Relationship Between Polycystic Ovary Syndrome and Early Menarche

Relação de Sop e Distúrbios Endócrinos com Menarca Precoce
Relación Entre el Síndrome de Ovarios Poliquísticos y la Menarca Temprana

RESUMO
Objetivo: Investigar a associação entre a menarca precoce e fatores endócrinos, com foco na obesidade, em mulheres com Síndrome dos Ovários Policísticos (SOP). **Método:** Estudo observacional com aplicação de questionário online a 198 mulheres com SOP. Foram analisados dados sobre idade da menarca, horário de sono e IMC. **Resultados:** A menarca aos 12 anos foi associada a um risco 2,17 vezes maior de obesidade. Mulheres que dormiam após a meia-noite apresentaram até 13,3 vezes mais chance de obesidade grau II. **Conclusão:** A qualidade do sono exerce maior influência sobre o risco de obesidade em mulheres com SOP do que a idade da menarca.
DESCRITORES: Síndrome dos Ovários Policísticos; excesso de peso; menarca.

ABSTRACT
Objective: To investigate the association between early menarche and endocrine factors, focusing on obesity in women with Polycystic Ovary Syndrome (PCOS). **Method:** Observational study based on an online questionnaire applied to 198 women with PCOS. Data on menarche age, sleep schedule, and BMI were analyzed. **Results:** Menarche at age 12 was associated with a 2.17-fold increased risk of obesity. Women who slept after midnight had up to a 13.3-fold higher chance of grade II obesity. **Conclusion:** Sleep quality has a stronger influence on obesity risk in women with PCOS than age at menarche.
DESCRIPTORS: Polycystic Ovary Syndrome; Obesity; Menarche

RESUMEN
Objetivo: Investigar la asociación entre la menarca temprana y los factores endocrinos, con enfoque en la obesidad, en mujeres con Síndrome de Ovarios Poliquísticos (SOP). **Método:** Estudio observacional basado en cuestionario en línea con 198 mujeres con SOP. Se analizaron datos sobre edad de menarca, horario de sueño e IMC. Resultados: La menarca a los 12 años se asoció a un riesgo 2,17 veces mayor de obesidad. Las mujeres que dormían después de la medianoche tuvieron hasta 13,3 veces más probabilidades de obesidad grado II. **Conclusión:** La calidad del sueño tiene más influencia en el riesgo de obesidad en mujeres con SOP que la edad de la menarca.
DESCRIPTORES: Síndrome de Ovarios Poliquísticos; Obesidad; Menarca

RECEIVED: 05/19/2025 **APPROVED:** 06/05/2025

How to cite this article: Krüger A, Reimer JP, Conceição NBT, Schwartz L, Pinto LH, Lima DD. Relationship Between Polycystic Ovary Syndrome and Early Menarche. Saúde Coletiva (Edição Brasileira) [Internet]. 2025 [acesso ano mês dia];15(97):16028-16039. Disponível em: DOI: 10.36489/saudecoletiva.2025v15i97p16028-16039

DOI: 10.36489/saudecoletiva.2025v15i97p16028-16039

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex disease with characteristic symptoms and unknown causes. This syndrome can be characterized as an endocrine-gynecological disorder, categorized as a disorder that causes hormonal changes and commonly affects women of childbearing age. [1]

Although it's a common disease, its etiology is not yet fully understood, but increasing evidence indicates that PCOS may result from a complex combination of several genes, being considerably influenced by epigenetics and environmental factors, with an emphasis on diet and lifestyle. [2]

As for the set of symptoms that can characterize this syndrome includes changes in the menstrual cycle, increased facial hair, multiple ovarian cysts, oily skin and the appearance of acne, hair loss, emotional instability, infertility, and weight gain. [3]

In this context, obesity, especially visceral adiposity, observed in both obese and non-obese women with PCOS, aggravates and intensifies the metabolic and reproductive outcomes associated with the syndrome. Obesity increases inflammatory adipokines, which enhance insulin resistance, promoting the formation of adipose tissue and decreasing lipolysis. Excess weight also makes the cells on the surface of the ovaries more sensitive to luteinizing hormone (LH), intensifying ovarian androgen production. [4]

