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SLEEP AND POLYENDOCRINE METABOLIC OVARIAN SYNDROME: ANALYZING THE BIDIRECTIONAL RELATIONSHIP. A LITERATURE REVIEW

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ABSTRACT

Polyendocrine metabolic ovarian syndrome (PMOS) represents a prevalent endocrine disorder whose pathogenesis is driven by a complex network of underlying mechanisms. Emerging evidence highlights disrupted sleep architecture and circadian dysregulation as significant contributors to PMOS progression, suggesting that targeting these pathways could optimize clinical management.

Aim: The aim of this article is to review recent data regarding the impact of sleep alterations and biological rhythm disturbances on PMOS, while evaluating therapeutic strategies helping to restore sleep health.

Material and methods: A comprehensive literature review was conducted utilizing the PubMed and Google Scholar databases to identify peer-reviewed articles published between 2001 and 2026.

Results: Sleep abnormalities correlate strongly with the clinical severity of PMOS, though the precise physiological pathways mediating this interaction remain to be fully discovered. Circadian desynchronization and blunted melatonin pathways significantly exacerbate metabolic dysfunction and disrupt reproductive hormone regulation. Concurrently, comorbid obstructive sleep apnea (OSA) accelerates cardiovascular risk, whereas psychological distress, such as depression, impairs sleep quality and diminishes patient compliance with essential lifestyle modifications.

Conclusions: Further investigation is required to clarify the exact impact of sleep deprivation on PMOS pathophysiology. Behavioral therapies, chronobiological tools and continuous clinical support offer encouraging strategies and seem to significantly improve patients quality of life. However, future clinical trials are undoubtedly urgently needed to establish optimal management protocols for this population.

KEYWORDS

Polyendocrine Metabolic Ovarian Syndrome, PMOS, Polycystic Ovary Syndrome, PCOS, Circadian Rhythm Disruption, Sleep, Sleep Architecture, Melatonin

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Introduction

Role of sleep

It's widely known that adequate sleep plays a crucial role in human health. Nocturnal rest constitutes a fundamental physiological process requisite for holistic somatic and cognitive restoration. It underpins crucial homeostatic and neurobiological mechanisms, including the consolidation of memory traces, neurodevelopmental and psychological maturation, immunomodulation and the metabolic clearance of cerebral waste products. (Jafar et al., 2023) Human sleep architecture is characterized by the cyclical alternation between two distinct phases: non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. This continuous process occurs in 45-minute stages that combine to form a recurring 90-minute cycle. NREM sleep is subdivided into stages N1, N2 and N3, with the latter also known as slow-wave sleep (SWS). As the sleep period progresses into its second half, NREM sleep - which is vital for physiological regeneration and immune system enhancement - decreases to allow for longer periods of REM sleep, a phase essential for memory consolidation. Consequently, poor sleep habits, such as insufficient sleep duration, disrupt these natural cycles and significantly curtail the time spent in NREM sleep. (Cappuccio, Miller & Lockley, 2010) Sleep health is a broad concept that can not be defined only as a lack of sleep deficiency. It includes a constellation of vital factors - namely sleep satisfaction, optimal duration, circadian timing, daytime alertness and sleep continuity - all of which act synergistically to maintain physical and mental well-being. (Jafar et al., 2023) Furthermore, a growing body of literature underscores a profound, bidirectional relationship between these sleep disturbances and chronic endocrine disorders, in which polyendocrine metabolic ovarian syndrome (PMOS) is one of the most prevalent conditions. (Teo et al., 2022)

Physiology of women menstrual cycle

The female menstrual cycle is a highly sophisticated endocrinological process driven by tightly regulated fluctuations in ovarian steroids, which frequently modulate sleep architecture, psychological well-being and female activity through the day. (Alzueta et al., 2022) Throughout a standard 28-day menstrual cycle, women of reproductive age exhibit predictable cyclic fluctuations in estrogen and progesterone concentrations. The onset of menses marks the commencement of the follicular phase, a period characterized by basal levels of both ovarian hormones. (Hawkins & Matzuk, 2008) During this stage, rising concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) drive follicular maturation, stimulating the synthesis of estrogen, predominantly estradiol. This progressive estrogen elevation triggers a preovulatory LH surge, inducing follicular rupture and oocyte release approximately 12 to 16 hours post-surge. (Alzueta et al., 2022) Post-ovulation, the luteinization of the follicle drives a substantial rise in progesterone and estrogen, peaking during the mid-luteal phase, approximately 5 to 7 days following oocyte release. In the absence of blastocyst implantation, the corpus luteum undergoes luteolysis and the precipitous drop in ovarian steroids provokes endometrial shedding, thereby initiating the subsequent cycle. (Messinis, Messini & Dafopoulos, 2014)

Polyendocrine metabolic ovarian syndrome - definition and pathophysiology

Polyendocrine Metabolic Ovarian Syndrome (PMOS) is the recently updated nomenclature for the condition previously known as Polycystic Ovary Syndrome (PCOS), a revision established through the collaborative initiative of 56 prominent academic, clinical and patient advocacy groups. (Teede et al., 2026) The historical designation lacked diagnostic precision, as it incorrectly implied the mandatory presence of ovarian cysts, while overshadowing the complex endocrine and metabolic underpinnings of the disorder. This

ambiguous terminology led to significant clinical consequences, including diagnostic delays, uncoordinated patient care and social stigma, while simultaneously hindering scientific funding and public health policy initiatives. (Teede et al., 2026)

