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Evaluation of Adipokine Levels (Betatrophin, Endotrophin and Meteorin-Like Protein) and their Relationship with Reproductive and Metabolic Disorders in Women with Polycystic Ovary Syndrome According to Body Mass Index

Objective — to show the disruptions in the reproductive, metabolic and adipokine (betatrophin, endotrophin and meteorin-like protein) levels in women with polycystic ovary syndrome (PCOS) according to their body mass index.

Materials and methods. This study was conducted on 160 women at the Chemistry Department, College of Science, Mustansiriyah University. The women were subdivided into 40 obese PCOS, 40 overweight PCOS, 40 normal-weight PCOS and 40 healthy women. The routine anthropometric, reproductive and metabolic characteristics, as well as the adipokines characteristics, were determined for all participants.

Results and discussion. Although betatrophin and endotrophin levels were increased statistically in PCOS compared with healthy women, meteorin-like protein levels significantly decreased. At the same time, betatrophin and endotrophin levels increased statistically as the degree of adiposity increased among PCOS subgroups. Meanwhile, meteorin-like protein levels statistically reduced as the degree of adiposity increased among PCOS subgroups. There were direct associations between betatrophin and endotrophin and body mass index, insulin, and homeostatic model assessment-insulin resistance in obese and overweight subgroups of PCOS. In contrast, inverse associations were noted between meteorin-like protein and body mass index, insulin, and homeostatic model assessment-insulin resistance in obese and overweight subgroups of PCOS.

Conclusions. The results from this study suggest that weight management significantly impacts the abnormalities in adipokines related to adiposity and its complications in PCOS.

Keywords

Adipokines, obesity, polycystic ovary syndrome.

A chronic endocrine condition among women throughout their reproductive age is polycystic ovary syndrome (PCOS), with a prevalence ranging from 8 to 13 % [30]. The recent clinically recognised criteria for PCOS diagnosis are the presence of at least two out of the following three characteristics after ruling out other possible causes: oligo-ovulation or anovulation, hyperandrogenism and the presence of multiple cysts in the ovaries as determined by ultrasound examination [18]. The precise identification of the aetiology of PCOS remains unclear. Nevertheless, some prior research has indicated a potential association between PCOS and a multitude of factors, such as family history, an improper lifestyle, the use of personal care products containing carcinogenic preservatives and obesity

[35]. About fifty percent of women diagnosed with PCOS have a body weight above the healthy range or even fall into the category of obesity [5]. Obesity increases the detrimental effects on both the reproductive and metabolic variables of PCOS due to an elevation of adaptive hyperinsulinaemia (HI), which in turn causes insulin resistance (IR). Furthermore, obesity leads to various complications related to PCOS, including glucose intolerance, dyslipidaemia and type 2 diabetes mellitus (T2DM) [32].

Recently, adipose tissue (AT) has been recognised to function as an endocrine organ because it releases a diverse range of signalling peptides that control many homeostatic processes, including nutrient intake, energy usage and insulin secretion and function [11]. The main peptides released from AT are adipokines, including betatrophin (β-Trophin), endotrophin (E-Trophin), and meteorin-like protein (Metrnl). Recent evidence suggests that the adipokine profile levels change in terms of the quantity and condition of AT due to obesity [10]. Therefore, in obesity, changes in the secretion of adipokines can cause reproductive and metabolic disruptions, which may be a significant factor in the onset of IR and related disorders, particularly PCOS [40]. Betatrophin, also called angiopoietin-like protein 8, is a novel adipokine that belongs to the angiopoietin-like protein family. It is mainly secreted by the liver and fatty tissues [17]. Betatrophin participates in many biological processes within the human body, particularly glucose tolerance during IR [1]. Moreover, previous studies have reported that β-Trophin has a role in regulating lipid metabolism [37]. Endotrophin is a soluble product from the breakdown of the A3 chain of collagen type IV by proteolysis, also called collagen type VI [23]. Endotrophin participates actively in diverse biological processes within the human body, such as inflammation, angiogenesis and fibrosis [36]. Endotrophin is a significant contributing factor to play a pivotal function in response to a metabolic problem [22]. Meteorin-like protein, also called Subfatin or Metrnl protein, is a novel adipokine mainly secreted by AT and during the exercise of skeletal muscles. Metrnl participates in diverse biological processes within the human body, including anti-inflammatory and insulin-sensitising activity [25]. Furthermore, increased Metrnl levels can stimulate energy expenditure and improve glucose tolerance [29]. The levels of these adipokines in women with PCOS were inconsistent compared with health women [15, 16, 19].

