

Research Article

Polycystic Ovary Syndrome in the Eye of Prostate-specific Antigen Among Nigerian Females

Collins Amadi^{1,2,*} , Johnbosco Chidozie Okafor³ , Ezra Agbo⁴ 

¹Department of Chemical Pathology, Rivers State University Teaching Hospital, Port Harcourt, Nigeria

²Department of Chemical Pathology, PAMO University of Medical Sciences, Port Harcourt, Nigeria

³Department of Chemical Pathology, University of Uyo Teaching Hospital, Port Harcourt, Nigeria

⁴Department of Chemical Pathology, Federal Medical Center, Abuja, Nigeria

Abstract

Introduction: The clinical relevance of raised total prostate-specific antigen (TPSA) in polycystic ovary syndrome (PCOS) is yet to be explored among Nigerians. To bridge this knowledge gap, we explored the clinical relevance of TPSA among PCOS patients in Nigeria. **Methods:** This case-controlled study was conducted between 2022 and 2024 in the Department of Chemical Pathology at the Rivers State University Teaching Hospital (RSUTH), Nigeria. Data from all eligible 240 PCOS patients were obtained and compared with age-matched controls and by TPSA status using descriptive/inferential parameters at $p < 0.05$. **Results:** PCOS patients had higher TPSA status (early follicular/mid-luteal phase) including higher BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), systolic blood pressure (SBP), luteinizing hormone (LH), follicle-stimulating hormone (FSH), total testosterone (TT), dehydroepiandrosterone-sulphate (DHEAS), fasting plasma glucose (FPG), fasting insulin (FINS), insulin-like growth factor 1 (IGF-1), HbA1c, total cholesterol (TChol), triglyceride (Tg), low-density lipoprotein cholesterol (LDL-C), high-sensitivity-C-reactive protein (hs-CRP), homocysteine, malondialdehyde (MDA), non-high-density lipoprotein cholesterol (non-HDL-C), Castelli risk index 1 and 2 (CRI-1/CRI-2), atherogenic index (AC), atherogenic index of plasma (AIP), visceral adiposity index (VAI), lipid accumulation product (LAP), free androgen index (FAI), homeostatic model assessment-insulin resistance (HOMA-IR), LH/FSH ratio, and Ferriman-Gallwey scores (FGS) but lower early-follicular phase estradiol (E2), sex hormone-binding globulin (SHBG), insulin-like growth hormone binding protein 1 (IGFBP-1), HDL-C, mid-luteal phase progesterone, superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and total antioxidant capacity (TAC) compared to healthy controls ($p < 0.05$, respectively). PCOS patients with higher TPSA status had more unfavorable anthropometric, clinical, hormonal, and metabolic profiles than those in the lowest tertile of TPSA status ($p < 0.05$, respectively). Among the PCOS patients, TPSA correlated positively with LH, FSH, TT, DHEAS, FPG, FINS, IGF-1, HbA1c, TChol, Tg, LDL-C, hs-CRP, homocysteine, MDA, non-HDL-C, CRI-1/CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR, LH/FSH ratio, and FGS but correlated negatively with E2, progesterone (early follicular/mid-luteal phases), SHBG, IGFBP-1, HDL-C, SOD, GSH-Px, and TAC ($p < 0.05$, respectively). TPSA was associated with oligo/amenorrhea, oligo/anovulation, hyperandrogenemia, Rotterdam phenotype A, moderate/severe FGS, overweight, generalized/abdominal obesity, hypertension, dyslipidemia, cardiovascular risk, oxidative stress risk, metabolic syndrome, and insulin resistance among PCOS patients ($p < 0.05$, respectively). TPSA level was a discriminative biomarker for PCOS diagnosis among the entire PCOS patients (AUC: 0.879; $p < 0.001$), however, a more robust discriminatory potential was observed among individuals with Rotterdam phenotype A (AUC: 0.935; $p < 0.001$). **Conclusion:** These findings indicate an association of TPSA with various adverse parameters in PCOS. Further studies are recommended to verify these findings.

*Corresponding author: collins338@yahoo.com (Collins Amadi)

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Keywords

Polycystic Ovary Syndrome, PCOS, Total Prostate-specific Antigen, TPSA

1. Introduction

Polycystic ovary syndrome (PCOS) or Stein-Leventhal syndrome, a classic syndrome of ovarian dysfunction, is the most common reproductive endocrine disorder affecting reproductive-aged women. Based on the diagnostic criteria applied, its prevalence has been reported to vary from 5.5% to 11.5% globally [1]. However, a 16.5% prevalence was recently documented among Nigerians [2]. Due to its heterogeneous clinical features, four major subtypes have been described [3]. Its classic form is usually characterized by cystic ovaries, irregular menstrual patterns, anovulatory cycles, and androgen excess [3]. It is usually associated with numerous health risks such as type 2 diabetes, hypertension, obesity, cardiovascular diseases, chronic liver disorders, endometrial hyperplasia, and infertility among others [3].

The precise etiologic basis of PCOS has remained elusive for decades since it was first described [3, 4]. In addition, its pathophysiology is also complex and somewhat unknown within the existing literature. However, there are bases to strongly believe that the diverse interplay of genetics, environmental, socio-demographic, and neuroendocrine factors play major vital roles in the evolution of the syndrome [4].

Although prostate-specific antigen (PSA), an androgen-dependent biomarker, has long been associated with the male prostate gland and its diverse benign and malignant pathologic processes, a large body of evidence indicates that the biomarker is also produced in some female tissues/organs including the periurethral Skene's gland (female equivalent of the male prostate gland), breast, ovary, and uterine endometrium where its synthesis still depends on the stimulatory actions of the female androgens [5].

However, the serum PSA level is very low in females compared to their male counterparts [6]. Still, due to the inherent androgen excess, PCOS culminates in the induction of unusually raised PSA synthesis from these androgen-sensitive tissues and organs [6]. Insulin-like growth factor 1 (IGF1) and high insulin levels can stimulate androgen synthesis leading to hyperandrogenemia in PCOS [7]. Hyperandrogenemia in PCOS, in addition to low sex hormone binding globulin (SHBG) concentrations, contributes to increased free androgen levels which exacerbate the condition [8]. In females, PSA is also produced under the stimulatory influence of progestins and glucocorticoids, but under the inhibitory influence of estrogens [5, 6].

Consequently, studies have been conducted aimed at exploring the clinical relevance of this raised PSA regarding its screening, diagnostic, and prognostic potential in PCOS management in recent times [5, 9]. However, most of these

previous studies have produced mixed results with none yet conducted among Nigerians [9].

To close this knowledge gap, we explored the clinical value of serum PSA among Nigerian PCOS patients.

2. Materials and Methods

2.1. Study Design, Site, and Duration

This was a prospective case-controlled observational study conducted in the Department of Chemical Pathology of one of the major tertiary health facilities [Rivers State University Teaching Hospital (RSUTH)] within the Niger Delta region of Nigeria. The study period spanned between January 2022 and September 2024. RSUTH has specialized clinical departments/units with adequate staff strength required for core clinical services, training, and research purposes. The Department of Chemical Pathology of the hospital has a well-equipped biochemical laboratory with diverse semi-automated and automated analyzers, a metabolic clinic/ward, and experienced biomedical scientists and laboratory physicians. Patients from different clinics/units are usually referred to the department from within and outside RSUTH for diverse biochemical investigations.

2.2. Ethical Considerations

The Rivers State Health Research Ethical Committee of the Rivers State Hospital Management Board (RSHMB) reviewed and approved the study protocol. All study populations agreed to participate and provided written and signed informed consent. The study strictly adhered to the RSHMB-recommended guidelines and the principles embodied and laid down in the Helsinki Declarations of 1964, revised in 2013.

2.3. Study Population

The study consisted of all eligible study populations who were referred to the Department of Chemical Pathology of RSUTH, from within and outside the hospital, for biochemical assessment following pelvic/transvaginal ultrasound scan evidence of PCOS and a gynecologist-confirmed PCOS clinical diagnosis on referral notes, or medical records, or laboratory request forms during the study period. For each

PCOS case identified and recruited (group 1), an age-matched healthy eumenorrheic non-hirsute participant (group 2) was selected as a healthy control.

2.4. Sample Size Determination

The calculated minimum sample size required for this study was approximately 240. The sample size was determined using a sample size mathematical formula for cross-sectional studies for characteristics in a population >10,000 using a 5% margin of error, 95% confidence interval, unlimited population size, and a reported 16.5% prevalence of PCOS previously documented in the study center [2, 10]. The result from the calculation was 212 each per case/control, we enrolled 240 in each group to account for an anticipated 10% dropout rate.

2.5. Eligibility Criteria

Criteria for inclusion were adults (aged ≥ 18 but ≤ 44 years) presenting for biochemical assessment for PCOS in the study center during the study period, having pelvic/transvaginal ultrasound evidence of PCOS, and having gynecologist-confirmed clinical diagnosis of PCOS in the referral notes, or medical records, or laboratory request forms upon recruitment. Criteria for exclusion included age $<18/>44$ years, current history of primary amenorrhea, having previous/current history of cigarette/alcohol intake, having adrenal gland and/or enzyme defects, androgen-secreting adrenal or ovarian tumors, Cushing's syndrome, hyperprolactinemia, thyroid dysfunction, idiopathic hirsutism, previous/current hepatic, renal, cardiovascular or pancreatic disorders including diabetes mellitus, on current/previous PCOS medications or progestins, glucocorticoids, any other form of hormonal/non-hormonal contraceptives. For any consented case identified and recruited, an age-matched (± 2 years) eumenorrheic non-hirsute healthy control adult was recruited from the general RSUTH staff population and other patient attendees to the hospital.

2.6. Sampling Method

A convenience sampling technique was employed to recruit participants until the target sample size was achieved.