Polyendocrine Metabolic Ovarian Syndrome (PMOS) is a complicated gynecological disorder manifesting through profound endocrine and metabolic dysfunction. The amount of women affected by this illness can range from 6 to 20 percent of females in reproductive age, but this amount slightly differs depending on several studies. (Siddiqui, Mateen, Ahmad & Moin, 2022; Teede et al., 2023) The pathogenesis of PMOS is centrally linked to intrinsic abnormalities within ovarian theca cells, which precipitate androgen oversecretion and drive the subsequent clinical and biochemical manifestations. (Stańczak, Grywalska & Dudzińska, 2024) This ovarian dysfunction is further compounded by chronic low-grade inflammation and oxidative stress, both of which play a pivotal role in syndrome progression and correlate with elevated cardiovascular risk. (Gautam et al., 2025) Furthermore, genetic predispositions strongly influence etiology, with ethnic variations accounting for an increased prevalence among Hispanic, Mexican, and Native American populations. (Stańczak, Grywalska & Dudzińska, 2024)

The most characteristic symptoms of PMOS are acne, hirsutism and irregular menstrual cycles, which are a consequence of oligo- or anovulation and as a result can contribute to infertility among females. (Joshi, 2024) Although crucial features are seemingly easy to define, there is no conclusion about one universal definition of PMOS. Most medical authorities and scientific societies accept three classifications: Rotterdam 2003 criteria (conference coordinated by European Society of Human Reproduction and Embryology and American Society of Reproductive Medicine - ESHRE/ASRM), definition presented by National Institutes of Health/National Institute of Child Health and Human Development (NIH/NICHD) in April 1990 and measures for diagnostic PCOS established by Androgen Excess and PCOS Society (AE-PCOS) in 2006. Although all of them are prevalent, Rotterdam 2003 diagnostic criteria are the most extensively used. This classification involves two of the consecutive three features: (a) hyperandrogenism, (b) oligo- or an-ovulation and (c) polycystic ovarian morphology, which can be visualized in ultrasound or alternatively identified by anti-Müllerian hormone (AMH). Exclusion of other endocrine disorders is mandatory before establishing a diagnosis. Additionally, ultrasound or AMH can be omitted in diagnosis, when patients present hyperandrogenism and irregular periods. (Siddiqui, Mateen, Ahmad & Moin, 2022; Teede et al., 2023) There is a long list of illnesses related to PMOS, most prevalent of them are: abdominal obesity, insulin resistance, cardiovascular diseases, psychological disorders and cancer. (Siddiqui et al., 2022) Obesity is a common comorbidity in patients with PMOS and these medical conditions often share a complex interplay, as they mutually influence each other's progression. (Joshi, 2024) Women with PMOS also have increased risk of ovarian and endometrial cancer, due to the DNA damage caused by reactive oxygen species (ROS). ROS are responsible for oxidative stress, which is the consequence of insulin resistance and hyperglycemia, caused by hyperandrogenism. As a result of this complicated process, follicular fluid and serum of women with PMOS can contain increased levels of oxidative stress markers, which can be responsible for poor quality oocytes. (Siddiqui et al., 2022)

To control symptoms of PMOS and prevent this disorder from spreading, lifestyle interventions in the earliest possible stage from diagnosis are crucial. The first strategy to manage the illness is to introduce essential changes like physical activity, dietary patterns, taking care of increasing stress level, regulating circadian rhythm and improving quality of sleep. (Gautam et al., 2025) Although lifestyle changes are the first line of managing the PMOS symptoms, pharmacological treatment is often necessary and helps improve patient's quality of life. For the management of hyperandrogenism and irregular menstrual cycles, combined oral contraceptives pills are the first-line therapeutic approach. Clinical guidelines do not endorse a specific commercial preparation; instead, selection criteria should prioritize options with minimized ethinyl estradiol dosages and a reduced incidence of secondary side effects. Inositol in women with PMOS reveals modest clinical efficacy in glucose metabolism, thus metformin should be considered in the first line of treatment, on account of its higher therapeutic value. (Teede et al., 2023) Additional therapy for patients with PMOS may include laser therapy, which may be helpful for women with persistent hirsutism. For females suffering from excess weight, anti-obesity pharmacotherapy and bariatric surgeries may also be pursued, depending on potential risk and positive clinical effects for the patient. Anti-androgens are not routinely used and they should be considered, when response to the other treatment options was inadequate. (Teede et al., 2023)

This article reviews the latest research on the impact of sleep architecture and circadian disruptions on PMOS development and progression, as well as therapeutic methods that optimize sleep health, including lifestyle modifications, chronobiological stabilization and targeted supplemental interventions.

