

Influence of Menstrual Cycle and Body Mass Index (BMI) on the Occurrence of Polycystic Ovary Syndrome (PCOS) in Women of Reproductive Age: A Literature Review

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Abstract:

Polycystic Ovary Syndrome (PCOS) is a complex endocrine condition that affects many reproductive-age women. It is characterized by irregular menstrual cycles, hyperandrogenism, and polycystic ovaries. Irregular menstrual cycles play a significant role in PCOS and can contribute to the risk of obesity, which, in turn, worsens PCOS symptoms. Research into the influence of menstrual cycles and Body Mass Index (BMI) on PCOS is crucial for a better understanding and more effective treatment of this condition. This literature review aims to analyze previous studies on PCOS, with a specific focus on how menstrual cycles and BMI affect its occurrence in women of reproductive age. The review synthesizes findings from various sources, including PubMed, Embase, and Google Scholar, to explore the complex relationship between these factors and PCOS. Several studies have shed light on different aspects of PCOS. For example, one study found a connection between high BMI and increased hair growth in women with PCOS. Another study delved into metabolomic differences, highlighting glycerophospholipid concentrations and their role in PCOS. PCOS was also associated with significant alterations in carbohydrate, lipid, and protein metabolism. Furthermore, research indicated that BMI had a notable impact on assisted reproductive outcomes in PCOS patients using a freeze-all strategy. Higher BMI was linked to a greater likelihood of early miscarriages in these individuals. In summary, this review provides a comprehensive understanding of PCOS by considering various aspects, including clinical, biochemical, and psychological factors. It emphasizes the importance of understanding the intricate relationship between menstrual cycles, BMI, and PCOS for better diagnosis and management. Early identification of menstrual irregularities and BMI assessment can aid in early PCOS detection. Lifestyle changes for weight management and hormonal therapies for menstrual cycle regulation are essential strategies for managing PCOS in reproductive-age women.

Keywords —Polycystic Ovary Syndrome (PCOS), Menstrual Irregularities, Body Mass Index (BMI), Reproductive-Age Women, Metabolomic Profile

A. INTRODUCTION

PCOS is a complex endocrine condition that affects a significant number of women of reproductive age. It is characterized by a combination of symptoms such as irregular menstrual cycles, hyperandrogenism (elevated androgen hormones), and polycystic ovaries (appearance of ovaries with multiple small cysts). Irregular menstrual cycles are one of the main symptoms of PCOS. It is typically marked by changes in cycle length, number of menstruation days, or intervals between menstrual periods (Teede et al., 2018).

Several studies mentioned that there is a complex interaction between menstrual cycles and BMI in PCOS. The irregular menstrual cycles in PCOS can contribute to an increased risk of obesity and elevated BMI. On the other hand, an elevated BMI can also exacerbate PCOS symptoms and lead to more severe hormonal imbalances (Cassar et al., 2016).

Research on the influence of menstrual cycles and body mass index (BMI) on Polycystic Ovary Syndrome (PCOS) holds significant importance for understanding and managing this condition. Irregular menstrual cycles are a common symptom of PCOS. Studying the impact of menstrual cycles in PCOS helps identify hormone patterns and changes that occur throughout the cycle, as well as their implications for women's reproductive health. Additionally, BMI is also linked to PCOS. Research on the influence of BMI in PCOS helps understand the relationship between obesity and this syndrome. Obesity can affect hormone levels in the body, including those associated with PCOS, such as insulin and sex hormones. Understanding the connection between BMI and PCOS can aid in managing the condition, including appropriate weight reduction strategies. Overall, researching the influence of menstrual cycles and BMI on PCOS is crucial for enhancing understanding and management of the condition, as well as developing more effective treatment approaches.

The aim of this literature review on the influence of menstrual cycles and body mass index (BMI) on the occurrence of Polycystic Ovary Syndrome (PCOS) in women of reproductive age is to gather and analyze previous research conducted in this area. The scope of this literature review will encompass various studies published in scientific journals related to the relationship between menstrual cycles, BMI, and PCOS occurrence in women of reproductive age. This may involve observational studies, retrospective studies, or intervention studies conducted in diverse populations of women."

