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Evaluation of Plasma Prolidase Level as a Diagnostic and Prognostic Biomarker for Polycystic Ovary Syndrome

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Abstract

Background: The key features of polycystic ovary syndrome (PCOS) are oligo-anovulation, hyperandrogenism, and polycystic ovaries. Elevated plasma prolidase activity is closely related to the pathophysiology of PCOS, in which increased ovarian stromal volume and atretic follicles may be accompanied by changes in extracellular matrix remodeling.

Objectives: Assessment of plasma prolidase levels in PCOS and to compare these levels between its different phenotypes as a marker for diagnosis and prognosis of the syndrome.

Patients and Methods: A case–control study included 44 women who were diagnosed with PCOS, and 48 healthy, ovulatory women. Plasma prolidase levels were measured and compared between the two groups and across different PCOS phenotypes.

Results: The mean prolidase level was significantly higher in PCOS (103.8 ± 82 ng/ml) than in controls (8.4 ± 4.1 ng/ml), the cut-off value (>31 ng/ml) was found to be 81.82% sensitive, 93.75% specific as a predictor of PCOS. The mean prolidase levels were higher in the PCOS group with ≥20 antral follicles; a positive correlation was found between prolidase level and the number of antral follicles in PCOS. Additionally, the mean prolidase levels varied significantly among the different PCOS phenotypes, with the polycystic ovary. hyperandrogenism oligo-anovulation (PHO) phenotype found to have the highest level.

Conclusion: Plasma prolidase has a potential to serve as a useful, inexpensive and easily assessable marker for the diagnosis of PCOS. Its levels were directrly correlated with the number of antral follicles in PCOS women, suggesting that it can be used as a tool to replase ultrasound imaging. Proidase levels vary significantly among the different PCOS phenotypes, so it could be used for monitoring the disease.

Keywords: Polycystic ovary syndrome, Prolidase, Rotterdam criteria.

Introduction

Polycystic Ovarian Syndrome (PCOS), also termed as hyperandrogenic anovulation (HA), or Stein–Leventhal syndrome, is one of the commonest endocrine diseases affecting females during reproductive life, as well as the young pre-pubertal girls (1). In addition, PCOS is a chronic disease that impacts women across their lifespan with expected lifelong sequelae like type II diabetes mellitus, dyslipidemia, cardiovascular disorders, as well as an increased risk of endometrial, breast, and ovarian carcinomas (2, 3). For this reason, early and correct diagnosis of PCOS is important not only to avoid eventual health

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morbidities but also to decrease economic burden (4). It is essential to recognize that PCOS is a syndrome with several possible etiologies and a wide range of features (5). The Rotterdam criteria are the most widely applied diagnostic criteria, which define the syndrome as a combination of hyperandrogenism and anovulation with polycystic ovaries (6). According to this definition four PCOS phenotypes are recognized in clinical practice: polycystic ovary morphology+ hyperandrogenism + oligo anovulation (PHO), oligo anovulation + hyperandrogenism (OH), polycystic ovary morphology+ hyperandrogenism (PH) and polycystic ovary morphology+ oligo anovulation (PO). The hyperandrogenism component of these criteria is marked by elevated levels of androgens, while the anovulation is represented by irregular menstruation, they do not present any difficulty in recognition. However, the major hurdle is to determine polycystic ovary by ultrasonography. Despite the availability of high-resolution ultrasound imaging, the detection of PCOS remains challenging, as most targeted patients are teenagers and young females, who are not willing to undergo transvaginal ultrasound scanning. Furthermore, obesity, a common feature of the syndrome, adds difficulty in trans-abdominal ultrasound imaging. In this manner, the identification of the ovarian morphology remains unclear (5). Additionally, till date, a common management strategy is applied for the patients independent on their phenotype, hence, there is a need for a marker in PCOS that is both qualitative and quantitative. This marker should possess both diagnostic as well as prognostic value and help in treating and monitoring the syndrome (7). Prolidase is an enzyme with multiple functions that carries the exclusive capacity to discredit amino dipeptides. It is engaged in the final step of collagen metabolism and possibly in the adjustment of peptide hormones (8). In mammals prolidases are detected in the cytoplasm and act initially to release proline in the last step of protein metabolism, especially throughout the synthesis and degeneration of collagen (9). Alterations in prolidase function were reported in various pathological conditions and malignancies like hypertension, erectile dysfunction and melanoma in addition to breast, lung and endometrial carcinoma (10, 11). In gynecology it has been linked to preeclampsia and early pregnancy loss (12, 13). Previous studies suggested that matrix – metalo-proteinase (MMP) can be engaged in the pathogenesis of PCOS through adjusting ovarian tissue remodeling. Some studies found that follicular fluid or the serum samples taken from PCOS patients contains elevated level of MMP-2 and MMP-9 compared to regularly ovulating women, clearly indicating increased gelatinolytic activity in association with PCOS (14). Since prolidase is considered as a member of MMP and a key enzyme of the extracellular matrix (ECM), hence elevated serum prolidase level might be closely related to the pathophysiology of PCOS, which is characterized by increased ovarian stromal volume, atretic follicles and accompanied with changes in extracellular matrix remodeling (15). However, few studies have focused on the value of prolidase, in pathogenesis of PCOS (9). Additionally, there is paucity in the information regarding its correlation with ovarian morphology and the clinical phenotypes of this syndrome. This study aimed to assess plasma prolidase levels in PCOS and to compare its levels between different PCOS phenotypes to investigate its utility as a marker for diagnosis and prognosis of PCOS.

