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Polycystic Ovary Syndrome - increased risk of depression development. Links and risk factors

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Abstract

PCOS is a common endocrine disorder affecting up to 6-10% of women in reproductive age. Patients suffer from many manifestations of this disease including symptoms of hyperandrogenism (hirsutism, acne, androgenetic alopecia), ovulation disorders, infertility, overweight and obesity, glucose-insulin homeostasis disorders (insulin resistance, type 2 diabetes). Many studies emphasize the relationship between the presence of PCOS in patients and the appearance of depression. The median incidence of depression in women with this syndrome was 36.6%, while in the group of women without PCOS it was 14.2%. The exact mechanism of this relationship is still unknown, but many factors may play an important role in it, e.g. increased BMI, infertility, high cortisol levels, body image, vitamin D deficiency or elevated inflammation markers.

Keywords: PCOS; depression; infertility; obesity

INTRODUCTION AND PURPOSE

PCOS is a common endocrine disorder affecting up to 6-10% of women in reproductive age. Patients suffer from many manifestations of this disease including symptoms of hyperandrogenism (hirsutism, acne, androgenetic alopecia), ovulation disorders, infertility, overweight and obesity, glucose-insulin homeostasis disorders (insulin resistance, type 2 diabetes). Many studies emphasize the relationship between the presence of PCOS in patients and the appearance of depression. The median incidence of depression in women with this syndrome was 36.6%, while in the group of women without PCOS it was 14.2%. The exact mechanism of this relationship is still unknown, but many factors may play an important role in it, e.g. increased BMI, infertility, high cortisol levels, body image, vitamin D deficiency or elevated inflammation markers.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting up to 6-10% of women in reproductive age. [1] In addition, there is a strong genetic correlation: 20-30% of sisters and 25-50% of mothers of women with this disorder also suffer from PCOS. Diagnosis is mostly based on the diagnostic criteria of the European Society of Human Reproduction and the American Society of Reproductive Medicine. They are: - clinical and/or biochemical markers of hyperandrogenism - ovulation disorders in the form of oligo- or anovulation - distinctive ultrasound (US) image [2] which is assessed according to the Rotterdam Criteria: 12 or more follicles from 2-9 mm in diameter or ovarian volume above 10 cm³. [3]

Symptoms of PCOS include:

- symptoms resulting from hyperandrogenism, such as hirsutism (medium or high severity occurs with a frequency of 60-80%), alopecia or excessive stimulation of the sebaceous glands leading for example to acne
- menstrual cycle disorders, which are the main cause of infertility in patients
- overweight and obesity, which are often affected by disorders of the glucose-insulin homeostasis: hyperinsulinemia, impaired glucose tolerance, and finally type 2 diabetes.

Many studies indicate a relationship between the occurrence of PCOS and the appearance of depression. The median incidence of depression in patients with this syndrome was 36.6%, while in the group of women without PCOS it was 14.2%.

The exact mechanism of the relationship between PCOS and the occurrence of depression is still unknown, but many factors are indicated that may play an important role in it. [2]

REVIEW

Abnormal BMI compared to normal BMI

Obesity is a global problem nowadays. In itself, it can result in increased cardiovascular risk, insulin resistance and abnormalities in the lipid profile. It is also associated with a weaker response of patients to infertility treatment and an increased risk of a complicated pregnancy. [3]

Women with PCOS and diagnosed obesity present significantly more aggravated symptoms, which include: irregular menstrual cycles, infertility, miscarriages, pregnancies complicated by hypertension, diabetes and signs of hyperandrogenism or metabolic syndrome.

Due to PCOS, patients are more likely to be obese, and their visceral adipose tissue index (VAI) is significantly higher than in the general population, both in obese and women with a normal body weight. [4]

The risk of being overweight or obese is 2-3 times higher in women suffering from PCOS (increased BMI and waist to hip ratio). In addition, the occurrence of eating disorders such as anorexia, bulimia or binge eating is more frequent. The probability of developing an eating disorder is higher in women with PCOS compared to the control group. Eating disorders apply to both the physical and mental condition of patients. Incorrect relationship with food is an additional factor that increases the risk of increased BMI and body weight. [5]

Since obesity as a disease is associated with an increased risk of depression in the general population, it seems reasonable that it may also affect the risk of depression in patients with PCOS. [6]

A cross-sectional analysis made in the Australian Longitudinal Study of Women's Health (ALWSH) compared a group of women with PCOS (n = 478) and without this syndrome (n = 8,134). Women with PCOS had a higher BMI (28.1 ± 7.2 kg/m²) than the non-PCOS group (25.1 ± 5.6 kg/m²). What is important, even after taking into account variables such as: high BMI, infertility and sociodemographic factors, the depression index was still higher in PCOS patients group. This indicates an independent influence of the syndrome on the occurrence of depression. It may be related to the awareness of having a permanent chronic disease or bothersome changes in appearance. [7]

Infertility

According to the WHO, infertility is defined as the absence of pregnancy after 12 months of regular sex without using any contraception. It is estimated that this problem affects at least 12% of couples in the world. [8] Polycystic ovary syndrome is the most common cause of infertility in women resulting from anovulation. [9] It affects up to 80% of cases in this type of infertility. [10]

Infertility is a cause of stress that affects many couples (more intensely women than men). Psychological symptoms reported by this include: anxiety, depression, sexual problems and low self-esteem. [8]

Kamboj et al. compared infertile and fertile women in terms of stress, anxiety, and depression. This cross-sectional study from North India showed that the group of infertile women had a higher percentage of individuals with high stress, anxiety, and depression compared to the group of fertile women.

