No Influence of Menstrual Cycle on Muscle Strength and Flexibility in Women Practising Strength Training

João Pedro Moraes de Souza, Tainá Maria de Souza Vidal, Keyla Brandão Costa, Aline de Freitas Brito, Manoel da Cunha Costa, Raphaella Christine Ribeiro de Lima, Marlene Salvina Fernandes da Costa, Wlaldemir Roberto dos Santos

School of Physical Education, University of Pernambuco, Recife, Pernambuco, Brazil

CORRESPONDING AUTHOR:

Wlaldemir Roberto dos Santos School of Physical Education University of Pernambuco 310 Arnóbio Marques St. Santo Amaro, Recife Pernambuco 50100130, Brazil E-mail: wlaldemir.santos@upe.br

DOI:

10.32098/mltj.03.2025.02

LEVEL OF EVIDENCE: 4

SUMMARY

Background. The menstrual cycle (MC) is a natural process of the female reproductive system, characterized by fluctuations in the hormones estrogen and progesterone, which can affect physical performance, particularly strength and flexibility.

Objective. To analyze the influence of the MC on muscle strength and flexibility in individuals practicing strength training, identifying variations throughout the different phases of the cycle.

Methods. An exploratory study included 15 amenorrheic university students (22.50 \pm 5.11 years) practicing strength training for at least 6 months, with a minimum of 3 weekly sessions. Participants with uncertain MC regularity, athletes, or those missing assessments were excluded. Sociodemographic, gynecological questionnaires, and the Menstrual Distress Questionnaire (MDQ) were administered. Muscle strength was measured via the 1-RM test for upper and lower limbs; flexibility by range of motion (goniometry) and the sit-and-reach test; subjective perception of exertion was recorded. Data were analyzed using ANOVA (p < 0.05).

Results. A significant difference was observed (p = 0.001) only in menstrual symptoms, with higher values during the menstrual phase and lower values in the postmenstrual phase (Δ : 120%). No significant differences were found in the other variables between the phases of the MC.

Conclusions. This study found no significant differences in flexibility or muscle strength across MC phases. Despite more intense symptoms during menstruation, physical performance was unaffected. Future research should explore the relationship between the MC and physical performance in women, especially in strength training.

KEY WORDS

Menstrual cycle; strength; flexibility.

INTRODUCTION

The menstrual cycle (MC) is a natural biological process that occurs monthly in women, from menarche to menopause, and is associated with fluctuations in sex hormones, primarily estrogen and progesterone (1). These hormonal fluctuations follow a predictable pattern in average 28-day cycles (2). The MC is commonly divided into three phases: the follicular phase, the ovulatory phase, and the luteal phase. The follicular phase begins with menstruation and extends

until ovulation, being further subdivided into the menstrual and post-menstrual periods. During this phase, there is a decline in estrogen and progesterone levels, followed by a gradual increase in estrogen, which stimulates the development of a dominant follicle, preparing the body for ovulation (1, 3).

During the ovulatory phase, which occurs right after the post-menstrual period of the follicular phase, the egg is released and transported toward the endometrium. This phase is characterized by high concentrations of estrogen

and progesterone. The ovulatory phase lasts an average of 24 to 48 hours and is followed by the luteal phase, which lasts approximately 14 days. The luteal phase is divided into two periods: the intermenstrual period (early luteal phase) and the premenstrual period (late luteal phase), which begins between the 23rd and 24th days after the onset of menstruation (4, 5). During the premenstrual period, estrogen and progesterone levels drop significantly due to the degeneration of the corpus luteum, in the absence of fertilization, preparing the body for the next MC (1, 6).