Patients and Methods

Study design: This is a case-control study that was carried out in the Gynecological Department at Azadi Teaching Hospital / Kirkuk over a period of nine months from November 2024-April 2025. The study has gained approval from the scientific council of gynecology and obstetrics / IRAQI Board for medical specializations. The study

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involved 92 females at reproductive age (18-40 years) who were recruited from the consultancy clinic, divided into two groups: 44 patients who were diagnosed as PCOS (case group) and 48 healthy ovulatory women as (control group).

Inclusion criteria: The patients in the PCOS group were selected according to the Rotterdam criteria (16), by the existence of two of the following criteria:

-oligo-ovulation and/or anovulation.

-Hyperandrogenism (clinically: presence of acne, hirsutism, alopecia).

-Polycystic ovaries as seen by ultrasound scan: (by finding of > 12 follicles / ovary of 2-9 mm in size and an ovarian volume of >10ml) (10).

And accordingly, four phenotypes were recognized in PCOS group:

-Polycystic ovary morphology + hyperandrogenism + oligo-anovulation (PHO): 24 patients.

-Oligo-anovulation + hyperandrogenism (OH): 6 patients.

-Polycystic ovary morphology + hyperandrogenism (PH): 10 patients.

-Polycystic ovary morphology + oligo-anovulation (PO): 4 patients.

The control group consist of healthy ovulatory women with normal ovarian morphology confirmed by ultrasound.

Exclusion criteria: Anovulation and hirsutism unrelated to PCOS, diabetes mellitus, thyroid disease, cardiovascular disease, history of ovarian drilling or surgery as well as taking drugs known to alter hormonal parameters or ovulatory function (ovulation induction and metformin) for the last 3 months.

Data collection tools: Women meeting the inclusion criteria were interviewed and informed about the study, informed consent was taken from them prior to their inclusion in the study and sample taking. Detailed history was taken including; age, obstetrical history, gynecological history including (subfertility, menstrual history and previous gynecological surgeries), history of chronic medical diseases and drug history. They were subject to complete physical examination including general examination for:

-Waist/hip ratio (WHR): waist circumference was measured in standing position, at the half of the distance between the lower ribs and crest of the pelvis, hip circumference was measured as the widest gluteal circumference a healthy WHR for women is ≤ 0.85 (17).

- Ferriman-Gallwey score: was done to evaluate patients for hirsutism & its severity a chart was used to provide scores, with a scale of 0-3 on 12 points in the body (upper lip, face, chin, jaw and neck, lower back, arm, thigh, chest, upper abdomen, upper back, lower abdomen and perineum), depending on severity. A score < 4 is regarded to be normal while a score ≥ 4 indicates hirsutism (13).

