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RESEARCH ARTICLE

THE RELATIONSHIP OF VITAMIN D TO*POLYCYSTIC OVARY SYNDROME* (*PCOS*) TEENAGERS AT KOTO TANGAH PADANG DISTRICT HIGH SCHOOL IN 2022

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Abstract

PCOS is characterized by increased ovarian and adrenal androgen secretion, hyperandrogenic symptoms such as hirsutism, acne and/or alopecia, menstrual irregularities, and polycystic ovaries. The prevalence of PCOS in 2016 was 6−21% of reproductive age worldwide. PCOS is the most common female endocrine disorder with a prevalence of around 4-6% in women of reproductive age in Indonesia. Vitamin D deficiency can increase PCOS symptoms. The research design was cross-sectional. The study was conducted at SMA N 7, SMA N 8 and SMA N 13 Padang in Koto Tangah District in May-August 2022. The research sample was high school students who experienced menstrual cycle disorders and were willing to agree to informed consent for the study with a sample size of 59 respondents. Vitamin D levels were examined using the 25-Hydroxyvitamin D ELISA Kit. Data were analyzed by chi-square test. The results showed that 86.4% of respondents experienced vitamin D deficiency. Statistically there was a relationship between PCOS in adolescents accompanied by hyperandrogens and vitamin D levels, there was a relationship between PCOS in adolescents accompanied by obesity and vitamin D levels, there was no relationship between PCOS in adolescents accompanied by acanthosis nigrican and vitamin D levels, and there was no relationship between PCOS in adolescents accompanied by hyperandrogens, obesity and acanthosis nigrican with vitamin D levels in SMA Koto Tangah District Padang in 2022. The conclusion of this study is that there is a relationship between PCOS in adolescents accompanied by hyperandrogens and vitamin D levels and there is a relationship between PCOS in adolescents accompanied by obesity and vitamin D levels.

Keywords: *Adolescent, PCOS, Vitamin D*

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INTRODUCTION

PCOS is characterized by increased ovarian and adrenal androgen secretion, hyperandrogenic symptoms such as hirsutism, acne and/or alopecia, menstrual irregularities, and polycystic ovaries. This syndrome is the most common cause of infertility in women, often becoming apparent during adolescence, and is primarily characterized by ovulatory dysfunction and androgen excess.[1,2] In addition, insulin resistance (IR) disorders are common in women with PCOS, who therefore have increased risk of type 2 diabetes.[3] The World Health Organization (WHO) in 2012 estimated that approximately 116 million women (3.4%) experienced PCOS worldwide. The prevalence of PCOS in 2016 was 6-21% in reproductive age worldwide.[4, 5] Polycystic Ovary Syndrome (PCOS) is the most common female endocrine disorder with a prevalence of around 4-6% among women of reproductive age in Indonesia.[6] Trends the prevalence of PCOS is increasing by 6-18%.[7, 8] Seventy-five percent of the female population, anovulatory infertility is caused by PCOS and in Indonesia, PCOS accounts for 8% -10% of infertility cases. Based on the results of the 2010 Riskesdas, it is known that the prevalence of irregular menstruation in women aged 10-59 years in West Sumatra Province is 19.1% and the average age of menarche is highest in the 13-14 year age range as much as 41.4%.[9] This is due to the role Insulin resistance in the pathophysiology of PCOS is influenced by a lifestyle with a high-calorie diet and a sedentary lifestyle.[7, 8]

The consequences of PCOS not only include reproductive problems, but also the risk of metabolic and cardiovascular disorders, gynecological neoplasms including endometrial, breast and ovarian cancer. Insulin resistance can be found in 50-80% of women with PCOS, 70-80% of PCOS patients who are obese and insulin resistant in 20-25% of PCOS patients who are slim. The risk of developing type 2 diabetes is ten times higher in PCOS patients, and 40% of PCOS patients will develop type 2 diabetes by age 40.[10, 11]

The clinical presentation of PCOS varies greatly by age, race, weight, and medication, with androgenic effects considered to be the most common mechanism responsible for the PCOS phenotype.[12] As a result, women with PCOS may see a variety of medical specialists, including gynecologists, internist, endocrinologist, or dermatologist.[2, 13]

In adolescents with PCOS complaints usually present with abnormal menstrual periods, hirsutism, and/or acne. Various patterns of menstrual irregularities can include primary amenorrhea, secondary amenorrhea, oligomenorrhea, and even excessive uterine bleeding.[14] A recent study found that PCOS was the most common underlying cause of adolescents hospitalized with abnormal uterine bleeding (AUB) and menorrhagia, accounting for 33% of admitted patients.