B. METHODS

This study employs a narrative literature review methodology to examine the existing body of knowledge related to Polycystic Ovary Syndrome (PCOS), specifically focusing on the influence of menstrual cycles and Body Mass Index (BMI). The objective of this review is to synthesize and analyze findings from previously conducted research studies, observational and interventional, to shed light on the relationship between these factors and the occurrence of PCOS in women of reproductive age.

The literature review involved a comprehensive search for articles and studies addressing PCOS, its correlates, and its impact. Searches were conducted in reputable academic databases, including but not limited to PubMed, Embase, and Google Scholar, to identify peer-reviewed articles, reviews, and relevant research papers. The primary inclusion criteria were articles that discussed PCOS and its association with menstrual cycles and BMI. Articles that explored the PICO elements (Population, Intervention or Exposure, Comparison, Outcome) were of particular interest in this study.

The study's Population (P) is women of reproductive age diagnosed with Polycystic Ovary Syndrome (PCOS), a multifaceted endocrine disorder prevalent among this specific demographic. The Intervention or Exposure (I) involves exploring the effects of two influential factors on PCOS: patterns of menstrual cycles and Body Mass Index (BMI). The investigation aims to uncover how these elements potentially contribute to the development and expression of PCOS in affected individuals.

The research question at the core of this narrative literature review is formulated as follows "How does the influence of menstrual cycle patterns and Body Mass Index (BMI) impact the occurrence of Polycystic Ovary Syndrome (PCOS) in women of reproductive age?". This research question serves as the foundation for the review, steering the investigation into existing literature to offer valuable insights into the intricate relationship between menstrual cycle patterns, BMI, and PCOS within the specified population. The PICO framework and the research question collectively establish a comprehensive structure for exploring the intersection of these factors and their implications for the occurrence of PCOS.

C. RESULT

- **Article Search Result**

| No | Author | Year | Title | Research Methods | Research Results |
|----|---|------|--|--|---|
| 1. | Samantha A, Inthrani R., Yionghuak, Angelica Win, Eu-Leong Yong a | 2021 | Effect of body mass index (BMI) on phenotypic features of polycystic ovary syndrome (PCOS) in Singapore women: a prospective cross-sectional study | Using a cross-sectional research design | Women with PCOS and high BMI have higher rates of oligomenorrhea (irregular menstrual cycles) and higher scores on the modified Ferriman-Gallwey scale (mFG), which measures hair growth. |
| 2. | Katarzyna O, Szymon P, Urszula M, Leszek P, Jan M | 2021 | Serum Metabolomics in PCOS Women with Different Body Mass Index | Using a combination of statistical analysis, multivariate analysis, and metabolomic data analysis techniques to investigate metabolomic profiles in patients with polycystic ovary syndrome (PCOS) | There were significant differences in serum metabolome profiles between groups of women with PCOS who had different BMI |
| 3. | MeitingQiu, M.D.,Yu | | Effect of body | Using a | Body mass index |

| | | | | | |
|--|--|--|---|----------------------------|---|
| Tao, M.D., Ph.D., Yanping Kuang, M.D., Ph.D., Yun Wang, M.D., Ph.D. | | | mass index on pregnancy outcomes with the freeze-all strategy in women with polycystic ovarian syndrome | retrospective cohort study | (BMI) has an influence on assisted reproductive outcomes in women with polycystic ovary syndrome (PCOS) using a freeze-all strategy. Obese patients with PCOS have a higher rate of early miscarriage |
|--|--|--|---|----------------------------|---|

Table 1. Data Extraction Result

• Evaluation of strengths weaknesses of existing research

| NO | TITLE | WEAKNESSES | STRENGTH |
|----|--|---|--|
| 1. | Effect of body mass index (BMI) on phenotypic features of polycystic ovary syndrome (PCOS) in Singapore women: a prospective cross-sectional study | <p>1. Relatively small sample size. This study included 160 women with PCOS and 160 healthy women without PCOS. A larger sample size may provide more representative results and may increase the statistical power of the study.</p> <p>2. Cross-sectional study design. This design only allows observation at a single point in time, so it cannot</p> | <p>1. Use of an appropriate control group. This study compared women with PCOS and healthy women without PCOS, allowing for a better comparison in identifying the effects of BMI on hair growth.</p> <p>2. Careful use of statistical analysis. This study used appropriate statistical analysis, including controls for relevant variables and the application of Bonferroni</p> |

