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Potential Applications of Creatine Supplements in Gynecology and Women's Health: Current Evidence and Future Perspectives

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Abstract

Background: Creatine is one of the most extensively studied dietary supplements and has traditionally been used to improve physical performance and muscle function. Increasing evidence suggests that its role extends beyond sports nutrition, with potential applications in women's health across different stages of the female lifespan.

Aim of the study: This review summarizes the biological functions of creatine, evaluates commercially available forms of supplementation, and critically discusses current evidence regarding its potential applications in gynecology and women's health, including the menstrual cycle, pregnancy, and menopause.

Materials and methods: A systematic review of PubMed (last 20 years) was conducted using the keywords: "creatine", "women's health", "menstrual cycle", "pregnancy", "menopause", and "gynecology".

Conclusions: Creatine supplementation is emerging as a promising supportive strategy in women's health beyond sports nutrition. Creatine monohydrate remains the preferred formulation because of its established efficacy and safety. Evidence suggests that creatine may improve hydration, reduce fatigue, and support physical performance during the reproductive years, while preclinical studies indicate potential fetal protective effects during pregnancy. In postmenopausal women, particularly when combined with resistance training, creatine may enhance lean body mass and muscle strength, with emerging evidence also supporting benefits for cognitive function. However, further large-scale randomized controlled trials are needed to confirm its long-term safety, optimal dosing, and clinical efficacy in female-specific conditions.

Keywords: *creatine, creatine monohydrate, women's health, gynecology, pregnancy, menopause, menstrual cycle, dietary supplements.*

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1. Introduction

Creatine is among the most widely used dietary supplements worldwide and has traditionally been associated with athletes and resistance-trained individuals seeking to improve physical performance and muscle function. Owing to its established efficacy, favorable safety profile, and widespread availability, creatine supplementation has become a common component of sports nutrition strategies. However, growing scientific interest in recent years has expanded its potential applications beyond athletic performance, highlighting possible roles in neurological health, aging, metabolism, and women's health [1, 2].

Women represent a unique population in which physiological and hormonal factors may influence creatine metabolism and responsiveness to supplementation. Fluctuations in sex hormones throughout the menstrual cycle, pregnancy, postpartum period, and menopause are accompanied by biological changes that may influence creatine metabolism, energy utilization, and tissue function. Increasing evidence suggests that creatine metabolism may be influenced by these hormonal changes, raising interest in its potential role across different stages of the female lifespan [1, 3].

Several female-specific physiological states are characterized by increased metabolic demands, fatigue, reduced physical capacity, impaired quality of life, and alterations in body composition. In addition, pregnancy and menopause are associated with substantial changes in musculoskeletal, neurological, and metabolic function. These observations have prompted researchers to investigate whether creatine supplementation may provide supportive benefits in selected aspects of women's health beyond its traditional use in sports nutrition [1, 2].

Particular attention has been directed toward the potential role of creatine during pregnancy, where experimental evidence suggests involvement in fetal and placental energy metabolism, and during menopause, where creatine supplementation has been investigated as a strategy to support muscle function, healthy aging, and overall well-being. Nevertheless, despite increasing interest and promising preliminary findings, many proposed applications remain incompletely understood and require further clinical investigation. Therefore, the aim of this review is to summarize current knowledge regarding the biological functions of creatine, commercially available forms of supplementation, and the potential applications of creatine in gynecology and women's health, while identifying areas requiring further research.

2. Effects of Creatine on the Human Body

Creatine is a naturally occurring nitrogen-containing compound synthesized primarily from the amino acids arginine, glycine, and methionine. Approximately 95% of total body creatine is stored in skeletal muscle, while the remaining amount is distributed among the brain, heart, and other tissues with high energy demands [5]. Within cells, creatine exists either in its free form or as phosphocreatine, a high-energy phosphate compound that plays a central role in cellular energy metabolism.

The primary physiological function of creatine is participation in the creatine–phosphocreatine system. Through the action of creatine kinase, phosphocreatine serves as an immediately available phosphate donor for the regeneration of adenosine triphosphate (ATP) from adenosine diphosphate (ADP). This mechanism enables rapid ATP resynthesis during periods of increased energy demand and is particularly important in tissues with fluctuating energy requirements, including skeletal muscle and the central nervous system [5, 6].

By increasing intramuscular phosphocreatine stores, creatine supplementation enhances the capacity for rapid ATP regeneration during short-duration, high-intensity activities. Consequently, supplementation has been associated with improvements in strength, power output, exercise performance, and training adaptations, particularly when combined with resistance exercise [5]. Increased intracellular creatine availability may also promote cellular hydration and support cellular energy homeostasis during periods of increased metabolic demand [6].