Few studies have examined the metabolic adipokine (β-Trophin, E-Trophin and Metrnl) levels among women with PCOS and healthy women. However, no research has investigated the linkage between these adipokines (β-Trophin, E-Trophin and Metrnl) and the severity of obesity in PCOS. Therefore, our paper attempts to show the levels of β-Trophin, E-Trophin and Metrnl in women with PCOS and their relationship with reproductive and metabolic disorders according to body mass index.

Materials and methods

To establish whether there is a linkage between β-Trophin, E-Trophin, and Metrnl levels and the severity of obesity in PCOS, the present cross-sectional work was conducted from 10 May 2024 to 10 October 2024 at the Chemistry Department, College of Science, Mustansiriyah University. A random sample of 160 women was recruited from private clinics in Baghdad City, aged 18 to 30, and subdivided into four groups: 40 obese (body mass index (BMI) ≥ 30 kg/m^2), 40 overweight (BMI 25.1—29.9 kg/m^2), 40 normal weight women with PCOS (BMI 18.5—24.9 kg/m^2), and 40 healthy women with normal weight as a control group for comparative purposes. The revised Rotterdam criteria were used to diagnose PCOS in this study [8], which require the presence of at least two of three symptoms: oligo/or amenorrhea, clinical/biochemical hypersecretion of androgens and polycystic ovary morphology observed through ultrasonography. Women with possible causes other than PCOS, such as tumours that secrete androgens, Cushing's syndrome, hypertension, diabetes mellitus and congenital adrenal hyperplasia, were ruled out. Furthermore, healthy women with irregular menstrual cycles, malignant or benign tumors, ovarian association diseases, and also autoimmune diseases were ruled out.

Five millilitres of each woman's venous blood were withdrawn during the first phase of the menstrual cycle, precisely on day 2, 3 or 4 of the menstrual cycle, after overnight fasting of at least 10 hours using a 5 mL disposable syringe. 5 mL were drawn and transferred into tubes with gel and left to clot at room temperature (25 °C) for 10 minutes. The tubes with gel were centrifuged for at least 7 minutes at 3000 round per minute to separate serum. The obtained serum was subdivided into two portions and stored until the hormonal, metabolic and adipokine markers were measured.

An electronic scale to the nearest 0.1 kg was used to measure the body weight of each woman. By dividing a woman's weight (measured in kg) by her square height (measured in m^2), BMI was determined. The ECLIA technique (Electrochemiluminescence Immunoassay) by Roche Cobas e-411 autoanalyser system (Roche-Hitachi Diagnostics, Japan) was employed to measure fasting serum of hormonal tests, including luteinising hormone (LH, mIU/mL), follicle-stimulating hormone

Table 1. **The statistical analysis of anthropometric. reproductive and metabolic parameters in the polycystic ovary syndrome subgroups and the healthy group**