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|----|---|---|---|
| | | <p>determine the cause-and-effect relationship between BMI, PCOS and hair growth. Longitudinal studies may provide a better understanding of this relationship.</p> <p>3. Use of mFG score to measure hair growth. The mFG score is a subjective method involving visual judgment, which may result in variation between raters. The use of objective methods or direct measurements may provide more accurate results.</p> | <p>correction to reduce the risk of type 1 error due to the large number of comparisons made.</p> <p>3. This study provides new understanding of the relationship between BMI, PCOS and hair growth in women. The finding that high BMI has an additional effect on hair growth in women with PCOS may provide new insights into the management of PCOS symptoms and patient self-esteem.</p> |
| 2. | Serum Metabolomics in PCOS Women with Different Body Mass Index | <p>1. The relatively small sample size may affect the generalizability of the findings of this study.</p> <p>2. This study only involved metabolomic analysis of serum so it did not consider metabolic changes that may occur in othe tissues or organs.</p> <p>3. This study was</p> | <p>1. This study utilizes advanced and comprehensive metabolomics analysis methods, which can provide deep insights into the metabolic changes that occur in PCOS.</p> <p>2. The multivariate analysis and statistical techniques used in this study allowed the identification of significant metabolic patterns and</p> |

| | | | |
|----|--|---|---|
| | | <p>observational in nature, so it was not possible to determine a cause-and-effect relationship between metabolic changes and PCOS.</p> <p>4. No control of environmental factors that may affect metabolic profile, such as diet and physical activity.</p> | <p>differences between the PCOS group and the control group.</p> <p>3. This study provides new information on potential biomarkers for PCOS, such as sphingomyelin C18:1, which can be used for diagnosis and monitoring of this condition.</p> <p>4. This study provides a better understanding of the role of lipid metabolism, insulin resistance and inflammation in the pathophysiology of PCOS.</p> |
| 3. | Effect of body mass index on pregnancy outcomes with the freeze-all strategy in women with polycystic ovarian syndrome | <p>1. This study is retrospective in nature, so it cannot determine the cause-and-effect relationship between BMI and reproductive outcomes with certainty.</p> <p>2. The data used in this study came from one medical center in China, so the generalizability of the results of this study is limited to the population studied.</p> | <p>1. This study used a large database, which may reduce the confounding factors associated with many variables that can affect pregnancy outcomes.</p> <p>2. This study provides important information on the influence of BMI on assisted reproductive outcomes in women with PCOS using the freeze-all strategy.</p> |

| | | | |
|--|--|---|--|
| | | <p>3. Some variables that may affect pregnancy outcomes, such as hormone levels and certain medical histories, were not available in the database used in this study.</p> | <p>3. This study provides practical recommendations that BMI may be an important factor to consider in assisted reproductive treatment in women with PCOS.</p> |
|--|--|---|--|

Table 2. Strength and Weaknesses of Studies

In an effort to gain a deeper understanding of Polycystic Ovary Syndrome (PCOS), several studies have been conducted to unveil the relationship between clinical characteristics, biochemical aspects, and their impact on patients' quality of life. (Amiri et al., 2019) conducted a comprehensive review that explored this connection. In their research, the authors made an intriguing discovery that provides new insights. They successfully identified a significant difference in glycerophospholipid concentrations between the PCOS patient group and the control group. This finding indicates that the biochemical aspect potentially plays a crucial role in the context of polycystic ovary syndrome.

Furthermore, (Cooney et al., 2017) also aimed to uncover another crucial aspect of PCOS, which is its impact on mental well-being. Through a systematic review and meta-analysis, they observed the prevalence of depression and anxiety symptoms in individuals with PCOS. The results of this analysis revealed concerning facts, including a significant level of depression and anxiety symptoms, even reaching moderate to severe levels. This finding provides us with a broader view of the complex impact of this syndrome on patients' psychological well-being.

Moreover, (Chong et al., 2018) contributed by developing MetaboAnalyst 4.0, an innovative metabolomic analysis tool characterized by transparency and integration. This tool not only facilitates the process of metabolomic data analysis but also introduces a new dimension to understanding metabolite profiles. With MetaboAnalyst 4.0, researchers can explore data more effectively, gain deeper insights, and comprehend metabolomic complexity in a holistic manner.

