scientific reports

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Serum levels of galanin-like peptide and alarin are highly correlated with polycystic ovary syndrome

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To compare the levels of galanin-like peptide (GALP) and alarin between patients with polycystic ovary syndrome (PCOS) and a control group, and to explore the correlations between GALP/alarin and PCOS. We selected a total of 103 PCOS patients and 89 non-PCOS control patients who visited the hospital during the same period. The PCOS patients and the controls were assigned by body mass index (BMI) into PCOS subgroup 1 and control subgroup 1 (18.5 < BMI < 24 kg/m^2) and into PCOS subgroup 2 and control subgroup 2 (BMI ≥ 24 kg/m^2). The general indices (weight, height, waist circumference, and hip circumference), serum sex hormone concentrations, biochemical indices, and GALP and alarin levels were measured for all subjects, and the differences in each index were compared between the two groups. (1) The BMI, waist-to-hip ratio (WHR), lipid accumulation product (LAP), total testosterone (total T), luteinizing hormone (LH) levels, fasting insulin (FINS), triglycerides (TG), alanine transaminase (ALT), HOMA-IR, and GALP and alarin concentrations were significantly higher and the AST/ALT ratio was significantly lower in the PCOS patients than in the controls. (2) Correlation analysis showed that serum GALP levels were positively correlated with BMI, WHR, LAP, total T, LH, FINS, TG, HOMA-IR, and alarin, and negatively correlated with AST/ALT. Serum alarin levels were correlated positively with BMI, WHR, LAP, total T, LH, FINS, TG, HOMA-IR, and GALP, and negatively with FSH and AST/ALT. Serum LAP, FINS, LH, and alarin were independent factors that influenced serum GALP levels, and serum FINS, LAP, LH, and GALP were independent factors that influenced serum alarin concentrations. The areas under the receiver operating characteristic curves (95% confidence intervals) for serum GALP and alarin levels in predicting PCOS were 0.78 (0.713, 0.847) and 0.828 (0.766, 0.889), respectively, and the cutoff values were 0.895 and 0.355, respectively. GALP and alarin were highly expressed in PCOS patients and closely associated with factors such as IR, HA, and obesity, and they showed favorable predictive values for PCOS.

Keywords Polycystic ovary syndrome, Galanin-like peptide, Alarin, Insulin resistance, Obesity

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disease that damages the reproductive health of many women of childbearing age worldwide[1]. The typical characteristics of PCOS include androgen excess, polycystic ovaries, and ovulatory dysfunction. The onset of PCOS is not only associated with genetic and environmental factors, but likely also with metabolic diseases such as obesity and insulin resistance[2]. However, the exact cause of PCOS remains unclear. Although women with PCOS reflect an increased risk of experiencing cardiovascular, metabolic, and neoplastic diseases[3], its long-term impacts cannot be readily measured due to its complex pathogenesis and periodic progression. Therefore, research on PCOS should not only focus on the treatment of its clinical manifestations, but investigators need to more assiduously explore its underlying pathogenesis and work to prevent its long-term complications.

Galanin-like peptide (GALP) belongs to the galanin family of neuropeptides and contains 60 amino acids. GALP-expressing cells are principally confined to the arcuate nucleus of the hypothalamus and the posterior pituitary gland, and it increases gonadotropin secretion by stimulating the release of GnRH into the pituitary portal vein blood[4]. In addition, GALP-positive neurons can project to several areas of the brain so as to regulate

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feeding behavior, body weight changes, energy metabolism, and reproductive capability. However, the specific mechanism underlying GALP's involvement in PCOS is still unelucidated. Alarin is another member of the galanin family of neuropeptides and contains 25 amino acids, with its N-terminal alanine and C-terminal serine residues resulting from the splice variant of GALP mRNA[5]. Alarin participates in the onset of insulin resistance through increased free fatty acids[6], and modulates the reproductive system by regulating the hypothalamic-pituitary-gonadal axis [7]. Therefore, it is speculated that PCOS patients may harbor abnormal alarin levels.

In this case–control study, we compared the serum GALP and alarin levels between PCOS patients and normally ovulating women, so as to explore the pathogenesis of PCOS and to provide further research directions for the early diagnosis of and effective interventions for PCOS.

Materials and methods

Participants and grouping

This study comprised 103 PCOS patients and 89 non-PCOS control patients who visited the Reproductive Clinic of the Second Affiliated Hospital of Shandong First Medical University between January 2022 and June 2023.