	Obese-PCOS (n = 40)	Overweight-PCOS (n = 40)	Normal Weight-PCOS (n = 40)	Healthy Women (n = 40)	P-value
Anthropometric Parameters					
Age, years	22.8 ± 2.3[a]	21.6 ± 3.7[a]	20.6 ± 2.5[a]	19.1 ± 2.1[a]	0.5971
Weight, kg	89.8 ± 10.7[a]	76.4 ± 16.3[b]	60.4 ± 14.9[c]	58.6 ± 14.2[c]	0.0001
BMI, kg/m^2	32.6 ± 3.9[a]	28.5 ± 2.3[b]	24.5 ± 2.1[c]	23.1 ± 1.8[c]	0.0001
Reproductive Parameters					
LH, mIU/mL	18.8 ± 4.5[a]	15.3 ± 2.6[b]	12.7 ± 2.1[c]	9.9 ± 1.7[d]	0.0001
FSH, mIU/mL	5.5 ± 1.7[a]	7.8 ± 1.9[b]	9.9 ± 1.5[c]	10.1 ± 1.1[c]	0.0311
LH/FSH ratio	3.4 ± 1.7[a]	1.9 ± 0.4[b]	1.3 ± 0.6[c]	0.98 ± 0.5[d]	0.0011
TT, ng/mL	1.89 ± 0.41[a]	1.41 ± 0.11[b]	1.11 ± 0.14[c]	0.53 ± 0.2[d]	0.0001
SHBG, nmol/L	35.6 ± 12.6[a]	46.2 ± 19.5[b]	54.4 ± 21.2[c]	58.2 ± 25.5[c]	0.0011
Metabolic Parameters					
Insulin, μIU/mL	16.9 ± 7.2[a]	14.6 ± 4.6[b]	9.1 ± 6.6[c]	8.3 ± 5.2[c]	0.0001
FBG, mg/dL	109.6 ± 7.9[a]	99.8 ± 6.5[b]	82.1 ± 10.9[c]	80.4 ± 6.4[c]	0.0158
HOMA-IR	4.6 ± 1.9[a]	3.6 ± 1.4[b]	1.8 ± 0.7[c]	1.6 ± 0.5[c]	0.0001
TC, mg/dL	192.2 ± 42.9[a]	171.1 ± 28.4[b]	158.8 ± 33.5[c]	156.2 ± 25.4[c]	0.0001
TG, mg/dL	154.5 ± 72.7[a]	139.9 ± 40.2[b]	127.8 ± 38.1[c]	124.1 ± 44.6[c]	0.0002
HDL-C, mg/dL	39.2 ± 12.8[a]	53.3 ± 11.2[b]	66.8 ± 10.8[c]	65.4 ± 13.2[c]	0.0365

(FSH, mIU/mL), total testosterone (TT, ng/mL), sex hormone-binding globulin (SHBG, nmol/L), insulin (μIU/mL) and metabolic tests, including blood glucose (FBG, mg/dL), total cholesterol (TC, mg/dL), triglycerides (TG, mg/dL) and high-density lipoprotein-cholesterol (HDL-C, mg/dL). To compute HOMA-IR (homeostatic model assessment-insulin resistance), the following standard formula was used: fasting glucose (mg/dL) X fasting insulin (μIU/L)/405. The ELISA (Enzyme-Linked Immunosorbent Assay) technique was employed to measure β-Trophin (0.5—100 ng/mL), E-Trophin (0.31—20 ng/mL) and Metrnl (31.2—2000 pg/mL) using commercial kits (MyBioSource, USA).

The computer program Prism, version 8.01 (GraphPad Software, Boston, New York, USA) was used to compute a one-way ANOVA (analysis of variance) at a 0.05 level of significance. Tukey's test was subsequently applied to indicate the probability of differences (P-value) among subgroups of PCOS and healthy group. The results are presented in terms of mean ± standard deviation (SD). To evaluate whether the studied parameters followed a Gaussian (normal) distribution, the Shapiro—Wilk normality test was utilised. A P-value of < 0.05 was considered statistically significant. The Pearson correlation coefficient was utilised to investigate the associations between adipokines and anthropometric, reproductive and metabolic parameters among subgroups of PCOS and the healthy group. The distinct letters (a, b, c and d) found in the same row in the table indicate that the three groups differ significantly. Significant differences between the three groups within a single parameter are indicated when all distinct letters are found in the same row. In contrast, when the same distinct letter is found in the same row for two or three groups, it indicates no significant difference within a single parameter.