-Body mass index (BMI): calculated by weight (in kilograms) divided by the square of height (in meters), BMI=Weight (Kg) /Square height (m^2) participant were classified according to BMI as: normal ($\leq$ 24.99 kg/m^2), overweight (25-29.99 kg/m^2) and obese ($\geq$ 30 kg/m^2) (18). Abdominal and/or transvaginal ultrasound examination was performed by experienced sonographers to visualize the ovaries for all women.

Sample collection for hormonal profile and prolidase level: All women were investigated for hormonal data including TSH, LH, FSH, Free testosterone, prolactin as well as prolidase levels. Five ml of blood was drowned from forearm and putted in an anticoagulant tube (containing EDTA) centrifuged and the top layer plasma was aspirated and stored at -20 degree.

Estimation of hormonal levels: TSH, LH, FSH, prolactin and free testosterone levels were measured using a fluorescence immunoassay technique by AFIAS machine, manufactured by Boditech Med Inc.'s technical services, South Korea. The tests use a sandwich immune-detection method. The detector antibodies in

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buffer bind to antigens in the sample forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized-antibodies on a test strip. More antigens in the sample will form the more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by the instrument for AFIAS test to show TSH, LH, FSH, prolactin and free testosterone concentration (19, 20).

Estimation of prolidase level: Measurement of prolidase activity in the plasma was done using enzyme-linked immune sorbent assay (ELISA) by YHB20200323720 kit produced by Shanghai Yanhui Biological Technology Co., Ltd., under the trade name YH Biosearch Laboratory. The plate has been pre-coated with human PEPD antibody. PEPD present in the sample is added and binds to antibodies coated on the wells. And then biotinylated human PEPD Antibody is added and binds to PEPD in the sample. Then Streptavidin-HRP is added and binds to the Biotinylated PEPD antibody. After incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of human PEPD. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm based on a standard curve (8). (Reference range: 2 ng/ml →600 ng/ml, sensitivity: 0.97 ng/ml).

Statistical Analysis

Statistical analysis of the data was done using version 25 of Statistical Package for Social Sciences (SPSS). The data expressed inform of mean, ranges and standard deviation. Categorized data were expressed in the form of percentages and frequencies. Independent t-test was applied for comparison between the continuous variables. To test association between continuous variables, the Pearson's correlation was applied. The receiver operating characteristic (ROC) curve was conducted for prolidase level as predictor of PCOS. A P – value at a level of < 0.05 was regarded as significant.

Results

Age, anthropometric and clinical characteristics of study groups: The age range of patients with PCOS was between 20-40 years with the mean age 28.6 ± 6.2 and the controls were between 18-38 years with the mean age 29 ± 5.3, there was no significant difference among the study groups in term of mean age (P value =0.79). There were no statistical differences in BMI and WHR between PCOS cases and controls. However, the mean of Ferryman-Gallwey score in cases (8.7 ± 2.8) was higher than in the controls (2.125 ± 0.7), with significant difference between the two groups (P value <0.001), as shown in Table 1. The distribution of cases and controls according to clinical and anthropometric characteristics, as well as the comparison of means of the anthropometric characteristics, are shown in Table 2. It was found that 47.7% of PCOS cases were nulliparous compared to 33.3% in the control group. Additionally, 9.1% of cases had history of one or more miscarriages compared to 16.7% in control group. However, there was no significant difference regarding parity and history of miscarriage among the two groups. (p value = 0.2) Of the PCOS cases 61.4% had history of subfertility, of which 56.8% were primary and 4.5% were secondary subfertility. This is compared to only 4.2% of women in the control group with history of subfertility, all of which were of primary type. Patients with PCOS had higher percentage of oligomenorrhoea (77.3%) in comparison to those in control group (4.2%). Women having PCOS had higher rate of subfertility and oligomenorrhoea compared to women in control group (P value < 0.001*). Regarding BMI, the highest proportion of PCOS cases (45.5%) were obese, while in the control group, the highest proportion (37.5%) of women had normal BMI. In addition, 13.6% of cases had abnormal WHR > 0.85 compared to 6.3% in the

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control group. However, there were no significant differences among the two groups regarding BMI and WHR. In relation to hirsutism, 90.9% of cases had Ferryman-Gallwey score ≥ 4, while none of the participants in the control group had a score ≥ 4, with statistically significant difference.

Table 1. Comparison in means of age and anthropometric data between study groups.