Collectively, these three studies form a more comprehensive understanding of polycystic ovary syndrome. From the interplay between clinical characteristics and biochemical profiles to its impact on patients' quality of life and mental well-being, along with the support of the latest metabolomic analysis tool, this literature provides valuable insights for medical practitioners, researchers, and individuals involved in PCOS management.

Findings

Women with Polycystic Ovary Syndrome (PCOS) and a high Body Mass Index (BMI) exhibit higher hair growth compared to healthy women with a normal BMI. The effect of high BMI on hair growth is also observed in women with PCOS. However, high BMI does not have an independent effect on other features of PCOS, such as menstrual cycle length and ovarian parameters. This research indicates that body weight has an additional effect on hair growth in women with PCOS, which can influence their self-esteem(Qiu et al., 2019).

There are differences in metabolite concentrations between women with Polycystic Ovary Syndrome (PCOS) and the control group. The main difference is observed in glycerophospholipid concentrations, with no specific trend for either upregulation or downregulation. Insulin resistance and high body weight have a greater influence on the level of acylcarnitine C2 than PCOS itself. Sphingomyelin (SM) C18:1 could potentially serve as a biomarker for PCOS and requires further investigation. No significant correlation was found between anthropometric and hormonal parameters with metabolomic outcomes.

PCOS alters the metabolic profile of patients, particularly in carbohydrate, lipid, and protein metabolism pathways. Plasma lipidomics in women with PCOS show evidence of decreased lipid oxidation. There's a connection between lipid metabolism and insulin resistance, as well as the roles of acylcarnitine and sphingolipids in inflammation triggered by obesity and PCOS pathophysiology. These findings provide new insights into the underlying biology of PCOS and could contribute to the development of improved diagnostic and therapeutic methods(Ożegowska et al., 2021).

The Body Mass Index (BMI) has a significant influence on assisted reproductive outcomes in women with Polycystic Ovary Syndrome (PCOS) undergoing a freeze-all strategy. The highest rate of live births occurs in PCOS patients with underweight and normal weight, gradually decreasing with increasing BMI. Obese PCOS patients experience higher rates of early miscarriages. This study suggests that BMI plays a role in pregnancy outcomes for women with PCOS undergoing IVF with a freeze-all strategy(Neubronner et al., 2021).

LITERATURE REVIEW

- **Polycystic Ovary Syndrome (PCOS)**

Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder that impacts a significant number of women in their reproductive years. It is characterized by a combination of symptoms, including irregular menstrual cycles, hyperandrogenism (elevated androgen hormone levels), and polycystic ovaries (ovarian appearance with numerous small cysts). The precise causes of PCOS remain elusive; however, factors such as genetics, insulin resistance, and imbalances in female sex hormones like estrogen and progesterone are thought to contribute to its development. The management of PCOS involves embracing a healthy lifestyle, incorporating elements such as a balanced diet, regular exercise, and weight management if necessary. Hormone therapy and medications can also be recommended to control symptoms and enhance fertility. While the exact etiology of PCOS continues to be investigated, the holistic approach to its management seeks to mitigate its impact on women's well-being and reproductive health (Teede et al., 2018).

- **PCOS Possible Risk Factors**

- Genetical Risk Factors

- There are several studies that stated that genomic studies in PCOS populations have shown that genetic factors play a role in the development of PCOS. (Day et al., 2017).

- Eating habits

- Unhealthy eating patterns, especially a diet high in sugar and simple carbohydrates, can increase the risk of PCOS (De Lima Nunes et al., 2019).

- **PCOS Pathophysiology**

- Upon diagnosis, PCOS manifests as a phenotype that embodies an intricate interplay of continuous neuroendocrine, metabolic, and ovarian dysfunctions. Throughout time, various hypotheses have been proposed concerning the direct physiological underpinnings of PCOS. PCOS results from the interplay of numerous proteins and genes, influenced by epigenetic and environmental factors. This specific segment of the article discusses the elements contributing to PCOS development in both human and preclinical models. Clinical and biochemical hyperandrogenism stands as a significant hallmark of PCOS. The onset of PCOS occurs during the early years of adolescence. However, the most crucial data emerges from clinical trials involving adult women, where there's a bias towards examining more severe phenotypes. Preclinical models utilizing animals and in vitro studies complement clinical research, benefitting from alternative

strategies to understand this intricate disease. Present clinical, experimental, and genetic evidence corroborate the involvement of neuroendocrine aspects in the pathophysiology of PCOS (Witchel et al., 2019).