The ethics committee of Mustansiriyah University/College of Science (BCSMU/0524/1116C on 03 May 2024) approved the study. Additionally, ethical consent was obtained from all subjects, and they were provided with comprehensive information about our study, including the purpose, procedures, benefits and confidentiality of the research. All the information listed above was clearly and understandably presented in a written consent form, and the researcher was present when the subjects completed the questionnaire.

Results and discussion

Table 1 illustrates the summary statistical analysis for anthropometric, reproductive and metabolic parameters in PCOS subgroups and the healthy group. The ANOVA revealed statistically significant differences in weight, BMI, LH, FSH, LH/FSH ratio, TT, SHBG, insulin, FBS, HOMA-IR, TC, TG and HDL-C between women with PCOS compared with healthy women, as well as among PCOS subgroups. On the other hand, no statistically significant differences in weight, BMI, FSH, SHBG, insulin, FBG, HOMA-IR, TC, TG and HDL-C were observed between women with and without PCOS in the normal-weight groups.

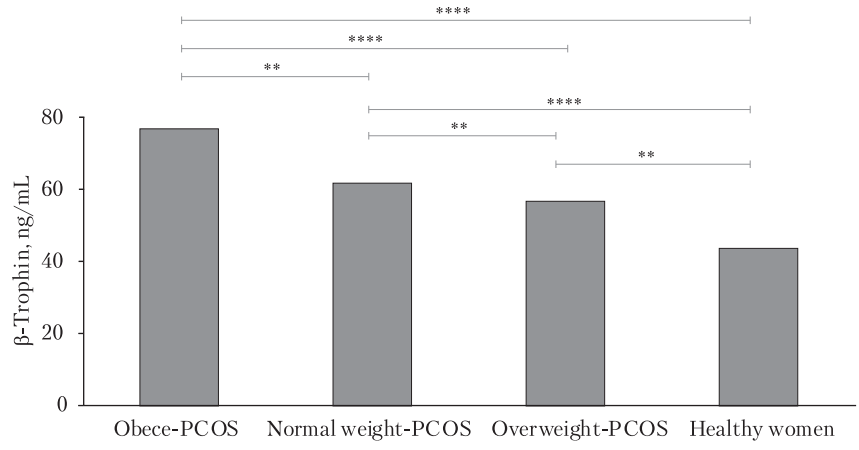

Fig. 1. **Betatrophin levels in polycystic ovary syndrome subgroups and the healthy group**

Note. **** indicates that the difference among means is highly statistically significant (p < 0.0001); ** indicates that the difference among means is statistically significant (p < 0.001).

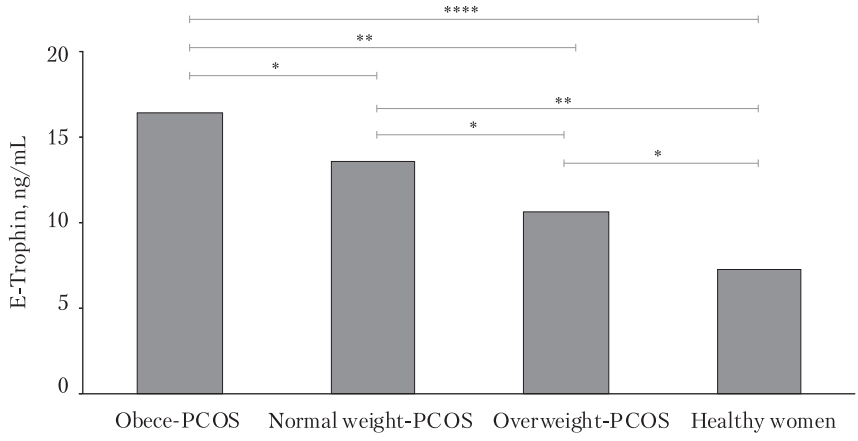

Fig. 2. **Endotrophin levels in polycystic ovary syndrome subgroups and the healthy group**

Note. **** indicates that the difference among means is highly statistically significant (p < 0.0001); ** indicates that the difference among means is statistically significant (p < 0.001); * indicates that the difference among means is statistically significant (p < 0.05).