Female physical performance can vary throughout the phases of the MC. In the post-menstrual period, the gradual increase in estrogen levels promotes anabolic responses, including enhanced muscle strength. Additionally, there is an increase in norepinephrine production, which directly impacts physical capacity, boosting muscular performance during this period (7). As the cycle progresses to the ovulatory phase, physical performance begins to decline, albeit subtly. During the ovulatory phase, there is a reversal in hormonal concentrations, marked by a significant decrease in estrogen levels, which reduces anabolic capacity. This effect is exacerbated by the rise in progesterone, which promotes catabolism and prepares the body for the luteal phase (7-9). For this reason, Blagrove et al. (8) suggest that the intensity and volume of strength training be adjusted according to the muscular responses of each MC phase, tailoring training to the performance characteristics of each period.

Additionally, flexibility may also vary throughout the MC due to increased levels of relaxin, particularly during the premenstrual period. This hormonal rise affects joints and ligaments, enhancing their elasticity and, consequently, range of motion (RM) (10). Similarly, but through different physiological mechanisms, during the menstrual and post-menstrual periods, the increase in estrogen and progesterone stimulates collagen synthesis and the activity of metalloproteinases, leading to greater ligament laxity and reduced tendon stiffness, factors that influence flexibility and RM (11).

Thus, the present study aims to analyze the influence of the MC on muscle strength and flexibility in individuals engaged in strength training, seeking to identify potential variations throughout the cycle's phases. The objective is to understand the physical responses that women may experience during the MC, enabling the formulation of more precise recommendations for adjusting training parameters, optimizing the effectiveness of programs, and minimizing discomfort or injury risks associated with hormonal fluctuations.

MATERIALS AND METHODS

Study type and population

This is an exploratory research study (12), conducted at the Biodynamics Laboratory (LABIO) of the Superior School of Physical Education at the University of Pernambuco (ESEF-UPE). The study was approved by the Human Research Ethics Committee (date of approval: November 11, 2019) of UPE, under opinion no. 3.696.219, following the ethical guidelines established by Resolution 466/12, which regulates research involving human subjects.

The sample selection was conducted through in-person invitations to all classes at ESEF-UPE, where the study's objectives, inclusion and exclusion criteria, as well as the risks and benefits of participation were presented. University students over 18 years old, eumenorrheic, without dysmetabolic issues, who had been engaged in strength training for at least six months, with a minimum frequency of three training sessions per week, and who agreed to participate voluntarily in the study were included. Participants who reported uncertainties regarding their MC regularity, those who were athletes in specific sports, who presented any injury to the musculotendinous complex, or those who missed any study assessments were excluded. Thus, 20 volunteers agreed to participate by signing the Informed Consent Form (ICF) and meeting the inclusion criteria. However, 5 were excluded for not attending one

Study design

After accepting and signing the ICF, a session was scheduled for explaining and familiarizing participants with the tests, as well as administering the sociodemographic questionnaire and gynecological history, aimed at characterizing the sample.

of the assessments, resulting in a final sample of 15 women.

The test battery was conducted at four distinct times: familiarization, menstrual period, post-menstrual period, and premenstrual period. The familiarization session was scheduled with a minimum interval of 72 hours before the expected date of menstruation, as reported by the volunteer. After familiarization, the volunteers were instructed to notify the researchers of the day their menstruation began for the first assessment, conducted during the menstrual period, specifically between the first and second day of menstruation. The second assessment occurred in the post-menstrual period, between the fourth and fifth day after the onset of menstruation, coinciding with the end of menstrual flow. Finally, the premenstrual assessment was conducted between the 23rd and 24th days after the onset of menstruation (4, 5).

During the familiarization session, a detailed explanation of the study was provided, according to the scheduled initial contact with each participant. At this time, body mass and height were measured, and the sociodemographic questionnaire and gynecological history were administered. Each volunteer was then subjected to an acclimatization session with the selected tests, starting with flexibility assessment, measured by RM using goniometry, considering shoulder and hip joint flexion and extension, with the right side as a reference (13). After the RM assessment, the flexibility of the posterior muscle chain was evaluated using the sit-and-reach test (SRT) with the Wells bench (5, 14, 15). Muscle strength was assessed using the one-repetition maximum (1-RM) test (5, 16), measuring the strength of the lower limbs (LL) and upper limbs (UP). At the end of the test battery, volunteers reported their effort using the scale subjective perception of exertion (SPE) (17).