Although PCOS was classically considered a cause of infertility in adults, it is now known that its onset can occur in childhood, so it should be considered in any adolescent with hirsutism, persistent acne, dysfunctional uterine bleeding and/or obesity. Identifying each of these complaints is a challenge in adolescence. On the other hand, a diagnosis of PCOS has long-term implications with an increased risk of infertility, metabolic syndrome, type 2 diabetes (T2DM) and cardiovascular disease.[10,14]

Vitamin D deficiency often occurs in women with PCOS, where 67-85% of women with PCOS have serum 25-hydroxy vitamin D [25(OH)D] concentrations <20 ng/ml. Vitamin D deficiency can increase PCOS symptoms. PCOS has a multigenic etiology and there are several extra-ovarian aspects to the pathophysiology of PCOS, but it is primarily caused by ovarian dysfunction. Altered gene expression of some tissues; such as ovaries, adipose and skeletal muscle; is known to contribute to this complex pathophysiology.[15,16]

Vitamin D deficiency conditions affect almost half of the world's population. Almost all ethnicities and age groups in the world are estimated to experience vitamin D deficiency. Research conducted in Indonesia and Malaysia with a sample of 504 Women of Childbearing Age (WCA) with an age range of 18 to 40 years found the prevalence of vitamin D deficiency to be 63% with an average serum 25(OH)D concentration was 48 nmol/L (19.2 ng/mL).[17]

The prevalence of Vitamin D deficiency is one of the nutritional problems related to health in WCA. Even though Indonesia is a tropical country, the prevalence of Vitamin D deficiency is quite high. WCA has a role The physiology of childbirth and menstruation which causes vulnerability to nutritional problems so needs attention. Vitamin D malnutrition causes various health impacts on women and their offspring.[17]

Measuring plasma Vitamin D levels as a screening for Vitamin D deficiency or insufficiency is not a routine examination. One of the reasons, among others, is that the cost of vitamin D examination is relatively expensive. Therefore, it is difficult to prevent long-term conditions that can result from Vitamin D deficiency or insufficiency, especially in WCA. Meanwhile, vitamin D levels below normal are associated with reproductive health problems in WCA.[17]

Women of childbearing age are women aged 15-49 years. At this age, the female reproductive organs have developed and are functioning optimally. In adolescent girls, the development of reproductive organs begins with puberty. Puberty itself is marked by the onset of menstruation (menarche), which is accompanied by physical, mental and social changes.[18]

The menstrual cycle is a sign of the maturation process of the reproductive organs which is influenced by the body's hormones. The role of the menstrual cycle is related to women's fertility levels. This cycle regularly occurs when a teenager reaches the age of 17 - 18 years, but can also occur after 3 - 5 years from the age of menarche. Normal menstrual patterns take place every 21 – 35 days, while menstrual days can last for 3 – 7 days.[18]

The menstrual cycle process sometimes has ups and downs and changes every month which can cause problems with menstrual disorders. The high prevalence of menstrual disorders is caused by various factors such as stress, lifestyle, physical activity, medical conditions, hormonal disorders and nutritional status. In previous research it was said that increasing body weight, stress and low physical activity can lengthen the menstrual cycle.[19]

Menstrual irregularity is a common feature of PCOS, occurring in more than 75% of the adult PCOS population, and is often the earliest clinical manifestation in adolescents.[20] The most frequent reason why patients with this syndrome come to the doctor is infertility (90%–95%) , disorders of the menstrual cycle (85-90% with oligomenorrhea and 30-40% with secondary amenorrhea), as well as other disorders such as hirsutism (70%) and acne (15-30%).[14]

With so many views on the effects of a lack of vitamin D levels, researchers are interested in conducting research on the effect of vitamin D on the clinical appearance of PCOS in adolescents with menstrual cycle disorders. We hypothesized that vitamin D deficiency would be associated with an increased risk of more PCOS clinical symptoms in adolescents. This research was conducted on adolescents because during adolescence significant and critical changes occur in growth, development and puberty.[4] It is hoped that examining vitamin D levels will enable early identification of adolescents with a high tendency to develop PCOS.

