RESEARCH ARTICLE

Testosterone level correlates significantly with luteinizing hormone to follicle-stimulating hormone ratio among women with polycystic ovary syndrome: A cross sectional study

[version 1; peer review: 1 approved with reservations]

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Abstract

Background: Polycystic ovary syndrome (PCOS), an endocrinological problem among women in the reproductive age, is characterized by chronic ovulatory dysfunction, hyperandrogenism, and elevated luteinizing hormone: follicle stimulating hormone (LH-FSH) ratio. The goal of this study was to examine if the blood LH-FSH ratio and total testosterone (TT) levels in Sudanese women with PCOS were linked. **Methods:** This cross-sectional study included 300 women with confirmed PCOS based on Rotterdam criteria. PCOS women mean (standard deviation): age 29.1(5.8) years; body mass index (BMI) 27.9±4.6 kg/m². Each participant underwent a clinical history, physical examination, and ovaries ultrasonogram. ASYS Expert Plus Microplate was used to quantify serum LH, FSH, and TT levels in fasting blood specimen drawn during the follicular phase of the menstrual cycle of women with PCOS.

Results: More than two-thirds of the participants (71.0%) had an aberrant LH-FSH ratio (cut-off>1.0), and 58.3% had hyperandrogenemia (TT>109.5 ng/dL). Hyperandrogenemic women had significantly increased LH-FSH ratio (P= 0.000). The LH-FSH ratio and serum TT were significantly positive correlated (r= 0.329, P= 0.000). Overall, 52.0% of women with PCOS exhibited menstrual cycle irregularity, and 59.0 % had a positive family history of PCOS. On logistic regression analysis, the LH-FSH ratio (odds ratio (OR) (95% confidence interval (CI)): 2.308 (1.698- 3.139, P= 0.000) was found to be positively related to hyperandrogenemia independently. Furthermore, when the LH-FSH ratio is greater than one, hyperandrogenemia can be distinguished from normoandrogenemia, area under the curve (AUC) = 0.726, P= 0.000, 95% CI: (0.668-0.785) with a serum TT

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?

view

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threshold of 109.5 ng/dL (sensitivity 70.0%, specificity 77.1%).

Conclusions: In women with PCOS, the serum LH-FSH ratio and TT have a strong relationship. Furthermore, LH-FSH ratio of greater than one can be used to distinguish between hyperandrogenic and non-hyperandrogenic PCOS women.

Keywords

PCOS, LH-FSH ratio, total testosterone, Hyperandrogenemia, Sudan

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Introduction

Polycystic ovary syndrome (PCOS) is a prevalent endocrine condition affecting women of reproductive age, with a reported frequency of 6 to 15%.^{1,2} PCOS is characterized by a female sex hormone imbalance and increased androgen production, which results in irregular or extended menstrual periods, obesity, and excessive hair growth.³ Genetic and epigenetic factors, as well as environmental variables have been identified as risk factors for intra-ovarian hyperandrogenism.³ PCOS is a challenging disorder to diagnose since it is a diverse condition with different characteristics. It is currently diagnosed using revised Rotterdam criteria, which has been recently approved by an international evidence-based PCOS guideline.^{4,5}

According to certain studies, the brain is both a regulator and an impacted organ in PCOS (the brain phenotype). The brain, which contains multiple receptors, and neurons with their neurotransmitters, produces a higher pulse frequency of gonadotropin. As a result, people with PCOS have more luteinizing hormone (LH) than follicle-stimulating hormone (FSH) secretion.⁶ Increased ovarian androgen production is caused by a change in the LH-FSH ratio. Furthermore, hyperandrogenemia lowers estrogen's negative feedback to the hypothalamus, resulting in increased LH pulse frequency. As a result, a vicious cycle is set in motion, causing a variety of clinical symptoms of PCOS, including hyperandrogenism.⁷ The goal of this study was to see possible link between the LH-FSH ratio and total testosterone levels in Sudanese women with PCOS.