The inclusion criteria for the PCOS patients were based on *the Rotterdam Criteria*[8] formulated by the American Society for Reproductive Medicine and the European Society of Human Reproduction and Embryology in 2003. Females treated for infertility during the same period who exhibited regular menstrual cycles (25 d < menstrual cycle < 35 d) were recruited as participants in the control group. None of the subjects possessed acute or chronic diseases—including diabetes, cardiovascular disease, thyroid disease, liver or kidney disease, autoimmune disease, malignant tumors, cognitive disorders, and acute or chronic inflammation. Patients who were administered hormonal therapy or any drug therapy in the previous three months were excluded. Data analysis of patient medical records in this study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Shandong First Medical University (Ethics approval number 202004014). All participants were informed regarding the purpose of this study and provided their informed consent.

Both the PCOS patients and controls were assigned to two subgroups according to body mass index (BMI): a PCOS subgroup 1 and control subgroup 1 (39 and 53 non-obese women, respectively, with $18.5 < BMI < 24$ kg/m^2), as well as a PCOS subgroup 2 and control subgroup 2 (64 and 36 overweight and/or obese women, respectively, with a $BMI \geq 24$ kg/m^2).

Methods

The weight, height, hip circumference (HC), and waist circumference (WC) of all subjects were measured by the same individual. The waist-to-hip ratio (WHR = WC [cm]/HC [cm]), BMI (body mass [kg]/height [m^2]), and lipid accumulation product (LAP= [WC (cm) − 58] ×triglyceride [TG {mmol/L}]) of each subject were also calculated.

Each subject came to the hospital in the early morning of the 2nd to 5th days of her menstrual cycle. After 15–30 min of sitting and resting, blood was drawn through the cubital vein (with the individual having fasted for over 12 h) to determine blood concentrations of reproductive endocrine hormones and biochemical indices, and 1 ml of serum was retained and frozen at − 80°C for the subsequent combined evaluation of serum GALP and alarin levels. Biochemical indices such as liver and kidney function, fasting blood glucose (FBG), and blood lipids were analyzed with a Hitachi 7600 automatic biochemical analyzer. Then, with a Beckman Coulter Gen-S automated analyzer, follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, estradiol (E2), prolactin (PRL), progesterone (P), and fasting insulin (FINS) were measured using a chemiluminescence method. We calculated the homeostasis model assessment of insulin resistance (HOMA-IR) as fasting insulin × fasting blood glucose/22.5. The serum levels of GALP (ELK Biotechnology Co., Ltd., catalog number: ELK9340, inter-assay variation: <10%) and alarin (Phoenix Pharmaceuticals Inc., catalog number: EK-026-34, inter-assay variation: <15%) were determined with an enzyme-linked immunosorbent assay (ELISA) kit.

Statistical methods

We conducted statistical analysis using SPSS 27.0, and all data were analyzed after fully controlling for confounding factors and by balancing baseline data. The measured data that conformed to a normal distribution are expressed as mean ± standard deviation, and compared between groups via independent-sample *t*-tests, and data that did not follow a normal distribution are expressed as M (P25, P75), and compared between groups via the Mann–Whitney U rank-sum test. The correlations between serum GALP or alarin concentrations and other parameters were evaluated via simple and multivariate stepwise regression analyses. Receiver operating characteristic (ROC) curves were constructed and areas under the ROC curves (AUCs) were applied to assess the value of GALP and alarin levels in predicting PCOS. We considered differences to be significant at $P < 0.05$.

Research technology roadmap

The research technology roadmap of the study was shown in Fig. 1.

Results

Comparisons of clinical indices, GALP, and Alarin between PCOS and controls

We herein evaluated 103 PCOS patients and 89 controls. The two groups were divided into two subgroups according to BMI: 39 and 64 cases in PCOS subgroups 1 and 2, and 53 and 36 cases in control subgroups 1 and 2, respectively.

BMI, WHR, LAP, total T, LH, FINS, TG, ALT, HOMA-IR, GALP, and alarin in the PCOS group were significantly higher than in controls, while the levels of AST/ALT were significantly lower than in the control group. There were no differences in other indices between the two groups (Table 1; Fig. 2).