The Rotterdam criteria are used in diagnosing PCOS in adult women, are different in adolescents where the existing diagnostic criteria often create problems in establishing a diagnosis because normal pubertal characteristics often overlap with PCOS symptoms.[20]

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Pelvic ultrasound findings are not recommended for the diagnosis of PCOS in adolescents or in women with gynecological age <8 years (<8 years post menarche) due to the high incidence of multi-follicular ovaries in this stage of life. Therefore, a diagnosis of PCOS may be considered in adolescents with persistent oligoamenorrhea 3 to 4 years postmenarche with clinical and/or biochemical hyperandrogenism after ruling out other disorders associated with irregular menstruation or hyperandrogenism. Even before a definitive diagnosis of PCOS, adolescents with clinical signs of androgen excess and oligomenorrhea/amenorrhea, hallmarks of PCOS, may be considered to be at risk for PCOS. Menstrual irregularities persisting 3 years after menarche are associated with PCOS in approximately 70% of cases, but when oligomenorrhea does not persist for 2 years, these adolescents are considered at risk for PCOS and require longitudinal evaluation to assess ongoing features of PCOS. Most of the clinical data available during adolescence relate to findings and outcomes in adult women[1,10, 21]

This research will be conducted on adolescent girls. According to the Republic of Indonesia Minister of Health Regulation number 25 of 2014, teenagers are residents with an age range of 10-18 years and this research will be conducted on high school age teenagers. Padang is the city with the highest number of female teenagers of high school and equivalent age in West Sumatra, with 29,532 out of a total of 143,058 female teenagers of high school and equivalent age in West Sumatra.[22] There are 71 public and private high schools spread across 11 sub-districts in Padang City. Koto Tangah District is the district with the largest number of high schools, namely 13 high schools consisting of 4 public high schools and 9 private high schools. [23] So this research will be conducted on female high school students in Koto Tangah District

Result

Characteristics of Research Respondents

Research was conducted on female students from SMA N 7, SMA N 8, and SMA N 13, Padang City, with a total of 59 research respondents who met the inclusion and exclusion criteria. This research was conducted to determine the relationship between vitamin D and clinical symptoms*PCOS* in teenagers. The research results were obtained as follows:

Table 5.1 Respondent Characteristics

Respondent Characteristics	f (%)
Age (years)	
a. 10-12	0
b. 13-15	2 (3,4)
c. 16-18	57 (96,6)
d. > 18	0
Post-menarche menstrual disorders	
a. 2-3 years	18 (30,5%)
b. > 3 years	41 (69,5%)
Vitamin D:	
a. Normal	8 (13,6)

b.	Less	51 (86,4)
BMI:		
a.	Not obese	
	Underweight (<18,5)	37 (62,7)
	Normal (18,5-22,9)	14 (23,7)
	Overweight (23-24,9)	21 (35,6)
b.	Obesity	2 (3,4)
	Obesity (25-29.9)	22 (37,3)
	Obesity II (>30)	18 (30,5)
		4 (6,8)
Clinical hyperandrogenism:		
a.	Not hyperandrogenous	29 (49,2)
b.	Clinical hyperandrogenism	30 (50,8)
Acanthosis nigricans:		
a.	Not acanthosis nigricans	43 (72,9)
b.	Acanthosis nigricans	16 (27,1)

Based on Table 5.1, it is known that the majority of respondents were in the 16-18 year age range, namely 57 respondents (96.6%), and the length of menarche was > 3 years in 41 respondents (69.5%). Most of the respondents experienced vitamin D deficiency, namely 51 people (86.4%), 37 respondents (62.7%) were not obese, 30 respondents (50.8%) had clinical hyperandrogenism, and 43 respondents (72) did not experience acanthosis nigricans. 9%).

Relationship of Vitamin D to *PCOS* in Adolescents Accompanied by Clinical Hyperandrogenism

The relationship between vitamin D levels and*PCOS* in adolescents accompanied by clinical hyperandrogenism can be seen in Table 5.2 below:

Table 5.2 Relationship between Vitamin D Levels and*PCOS* Accompanied by Clinical Hyperandrogenism

Vitamin D	Clinical Hyperandrogenism				Amount		p-Value
	Clinical Hyperandrogenism		Not Hyperandrogen				
	(f)	%	(f)	%	(f)	%	
Less	30	58,8	21	41,2	51	100	0,002
Normal	0	0	8	100	8	100	

Based on Table 5.2, it can be concluded that the majority of respondents with low vitamin D levels, namely 30 respondents (58.8%) experienced clinical hyperandrogenism and all respondents with normal vitamin D levels, namely 8 respondents (100%) did not experience

hyperandrogenism. The results of statistical tests show that there is a relationship between vitamin D and clinical hyperandrogenism in adolescents who experience it*PCOS* (p<0,05).