Methods

Study design

This was an observational study with a cross-sectional design. The study was conducted between October 2020 and September 2021 in Khartoum- Sudan. Various infertility centers clinics were visited to select the study sample, using a convenience sampling method. The inclusion criteria were women with confirmed PCOS based on Rotterdam criteria,⁵ where at least two of the following criteria were fulfilled: oligomenorrhoea/anovulation (delayed menses >35 days or <8 spontaneous hemorrhagic episodes/year), hyperandrogenism (clinical hirsutism using modified Ferriman-Gallwey score of ≥ 8 or biochemical) and morphology of polycystic ovaries on ultrasonography (12 or more follicles in each ovary measuring 2 to 9 mm in diameter, and/or increased ovarian volume >10 mL³). Women with systemic disease (cardiovascular disease and diabetes mellitus), on medication prior to the study (oral contraceptives, glucocorticoids, ovulation induction agents, and estrogenic or anti-androgenic) were excluded from the study.^{4,5}

Sample size calculation

At the time of the study, there was no published data about the prevalence of PCOS in Sudan. For this, the prevalence of PCOS in unspecified populations 3–10%.⁸ The sample size was determined based on the following equation⁹:

$$n = (Z_{1-\alpha/2})^2 \times P(1 - P) \div d^2$$

where:

n = sample size

$Z_{1-\alpha/2}$ = 1.96 for 95% confidence level

d = Desired margin of error, expressed as a decimal (0.05)

P = Prevalence of the disease (10.0%)

n = 138

Ethical considerations

The study protocol was approved by the Federal Ministry of Health at Khartoum- Sudan. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration. The study objective was explained to potential participants, and those who agreed to participate provided a signed consent before the start of the study.

Procedure

After signing an informed consent form, the socio-demographic characteristics, medical and gynecological history were taken from each patient using a questionnaire. The detailed medical and gynecological history (menstrual pattern, fertility, hirsutism) were taken from all patients included in the study. Then full general and pelvic examinations were performed.

Following standard protocols, weight was measured twice. After calibration, OMRON BF508I Body Fat Scales (China) were utilized. Women were told to remove their bulky attire. The weights were calculated to within 0.1 kg. After calibration, ladies were requested to remove their shoes and a portable stadiometer (SECA-213 model, Germany) was used to measure their height twice. Quetelet's BMI was estimated using a conventional formula (weight in kilograms divided by height in meters²). Underweight (<18.5 kg/m²), normal (18.5-24.9 kg/m²), overweight (25.0-29.9 kg/m²), and obese (30 kg/m²) were the BMI categories used by the WHO.¹⁰ During the follicular phase, ultrasonography was performed by Mindray (model: DP-50, Germany) and vaginal transducer where presence or absence of ovarian cysts were conformed or excluded. If cysts were seen, then the volume as well as the number of small follicles were determined, in each ovary.

Methods of sampling and analysis

Women were asked to come back on days 2-5 after a spontaneous menstruation or on a convenient day if they had amenorrhea. In a fasting state, 5 mL venous blood was collected between the hours of 8 a.m. and 9 a.m. The blood was centrifuged using Hettich (D-78532 Tuttlingen: Germany), then plasma obtained, and kept at -20 °C until the assay. Enzymes linked immunosorbent assay (ELISA); ASYS (model: Expert Plus; type G020150; serial nr: 28382; Austria) was used to quantify serum LH, FSH by indirect method, and TT competitive methods.

Statistical analysis

Data was coded, and statistical analysis was performed with social package of statistical science version 26.0 (SPSS Inc., IBM, Chicago, IL, USA). The Kolmogorov–Smirnov was used for testing the normality of continuous data. All data was skewed. Continuous variables were presented as mean with standard deviation, and median with interquartile ranges. Whereas qualitative data was expressed with frequency (%). Mann-Whitney U test, and Chi-square test for qualitative variables were used to assess the relationship between LH-FSH ratio groups and androgen status. The association between the LH-FSH ratio, serum TT, and BMI was tested using Spearman's correlation test. The link between the LH-FSH ratio >1 and other factors was investigated using binary logistic regression analysis. The serum LH-FSH ratio was studied using a receiver-operating characteristic (ROC) curve to see if it might distinguish androgen status.