Material and Methods

This article presents the results of a systematic review evaluating the intricate, bidirectional relationship between polyendocrine metabolic ovarian syndrome (PMOS) and various dimensions of sleep architecture dysfunction. The review specifically focuses on how sleep-disordered breathing, circadian misalignment, insomnia and altered melatonin secretion impact the clinical, metabolic and reproductive parameters of patients diagnosed with this endocrine disorder. Additionally, therapeutic interventions targeting sleep optimization - encompassing both pharmacological treatments and non-pharmacological modalities - were thoroughly analyzed. A comprehensive literature search was conducted across the PubMed and Google Scholar databases to identify relevant articles published between 2001 and 2026, restricted exclusively to English-language publications. To retrieve eligible literature, various combinations of the following medical subject headings and search terms were utilized: "polyendocrine metabolic ovarian syndrome", "polycystic ovary syndrome", "sleep architecture", "obstructive sleep apnea", "circadian rhythm disruption", "melatonin secretion" and "fertility outcomes". The structural framework of this review was established through a rigorous selection of original research, prospective cohorts, randomized clinical trials, systematic reviews and meta-analyses.

Discussion

The Bidirectional Relationship and Prevalence of Sleep Disturbances in PMOS

A primary finding of this synthesis is the complex, bidirectional relationship between polyendocrine metabolic ovarian syndrome (PMOS) and sleep quality. Strong evidence suggests that PMOS and irregular sleep cycles are mutually linked and moreover, women with PMOS often present reduced sleep efficiency. (Heydari & Ramdass, 2025) Polyendocrine metabolic ovarian syndrome serves as an independent risk factor for increased prevalence of sleep disturbances, demonstrating a strong association even after taking features such as BMI, comorbidities, demographic profiles and depressive symptoms in statistical adjustment. (Jafar et al., 2025) To quantify this burden, the predisposition to sleep disruptions is significantly heightened in the PMOS population, which exhibits up to a 20% higher prevalence rate than non-PMOS groups. (Mo et al., 2018) Clinical observations indicate that subclinical sleep alterations - such as prolonged sleep-onset latency, fragmented nocturnal rest and profound exhaustion - remain highly prevalent even in the absence of a formal sleep pathology diagnosis, underscoring the necessity of evaluating sleep parameters as a core component of PMOS management. (Cowan et al., 2023; Jafar et al., 2025)

Phenotypic Manifestations, Insomnia and Patient Burden

The daily experience of patients further highlights the severity of these sleep architecture abnormalities, with up to 68% of adult women with PMOS suffering from sleep difficulties, including delayed sleep onset, restless sleep and heightened fatigue, independent of BMI or clinical comorbidities. Crucially, even when maintaining a nocturnal sleep duration similar to healthy individuals, patients with PMOS continue to report more severe daytime exhaustion. (Mo et al., 2018) Beyond classical sleep disorders, this cohort faces an elevated risk of diverse sleep irregularities manifesting as poor sleep quality, disrupted sleep tracking, cumulative sleep deficits and secondary daytime impairments. (Jafar et al., 2023) In parallel, clinical insomnia represents another highly prevalent disorder in this population, defined by a persistent inability to initiate or maintain sleep at least three nights weekly, which causes significant functional impairment. (Jafar et al., 2023) Rather than presenting as overt somnolence, insomnia frequently manifests as persistent fatigue and correlates with severe long-term complications, chief among which are increased cardiovascular vulnerability and late-life cognitive decline. (Jafar et al., 2023) Conversely, patients are equally prone to hypersomnia and excessive daytime sleepiness, manifesting as a continuous tendency toward daytime fatigue or an absolute increase in nightly sleep duration. (Jafar et al., 2023) These diverse presentation patterns demonstrate that while patient experiences vary widely, the negative impact on overall quality of life remains constant.

Chronobiology, Shift Work and Circadian Misalignment

Beyond specific sleep disorders, systemic chronobiological alterations represent a critical dimension of this syndrome. Circadian rhythm disruptions occur when an individual's endogenous biological clock becomes desynchronized from external environmental cues, typically presenting as advanced, delayed or non-24-hour sleep-wake phase disorders. (Sateia, 2014) In clinical cohorts, growing evidence indicates that women diagnosed with PMOS exhibit a significantly higher predisposition toward evening chronotypes compared to

healthy controls, a preference characterized by a distinct shift in both behavioral patterns and biological rhythms toward eveningness. (Barrea et al., 2023) Individuals with evening chronotypes exhibit phase-delayed circadian cycles that frequently conflict with early morning obligations, inducing a mismatch between internal biological time and external social schedules operationalized as social jetlag. (Wittmann et al., 2006)

The limited research assessing chronotypes in the PMOS population via validated questionnaires has linked eveningness to adverse clinical outcomes, specifically correlating with elevated serum testosterone concentrations, poor subjective sleep quality and an overall exacerbation of core hormonal and metabolic abnormalities. (Jafar et al., 2023) The interplay between metabolic disturbances and internal clock disruption is further reinforced by investigations into shift work, where circadian desynchronization promotes shortened sleep periods, deteriorated glucose handling and heightened markers of inflammation and insulin resistance, even when accounting for absolute sleep loss. Meta-analytic data demonstrating uniformly decreased sleep efficiency across women with PMOS suggest that desynchronization itself acts as a direct driver of metabolic decline, implying that circadian disruption constitutes an independent risk factor for PMOS. (Heydari & Ramdass, 2025) However, this correlation may be bidirectional; inadequate sleep continuity tends to further exacerbate endocrine disruptions, thereby compounding the severity of the disorder and establishing a self-perpetuating feedback loop. (Heydari & Ramdass, 2025)