Relationship of Vitamin D to*PCOS* in Adolescents with Obesity

The relationship between vitamin D levels and*PCOS* in adolescents accompanied by obesity can be seen in Table 5.3 below:

Table 5.3 Relationship between Vitamin D Levels and Obesity

Vitamin D	Obesity				Amount		p-Value
	Obesity		Not Obese				
	(f)	%	(f)	%	(f)	%	
Less	22	43,1	29	56,9	51	100	0,02
Normal	0	0	8	100	8	100	

Based on Table 5.3, it can be concluded that the majority of respondents with deficient vitamin D levels, namely 29 respondents (56.9%) were not obese and all respondents with normal vitamin D levels, namely 8 respondents (100%) were also not obese. The results of statistical tests show that there is a relationship between vitamin D and obesity in adolescents who experience it*PCOS* (p<0,05).

Relationship of Vitamin D to*PCOS* in Adolescents Accompanied by Acanthosis Nigricans

The relationship between vitamin D levels and*PCOS* in adolescents accompanied by acanthosis nigricans can be seen in Table 5.4 below:

Table 5.4 Relationship between Vitamin D Levels and Acanthosis Nigricans

Vitamin D	Acanthosis Nigricans				Amount		p-Value
	Acanthosis Nigricans		Not Acanthosis Nigricans				
	(f)	%	(f)	%	(f)	%	
Less	16	31,4	35	68,6	51	100	0,093
Normal	0	0	8	100	8	100	

Based on Table 5.4, it can be concluded that the majority of respondents with deficient vitamin D levels, namely 35 respondents (68.6%) did not experience acanthosis nigricans and all respondents with normal vitamin D levels, namely 8 respondents (100%) did not experience acanthosis nigricans. The results of statistical tests show that there is no relationship between vitamin D and acanthosis nigricans in adolescents who experience it*PCOS* (p>0,05).

Relationship of Vitamin D to*PCOS* in Adolescents Accompanied by Clinical Hyperandrogenism, Obesity, and*Acanthosis Nigricans*

The relationship between vitamin D and*PCOS* in adolescents accompanied by clinical hyperandrogenism, obesity, and acanthosis nigricans can be seen in Table 5.5 below:

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Table 5.5 Relationship of Vitamin D with Clinical Hyperandrogenism, Obesity, and Acanthosis Nigricans

Vitamin D	Clinical Symptoms				Amount		p-Value
	Of		No				
	(f)	%	(f)	%	(f)	%	
Less	11	21,6	40	78,4	51	100	0,33
Normal	0	0	8	100	8	100	

Based on Table 5.5, it can be concluded that the majority of respondents with deficient vitamin D levels, namely 40 respondents (78.4%) did not experience clinical symptoms (hyperandrogenism, obesity and acanthosis nigricans) and all respondents with normal vitamin D levels were 8 respondents (100%) did not experience clinical symptoms (hyperandrogenism, obesity, and acanthosis nigricans). The results of statistical tests show that there is no relationship between vitamin D levels and clinical hyperandrogenism, obesity and acanthosis nigricans in adolescents who experience*PCOS* (p>0,05).

Discussion

Characteristics of Research Respondents

In 59 research samples conducted at high schools in Koto Tangah District, the dominant age was 16-18 years. This age group is late adolescence, in accordance with the Indonesian Ministry of Health in 2009 which states that the 12-16 year age group is categorized as early adolescence, and 17-25 is categorized as late adolescence. This late adolescent age group is dominant because the sample for this study is high school students, who have gone through at least 9 years of previous education in elementary and middle school, so the average age of students entering high school is 16 years old. This is in accordance with data from statistical data published by the Ministry of Education and Culture regarding the largest age group among high school students in Indonesia in the 2020/2021 academic year is the 16-18 year age group.[23]