Beyond skeletal muscle, creatine plays an important role in tissues involved in cognition, neurological function, and reproduction. Creatine is also present in high concentrations in the brain, where it contributes to maintaining cellular energy homeostasis. Emerging evidence suggests that creatine supplementation may influence mood, cognitive performance, and fatigue, although the magnitude of these effects appears to vary among populations and clinical settings.

In women, creatine metabolism may be influenced by hormonal status and life-stage-specific physiological changes. Research suggests that women may exhibit lower endogenous creatine synthesis and lower dietary creatine intake than men, while fluctuations in estrogen and progesterone may affect creatine kinase activity and creatine homeostasis. These observations provide a biological rationale for investigating creatine supplementation in female-specific conditions such as pregnancy, postpartum recovery, and menopause.

3. Commercially Available Forms of Creatine

Several forms of creatine are currently available as dietary supplements, including creatine monohydrate, creatine hydrochloride (HCl), creatine ethyl ester (CEE), creatine citrate, creatine nitrate, creatine pyruvate, magnesium creatine chelate, and buffered creatine preparations. Many of these products have been introduced with claims of enhanced bioavailability, improved solubility, superior absorption, or reduced adverse effects compared with traditional creatine monohydrate.

Creatine monohydrate remains the most extensively studied and widely used form of creatine supplementation. It demonstrates high bioavailability, well-established efficacy, and an excellent safety profile across numerous clinical and sports-related studies. Supplementation with creatine monohydrate has consistently been shown to increase muscle creatine and phosphocreatine concentrations, making it the reference standard against which alternative formulations are compared [5, 7].

Creatine hydrochloride has gained popularity primarily because of its greater water solubility. Despite this improved solubility, currently available evidence does not demonstrate superior biological effectiveness compared with creatine monohydrate [7]. Similarly, creatine ethyl ester was developed to enhance cellular uptake through structural modification of the creatine molecule. However, comparative investigations have not demonstrated superior increases in muscle creatine content, muscle mass, strength, or exercise performance relative to creatine monohydrate. Furthermore, creatine ethyl ester appears to undergo greater conversion to creatinine under acidic conditions following ingestion, potentially reducing its effectiveness [8].

Other commercially available formulations, including creatine citrate, pyruvate, nitrate, buffered creatine, and magnesium creatine chelate, have been investigated in a limited number of studies. Although some have been proposed to offer theoretical physicochemical or pharmacokinetic advantages, current evidence remains insufficient to establish meaningful advantages over creatine monohydrate regarding efficacy or safety. Creatine monohydrate remains the preferred form of creatine supplementation owing to its extensive scientific evidence, well-established efficacy, favorable safety profile, and cost-effectiveness.

4. Effects of Creatine Supplementation in Women in Reproductive Years

4.1 The Menstrual Cycle and Hormonal Phases

Across the menstrual cycle, women go through two hormonally distinct stages, the follicular and luteal phases, where estrogen and progesterone are rising and falling, reshaping everything from hydration to energy metabolism. The physiological changes during the cycle are experienced by each and every woman in areas like sport performance, sleep and fatigue, and fluid distribution [1, 9, 10].

A study of 30 moderately physically active women, naturally menstruating or using hormonal contraceptives, assessed whether daily consumption of 20 g (4×5 g) of creatine monohydrate for 5 days affects fluid distribution across menstrual phases. In the examined group there was a significant increase in parameters like total body water, extracellular fluid and intra-cellular fluid after consuming creatine monohydrate in the luteal phase. Supplementing creatine improved hydration status in the luteal phase, without a significant increase in body mass. That study did not explore the impact of hydration markers on thermoregulation, however previous research has demonstrated that increased total body weight and intra-cellular fluid are connected with better exercise performance and thermoregulatory outcomes [9].

Moreover it is widely recognised that hormones do not just affect how the body feels across the cycle, they also affect the creatine metabolism itself. As estrogen and progesterone shift, the creatine production in the body does, how efficiently it is moved into tissues and how active the creatine kinase enzyme is. This pattern evolves across a woman's reproductive life [10, 3]. Animal studies back this up – research in rodents found that creatine kinase activity tracks estrogen's rise and fall across the cycle and does not stay constant [11].

Estrogen peaks during the luteal phase, when there is an elevation in protein catabolism and reduction in carbohydrate storage. Creatine supports muscle protein kinetics, glycogen regulation and reduces oxidative stress, which makes the luteal phase the time of the cycle, when creatine supplementation could benefit the most. The increase in creatine kinase levels may also reduce muscle damage after sport performance and reduce general fatigue after a sprint test [3, 2].