Anthropometric data	Cases	Controls	P Value
Age (years)	28.6 ± 6.2	29 ± 5.3	0.79
Body Mass Index (BMI) (kg/m^2)	28.7 ± 4.1	27.35 ± 4.8	0.15
Waist/ Hip Ratio (WHR)	0.8 ± 0.04	0.8 ± 0.03	0.06
Ferriman-Gallwey score	8.7 ± 2.8	2.125 ± 0.7	< 0.0001*
* The difference was statistically significant (Student T test; P< 0.0001)			

Table 2. Comparison in means of age and anthropometric data between study groups.

Variables	Cases N=44		Controls N=48		P Value
	No	%	No	%	
Parity					
P0	21	47.7	16	33.3	0.2
P1+	23	52.3	32	66.7	
Miscarriage					0.28
None	40	90.9	40	83.3	
One or more	4	9.1	8	16.7	
Subfertility					< 0.001*
None	17	38.6	46	95.8	
yes	27	61.4	2	4.2	
→Primary	→25	56.8	→2	4.2	
→Secondary	→ 2	4.5	→0	0	
Menstrual Cycle					< 0.001*
Regular	10	22.7	46	95.8	
Oligo-menorrhea	34	77.3	2	4.2	
BMI					
Normal	10	22.7	18	37.5	0.278
Overweight	14	31.8	14	29.1	
Obese	20	45.5	16	33.3	
Waist/Hip Ratio					
≤ 0.85	38	86.4	45	93.7	0.053
> 0.85	6	13.6	3	6.3	
Ferriman-Gallwey score					<0.001*
< 4	4	9.1	48	100.0	
≥4	40	90.9	0	0.0	
* Statistically significant association (T test, p < 0.001)					

Hormonal profile and prolidase level in study groups: Table 3 shows the hormonal profile of patients with PCOS and those in control group, revealing significantly higher mean levels of the hormones (TSH, LH, free testosterone, prolactin) in PCOS cases compared to controls (p-value < 0.0001). However, the mean value of the FSH hormone was lower in PCOS (4.8±1.5) than in the control group (9.5±5.2), (p-value < 0.0001). The mean prolidase level in PCOS group (103.8 ± 82) was significantly higher in comparison with the control group (8.4 ± 4.1) (P value ≤ 0.0001*).

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Table 3. Comparison of the study groups according to means of hormonal data and prolidase level.

Hormonal Data	Cases	Controls	P value
Thyroid Stimulating Hormone (TSH) (µ IU/ml)	2.4 ± 0.8	1.1 ± 0.7	< 0.0001*
Follicle Stimulating Hormone (FSH) (mIU/ml)	4.8 ± 1.5	9.5 ± 5.2	< 0.0001*
Luteinizing Hormone (LH) (mIU/ml)	9.9 ± 3.6	5.5 ± 3.9	< 0.0001*
Free Testosterone (nmol/ml)	2.5 ± 0.8	0.6 ± 0.5	< 0.0001*
Prolactin (ng/ml)	19.2 ± 4.1	15.2 ± 4.3	< 0.0001*
Prolidase (ng/ml)	103.8 ± 82	8.4 ± 4.1	<0.0001*
* The differences were statistically significant (Student T test; P< 0.0001)			

Receiver Operator Characteristic (ROC) curve analysis was constructed for evaluation of the potential of prolidase biomarker as predictor for PCOS as shown in Figure 1. Based on the area under the curve (AUC = 85.5%) the cut-off value of prolidase was 31ng/ml, specifically, plasma prolidase level > 31 ng/ml is found to be predictive for PCOS. The cut-off value of prolidase was reported with a sensitivity of 81.82% (representing the proportion of observations that are predicted to be positive when the women had PCOS) and specificity of 93.75% (represents the proportion of observations that are predicted to be negative when women are not having PCOS), with a positive predictive value of 100% and negative predictive value of 85.71%. Youden's Index = 0.7557 that is a relatively high value, suggesting that 31 ng/ml is a good cutoff point for diagnosing PCOS.