After the familiarization phase, the same evaluations were conducted during the other three phases of the cycle (menstrual, post-menstrual, and premenstrual), with the addition of completing the Menstrual Distress Questionnaire (MDQ) (18) at the beginning of each assessment for the respective phase of the MC.

All assessments were conducted in the LABIO at ESEF-UPE, with temperature controlled at 22 degrees Celsius (71.6 degrees Fahrenheit) during the evaluations and without the presence of any ambient sounds, except for the commands for performing the tests. All assessments and reassessments were conducted by a single evaluator, using the same instruments and procedures throughout. The tests and retests were performed between 11:00 AM and 1:00 PM.

Collection instruments

The sociodemographic questionnaire and gynecological history aimed to characterize the sample. The sociodemographic questionnaire assessed personal health conditions and lifestyle, specifying training history characteristics. The gynecological history investigated information regarding contraceptive use, obstetric history, and menstrual history. Menstrual symptomatology was assessed using an adapted version of the MDQ (18), consisting of 27 items that address the main symptoms associated with menstruation. Each item is scored on a scale from 0 to 4 points, where 0 = no symptom; 1 = mild symptom; 2 = moderate symptom; 3 = severe symptom; and 4 = unbearable symptom. A higher score indicates greater reported symptomatology. The MDQ was administered during the assessments in the menstrual, post-menstrual, and premenstrual periods.

RM was assessed using goniometry, with a universal acrylic goniometer from the Carci brand, to measure active flexion and extension of the shoulder and hip joints, using the right side as a reference. Shoulder flexion and extension were measured in the anatomical position, with the palm in a neutral position at 0 degrees of abduction, adduction, and rotation. Under the researcher's instruction, the participant actively performed the maximum possible RM in flexion, with the value verified and recorded in a data collection instrument. Next, the participant performed the extension movement, with the angle also noted. Hip RM was evaluated with the participant in a supine position for flexion and in a prone position for extension. In both positions, the movement started at 0 degrees of abduction, adduction, and rotation, and under the researcher's instruction, the participant performed the maximum RM, with the angle recorded in a data collection instrument (13). For this study, the average RM obtained in flexion and extension for each segment (shoulder and hip) was adopted, resulting in a single mean for each.

The flexibility of the posterior muscle chain was assessed using the SRT (5, 14, 15), which measures flexibility in the posterior region of the spine and lower limbs. A wooden Wells orthopedic box (Zapmédica brand, dimensions: $30.5 \text{ cm} \times 30.5 \text{ cm} \times 30.5 \text{ cm}$) was used. Participants were instructed to sit on their ischial tuberosities, barefoot, with their feet apart and soles resting on the base of the box, knees fully extended, and hands stacked with middle fingers aligned. In the initial position, participants were to take a deep breath, and upon exhaling, slide along the measuring line as far as possible, holding the position for approximately 3 seconds to validate the measurement. In each session, three attempts were made, and the average of the three results was included in the analysis. The zero point of the scale aligns with the foot support and advances approximately \pm 28 cm toward the participant.

Muscle strength was assessed using the 1-RM test (5, 16). To evaluate the strength of the LL, a horizontal leg press machine was used, which primarily performs knee and hip extension actions. For the UP, a chest press machine was employed, which primarily facilitates horizontal shoulder adduction, scapular abduction, and elbow extension. Both machines were from the Movement brand and were equipped with fixed weight bars, cushioning, automatic counters, and timers.