Results

In total, 350 Women were screened; 300 of them fulfilled the inclusion criteria.¹¹ Their mean (SD) age was 29.1 (5.8) years, and BMI 27.9 (4.6) kg/m². Overall; 30.3% (n=91) of women were obese based on their BMI, and 59.0% (n=117) had positive family history to PCOS. More than half (52.3%, n=157) of women had menstrual cycle irregularity. More than two-thirds of them (71.0%, n= 213) had altered LH-FSH ratio with cut-off > 1.0. According to their serum TT (> 109.5 ng/dL), 58.3% (n= 175) had hyperandrogenemia.

Women with LH- FSH ratio >1 (based on their serum LH-FSH ratio) had significantly increased serum TT level (P = 0.000), and 70.0% of them had TT> 109.5 ng/dL. 55.4% (n= 118) of them had positive family history to PCOS, compared with counterpart. There were no significant differences in age, BMI, and menstrual cycle frequency irregularity between groups (Table 1).

In comparison to their counterpart, women with hyperandrogenemia (serum TT > 109.5 ng/dL) had significant increase in LH-FSH ratio (P= 0.000). Furthermore; obesity was found in 30.9% (n= 54) of them based on their BMI (Table 2).

As shown in Figure 1, the Spearman's correlation revealed that serum LH-FSH ratio was significantly correlated with serum TT (ng/dL) (r= 0.329, P= 0.000). However; both LH-FSH ratio and TT were insignificantly correlated with BMI among women with PCOS (results not shown on figure).

As shown in Table 3, the serum LH-FSH ratio (odds ratio (OR) (95% confidence interval (CI)): 2.308 (1.698-3.139, P = 0.000) was independently related to androgen status and can be used as a predictor in women with PCOS.

According to the ROC curve analysis; LH-FSH ratio>1 can distinguish hyperandrogenemia from normoandrogenemia in women with PCOS (AUC = 0.726, P=0.000, 95% CI: 0.668-0.785; sensitivity 70.0%, specificity 77.1%) at TT threshold 109.5 ng/dL (Figure 2).

Discussion

In the present study, the link between serum LH-FSH ratio and total testosterone level were investigated in a cross-sectional analysis of 300 Sudanese women with PCOS. The study revealed that 30.3% of women were obese based on their BMI. Obesity was found in 50–80 % of women with PCOS, according to McCartney and Marshall.¹² This may differ depending on race, ethnicity, location, and environmental factors (physical activity, diet, stress).

Table 1. Characteristics of the study population (n= 300) based on LH-FSH ratio.