2.7. Data Collection

On the first day of presenting in the metabolic unit of the department, patients were identified, counseled, and educated about the study to obtain consent. If consented, a semi-structured questionnaire was administered by trained research assistants to obtain baseline socio-demographic, past medical history, gynecologic, and clinical data, and to ascertain eligibility status. If eligibility is confirmed, vital clinical parameters were obtained followed by the anthropometric measurements and specimen acquisition for laboratory analysis. Socio-demographic data included age, cigarette, and alcohol consumption status. Past medical history data in-

cluded adrenal, thyroid, hepatic, renal, cardiovascular, pancreatic, and anterior pituitary disorders, hyperprolactinemia, and diabetes mellitus. The clinical data included systolic blood pressure (SBP), diastolic blood pressure (DBP), and hirsutism assessment based on the modified Ferriman-Gallwey score (FGS) rating. The anthropometric data included height, weight, waist circumference (WC) obtained with a non-stretchable measuring tape placed at the approximate midpoint between the lower border of the last palpable rib and the top of the iliac crest at the end of expiration, hip circumference (HC) obtained with the non-stretchable measuring tape placed around the widest portion of the buttocks using the greater trochanter of the femur as a landmark, and the calculated body mass index (BMI)/waist-hip ratio (WHR).

Following the initial assessment on the first day of presentation, the patients were counseled to present during the early follicular phase (day 3-4) of a spontaneous cycle (natural), or progestogen-induced (dydrogesterone 10 mg/day for 5 days) cycle, or randomly for women who have a negative progesterone challenge test, for fasting venous blood collection for early follicular phase laboratory parameters and to present again during the mid-luteal phase (days 21-23) for a second phase of non-fasting venous blood collection for mid-luteal phase laboratory parameters.

2.8. Laboratory and Quality Assurance Protocols

2.8.1. Laboratory Parameters

The laboratory parameters obtained during the early follicular phase (day 3-4) included follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone, prolactin, total testosterone (TT), thyroid-stimulating hormone (TSH), 8-10 am cortisol, total PSA (TPSA), insulin-like growth factor binding protein 1 (IGFBP-1), insulin-like growth factor 1 (IGF-1), sex hormone binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEAS), free androgen index (FAI), glycated hemoglobin A1c (HbA1c), fasting insulin/glucose, homeostatic model assessment-insulin resistance (HOMA-IR), total cholesterol (TChol), triglyceride (Tg), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), hs-C-reactive protein (hs-CRP), homocysteine, malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), total anti-oxidant capacity (TAC), Castelli risk index 1 (CRI-1), Castelli risk index 2 (CRI-2), atherogenic coefficient (AC), atherogenic index of plasma (AIP), visceral adiposity index (VAI), and lipid accumulation product (LAP). The laboratory parameter obtained during the mid-luteal phase (days 21-23) was serum progesterone.

2.8.2. Specimen Management and Laboratory Analysis

Specimen acquisition was done using standardized proto-

cols and all laboratory analysis was done in the Department of Chemical Pathology of RSUTH. During the early follicular phase, six milliliters (10 ml) of fasting venous whole blood was acquired (8-10 am) aliquoted as follows: 4 ml into plain, 3 ml into ethinyl-di-amine-tetra-acetic (EDTA), and 3 ml into fluoride oxalate specimen tubes. During the mid-luteal phase, 3 ml of non-fasted venous whole blood was acquired into plain specimen tubes. Acquired specimens in plain tubes were allowed to clot undisturbed at room temperature and were later centrifuged at 1500 g for 10 minutes. The serum supernatant was later transferred with Pasteur's pipette into plain tubes until analyzed. Processed serum was analyzed for FSH, LH, E2, progesterone, prolactin total testosterone, TSH, cortisol, TPSA, SHBG, DHEAS, and fasting insulin on an automated immunoassay analyzer (Architect i2000, Abbott Laboratories, Abbott Park, IL, USA).

The processed serum was also analyzed for hs-CRP, homocysteine, IGFBP-1, and IGF-1 using the enzyme-linked immunoassay (ELISA) methodology using standard reagent kits (Elabscience, Houston, USA). Fasting glucose was analyzed on an automated chemistry analyzer (BS200, Mindray, China) using the fluoride oxalate tube-acquired plasma specimen. HbA1c was analyzed by ion-exchange chromatography methodology on a high-performance liquid chromatography system (D10, Biorad, USA) using the EDTA tube-acquired venous whole blood specimen. EDTA-tube processed plasma was also used for the analysis of TChol, Tg, and HDL-C on an automated chemistry analyzer (BS200, Mindray, China). Serum MDA level (institutional reference value: 1.3-1.4 nmol/L) was determined as a measure of thiobarbituric acid reacting substances according to the method of Yagi [11]. Serum activity of GSH-Px (institutional reference value: ≥ 220 U/mL) was determined using dithiodinitrobenzoic acid based on the Mishra and Fridovich method [12], serum SOD activity (institutional reference value: ≥ 125 U/mL) was estimated using the principle of inhibition of auto-oxidation of adrenaline based on the Rostruck and Pope method [13], while serum TAC status (Institutional reference value: 300-500 $\mu\text{mol/L}$) was estimated via the ferric reducing ability of plasma method based on the Koracevic methods [14] as recently reviewed by Katerji and colleagues [15].

2.8.3. Quality Assurance

The utilized study questionnaire was explored for reliability and validity using appropriate methodologies. Two levels of control sera were used to monitor intra-assay and inter-assay analytic precision, and at all times, the intra- and inter-assay coefficients of variation were below 5% and 10%, respectively.

2.9. Variable Definitions/Stratifications

2.9.1. PCOS Diagnostic Criteria

This was based on Rotterdam revised 2003 consensus cri-

teria which is defined as the presence of at least two of the following three features [16, 17]; 1) Chronic oligo-ovulation/anovulation; 2) Clinical and/or biochemical hyperandrogenism; and 3) Transvaginal ultrasound scan polycystic ovary morphology [16, 17].

2.9.2. Menstrual/Ovulatory Patterns

These disorders included amenorrhea, oligomenorrhea, hypomenorrhea, hypermenorrhea, and irregular menstrual intervals and were defined based on the participants' history. Menstrual disorders were diagnosed as oligomenorrhea when menstrual cycles lasted more than 35 days or occurred less than nine times a year. Amenorrhea was defined as the absence of menses for 3 months in a woman with previously normal menstruation, or six months for women with a history of oligomenorrhoea. Eumenorrhea was defined as regular menstrual cycle of 26 - 34 days in length with cycle menstrual bleeding time of 3-5 days.

The ovulatory cycle was defined biochemically by a mid-luteal phase (day 21-23) menstrual cycle serum progesterone of ≥ 9.5 nmol/l (≥ 3.0 ng/ml) with normal menstrual cycle length without a previous history of oligomenorrhoea/amenorrhoea. The anovulatory cycle was defined biochemically by a mid-luteal phase (day 21-23) menstrual cycle serum progesterone of < 3.0 ng/ml (< 9.5 nmol/l) with clinical presence of oligomenorrhea/amenorrhea.

2.9.3. Hyperandrogenism/Hirsutism

Hyperandrogenism was defined based on serum levels of androgens (serum TT and calculated FAI) in addition to clinical findings (acne, oily skin, hirsutism, and male pattern hair loss - androgenic alopecia). Serum TT level > 2.8 nmol/L (based on institutional reference value) was defined as biochemical hyperandrogenism. FAI was calculated as (total testosterone)/SHBG $\times 100$ and the cut-off point $\geq 5\%$ was considered hyperandrogenism as previously described [18].

Hirsutism, as clinical evidence of hyperandrogenism, was defined based on the modified Ferriman-Gallwey rating score [18], which examines coarse terminal hairs in nine body areas (i.e. upper lip, chin, chest, upper and lower abdomen, thigh, upper and lower back and upper arms). In this modified scoring system, 9 androgen-dependent body sites were evaluated. The severity of hirsutism in each section was scored from 0 (no significant terminal hair growth) to 4 (severe terminal hair growth). A total score of < 6 was considered non-hirsute while a score ≥ 6 was considered hirsute which was further graded as mild (6-15), moderate (16-24), and severe hirsutism (≥ 25) [19].

2.9.4. Polycystic Ovary Morphology

Polycystic ovary morphology on transvaginal ultrasound scan was defined as the presence of 12 or more follicles measuring 2-9 mm in diameter and/or at least one enlarged ovary measuring > 10 cm³ [16, 17].

2.9.5. Rotterdam Phenotypes

The Rotterdam criteria for PCOS identifies 4 phenotypes based on the presence of hyperandrogenism (HA), oligo-anovulation (OA), and polycystic ovary morphology (PCOM) as previously described [16, 17]: Phenotype A (classic/frank PCOS): HA, OA, and PCOM, Phenotype B (classic non-polycystic ovary PCOS): HA and OA, but no PCOM Phenotype C (non-classic ovulatory PCOS): HA and PCOM, but with ovulatory cycles and Phenotype D (non-classic mild/normoandrogenic PCOS): OA and PCOM, but no clinical or biochemical hyperandrogenism.

2.9.6. Insulin Resistance/TPSA

HOMA-IR was calculated as [fasting glucose (mmol/l) x fasting insulin (pmol/l)]/135 and a value ≥ 2.0 were defined as insulin resistance (IR) [20].

Serum TPSA was graded as tertile 1: low (≤ 0.35 $\mu\text{g/L}$), tertile 2: intermediate (0.36 - 0.65 $\mu\text{g/L}$), and tertile 3: high (≥ 0.66 $\mu\text{g/L}$) serum TPSA status.

2.9.7. Lipid Parameters

LDL-C was calculated using the Friedewald formula [$\text{LDL-C (mmol/L)} = \text{TChol} - \text{HDL-C} - \text{Tg}/2.2$] with all parameters in mmol/L [21]. Non-HDL-C was calculated as the mathematical difference between the TChol and HDL-C concentrations ($\text{non-HDL-C} = \text{TChol} - \text{HDL-C}$, mmol/L) [22]. CRI-1 was defined as the ratio of TChol to HDL-C (TC/HDL-C), while CRI-2 was defined as the ratio of LDL-C to HDL-C (LDL-C/HDL-C) [22]. AC was calculated using the following formula: $\text{AC} = \text{TChol} - \text{HDL-C}/\text{HDL-C}$ or $(\text{Non-HDL-C})/(\text{HDL-C})$ [22]. AIP was defined as a logarithmically transformed ratio of molar concentrations of Tg to HDL-C (Log Tg/HDL-C) [22, 23]. VAI was calculated using WC, BMI, Tg, and HDL-C in the following formula: $\text{VAI} = [\text{WC}/36.58 + (1.89 \times \text{BMI})] \times (\text{Tg}/0.81) \times (1.52/\text{HDL-C})$ [22, 24]. LAP was calculated with WC in cm and Tg in mmol/L as an index for estimation of excessive lipid accumulation using the following formula: $\text{LAP} = (\text{WC [cm]} - 58) \times \text{Tg [mmol/L]}$ for women [22, 23].