In another study, Gordon et al. observed that creatine supplementation was linked to a 5% decrease in fatigue index compared to placebo group (less than 1% change) – an interaction that did reach statistical significance ($p=0.048$). This suggests creatine may meaningfully neutralise the sprint-performance decline typically seen in the luteal phase. It opens a useful base for dietary planning in female athletes. Another measured parameter – heart rate variability, was lower in both groups in luteal phase. It is connected with worse regeneration, but creatine monohydrate did not seem to impact its value [12].

However, creatine consumption is also connected with concerns about weight gain especially among women. There is observed an increase of water weight (but not fat gain) during consumption of loading doses of creatine, mostly observed among males. Furthermore, combining creatine with a high carbohydrate intake (1 g/kg body weight) can result in additional weight gain and it should be taken under consideration while starting the supplementation. Definitely further research is needed on creatine's impact during the follicular phase and among women with amenorrhea [3]. Supplementation regimens should be established on the basis of an observation of the menstrual cycle and individual response.

4.2 Pregnancy

Creatine can impact pregnancy and fetus development in many directions. Supplementing creatine and adding creatine to the list of specialist recommendations are widely discussed and are still a promising direction of research. Analysis of NHANES data from years 2011-2018 found that roughly 6 out of 10 pregnant women in the US consumed less creatine than recommended for an adult female [13]. This evidence is even more concerning because women generally synthesise about 20% less creatine and consume 30-40% less in diet than men [1].

Two obstetric complications remain especially hard to prevent: hypoxic encephalopathy in the newborn and premature birth. They are often present alongside issues such as intrauterine infection or chronic fetal hypoxia. The demands of pregnancy itself compound this risk. Even in an uncomplicated pregnancy, the placenta generates oxygen and nitrogen-based free radicals at an elevated rate, because the body in general is running at a heightened metabolic pace [14].

Creatine supplementation supports the development of the neurological system, is neuroprotective and reduces the risk of birth complications and reduces mortality [4]. In animal studies on pregnant spiny mice it has been proven that creatine loading before birth

protects skeletal muscles from asphyxia-induced damages and improves motor performance ($P<0.05$) [15], prevents functional changes in the diaphragm ($P<0.05$) [16] and supports renal excretory function [17]. Many animal studies reported that maternal creatine supplementation prevented and improved postnatal growth [4, 18].

It seems creatine supplementation did not show any significant adverse effects. However to establish a clinical consensus of the dosage and tolerance there is needed more evidence, especially from clinical trials among pregnant women.

5. Effects of Creatine Supplementation in Postmenopausal Women

Menopause is a natural biological process characterized by the permanent cessation of ovarian function and a marked decline in circulating estrogen levels. Beyond the loss of reproductive capacity, estrogen deficiency induces physiological changes that affect multiple organ systems, particularly the musculoskeletal and nervous systems. Postmenopausal women experience an accelerated decline in skeletal muscle mass and strength, contributing to reduced physical performance and an increased risk of sarcopenia. At the same time, enhanced bone resorption results in progressive reductions in bone mineral density, predisposing women to osteoporosis and fragility fractures. Menopause has also been associated with cognitive symptoms, including impairments in memory, attention, and executive function, which may be partly attributed to altered cerebral energy metabolism and reduced neuroprotective effects of estrogen.

Given the important role of creatine in cellular energy homeostasis, particularly in skeletal muscle and the brain, creatine supplementation has emerged as a promising nutritional strategy to counteract several adverse consequences of menopause [19, 20, 21].

A recent systematic review and meta-analysis by Naddafha et al. (2026), including seven randomized controlled trials (n = 608 postmenopausal women), evaluated the effects of creatine monohydrate supplementation on body composition, muscle strength, and bone outcomes. Across interventions lasting 12–104 weeks, creatine was most commonly administered as creatine monohydrate at doses ranging from 1 to 5 g/day (with some protocols including a loading phase or higher doses ≥5 g/day), either alone or combined with resistance training. The analysis showed a small but significant increase in lean body mass (+0.37 kg) and an improvement in lower-body strength, with leg press 1RM increasing by

approximately +7.5 kg, particularly when creatine was used at ≥5 g/day alongside resistance training, while no meaningful effects were observed on bone mineral density [22].

In contrast to the majority of studies reporting no significant effects of creatine on bone mineral density, a randomized controlled trial by Chilibeck et al. (2015) provided somewhat different findings. In this 12-month, double-blind study, the effects of creatine monohydrate supplementation combined with resistance training were investigated in postmenopausal women. The study included 47 participants (mean age ~57 years) who received either creatine monohydrate (0.1 g/kg body mass/day) or placebo during a supervised resistance training program performed three times per week. Although no significant differences were observed in total lumbar spine or hip bone mineral density, creatine supplementation was associated with a smaller reduction in femoral neck BMD, corresponding to −1.2% in the creatine group compared with −3.9% in the placebo group ($p < 0.05$). In addition, beneficial effects were observed in femoral bone geometry, including increased subperiosteal width, suggesting improved bone strength. Greater gains in upper-body strength were also reported in the creatine group. However, no significant differences were found in overall body composition or several other bone-related outcomes [23].