Variables	LH-FSH ratio (cut-off > 1.0)		Total	P- value
	Normal (n=87.0)	High (n=213.0)		
Age/year				
Mean (SD) [#]	29.5 (5.9)	28.9 (5.9)	29.1 (5.9)	0.538*
Median (SEM) [†]	29.0 (0.63)	29.0 (0.40)	29.0 (0.34)	
Q1-Q3	25.0-34.0	25.0-33.0	25.0-33.0	
BMI kg/m²				
Mean (SD) [#]	29.2 (4.7)	28.2 (4.5)	28.5 (4.6)	0.101*
Median (SEM) [†]	29.0 (0.51)	28.3 (0.31)	28.4(0.3)	
Q1-Q3	25.91-32.03	24.98-30.67	25.3-30.8	
Normal weight	16.0 (18.5) [‡]	53.0 (24.9)	69.0 (23.0)	
Overweight	41.0 (47.1)	99.0 (46.5)	140.0 (46.7)	
Obese	30.0 (34.5)	61.0 (28.6)	91.0 (30.3)	
F. C				
Yes	59.0 (67.8) [‡]	118.0 (55.4)	117.0 (59.0)	0.047*
No	28.0 (32.2)	95.0 (44.6)	123.0 (41.0)	
M.C (n, %)[‡]				
Regular	39.0 (44.8) [‡]	104.0 (48.8)	143.0 (47.7)	0.529*
Irregular	48.0 (55.2)	109.0 (51.2)	157.0 (52.3)	
TT ng/dL				
Mean (SD) [#]	118.3 (106.2)	256.2(164.2)	216.3 (162.1)	0.000*
Median (SEM) [†]	86.0 (11.39)	270.0 (11.25)	184.0 (9.4)	
Q1- Q3	48.0-134.0	86.4-400.0	70.0-390.0	
≤109.5ng/dL	61.0 (70.1) [‡]	64.0 (30.0)	125.0 (41.7)	0.000*
> 109.5 ng/dL	26.0 (29.9)	149.0 (70.0)	175.0 (58.3)	
AMH				
Mean (SD) [#]	6.7 (2.5)	7.4 (3.4)	7.2 (3.2)	0.345*
Median (SEM) [†]	5.9 (0.27)	6.2 (0.23)	6.2 (0.2)	
Q1- Q3	5.1-7.6	5.1-8.35	5.1-7.8	

BMI: body mass index; FC: family history; M.C; Menstrual cycle; TT: total testosterone; AMH: anti muller's hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone.

[#]Mean= Geometric mean; SD= standard deviation;

[†]= Median; S.E.M= Standard Error of Mean, Q1-Q3= Interquartile Ranges,

[‡]Values are numbers and percentages;

*P-value were obtained using Mann-Whitney test; and P[#] were obtain using Chi- Square test.

The most common clinical symptom of women diagnosed with PCOS, according to Malini and George,¹³ is a greater LH-FSH ratio. The LH-FSH ratio in healthy women is 1:1. In PCOS, the LH level is higher than the FSH level, resulting in increased ovarian androgen production and ovulatory failure. Various LH-FSH ratio cut-offs have been proposed. However, the cut-off more than 1.0 was found to be the most successful in diagnosing PCOS in terms of sensitivity and specificity.^{14,15}

According to our findings, 71.0% of women with PCOS exhibited an abnormal LH-FSH ratio with a cut-off of >1. Morshed *et al.* reported that 71.0% PCOS patients (cut-off more than 1.0) exhibited an aberrant LH-FSH ratio.¹⁶ According to Nath *et al.*,¹⁷ 70.58% of women with PCOS have an increased LH-FSH ratio. As a result, the authors proposed that the LH-FSH ratio is one of the defining characteristics of PCOS women.¹⁷

Study revealed 58.3% of women with PCOS had hyperandrogenemia (cut-off TT more than 109.5 ng/dL). Furthermore, the findings showed a statistically significant difference in the frequency of hyperandrogenemia between the changed and

Table 2. Characteristics of the study population (n= 300) based on androgenemia.