2.9.8. BMI/WHR

BMI was calculated by applying Quetelet's equation, that is, $\text{weight (kg)}/\text{meter}^2$ [25]. BMI was categorized as underweight (<18.5), normal weight (18.5 - 24.9), overweight (25.0 - 29.9), and obese (≥ 30) [25]. Based on the World Health Organization (WHO) definition, a WHR ratio of ≥ 0.85 was defined as abdominal (central) obesity [26].

2.9.9. Hypertension, Dyslipidemia, and Metabolic Syndrome

Hypertension was defined as an average systolic blood pressure ≥ 140 mmHg, average diastolic blood pressure ≥ 90 mmHg, or self-reported current anti-hypertensive medications

as previously described [27]. Dyslipidemia was defined based on the National Cholesterol Education Program - Adult Treatment Panel 111 as the history of taking anti-hyperlipidemic drugs or lipoprotein disorders according to NCEP ATP III ($\text{TChol} > 5.17$ mmol/l or $\text{Tg} > 1.7$ mmol/l or $\text{HDL-C} < 1.30$ mmol/l or $\text{LDL-C} > 3.4$ mmol/l) [28]. The was defined based on the 2002 NCEP-ATP 111 guidelines.

According to the NCEP ATP III definition, metabolic syndrome is present in a female if 3 or more of the following 5 criteria are met: $\text{WC} \geq 88$ cm, arterial blood pressure $\geq 130/85$ mmHg, Tg level > 1.7 mmol/L, fasting HDL-C < 1.30 mmol/L, and FPG > 5.1 mmol/L [28].

2.9.10. Cardiovascular/Oxidative Stress Risk

This was defined using the institutional reference values of serum hs-CRP and homocysteine levels. A serum hs-CRP level (institutional reference value: < 9.5 nmol/L) ≥ 9.5 nmol/L (1.0 mg/L) and/or serum homocysteine level (institutional reference value 5.0 - 15.0 $\mu\text{mol/L}$) ≥ 15.0 $\mu\text{mol/L}$ was defined as raised cardiovascular risk. This was defined as raised serum MDA levels (institutional reference value: 1.3 - 1.4 nmol/L) ≥ 1.4 nmol/L with concomitant reduction of SOD activity (institutional reference value: ≥ 125) of < 125 U/mL and/or GSH-Px activity (institutional reference value: ≥ 220) of ≤ 220 U/mL and/or reduced TAC levels (institutional reference value: 300 - 500 $\mu\text{mol/L}$) of < 300 $\mu\text{mol/L}$.

2.10. Data Management

Data management and analyses were done using Statistical Package for Social Sciences (SPSS) software for Windows version 25. Continuous data were initially evaluated for conformity to a normal distribution pattern using the Shapiro-Wilk tests. Continuous data violating the normal distribution patterns were log-transformed before analysis, expressed using means \pm standard deviations, and compared by independent student t-test or analysis of variance (ANOVA), as appropriate. Categorical data were reported as counts/percentages and compared with the Chi-square or Fisher's exact tests, as appropriate. Crude/adjusted linear and logistic regression models were used to evaluate relationships and associations between dependent and independent variables. Receiver operating characteristic (ROC) curve analysis was used to determine the discriminatory potential of TPSA for PCOS diagnosis. All statistical analysis was performed at 95% confidence intervals and an alpha value < 0.05 was deemed statistically significant.

3. Results

During the study, 369 clinically diagnosed and transvaginal ultrasound-confirmed females with PCOS presented for biochemical evaluation/confirmation in the study setting. However, only 240 met the eligibility criteria and were recruited after consent to participate in the study.

Table 1. Comparison of demographic, laboratory and clinical parameters among PCOS patients and healthy controls.

Variables	PCOS Cases, n = 240 Mean \pm SD/n (%)	Healthy Controls, n = 240 Mean \pm SD/n (%)	p-value
A. Early follicular phase			
Age, mean, years	32.22 \pm 3.76	31.86 \pm 3.59	0.307
BM1, kg/m ²	32.84 \pm 3.08	29.94 \pm 3.17	0.032*
WC, cm	83.64 \pm 7.17	79.54 \pm 7.50	<0.001*
Hip circumference, cm	109.69 \pm 8.35	98.32 \pm 8.11	<0.001*
Waist-hip ratio	0.85 \pm 0.68	0.78 \pm 0.40	0.016*
SBP, mmHg	138.86 \pm 9.55	134.73 \pm 9.14	0.006*
DBP, mmHg	80.11 \pm 5.08	79.78 \pm 5.02	0.117
Serum LH, IU/L	29.44 \pm 3.07	4.12 \pm 1.04	<0.001*
Serum FSH, IU/L	13.93 \pm 2.18	3.97 \pm 1.01	<0.001*
Serum E2, pmol/L	146.56 \pm 11.87	169.66 \pm 10.14	<0.001*
Serum progesterone, nmol/L	2.18 \pm 1.56	2.71 \pm 1.69	0.057
Serum prolactin μ g/L	16.70 \pm 2.15	15.54 \pm 2.68	0.206
Serum TT, nmol/L	4.11 \pm 1.21	1.07 \pm 0.33	<0.001*
Serum TSH, mIU/L	2.71 \pm 0.70	2.64 \pm 0.84	0.216
Serum cortisol (8-10 am), nmol/L	189.11 \pm 9.61	190.03 \pm 9.72	0.344
Serum DHEAS, μ mol/L	4.96 \pm 1.03	3.18 \pm 0.96	<0.001*
Serum SHBG, nmol/L	17.42 \pm 3.10	56.90 \pm 5.37	<0.001*
FPG, mmol/L	6.10 \pm 1.17	4.08 \pm 1.05	<0.001*
Fasting serum insulin, pmol/L (IR > 174)	214.92 \pm 12.53	79.44 \pm 6.60	<0.001*
Serum IGFBP-1, μ g/L	2.55 \pm 1.05	9.88 \pm 1.85	<0.001*
Serum IGF-1, nmol/L	49.34 \pm 5.62	13.43 \pm 2.65	<0.001*
HbA1c, mmol/mol	56.33 \pm 7.44	32.58 \pm 3.40	<0.001*
Plasma TChol, mmol/L	5.16 \pm 1.40	4.17 \pm 1.13	<0.001*
Plasma Tg, mmol/L	2.67 \pm 0.34	1.50 \pm 0.14	<0.001*
Plasma HDL-C, mmol/L	1.27 \pm 0.87	2.17 \pm 1.11	<0.001*
Plasma LDL-C, mmol/L	3.10 \pm 0.78	1.60 \pm 0.22	<0.001*
Plasma Non-HDL-C, mmol/L	3.78 \pm 1.43	2.13 \pm 1.02	<0.001*
Serum hs-CRP, nmol/L	22.75 \pm 3.60	6.71 \pm 1.17	<0.001*
Serum homocysteine, μ mol/L	13.79 \pm 2.62	5.11 \pm 1.20	<0.001*
Serum malondialdehyde, nmol/L	1.63 \pm 0.89	1.31 \pm 0.68	<0.001*
Serum superoxide dismutase, U/mL	10.34 \pm 1.41	138.82 \pm 6.39	<0.001*
Serum glutathione peroxidase, U/mL	116.14 \pm 8.70	327.17 \pm 28.66	<0.001
Total serum anti-oxidant capacity, μ mol/L	205.77 \pm 12.08	414.00 \pm 9.44	<0.001*
CRI-1	3.67 \pm 0.91	2.10 \pm 0.32	<0.001*

	PCOS Cases, n = 240	Healthy Controls, n = 240	p-value
Variables	Mean \pm SD/n (%)	Mean \pm SD/n (%)	
CRI-2	0.98 \pm 0.07	0.66 \pm 0.04	0.016*
AC	2.91 \pm 0.14	1.42 \pm 0.03	<0.007*
AIP	0.22 \pm 0.09	0.08 \pm 0.01	<0.001*
VAI	2.43 \pm 0.88	1.47 \pm 0.17	<0.001*
LAP	82.33 \pm 6.99	49.41 \pm 4.51	<0.001*
FAI,%	7.70 \pm 2.22	2.10 \pm 1.64	<0.001*
HOMA-IR	3.20 \pm 0.88	0.88 \pm 0.05	<0.001*
LH/FSH ratio	2.81 \pm 1.04	1.01 \pm 0.06	<0.001*
TPSA, μ g/L	0.97 \pm 0.12	0.10 \pm 0.01	<0.001*
Ferriman-Gallwey score	15.93 \pm 2.33	0.09 \pm 0.10	<0.001*
B. Mid-luteal phase			
Serum progesterone, nmol/L	5.55 \pm 2.97	49.80 \pm 3.21	<0.001*
Serum TPSA, μ g/L	0.99 \pm 0.18	0.09 \pm 0.01	<0.001*
C. Data categories/strata			
Menstrual patterns			<0.001*
Eumenorrhea	15 (6.3)	240 (100.0)	
Oligomenorrhoea	155 (64.6)	0 (0.0)	
Amenorrhea	70 (29.1)	0 (0.0)	
Ovulatory patterns			<0.001*
Normo-ovulatory cycle	20 (8.3)	240 (100.0)	
Oligo/Anovulatory cycle	220 (91.7)	0 (0.0)	
Hyperandrogenism			<0.001*
Negative; positive	19 (7.9); 221 (92.1)	240 (100.0); 0 (0.0)	
Polycystic ovary morphology			<0.001*
Negative; positive	36 (15.0); 204 (85.0)	240 (100.0); 0 (0.0)	
Rotterdam phenotypes			NA
Type A	165 (68.8)	--	
Type B	36 (15.0)	--	
Type C	20 (8.3)	--	
Type D	19 (7.9)	--	
Ferriman-Gallwey scores		--	0.002*
Non-hirsute	2 (0.8);	240 (100.0)	
Mild	22 (9.2)	0 (0.0)	
Moderate	98 (40.8)	0 (0.0)	
Severe	108 (45.2%)	0 (0.0)	
BMI status, kg/m ²			0.002*
Normal weight	60 (25.0);	120 (50.0)	