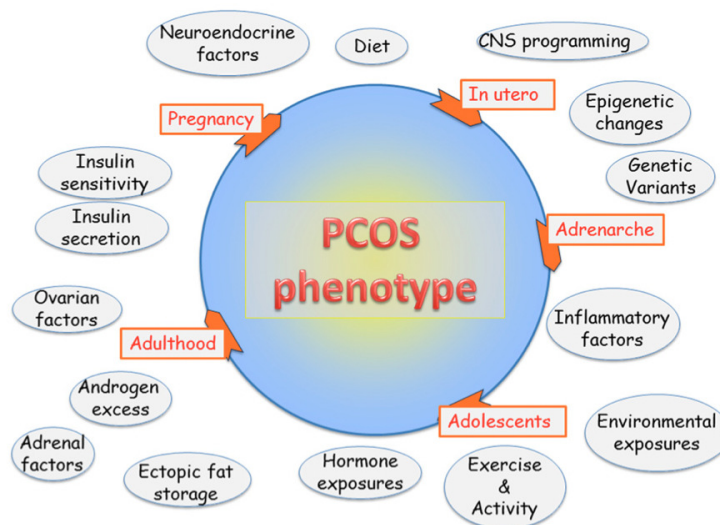


Figure 1. PCOS Phenotype(Witchel et al., 2019)

- **Menstrual Cycle Correlation with PCOS**

A lengthy and irregular menstrual cycle, a characteristic of polycystic ovary syndrome (PCOS), has been linked to higher androgen levels and lower sex hormone-binding globulin levels. These hormonal fluctuations can elevate the risk of specific histological subtypes of ovarian cancer(Harris et al., 2017).

Menstrual cycle disturbances stand as a key characteristic of polycystic ovary syndrome (PCOS). Research indicates a correlation between menstrual cycle irregularities and PCOS. Patients with PCOS experience ovulation disruptions, leading to irregular or oligomenorrheic menstrual cycles(Amiri et al., 2019). Patients with PCOS exhibit a notably high prevalence of oligo- or anovulation, which subsequently leads to disruptions in the menstrual cycle pattern. In this scenario, irregular or even absent ovulation can disturb the balance of reproductive hormones, resulting in irregular, infrequent, or occasionally absent menstrual periods(Cooney et al., 2017).

- **The Role of Reproductive Hormones in Menstrual Cycle in PCOS**

- Folicle Stimulating Hormone (FSH)

In the early stages of a normal menstrual cycle, the hypothalamus releases gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary gland to produce follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Increased FSH stimulates the development of ovarian follicles, leading to the production of estrogen. Elevated LH triggers the release of the egg (ovulation) and the transformation of the follicle into the corpus luteum, which produces progesterone.(Teede et al., 2018).

- **Progesterone**

Progesterone is produced by the corpus luteum after ovulation and plays a role in preparing the endometrium to receive the embryo. In PCOS, ovulation disorders are common, so adequate progesterone production may be inhibited (Teede et al., 2018).

- **Impact of menstrual cycle disorders on clinical manifestations of PCOS**

- **Metabolic Disorders**

Menstrual cycle disorders in PCOS are also associated with an increased risk of metabolic disorders, such as insulin resistance, type 2 diabetes, and metabolic syndrome. Hormonal imbalances caused by menstrual cycle disorders in PCOS may affect tissue sensitivity to insulin and contribute to metabolic disorders (Teede et al., 2018).

- **Cardiovascular Disease**

The menstrual cycle disorders that occur in PCOS are associated with an increased risk of cardiovascular disease, including heart disease, stroke, and peripheral arterial disease. Hormonal imbalances and insulin resistance in PCOS may contribute to vascular inflammation and dysfunction (Shaaban et al., 2019).

- **Psychological Problems and Psychosocial Wellbeing**

Irregular menstrual cycle disorders or absence of menstruation in PCOS may also impact the psychological well-being and psychosocial well-being of women with this condition. Clinical manifestations associated with menstrual cycle disorders may affect body image, self-confidence, and general quality of life (Dokras et al., 2018).

