Family history of PCOS, obesity, low fiber diet, and low physical activity increase the risk of PCOS

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Background: Polycystic ovarian syndrome (PCOS) is a common endocrine disorder and leading cause of prolonged anovulation. PCOS has been linked to a variety of long-term health problems, including: heart disease; metabolic syndrome; and diabetes. It is interesting to know the risk factors for PCOS in local settings.

Objective: The aim of this research is to identify PCOS risk factors in our own settings (Asri Medical Center in Yogyakarta), so that we could identify the specific preparation to avoid having disorders personalized in local characteristics.

Methods: This is a descriptive-analytic cross-sectional study. The research was carried out at Asri Medical Center in Yogyakarta, Indonesia, with a total sample size of 92 people who met the inclusion and exclusion criteria. They were divided into two groups: non-PCOS and PCOS. Data were retrieved using the questionnaire. The variables evaluated were nutritional status, physical activity, carbohydrate diet, fiber diet, family history of diabetes, family history of PCOS, and age of menarche. The data was analyzed using the Chi-square test.

Results: Family history of PCOS, obesity, low physical activity and a low-fiber diet proved to differ significantly between the two groups (p<0.05).

Conclusion: Family history of PCOS, obesity, low physical activity, low fiber diet had a substantial impact on the occurrence of PCOS.

Latar Belakang: Polycystic ovarian syndrome (PCOS) adalah gangguan endokrin umum dan merupakan penyebab penting anovulasi kronis pada wanitaPCOS terkait dengan banyak masalah kesehatan jangka panjang seperti penyakit kardiovaskular, penyakit sindrom metabolik, dan diabetes. Penting untuk menyelidiki faktor-faktor yang meningkatkan risiko PCOS.

Tujuan: Tujuan dari penelitian ini adalah untuk mengetahui faktor risiko PCOS sehingga wanita yang memiliki faktor risiko dapat mengantisipasi untuk menghindari PCOS.

Metode: Penelitian ini merupakan penelitian deskriptif analitik dengan desain penelitian cross sectional. Pengambilan sampel dilakukan di Asri Medical Center Yogyakarta, dengan jumlah sampel sebanyak 92 orang yang memenuhi kriteria inklusi dan eksklusi. Sampel dibagi menjadi 2 yaitu kelompok kontrol (non PCOS) dan kelompok PCOS. Kuesioner digunakan untuk pengambilan data. Variabel yang diamati adalah status nutrisi, aktivitas olahraga, diet karbohidrat, diet serat, riwayat keluarga DM, riwayat keluarga dengan PCOS.
INTRODUCTION

PCOS is one of the most frequent type of endocrine disorder that affects women of childbearing age. Depending on the diagnostic criteria used in different parts of the world, the prevalence varies significantly. PCOS affects 5–10% of the world’s reproductive-age population. Several studies have lately documented an increase in PCOS prevalence due to higher calorie intake, high carbohydrate intake, high fiber intake, and rarely exercise, as well as the tendency to gain weight, which promotes insulin resistance. The Rotterdam criteria are widely used to establish the diagnosis of PCOS. These criteria include 2 of the following 3 symptoms; anovulation, clinical and/or laboratory hyperandrogenism and ultrasound features typical of PCOS. Approximately 50–70% of women with PCOS exhibit hyperandrogen-related clinical symptoms, and 65–95% have increased insulin resistance. Genetic factors can influence the occurrence of PCOS but the association between its variables, on the other hand, is still uncertain. Consumption of junk food and a high-carbohydrate diet raises the risk of insulin resistance, which can lead to PCOS. Due to the hyperinsulinemia and insulin resistance caused by PCOS, one of the hazards is a lack of physical exercise. Obesity is the next most common risk factor. The sensitivity of pancreatic beta cells to elevated blood sugar is reduced as the result of obesity. The tissue’s sensitivity to insulin will decrease as a result of this condition, and the pancreas’ beta cells will instantly compensate by boosting insulin synthesis, resulting hyperinsulinemia. By complex processes, hyperinsulinemia increases androgen production. The age of menarche is another factor that may influence the occurrence of PCOS. The early maturation of the adrenal cortex reticular zone promotes an increase in androgen production, resulting in a younger age of menarche. Increased androgen levels, also known as hyperandrogenism, are thought to have a role in the development of PCOS. Those factors that are described above could be different in our local setting in Yogyakarta. As the term of personalized medicine is increasingly prominent, it is necessary to find out the evidence of the specific characteristics in our own local settings.