	PCOS Cases, n = 240	Healthy Controls, n = 240	p-value
Variables	Mean \pm SD/n (%)	Mean \pm SD/n (%)	
Overweight	69 (28.8)	62 (25.8)	
Obese	111 (46.2)	58 (24.2)	
Abdominal obesity			<0.001*
Negative; positive	69 (28.8); 171 (71.2)	175 (72.9); 65 (27.1)	
Hypertension			<0.001*
Negative; positive	84 (35.0); 156 (65.0)	148 (61.7); 92 (38.3)	
Dyslipidemia			<0.001*
Negative; positive	78 (32.5); 162 (67.5)	184 (76.7); 56 (23.3)	
Cardiovascular risk			<0.001*
Negative; positive	56 (23.3); 184 (76.7)	224 (93.3); 16 (6.7)	
Oxidative stress risk			<0.001*
Negative; positive	64 (26.7); 176 (73.3)	226 (94.2); 14 (5.8)	
Metabolic syndrome			<0.001*
Negative; positive	81 (33.8); 159 (66.2)	184 (76.7); 56 (23.3)	
Insulin resistance			<0.001*
Negative; positive	68 (28.3); 172 (71.7)	204 (85.0); 36 (15.0)	
Early follicular phase TPSA status, μ g/L			0.017*
Tertile 1: Low	56 (23.3%)	240 (100.0%)	
Tertile 2: Intermediate	69 (28.8%)	0 (0.0%)	
Tertile 3: High	115 (47.9%)	0 (0.0%)	

*Statistically significant; NA: not applicable; BMI: body mass index; WC: waist circumference; FSH: follicle-stimulating hormone; LH: luteinizing hormone; E2: estradiol; TT: total testosterone; TSH: thyroid-stimulating hormone; DHEAS: dehydroepiandrosterone sulphate; SHBG: sex hormone binding globulin; FPG: fasting plasma glucose; IGFBP-1: insulin-like growth factor binding protein 1; IGF-1: insulin-like growth factor 1; HbA1c: glycated hemoglobin A1c; TChol: total cholesterol; Tg: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CRI-1: Castelli risk index 1; CRI-2: Castelli risk index 2; AC: atherogenic coefficient; AIP: atherogenic index of plasma; VAI: visceral adiposity index; LAP: lipid accumulation product; FAI: free androgen index; HOMA-IR: homeostatic model assessment of insulin resistance; TPSA: total prostate-specific antigen

Table 1 depicts the demographic, clinical, anthropometric, and laboratory comparisons between the PCOS patients and healthy controls during the follicular and mid-luteal phases of the menstrual cycle. From Table 1 as shown, the PCOS patients had higher TPSA status (early follicular/mid-luteal phase) including higher BMI, WC, HC, WHR, SBP, TPSA (early follicular/mid-luteal phase), LH, FSH, TT, DHEAS, FPG, FIN, IGF-1, HbA1c, TChol, Tg, LDL-C, hs-CRP, homocysteine, MDA, and raised calculated values of non-HDL-C, CRI-1, CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR., LH/FSH ratio, and Ferriman-Gallwey scores (FGS) but lower early follicular phase E2, SHBG, IGFBP-1, HDL-C, mid-luteal phase progesterone, SOD, GSP-Px, and TAC values compared to the healthy controls ($p < 0.05$, respectively) (Table 1). Higher rates of oligo/amenorrhea, oli-

go/anovulation, hyperandrogenism, polycystic ovary morphology, moderate/severe FGS, general overweight/obesity status, abdominal (central) obesity, hypertension, dyslipidemia, cardiovascular risk, oxidative stress risk, metabolic syndrome, and insulin resistance was observed among the PCOS patients compared to the healthy controls ($p < 0.05$, respectively) (Table 1). Among the PCOS patients, Rotterdam phenotype A (68.8%; $n=165$) was the most predominant followed by type B (15.0%; $n=36$), type C (8.3%; $n=20$), and type D (7.9%; $n=19$) ($p < 0.05$, respectively) (Table 1). The majority of the PCOS patients also presented with higher tertile levels (third tertile) of TPSA status (47.9%; $n=115$) during the early follicular phase ($p < 0.05$) (Table 1).

Table 2 depicts the demographic, clinical, anthropometric, and laboratory comparisons by TPSA tertiles during the fol-

licular and mid-luteal phases of the menstrual cycle among PCOS patients. From Table 2, the PCOS patients within the third tertile of TPISA status had higher BMI, WC, hip circumference, WHR, TPISA (early follicular/mid-luteal phase), LH, FSH, TT, DHEAS, FPG, FIN, IGF-1, HbA1c, TChol, Tg, LDL-C, hs-CRP, MDA, raised calculated values of non-HDL-C, CRI-1, CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR., LH/FSH ratio, and FGS but lower early follicular phase E2, SHBG, IGFBP-1, HDL-C, mid-luteal phase progesterone, SOD, GSH-Px, and TAC values compared to those

in the lower tertiles ($p < 0.05$, respectively) (Table 2). The majority of the PCOS patients in the highest tertile of TPISA status (third tertile) presented with oligo/amenorrhea, oligo/anovulation, hyperandrogenism, polycystic ovary morphology, Rotterdam PCOS phenotype A, moderate/severe FGS, generalized overweight/obesity status, abdominal (central) obesity, hypertension, dyslipidemia, cardiovascular risk, oxidative stress risk, metabolic syndrome, and insulin resistance compared to those within the lowest tertile of TPISA status ($p < 0.05$, respectively) (Table 2).

Table 2. Comparison of parameters among PCOS patients by PSA categories.

Variables	Tertile 1: Low TPISA Status (n=56)	Tertile 2: Intermediate TPISA Status (n=69)	Tertile 3: High TPISA Status (n=115)	p-value
	Mean \pm SD/n (%)	Mean \pm SD/n (%)	Mean \pm SD/n (%)	
A. Early follicular phase				
Age, mean, years	30.07 \pm 3.11	32.61 \pm 3.74	34.93 \pm 3.90	<0.001*
BMI, kg/m ²	29.56 \pm 3.10	31.88 \pm 3.29	32.91 \pm 3.67	0.027*
WC, cm	95.60 \pm 7.88	100.10 \pm 8.43	102.67 \pm 9.11	0.016*
Hip circumference, cm	102.77 \pm 8.10	114.44 \pm 8.46	116.70 \pm 8.67	<0.001*
Waist to hip ratio	0.83 \pm 0.55	0.85 \pm 0.78	0.89 \pm 0.90	<0.001*
SBP, mmHg	132.17 \pm 8.89	136.71 \pm 9.18	139.64 \pm 9.71	<0.001*
DBP, mmHg	79.09 \pm 5.03	80.07 \pm 5.04	80.19 \pm 5.05	0.0220
Serum LH, IU/L	13.98 \pm 3.66	24.37 \pm 4.70	35.77 \pm 5.11	<0.001*
Serum FSH, IU/L	11.91 \pm 2.45	12.04 \pm 2.67	13.83 \pm 2.85	0.017*
Serum E2, pmol/L	155.76 \pm 10.53	146.51 \pm 10.67	134.93 \pm 10.44	<0.001*
Serum progesterone, nmol/L	2.01 \pm 1.46	1.71 \pm 1.19	1.44 \pm 1.07	0.014*
Serum prolactin, μ g/L	14.18 \pm 2.23	15.05 \pm 2.12	13.98 \pm 2.03	0.206
Serum TT, nmol/L	3.52 \pm 1.13	5.51 \pm 1.49	5.93 \pm 0.74	<0.001*
Serum TSH, mIU/L	2.40 \pm 0.42	2.67 \pm 0.71	2.45 \pm 0.70	0.422
Serum cortisol (8-10 am), nmol/L	181.24 \pm 8.96	180.52 \pm 9.44	180.92 \pm 9.55	0.337
Serum DHEAS, μ mol/L	4.06 \pm 1.10	5.14 \pm 1.23	6.38 \pm 1.17	<0.001*
Serum SHBG, nmol/L	16.16 \pm 3.03	14.05 \pm 2.26	12.71 \pm 2.04	<0.001*
FPG, mmol/L	4.45 \pm 1.06	5.39 \pm 1.51	6.84 \pm 2.47	<0.001*
Fasting insulin, pmol/L	171.76 \pm 9.67	198.86 \pm 10.75	223.17 \pm 12.66	<0.001*
IGFBP-1, μ g/L	3.45 \pm 1.67	2.10 \pm 1.34	1.89 \pm 0.98	<0.001*
IGF-1, nmol/L	41.56 \pm 5.20	47.71 \pm 5.44	50.77 \pm 5.81	<0.001*
HbA1c, mmol/mol	50.87 \pm 5.03	59.79 \pm 5.07	64.52 \pm 6.14	<0.001*
Plasma TChol, mmol/L	4.96 \pm 1.09	5.24 \pm 1.29	5.33 \pm 1.46	<0.001*
Plasma Tg, mmol/L	1.96 \pm 0.19	2.49 \pm 0.22	2.98 \pm 0.47	<0.001*
Plasma HDL-C, mmol/L	1.38 \pm 0.90	1.24 \pm 0.66	1.16 \pm 0.43	0.019*
Plasma LDL-C, mmol/L	2.87 \pm 0.54	3.27 \pm 0.85	3.43 \pm 0.96	0.003*