Thus, when considering how obesity affects the quality of life of people with PCOS, we must consider other factors that may be associated, such as sleep quality and its interrelationship with excess weight and the syndrome. [5]

However, growing evidence has linked melatonin to protection against obesity, going beyond its role in sleep patterns. This substance influences not only sleep-wake cycles, but also plays a role in protecting against obesity and metabolic disorders by affecting the processing of glucose and lipids. [6]

This study aims to analyze the influence of endocrine and sleep disorders in women with PCOS and obesity. This raises the question of contributing factors to excess weight, which can be managed and prevent complications and comorbidities in women prone to obesity.

METHOD

Study design

This study was conducted through an online survey of women diagnosed with PCOS. It was developed virtually via the GoogleForms® platform due to the COVID-19 pandemic. It was a survey on the presence of risk factors for DM II, such as overweight and diet, sedentary lifestyle and sleep quality; in groups of women with diabetic and non-diabetic PCOS, for comparison purposes.

Ethical issues in research

As it involved human beings, the legislation - Law No. 14,874/2024, in force in Brazil - was respected, and this project was submitted to the Research Ethics Committee (CEP) of UNIVILLE, where it was reviewed and approved, obtaining approval protocol with registration CAA 26897719.0.0000.5366.

Definition of population and sample

The study population consisted of women who reported having been diagnosed with PCOS. Women who underwent bariatric surgery, exercised regularly (more than three days a week), or were under regular nutritional monitoring, as well as those who did not agree to participate in the study or who did not complete the questionnaire, were excluded from the study.

Research development

An observational study was carried out, involving document analysis and interviews, in which data were obtained from the analysis of responses made from a virtual questionnaire. The data and information collected

DOI: 10.36489/saudecoletiva.2025v15i97p16028-16039

corresponded to: [a] Patient characteristics: age, family history, general habits; [b] data related to the dependent variable (BMI); and [c] data on independent variables: sleep quality and BMI.

Data collection

Patient data was collected using a questionnaire. Data were recorded on a standard form developed by the researchers; available on an online GoogleForms® platform, from May to August 2021. The data were then plotted in an Excel® spreadsheet and grouped according to the study variables previously identified above.

Data analysis

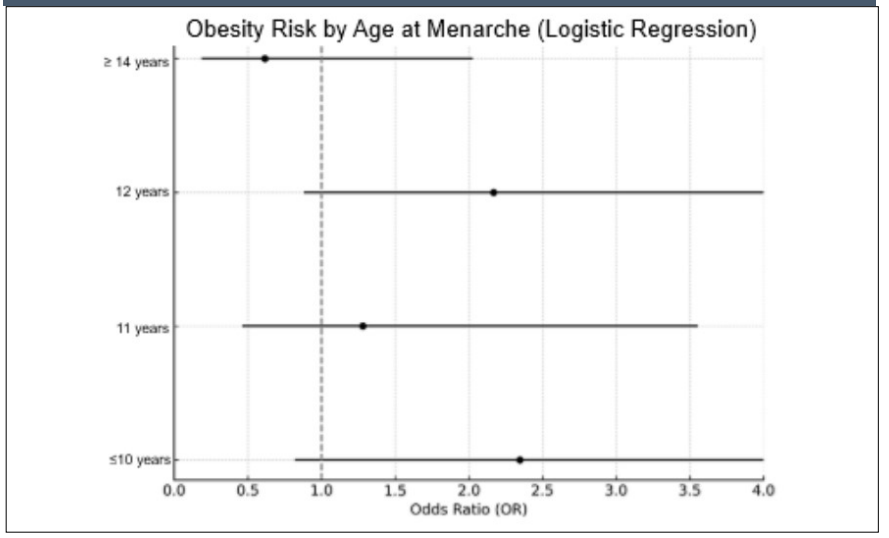
The data were evaluated for correlations between variables using logistic regression, presenting the odds ratios (OR) of each independent variable on the patient's weight classification.