Initially, on each machine, starting with the horizontal leg press, the participant performed a warm-up with full range of motion for the knee and hip, executing 12 repetitions at 40% to 60% of the maximum load estimated by

the participant. After 2 minutes, the load was adjusted to the maximum estimated weight. If the participant successfully completed the 1-RM (characterized by full range of motion during the exercise, specifically full extension of the knee and hip in the concentric phase of the movement), she rested for an additional 3 to 5 minutes, and the procedure was repeated for up to three attempts. If the participant was unable to complete the movement correctly, the test was terminated, and the load obtained from the last successful attempt was validated as the maximum load. The same procedure was followed for the chest press, with the participant performing the complete concentric movement of horizontal shoulder adduction, scapular abduction, and elbow extension.

Effort during the activities was measured using the SPE (17). At the end of the assessments for each respective period, participants rated their perceived level of effort for completing the tests on a scale of 1 to 10 (where 1 = very light activity; 2-3 = light activity; 4-6 = moderate activity; 7-8 = vigorous activity; 9 = very hard activity; and 10 = maximum effort). A higher score indicated greater perceived exertion.

Data analysis and processing

All data were recorded in collection instrument forms, tabulated in electronic spreadsheets, and subsequently analyzed. For data treatment, exploratory inspections were conducted to identify extreme values (outliers), as well as to check for normality of distribution and homogeneity of data. Statistical analyses included descriptive and inferential techniques, either parametric or non-parametric, as necessary, and the characterization of the sample was presented. Repeated measures ANOVA was used to compare the menstrual, post-menstrual, and pre-menstrual periods. Statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp.). The significance level was set at p < 0.05 for all analyses.

RESULTS

The sample consisted of 15 volunteers, with an average age of 22.50 (\pm 5.11) years. They had been practicing strength training for an average of 3 (\pm 0.71) years, with an average weekly frequency of 4 (\pm 0.97) days. Regarding gynecological conditions, menarche occurred at an average age of 11 (\pm 1.16) years, and 20% of the participants reported using contraceptives. The characteristics of the sample are detailed in **table I**.

When analyzing the differences in flexibility (RM and flexibility of the posterior muscle chain), muscular strength, perceived exertion, and menstrual symptoms during the three phases of the MC (menstrual, post-menstrual, and pre-menstrual), significant differences (p < 0.001) were observed only in menstrual symptoms. Using the MDQ, higher scores were found during the menstrual period (score: 36.27 ± 19.71) and lower scores during the post-menstrual period (score: 16.53 ± 11.53 ; Δ : 120%) (table II).

When comparing the participants who used (80%) and did not use (20%) contraceptives, no significant differences (p > 0.05) were observed in any of the measured variables (**figure 1**).

DISCUSSION

In this study, no significant differences were found in flexibility, muscle strength, or SPE between the phases of the MC (menstrual, post-menstrual, and pre-menstrual). The only significant variation observed was in the menstrual symptoms reported during the MC, with higher values during the menstrual phase (p < 0.001), as assessed by the MDQ.

Variations in women's physical performance may be directly associated with the phases of the MC due to hormonal fluctuations, primarily of estrogen and progesterone (1, 6). The follicular phase is subdivided into two periods of the MC: menstrual and post-menstrual. The first four days of

Table I. Sample characterization (n = 15).

n = 15	Mean (Md) ± SD	Minimum	Maximum	P-value
Age (years)	$22.50 (21.00) \pm 5.11$	19	40	0.001*
Mass (kg)	$62.90 (65.40) \pm 7.76$	48.00	71.70	0.084
Height (cm)	$163.00 (162) \pm 5.08$	155	171	0.709
BMI (kg/m²)	$23.70 (24.0) \pm 2.91$	17.40	28.00	0.708

BMI: Body Mass Index; *p < 0.001: Significance value of the normality test (Shapiro-Wilk).

