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A SCRUPULOUS EVALUATION OF POLYCYSTIC OVARIAN SYNDROME IN MALAYSIAN ADOLESCENT FEMALES: A SYSTEMATIC REVIEW

Jaya Balan Valliappan[1], Hema Ramachandran[2], Ratnarajan Thivakulan[3], Karthikeyan Murugesan[4], Ashok Gnanasekaran[5], Jyotsna Sinha[6], Pugazhandhi Bakthavatchalam*

Authors Affiliations:

[1]Professor, Department of O&G, Faculty of Medicine, Quest International University, Ipoh, Perak, 30250, Malaysia.

[2]Senior Lecturer, School of Biological Sciences, Quest International University, Ipoh, Perak, 30250, Malaysia.

[3]Internal Medicine, Manipal College of Medical Sciences, Pokhara, Nepal.

[4]Associate Professor, Department of Microbiology, Faculty of Medicine, Quest International University, Ipoh, Perak, 30250, Malaysia.

[5]Associate Professor, Department of Microbiology, Faculty of Medicine, Quest International University, Ipoh, Perak, 30250, Malaysia.

[6]D.Y.Patil Medical College and Hospital, Kolhapur, Maharashtra; Contractual Medical Officer, Bihar Health Govt., Bihar, India.

ABSTRACT

Women of reproductive age are frequently affected by the endocrinopathy known as a polycystic ovarian syndrome (PCOS). Since it was first described by Stein and Leventhal in 1935, this disease has been known to cause obesity, which accounts for at least 80% of ovulatory infertility. Obesity and PCOS are complicatedly related. Some women experience the first PCOS symptoms soon after they start their periods. According to my research, women with PCOS either create too much insulin or their insulin does not function as it should. As a result, insulin resistance is a frequent observation in PCOS. In women with PCOS compared to weight-contingent reproductively normal women, insulin action on skeletal muscle decreased by 35–40%, and this condition is made worse by obesity. Additionally, according to some research, up to 80% of women with PCOS are overweight or obese. Additionally, when weight increases, insulin resistance increases, and the level of circulating insulin rises, high levels of insulin are linked to obesity, making it possible to analyse the interplay between weight and insulin resistance. As a result, the level of testosterone will rise, which will disrupt follicular growth and development and result in polycystic ovarian morphology. There are so two approaches to connecting obesity and PCOS. I will first discuss how PCOS can induce obesity, and then I will discuss how obesity can cause PCOS. According to my investigations, women who are obese are more likely than the general population to develop PCOS because of insulin resistance. In the meantime, PCOS-afflicted women's obesity is exacerbated by rising androgen levels. The risk factors linked to an increased risk of PCOS in obese women include increased levels of luteinizing hormone (LH), hyperinsulinemia, and elevated levels of hyper-androgens. These risk factors also contribute to obesity in PCOS patients.

Keywords: Polycystic ovarian syndrome; obesity; insulin resistance; hyperinsulinemia;

hyperandrogenism; luteinizing hormone (LH)

INTRODUCTION

One of the most prevalent endocrine conditions, polycystic ovarian syndrome (PCOS) affects 5 to 10% of women of reproductive age or those who have oligo-anovulation (1). Additionally, it is a condition marked by unexplained hyperandrogenism (2), abnormal gonadotropin secretion, and insulin resistance as a result of significant impairments in insulin action and -cell function. This gradually raises the risk of type 2 diabetes and glucose intolerance. Instead of hirsutism or anovulation, the broad spectrum of this heterogeneous condition appears to include atypical cases of hyperandrogenemia with central obesity and signs of insulin resistance (2). The PCOS diagnosis is still debatable. The Androgen Excess and PCOS Society published diagnostic criteria in 2009 that characterize PCOS as the concomitant presence of hyperandrogenism and ovarian dysfunction (ovulatory dysfunction and/or polycystic ovarian morphology) (3).

While this is happening, the diagnosis for this syndrome is made on the basis of irregular cycles, hyperandrogenism, and ovaries that seem typically polycystic (4). Women in this category will often have an intercycle gap of more than 35 days, and ultrasonography will show polycystic ovaries and clinical or laboratory indications of hyperandrogenism (5). Due to irregular ovulation, patients are frequently infertile in most cases (5). Hyperandrogenism is still the syndrome's defining clinical feature, though. Regarding individual reviews, the following sections of this review article will go into more detail on how obesity increases the likelihood of metabolic dysfunction and magnifies the clinical severity of the illness. By offering a narrative overview of qualitative studies that show how obese women have a higher risk of PCOS than the general population, this paper makes a small dent in that gap.