RESULTS

Based on the analysis of a group of women with PCOS, totaling 198 registered in the Unified Health System, 65.15% were overweight, 32.82% were of normal weight, and 2.02% were underweight, when compared to women of normal weight (BMI 18.50 to 24.99) and grade III obesity (BMI greater than 40).

To analyze the influence of menarche, we considered women as non-obese (BMI < 30) and obese (BMI ≥ 30) were considered. The data were submitted to linear regression, which obtained the data shown in Figure 1:

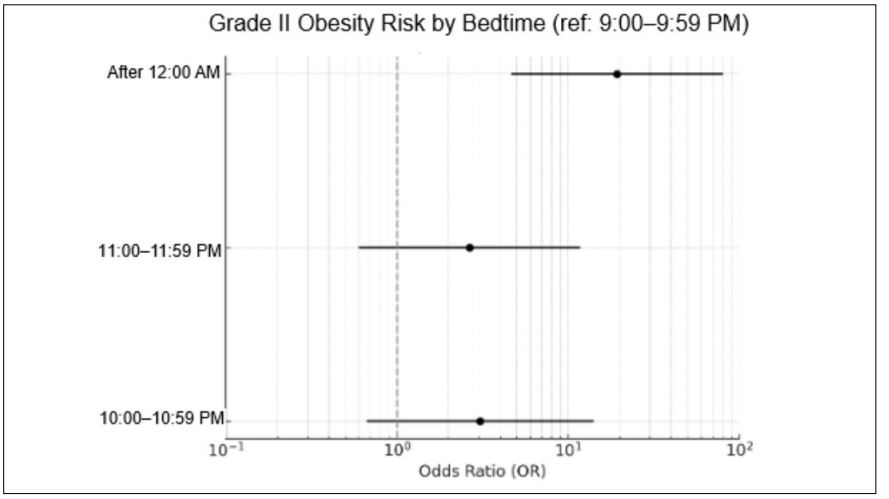
Figure 1: Relative risk of obesity according to age at menarche. Logistic regression graph showing the odds ratios (OR) and respective 95% confidence intervals (95% CI) for obesity in women, based on age at menarche.



The reference category was menarche at age of 13, used as a control. A trend towards a higher chance of obesity was observed among women with early menarche (≤10 to 12 years), with age of 12 associated with an OR of 2.17 (= 0.009), suggesting more than twice the chance of obesity compared to the reference group. The vertical dashed line indicates OR = 1, corresponding to the absence of effect.

Regarding sleep quality, expressed in the condition of sleeping before 10 p.m., the risk was expressed in Figure 2

Figure 2: Odds ratio (OR) graph for grade II obesity according to usual bedtime, taking as reference group women who sleep between 9:00 p.m. and 9:59 p.m. as the reference group. Each point represents the estimated OR with a 95% confidence interval (95% CI), and the dotted line at OR = 1 indicates no association.



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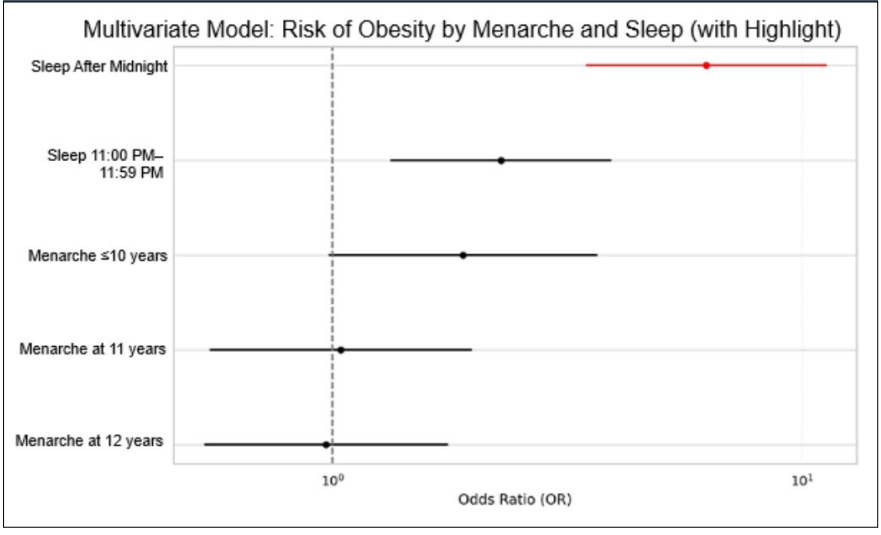
The results indicate that, compared to the reference group, sleeping between 10:00 p.m. and 10:59 p.m. is associated with a 5.5 times greater chance of grade II obesity (95% CI: ~3.5 – 8.5). Sleeping between 11:00 p.m. and 11:59 p.m. is associated with a 7.3 times greater chance (95% CI: ~4.6 – 11.4). Most strikingly, sleeping after midnight is associated with a 13.3 times greater chance (95% CI: ~8.2 – 21.4).