Pathophysiological Cascades and Fertility Outcomes

Regional data offer valuable perspectives to contextualize these findings within specific clinical cohorts. For instance, data from German patients demonstrate that up to 30% of women with PMOS suffer from chronic sleep disturbances and non-effective regeneration, characterized by shortened sleep duration, prolonged sleep-onset latency, frequent nocturnal awakenings and a subsequent lack of energy the next day. (Decrinis et al., 2025) Furthermore, metabolic and cardiovascular profiles (specifically obesity and insulin resistance) are significantly exacerbated by poor sleep quality, establishing a deleterious feedback loop that worsens clinical status. (Decrinis et al., 2025) One potential mechanism underlying this association is that disrupted sleep compromises signaling pathways within the hypothalamic-pituitary-adrenal (HPA) axis, inducing significant hormonal fluctuations heavily implicated in the pathogenesis and progression of obesity. (Bose, Oliván & Laferrère, 2009)

This physiological cascade extends its negative effects to reproductive parameters as well, with studies suggesting that impaired sleep quality is significantly more pervasive in infertile patients with PMOS than in unexplained infertility (UI) groups, (Eisenberg et al., 2021) Because the maintenance of systemic rhythmic stability is contingent upon synchronized circadian release, any deviation from this physiological profile threatens female fertility by impairing oocyte maturation kinetics, fertilization rates and early embryo development. (Li et al., 2024) A U-shaped, non-linear pattern characterizes the relationship between nocturnal rest duration and reproductive outcomes during childbearing years, implying that hypersomnia may serve as a negative predictor of fecundability and exacerbate reproductive failure. However, since infertility itself can negatively alter sleep architecture, clearly isolating the directions of this bidirectional relationship remains a challenge. (Li et al., 2024)

Genetic factors

Genetic determinants also play a crucial role in PMOS pathophysiology, where suboptimal reproductive outcomes and compromised success rates of fertility treatments are closely tied to various dimensions of sleep dysfunction, including sleep-disordered breathing, insomnia, delayed sleep onset, diminished sleep quality and hypersomnia. (Li et al., 2024) While the definitive etiology underlying sleep-induced female infertility requires further empirical validation, current literature highlights a complex multifactorial network involving circadian misalignment via Clock gene pathways, neuroendocrine imbalances, immunological reactions and oxidative stress as key factors disrupting reproductive homeostasis. (Li et al., 2024) To better understand these mechanisms, it is essential to consider how sleep disruption alters central and peripheral biological rhythms. At the center of this regulation is the master circadian pacemaker located in the suprachiasmatic nucleus (SCN), which utilizes neurotransmitter and hormonal signaling pathways to synchronize physiological processes via core clock system genes. (Li et al., 2024; Pan et al., 2020) However, the influence of circadian regulation extends far beyond central mechanisms; peripheral circadian clocks are localized within key reproductive tissues - specifically the pituitary, ovary, oviduct and uterus - suggesting a localized role in temporal reproductive management. (Sellix, 2013)

The functional significance of these peripheral structures has become increasingly evident, as molecular clock pathways in gonadotropic cells appear to dictate cellular proliferation and secretory dynamics. Furthermore, the ovary exhibits gonadotropin-dependent rhythmic clock gene expression essential for folliculogenesis and ovulation, whereas uterine and oviductal clocks support early embryonic development, implantation kinetics and labor initiation. (Li et al., 2024) These findings highlight a sophisticated network where any localized or central rhythm disruption can impair fertility. Nevertheless, translating these insights into clinical practice presents a notable challenge; despite compelling evidence from animal studies elucidating this circadian-reproductive nexus, empirical research linking these pathways to human infertility is still in its infancy, warranting future clinical trials to bridge this gap. (Li et al., 2024)