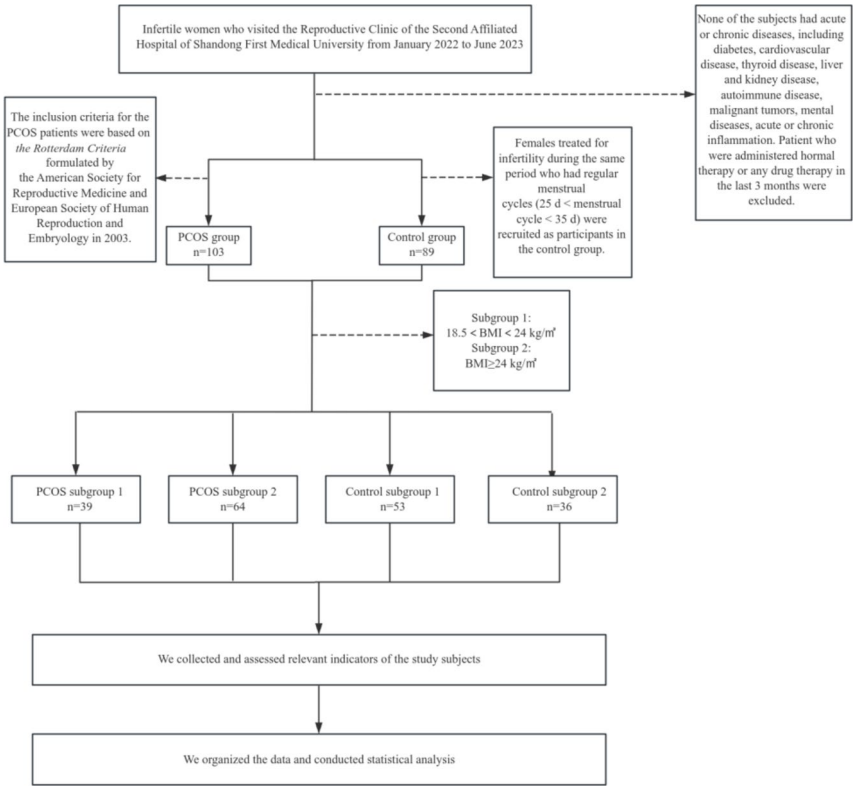

Fig. 1. Research technology roadmap.

	PCOS group ($n=103$)	Control group ($n=89$)	P
BMI (kg/m^2)	25.09 (23.03, 29.41)	22.72 (20.44, 26.22)	< 0.001**
WHR	0.79 ± 0.058	0.77 ± 0.046	0.002**
LAP	23.40 (12.15, 52.47)	16.20 (7.45, 24.58)	0.001**
P (ng/ml)	0.52 (0.42,0.66)	0.55 (0.42,0.71)	0.257
E_2 (pg/ml)	38.00 (27.35,45.62)	35.07 (27.58,49.08)	0.610
PRL (ng/ml)	11.50 (8.33,14.02)	12.38 (9.26,16.57)	0.144
total T (ng/dL)	25.26 (19.80,32.11)	17.46 (14.79,22.34)	< 0.001**
FSH (mIU/mL)	6.73 ± 1.43	6.85 ± 1.55	0.580
LH (mIU/mL)	6.39 (4.62,9.95)	3.94 (2.99,5.54)	< 0.001**
FINS (mU/L)	14.76 (10.89,23.10)	10.15 (6.91,16.49)	< 0.001**
TC (mmol/L)	4.58 (4.19,5.08)	4.59 (4.08,5.22)	0.779
TG (mmol/L)	1.09 (0.76,1.80)	0.97 (0.66,1.35)	0.010*
FBG (mmol/L)	5.32 ± 0.39	5.25 ± 0.40	0.258
ALT (U/L)	15.00 (11.00,23.00)	13.00 (10.00,19.00)	0.038*
AST (U/L)	16.00 (13.00,19.00)	16.00 (14.00,17.75)	0.761
AST/ALT	0.94 (0.80,1.28)	1.12 (0.91,1.46)	0.016*
BUN (mmol/L)	4.08 (3.58,4.96)	4.21 (3.64,5.11)	0.841
Cr (mol/L)	51.40 (45.80,56.80)	52.25 (46.90,57.60)	0.415
HOMA-IR	3.61 (2.47,5.36)	2.29 (1.66,3.95)	< 0.001**
GALP (ng/ml)	1.44 (0.96,1.69)	0.58 (0.40,0.82)	< 0.001 **
Alarin (ng/ml)	0.54 (0.40, 0.66)	0.23 (0.20, 0.34)	< 0.001 **

Table 1. Comparisons of clinical indices and serum GALP and Alarin concentrations between PCOS patients and controls. *$P < 0.05$; **$P < 0.01$.