These findings suggest a significant relationship between late bedtimes and a higher prevalence of grade II obesity in women in the study sample.

By performing a linear regression and calculating OR calculation with adjustments, grouping the two categories of variables, we obtained the data shown in Figure 3.

Figure 3: This graph presents the results of a multivariate logistic regression that analyzed the association between age at menarche, usual bedtime, and risk of obesity risk in the study population. While early menarche plays a relevant role in isolation, its influence increases when we adjust for the sleep factor, indicating that late bedtime has a significant cumulative effect in this group.



Based on the adjusted multivariate model, which simultaneously considers the effects of age at menarche and bedtime, the variable with the greatest impact on obesity is clearly bedtime.

Bedtime, especially after midnight, is the most impactful factor in obesity among those analyzed, even when considered along with age at menarche. While early menarche may play a relevant role in isolation, its influence is attenuated when we adjust for the sleep factor, indicating that late sleep has a more robust and independent effect.

DISCUSSION

Understanding PCOS has become extremely important from a women's health perspective, since it is the most common reproductive endocrine disorder affecting women of reproductive age. Its etiology is still unknown, but it is believed that its origin is multifactorial and involves polygenic genetic alterations, the development of which is influenced to some degree by environmental factors, such as diet and the development of obesity. Its pathophysiology involves an alteration in the pulsatility of the release of the hormone GnRH, leading to an increase in the release of LH and a decrease in FSH. As a result, the complete growth and maturation of the follicles is hindered, so that they stop developing at intermediate stages, giving the ovary the characteristic polycystic morphology.[7]

It is worth highlighting the factors that contribute to the impact and consequences of excess weight in PCOS, in which excess weight is quite recurrent, due to metabolic and hormonal disorders. The intestinal microbiota, for example, seems to play an important role in the manifestations of PCOS, since in dysbiosis, the diversity of bacterial species is reduced, impairing intestinal permeability [8] and influencing hyperandrogenism, since dysbiosis activates the individual's immune system, which can cause hyperinsulinemia, which would increase androgen production. Therefore, although further studies are still needed regarding the treatment of PCOS, the use of probiotics reduces the body's inflammatory process, thereby reducing testosterone levels and improving the quality of life of patients. [9]

Moreover, sleep disorders also play an important role in the high BMI of patients with PCOS. The syndrome influences this disorder, since it can reduce the time spent in REM sleep,5 the deep sleep that promotes rest and recovery, which consequently leads to a state of drowsiness during the day, making it difficult to perform physical activities, in addition to promoting nutritional disorders, due to increased appetite, regulated by the secretion of leptin during sleep. The decrease in melatonin also influences this pathogenesis, since this hormone is important in maintaining ovarian health. Therefore, in agreement with the literature, there is an impact of sleep disorders on excess weight in patients with PCOS.