PCOS is a form of hormonal disorder that most often occurs in adolescents with varying clinical symptoms. Teenagers who experience*PCOS* can affect the menstrual cycle, fertility levels, psychology, and metabolic disorders such as obesity. Signs and symptoms*PCOS* often begins to appear in adolescence but in some women the symptoms*PCOS* it doesn't even appear until early adulthood.[110] The results of research on teenagers in Bangladesh using the Rotterdam criteria showed that 9.13% of teenagers experienced*PCOS*. The endocrinologist community suggests a diagnosis*PCOS* In female adolescents, this should be determined based on the presence or absence of clinical symptoms of hyperandrogenism.[111]

The average age of menarche for this research sample was 12.5 years in accordance with the results of the 2017 Indonesian Demographic and Health Survey report which stated that the age of menarche varied between 10 - 16 years with an average onset of 12.4 years. The majority of adolescents (76.6%) have an age of menarche ranging from 12-14 years with the initial occurrence being less than 8 years and the latest occurring at the age of 17 years.[112]

In this study, 22 (37.3%) students with menstrual disorders were obese and 2 were overweight. The obesity rate in this research sample is higher than the incidence of obesity in

adolescents, which is based on Basic Health Research data, the prevalence obesity in adolescents aged 16-18 years in Indonesia in 2013 was 7.3%. The incidence of obesity tends to increase every year, where in 2007, the incidence of obesity in adolescents was still 1.4%. West Sumatra is included in 15 provinces that have an obesity prevalence above the national figure.[61]

The prevalence of obesity in adolescents, based on data from the West Sumatra Provincial Health Service, is 6.5%. Based on data from the Padang City Health Service, obesity in adolescents is included in the 10 most common diseases in high school (SMA) adolescents in Padang City with a prevalence of 10.3% in 2012-2013, exceeding the national prevalence of 10%.

The high rate of obesity in this sample is due to the research sample being patients with menstrual disorders who are at risk for PCOS. Obesity is a common characteristic and one of the clinical manifestations of PCOS. There is evidence that obesity, especially abdominal obesity, worsens the clinical and endocrine features of PCOS syndrome. Variations in the prevalence of obesity in each population are associated with lifestyle factors and genetic factors. It is estimated that 38-88% of women with*PCOS* are obese. Weight loss is known to reduce androgen levels and have a positive impact on patient fertility*PCOS* who are obese. The risk of anovulatory infertility will increase in women with BMI ≥ 24.[112] Obesity is closely related to insulin resistance which can cause hyperandrogenemia.[113]

Vitamin D plays a role in the process*PCOS*. As many as 67-85% of women with*PCOS* have a vitamin D deficiency.[4] The results of this study showed that the majority of respondents experienced vitamin D deficiency (≤ 20 ng/mL). This is in line with research conducted by Trummer*et al* (2019) which serum levels of vitamin D in women with*PCOS* tends to be low or even deficient. Vitamin D status is closely related to the occurrence of insulin resistance, one of the main characteristics of the phenotype*PCOS.* Vitamin D can suppress pro-inflammatory cytokines and increase insulin receptor expression, resulting in increased insulin synthesis and release. Insulin resistance is associated with an increased risk of several metabolic disorders, including type 2 diabetes mellitus and cardiovascular disease. Metabolic disorders in*PCOS* related to ovarian physiology.[114] The correlation between the pathogenesis of insulin resistance and vitamin D deficiency places hypovitaminosis as a causative factor in the occurrence of metabolic syndrome in women who suffer from it*PCOS*.[115]

Previous studies have shown that changes in intracellular calcium concentrations caused by vitamin D deficiency can trigger abnormal ovulation in women with*PCOS*. Vitamin D deficiency is a risk factor*PCOS* and is associated with increased levels of androgen hormones in cases*PCOS*.[116] A number of research results show that vitamin D deficiency is associated with insulin resistance, impaired glucose and lipid metabolism, and infertility (a condition that often occurs in women with*PCOS*).[115]

The incidence of clinical hyperandrogenism in this study was 50.8%. The incidence of hyperandrogenism is in line with the prevalence of clinical hyperandrogenism in patients*PCOS*, where the incidence of hirsutism in*PCOS* occurs in 70 – 80% of cases, which usually begins in early late adolescence.[113]

The incidence of clinical hyperandrogenism in this study is in line with the incidence of hyperandrogenism in patients*PCOS* This is because hirsutism generally begins in early adolescence. In this study the students were aged around 16-18 years which makes it possible for this clinical condition to have appeared in the sample of this study. The incidence of hirsutism is also influenced by cultural and ethnic factors. In general, a small percentage of Asian women show hirsutism. The incidence of hirsutism in Caucasian women is 60-70%,

while in Japanese women it is 30%. Davis et al reported a prevalence of hirsutism in PCOS of 5% in a Southeast Asian population.[119]