Figs. 1, 2 and 3 compare the serum levels of adipokines (β-Trophin, E-Trophin and Metrnl) in PCOS subgroups with those of the healthy group. The statistical analysis indicated that the β-Trophin level was statistically higher in PCOS subgroups than in the healthy group (75.1 ± 9.6 ng/mL *vs* 63.6 ± 9.8 ng/mL *vs* 54.7 ± 12.3 ng/mL *vs* 41.4 ± 11.8 ng/mL; p = 0.0001), as shown in Fig. 1. In the same way, the level of E-Trophin was statistically higher in PCOS subgroups than in the healthy group (17.1 ± 1.4 ng/mL *vs* (13.8 ± 1.1) ng/mL *vs* 11.2 ± 1.6 ng/mL *vs* 7.7 ± 1.9 ng/mL; p = 0.001), as shown in Fig. 2. Conversely, the level of Metrnl was statistically lower in PCOS subgroups than in the healthy group (1485.5 ± 188.3 pg/mL *vs* 1641.1 ± ± 197.9 pg/mL *vs* 1749.2 ± 156.6 pg/mL *vs* 1803.7 ± 137.4 pg/mL; p = 0.0001), as shown in Fig. 3.

Tables 2, 3 and 4 display the linear regression analysis between adipokines (β-Trophin, E-Trophin and Metrnl) and anthropometric, reproductive and metabolic characteristics in PCOS subgroups and the healthy group. Although the Pearson correlation coefficient from this study showed a significant direct association between β-Trophin and BMI, insulin, HOMA-IR, TC and TG in the obese and overweight subgroups of PCOS, β-Trophin was statistically inversely correlated with SHBG in the obese PCOS group (Table 2). Likewise, E-Trophin showed a significant direct association with BMI, LH/FSH ratio, insulin and HOMA-IR in the obese and overweight PCOS subgroups (Table 3). Metrnl showed an inverse association with BMI, insulin and HOMA-IR in the obese and overweight PCOS subgroups. Also, Metrnl showed an inverse relationship with TC and TG only in the obese PCOS group (Table 4).

On the other hand, simple linear regression did not indicate any statistically significant correlation

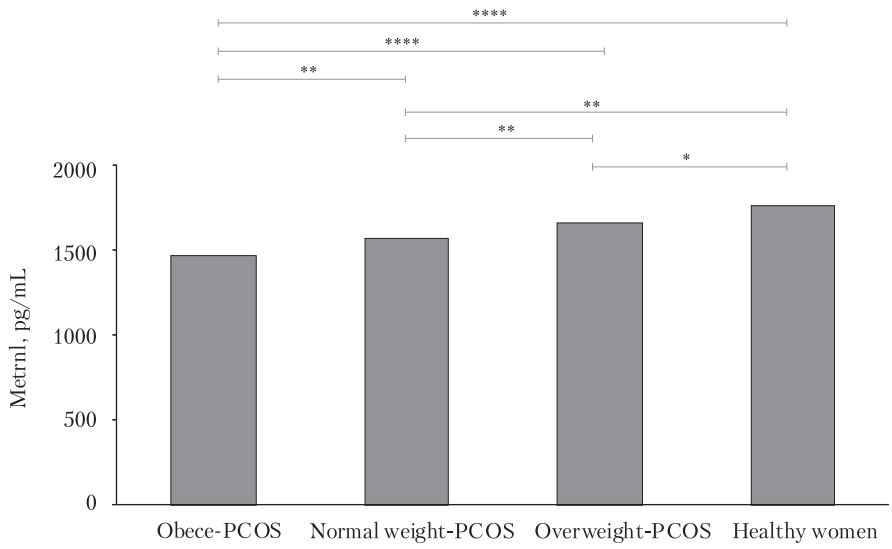

Fig. 3. **Meteorin-like protein levels in polycystic ovary syndrome subgroups and the healthy group**