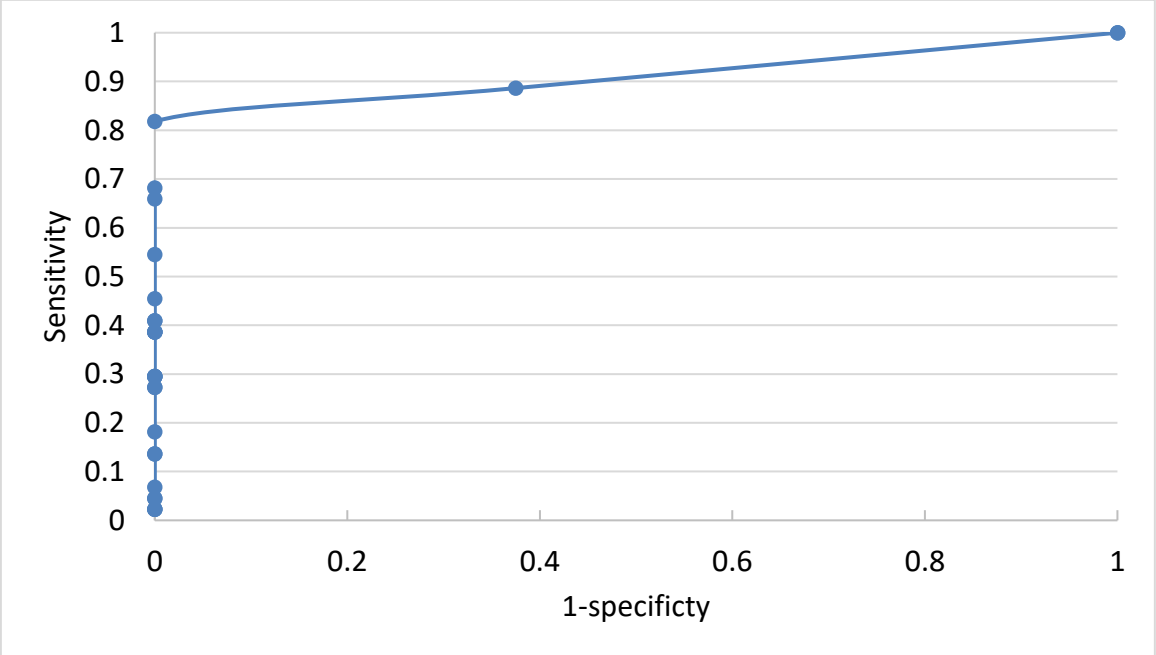

Figure 1. Receiver Operator Curve (ROC) for the cut-off point of plasma prolidase as a predictor for PCOS.

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Prolidase level according to the number of antral follicles in PCOS: Women with PCOS were sub-divided into 3 groups according to the number of antral follicles in the ovary, as shown in Table 4. The mean plasma prolidase level appears to be higher with increasing numbers of ovarian antral follicles, with statistically significant differences between the 3 subgroups using the ANOVA test (p-value < 0.0001*). Further analysis of the data by Post Hoc Multiple Comparisons showed that the mean prolidase levels were higher in the group with ≥ 20 antral follicles compared to group of patients with fewer than 15 antral follicles and those with 15-19 antral follicles (p-value = 0.001). Although the level of prolidase in the group with 15-19 antral follicles was higher than that reported in the group fewer than 15 antral follicles, the difference between the groups was not significant (p-value = 0.341).

Table 4. Differences in mean prolidase level among the diseased group by number of antral follicles in the ovaries.

No of antral follicles in the Ovaries	No. of Patients	Mean prolidase level (ng/ml)	post hoc multiple comparisons	P value
Less than 15 antral follicles	7	21.2 ± 5.9	<15 * 15-19 <15 * ≥20	0.341 0.000*
15-19 antral follicles	15	68.4± 44.9	15-19 * <15 15-19* ≥20	0.341 0.001*
20 antral follicles & More	22	154±81.1	≥20 * <15 ≥20 * 15-19	0.000* 0.001*
*Statistically Significant Differences (ANOVA, Bonferroni Post Hoc Multiple Comparisons)				

Furthermore, the Pearson correlation test showed that there was a positive correlation (r= 0.7) between number of antral follicles in the ovaries in PCOS cases and plasma prolidase levels (p < 0.001) as shown in Figure 2.