- **Relationship between BMI and PCOS**

Obesity is a risk factor for PCOS. Women who are obese have a higher chance of developing PCOS compared to those with normal BMI (Nandi et al., 2014).

Obesity is often associated with insulin resistance, a condition in which the body does not respond well to insulin. Insulin resistance in PCOS can trigger increased production of the hormone insulin by the pancreas. High levels of insulin in the body can stimulate the production of androgen hormones by the ovaries and affect the normal function of ovarian cells. This can lead to irregular follicular growth, irregular ovulation, and hormonal imbalance in PCOS (Nandi et al., 2014).

Obesity is associated with chronic low-level inflammatory conditions in the body. Excess fat cells can produce proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α). These chronic inflammatory conditions can affect ovarian hormone production, disrupt hormonal balance, and worsen PCOS symptoms (Ricciotti & FitzGerald, 2011). Obesity can also affect ovulation in PCOS. The high levels of insulin and leptin hormones associated with obesity can affect the secretion of ovarian hormones, such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which regulate ovulation. Ovulation disorders in PCOS can lead to no ovulation or irregular ovulation (Lim et al., 2013).

- **Impact of BMI on PCOS symptoms and complications**

- Hyperandrogenism

- Being overweight or obese, which is reflected in increased BMI, may exacerbate symptoms of hyperandrogenism in PCOS, such as hirsutism (excessive hair growth in unusual areas) and acne (Lim et al., 2013).

- Insulin Resistance and Metabolic Disorders

- Obesity, indicated by increased BMI, contributes to insulin resistance in PCOS. Insulin resistance can affect glucose and fat metabolism, leading to an increased risk of type 2 diabetes, metabolic syndrome, and lipid metabolism disorders (Teede et al., 2018).

- Pregnancy Complication

- Obesity, reflected in increased BMI, may increase the risk of pregnancy complications in PCOS, including gestational diabetes, preeclampsia, and preterm birth (Cassar et al., 2016).

D. DISCUSSION AND CONCLUSION

Studies have shown the influence of menstrual cycle and body mass index (BMI) on the incidence of PCOS in fertile women. Irregular menstrual cycles or absence of menstruation (amenorrhea) can be a major clinical symptom of PCOS and is one of its diagnostic criteria.

Menstrual cycle disorders in PCOS are often related to hormonal imbalances, including increased luteinizing hormone (LH) and decreased follicle-stimulating hormone (FSH).

In addition, overweight and obesity, reflected in increased BMI, are also closely associated with the incidence of PCOS. Obesity can worsen PCOS symptoms and affect hormonal function, including insulin resistance and increased production of androgen hormones. Insulin resistance is a mechanism associated with PCOS and may affect glucose regulation and lipid metabolism. Increased production of androgen hormones, such as testosterone, is also a characteristic of PCOS that may affect reproductive hormone balance.

From this discussion, it can be concluded that menstrual cycle disorders and BMI play an important role in the incidence of PCOS in fertile women. Menstrual cycle disorders, such as amenorrhea or menstrual irregularities, can be clinical symptoms indicative of PCOS. At the same time, a high BMI, which reflects overweight or obesity, also contributes to the risk of PCOS.

It is important to remember that the relationship between menstrual cycle, BMI and PCOS is complex and interrelated. Menstrual cycle disorders can affect reproductive hormones, which in turn can affect BMI and the incidence of PCOS. Conversely, high BMI can also affect hormone regulation and exacerbate PCOS symptoms. A therapeutic approach involving weight management, lifestyle changes, menstrual cycle regulation, and management of insulin resistance can provide significant benefits in the management of PCOS.

- Improved diagnostics

Understanding the influence of menstrual cycle and BMI on the incidence of PCOS can help in a better diagnostic process. Identification of menstrual cycle disorders and assessment of BMI can be used as early indicators in evaluating the possibility of PCOS in fertile women.

- Weight Management

Healthy weight management and BMI reduction can be an important strategy in the management of PCOS in fertile women. Approaches involving lifestyle changes, such as a balanced diet and regular physical activity, can help reduce the symptoms and complications of PCOS.

- Menstrual Cycle Regulation

Regulation of the menstrual cycle through hormonal therapy or other strategies can be an important aspect of PCOS management. Approaches involving hormone control, such as

hormonal contraception, can help improve menstrual cycle disturbances and reduce symptoms associated with PCOS.

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