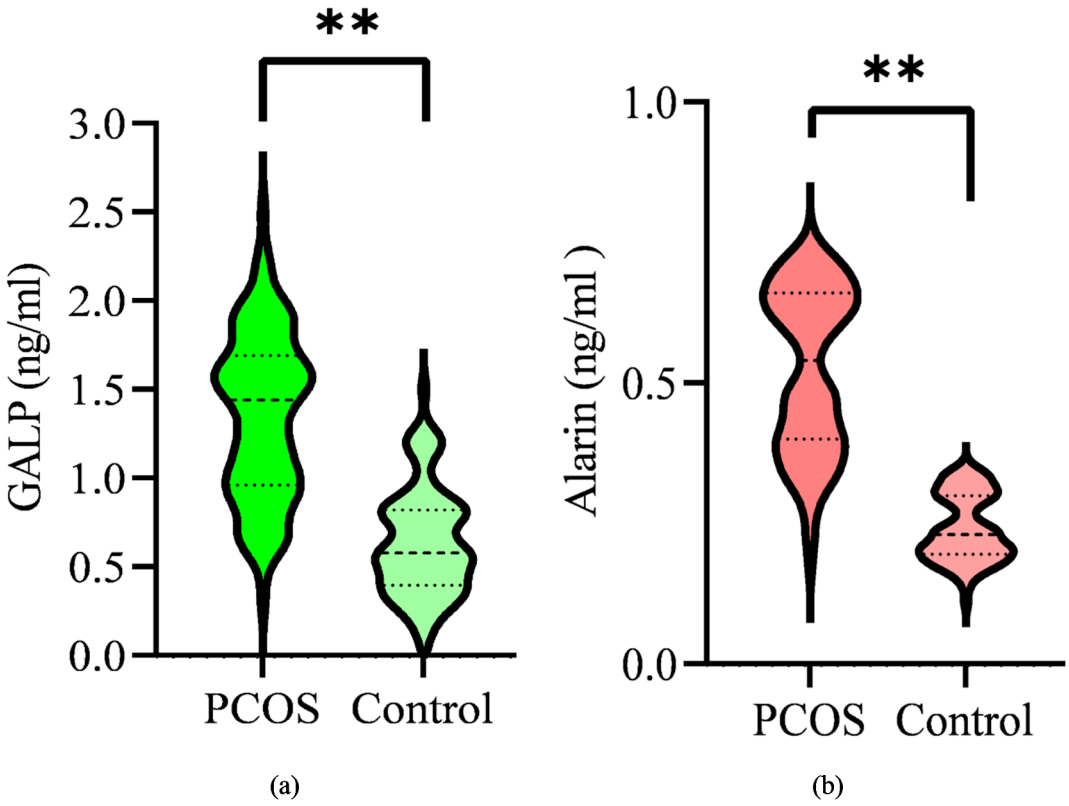

Fig. 2. Comparisons of serum GALP and alarin concentrations between PCOS and control groups. (**a**) GALP; (**b**) alarin.

Subgroup comparisons of clinical indices, GALP, and Alarin in PCOS patients and controls

FINS, TG, ALT, HOMA-IR, GALP, and alarin were significantly lower, and the levels of LH and AST/ALT were significantly higher, in PCOS subgroup 1 than in PCOS subgroup 2. Other indices did not differ between the two subgroups (Table 2). FINS, ALT, HOMA-IR, GALP, and alarin in control subgroup 1 were also significantly attenuated relative to control subgroup 2 (Table 3).'

Simple correlation analysis of GALP or Alarin with other indices

Serum GALP levels were correlated positively with BMI, WHR, LAP, total T, LH, FINS, TG, HOMA-IR, and alarin, negatively correlated with AST/ALT, and not correlated with other indices. Serum alarin levels were positively correlated with BMI, WHR, LAP, total T, LH, FINS, TG, HOMA-IR, and GALP, negatively correlated with FSH and AST/ALT, and not correlated with other indices (Table 4).

Multiple Stepwise regression analysis between GALP or alarin and influencing factors

Serum LAP, FINS, LH, and alarin levels were independent influencing factors of serum GALP levels ($P<0.05$) (Table 5). Serum FINS, LAP, FSH, and GALP levels were independent influencing factors of serum alarin levels ($P<0.05$) (Table 6).

Efficacy of serum GALP and alarin levels in predicting PCOS

We constructed ROC curves for serum GALP and alarin levels in predicting PCOS, and found that the areas under the curves (AUCs, 95% CI) were 0.78 (0.713, 0.847) ($P<0.001$) and 0.828 (0.766, 0.889) ($P<0.001$), respectively, and the cutoff values were 0.895 and 0.355, respectively (Fig. 3).

Discussion

When we compared serum GALP and alarin levels, and various metabolic indices between PCOS patients and infertile, non-PCOS patients, we ascertained that serum GALP and alarin were highly expressed in PCOS patients.