Variables	Tertile 1: Low TPSA Status (n=56)	Tertile 2: Intermediate TPSA Status (n=69)	Tertile 3: High TPSA Status (n=115)	p-value
	Mean \pm SD/n (%)	Mean \pm SD/n (%)	Mean \pm SD/n (%)	
Plasma Non-HDL-C, mmol/L	2.90 \pm 0.96	3.45 \pm 1.30	3.89 \pm 1.56	0.012*
Serum hs-CRP, nmol/L	20.13 \pm 3.22	24.60 \pm 3.41	27.88 \pm 3.81	<0.001*
Serum homocysteine, μ g/L	12.79 \pm 2.16	16.56 \pm 2.70	18.46 \pm 2.85	<0.001
Serum malondialdehyde, nmol/L	1.41 \pm 0.36	1.68 \pm 0.91	1.79 \pm 0.96	<0.001*
Serum superoxide dismutase, U/mL	11.21 \pm 1.32	9. \pm 1.17	7.44 \pm 1.08	<0.001*
Serum glutathione peroxidase, U/mL	102.51 \pm 8.11	94.62 \pm 7.63	83.30 \pm 6.56	<0.001*
Total serum anti-oxidant capacity, μ mol/L	217.55 \pm 12.79	186.40 \pm 11.32	171.57 \pm 10.18	<0.001*
CRI-1	2.98 \pm 0.64	3.57 \pm 0.78	3.90 \pm 0.94	0.004*
CRI-2	0.71 \pm 0.05	0.89 \pm 0.06	1.16 \pm 0.12	0.013*
AC	2.16 \pm 0.09	2.97 \pm 0.16	3.17 \pm 0.14	<0.001*
AIP	0.20 \pm 0.08	0.26 \pm 0.14	0.32 \pm 0.26	<0.001*
VAI	2.10 \pm 0.51	2.89 \pm 0.96	3.17 \pm 1.33	0.006*
LAP	66.57 \pm 5.11	87.80 \pm 7.12	91.54 \pm 7.83	<0.001*
FAI, %	7.01 \pm 1.02	8.66 \pm 1.55	9.79 \pm 1.77	<0.001*
HOMA-IR	2.77 \pm 0.76	3.16 \pm 0.86	3.93 \pm 0.90	<0.001*
LH/FSH ratio	1.47 \pm 1.23	2.17 \pm 1.44	2.98 \pm 1.34	<0.001*
Ferriman-Gallwey score	15.41 \pm 2.11	16.89 \pm 2.34	18.23 \pm 2.71	<0.001*
B. Mid-luteal phase				
Serum progesterone, nmol/L	6.61 \pm 2.74	4.97 \pm 1.98	3.72 \pm 1.76	<0.001*
C. Categories of data				
Menstrual pattern				<0.001*
Eumenorrhea	15 (26.8)	0 (0.0)	0 (0.0)	
Oligomenorrhea	41 (73.2)	14 (20.3)	100 (87.0)	
Amenorrhea	0 (0.0)	55 (79.8)	15 (13.0)	
Ovulatory patterns				
Ovulatory cycle	14 (25.0)	4 (5.8)	2 (1.7)	<0.001*
Oligo/Anovulatory cycle	42 (75.0)	65 (94.2)	113 (98.3)	
Hyperandrogenism				<0.001*
Negative; positive	16 (28.6); 40 (71.4)	2 (2.9%); 67 (97.1)	1 (0.9); 114 (99.1)	
Polycystic ovary morphology				<0.001*
Negative; positive	30 (53.6); 26 (46.4)	4 (5.8%); 65 (94.2)	2 (1.7%); 113 (98.3)	
Rotterdam phenotypes				<0.001*
Type A	2 (3.6)	66 (95.8)	97 (84.3)	
Type B	19 (33.9)	1 (1.4)	16 (13.9)	
Type C	18 (32.4)	1 (1.4)	1 (0.9)	
Type D	17 (30.1)	1 (1.4)	1 (0.9)	

Variables	Tertile 1: Low TPSA Status (n=56)	Tertile 2: Intermediate TPSA Status (n=69)	Tertile 3: High TPSA Status (n=115)	p-value
	Mean \pm SD/n (%)	Mean \pm SD/n (%)	Mean \pm SD/n (%)	
Ferriman-Gallwey scores				<0.001*
Non-hirsute	2 (3.6)	0 (0.0)	0 (0.0)	
Mild	15 (26.8)	2 (2.9)	5 (4.3)	
Moderate	35 (62.5)	48 (69.6)	15 (13.1)	
Severe	4 (7.1)	19 (27.5)	95 (82.6)	
BMI status, kg/m ²				0.002*
Normal weight	49 (87.5)	8 (11.6)	3 (2.6)	
Overweight	3 (5.4)	37 (53.6)	29 (25.2)	
Obese	4 (7.1)	24 (34.8)	83 (72.2)	
Abdominal obesity				<0.001*
Negative; positive	46 (82.1); 10 (17.9)	20 (29.0); 49 (71.0)	3 (2.6); 112 (97.4)	
Hypertension				<0.001*
Negative; positive	50 (89.3); 6 (10.7)	24 (34.8); 45 (65.2)	10 (8.6); 105 (91.4)	
Dyslipidemia				<0.001*
Negative; positive	40 (71.4); 16 (28.6)	30 (43.5); 31 (56.5)	8 (7.0); 107 (93.0)	
Cardiovascular risk				<0.001*
Negative; positive	50 (89.3); 6 (10.7)	5 (7.2); 64 (92.8)	1 (0.9); 114 (99.1)	
Oxidative stress risk				<0.001*
Negative; positive	49 (87.5); 7 (12.5)	14 (20.3); 55 (79.7)	1 (0.9); 114 (99.1)	
Metabolic syndrome				<0.001*
Negative; positive	54 (96.4); 2 (3.6)	20 (29.0); 49 (71.0)	7 (6.1); 108 (93.9)	
Insulin Resistance				<0.001*
Negative; positive	50 (89.3); 6 (10.7)	13 (18.8); 56 (81.2)	5 (13.0); 110 (87.0)	

*Statistically significant; TPSA: total prostate-specific antigen; BMI: body mass index; WC: waist circumference; FSH: follicle-stimulating hormone; LH: luteinizing hormone; E2: estradiol; TT: total testosterone; TSH: thyroid-stimulating hormone; DHEAS: dehydroepiandrosterone sulphate; SHBG: sex hormone binding globulin; FPG: fasting plasma glucose; IGFBP-1: insulin-like growth factor binding protein 1; IGF-1: insulin-like growth factor 1; HbA1c: glycated hemoglobin A1c; TChol: total cholesterol; Tg: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CRI-1: Castelli risk index 1; CRI-2: Castelli risk index 2; AC: atherogenic coefficient; AIP: atherogenic index of plasma; VAI: visceral adiposity index; LAP: lipid accumulation product; FAI: free androgen index; HOMA-IR: homeostatic model assessment of insulin resistance

Table 3 depicts the results of the crude and adjusted linear regression models between TPSA and various significant biochemical/clinical parameters during the early follicular phase and mid-luteal phase among PCOS patients. From the Table 3, as shown, TPSA correlated positively with LH, FSH, TT, DHEAS, FPG, fasting insulin, IGF-1, HbA1c, TChol, Tg,

LDL-C, hs-CRP, MDA, non-HDL-C, CRI-1, CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR, LH/FSH ratio, and FGS but correlated negatively with E2, progesterone (early follicular/mid-luteal phase), SHBG, IGFBP-1, HDL-C, SOD, GSH-Px, and TAC following crude and adjusted linear regression models ($p < 0.05$, respectively) (Table 3).

Table 3. Relationships between serum TPSA and biochemical parameters among the PCOS patients.

Early Follicular Phase TPSA, µg/L	Crude Linear Regression			Adjusted Linear Regression**		
	B	SE	p-value	B	SE	p-value
A. Early follicular phase						
Serum LH (IU/L)	0.558	0.116	<0.001*	0.660	0.096	<0.001*
Serum FSH (IU/L)	0.102	1.143	0.360	0.099	1.200	0.038
Serum E2	-0.609	0.041	<0.001*	-0.598	0.052	<0.001*
Serum progesterone, (nmol/L)	-0.142	1.270	0.217	-106	1.220	0.188
Serum TT, nmol/L	0.689	0.096	<0.001*	0.710	0.088	<0.001*
Serum DHEAS	0.558	0.077	<0.001*	0.511	0.080	<0.001*
Serum SHBG, nmol/L	-0.665	0.069	<0.001*	-0.609	0.076	<0.001*
FPG, mmol/L	0.579	0.089	<0.001*	0.593	0.081	<0.001*
Fasting insulin, pmol/L	0.487	0.110	0.007*	0.499	0.081	0.002*
IGFBP-1, µg/L	-0.601	0.093	<0.001*	-0.587	0.091	<0.001*
IGF-1, nmol/L	0.617	0.086	<0.001*	0.602	0.096	<0.001*
HbA1c, mmol/mol	0.575	0.101	<0.001*	0.601	0.094	<0.001*
Plasma TChol, mmol/L	0.445	0.078	0.001*	0.409	0.097	0.004*
Plasma Tg, mmol/L	0.560	0.074	<0.001*	0.517	0.059	<0.001*
Plasma HDL-C, mmol/L	-0.650	0.044	<0.001*	-0.611	0.057	<0.001*
Plasma LDL-C, mmol/L	0.590	0.083	<0.001*	0.588	0.089	<0.001*
Plasma Non-HDL-C, mmol/L	0.484	0.116	0.007*	0.440	0.121	0.011*
Serum hs-CRP, nmol/L	0.603	0.045	<0.001*	0.624	0.039	<0.001*
Serum homocysteine, µg/L	0.577	0.067	<0.001*	0.507	0.081	<0.001*
Serum malondialdehyde, nmol/L	0.478	0.103	<0.001*	0.433	0.121	<0.001*
Serum superoxide dismutase, U/L	-0.499	0.116	0.012*	-0.482	0.117	0.037*
Serum glutathione peroxidase, U/L	-0.585	0.111	<0.001*	0.622	0.081	<0.001*
Total serum anti-oxidant capacity, µmol/L	-0.655	0.067	<0.001*	0.614	0.085	<0.001
CRI-1	0.670	0.094	<0.001*	0.689	0.085	<0.001*
CRI-2	0.389	0.116	0.003*	0.377	0.118	0.016*
AC	0.577	0.092	<0.001*	0.504	0.079	<0.001*
AIP	0.640	0.034	<0.001*	0.670	0.030	<0.001*
VAI	0.530	0.098	<0.001*	0.536	0.101	<0.001*
LAP	0.616	0.041	<0.001*	0.603	0.052	<0.001*
FAI,%	0.691	0.097	<0.001*	0.695	0.087	<0.001*
HOMA-IR, mmol/L	0.560	0.098	<0.001*	0.570	0.100	<0.001*
LH/FSH ratio	0.611	0.077	<0.001*	0.643	0.066	<0.001*
Ferriman-Gallwey score	0.433	0.095	<0.001	0.427	0.100	<0.001*