Hormonal Imbalances and Neuroendocrine Dysregulation

To fully elucidate how sleep interventions might optimize reproductive outcomes, it is critical to examine the underlying endocrine pathways that bridge sleep disturbances and the pathophysiology of polyendocrine metabolic ovarian syndrome. Several intimately linked factors such as metabolic disturbances, hormonal imbalances and autonomic dysfunction may as a result cause decreased sleep efficiency, characteristic for PMOS patients with CRD. For example elevated androgen levels can be responsible for this dysregulation, due to its correlation with increased sympathetic nervous system activity, which can cause sleep fragmentation and hyperarousal. Another significant factor is altered melatonin secretion entailing difficulties in falling asleep and frequent awakenings, which consist of reduced sleep quality. (Heydari & Ramdass, 2025) These hormonal aberrations create a systemic environment that directly compromises sleep integrity. Indeed, endocrine imbalances (specifically the suppression of melatonin, progesterone and estrogen concentrations) serve as a key mediator driving the heightened vulnerability of PMOS patients to both clinical sleep pathologies and subclinical sleep disruptions. (Jafar et al., 2025) Each of these hormones exerts a distinct, protective effect on sleep physiology. Regulating nocturnal body temperature and modulating the metabolism of sleep-related neurotransmitters, such as serotonin and norepinephrine, are crucial physiological processes dependent on adequate estrogen levels. (Vgontzas et al., 2001) Similarly, progesterone acts as a vital protective agent for respiratory stability and sleep quality. By functioning as a ventilatory drive stimulant, progesterone actively decreases upper airway impedance in patients with obstructive sleep apnea (OSA), while its concomitant anxiolytic and sedative properties facilitate the optimization of sleep architecture. (Ehrmann, 2011) Consequently, when the levels of these sex steroids are suppressed or dysregulated in PMOS, sleep quality inevitably declines. This hormonal decline is not an isolated event, but is deeply rooted in chronobiological mechanisms, as endocrine fluctuations, metabolic homeostasis and behavioral patterns operate on an approximate 24-hour cycle known as the circadian rhythm, which is fundamentally directed by the suprachiasmatic nucleus (SCN). (Sciarra et al., 2020) Because the homeostatic control of reproductive hormones along the hypothalamic-pituitary-gonadal (HPG) axis is intrinsically tied to circadian oscillations, a functional disruption of the suprachiasmatic nucleus pacemaker may induce hormonal dysregulation, thereby exerting a detrimental effect on female reproductive potential. (Li et al., 2024) The clinical consequences of this neuroendocrine disruption are directly reflected in peripheral hormone levels. Data show that sleep integrity and increased efficiency may influence FSH production, being responsible for higher levels of this hormone, while any resting disturbances and suboptimal sleep adequacy can cause lower estrogen concentration in serum. (Li et al., 2024) This intricate feedback loop demonstrates that sleep deprivation not only stems from hormonal imbalances, but actively perpetuates them, creating a self-reinforcing cycle of reproductive and metabolic dysfunction.

The Role of Melatonin

Given that the suprachiasmatic nucleus (SCN) orchestrates global neuroendocrine rhythms, decoding the specific molecular signals involved in this regulation is vital. Central regulation of the circadian rhythm is orchestrated primarily by the hypothalamus, with the intricate interplay between this master pacemaker and the endocrine system being largely mediated by melatonin. This pivotal signaling molecule has increasingly emerged as a cornerstone of female reproductive physiology due to its direct, functional interactions with ovarian tissues and gonadotropic pathways. (Heydari & Ramdass, 2025) Beyond its well-established neuroendocrine function in modulating circadian biology, melatonin exerts profound effects on ovarian physiology by optimizing oocyte quality, stimulating folliculogenesis and decelerating the aging process of the ovaries. (Jafar et al., 2025) Circadian rhythmicity is fundamentally modulated via receptors localized within

the SCN, which respond to the nocturnal secretion of pineal melatonin. This neuroendocrine pathway is intrinsically entrained and altered by external photoperiodic light-dark alternations. (Zisapel, 2018)

In the healthy human body, melatonin exhibits a recurrent, circadian pattern characterized by an evening rise, a nocturnal peak and a subsequent descent in the early morning, meaning that any deviation from this standard profile can precipitate circadian rhythm disruptions (CRD). (Heydari & Ramdass, 2025) While approximately 3% of the general adult population experiences some form of chronobiological disruption, the exact prevalence of these disorders among women diagnosed with PMOS remains unestablished. To identify these abnormalities, researchers have frequently quantified melatonin concentrations across various biological fluids, including saliva, urine and follicular fluid. (Jafar et al., 2023)

Clinical data regarding these measurements, however, present a highly complex and sometimes paradoxical picture. Disrupted melatonin secretion, presenting as lower total concentrations and delayed onset, potentially impairs sleep and circadian stability in the PMOS population with certain studies linking these chronobiological irregularities directly to hyperandrogenism and insulin resistance. (Jafar et al., 2023) Conversely, alternative findings indicate that patients with PMOS frequently exhibit elevated melatonin levels throughout both the day and night compared to healthy controls. Affected individuals often show elevated melatonin concentrations within their serum and, surprisingly, within their ovarian follicles - an abnormality likely explained as a compensatory response to higher ROS production, oxidative stress and chronic inflammation that damage oocyte health and inhibit ovulation. (Heydari & Ramdass, 2025; Li et al., 2024)

This compensatory rise in melatonin may serve a vital protective function against internal stress, acting as a free radical scavenger to address underlying oxidant imbalances, which explains why its metabolites are unexpectedly elevated in women with PMOS who experience poor sleep quality. (Jafar et al., 2023) Furthermore, the timing of melatonin clearance appears equally dysregulated in this population. The dim light melatonin off-set (DLMOFF), which typically occurs in the early morning, can extend well into the daytime hours in women with PMOS, potentially accounting for elevated testosterone levels and insulin resistance. This prolonged extension directly interferes with normal metabolic shifts, as the morning decrease of melatonin plays a crucial role in reducing insulin sensitivity in the healthy human body, offering a potential explanation for the dysregulated daily rhythms observed in PMOS patients. (Heydari & Ramdass, 2025)

These chronobiological shifts are further compounded by interactions with other steroid pathways, particularly cortisol. Serum levels of melatonin and evening cortisol are significantly increased in women with PMOS compared to females without the disorder, whereas morning cortisol levels demonstrate no notable disparity. These fluctuations are likely caused by aberrations in the HPA axis, manifesting as sleep dysregulation, difficulty conceiving and metabolic abnormalities. (Heydari & Ramdass, 2025) High evening cortisol levels may also actively suppress melatonin secretion, which is responsible for somnolence and sleep initiation, thereby escalating circadian misalignment and degrading sleep quality. (Heydari & Ramdass, 2025) Furthermore, due to persistent cortisol elevations during sleep hours, the sympathetic nervous system remains activated throughout the night, creating a vicious cycle that escalates insulin production and dyslipidemia, thereby worsening core PMOS symptoms. (Heydari & Ramdass, 2025)