Note. **** indicates that the difference among means is highly statistically significant ($p < 0.0001$); ** indicates that the difference among means is statistically significant ($p < 0.001$); * indicates that the difference among means is statistically significant ($p < 0.05$).

Table 2. **Correlations between β-Trophin and anthropometric, reproductive and metabolic characteristics in PCOS subgroups and the healthy group**

	β-Trophin							
	Obese-PCOS		**Overweight-PCOS**		**Normal Weight-PCOS**		**Healthy Women**	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Anthropometric Parameters								
Weight	0.823	0.202	0.544	0.182	0.362	0.546	0.202	0.279
BMI	0.482	0.003**	0.477	0.012*	0.523	0.202	0.456	0.621
Reproductive Parameters								
LH	0.279	0.089	0.329	0.166	0.815	0.097	0.321	0.062
FSH	–0.112	0.654	–0.014	0.881	–0.111	0.885	–0.279	0.089
LH/FSH ratio	0.081	0.852	0.023	0.919	0.347	0.091	–0.271	0.272
TT, ng/mL	0.273	0.109	0.442	0.394	0.528	0.340	0.597	0.825
SHBG	–0.310	0.017*	–0.238	0.086	–0.014	0.942	–0.030	0.874
Metabolic Parameters								
Insulin	0.535	0.001**	0.499	0.004**	0.552	0.201	0.335	0.062
FBG	0.276	0.205	0.111	0.885	0.089	0.961	0.318	0.226
HOMA-IR	0.616	0.001**	0.711	0.001**	0.545	0.111	0.646	0.110
TC	0.352	0.031*	0.509	0.033*	0.422	0.211	0.179	0.494
TG	0.227	0.041*	0.301	0.046*	0.387	0.425	0.111	0.732
HDL-C	–0.416	0.211	–0.07	0.696	–0.361	0.761	–0.106	0.781

Note. r — linear correlation coefficient; * indicates a significant association between the two variables; ** indicates a highly significant association between the two variables.

between β-Trophin and E-Trophin in PCOS subgroups or the healthy group. Instead, Metrnl has a significant inverse association with β-Trophin ($r = –0.385$; $p = 0.021$) and E-Trophin ($r = –0.428$; $p = 0.001$) in the PCOS subgroup only.

There is a large volume of published studies describing the detrimental effects of varying degrees of adiposity on both metabolic and reproductive indicators of PCOS due to elevated adaptive insulin levels, which in turn cause IR. Furthermore, recent evidence suggests that the adipokine profile levels change according to the quantity and condition of AT due to obesity in PCOS [40]. The findings from the current investigation demonstrated that the

Table 3. **Correlations between endotrophin and anthropometric, reproductive and metabolic characteristics in PCOS subgroups and the healthy group**