Variables	Androgenemia (cut-off > 109.5 ng/dL)		P- value
	≤ 109.5 (n=125)	>109.5 (n=175)	
Age/year			
Mean (SD) [#]	29.3 (5.9)	28.9 (5.8)	0.434*
Median (SEM) [†]	29.0 (0.5)	29.0 (0.4)	
Q1-Q3	25.0-34.0	24.0-33.0	
BMI kg/m²			
Mean (SD) [#]	28.5 (4.7)	28.4 (4.5)	0.962*
Median (SEM) [†]	28.5 (0.4)	28.3 (0.3)	
Q1-Q3	25.1-30.4	25.3-30.8	
Normal weight	30.0 (24.0) [‡]	39.0 (22.3)	0.935 [#]
Overweight	58.0 (46.4)	82.0 (46.9)	
Obese	37.0 (29.6)	54.0 (30.9)	
Family history			
Yes	81.0 (64.8) [‡]	96.0 (54.9)	0.084 [#]
No	44.0 (35.2)	79.0 (45.1)	
Menstrual Cycle n (%)[‡]			
Regular	57.0 (45.6) [‡]	86.0 (49.1)	0.545 [#]
Irregular	68.0 (54.4)	89.0 (50.9)	
LH- FSH ratio			
Mean (SD) [#]	1.32 (1.0)	2.15 (1.2)	0.000*
Median (SEM) [†]	1.06 (0.09)	1.91 (0.09)	
Q1- Q3	0.75-1.49	1.29-2.58	
≤1	61.0 (48.8) [‡]	26.0 (14.9)	0.000[#]
>1	64.0 (51.2)	149.0 (85.1)	
AMH			
Mean (SD) [#]	7.2 (3.3)	7.1 (3.0)	0.883*
Median (SEM) [†]	5.9 (0.2)	6.2 (0.2)	
Q1- Q3	5.1-7.8	5.0-7.6	

[#]Mean= Geometric mean; SD= standard deviation;

[†]= Median; SEM= Std. Error of Mean, Q1-Q3= Interquartile Ranges,

[‡]Values are numbers and percentages;

^{*}P-value were obtained using Mann-Whitney test; and [#]P were obtain using Chi- Square test. BMI: body mass index; FC: family history; M.C; Menstrual cycle; TT: total testosterone; AMH: anti mullein's hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone

normal LH-FSH ratio groups demonstrated that an altered LH-FSH ratio with a cut-off of 1.0 was associated with androgen status in women with PCOS. Moreover, the LH-FSH ratio was linked to a higher level of serum TT. Alexiou *et al.*, reported hyperandrogenemia was present in 78.2% of PCOS.¹⁸ Livadas and his colleagues reported that prevalence of hyperandrogenemia was 58.8%.¹⁹ The imbalance in LH: FSH causes proliferation of ovarian theca cells leading to increased steroidogenesis, and ultimately leading to hyperandrogenemia in PCOS women.²⁰

In the hyperandrogenic group LH-FSH ratio was higher and differed significantly from the value of the normoandrogenic group. This may suggest that LH-FSH ratio has an independent relation with TT, which is consistent with previous studies.^{13,21}

In regression analysis our study observed that LH-FSH ratio>1 was significantly positive independently associated to hyperandrogenemia. Moreover, ROC analysis indicated that serum LH-FSH ratio>1 was significantly discriminate

Figure 1. Spearman correlation between LH-FSH ratio and serum TT (ng/mL); significant positive correlation ($r = 0.329$, $P = 0.000$). LH-FSH: luteinizing hormone to follicle-stimulating hormone, TT: total testosterone.

Table 3. multivariable logistic regression analysis for hyperandrogenemia (cut-off > 109.5 ng/dL).

	B	Std. Error	Wald	sig	OR	Lower Bound	Upper Bound
Age by years	-0.004	0.021	0.039	0.844	0.996	0.955	1.038
F.H	-0.260	0.260	0.997	0.318	0.771	0.463	1.284
AMH	-0.060	0.042	2.009	0.156	0.942	0.866	1.023
LH-FSH ratio	0.837	0.157	28.47	0.000	2.308	1.698	3.139

Binary logistic regression analysis was done. OR: odds ratio; CI: confidence interval; F.H: have positive family history of PCO; AMH: anti muller's hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone

Diagonal segments are produced by ties.

Figure 2. Receiver operator characteristics (ROC) curves, serum LH-FSH ratio > 1 as discriminator androgen statuses among PCOS women; Area under the curve (AUC) = 0.726, $P = 0.000$, 95% confidence interval (CI) (0.668-0.785) with cut-off 109.5 ng/dL (sensitivity 70.0%, specificity 77.1%).

androgen statuses among PCOS women with cut-off to serum TT 109.5 ng/dL. The studies^{13,21} also demonstrate that an LH-FSH ratio greater than 1.0 is enough to generate significant testosterone production from the ovaries, resulting in hyperandrogenemia.