METHODS

Design and subjects

This is a cross-sectional research with an analytic observational design. This study undertaken from May to August 2019 at the Asri Medical Center Hospital in Yogyakarta, Indonesia.

Data Collection

In this study, a purposive sample method was adopted. The inclusion criteria were all women who had menstruation issues and were willing to participate in the study. Whereas women with menstrual issues who also had liver disease, diabetes, kidney disease, or other causes of anovulatory infertility were excluded. The study included 46 women with PCOS diagnosed using the Rotterdam criteria, as well as 46 women with other menstrual problems. The data was gathered from the patient’s medical records and also questionnaire. Diabetes mellitus (DM) in the family, PCOS in the family, age of menarche, nutritional status, physical activity, carbohydrate diet, and fiber diet are some of the questions asked. Nutritional status is measured by BMI (Obesity: >30; Overweight: 25-30, normal:<25). Physical activity is assessed by frequency of doing exercise in a week (high ≥ 3 times/week; low: < 3 times/week). Carbohydrate diet is assessed by the frequency of consuming high-carbohydrate foods beyond large meals (high: >3 times/week; low: <3 times/week), a high-fiber diet is assessed with frequency
consuming high-fiber foods (high: >3 times/week; low: <3 times/week).

The Health Research Ethics Committee of the Faculty of Medicine and Health Science, University of Muhammadiyah Yogyakarta, Indonesia has given its approval to this study (150/EP-FKIK-UMY/IV/2019).

**Statistical analysis**

Bivariate data analysis was done using the Chi-square test with a significance threshold of p<0.05 and Confidence Interval=95%.

**RESULTS**

**Group characteristics**

A total of 46 PCOS patients and 46 non-PCOS individuals participated in the study. The existence of a family history of PCOS, obesity, low physical activity, and a low-fiber diet were all linked with the incidence of PCOS. Based on the research that has been conducted, the following results were obtained using the Chi square test. Family history of PCOS, obesity, low physical activity and a low-fiber diet proved to differ significantly between the two groups (p<0.05, Table 1).

<table>
<thead>
<tr>
<th>Table 1. Risk factor of PCOS</th>
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<td>Variable</td>
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<tr>
<td>Family history of Diabetes Mellitus</td>
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<td>Yes</td>
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<td>No</td>
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<tr>
<td>Family history of PCOS</td>
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<td>Yes</td>
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<td>No</td>
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<tr>
<td>Age of menarche</td>
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<td>&lt;12 years old (early)</td>
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<td>12-16 years old (normal)</td>
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<td>&gt;16 years old (late)</td>
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<tr>
<td>Nutritional status</td>
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<td>Obesity</td>
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<td>Overweight</td>
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<td>Normal</td>
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<td>Physical activities</td>
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<td>Carbohydrate diet</td>
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*p<0.05
DISCUSSION

There was a relationship between PCOS incidence and a family history of PCOS in this study, however it was not associated to a family history of diabetes mellitus. Genetic factors have a role in the pathophysiology of PCOS. Although this genetic explanation has not been verified, various theories suggest that PCOS is inherited by an autosomal dominant gene and several candidate genes that may impact PCOS occurrence.

The pathophysiology of PCOS is linked to an inherited genetic component; genetic factors influence the PCOS phenotype in at least 10% of cases. Several chromosomal locations and potential genes for PCOS have been found through genome-wide association studies (GWAS). According to a meta-analysis, polymorphisms in the steroidalogenic acute regulatory gene (StAR), gonadotropin-releasing hormone receptor (GnRHR), follicle stimulating hormone receptor (FSHR), fat mass and associated obesity, insulin receptor (IR), IR substrate (IRS), vitamin D receptor (VDR) are all involved in the pathophysiology of PCOS. Despite the fact that most women with PCOS have insulin resistance, pancreatic B cell dysfunction, poor glucose tolerance, and/or type 2 diabetes, PCOS does not appear to be associated with genetic changes that increase the risk of type 2 diabetes. Family history of DM, on the other hand, is linked to the phenotype of PCOS. Sex Hormone Binding Globulin (SHBG) and Free Androgen Index (FAI) are both associated with a family history of DM. PCOS individuals with a family history of diabetes have higher rates of Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and FAI. A family history of diabetes is associated with elevated hemoglobin A1c (HBA1c) levels in PCOS women.