Prolidase level in PCOS phenotypes: Table 5 shows the mean prolidase level in the different PCOS phenotypes Although there were statistically significant differences in mean plasma prolidase level between the four PCOS phenotype groups (P = 0.007), the PHO phenotype had the highest prolidase level (146.3 ± 79.7) and the OH phenotype had the lowest recorded level of this biomarker (19.2 ± 2.5). However, Post Hoc Multiple Comparisons showed that the differences in mean plasma prolidase were only statistically significant between patients with OH phenotype had the lowest recorded level of this biomarker (19.2 ± 2.5). However, Post Hoc Multiple Comparisons showed that the differences in mean plasma prolidase were only statistically significant between patients with OH in relation to those with PHO and PH phenotypes (p-value = 0.005 and 0.028, respectively), while the rest of the differences failed to reach a statistically significant values.

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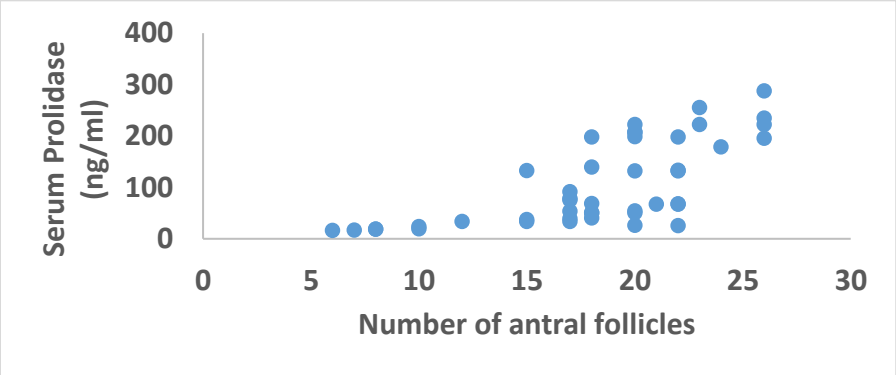

Figure 2. Correlation between Number of ovarian antral follicles and Prolidase level (r=0.7, P < 0.001).

Table 5. Differences in mean Prolidase level among the PCOS group according to phenotype.

Classification by clinical phenotype	No. of patients	Mean Prolidase level (ng/ml)	Bonferroni Post Hoc Multiple Comparisons	P-value
Oligo-menorrhea+ Hyperandrogenism (OH)	6	19.2 ± 2.5	OH * PO OH * PH OH* PHO	0.092 0.028* 0.005*
Polycystic ovary + Oligo-menorrhea (PO)	4	144.6 ± 77.9	PO * OH PO * PH PO * PHO	0.092 1.000 1.000
Polycystic ovary + Hyperandrogenism (PH)	10	137.6 ± 88.88	PH * OH PH * PO PH* PHO	0.028* 1.000 1.000
Polycystic ovary + Hyperandrogenism + Oligo-menorrhea (PHO)	24	146.3 ± 79.7	PHO * OH PHO * PO PHO * PH	0.005* 1.000 1.000
*Statistically Significant Differences (ANOVA, Bonferroni Post Hoc Multiple Comparisons)				

Discussion

PCOS is characterized by variable types of clinical manifestations. It consists of various physiological, metabolic, reproductive and gynecological dysfunctions making the diagnosis and monitoring of the syndrome challenging as no single diagnostic laboratory measure or diagnostic parameter appears to be sufficient (7). The core findings of the current study were firstly an elevated plasma prolidase level in PCOS that was strongly correlated with ovarian morphology and AFC and markedly changing across PCOS phenotypes reflecting specific aspects of the pathophysiology of the syndrome, secondly it provided a specific plasma prolidase cut off value for diagnosing PCOS. According to the distribution of study participants by demographic