The incidence of acantosis nigrican in this study was 27.1%. The occurrence of acantosis nigrican is considered a marker of insulin resistance in the skin. Acanthosis nigricans can be found in individuals with or without*PCOS*. Insulin resistance causes hyperinsulinemia, which is believed to stimulate the growth of keratinocytes and dermal fibroblasts, resulting in characteristic skin changes. In this study, 12 students with achantosis nigrican had an obese BMI, both of which were associated with obesity. This is in line with research where acanthosis nigricans occurs more often in obese women with*PCOS* (50 percent incidence) compared to women with*PCOS* and normal body weight (5 to 10 percent).[115]

Relationship of Vitamin D to*PCOS* in Adolescents Accompanied by Clinical Hyperandrogenism

The results of this study show that there is a relationship between vitamin D levels and*PCOS* in adolescents accompanied by clinical hyperandrogenism and it is known that the majority of respondents with low levels of vitamin D experience clinical hyperandrogenism. This is in line with Davis' research*et al* (2019). They conducted research on women who experienced it*PCOS* by grouping them according to the Rotterdam criteria and research results found a high prevalence of vitamin D deficiency in cases*PCOS* with hyperandrogenism.[117]

Vitamin D deficiency is known to contribute to its occurrence*PCOS*. *PCOS* It is estimated that it can occur in one in five women which is related to insulin resistance and hyperandrogenism which can be influenced by vitamin D metabolism.[118] Hasil penelitian Kılınç*et al* (2019) it is known that there is a relationship between 25-OH-D levels and gonadotropin hormones during puberty. Total testosterone levels were higher and inhibin B lower in adolescent girls who had 25OH-D deficiency compared to adolescents with normal 25OH-D levels. Therefore, 25OH-D was concluded to have an influence on gonad function during the early period of life.[119] Vitamin D is thought to improve fertility by modulating androgenic activity. Vitamin D is able to influence the expression and activity of several enzymes involved in the production of sex hormones.[115]

Hyperandrogens in*PCOS* can occur since puberty. Manifestations of hyperandrogenism can be accompanied by no symptoms or even classic symptoms (acne, hirsutism, etc*alopecia*) to experience ovulatory and menstrual dysfunction. Symptoms of hyperandrogenism not only affect physical and psychological health but also have a significant relationship with pregnancy complications such as premature labor and preeclampsia. In women who experience*PCOS* known rate*Sex Hormone Binding Globulin* (*SHBG*) low.*SHBG* has an important role in regulating androgen levels. Insulin resistance and hyperinsulin contribute to the occurrence of hyperandrogens by causing reduced production*SHBG* in the heart. One study found that there was a positive correlation between serum vitamin D levels and SHBG levels.[120]

Shan *et al* (2022) found that vitamin D levels in Chinese women with*PCOS* low, especially those experiencing hyperandrogenism. There is a negative correlation between 25(OH)D and hyperandrogenism. Vitamin D is related to manifestation*PCOS* including ovulatory dysfunction and hyperandrogenism.[121] Vitamin D may have a beneficial effect on insulin response and androgen levels in cases*PCOS*. Women who experience*PCOS* had higher testosterone levels than the control group. Clinical signs of hyperandrogenism include hirsutism,*acne*, and*alopecia* in women with*PCOS*. Low vitamin D levels are associated with high hirsutism scores, and the analysis results show that there is a negative correlation

between serum vitamin D3 levels and hirsutism scores. Someone who experiences hirsutism has lower vitamin D levels than people who do not experience hirsutism.[101]

The reason that not everyone who is deficient in vitamin D experiences hyperandrogenism is because this research can also be caused by the modified Ferriman-Gallwey score, there is still no standard value that can be used as a guide in diagnosing hirsutism. Various studies have suggested different cut-off values for the Ferriman-Gallwey grading system in different racial groups. For example, a score of 6 is recommended for Japanese women, 3 for Thai women, 8 for Caucasian women, and 10 for Turkish women. In Chinese women, there have been two studies on the cut-off value of the Ferriman-Gallwey score.[119] Because in Indonesia itself there is no set standard value, in this research the value is*cut off* used to follow the Thai race, namely ≥3. Possible value*cut off* in this research sample it should be lower than the value used, so that samples that actually already have clinical hirsutism are not diagnosed.