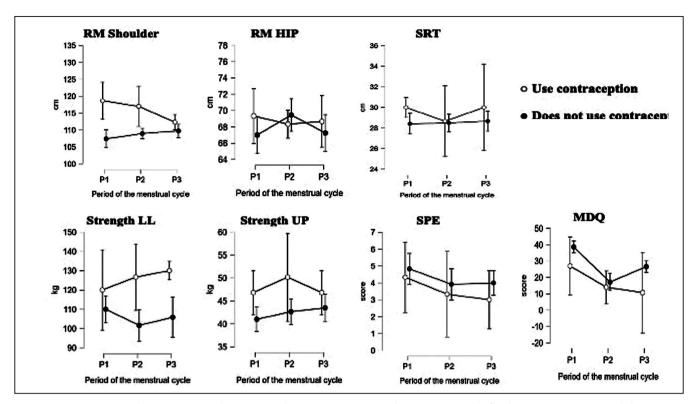


Figure 1. Comparison between periods (menstrual, post-menstrual and pre-menstrual) of volunteers who use and do not use contraceptives.

P1: Menstrual period; P2: Post-menstrual period; P3: Pre-menstrual period; RM: Range of motion; SRT: Sit and reach test; LL: Lower limbs; UP: Upper Limbs; SPE: Subjective perception of exertion; MDQ: Menstrual Distress Questionnaire.

Table II. Comparison between periods (menstrual, post-menstrual and pre-menstrual).

	Menstrual	Post-menstrual	Pre-menstrual	P-value
RM Shoulder (cm)	109.66 ± 13.25	110.56 ± 9.63	110.26 ± 10.25	0.833
RM Hip (cm)	67.47 ± 9.31	69.23 ± 9.42	67.53 ± 11.24	0.369
SRT (cm)	28.73 ± 13.68	28.53 ± 14.51	28.933 ± 13.30	0.823
Strength LL (kg)	112.00 ± 41.48	106.67 ± 43.93	110.67 ± 10.33	0.619
Strength UP (kg)	42.17 ± 9.15	44.17 ± 12.22	44.17 ± 10.10	0.456
SPE (score)	4.73 ± 1.87	3.80 ± 2.00	3.80 ± 1.82	0.170
MDQ (score)	36.27 ± 19.71	16.53 ± 11.53	23.40 ± 21.04	0.001*

RM: Range of motion; SRT: Sit and reach test; LL: Lower limbs; UP: Upper Limbs; SPE: Subjective perception of exertion; MDQ: Menstrual Distress Questionnaire; *p < 0.001: Significant difference.

menstruation correspond to the flow phase, known as the menstrual period or early follicular phase. Next, we enter the late follicular phase or post-menstrual period, when the flow has ceased and the body transitions towards ovulation (1). During the follicular phase (menstrual and post-menstrual periods), estrogen and progesterone levels increase, particularly in the early follicular phase (menstrual period), with concentrations rising as the late follicular phase

(post-menstrual period) approaches. The peak of these hormones marks the end of the late follicular phase and the transition to ovulation (3).

The ovulatory phase lasts an average of 24 to 48 hours, and after it concludes, the luteal phase begins, lasting approximately 14 days. This phase is divided into two periods: the intermenstrual period (early luteal phase) and the pre-menstrual period (late luteal phase), which starts at the end of the luteal phase, around the 23rd or 24th day after the onset of menstruation (4, 5). During this phase, there is a sharp drop in estrogen and progesterone levels due to the degeneration of the corpus luteum (in the absence of fertilization), preparing the body for the onset of the menstrual period (1, 6).

These hormonal fluctuations can trigger a variety of symptoms in women, affecting connective tissues and muscle function. This may influence joint stability (altering RM and muscle flexibility), muscle strength, and consequently the SPE during exercise, depending on the stage of the MC (11, 19, 20, 21), or even increase the incidence of injuries at the myotendinous junction, due to inefficient flexibility (22). The increase in estrogen and progesterone (menstrual and post-menstrual period) promotes collagen synthesis and the activity of enzymes like metalloproteinases, which degrade the extracellular matrix and lead to tissue remodeling. This can result in greater ligament laxity and decreased tendon stiffness, directly affecting flexibility and, as a consequence, RM (11). Regarding muscle strength, elevated levels of these hormones may influence neuromuscular transmission and excitation-contraction coupling, affecting muscle contraction efficiency and, consequently, strength and SPE (19, 20). The premenstrual period (late luteal phase) is characterized by a sharp decline in estrogen and progesterone, which induces a sedative effect on the activation of the muscular system by the central nervous system, directly impacting muscle strength. Additionally, this significant drop can lead to exacerbated sensory activations, contributing to pain, increased water retention, and edema, which may influence range of motion. Hormonal changes during this phase also affect neurotransmitters linked to the limbic system and prefrontal cortex, leading to mood changes and decision-making difficulties. This set of symptomatic conditions is known as premenstrual tension (PMT) and can cause physical performance alterations due to the psychophysical disturbances mentioned (23).