There are several solid points in the present research. A high sample size was used in this study. It looked at the relationship between the LH-FSH ratio >1 and TT in Sudanese women PCOS. It is the first study to use an LH-FSH ratio greater than 1 to distinguish hyperandrogenic status in PCOS Sudanese individuals. Our research can be used as a starting point for further research. To compute the free testosterone index, serum sex hormone binding globulin or free testosterone were not assessed. Furthermore, we lack population-specific data on serum TT reference ranges.

Conclusions

Sudanese women with PCOS are prone to androgenemia. Furthermore, among women with PCOS, the LH-FSH ratio was found to be substantially linked with total testosterone. The finding of this study may aid in a better understanding of the pathophysiology and management of hyperandrogenemia in PCOS women of Sudanese descent.

Data availability

Figshare: PCOS in Sudan. <https://doi.org/10.6084/m9.figshare.19102715>.¹¹

- Note: FH: family history; MC: menstrual cycle; AMH: anti muller's hormone

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

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The scientific study was well ignited and carried out. However, the following requests need to be corrected. In addition, some suggestions should be clarified in the introduction and discussion.

- Different scientific articles give different cut-off values of 2: 1 or 3: 1 in the introduction, as is the case with other populations. And since other values have emerged, the reasons for this should be discussed in the discussion
- In premenopausal women, the LH / FSH ratio is typically 1: 1 does the ratio change with age? should be referred to in the discussion
- Women with PCOS in European populations tend to be overweight or obese with occasional normal body weight, how does this apply to Sudanese women?
- Does body fat affect LH and FSH levels? I recommend the Figure 2 in (Szczuko *et al.* 2014) ¹. It is also worth checking PCOS phenotypes
- Authors should explore the biochemical evidence of an increase in testosterone levels as well as a high free androgen index (FAI index)
- Correct the level of testosterone and FAI index² and briefly write down if there are differences in the cut-off point
- The conclusion should apply to women from Sudan. The LH / FSH ratio in other populations in the PCOS female group was already known

References

1. Szczuko M, Zapałowska-Chwyc M, Maciejewska D, Drozd A, et al.: High glycemic index diet in

PCOS patients. The analysis of IGF I and TNF- α pathways in metabolic disorders. *Med Hypotheses*. 2016; **96**: 42-47 [PubMed Abstract](#) | [Publisher Full Text](#)

2. Szczuko M, Zapałowska-Chwyć M, Maciejewska D, Drozd A, et al.: Significant Improvement Selected Mediators of Inflammation in Phenotypes of Women with PCOS after Reduction and Low GI Diet. *Mediators Inflamm*. 2017; **2017**: 5489523 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am an expert in the field of nutrition, including PCOS. I have written a total of over 10 papers on various aspects of PCOS

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 18 Apr 2022

Ghada Elfadil, Sudan University of Science and Technology, Khartoum, Sudan

- **Reviewer comment:** The conclusion should apply to women from Sudan. The LH / FSH ratio in other populations in the PCOS female group was already known.
- **Author response:** Tola et al found that in Sudanese women with PCOs the cut- off more than 1 has a diagnostic power of PCOS with sensitivity and specificity 72%, 76% respectively (Tola H, Abbas M, Alhassan EA, et al.: Assessment of the Role of the Anti-Mullerian Hormone, Luteinizing Hormone/Follicle Stimulating Hormone Ratio in the Diagnosis of Polycystic Ovary Syndrome in Sudanese Women. Open Access Maced J Med Sci. 2018; 6:1244-1247).