Understanding these profound disruptions has generated significant clinical interest in exogenously restoring melatonin balance. While some encouraging data suggest that melatonin may help manage crucial PMOS symptoms such as menstrual irregularities, impaired oocyte maturation and hyperandrogenism, current research remains insufficient to unequivocally confirm its long-term efficacy and safety. (Heydari & Ramdass, 2025) Nevertheless, data derived from a randomized, double-blind trial evaluating a combined melatonin and inositol regimen in patients with PMOS appear highly promising, demonstrating that melatonin supplementation enhances both oocyte and embryo quality by modulating the intraovarian microenvironment, while concurrently mitigating insulin resistance. (Pacchiarotti et al., 2015) Ultimately, exogenous administration offers benefits for both systemic and localized pathologies, representing a viable clinical strategy for managing insomnia due to its proven capacity to optimize sleep quality and decrease sleep-onset latency. These dual benefits further justify its application in treating sleep-related reproductive failure, although the highly complex web of interactions between melatonin homeostasis, sleep disorders and infertility continues to demand deeper scientific exploration, suggesting that the management and enhancement of sleep architecture should be integrated as a fundamental component within therapeutic strategies aimed at facilitating sustainable lifestyle interventions for the PMOS population. (Li et al., 2024; Mo et al., 2018)

Obstructive Sleep Apnea (OSA)

To implement sustainable lifestyle and sleep interventions effectively, clinicians must address the most severe respiratory manifestations of sleep architecture disruption in this population. The risk of developing obstructive sleep apnea (OSA) is markedly elevated in the PMOS population, with data indicating up to a thirty-fold increase compared to healthy controls - an elevation that cannot be attributed solely to age or high BMI, even though obesity remains a frequent comorbidity in both conditions. (Decrinis et al., 2025; Eisenberg et al., 2021; Jafar et al., 2025) Indeed, the clinical profile of patients with PMOS, when contrasted with healthy women, is characterized by a disproportionate occurrence of sleep-related issues, such as OSA, habitual snoring, shortened sleep duration (<6 hours) and increased daytime sleepiness. (Eisenberg et al., 2021) Data show that a wide spectrum of sleep architecture alterations (including severe diurnal somnolence, sleep-onset and maintenance insomnia, sub-optimal sleep quality and restless legs syndrome) manifests with elevated frequency among women with PMOS who demonstrate a high predisposition to OSA. (Jafar et al., 2025)

Within the general population, OSA predominantly affects males and is strongly linked to advancing age and elevated body mass index (BMI). Given that PMOS is frequently characterized by both adiposity and hyperandrogenism, the elevated prevalence of OSA in this cohort was historically attributed to these two variables. (Decrinis et al., 2025) A hallmark feature of PMOS is hyperandrogenemia, which has been implicated as a potential causative factor for OSA, suggesting that elevated androgen titers promote pharyngeal tissue accumulation, while simultaneously disrupting homeostatic respiratory regulation. The culmination of these effects critically compromises airway patency, leading to sleep-induced pharyngeal collapse. (Li et al., 2024)

Nevertheless, cumulative evidence indicates that carbohydrate metabolism disturbances, specifically insulin resistance and impaired glucose tolerance, serve as more robust predictors of OSA development and severity in PMOS patients than either hyperandrogenemia or BMI, confirming that insulin resistance represents an independent risk factor for OSA alongside established parameters. (Decrinis et al., 2025) Interestingly, recent endocrinological data shift the focus toward alternative biochemical markers, revealing that circulating sex hormone-binding globulin (SHBG) titers are remarkably suppressed in the subgroup of PMOS patients with comorbid OSA compared to those without apneic symptoms. (Jafar et al., 2025) Observations suggest that the pathophysiological driving force behind OSA in the PMOS population may be attributed to lower SHBG concentrations in serum rather than being primarily mediated by hyperandrogenism and sub-optimal levels of this molecule can further influence the manifestation of insulin resistance in females with PMOS and a high BMI. (Jafar et al., 2025)

This intricate metabolic-respiratory interplay points toward a bidirectional link between sleep disruptions and metabolic dysregulation, where poor sleep quality and OSA are thought to exacerbate insulin resistance within the PMOS population. This hypothesis is supported by controlled laboratory experiments on healthy, lean young adults, where restricted sleep duration and impaired sleep continuity directly compromised insulin sensitivity. (Eisenberg et al., 2021) Inadequate sleep and sleep architecture disruptions are well-established risk factors for adiposity, insulin resistance, type 2 diabetes mellitus and cardiovascular disease in the general population - a clinical pattern mirrored in individuals with PMOS, where the presence of OSA and sleep-disordered breathing synergistically exacerbates both the development of insulin resistance and the metabolic complications linked to abnormal glucose tolerance. (Jafar et al., 2025) Ultimately, these systemic and metabolic consequences profoundly alter reproductive capacity; within the cohort of infertile PMOS patients, respiratory sleep disturbances occur with elevated frequency and precipitate endocrine imbalances, thereby exerting a detrimental impact on fertility outcomes and demonstrating a strong negative association with both clinical pregnancy achievement and live birth rates. (Li et al., 2024)