Definition of PCOS:

PCOS is a diverse complicated condition with an unknown origin that affects women's metabolisms in the long run by causing hyperandrogenism, subfertility, infertility, and irregular ovulatory and menstrual cycles (6). It is also widely recognized as the most prevalent metabolic condition in females. Stein and Leventhal were the first to characterize this condition. Androgen excess, ovulatory failure, and the formation of polycystic ovaries are the three primary characteristics of the polycystic ovarian syndrome (PCOS) (7). There are numerous potential diagnostic standards for PCOS that are carefully examined. Notably, the Evidence-based Methodology Workshop Panel on Polycystic Ovarian Syndrome at the National Institutes of Health (NIH) made the following suggestions in 2012 (8):

1. Changing the name of the condition to more accurately represent the intricate interactions between the hypothalamus, pituitary, ovary, and adrenal glands that characterize the syndrome
2. Preserving the inclusive, broad diagnostic standards of Rotterdam

Epidemiology

The prevalence of polycystic ovarian syndrome (PCOS) varies depending on the diagnostic standards used to classify the condition. For instance, the National Institutes of Health (NIH)

classified 456 (55 percent) of 827 women with World Health Organization (WHO) class II oligoovulation (estrogenic normogonadotropic ovulatory dysfunction) as having PCOS in 1990 based on the criteria of irregular menses, biochemical and clinical hyperandrogenism, with other causes of hyperandrogenism excluded (9). Using the more stringent Rotterdam 2003 criteria, which requires two out of the three of the following factors: oligo- and anovulation, clinical and biochemical evidence of hyperandrogenism, and polycystic ovaries, 754 (91%) women were classified as having PCOS.

MATERIAL AND METHODS

A narrative review was conducted to investigate the theory that women who are obese are more likely than the general population to develop PCOS and to identify obesity as a side effect of PCOS.

Finding the link between PCOS and obesity is the review's main objective. Keyword searches of the Medline, NCBI, PubMed, An International Journal of Obstetrics and Gynaecology (BJOG), and International Bibliography of the Social Sciences (IBSS) databases helped find the studies that were included in the review. Obesity, PCOS, glucose tolerance, anovulation, and hyperandrogenism were searched keywords along with qualitative research to find relevant materials. WebMD PCOS and Weight Gain; Polycystic Ovarian Syndrome (PCOS) and Obesity by William Hignett, MPH, and Ted Kyle, RPh, MBA; A Guide to Understanding Polycystic Ovarian Syndrome (PCOS) by W Colin Duncan, 2014; Identifying Children at Risk for Polycystic Ovary Syndrome by Robert L. Rosenfield, 2007; Treating Infertility in Polycystic Ovary Syndrome by Peter Ko.

The investigations that are part of this publication are constrained by their small size and narrow scope. Evaluations of methodological quality were not employed to remove papers from the study because this is not a systematic review type and just a few articles were discovered to describe this research.

RESULTS

In women who have PCOS, obesity is a common feature. Based on the articles studied, most of the authors conclude that PCOS occurs both in obese and non-obese patient.

However, in those who are obese, it will worsen PCOS as obese women have higher risk for metabolic dysfunction. Obesity is a complication of PCOS as it develops. As we study the details about PCOS, insulin resistance is one of the main drivers to develop a polycystic ovary. With the presence of obesity, this insulin resistance worsens.

In addition, obesity exacerbates the PCOS phenotype of an affected individual. Weight reduction among obese women has been proven to improve stable androgen levels, insulin sensitivity and ovulation rate. Thus, improve PCOS.

Though obesity is one of the risk factors causing PCOS, the present study shows that obesity is not essential to make the diagnosis of PCOS. Even though obese women are at a higher risk of PCOS, body weight is not a limiting factor for the occurrence of PCOS.

DISCUSSION:

Pathogenesis of PCOS

The biology of the ovary has six stages of development that can be used to explain PCOS's antecedents.

The first is the ovarian follicle's synthesis of sex steroids, specifically estradiol. Theca cells and granulosa cells are the steroidogenic layers of the ovarian follicle, and LH induces the formation of androgen from cholesterol in outer theca cells, and FSH then encourages the conversion of androgens into estrogens in inner granulosa cells (9). The two-cell, two-gonadotropin model of estrogen production is another name for this (9).

Second, increased exposure to androgens, which have an impact on follicular growth and development, is linked to the development of PCOS (4). A polycystic ovary has an increased number of tiny antral follicles, which are little fluid-filled follicles that may be seen with the unaided eye (4). They are not "cysts" because they have healthy oocytes that may develop properly if FSH is administered to them exogenously (12). As a result, the ovarian "cysts" in PCOS are really just stopped follicles with atresia, which is a decreased rate of cell proliferation. Therefore, testosterone stimulates follicular formation and survival, then inhibits it later, leading to the morphology of polycystic ovaries (4). Ironically, the morphology is connected to a rise in endogenous androgens in some way. Pathologically, the level of androgen increases endogenously when there are androgen-secreting tumors and late-onset congenital adrenal hyperplasia where the secretion of adrenal androgen level is increased (13). Therefore, as the ovary responds to the increased level of androgen, polycystic morphology develops, and follicular growth later gets inhibited (4). Thus, this results in an increased level of anovulation (4).