	E-Trophin							
	Obese-PCOS		**Overweight-PCOS**		**Normal Weight-PCOS**		**Healthy Women**	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Anthropometric Parameters								
Weight	0.383	0.090	0.315	0.767	0.247	0.188	0.293	0.129
BMI	0.535	0.005**	0.482	0.006**	0.053	0.911	0.107	0.053
Reproductive Parameters								
LH	0.014	0.972	0.299	0.667	0.121	0.630	0.972	0.097
FSH	–0.338	0.517	–0.358	0.514	0.097	0.815	0.071	0.921
LH/FSH ratio	0.399	0.019**	0.373	0.026*	0.181	0.862	0.023	0.919
TT, ng/mL	0.138	0.271	0.269	0.328	0.197	0.432	0.635	0.199
SHBG	–0.113	0.799	–0.028	0.552	–0.388	0.341	–0.341	0.142
Metabolic Parameters								
Insulin	0.785	0.001**	0.733	0.002**	0.541	0.221	0.059	0.798
FBG	0.532	0.444	0.156	0.660	0.525	0.433	0.523	0.444
HOMA-IR	0.811	0.001**	0.721	0.003**	0.441	0.424	0.044	0.716
TC	0.166	0.173	0.603	0.505	0.188	0.595	0.180	0.213
TG	0.191	0.217	0.111	0.885	0.772	0.199	0.128	0.123
HDL-C	–0.863	0.448	–0.245	0.332	0.952	0.169	0.263	0.438

Note. r — linear correlation coefficient; * indicates a statistically significant association between the two variables; ** indicates a highly statistically significant association between the two variables.

Table 4. **Correlations between meteorin-like protein and anthropometric, reproductive and metabolic characteristics in PCOS subgroups and the healthy group**

	Metrnl							
	Obese-PCOS		**Overweight-PCOS**		**Normal Weight-PCOS**		**Healthy Women**	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Anthropometric Parameters								
Weight	–0.351	0.129	–0.288	0.334	–0.175	0.461	–0.100	0.676
BMI	–0.535	0.005**	–0.482	0.002**	–0.352	0.212	–0.645	0.216
Reproductive Parameters								
LH	0.311	0.245	0.014	0.972	0.097	0.815	0.222	0.206
FSH	0.211	0.362	0.414	0.181	0.162	0.581	0.497	0.089
LH/FSH ratio	0.108	0.258	0.302	0.199	0.473	0.901	0.712	0.227
TT, ng/mL	–0.266	0.382	–0.377	0.159	–0.099	0.931	–0.356	0.322
SHBG	0.603	0.505	0.313	0.059	0.361	0.118	0.285	0.223
Metabolic Parameters								
Insulin	–0.752	0.001**	–0.535	0.004**	0.552	0.801	0.533	0.620
FBG	0.266	0.251	0.122	0.483	0.197	0.691	0.183	0.262
HOMA-IR	–0.811	0.001**	–0.666	0.001**	0.645	0.315	0.466	0.353
TC	–0.553	0.012*	0.905	0.333	0.318	0.318	0.197	0.494
TG	–0.371	0.011*	0.251	0.646	0.106	0.160	0.372	0.273
HDL-C	0.641	0.112	0.297	0.391	-0.631	0.553	0.351	0.372

Note. r — linear correlation coefficient; * indicates a significant association between the two variables; ** indicates a highly significant association between the two variables.

β-Trophin levels were were significantly higher in PCOS than in the healthy group. These results are broadly consistent with those observed by M. Calan et al. [7]. Additionally, the post hoc analysis in the current study showed statistical differences in the β-Trophin levels among PCOS subgroups. Simple linear regression analysis in the current investigation predicted that β-Trophin was directly associ-

ated with BMI, insulin and HOMA-IR in obese and overweight PCOS subgroups. These significant correlations are very similar to the previous reports [20, 33]. The findings from the present study indicate that β-Trophin participates in the progression of IR markers, including BMI, fasting insulin and HOMA-IR. β-Trophin plays a significant role in regulating the pancreas β-cells and production of fats [14]. β-Trophin was recently recognised as a considerable stimulator for replicating β-cells and promoting glucose tolerance [27]. PCOS is mainly characterised by the development of IR, which causes pancreatic β-cells to respond by increasing their proliferation and insulin production in order to meet the rising demand for insulin. However, insulin secretion decreases as β-cell activity declines over time [38]. Therefore, the present study hypothesised that compensatory hypersecretion of β-Trophin from AT resulted from a response to the severity of IR in women with PCOS based on their BMI. On the other hand, β-Trophin was directly associated with TC and TG in obese and overweight subgroups of PCOS. Recent investigations in animal trials have shown a correlation between β-Trophin and lipid metabolism [4]. Also, there is strong evidence indicating that the expression of β-Trophin could be enhanced by obesity and HI, which result in elevated levels of TG and IR rather than improving glucose metabolism [24]. A previous study by Erbag et al. contrasted with the present study, noting that β-Trophin levels statistically decreased in PCOS compared with the healthy group. Also, the associations between β-Trophin and BMI, fasting insulin, and HOMA-IR were inverse in women with PCOS [13]. The contradictory results between the current study and the previous one could be attributed to variations in sample size, ethnicities, ages or even the laboratory kits utilised [19].