Early Follicular Phase TPSA, µg/L						
	Crude Linear Regression			Adjusted Linear Regression**		
	B	SE	p-value	B	SE	p-value
Mid-luteal Phase TPSA, µg/L						
B. Mid-luteal phase						
Serum progesterone, nmol/L	-0.616	0.076	0.002*	-0.654	0.061	<0.001*

*Statistically significant; TPSA: total prostate-specific antigen; BMI: body mass index; WC: waist circumference; FSH: follicle-stimulating hormone; LH: luteinizing hormone; E2: estradiol; TT: total testosterone; TSH: thyroid-stimulating hormone; DHEAS: dehydroepiandrosterone sulphate; SHBG: sex hormone binding globulin; FPG: fasting plasma glucose; IGFBP-1: insulin-like growth factor binding protein 1; IGF-1: insulin-like growth factor 1; HbA1c: glycated hemoglobin A1c; TChol: total cholesterol; Tg: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CRI-1: Castelli risk index 1; CRI-2: Castelli risk index 2; AC: atherogenic coefficient; AIP: atherogenic index of plasma; VAI: visceral adiposity index; LAP: lipid accumulation product; FAI: free androgen index; HOMA-IR: homeostatic model assessment of insulin resistance

**adjusted for age, BMI, WC, LH (early follicular phase), FSH (early follicular phase), E2, TT, DHEAS, SHBG, FPG, fasting insulin, IGFBP-1, IGF-1, HbA1c, TChol, Tg, HDL-C, LDL-C, CRI-1, CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR, LH/FSH ratio, progesterone (mid-luteal phase), Ferriman-Gallwey rating score, ovulatory pattern status, and Rotterdam phenotypes

Table 4. Association between TPSA and Ovulatory Patterns, PCOS Phenotypes, and Ferriman-Gallwey Scores among the PCOS Patients.

	TPSA, µg/L					
	Crude Logistic Regression			Adjusted Logistic Regression**		
	OR	95% CI	p-value	OR	95% CI	p-value
Menstrual patterns						
Eumenorrhea	1.0			1.0		
Oligomenorrhoea	2.881	1.956 – 3.518	<0.001*	2.244	1.788-2.916	<0.001*
Amenorrhea	4.557	3.442 – 5.656	<0.001*	4.227	3.067-5.400	<0.001*
Ovulatory patterns						
Ovulatory cycle (reference)	1.0			1.0		
Oligo/Anovulatory cycle	7.224	6.379 – 8.655	<0.001*	6.788	5.710 – 7.670	<0.001*
Hyperandrogenism						
Negative (reference)	1.0			1.0		
Positive	2.559	1.611 – 3.055	<0.001*	2.661	1.701-3.217	<0.001*
Polycystic ovary morphology						
Negative (reference)	1.0			1.0		
Positive	2.347	1.664-3.188	<0.001*	2.116	1.488-2.988	<0.001*
Rotterdam phenotypes						
Type A	5.9756	4.581 – 7.113	<0.001*	5.884	4.633 – 6.916	<0.001*
Type B	1.107	0.510 – 1.956	0.104	1.097	0.491 – 1.884	0.124
Type C	1.089	0.473 – 1.832	0.162	1.038	0.441 – 1.790	0.170
Type D (reference)	1.0			1.0		
Ferriman-Gallwey score						

	TPSA, µg/L					
	Crude Logistic Regression			Adjusted Logistic Regression**		
	OR	95% CI	p-value	OR	95% CI	p-value
Mild (reference)	1.0			1.0		
Moderate	3.444	2.876 – 4.671	0.014*	3.309	2.780 – 4.563	0.005*
Severe	5.997	4.456 – 6.089	<0.001*	6.100	4.970 – 7.104	<0.001*
BMI status, kg/m ²						
Normal weight (reference)	1.0			1.0		
Overweight	1.883	1.105-2.619	<0.001*	1.716	1.008-2.554	<0.001*
Obese	2.444	1.700-3.189	<0.001*	2.233	1.513-3.088	<0.001*
Abdominal obesity						
Negative (reference)	1.0			1.0		
Positive	3.166	2.416-4.227	<0.001*	2.915	2.211-4.077	<0.001*
Hypertension						
Negative (reference)	1.0			1.0		
Positive	1.872	1.288-2.566	<0.017*	1.816	1.207-2.450	<0.022*
Dyslipidemia						
Negative (reference)	1.0			1.0		
Positive	5.991	4.965-6.577	<0.001*	5.610	4.598-6.244	<0.001*
Cardiovascular risk						
Negative (reference)	1.0			1.0		
Positive	6.515	5.610-7.276	<0.001*	6.644	5.782-7.356	<0.001*
Oxidative stress risk						
Negative (reference)	1.0			1.0		
Positive	2.334	1.611-3.276	<0.001*	2.169	1.487-3.013	<0.001*
Metabolic syndrome						
Negative (reference)	1.0			1.0		
Positive	5.775	4.874-6.570	<0.001*	5.917	4.948-6.786	<0.001*
Insulin resistance						
Negative (Reference)	1.0			1.0		
Positive	4.776	3.678-5.789	<0.001*	5.110	3.987-5.770	<0.001*

*Statistically significant; TPSA: total prostate-specific antigen; OR: odd ratio; CI: confidence interval; **adjusted for age, BMI, WC, LH (early follicular phase), FSH (early follicular phase), E2, TT, DHEAS, SHBG, FPG, fasting insulin, IGFBP-1, IGF-1, HbA1c, TChol, Tg, HDL-C, LDL-C, CRI-1, CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR, LH/FSH ratio, progesterone (mid-luteal phase), Ferriman-Gallwey rating score, ovulatory pattern status, and Rotterdam phenotypes

Table 4 depicts the crude and adjusted logistic regression models of the association between TPSA and ovulatory patterns, PCOS phenotypes, and Ferriman-Gallwey scores. From Table 4, TPSA was associated with oligo/amenorrhea, oligo/anovulatory

cycle, hyperandrogenism, Rotterdam phenotype type A, moderate/severe FGS, generalized overweight/obesity, abdominal (central) obesity, hypertension, dyslipidemia, cardiovascular risk, oxidative risk, metabolic syndrome, and insulin resistance fol-

lowing the crude and adjusted logistic regression models ($p < 0.05$, respectively) (Table 4).

Table 5 shows the discriminatory potentials of TPSA for PCOS diagnosis among the entire PCOS patients and by different PCOS phenotypes using the ROC curve analysis. From Table 5, TPSA level was a discriminative biomarker for the

diagnosis of PCOS among the entire PCOS patients (AUC: 0.879; CI: 0.814-0.944; SE: 0.033; $p < 0.001$), however, a more robust discriminatory potential of TPSA was observed among individuals with the Rotterdam phenotype type A (AUC: 0.935; CI: 0.857-1.000; SE: 0.021; $p < 0.001$) compared to the entire PCOS patients.

Table 5. Discriminatory potentials of TPSA for PCOS diagnosis among the entire PCOS patients and by PCOS phenotypes.

Statistical Properties	PCOS Phenotypes				
	Overall, n=240	A, n=165	B, n=36	C, n=20	D, n=19
AUC of ROC curve	0.879	0.935	0.765	0.505	0.423
95% CI	0.814-0.944	0.857-1.000	0.703-0.845	0.421-0.597	0.330-0.507
SE	0.033	0.021	0.143	1.209	1.246
p-value	<0.001*	<0.001*	0.024*	0.211	0.431

*Statistically significant; AUC: area under the ROC curve; ROC: receiver-operating characteristics; CI: confidence interval; SE: standard error

4. Discussion

4.1. Major Findings

The current study was set to evaluate the clinical value of PSA in PCOS among indigenous Nigerians by exploring its relationship with diverse anthropometric, clinical, hormonal, and metabolic profiles of PCOS. Following analysis, the PCOS patients had higher TPSA status (early follicular/mid-luteal phase) including higher BMI status, WC, HC, WHR, SBP, LH, FSH, TT, DHEAS, FPG, FINS, IGFBP-1, IGF-1, HbA1c, TChol, Tg, LDL-C, hs-CRP, homocysteine, MDA, non-HDL-C, CRI-1, CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR, LH/FSH ratio, and FGS but lower early-follicular phase E2, SHBG, HDL-C, mid-luteal phase progesterone, SOD, GSH-Px, TAC compared to healthy control which indicates adverse anthropometric, clinical, hormonal, and metabolic profiles among the PCOS patients compared to the healthy controls. In addition, the PCOS patients with higher tertile of TPSA status had more unfavorable anthropometric, clinical, hormonal, and metabolic profiles compared to those with the lowest tertile of TPSA status. Among the studied PCOS patients, TPSA correlated positively with LH, FSH, TT, DHEAS, FPG, FINS, IGF-1, HbA1c, TChol, Tg, LDL-C, hs-CRP, homocysteine, MDA, non-HDL-C, CRI-1/CRI-2, AC, AIP, VAI, LAP, FAI, HOMA-IR, LH/FSH ratio, and FGS but correlated negatively with E2, progesterone (early follicular/mid-luteal phases), SHBG, IGFBP-1, HDL-C, SOD, GSH-Px, and TAC. TPSA was associated with oligomenorrhoea /amenorrhoea, oligo/anovulation, hyperandrogenism, Rotterdam phenotype A, moderate/severe FGS, overweight,

generalized/abdominal obesity, hypertension, dyslipidemia, cardiovascular risk, oxidative stress risk, metabolic syndrome, and insulin resistance among the PCOS patients. TPSA level was also observed to be a discriminative biomarker for the diagnosis of PCOS among all PCOS patients, however, a more robust discriminatory potential of TPSA was observed among individuals with the Rotterdam phenotype A.