GALP is a hypothalamic peptide located in the arcuate nucleus that stimulates the release of GnRH from the hypothalamus and GT1-7 cells (a GnRH neuronal cell line). Takatsu et al. found that GALP immunoreactive fibers were densely distributed in the medial preoptic area of the hypothalamus, which is known to be associated with the regulation of feeding and reproduction[9]. Some researchers also demonstrated that the central administration of GALP stimulated GnRH-mediated LH secretion in rats. Since GALP was shown to be involved in GnRH-mediated LH secretion, it may constitute a mediator of the augmented GnRH pulse frequency and LH pulsatility that are characteristic of PCOS[10]. Lawrence et al.[4] discerned that GALP expression was regulated by

	PCOS subgroup 1 ($n=39$)	PCOS subgroup 2 ($n=64$)	*P*
P (ng/ml)	0.60 ± 0.24	0.52 ± 0.21	0.069
E_2 (pg/ml)	39.18 (31.50, 49.08)	36.91 (25.93, 43.21)	0.227
PRL (ng/ml)	11.68 (8.04, 14.31)	11.49 (9.35,13.84)	0.935
total T (ng/ml)	26.95 ± 10.84	25.82 ± 9.83	0.588
FSH (mIU/mL)	7.19 ± 1.54	6.55 ± 1.45	0.056
LH (mIU/mL)	7.80 (5.27, 12.52)	5.74 (3.53,9.05)	0.009**
FINS (mU/L)	10.94 (9.30,12.60)	21.00 (14.27,28.83)	< 0.001**
TC (mmol/L)	4.54 (4.19,4.96)	4.59 (4.18,5.16)	0.552
TG (mmol/L)	0.79 (0.72,1.09)	1.56 (0.90,2.10)	< 0.001**
FBG (mmol/L)	5.25 (5.05,5.46)	5.33 (5.16,5.63)	0.162
ALT (U/L)	11.00 (9.00,15.00)	18.00 (14.00,25.00)	< 0.001**
AST (U/L)	15.00 (13.00,17.00)	17.00 (14.00,19.00)	0.098
AST/ALT	1.23 (0.96,1.71)	0.88 (0.73,1.09)	< 0.001**
BUN (mmol/L)	4.08 (3.58,4.68)	4.08 (3.57,5.05)	0.830
Cr (mol/L)	50.50 (45.80,56.00)	52.00 (45.78,57.10)	0.373
HOMA-IR	2.48 (2.00,3.12)	4.72 (3.37,7.20)	< 0.001**
GALP (ng/ml)	0.91 ± 0.25	1.62 ± 0.34	< 0.001**
Alarin (ng/ml)	0.40 (0.34,0.47)	0.64 (0.58,0.68)	0.001**

Table 2. Subgroup analysis of clinical indices and GALP and Alarin concentrations in PCOS patients. *$P < 0.05$; **$P < 0.01$.

	Control subgroup 1 ($n=53$)	Control subgroup 2 ($n=36$)	*P*
P (ng/ml)	0.58 (0.45, 0.74)	0.55 (0.40,0.67)	0.533
E_2 (pg/ml)	38.27 (30.43,53.24)	32.26 (25.13,44.24)	0.245
PRL (ng/ml)	12.86 (10.69,17.77)	10.68 (8.31,15.59)	0.080
total T (ng/ml)	17.23 (14.61,20.33)	19.33 (15.80,24.49)	0.111
FSH (mIU/mL)	7.36 (6.42,8.57)	6.42 (5.43,7.79)	0.054
LH (mIU/mL)	4.48 (3.22,5.84)	3.22 (2.64,4.64)	0.225
FINS (mU/L)	8.72 (5.31,11.08)	15.90 (9.51,22.18)	< 0.001**
TC (mmol/L)	4.71 ± 0.97	4.61 ± 0.72	0.525
TG (mmol/L)	0.89 (0.58, 1.34)	1.08 (0.77, 1.42)	0.079
FBG (mmol/L)	5.13 ± 0.38	5.47 ± 0.44	0.427
ALT (U/L)	12.50 (9.25,16.00)	14.50 (11.00,20.00)	0.015*
AST (U/L)	15.00 (14.00,17.75)	16.00 (14.25,17.75)	0.341
AST/ALT	1.23 (1.07,1.50)	1.03 (0.75,1.33)	0.076
BUN (mmol/L)	4.08 ± 1.08	4.55 ± 0.87	0.611
Cr (mol/L)	52.35 ± 7.99	52.55 ± 8.30	0.888
HOMA-IR	1.93 (1.24,2.62)	3.83 (2.25,5.31)	< 0.001 **
GALP (ng/ml)	0.53 ± 0.22	0.80 ± 0.33	0.028*
Alarin (ng/ml)	0.21 (0.19, 0.24)	0.31 (0.29, 0.33)	< 0.001 **