Extending the current evidence base on creatine and menopausal health, the randomized controlled CONCRET-MENOPA trial by Korovljev et al. investigated the effects of different low-dose creatine formulations on neurocognitive and metabolic outcomes in perimenopausal and postmenopausal women. In this 8-week, double-blind study, 36 participants (mean age ~50 years) were randomized to receive either creatine hydrochloride at doses of 750 mg/day or 1500 mg/day, creatine hydrochloride combined with creatine ethyl ester, or placebo. The study primarily focused on brain bioenergetics and cognitive performance rather than musculoskeletal endpoints. Results demonstrated that medium-dose creatine hydrochloride significantly improved reaction time compared with placebo ($p < 0.01$) and was associated with an increase in frontal brain creatine concentrations ($p < 0.01$). In addition, a trend toward improved mood-related outcomes was observed, although not all between-group differences reached statistical significance. No safety concerns or adverse events were reported [24].

Table 1

Summary of key findings on creatine's effects during the menstrual cycle, pregnancy, and menopause, with the primary studies referenced in the source

Life Stage	Main Observed Effects	Dosage / Protocol	Study (authors, year)
Menstrual cycle – luteal phase	Improved hydration status (increased total body water, extracellular and intracellular fluid) without significant increase in body mass	20 g/day (4×5 g) for 5 days	Moore, Gordon, Cabre, et al. (2023)
Menstrual cycle – luteal phase	Reduced fatigue index (~5% decrease vs. <1% in placebo, p=0.048); no effect on heart rate variability	Loading dose protocol	Gordon, Moore, Patterson, et al. (2023)
Menstrual cycle – general	Creatine kinase activity fluctuates in line with estrogen levels across the cycle (animal study)	—	Somjen et al. (1991) – rat study
Pregnancy	Insufficient creatine intake in ~6 out of 10 pregnant women in the US (NHANES analysis)	—	Ostojic, Forbes, Candow (2022)
Pregnancy	Potential fetal neuroprotection, reduced risk of hypoxic encephalopathy and birth complications (Cochrane review)	—	Dickinson, Bain, Wilkinson, et al. (2014) – Cochrane
Pregnancy (animal studies)	Protection of skeletal muscle from asphyxia-induced damage, improved motor performance	Prenatal supplementation in spiny mice	LaRosa et al. (2016) – skeletal muscle
Pregnancy (animal studies)	Prevention of structural and functional changes in the diaphragm after birth asphyxia	Same as above	LaRosa et al. (2016) – diaphragm
Pregnancy (animal studies)	Support of renal excretory function	Same as above	Ellery, LaRosa, Kett, et al. (2016)
Menopause / postmenopause	Small but significant increase in lean body mass (+0.37 kg) and lower-body strength (leg press 1RM +7.5 kg); no meaningful effect on bone mineral density	1–5 g/day (some protocols with loading phase, ≥5 g/day), often combined with resistance training; 12–104 weeks	Naddafha, Antonio, Kreider, Stout (2026) – meta-analysis of 7 RCTs, n=608
Menopause / postmenopause	Smaller reduction in femoral neck BMD	0.1 g/kg body mass/day + resistance	Chilibeck, Candow, Landeryou, et al.

	(−1.2% vs. −3.9% in placebo, $p<0.05$); improved femoral bone geometry; greater upper-body strength gains	training 3×/week, 12 months	(2015), n=47
Perimenopause / menopause	Significant improvement in reaction time ($p<0.01$) and increased frontal brain creatine concentration ($p<0.01$); trend toward improved mood	Creatine HCl 750 mg/day or 1500 mg/day (± ethyl ester), 8 weeks	Korovljev, Ostojic, Panic, et al. (2026) – CONCRET-MENOPA, n=36

6. Conclusions

Creatine supplementation is emerging as a promising supportive strategy in women's health beyond sports nutrition. Creatine monohydrate remains the preferred formulation because of its established efficacy and safety. Evidence suggests that creatine may improve hydration, reduce fatigue, and support physical performance during the reproductive years, while preclinical studies indicate potential fetal protective effects during pregnancy. In postmenopausal women, particularly when combined with resistance training, creatine may enhance lean body mass and muscle strength, with emerging evidence also supporting benefits for cognitive function. However, further large-scale randomized controlled trials are needed to confirm its long-term safety, optimal dosing, and clinical efficacy in female-specific conditions.

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