4.2. Relationship with Previous Studies

Our findings of adverse anthropometric, clinical, hormonal, and metabolic profiles among the PCOS patients compared to the healthy controls are well-documented in previous similar studies [22]. In addition, several aspects of the current findings align with observations from similar previous studies within the existing literature regarding TPSA status and its relationships with diverse anthropometric, clinical, hormonal, and metabolic features in PCOS [29-35].

In an Iranian case-controlled study reported by Madanian and colleagues aimed to compare 32 PCOS patients to 32 age-matched controls through metabolic measures and serum TPSA level, the authors found mean serum TPSA, FGS, LH/FSH, TT, DHEAS, and 17(α)-hydroxyprogesterone levels were higher in PCOS ($p < 0.001$, respectively) compared to healthy controls [29]. TPSA levels > 0.07 ng/ml yielded a sensitivity of 91% and specificity of 82% and was helpful as a diagnostic tool for women with PCOS. The authors also observed that the circulating androgens and hirsutism were associated with higher levels of TPSA in PCOS women which led the authors to conclude that there was a direct correlation between TPSA, hirsutism, and hyperandrogenic state [29].

In another similar study conducted in Poland by Rudnicka and colleagues aimed to assess the concentration of TPSA and

free PSA (fPSA) in 165 patients with PCOS and 40 healthy controls, to establish the relationship between TPSA and fPSA and hormonal parameters, and determine the performance of PSA in diagnosis of PCOS [30], the authors observed that TPSA was higher in PCOS group versus controls but found fPSA to be below the lower detection levels among all patients. The authors also found mean FAI to be 4.31% in PCOS patients versus 1.79% in controls ($p < 0.001$), and observed that TPSA correlated with TT ($r = 0.173$; $p = 0.027$) and FAI ($r = 0.2603$; $p = 0.001$) but not with BMI, FSH, LH, E2, DHEAS, progesterone, and insulin.

The AUC for FAI was 82.1%, threshold of 2.56 nmol/l, for TT AUC 80.5%, a threshold of 0.54 ng/ml, for TPSA AUC 66.3%, a threshold of 0.005 ng/ml, and for androstenedione AUC 62.7%, threshold 3.95 ng/ml.

Based on their findings, the authors concluded that FAI was the best marker for hyperandrogenic status and has better accuracy for TT and TPSA serum levels in the diagnostic evaluation of PCOS [30].

From Bangladesh, Hurjahan-Banu and colleagues found serum PSA and TT level were significantly higher among 40 PCOS subjects than 25 controls (0.05 ± 0.01 vs. 0.04 ± 0.01 ng/ml; $p < 0.02$; 40.18 ± 21.12 vs. 28.92 ± 13.65 ng/dl; $p < 0.01$, respectively) and found PSA positively correlated with observed polycystic ovaries by USG in the PCOS group ($r = 0.397$, $p = 0.011$) but not with either testosterone ($r = 0.075$, $p = 0.644$) or hirsutism score ($r = 0.012$, $p = 0.940$), which contrast with our study [31].

From Iraq, Ibrahim and colleagues found mean serum TPSA levels significantly higher in 50 PCOS women compared to 50 control women (0.15 ± 0.09 , 0.016 ± 0.003 ; $p < 0.05$) with PCOS women having a significant positive correlation with FGS, LH/FSH ratio, and serum TT with r values: 0.964, 0.988, 0.922 respectively. There was a strong correlation between serum PSA levels with the degree of hirsutism as evaluated by FGS. Serum PSA level in the 1st group (FGS 4-8) was 0.07 ± 0.009 , in the 2nd group (FGS 9-12) was 0.1 ± 0.06 and in the 3rd group (FGS 13-16) was 0.3 ± 0.03 . The authors concluded that TPSA level was significantly higher in women with PCOS and correlated positively with LH/FSH, TT, and FGS, and that a higher FGS score of hirsutism correlates with a higher serum TPSA level [32].

Reporting from Sudan in a cross-sectional study, Mohajir Hussein and colleagues found significant difference between the mean TPSA in PCOS cases ($n = 50$) (0.025 ± 0.013 ng/ml) than normal fertile control subjects ($n = 40$) (0.004 ± 0.005 ng/ml; $p = 0.001$), and infertile patients without PCOS ($n = 11$) (0.013 ± 0.005 ; $p = 0.004$) and very weak, insignificant, negative correlation of TPSA and anti-mullerian hormone ($r = -0.132$, $p = 0.360$). However, the authors found the AUC following ROC curve analysis for TPSA regarding the fertile controls to be 0.924 (92.4%), 0.790 (79.0%) regarding infertile without PCOS, and 0.501 (50.1%) for the infertile PCOS cases [33].

In Turkey, Vural and colleagues recruited 43 females and 43 age-matched health controls to determine if TPSA levels

was increased in PCOS and the possibility of TPSA being used as a diagnostic marker of hyperandrogenism in a prospective case-controlled study [34]. The authors observed that the mean BMI, WHR, FGS, LH/FSH, Tg, VLDL TT, and DHEAS were demonstrated to be higher with lower SHBG in PCOS cases than the healthy controls ($p < 0.005$, respectively). In addition, serum TPSA levels were found to be significantly higher in PCOS (PSA: 0.026 ± 0.023 ng/mL in PCOS versus PSA: 0.009 ± 0.008 ng/mL in healthy controls, $p < 0.001$). Positive correlations between PSA and FGS ($r = 0.417$, $p < 0.001$), PSA and TT ($r = 0.456$, $P = 0.03$), and between PSA and DHEAS ($r = 0.268$, $p = 0.02$) with a negative correlation between SHBG and PSA ($r = -0.40$, $p = 0.04$). These findings led Vural and colleagues to conclude that PSA appears to be a promising marker of endogenous androgen excess in females suffering from PCOS [34].

In another case-control study conducted in Turkey aimed to assess the diagnostic value of TPSA and fPSA in women with 62 PCOS patients (group A=42 anovulatory PCOS; group B=20 ovulatory PCOS) and 35 healthy controls by UkinC and colleagues, the authors found that in group A, a TPSA level > 10 pg/ml yielded a sensitivity of 73.2%, a specificity of 80%, and a diagnostic accuracy of 73%, with a positive predictive value of 88.2% and a negative predictive value of 59.3% and a fPSA level of greater than 2.1 pg/ml yielded a sensitivity of 71.2%, a specificity of 80.4%, and a diagnostic accuracy of 87%, with a positive predictive value of 87.2% and a negative predictive value of 58.4%. In group B, a PSA level > 10 pg/ml yielded a sensitivity of 65%, a specificity of 80%, and a diagnostic accuracy of 73%, with a positive predictive value of 76.5% and a negative predictive value of 69.6% and a fPSA level > 2.1 pg/ml yielded a sensitivity of 65.4%, a specificity of 80.4%, and a diagnostic accuracy of 87%, with a positive predictive value of 75.5% and a negative predictive value of 68.4%. These findings led authors to conclude that circulating androgens and hirsutism are independently associated with the degrees of PSA and fPSA in PCOS women and that increased plasma levels of PSA (> 10 pg/ml) and fPSA (> 2.1 pg/ml) could be helpful as a diagnostic tool for women with ovulatory or anovulatory PCOS [35].

4.3. Mechanistic Considerations

The mechanisms underlying the increased TPSA in PCOS have attracted immense attention [34-36]. However, a large number of research evidence seems to link this to the up-regulation of PSA-specific gene expression in hormone-responsive tissues secondary to hyperandrogenemia inherent in these patients of PCOS as concluded by Vural and colleagues [34], and as was earlier clarified by Zarghami and colleagues [36]. Hyperandrogenism is considered the major clinical hallmark of the diverse metabolic disturbances in PCOS [37]. This was corroborated in this current study where we observed TPSA status association with all diverse biochemical and metabolic indices usually linked to hyper-

androgenemia in PCOS such as menstrual disorders, ovulatory dysfunctions, metabolic syndrome, and its associated features (obesity, dyslipidemia, hypertension, hyperglycemia), FGS, cardiovascular risk, insulin resistance, etc, as previously described [37, 38].

4.4. Relevance to Clinical Practice and Future Studies

The current study findings inform the need to engage the use of TPSA as an index of hyperandrogenemia which seems to underline most of the anthropometric, clinical, biochemical, and metabolic disturbances in Nigerian females with PCOS. However, future studies should be geared toward a detailed evaluation of the parameters that influence TPSA among Nigerian females with PCOS.

4.5. Strength and Limitations

The study was strengthened by its relatively large sample size. Yet, the study was limited by some factors which are potential areas for improvement in future studies. As with most observational studies, the findings here do not in any way infer causality but mere association. The study was also a single-center study, so its findings may not reflect the larger population within the studied region and must be interpreted with caution.

5. Conclusion

Compared to healthy age-matched controls, PCOS patients had higher TPSA status including other adverse anthropometric, clinical, hormonal, and metabolic profiles. In addition, those PCOS patients with higher TPSA status had more unfavorable anthropometric, clinical, hormonal, and metabolic profiles compared to those with the lowest TPSA status. TPSA correlated significantly with diverse hormonal and metabolic parameters among the PCOS patients and was also associated with oligo/amenorrhea, oligo/anovulation, hyperandrogenism, Rotterdam phenotype A, moderate/severe FGS, overweight, generalized/abdominal obesity, hypertension, dyslipidemia, cardiovascular risk, oxidative stress risk, metabolic syndrome, and insulin resistance among the PCOS patients. Serum TPSA level was a discriminative biomarker for the diagnosis of PCOS among the entire PCOS patients, however, a more robust discriminatory potential of TPSA was observed among individuals with the Rotterdam phenotype A. The current findings indicate a relationship between TPSA and diverse features in PCOS directly related to the hyperandrogenemia inherent in PCOS.