- **Reviewer comment:** Correct the level of testosterone and FAI index² and briefly write down if there are differences in the cut-off point.
- **Author response:** Hyperandrogenemia based on estimation of TT level, while the gold standard is serum free testosterone by equilibrium dialysis, which is complex, expensive and labor-intensive. Therefore, surrogate markers such as the free androgen index (Szczuko, M., Zapałowska-Chwyć, M., Maciejewska, D., Drozd, A., Starczewski, A., & Stachowska, E. (2017). Significant Improvement Selected Mediators of Inflammation in Phenotypes of Women with PCOS after Reduction and Low GI Diet. *Mediators of inflammation*, 2017, 5489523) or calculated free and bioavailable testosterone can be used to assess hyperandrogenemia (Ożga, K., Krzyczkowska-Sendrakowska, M., Hubalewska-Dydejczyk, A., Gilis-Januszewska, A., Ratajczak, M., Ratajczak, M., Chaykivska, Z., & Jach, R. (2019). The value of the free androgen index depends on the phenotype of polycystic ovary syndrome - a single-centre experience. *Endokrynologia Polska*, 70(4), 330–335)
- **Reviewer comment:** Does body fat affect LH and FSH levels? I recommend the Figure 2 in (Szczuko *et al.* 2014) ¹. It is also worth checking PCOS phenotypes.
- **Author comment:** Obesity augments the androgen production by stimulating LH, which in turn leads to hyperandrogenism (Glueck, C.J., Goldenberg, N., 2019 Mar 1. Characteristics of obesity in polycystic ovary syndrome: etiology, treatment, and genetics. *Metabolism* 92, 108–120). Leptin, an appetite-controlling adipokine has a direct impact on the neuroendocrine and reproductive function of obese PCOS women(Szczuko, M., Zapałowska-Chwyć, M., Maciejewska, D., Drozd, A., Starczewski, A., & Stachowska, E. (2016). High glycemic index diet in PCOS patients. The analysis of IGF I and TNF- α pathways in metabolic disorders. *Medical hypotheses*, 96, 42–47)
- **Reviewer comment:** Women with PCOS in European populations tend to be overweight or obese with occasional normal body weight, how does this apply to Sudanese women?
- **Author Response:** Among Sudanese PCOS women in this study we found that 30.3% were obese and 46.7% were overweight.
- **Reviewer comment:** In premenopausal women, the LH / FSH ratio is typically 1: 1 does the ratio change with age? should be referred to in the discussion.
- **Author response:** No diagnostic criteria are presently available for PCOS for premenopausal and menopausal women, the condition can still be suspected in case of a previous diagnosis of the condition, a chronic history of irregular menstrual cycles and hyperandrogenism, and/or polycystic ovarian morphology during the reproductive period (Çelik, Ö., & Köse, M. F. (2021). An overview of polycystic ovary syndrome in aging women. *Journal of the Turkish German Gynecological Association*, 22 (4), 326–333) .
- **Reviewer comment :** Different scientific articles give different cut-off values of 2: 1 or 3: 1 in the introduction, as is the case with other populations. And since other values have emerged, the reasons for this should be discussed in the discussion.

- **Author response:** A number of studies have proposed appropriate cut-off values for the LH:FSH ratio in PCOS patients. however, the optimal cut-off threshold remains unclear because of the varying sensitivity and specificity. Hsu et al. suggested that an LH/FSH ratio of >1 offered the best combination of sensitivity and specificity for the diagnosis of PCOS (Hsu MI, Liou TH, Liang SJ, Su HW, Wu CH, Hsu CS. Inappropriate gonadotropin secretion in polycystic ovary syndrome. Fertil Steril 2009;91:1168-74). while, in contrast, Papaleo et al ; postulated that an LH/FSH ratio of ≥ 2 is the characteristic feature of abnormal gonadotropin secretion in PCOS patients (Papaleo E, Doldi N, De Santis L, Marelli G, Marsiglio E, Rofena S, et al. Cabergoline influences ovarian stimulation in hyperprolactinaemic patients with polycystic ovary syndrome. Hum Reprod 2001;16:2263-6).

Competing Interests: No competing interest

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