Although physiological conditions suggest potential changes in physical performance, this study did not observe any significant variation (p > 0.05). Regarding muscle strength, some studies support this result. For instance, Pereira *et*

al. (5), comparing muscle strength across three phases of the MC in 20 women engaged in strength training using the 1-RM test, found no significant difference. Similarly, Thompson et al. (24) observed that muscle strength did not change throughout the MC in a study evaluating the muscle performance of 30 trained women. Furthermore, Romero-Moraleda et al. (25) found that 13 eumenorrheic trained women exhibited similar muscle strength performance across different MC phases. Likewise, Jonge et al. (26) did not identify any variations in muscle strength or fatigue (equivalent to SPE) when evaluating 19 trained women across the MC.

On the other hand, Rodrigues *et al.* (27) observed that in the late follicular phase (post-menstrual period), strength was greater than in the early follicular phase (menstrual period) when assessing muscle strength through the 1-RM test in 15 women who had been engaged in strength training for at least three years. These differences suggest that as physical performance improves with increased training duration, hormonal fluctuations may elicit different physical responses during various phases of the MC. This could be attributed to the fact that the authors evaluated women with a more extensive training history (over three years), unlike this study and others, such as Pereira *et al.* (5), which found no differences in women who had been training for at least six months, a criterion that was also used to include participants in this study's sample.

This hypothesis is supported by the studies of Pournasiri *et al.* (28), who assessed the muscle strength of 37 athletes from various sports with a minimum training history of three years, using isokinetic analysis of knee extensors and flexors. The results revealed that the athletes exhibited higher strength indices in the post-menstrual period compared to the menstrual and pre-menstrual periods.

Regarding flexibility, Ghangrekar *et al.* (29) corroborate the results of this study by not observing variations in joint instability across the three phases of the MC, assessing 90 women who had been exercising for at least three months. On the other hand, Miyazaki and Maeda (10), when correlating the MC with the flexibility of 16 young, healthy women who did not engage in sports or specific training involving strength or flexibility, observed, through knee extension using an isokinetic dynamometer, that passive stiffness decreased during the ovulatory and luteal phases, suggesting changes in the flexibility of the posterior muscular chain of the LL during these phases.

In contrast to this study, Pereira *et al.* (5), when assessing flexibility through the SRT in 20 trained women, found higher levels of flexibility in the post-menstrual period.

These differences may stem from secondary training practices, as in the study by Miyazaki and Maeda (10), the participants did not engage in strength or flexibility training, unlike in this study, where all participants practiced strength training, which may explain a lower susceptibility to performance changes related to hormonal fluctuations. In Pereira *et al.*'s (5) study, which also involved women engaged in strength training, it was not evaluated whether the participants engaged in additional training besides strength training. Depending on the specificity of the physical training performed, there may be a greater involvement of flexibility, making women more sensitive to variations in this capacity throughout the MC.

Regarding MC symptomatology, we observed that the highest sensitivity occurred during the menstrual period (p < 0.001). These findings are related to the negative physical and emotional symptoms, measured by the MDQ, that some women experience during the late luteal phase and that tend to improve at the onset of menstruation, characteristics commonly associated with PMT. Although the exact mechanisms of PMT are not fully understood, Boboc and Oinonen (30) suggest that there is evidence indicating that hormonal sensitivity may contribute to symptoms not only during the premenstrual phase but throughout the luteal phase. Schmidt *et al.* (31) argue that the variations causing physical and emotional changes associated with PMT are not due to hormonal fluctuations but rather hypersensitivity to abrupt hormonal changes.