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data, no significant differences were found in means of age, BMI, WHR, parity and miscarriage rates, which align with the results of N. Hilali et al. in their study (21). In contrast, Bhatnager R. et al. study (22) found no considerable difference regarding age between studied groups, but the PCOS subjects had considerably elevated BMI and WHR than the control participants. They related this to metabolic changes associated with the syndrome that can lead to anovulation. This inconsistency may be related to the difference in the characteristic and nature of the selected populations in the different studies. On the other hand, our study showed significantly higher rates of subfertility, menstrual cycle irregularity, and abnormal Ferriman-Gallwey scores in PCOS group compared to the control group. These may be related to peripheral biosynthesis and aromatization of estrogens and reduced levels of sex hormone-binding globulin, leading to elevated levels of free androgens, in addition to raised insulin levels that can lead to exaggerated ovarian androgen production. Similar observation was noted in the previous studies (21, 23). Our data revealed that TSH significantly elevated in PCOS subjects compared to controls. In contrast, other two studies by Bhatnager et al found that TSH levels did not significantly differ in PCOS and normal women (22, 23). We also detected higher testosterone, LH and prolactin levels in patients with PCOS than their controls. Consistent finding was revealed by the study of Hilali et al. (21). While in Bhatnager et all's study (22), prolactin levels were not significantly different between studied groups. Conversely, FSH levels were lower in PCOS group compared to controls, which agrees with other studies (22-24). However, in their study Hilali et al (21) found no difference in FSH level between the two groups. Difference in the hormonal profiles across studies may be related to the variations in the inclusion criteria applied for patients' selection, as well as the differences in the clinical phenotypes of the studied PCOS women. In our study we detected higher mean prolidase level in the plasma sample of PCOS patients (103.8 ± 82 ng/ml) than the control group (8.4 ± 4.1 ng/ml), indicating that raised prolidase levels could be potentially associated with the pathogenesis of PCOS. Since prolidase is an important regulator for ECM remodeling, it is suggested that prolidase may play a role in folliculogenesis and any changes in follicular development might be reflected in its serological levels (25). Till date, there are scarce studies published analyzing the role of prolidase in PCOS and all stated that prolidase activity was elevated in PCOS compared to normal women (21, 23, 26). On further evaluation of our potential biomarker (prolidase), the cut-off value of (>31ng/ml), was found to be (81.82%) sensitive and (93.75%) specific as a predictor for PCOS. In comparison, Bhatnager et al. (23) used the Mayara method, which is a biochemical assay designed to accurately measure prolidase enzyme activity in human samples particularly erythrocytes but it has been adopted for use in serum or plasma as well, for estimating prolidase levels in the serum, finding that the (cut-off value of plasma prolidase was 621.54 U/l), with a sensitivity of (93.76%) and a specificity of (89.34%). This difference in cut-off level with our study may be related to the difference in the method and units used for prolidase level estimation. Prolidase levels were further analyzed based on the number of antral follicles in PCOS groups. It was found that prolidase values increase with increasing number of antral follicles in ovaries, with patients having > 20 antral follicles recording the significantly highest prolidase level. Furthermore, Pearson correlation analysis of the data demonstrated that prolidase levels were positively correlated with the number of antral follicles, which can be related to the fact that the number of antral follicles in the ovaries reflect the changes within the ovarian ECM, which in turn is

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excellently reflected by plasma prolidase level in PCOS women. Consistent results were obtained in a single study by Syabakhash et al (26) in patients with PCOS, where prolidase activity was positively correlated with total oxidant status (TOS) as well as with follicle number. During prolidase analysis according to clinical phenotype of PCOS patients, the current study found a significant difference in prolidase level between different subgroups. Patients in the (POH) phenotype was found to have highest prolidase level, followed by (PO) phenotype, while the lowest level was recorded in (OH) phenotype. The highest prolidase levels in (POH) phenotype, which holds the whole key features of the syndrome, reflect the severity of the condition in this phenotype. Additionally, the relatively higher prolidase activity measured in (PO) phenotype might be related to the presence of oligomenorrhoea with polycystic ovarian morphology, reflecting an increasing number of unovulating antral follicles. These findings indicate that prolidase levels are more closely related to the features of PCOS and oligo menorrhea than to hyperandrogenism. Therefore, we suggest that prolidase might play a crucial role in the interaction of genotype and phenotype in PCOS. This was in accordance with the results of Bhatnager et al. (23), which was the only study we found evaluating the prolidase level in relation to the clinical phenotype. Finally, this study has several limitations. First, the sample size was small, and the second most significant point is that the proportion of the ovarian source of prolidase in the blood is unclear, making it difficult to assess the source of the detected prolidase activity.