Table 3. Subgroup analysis of clinical indices and GALP and Alarin concentrations in control patients. *$P < 0.05$; **$P < 0.01$.

insulin, leptin, and blood glucose levels, and in turn affected the secretion of ovarian hormones. However, there are only two reports on potential correlations between GALP and PCOS. Li et al.[11] uncovered no significant differences in GALP protein or mRNA expression among a PCOS model group, an electroacupuncture group, a sham acupuncture group, and a normal control group in rats. Demirpence et al.[12] found significantly elevated serum GALP levels in PCOS patients, and their study revealed that the GALP levels were negatively correlated with 25-hydroxyvitamin D levels and positively correlated with total T levels, but not with other parameters such as IR. We found that GALP levels in the PCOS group were also significantly higher than in the control group and positively correlated with total T, supporting the results of Demirpence et al. However, in contrast, we determined that GALP levels were positively correlated with FINS, TG, and HOMA-IR—suggesting that GALP was not only involved in hormonal regulation, but that it was also closely associated with glucose and lipid metabolism. In addition, Fraley et al.[13] showed that insulin might influence GALP gene expression via the central nervous system (CNS). Research has revealed that GALP enhanced the expression of uncoupling protein

Indices	GALP ($n=192$)		Alarin ($n=192$)	
	r	*P*	*r*	*P*
BMI	0.654	< 0.001**	0.603	< 0.001**
WHR	0.428	< 0.001**	0.435	< 0.001**
LAP	0.538	< 0.001**	0.514	< 0.001**
P	−0.024	0.741	−0.086	0.238
E_2	0.017	0.811	−0.017	0.819
PRL	−0.132	0.068	−0.178	0.214
total T	0.285	0.002**	0.364	0.001**
FSH	−0.129	0.074	−0.161	0.026*
LH	0.192	0.008**	0.22	0.002**
FINS	0.499	< 0.001**	0.513	< 0.001**
TC	0.048	0.511	0.047	0.496
TG	0.299	< 0.001**	0.329	< 0.001**
FBG	0.125	0.084	0.186	0.013*
AST/ALT	−0.299	0.035*	−0.309	0.002**
BUN	0.012	0.872	0.056	0.439
Cr	0.003	0.972	−0.01	0.810
HOMA-IR	0.493	< 0.001**	0.513	< 0.001**
Alarin	0.818	< 0.001**		

Table 4. Simple correlation analysis between GALP or Alarin concentrations and other indices. *$P < 0.05$; **$P < 0.01$.

	B	Standard errors for B	B (Standardized coefficient)	t	*P*
LAP	0.004	0.001	0.241	3.015	0.003
Alarin	0.435	0.212	0.148	2.049	0.042
FINS	0.011	0.005	0.201	2.495	0.013
LH	0.018	0.008	0.149	2.322	0.021

Table 5. Multiple Stepwise regression analysis between GALP and influencing factors.

	B	Standard errors for B	B (Standardized coefficient)	t	*P*
FINS	0.004	0.002	0.219	2.757	0.006
GALP	0.055	0.024	0.162	2.292	0.023
LAP	0.001	0.000	0.171	2.139	0.034
FSH	−0.015	0.007	−0.128	−2.021	0.045

Table 6. Multiple Stepwise regression analysis between alarin and influencing factors.

1 (UCP1) in the brown adipose tissue (BAT) of high-fat diet-induced obese mice by activating their sympathetic nervous system (SNS), while also increasing the expression of adipose tissue triglyceride lipase (ATGL) and hormone-sensitive lipase (HSL) genes in white adipose tissue (WAT); this then enhanced the expression of phosphorylated protein in HSL, promoting lipolysis. These data also indicate that GALP may regulate peripheral lipid metabolism through the SNS[14]. Fang et al.[15] showed that serum GALP concentrations in obese subjects were significantly higher than in their healthy control group and were associated with elevated triglyceride levels, but not with insulin sensitivity. After subgroup analysis based on BMI, the GALP levels were significantly higher in our PCOS subgroup 2 relative to PCOS subgroup 1, and in control subgroup 2 versus control subgroup 1. Thus, GALP levels in the obese or overweight groups were significantly augmented, consistent with the results of Fang et al.[15], and re-confirmed the correlation between GALP and obesity. These results suggest that weight loss may assist in reducing GALP levels, thereby further improving glucose and lipid metabolism and endocrine function in PCOS patients. However, the specific pathway by which GALP is involved in PCOS remains unclear, and this necessitates additional clinical trials.