Relationship of Vitamin D to*PCOS* in Adolescents with Obesity

In this study, it was found that more people in the obese group experienced vitamin D deficiency and there was a clinical relationship*PCOS* in adolescents accompanied by obesity with vitamin D levels.*PCOS* is an obesity-related condition, where weight gain and obesity contribute to the development*PCOS* and also development*PCOS* can contribute to weight gain.[124] This is also what happened in this research. This condition occurs because obesity is caused by multifactors, including genetics, physical activity, diet and hormonal disorders.

The results of this study are in line with the results of previous research showing that vitamin D deficiency often occurs in women who suffer from it*PCOS*, especially in women who are obese and have insulin resistance.[122] Obesity is known to be a risk factor for hypovitaminosis D and the association between obesity, hypovitaminosis D, and*PCOS* proven.[123]

Obesity is a condition where there is excessive fat accumulation, where abdominal fat is the main risk factor for insulin resistance. Obesity accompanied by insulin resistance is often associated with low 25(OH)D concentrations. A research result shows that there is a relationship between 25(OH)D levels ≤20 ng/mL and the risk of obesity in the non-obese group after being followed for four years.[124] Lumme Research*et al* (2019) found out the average BMI in women who experienced it*PCOS* higher than the control group. Woman with*PCOS* and high BMIs experience a greater deficiency in 25(OH)D levels than women with normal BMIs.[101]

Research conducted by Aghadavod*et al* (2017) shows the average vitamin D levels of teenagers*PCOS* with*overweight* namely 1.6 ± 0.9 nmol/ml while in adolescents*PCOS* with normal body weight, namely 4.5 ± 1.7 nmol/ml. Previous studies have described possible mechanisms by which low serum 25(OH)D is associated with obesity. Insulin resistance and obesity are associated with reduced secretion*growth hormone* (GH) in patients*PCOS*. This may be the cause of decreased 25(OH)D levels because GH significantly increases expression*renal 1-a-hydroxylase* and of course serum 25(OH)D levels.[125]

Several studies have found an inverse association between BMI and serum 25(OH)D levels in women with*PCOS*. 25(OH)D levels in women*PCOS* who are obese are 27-56% lower than women with*PCOS* who are not obese. The results of other studies show that low 25(OH)D levels are significantly determined by the level of adiposity (BMI and total fat mass). There is a possibility of a high prevalence of vitamin D deficiency in women with*PCOS* associated with obesity because vitamin D is fat soluble.

Relationship of Vitamin D to*PCOS* on Involved Adolescents*Acanthosis Nigricans*

The results of this study show that there is no relationship between vitamin D and*PCOS* in adolescents accompanied*acanthosis nigricans*. *Acanthosis nigricans* closely related to insulin resistance and metabolic syndrome. Lesions caused by*acanthosis nigricans* is a result of high concentrations of insulin binding to the receptor*insulin-like growth factor* (IGF) thereby increasing the formation of epidermal cells in the form of plaque.[126]

Previous research conducted on a group of teenagers with obesity identified teenagers who experienced it*PCOS* more joined*acanthosis nigricans*. *Acanthosis nigricans* in women with*PCOS* varies greatly depending on age, weight, pubertal status, PCOS phenotype, insulin resistance, obesity, and genetic characteristics. With a prevalence of around 30-50% or even 70-90% in women*PCOS* accompanied by obesity,*acanthosis nigricans* is one of the clinical signs most frequently found in cases*PCOS* which is accompanied by acne, hirsutism and alopecia.*Acanthosis nigricans* more often found in women with obesity*PCOS* compared to women of normal weight. Higher androgen levels contribute to hirsutism and*acanthosis nigricans*.[126]

Acanthosis nigricans become one of the clinical signs*PCOS*. This research is not in line with previous research which concluded that as many as 60.9% of research respondents experienced vitamin D3 deficiency*acanthosis nigricans*. As many as 75% experienced pigmentation abnormalities in the elbows and knees, 60% in the axilla, 58.8% in the knuckles, and 50% in the neck. There is a negative correlation between vitamin D3 and severity*acanthosis nigricans*. Patients who experience*acanthosis nigricans* in the axilla there is a vitamin D3 deficiency and this has been tested statistically.[126]

This happened because in this study insulin resistance was assessed only on a clinical basis, where acantosis nigricans was found. Acantosis nigricans is most often associated with diabetes and insulin resistance, but although rare it can also be a sign of internal malignancy and can also occur due to hormonal disorders or with the use of certain drugs such as systemic glucocorticoids and oral contraceptives. So the condition of acantosis nigricans does not always indicate insulin resistance. Apart from that, in this study, the number of students with acantosis nigricans was only a small percentage, namely 16 students and all of them had other clinical PCOS in the form of clinical hyperandrogenism and obesity. So it cannot describe the effect of acantosis nigricans itself on vitamin D levels.