Conclusion

Plasma prolidase has a potential to serve as a useful, inexpensive and easily assessable marker for the diagnosis and screening of PCOS. Prolidase levels were directly correlated with number of antral follicles in the ovaries of PCOS women, suggesting that it can be considered as a promising tool replacing ultrasound and its related difficulties. Prolidase levels vary significantly among the different phenotypes of PCOS, indicating that they are closely correlated with the severity of the syndrome and can be utilized as markers for monitoring, progression of the syndrome and they can be used to monitor response to treatment.

Source of funding: No source of funding.

Ethical clearance: This study was conducted in the Gynecological Department at Azadi Teaching Hospital, Kirkuk, over a period of nine months from November 2024 to April 2025. Ethical approval for this study was obtained from the Scientific Council of Gynecology and Obstetrics / Iraqi Board for Medical Specializations.

Conflict of interest: None.

Use of Artificial Intelligence (AI): The authors state they did not use any generative AI tools for creating or editing the manuscript's language.

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تقييم مستوى انزيم البروليديز في بلازما الدم كمؤشر حيوي تشخيصي وانذاري لمتلازمة تكييس المبايض

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الملخص

الخلفية: السمات الرئيسية لمتلازمة تكيس المبايض هي قلة الإباضة، وفرط الأندروجين، وتكيس المبايض. يرتبط ارتفاع نشاط بروليديز البلازما ارتباطًا وثيقًا بالفيزيولوجيا المرضية لمتلازمة تكيس المبايض، حيث قد يصاحب زيادة حجم سدى المبيض والجريبات الغارية تغيرات في إعادة تشكيل المصفوفة خارج الخلية.

الأهداف: تقييم مستويات بروليديز البلازما في متلازمة تكيس المبايض ومقارنة مستواها بين أنماطها الظاهرية المختلفة كمؤشر لتشخيص المتلازمة وتوقع سيرها.

المرضى والطرق: شملت دراسة الحالة والشاهد ٤٤ امرأة شُخِّصت بمتلازمة تكيس المبايض، و٤٨ امرأة سليمة التبويض. تم قياس مستوى بروليديز البلازما ومقارنته بين النساء في المجموعتين وبين الأنماط الظاهرية المختلفة لمتلازمة تكيس المبايض.

النتائج: كان متوسط مستوى البروليداز (١٠٣,٨ ± ٨٢ نانوغرام/مل) أعلى بشكل ملحوظ لدى المصابات بمتلازمة تكيس المبايض منه لدى مجموعة الضوابط (٨,٤ ± ٤,١ نانوغرام/مل)، ووُجد أن قيمة القطع (<٣١ نانوغرام/مل) حساسة بنسبة ٨١,٨٢٪، ونوعية ٩٣,٧٥٪ كمؤشر لمتلازمة تكيس المبايض. كان متوسط مستويات البروليداز أعلى في مجموعة متلازمة تكيس المبايض مع ≤٢٠ جريب غاري، ووُجد ارتباط إيجابي بين مستوى البروليداز وعدد الجريبات الغارية في متلازمة تكيس المبايض. بالإضافة إلى ذلك، اختلف متوسط مستويات البروليداز بشكل كبير بين الأنماط الظاهرية المختلفة لمتلازمة تكيس المبايض، حيث وُجد أن النمط الظاهري لتكيس المبايض + فرط الأندروجين + قلة الإباضة يظهر اعلى مستوى للبروليداز.

الاستنتاج: يتمتع إنزيم البروليديز البلازمي بإمكانية استخدامه كمؤشر مفيد، وغير مكلف، وسهل التقييم لتشخيص متلازمة تكيس المبايض. وقد ارتبطت مستوياته ارتباطًا مباشرًا بعدد الجريبات الغارية لدى النساء المصابات بمتلازمة تكيس المبايض، مما يشير إلى إمكانية استخدامه كأداة بديلة للتصوير بالموجات فوق الصوتية. وتختلف مستويات البروليديز اختلافًا كبيرًا باختلاف أنماط متلازمة تكيس المبايض، لذا يمكن استخدامه لمراقبة المرض.

الكلمات المفتاحية: متلازمة تكيس المبايض، البروليديز، معايير روتردام.

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