Alarin is a regulatory peptide that is widely expressed in the CNS and peripheral tissues of humans and rodents, is involved in multiple physiologic functions (e.g., ingestive behaviors, sugar metabolism, body temperature regulation, and reproduction), and is associated with various diseases (e.g., obesity, metabolic syndrome, type 2 diabetes mellitus [T2DM], and hypertension)[16–20]. A majority of studies on alarin have

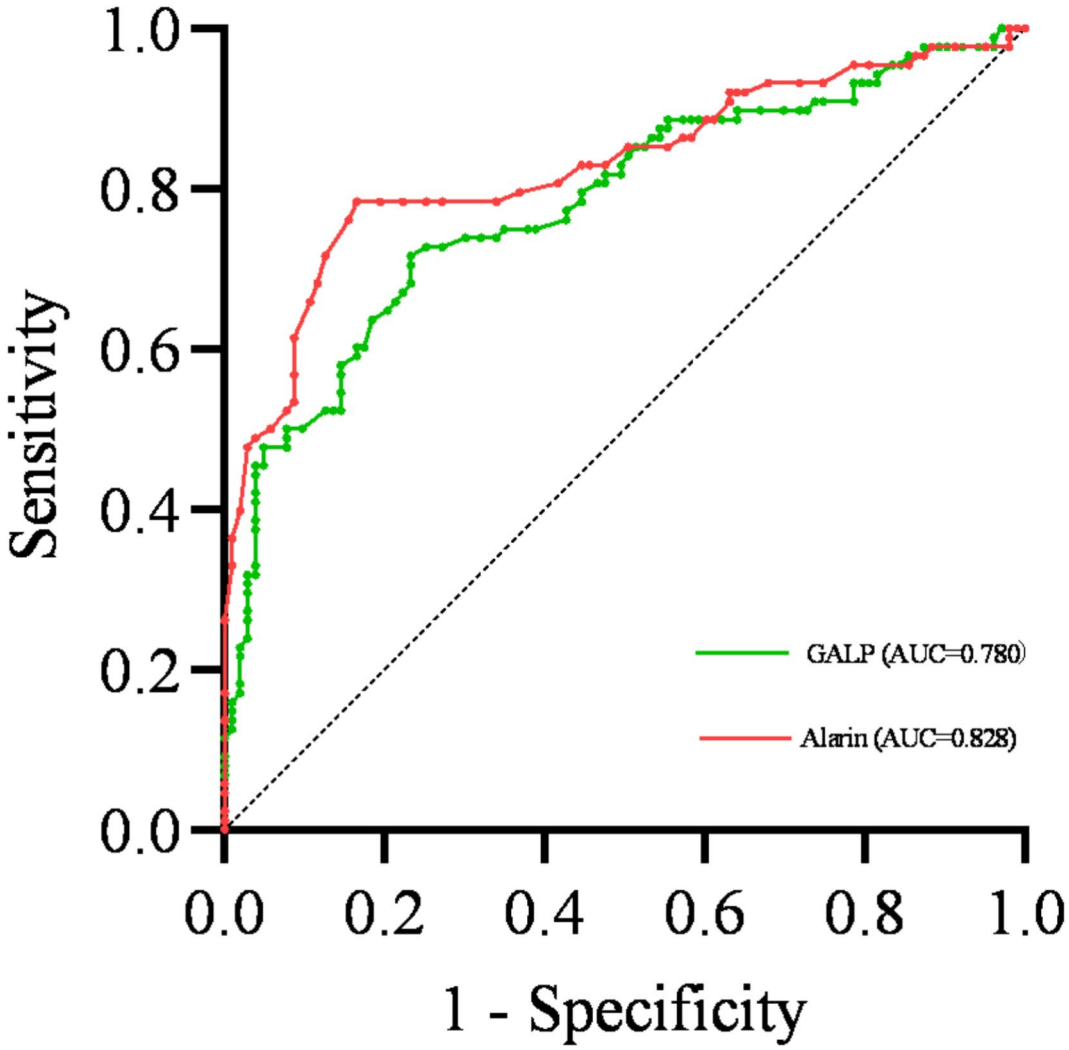

Fig. 3. ROC curves for serum GALP and alarin levels used in the prediction of PCOS.