Relationship of Vitamin D to*PCOS* in Adolescents Accompanied by Clinical Hyperandrogenism, Obesity, and*Acanthosis Nigricans*

The results of this study show that there is no relationship between vitamin D levels and*PCOS* in adolescents accompanied by clinical hyperandrogenism, obesity, and*acanthosis nigricans*. The discrepancy in the results of this study can be influenced by other factors underlying the etiology of its occurrence*PCOS*, in addition to the involvement of genetic manifestations*PCOS* can be influenced by*life style*. Although genetic factors clearly contribute to the severity of androgen excess and/or insulin resistance in the PCOS phenotype, environmental factors, which influence body weight, are also relevant as an etiology of clinical severity.*PCOS*.[6]

Women with*PCOS* may already indicate metabolic complications. Insulin resistance is even found in 20-30% of patients*PCOS* with normal weight.*Acanthosis nigricans,* acne, hirsutism, and high BMI are the most practical tools to increase awareness of cases*PCOS* in addition to menstrual cycle anomalies.[126]

Vitamin D deficiency increases the production of parathyroid hormone and an increase in parathyroid hormone is associated with*PCOS*, anovulatory infertility, and increased testosterone. It is known that vitamin D deficiency combined with calcium deficiency can trigger abnormal menstruation associated with*PCOS*. Low 25(OH)D levels are associated with long menstrual cycles in normal women and vitamin D supplementation increases follicle formation and restores menstrual cycles in women with*PCOS*.[101]

A study was conducted on 175 women with*PCOS* (mean age 16.8 ± 1.7 years) and it is known that 77.7% of them experienced*acanthosis nigricans,* menstrual cycle disorders (88%),*overweight* and obesity (69%), and hirsutism (94%). Vitamin D deficiency often occurs in women who suffer from it*PCOS*. About 67-85% of women with*PCOS* have a serum 25-(OHD) level < 20ng/mL. Vitamin D deficiency can worsen clinical symptoms*PCOS*. Several studies show that vitamin D supplementation can overcome insulin resistance and reduce serum androgen levels.[111]

Hyperandrogens interfere with follicular development so that they cannot produce mature follicles. This results in reduced estrogen produced by the ovaries and no LH surge which triggers ovulation. Besides that, insulin resistance causes a state of hyperinsulinemia which leads to a state of hyperandrogenism, because insulin stimulates androgen secretion and inhibits hepatic SHBG secretion so that androgens are free to bind. In some cases it is followed by clinical signs*acanthosis nigricans*.[112]

Metabolic changes in cases*PCOS* associated with dysfunction of vitamin D and calcium metabolism which is important in follicle development and normal glucose metabolism. Several research results show patients*PCOS* especially those who are obese, have lower serum vitamin D levels and this is associated with hyperandrogenism, metabolic syndrome, insulin resistance, and increased BMI.

Conclusion

a. Most of the respondents were in the age range of 16-18 years, most of the duration of menarche was > 3 years, most of the respondents experienced vitamin D deficiency, a small number of respondents were obese, most of the respondents experienced clinical hyperandrogenism, and a small number of respondents experienced*acanthosis nigricans*.

b. There is a relationship*PCOS* in adolescents accompanied by clinical hyperandrogenism with vitamin D levels in high school in Koto Tangah District, Padang in 2022.

c. There is a relationship*PCOS* in adolescents accompanied by obesity with vitamin D levels in high schools in Koto Tangah District, Padang in 2022.

d. There is no relationship*PCOS* in adolescents accompanied by Acantosis nigrican with vitamin D levels in high schools in Koto Tangah District, Padang in 2022.

e. There is no relationship*PCOS* in adolescents accompanied by clinical hyperandrogenism, obesity, and acantosis nigrican with vitamin D levels in high school in Koto Tangah District, Padang in 2022.

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