Abbreviations

AC Atherogenic Coefficient

AIP	Atherogenic Index of Plasma
BMI	Body Mass Index
CRI-1	Castelli Risk index 1
CRI-2	Castelli Risk index 2
DHEAS	Dehydroepiandrosterone Sulphate
DBP	Diastolic Blood Pressure
E2	Estradiol
EDTA	Ethyl Diamine Tetra-acetic Acid
FSH	Follicle-stimulating Hormone
FPG	Fasting Plasma Glucose
FGS	Ferriman-Gallwey Score
FIN	Fasting Insulin
GSH-Px	Glutathione Peroxidase
HA	Hyperandrogenism
HbA1c	Glycated Hemoglobin A1c
HC	Hip Circumference
HDL-C	High-density Lipoprotein Cholesterol
hs-CRP	High-sensitivity C-reactive Protein
HOMA-IR	Homeostatic Model Assessment of Insulin Resistance
IGF-1	Insulin-like Growth Factor 1
IGFBP-1	Insulin-like Growth Factor Binding Protein
IR	Insulin Resistance
LH	Luteinizing Hormone
LDL-C	Low-density Lipoprotein Cholesterol
LAP	Lipid Accumulation Product
MDA	Malondialdehyde
OA	Oligo-anovulation
PCOS	Polycystic Ovary Syndrome
PCOM	Polycystic Ovary Morphology
RSUTH	Rivers State University Teaching Hospital
SBP	Systolic Blood Pressure
SHBG	Sex Hormone-binding Globulin
SOD	Superoxide Dismutase
PSA	Prostate-specific Antigen
TPSA	Total Prostate-specific Antigen
TT	Total Testosterone
TChol	Total Cholesterol
Tg	Triglyceride
TAC	Total Anti-oxidant Capacity
VAI	Visceral Adiposity Index
WC	Waist Circumference
WHR	Waist Hip Ratio

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Author Contributions

Collins Amadi: Conceptualization, Data curation, Formal

Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Johnbosco Chidozie Okafor: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Ezra Agbo: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

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The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author (CA) upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Salari N, Nankali A, Ghanbari A, Jafarpour S, Ghasemi H, Dokaneheifard S, et al. Global prevalence of polycystic ovary syndrome in women worldwide: a comprehensive systematic review and meta-analysis. *Arch Gynecol Obstet.* 2024; 310(3): 1303-14.
- [2] Felix OE, Florence KM, Moses BE. Prevalence of polycystic ovarian syndrome in women of childbearing age within Port Harcourt metropolis in Nigeria using sonographic evaluation. *Health Sc J.* 2022; 16(7): 1-4.
- [3] Unfer V, Kandaraki E, Pkhaladze L, Roseff S, Vazquez-Levin MH, Laganà AS, et al. When one size does not fit all: reconsidering PCOS etiology, diagnosis, clinical subgroups, and subgroup-specific treatments. *Endo Metab Sci.* 2024; 15: 100159.
- [4] Harada M. Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research. *Reprod Med Biol.* 2022; 21(1): e12487.
- [5] Wu ZH, Tang Y, Niu X, Pu FF, Xiao XY, Kong W. Prostatic-specific antigen (PSA) levels in patients with polycystic ovary syndrome (PCOS): a meta-analysis. *J Ovarian Res.* 2019; 12(1): 94. <https://doi.org/10.1186/s13048-019-0569-2>
- [6] Nagaraj S, Naik AL, Pratibha K, Kumar VK. Prostate-specific antigen in women with PCOS and its correlation with total testosterone. *Int J Biotech Biochem.* 2019; 15(2): 87-95.
- [7] Li X, Lin S, Yang X, Chen C, Cao S, Zhang Q, et al. When IGF-1 meets metabolic inflammation and polycystic ovary syndrome. *Int Immunopharmacol.* 2024; 138: 112529.
- [8] Kanbour SA, Dobs AS. Hyperandrogenism in women with polycystic ovarian syndrome: Pathophysiology and controversies. *Androgens: Clin Res Therap.* 2022; 3(1): 22-30.
- [9] Maleki-Hajiagha A, Razavi M, Rezaeinejad M, Sepidarkish M, Mehri A, Vesali S, et al. Serum prostate-specific antigen level in women with polycystic ovary syndrome: a systematic review and meta-analysis. *Horm Metab Res.* 2019; 51(04): 230-42.
- [10] Naing L, Winn T, Rusli BN. Practical issues in calculating the sample size for prevalence studies. *Arch Orolfac Sci.* 2006; 1: 9–14.
- [11] Yagi K. Free Radicals in Diagnostic Medicine. Lipid peroxides and related radicals in clinical medicine. In: Armstrong D (ed). New York: Plenum Press; 1994: 1-15.
- [12] Misra HP, Fridovich I. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. *J Biol Chem.* 1972; 247(10): 3170-5.
- [13] Rotruck JT, Pope AL, Ganther HE, Swanson AB, Hafeman DG, Hoekstra W. Selenium: biochemical role as a component of glutathione peroxidase. *Science.* 1973; 179(4073): 588-90.
- [14] Koracevic D, Koracevic G, Djordjevic V, Andrejevic S, Cosic V. Method for the measurement of antioxidant activity in human fluids. *J Clin Pathol.* 2001; 54(5): 356-61.
- [15] Katerji M, Filippova M, Duerksen-Hughes P. Approaches and Methods to Measure Oxidative Stress in Clinical Samples: Research Applications in the Cancer Field. *Oxid Med Cell Longev.* 2019; 2019: 1279250. <https://doi.org/10.1155/2019/1279250>
- [16] Chang S, Dunaif A. Diagnosis of Polycystic Ovary Syndrome: Which Criteria to Use and When? *Endocrinol Metab Clin North Am.* 2021; 50(1): 11-23. <https://doi.org/10.1016/j.ecl.2020.10.002>
- [17] Livadas S, Diamanti-Kandarakis E. Polycystic ovary syndrome: Definitions, phenotypes, and diagnostic approach. *Front Horm Res.* 2013; 40: 1–21.
- [18] Rahmatnezhad L, Moghaddam-Banaem L, Behrouzi Lak T, Shiva A, Rasuli J. Free androgen index (FAI)'s relations with oxidative stress and insulin resistance in polycystic ovary syndrome. *Sci Rep.* 2023; 13(1): 5118. <https://doi.org/10.1038/s41598-023-31406-0>
- [19] Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrinol Metab* 1961; 21: 1440-7.
- [20] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia.* 1985; 28: 412–9.

- [21] Friedewald WT, Levy RL, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge Clin Chem 1972; 18: 499-502.
- [22] Emokpae MA, Van-Lare TO, Babatunde EM. Cardiovascular risk is independently associated with body mass index in women with polycystic ovarian syndrome in Lagos, Nigeria. Fertil Reprod. 2024; 6(03): 143-9.
- [23] Glintborg D, Rubin KH, Nybo M, Abrahamsen B, Andersen M. Cardiovascular disease in a nationwide population of Danish women with polycystic ovary syndrome. Cardiovasc Diabetol. 2018; 17: 1-2.
- [24] Kałużna M, Czapka-Matyasik M, Kompf P, Moczko J, Wachowiak-Ochmańska K, Janicki A, et al. Lipid ratios and obesity indices are effective predictors of metabolic syndrome in women with polycystic ovary syndrome. Ther Adv Endocrinol Metab. 2022; 13: 20420188211066699. <https://doi.org/10.1177/20420188211066699>
- [25] WHO. Physical Status: The Use and Interpretation of Anthropometry: Report of a World Health Organization (WHO) Expert Committee. Geneva, Switzerland: World Health Organization; 1995.
- [26] World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation, Geneva, 8-11 December 2008 [Internet]. Geneva: World Health Organization; c2011 [cited 2024 December 3]. Available from: <http://www.who.int/iris/handle/10665/44583>
- [27] Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA. 2010; 303: 2043-2050. <https://doi.org/10.1001/jama.2010.650>
- [28] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106(25): 3143-421.
- [29] Mardanian F, Heidari N. Diagnostic value of prostate-specific antigen in women with polycystic ovary syndrome. J Res Med Sci. 2011; 16(8): 999-1005.
- [30] Rudnicka E, Radowski S, Suchta K. Prostate-specific antigen (PSA) in diagnosis of polycystic ovarian syndrome - a new insight. Gynecol Endocrinol. 2016; 32(11): 931-935.
- [31] Hurjahan-Banu HM, Sukanti-Shah NA, Sadiqa-Tuqan TS, Fariduddin M. Prostate-specific antigen is raised in polycystic ovary syndrome. Endocrinol Metab Int J. 2018; 6(4): 297-300.
- [32] Ibrahim WW, Salah RK, Abbas WM. Serum prostate-specific antigen level in women with polycystic ovary syndrome. J Fac Med Baghdad. 2016; 58(2): 136-9.
- [33] Mohajir Hussein AM, Hussein E, Eltom A. Assessment of serum Prostate-specific antigen (PSA) level among Sudanese women with polycystic ovarian syndrome In Khartoum state. Sch J Appl. Med Sci. 2017; 5: 1288-96.
- [34] Vural B, Ozkan S, Bodur H. Is prostate-specific antigen a potential new marker of androgen excess in polycystic ovary syndrome? J Obstet Gynaecol Res. 2007; 33(2): 166-73.
- [35] UKINC K, Ersoz HO, Erem C, Hacıhasanoglu AB. Diagnostic value of prostate-specific antigen (PSA) and free prostate-specific antigen (fPSA) in women with ovulatory and anovulatory polycystic ovary syndrome. Endocrine. 2009 Feb; 35(1): 123-9.
- [36] Zarghami N, Grass L, Diamandis EP. Steroid hormone regulation of prostate-specific antigen gene expression in breast cancer. Br J Cancer. 1997; 75: 579-588.
- [37] Sanchez-Garrido MA, Tena-Sempere M. Metabolic dysfunction in polycystic ovary syndrome: Pathogenic role of androgen excess and potential therapeutic strategies. Mol Metab. 2020; 35: 100937. <https://doi.org/10.1016/j.molmet.2020.01.001>
- [38] Green KI, Amadi C. The impact of BMI on the plasma glucose and lipid status of women with polycystic ovary syndrome. Int J Res Med Sci. 2018; 6: 3832-7.

Research Field

Collins Amadi: General endocrinology, Metabolic Disorders, Cancer Biochemistry, COVID-19 Biochemistry, Clinical Nutrition

Johnbosco Chidozie Okafor: General Endocrinology, Metabolic Disorders, Cancer Biochemistry, COVID-19 Biochemistry, Clinical Nutrition

Ezra Agbo: General Endocrinology, Metabolic Disorders, Cancer Biochemistry, COVID-19 Biochemistry, Clinical Nutrition