DOI: 10.36489/saudecoletiva.2025v15i97p16028-16039

In this sense, the research found evidence in the literature that impaired intestinal microbiota and sleep quality negatively influence the manifestations of the syndrome, the latter being the most prevalent cause. Furthermore, in relation to menarche and its influence on the development of the pathology, no studies were found that demonstrate such a correlation. Therefore, sleep quality is important to prevent negative effects of PCOS, such as excess weight, in addition to changing habits, with a healthy diet and physical activity, which is essential to maintain a healthy intestinal microbiota, nutritional adjustments and the energy balance necessary for the proper functioning of the body and the patient's quality of life.

Among the hypotheses related to PCOS, two stand out: age at menarche and quality of sleep. Since the dependent variable was excess weight, there was no relationship with the age at which the patient had menarche, but the group with menarche under 10 years of age had a lower chance of having normal weight, and a 20% chance of being overweight or obese grade II. On the other hand, of the 198 women with PCOS registered with the SUS, more than 65% were overweight.

Thus, it is concluded that the most likely hypothesis related to excess weight is sleep quality, since a total of 81.82% of patients with grade II obesity slept after midnight, with a correlation between these variables.

Melatonin – an agent that regulates the sleep-wake cycle – is very important in controlling food intake, energy expenditure and accumulation in adipose tissue. According to Thannickal (2020), reduced sleep hours with a melatonin deficit are related to a greater chance of weight gain. In view of this, this condition implies the adoption of physical activity practices, as well as the quality of sleep daily, in order to achieve better weight control.[13]

Regarding the quality of sleep among women with PCOS, there was a big difference in those who slept after midnight, who tended to produce less melatonin, since 81.82% had type II obesity. In addition, the reduction of sleep increases appetite due to the dysfunction of some proteins, which can trigger obesity.[10] Leptin, for example, is released during sleep and promotes the feeling of satiety, so sleep deprivation can reduce its serum concentration, impairing its ability to trigger a signal in the body's energy balance. Like leptin, the secretion of ghrelin, responsible for preprandial hunger, is also influenced by sleep. Thus, the two proteins mentioned form a relationship involving appetite and satiety, and changes in their concentrations, caused by sleep dysfunctions, can lead to nutritional imbalances and, eventually, obesity.

Furthermore, poor sleep quality and the consequent decrease in melatonin secretion can also influence ovarian health. Melatonin can delay folliculogenesis and prevent excessive proliferation of granulosa cells, which are responsible for the production of estradiol, in PCOS. [11] This hormone eliminates free radicals from the ovaries, as it acts on ovarian follicle cells, thus reducing oxidative stress that could damage the eggs, in addition to stimulating ovarian function in patients with PCOS. [12]

According to Thannickal (2020), PCOS is a risk factor for sleep disorders, and women with the disease tend to have difficulty with weight control and diet. Lifestyle interventions, such as physical activity, have shown good results in regulating the menstrual cycle and reducing androgen levels. However, poor sleep quality leads to excessive daytime sleepiness, which makes it difficult to implement these lifestyle changes. Thus, the data demonstrate the correlation between BMI and melatonin, which can negatively affect the manifestations of PCOS. [13]

CONCLUSION

Studies demonstrate the importance of melatonin, a regulatory agent of the sleep-wake cycle, in controlling glucose metabolism, modulating humoral immune activity, vascular tone, and regulating human reproductive function.

In addition, they relate the reduction in sleep hours to a melatonin deficit and a greater chance of weight gain, due to changes in the control of food intake with energy expenditure and accumulation in adipocytes. This study shows the interference of sleep hours and age at menarche with obesity. Hours of sleep may be a non-modifiable factor, unlike early menarche (before age of 10).

This condition requires attention to the adoption of physical activity practices and quality sleep quality practices, with a focus on patients with PCOS, who will benefit both in terms of weight control and BMI. In addition, factors such as diet and intestinal flora will be evaluated at a later date. [13]

ACKNOWLEDGMENTS

Univille for the Research Support Fund (FAP) and the Extension Support Fund (FAEX), the ECOSAM project at UNIVILLE, and the Municipal Health Secretariat of Joinville for the partnership via INOVA.

DOI: 10.36489/saudecoletiva.2025v15i97p16028-16039

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