When considering physical performance and, consequently, sports performance, it is essential to recognize the influence of physical and emotional aspects on performance. PMT can lead to a reduction in performance throughout the MC due to the cyclical recurrence of symptoms that affect the behavioral dimension (fatigue, insomnia, dizziness, *etc.*), the psychological dimension (irritability, depressed mood, anxiety, restlessness, *etc.*), and the physical dimension (headaches, tenderness, swelling, muscle and joint pain, *etc.*), with these symptoms decreasing rapidly after the onset of menstruation (32).

Although this study identified relationships between negative symptoms and the MC, particularly during the menstrual period, no other variables were observed that could reflect the magnitude of the influence of these changes on performance. The study did not find significant differences in the evaluated capacities, such as strength and flexibility.

Another relevant point to discuss is the absence of significant differences between women who use and do not use contraceptives. Studies such as that of Romero-Moraleda *et al.* (25) indicate that contraceptives may minimize the natural

hormonal fluctuations of the MC, which could theoretically result in less variation in physical performance throughout the cycle. However, in this study, no significant variations were found between the groups. This suggests that, regardless of contraceptive use, other factors, such as the level and type of training, may play a more determining role in strength, flexibility, and perceived exertion performance. This finding reinforces the need for further studies specifically investigating the impact of contraceptives on physical performance in trained women to determine whether there is indeed an attenuation of the effects of the MC.

As limitations, the study could have explored other performance-related capacities, such as physical and emotional aspects. Additionally, the sample consisted predominantly of women with an average age of $22.50~(\pm~5.11)$ years who practiced only strength training. Including women from varied age groups and those participating in other physical and sports modalities could provide a more comprehensive and accurate view of the variations in performance associated with PMT. Analyzing these additional variables could reveal direct relationships with the increased symptomatology reported during the menstrual period, offering a more complete understanding of the impact of PMT on physical and sports performance.

The findings of this study have important practical implications, especially for physical education professionals and coaches working with women. Although no significant differences were observed in physical performance variables during the different phases of the MC, it is advisable that training plans consider individual variability in menstrual symptoms. Continuous monitoring of the MC and SPE can be an effective strategy for adjusting training load as needed, without compromising performance. Additionally, it is crucial for athletes to be educated about the potential influences of the MC on performance, enabling them to adjust their physical and mental preparation according to their needs, thus fostering greater confidence in continuous training throughout the cycle.

CONCLUSIONS

In this study, no significant variations were observed in flexibility and muscular strength throughout the different phases of the MC, and these variables had no impact on SPE. Although the literature documents physiological variations throughout the MC, the results obtained did not indicate significant changes in the performance of the assessed physical capacities.

The symptomatology, as expected, showed greater intensity

during the menstrual period. However, this manifestation did not seem to influence the performance in the analyzed capacities, suggesting that, despite the reported physical and emotional discomfort, it does not directly affect physical performance.

Given the importance of understanding possible variations in female physical performance throughout the MC to optimize training prescriptions and maximize sports performance, it is recommended that future studies include a more diverse sample, encompassing women of different ages and sports modalities. These studies could further investigate the influence of the MC on performance variables, providing more robust guidelines to enhance the performance of women, particularly among those engaged in strength training.

FUNDINGS

The National Council for Scientific and Technological Development (CNPq) provided the research scholarship that was essential for the completion of this study.

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

JPMS, WRS: investigation, data collection, writing – original draft. KBC, AFB, MCC, RCRL: writing – review & editing, formal analysis. TMSV, MSFC: formal and statistical analysis. WRS: supervision & editing. WRS, JPMS: funding acquisition.

ACKNOWLEDGEMENTS

We would like to thank the National Council for Scientific and Technological Development (CNPq).

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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