomotor symptoms and preserving bone density. The document reinforces that, for healthy and symptomatic women, the balance between risks and

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The benefits are overwhelmingly favorable. This view establishes the basis for modern management, with a focus in the restoration of hormonal homeostasis, which previous authors, such as Santoro et al. (2021), They described it as lost.

However, the practical application of TRH requires a rigorous analysis of the start time. concept on which Cho et al. (2023) introduce a cautious perspective from cardiology. While Faubion et al. (2022) focus on symptomatic relief, this study emphasizes that the Cardiovascular protection depends strictly on the 10-year "window of opportunity" after the Menopause. The authors warn against initiating therapy in vessels already compromised by atherosclerosis. It can be harmful, contrary to the protective effect observed in young women. Thus, the Therapeutic indication ceases to be universal and becomes a precise calculation of age and time. exposure to estrogen deficiency.

Disagreements regarding vascular risk are largely resolved by the careful selection of the route. of administration, as discussed by Vigneswaran and Hamoda (2022). The authors argue that The transdermal route should be preferred, especially for women with risk factors. metabolic disorders occur by avoiding the first-pass hepatic effect. Unlike the oral route, which It stimulates the synthesis of pro-coagulant factors and elevates C-reactive protein; the use of patches or gels It maintains inflammatory neutrality and presents a lower risk of thromboembolic events. This Technical distinction is fundamental to aligning symptom relief with safety requirements. cardiovascular guidelines established by Cho et al. (2023) and Oliveira et al. (2024).

Further refining the safety of the therapeutic scheme, Flores, Pal and Manson (2021) They make a decisive contribution regarding the use of micronized progesterone, a formulation chemically identical to the natural hormone produced by the ovaries, in comparison to synthetic progestogens. The review clarifies that this natural version does not negate the benefits. estradiol-associated vascular disorders and present a significantly higher risk profile for breast cancer. lower than that of synthetic options. Unlike older artificial progestins, the Micronized milk is metabolically neutral, meaning it does not worsen insulin resistance. discussed by Paschou et al. (2024). Therefore, the careful selection of the progestogen completes the tripod. Safety: right dose, right route, and right molecule.

Despite advances in hormone prediction, it is necessary to acknowledge important limitations. methodological changes that affect current clinical practice. Moolhuijsen and Visser (2020) emphasize that, Although AMH is superior to FSH, the lack of universal standardization among the different assays Laboratory testing remains a challenge. This technical variability can generate reference values. These differences make it difficult to create rigid global protocols. Therefore, the interpretation of Results should be interpreted cautiously, considering that the accuracy of the biomarker depends directly on...

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sensitivity of the assay used in each institution.

One remaining challenge in the literature relates to the need for greater data robustness.
Longitudinal studies targeting specific subgroups. Although extensive follow-ups exist.
For the female population in general, Nelson et al. (2023) observe that most of these studies
It focuses on healthy profiles, which limits the understanding of HRT behavior in women.
with autoimmune diseases or rare metabolic conditions. This selectivity in the samples of
In the long term, it becomes difficult to generalize guidelines for highly complex patients. Therefore,
Evidence-based medicine should, in the coming years, seek clinical follow-up.
more diversified, aiming to consolidate therapeutic safety for these sub-populations
represented and promote genuine therapeutic equity.

Looking ahead to the future, the integration of artificial intelligence into
Biomarker monitoring promises to revolutionize menopause management. Gatenby and Simpson
(2024) suggest that predictive algorithms could combine AMH, FSH, and androgen data.
to calculate, in real time, the exact dose of hormone needed. This is an evolution towards medicine.
Digital precision would allow for dynamic therapeutic adjustments, further minimizing the risks of
adverse effects. The expectation is that the technology will transform the climate transition in a period
Monitored with the same rigor as other chronic conditions.

In addition to improvements in HRT, the literature is beginning to explore non-hormonal treatment pathways.
Highly effective hormonal therapy for women with absolute contraindications. Santoro et al. (2021)
They discuss the emergence of new neurochemical receptor antagonists that act directly.
in the thermoregulatory center of the hypothalamus. These drugs offer a promising alternative for
Relief from hot flashes, without the systemic risks associated with estrogen exposure. This advance
This represents a milestone for breast cancer survivors or patients with a history of breast cancer.
Thrombophilia, broadening the range of multidisciplinary care.

In summary, the evidence analyzed in this discussion consolidates the understanding of
Menopause as a critical multisystem health milestone. The integration of biomarkers.
sensitive factors, such as AMH, combined with therapeutic choices based on the window of opportunity and in
Safe routes of administration ensure robust and individualized clinical management. Analyses
The findings gathered here reinforce the need for an interdisciplinary approach, in which diagnostic precision is paramount.
Pharmacological safety and health go hand in hand. The ultimate goal should always be the promotion of a
healthy and active aging in women, with the metabolic and vascular risks properly managed.
mitigated.

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FINAL CONSIDERATIONS

This review achieved its objective by demonstrating that menopause transcends the sphere. reproductive, configuring itself as a physiological event with a broad systemic and metabolic impact. and cardiovascular. It became evident that hormone replacement therapy, when initiated within the window of The right opportunity, managed through safe channels, represents the most effective clinical strategy. to mitigate symptoms and prevent long-term morbidity. In this context, laboratory evaluation Continuous testing has proven to be an indispensable pillar for the early confirmation of ovarian failure. both for risk stratification and safe monitoring of women's health throughout their lives. The therapeutic intervention.

The impact of this study on society lies in the necessary paradigm shift in Regarding female aging. Considering the significant increase in life expectancy, Ensuring that women go through menopause in good health means drastically reducing the incidence. of chronic diseases with high social and personal costs, such as osteoporosis, diabetes, and other conditions coronary. Disseminating this evidence-based knowledge empowers patients and This will alert public health authorities to the urgency of treating menopause not only as the end of fertility. but also as a critical window for prevention, promoting active aging and with high quality of life.

Within this network of multidisciplinary care, the role of the biomedical professional becomes evident. fundamental. This professional is the technical and scientific agent responsible for ensuring accuracy, The reproducibility and excellence of the tests that underpin clinical decision-making. Since the rigorous execution and interpretation of complex hormone dosages, such as the hormone

At the forefront of diagnostic medicine. Its analytical rigor ensures the issuance of accurate reports. highly reliable, allowing therapy to be truly individualized and safe for each patient.

Finally, as a future perspective, it is suggested that new research be conducted focusing on... Universal standardization of laboratory assays for emerging ovarian markers, aiming to greater homogeneity in global reference values. Further development is also recommended. longitudinal studies that investigate the behavior of hormone replacement therapy in populations with specific comorbidities and rare diseases. Furthermore, the exploration of predictive technologies, such as the application of artificial intelligence in cross-referencing laboratory data, and continuous research. through more efficient non-hormonal therapeutic pathways represent promising avenues for To consolidate precision medicine in women's health.

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