Infertility is a factor of social, biological, and cultural trauma. That might be a stress trigger, which in the long term causes psychological disorders in the form of anxiety, depression, and cognitive impairment. [11]

High cortisol levels

Stress in everyday life can cause many medical conditions. Fears and stress resulting from the PCOS very often arise from changes in external appearance - hirsutism, obesity, acne. [12]

Corticotropin releasing hormone is secreted during stressful situations. This induces the release of adrenocorticotropic hormone (ACTH) from the pituitary and glucocorticoids from the adrenal glands. For this reason, the activity of the hypothalamic–pituitary–adrenal (HPA) axis in women with PCOS increases cortisol production. [13]

Cortisol is a known biomarker of stress-related changes. A study by Dr. Barnali Ray Basu et. al showed that in the saliva of patients with PCOS higher levels of cortisol occur in comparison to the control group. This suggests higher levels of stress in women with PCOS. [14]

As described before chronic stress causes activation of the HPA axis. Obesity is more common in PCOS patients compared to healthy women. In obese patients, such stimulation (of the HPA axis) is more common compared to normal-weight patients. In addition, cortisol released into the system promotes central fat composition (visceral and intra-abdominal areas). [12]

The HPA axis activation and elevated cortisol levels are described as possible causes of depression in the general population; therefore, also in patients with PCOS, a possible relationship between the occurrence of depression and high levels of the above hormone is expected. [15]

Body image

Body image consists of the state of health, physical appearance, individual skills, and the sense of self-attractiveness. Physical and mental changes associated with PCOS negatively affect the perception of one's own body. It also influences social behaviour and interpersonal relationships. [16]

The decrease in self-esteem is strongly associated with obesity or overweight, acne, androgenetic alopecia and hirsutism. In a study conducted by M. Himelein and S. Thatcher, a higher percentage of depression and dissatisfaction with body appearance was found in women with PCOS compared to the control group. According to the results, negative body image does not only depend on being overweight or obese. Women with PCOS showed greater dissatisfaction with their appearance with an indication of features such as complexion, visible facial hair, facial features, general appearance. [17]

A case-control study performed by Yıldı Arzu Abal, Bulat Aytek Şik draws attention to the relationship between body perception and sexual health. 74.23% of women with PCOS and 44.2% of healthy women experienced dysfunction in this area, therefore it seems that the presence of PCOS syndrome is an important factor affecting sexual functions.

Hirsutism and irregular menstrual cycles turned out to be the most important factors in this relation (between body image and sexual functions). Irregular menstrual cycles increase the risk of sexual dysfunction 2.99 times, while hirsutism 2.43 times. [16]

Vitamin D

Vitamin D deficiency increases the risk of many chronic diseases, including obesity, insulin resistance, type 2 diabetes, cardiovascular diseases and psychological disorders. Women with PCOS often suffer from insulin resistance that raises inflammatory markers and leads to diabetes. [18]

These disorders (IR, metabolic syndrome, cardiovascular diseases) are associated with vitamin D deficiency. This is due to the fact that vitamin D regulates glucose-insulin homeostasis by specific Vitamin D Receptor-VDR (also located in pancreatic beta cells). VDR functions include activating the transcription of the human insulin receptor gene, stimulating the expression of insulin receptor, and increasing insulin mediated glucose transport [19]

Obesity is a well-known risk factor for vitamin D deficiency. Women with PCOS coexisting with obesity had lower levels of this vitamin than women with normal weight and PCOS. [18] About 67-85% of patients with PCOS suffer from vitamin D deficiency.

An 8-week double-blind randomized clinical trial- RCT by Kaviani et al. found that increasing circulating 25(OH) D concentrations (8 weeks supplementation) in patients with mild to moderate depression resulted in significant recuperation from depression severity in comparison to the control group. [19]

Inflammatory

Many studies emphasize that PCOS is associated with elevated markers of inflammation. This observation suggests that this syndrome is a state of chronic low-grade inflammation. [20]

White blood cells (WBC) and C-Reactive Protein (CRP) are significantly elevated compared to women of similar age, BMI and normal ovulation. There is a correlation between the presence of elevated inflammatory markers and insulin resistance, BMI and visceral adipose tissue index. [21]

In addition, the previously described vitamin D deficiency causes an increase in inflammatory markers and is itself associated with an increased risk of mood disorders. [12]

Many researchers suggest that the inflammatory process may have an impact on the prevalence of depression in the general population, which may indicate a link between an increased percentage of women with depression and coexisting PCOS. [13]

There is still not enough research to explain the problem of low-grade inflammation coexisting with PCOS. Well-planned prospective research is necessary to thoroughly investigate this issue and understand its significance. [22]

SUMMARY

Polycystic ovary syndrome is a multidisciplinary disease requiring a holistic approach to patients. Data from many studies confirm that it causes a more frequent occurrence of depression. This significantly affects the quality of life and health of women.

This review gathers potential factors that are suspected to be potential causes of mood disorders in women with PCOS (increased BMI, infertility, high cortisol levels, body image, vitamin D deficiency and elevated inflammation markers). Determining the cause of the disorder is crucial to optimizing treatment and providing real help for patients who suffers from PCOS.

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