focused on diabetes and metabolic syndrome. For example, Fang et al.[21]showed that alarin levels in patients with metabolic syndrome were significantly higher than in the control group, and were positively correlated with FBG, BMI, glycosylated hemoglobin (HbA1c), and HOMA-IR; meanwhile, Zhou et al.[22] ascertained that alarin levels significantly increased in newly diagnosed T2DM patients compared to controls. Similarly, Hu et al.[6] determined that the alarin levels in patients with impaired glucose tolerance (IGT) and T2DM were higher than in healthy individuals, and that the plasma alarin levels in T2DM patients rose significantly relative to patients with IGT—suggesting that alarin plays a role in the onset and development of diabetes. Fraley et al.[24] administered alarin via intravenous injection to mice and observed an induction of FOS protein immunoreactivity in several areas of the hypothalamus that regulate food intake, body weight, and the secretion of LH. Animal experiments have indicated that alarin promoted the secretion of LH by affecting GnRH secretion in the hypothalamus[23], and Yildirim et al.[25] found alarin levels to be significantly higher in infertile women with diminished ovarian reserve and to be significantly correlated with serum LH concentrations. However, there are only two extant reports on a potential correlation between alarin and PCOS, and their results are divergent. A case–control study showed elevated serum alarin concentrations in PCOS patients that were positively correlated with LH and anti-Müllerian hormone (AMH) levels, and significantly negatively correlated with HDL and FSH concentrations[26]. Similarly, Yang et al.[27] ascertained that alarin was highly expressed in PCOS patients. However, in contrast to the study by Gorkem et al., Yang et al. found no correlation between alarin and FSH, LH, or HDL; instead, it was positively correlated with BMI, WPR, FBG, fasting insulin, HOMA-IR, E_2, TG, high-sensitivity C-reactive protein, and IL-6. We herein found that the serum alarin levels in the PCOS group were significantly higher than in the control group, and that they were correlated positively with LH and negatively with FSH, congruent with the results of Gorkem et al. In addition, serum alarin levels were positively correlated with BMI, WHR, LAP, FINS, TG, and HOMA-IR, consistent with the data of Yang et al.[27]. These data suggest that alarin may be closely associated with obesity, dyslipidemia, and insulin resistance. Distinct from the results of Gorkem et al. and Yang et al., we found alarin levels to be positively correlated with total T, suggesting that alarin may be important in inducing PCOS by affecting testosterone levels. The disparities among these studies may be related to racial differences

in research samples, regional differences, diversity of selection criteria, and sample size. Some scholars who have studied the relationship between alarin levels and obesity in children demonstrated that circulating alarin in obese children was significantly higher than in the respective control group[28], depicting an effect of alarin on obesity. Other authors have reported that serum alarin levels in obese patients were higher than in normal-weight individuals, and that they were correlated with factors such as BMI and IR[7]. After subgroup allocation based on BMI, we found that alarin levels in PCOS subgroup 2 and control subgroup 2 were significantly higher than in the corresponding normal-weight subgroups, suggesting that alarin may be related to the development of obesity. However, we still need to further examine the mechanisms by which alarin is involved in IR and obesity, and discern its impact on the onset and development of PCOS so as to improve the accuracy of PCOS diagnosis and to foster effective treatment.

This study indicates that there are abnormal levels of GALP and alarin in the bodies of patients with PCOS. Our ROC curve analysis showed that serum levels of GALP and alarin could be used to predict the occurrence of PCOS, thus providing a method for the early diagnosis of PCOS. However, due to the limitations inherent to the selection of subjects, our results may be affected by this confounder. In addition, due to the multifactorial nature of the pathogenic mechanisms underlying PCOS, its development cannot be revealed using a single model. Therefore, we expect to increase sample size in the future. We also postulate that methods will be improved by initiating prospective cohort studies that further clarify the changes in serum GALP and alarin levels during the onset and development of PCOS, and posit that this will elucidate potential pathophysiologic mechanisms that are operational in PCOS.

Data availability

All data sharing and collaboration requests should be directed to the corresponding author.

Received: 13 August 2024; Accepted: 6 March 2025
Published online: 22 March 2025

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Author contributions
M.L.: Wrote the main manuscript text, X.Z.: Statistical Analysis and Experimental guidance, Z.S.: Experimental operation, H.W.: Data Collection, X.S.: Study Design, W.Z.: Funds Collection, Data Interpretation.

Funding
This study was supported by the Natural Science Foundation of Shandong Province (ZR2016HL04); the Development of Science and Technology Plan of Shandong Province Medicine and Health Care (2015WS0100); Science and Technology Innovation Development Project of Taian City (2020NS266).

Declarations

Competing interests
The authors declare no competing interests.

Ethical approval
Data analysis of patient medical records in this study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Shandong First Medical University (Ethics approval number 202004014). All participants were informed with regards to the purpose of this study and provided their informed consent.

Additional information
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