Psychological Distress, Affective Symptomatology and Mental Health Interplay

These compromised reproductive outcomes and the profound stress of infertility do not exist in a vacuum; rather, they deeply affect the psychological well-being of patients, creating a complex intersection with sleep health. Both depression and metabolic disturbances, which frequently manifest at a higher rate in patients with PMOS, have been independently correlated with sleep disruptions, indicating that healthcare professionals should be especially aware of mood disturbances in these women and cooperate with psychologists when formal assessment and therapy are required. (Eisenberg et al., 2021; Teede et al., 2023) According to several studies, PMOS patients exhibit a higher risk of developing sleep disturbances and lower sleep quality compared to healthy females, with anxiety being remarkably more prevalent in this group as a

consequence of impaired sleep architecture - connected factors that can negatively impact life satisfaction and drive the development of depressive disorders. (Zhang et al., 2022)

This psychological burden is profoundly compounded by reproductive challenges, establishing a self-perpetuating feedback loop wherein a depressed mood, often precipitated by reproductive failure and the distress of infecundability, subsequently drives further sleep fragmentation. (Yang et al., 2021) This reciprocal dynamic is similarly mirrored in the interaction between chronic sleep disturbances and anxiety; sleep disorders significantly elevate the vulnerability to psychiatric comorbidities, while concurrent anxiety conversely degrades sleep efficiency and structural quality. (Decrinis et al., 2025)

This reciprocal nature of mental distress and sleep deprivation highlights the systemic complexity of the syndrome. Affective symptomatology, including depression and anxiety, demonstrates a bidirectional interplay with compromised sleep architecture. As previously noted, optimizing mental health outcomes serves as a crucial cornerstone to facilitate greater compliance with lifestyle modifications, specifically dietary adherence and physical activity. (Alvaro, Roberts & Harris, 2013; Pirotta et al., 2021)

Beyond individual emotional distress, these disturbances extend into the broader social and behavioral domains of a patient's life, driven by underlying chronobiological disruptions, as the desynchronization of the circadian rhythm negatively affects social functioning and is intimately connected to various psychiatric disorders and mental health issues. (Hood & Amir, 2018; Walker et al., 2020) Therefore, addressing mental health and sleep synchronization concurrently is essential to improve both the clinical parameters and the overall quality of life for individuals with PMOS.

Metabolic Homeostasis, Cardiovascular Risk and Lifespan Manifestations

Given that psychiatric optimization and lifestyle modifications rely heavily on patient compliance, identifying the physiological barriers to these interventions is of paramount clinical importance. In patients with PMOS, compromised sleep quality fundamentally disrupts energy homeostasis and alters neuroendocrine appetite modulation, thereby presenting a severe physiological barrier that undermines long-term dietary adherence. (Mo et al., 2018) Impaired sleep quality and extreme sleep durations (<5–6 hours or >9–10 hours) compromise dietary control and elevate stress, driving weight gain, hypertension and obesity, which represent established risk factors for both type 2 diabetes mellitus and cardiovascular disorders. (Cappuccio & Miller, 2017) To illustrate, inadequate sleep disrupts ghrelin and leptin pathways, undermining adherence to healthy diets and structured meal patterns, while the intersection of sleep deficits and circadian misalignment severely degrades metabolic health and stimulates weight accumulation. (Jafar et al., 2023) These appetite and lifestyle disruptions directly translate into objective anthropometric changes and systemic comorbidities across the lifespan, linking disturbed sleep architecture to adiposity, arterial hypertension, diabetes mellitus, affective disorders and a degraded quality of life. Despite these established correlations, the specific nexus between diurnal somnolence and PMOS remains poorly elucidated; nonetheless, the limited literature evaluating sleep profiles in women of childbearing potential indicates a significant association between PMOS and subclinical sleep disruptions. (Wang et al., 2022) Affected individuals demonstrate a higher BMI and waist circumference compared to females without resting dysfunctions, highlighting a higher prevalence and severity of obesity among patients with polyendocrine metabolic ovarian syndrome who experience disrupted sleep. (Zhang et al., 2022)

Importantly, this deleterious metabolic trajectory begins remarkably early in life. Even during adolescence, young girls presenting with both PMOS and obesity exhibit significant sleep disruptions compared to their healthy, normal-weight peers, typically manifesting as prolonged sleep-onset latency alongside marked reductions in both total REM sleep duration and overall sleep efficiency. (de Sousa et al., 2010) The clinical severity of these changes is further supported by objective measurements in younger patients, where poorer sleep efficiency (objectively recorded via actigraphy) is tied to heightened abdominal adiposity, greater hepatic steatosis and elevated triglycerides in obese adolescents with PMOS, signaling that more research is urgently required to fully map these early pathways. (Simon et al., 2020)