Our findings indicate a link between obesity and the occurrence of PCOS. Patients with a family history of obesity had a greater percentage of body fat than those who did not. PCOS individuals who are obese are more prone to have irregular menstrual cycles and maturation of ovarian follicles. Obesity appears to trigger insulin resistance that causing PCOS, and women with PCOS appear to be more prone to obesity. Obese PCOS women were shown to have higher systolic and diastolic blood pressure, as well as fasting blood sugar, insulin, HOMA-IR, total cholesterol, and triglycerides. In roughly 50-70 percent of PCOS women, and 95 percent of obese PCOS women, IR occurs. Obesity causes changes in adipokine production, such as a decrease in adiponectin and an increase in leptin, which leads to an increase in proinflammatory cytokines. Obesity and insulin resistance enhance the release of inflammatory cytokines such as high-sensitivity CRP (hs-CRP), IL-6, IL-18, and tumor necrosis factor alpha (TNF-a) in PCOS women, which is one of the low-grade chronic inflammatory illnesses. This increase in proinflammatory cytokines regulates IR by boosting IRS-1 serine phosphorylation and reducing Akt substrateof 160 kDa (AS160) phosphorylation, resulting in a decrease in the expression of the glucose transporter type 4 (GLUT-4) and decreasing glucose transport into cells. Obesity reduces the ability of the body’s cells to fight insulin. The sensitivity of pancreatic beta cells to elevated blood sugar is reduced as a result of obesity. Because the tissue's sensitivity to insulin reduced, pancreatic beta cells will be instantly adjusted by boosting insulin synthesis, resulting in hyperinsulinemia. By a variety of processes, hyperinsulinemia increases androgen production.

On the other hand, PCOS also linked to a poor diet. The diet in question involves the proportion, quantity, variety, or a mix of different drinks and meals, as well as the frequency with which they are typically consumed. A healthy diet consists of foods that meet the body’s energy requirements. However, there are a few PCOS women who consume more food than their bodies require. Dietary habits such as overeating in junk food and consuming macronutrients in excess of the body’s requirements can increase the risk of polycystic ovaries. Content high carbohydrate, high calorie, and low fiber content
in junk and fast food raises the risk of insulin resistance, which can lead to PCOS.\textsuperscript{23} This study found no link between excessive carbohydrate consumption in the diet and the occurrence of polycystic ovarian syndrome. Previous research has suggested that a high-carbohydrate diet can raise the risk of polycystic ovarian syndrome in women.\textsuperscript{7} This disparity might be attributed to discrepancies in measuring methodologies. In this study, measures were taken solely through the completion of questionnaires, with no in-depth dietary assessment.

The findings of this study revealed that there was no statistically significant difference in menarche age between the PCOS and non-PCOS groups. In comparison to normal girls, PCOS girls have a wide range of menarche ages. Menarche onset is influenced by a number of factors, including BMI and genetic variance. PCOS women have a delayed beginning of menarche due to delayed follicular development in prepubertal, hormonal imbalances of estradiol, progesterone, and androgens, and hormonal imbalances of estradiol, progesterone, and androgens. Girls who are later diagnosed with PCOS may have primary amenorrhea as a consequence. Menarche may occur early in PCOS girls who have a history of deliveries with dysmaturity and smaller for gestational age newborns. Menarche appears earlier in PCOS girls with a high BMI. Furthermore, genetic variations can influence the age of menarche in women with PCOS.\textsuperscript{24,25}

This research discovered a link between low physical activity and the occurrence of PCOS. Low physical activity might contribute to the development of PCOS, which is characterized by hyperinsulinemia and insulin resistance. Physical activity that is sufficient and consistent is directly tied to the metabolism of stored glucose in the muscles for use as energy, and if the glucose level is low, the muscle will compensate by pulling glucose from the bloodstream. This is what causes blood glucose levels to drop, allowing for better blood glucose control.\textsuperscript{8} Insulin secretion and sensitivity are affected by physical exercise in patients with polycystic ovarian syndrome. Excessive fat accumulation occurs in the absence of physical activity, resulting in an increase in the amount of free fatty acids (FFA) and triglyceride levels.\textsuperscript{21} In PCOS women, this low-density lipoproteins (LDL) saturated fat inhibits insulin action, resulting in hyperinsulinemia. Insulin resistance will diminish and insulin sensitivity will rise when you get enough exercise or physical activity. Long-term calorie restriction (5-6 months) and increased physical activity can result in weight loss of 5-10% of the original weight. IR and hyperandrogenism, as well as menstrual function and fertility, can all be affected by this disorder. Additionally, it has the potential to promote long-term metabolic health.\textsuperscript{23}

**CONFLICT OF INTEREST**

Family history of PCOS, obesity, low physical exercise, a low-fiber diet were major PCOS risk factors.

**ACKNOWLEDGEMENT**

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