Thirdly, ovarian androgen synthesis increases at the point when circulating LH concentrations are higher than FSH concentrations. LH pulse amplitude and frequency, as well as higher baseline LH concentrations, are more common in women with this syndrome. Chronic anovulation is caused by an imbalance in the LH: FSH ratio (16). This enhanced exposure of the ovary to androgen may be the result of prenatal programming (4).

Fourth, how androgen bioavailability is regulated by the sex hormone binding protein (SHBG). A protein in the blood called SHBG binds to and blocks androgens (4). This sex hormone has an inverse relationship with weight in terms of PCOS and obesity (17). As women gain weight, SHBG will decline and androgen availability will eventually rise (17). So PCOS will get worse. On the other hand, as weight drops, SHBG rises and androgen availability consequently falls, leading to better PCOS (17). As a result, weight is a crucial sign of how LH affects the ovary. Obesity causes it to be accentuated.

Fifth stage: Insulin can increase androgen levels at a specific LH concentration because it multiplies the effects of LH on theca cells. As a result, even at a normal LH concentration, ovarian androgen can increase. More insulin concentrations are required to boost glucose absorption in tissues when there is peripheral insulin resistance (18). In combination with insulin resistance, this hyperinsulinemia will increase the production of androgen in the ovary (4). If the insulin resistance gets worse, insulin concentrations rise, and androgen levels rise as a result, which makes PCOS

worse.

The most crucial step in the relationship between obesity and PCOS is the final one. Given the preceding knowledge from the five stages, it seems to sense that changes in insulin levels and SHBG, both of which can affect androgen concentrations, can affect weight. Weight gain is a result of high insulin levels (19). As a result, insulin resistance and blood insulin levels will grow as weight increases (20). SHBG will decrease as women's weight rises. Furthermore, even insulin by itself can stop the liver from producing SHBG (21). As a result, these risk factors will produce an increase in the level of androgen production in the ovary, which causes PCOS.

Relationship between PCOS and obesity

Understanding the pathophysiology of how obesity has exacerbated many of the metabolic and reproductive problems associated with PCOS has allowed us to examine the relationship between PCOS and obesity. Weight loss is always recommended for PCOS patients as it will help with both non-fertility and fertility-related issues. It has been demonstrated that losing 10% of body weight increases the likelihood of ovulation, pregnancy, and a regular menstrual cycle. According to some research, as much as 80% of women with PCOS are overweight or obese (22).

Because obesity makes PCOS worse, it might be classified as a complication of the condition. We know that obesity worsens PCOS, which is also linked to problems in insulin sensitivity. Hyperinsulinemia will be the main factor causing PCOS to worsen and develop in order to link it to obesity. Women with PCOS first create too much insulin or their insulin does not function properly. Insulin levels are high in the bloodstream due to insulin resistance rather than being used by the muscular tissues. Consequently, insulin resistance is a common observation in PCOS. When compared to weight-contingent, reproductively normal women, PCOS patients' insulin action on skeletal muscle decreased by 35–40%, and obesity made this condition worse (22). Additionally, according to some research, up to 80% of women with PCOS are overweight or obese. Additionally, when weight increases, insulin resistance increases, and the level of circulating insulin rises, high levels of insulin are linked to obesity, making it possible to analyze the interplay between weight and insulin resistance. As a result, the level of androgen will rise and influence how the ovary develops and grows its follicles, leading to polycystic ovarian morphology. Up to 75% of PCOS-afflicted females are obese or overweight (22).

CONCLUSION

In conclusion, there is a complicated association between PCOS and obesity. In order to comprehend and establish the connection between PCOS and obesity, this research study includes a wide range of alternate viewpoints on many aspects of PCOS. In order to connect obesity and PCOS, a narrative review study based on relevant keyword searches was carried out with the goals of determining how PCOS can induce obesity and, secondly, how obesity can cause PCOS.

According to my investigations, women who are obese are more likely than the general population to have PCOS because of metabolic inefficiency. In the meantime, PCOS-afflicted women's obesity is exacerbated by rising androgen levels. Understanding the progression of the syndrome

and the difficulties that arise as it gets worse helped to clarify how obesity might exacerbate PCOS. As is well known, PCOS patients are more likely to have insulin resistance and -cell dysfunction. Weight is inversely correlated with the sex hormone binding protein (SHBG), which controls the bioavailability of androgens. As women gain weight, SHBG will decline and androgen availability will eventually rise. So PCOS will get worse. For PCOS women who are obese, weight loss and lifestyle modifications will always be the first line of treatment. It has been determined that this method of treatment is superior to medical intervention. Such changes have been successful in improving infertility and restoring ovulation in obese women with PCOS. Most importantly, hyperandrogenism is improved in obese PCOS women who lose up to 10% of their body weight.

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Authors declare no competing interest

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