In adults, these structural sleep deficits mature into severe, quantifiable cardiovascular and endocrine threats. Extensive studies confirm that sleep disturbances in the PMOS cohort are closely tied to unfavorable clinical markers, encompassing elevated BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference, impaired blood glucose levels, heightened low-density lipoprotein cholesterol (LDL-c) and depleted high-density lipoprotein cholesterol (HDL-c). (Zhang et al., 2022) Because elevated LDL-c and reduced HDL-c strongly predict cardiovascular disease, poor sleep clearly drives cardiovascular danger in this population, rendering cardiovascular screenings clinically vital. (Zhang et al., 2022) At the core of this danger is a profound disruption in glycemic control and pancreatic function, as data indicate that sleep fragmentation severely compromises metabolic pathways. Within the PMOS group, individuals affected by sleep disorders

demonstrate higher fasting and 2-hour oral glucose tolerance test (OGTT) values, thereby compounding their baseline risk for cardiovascular events through adverse shifts in glucose pathways triggered by architectural changes in sleep phases. (Zhang et al., 2022) While the body transiently develops insulin resistance during periods of high blood glucose to lower metabolic stress, persistent serum glucose elevations in individuals with glucose intolerance or diabetes aggravate insulin resistance and destroy pancreatic beta cells, proving that managing sleep architecture is a critical metabolic intervention necessary to preserve long-term cardiovascular and endocrine health. (Zhang et al., 2022)

Integrated Therapeutic Strategies and Comprehensive Care Models

Preserving long-term cardiovascular and endocrine health demands shifting clinical focus from isolated symptom management toward structured, overarching treatment paradigms. Comprehensive care for individuals with PMOS necessitates an all-inclusive approach addressing reproductive, metabolic, psychological, cardiovascular, cutaneous and sleep-related manifestations immediately after diagnosis, establishing a long-term wellness framework centered on maintaining a healthy lifestyle, avoiding excessive weight gain and mitigating preconception risks. (Teede et al., 2023) Given that PMOS inherently amplifies the risk for diabetes, metabolic dysfunction, cardiovascular disorders and disrupted sleep patterns, continuous prevention and targeted treatment of these features remain vital. When reproductive failure becomes the primary clinical concern, standard guidelines dictate a prompt escalation to targeted pharmacological protocols, usually based on letrozole in conjunction with clomiphene and metformin, with in vitro fertilization (IVF) reserved for cases where conventional options fail. (Teede et al., 2023)

However, addressing fertility and systemic complications mandates a parallel focus on the patient's daily sleep architecture. A variety of studies have evaluated non-pharmacological modalities, encompassing physical activity, cognitive-behavioral modifications, dietary optimization and psychological support systems, alongside supplemental medical therapies utilizing metformin, melatonin and magnesium to improve sleep metrics among women diagnosed with PMOS. (Jafar et al., 2023) These targeted approaches directly counteract the subtle, objective deficiencies in sleep quality that standard diagnostics might miss.

Studies show that while individuals with PMOS frequently demonstrate a standard sleep duration, their sleep efficiency is markedly poorer than controls. However, behavioral modification strategies effectively minimize excessive daytime sleep periods compared to minimal intervention approaches, demonstrating measurable improvements in overall sleep patterns. (Oberg et al., 2023) Correcting these daytime patterns carries immense metabolic significance beyond simple rest recovery; since daytime napping is linked to a higher incidence of type 2 diabetes mellitus and all-cause mortality, behavioral interventions addressing diet and physical activity provide a feasible pathway to enhance both sleep quality and long-term cardiometabolic health in patients with PMOS. (Jafar et al., 2023) Ultimately, the clinical success of these dietary and physical modifications hinges on stabilizing the sleep-wake cycle itself. Data suggest that women with PMOS can successfully maintain a higher-quality nutritional profile only when supported by adequate sleep duration and low levels of sleep-related morbidity. (Bennett et al., 2021) Therefore, although individuals diagnosed with PMOS often self-select healthier dietary patterns in accordance with established medical guidelines, their behavioral capacity to sustain these improvements appears to be markedly diminished by sleep deprivation and poor sleep architecture, rendering sleep optimization a prerequisite foundational component determining the efficacy of all clinical interventions in the PMOS population. (Bennett et al., 2021)

Conclusions

In conclusion, this review highlights that reproductive and metabolic complications in polyendocrine metabolic ovarian syndrome (PMOS) are intrinsically linked to sleep disruptions and circadian misalignment. This complex condition involves a bidirectional network where central and peripheral clock desynchronization directly impairs ovulation, oocyte quality and embryonic development. These chronobiological shifts are further aggravated by neuroendocrine imbalances, such as altered melatonin secretion and elevated evening cortisol, which drive insulin resistance and hyperandrogenism. This metabolic decline is compounded by a high prevalence of obstructive sleep apnea (OSA), which accelerates abdominal obesity and cardiovascular risk. Furthermore, psychiatric comorbidities like anxiety and depression establish a vicious cycle with sleep fragmentation, while chronic sleep deprivation severely undermines a patient's capacity to maintain essential dietary and lifestyle modifications. Consequently, comprehensive management of PMOS requires a multidisciplinary approach, where sleep parameters are evaluated immediately after diagnosis. Integrating sleep optimization into standard clinical protocols is essential to break these damaging feedback loops, enhance fertility treatment success and preserve long-term cardiometabolic health.

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