Another significant finding in this study was that E-Trophin levels statistically increased women with PCOS compared to healthy women. Equally important, in the current study, linear regression revealed that E-Trophin was directly correlated with BMI, LH/FSH ratio, fasting insulin and HOMA-IR in obese and overweight PCOS subgroups. These results are consistent with those observed by G. Guney et al. [16]. The post hoc analysis in the current study showed statistical differences in E-Trophin levels among PCOS subgroups. This study is the first to report on E-Trophin levels in women with PCOS based on their BMI. The correlation between E-Trophin with fasting insulin and HOMA-IR in the current investigation further supports the idea of the influence of E-Trophin on the balance of energy and insulin sensitivity regulation [21, 36]. Besides that, a recent investigation on animals noted that chronic exposure to E-Trophin in mice caused impaired glucose and insulin tolerance [21]. A significant correlation between E-Trohin and LH/FSH ratio in the present investigation confirms the association between E-Trophin and androgens. Not only does the unusual signalling pathway for expression of transforming growth factor beta-1 (TGF-β1) have a substantial role in the progression of fibrosis, but also increased TGF-β1 expression enhances the activation of theca-interstitial cells and results in elevated androgen levels observed in PCOS [6]. Researchers have demonstrated a reciprocal association between ovarian theca and AT cells with androgen levels [3]. A recent study conducted by Ostinelli et al. has noted that androgens could be substantially produced due to abnormalities of AT, and its abnormalities are more prevalent in PCOS, which could affect the structure of AT [31].

Unlike β-Trophin and E-Trophin, the Metrnl level was statistically decreased in PCOS compared with the healthy group. Moreover, the current post hoc analysis showed significant differences in the Metrnl levels among PCOS subgroups. Correspondingly, in the current study, linear regression analysis revealed that Metrnl has an inverse statistical association with BMI, fasting insulin, and HOMA-IR in PCOS subgroups who were obese and overweight. These results match those observed in an earlier study by A.A. Majeed et al. [28]. Metrnl is a novel adipokine identified in the last decade that exhibits remarkable expression in subcutaneous fat for humans and rodents. Moreover, Metrnl is present in the bloodstream, exercising skeletal muscles and AT during exposure to cold [25]. Metrnl increased insulin sensitivity by activating the pathway of peroxisome proliferation-activated receptor gamma (PPAR-γ) [12]. Metrnl was elevated in obese/diabetic mice, resulting in enhanced energy expenditure and genes related to anti-inflammatory cytokine production and increased glucose tolerance [34]. The associations between the level of Metrnl and metabolic markers such as BMI, insulin and HOMA-IR in prior research results are conflicting. The findings of T2DM and obesity involving IR, such as PCOS, indicated an inverse statistical correlation between Metrnl and both BMI and HOMA-IR [2, 9]. In contrast to the findings of the present study, previous work by D. Löffler et al. showed a direct statistical association between Metrnl and both BMI and HOMA-IR [26]. The inconsistency between the findings of the present study and the literature indicated above may be due to the associations with the severity of metabolic abnormalities that may not be noticed in less severe disruptions of carbohydrate

metabolism. The duration of metabolic disease and the concurrent condition or related health concern may also have effects.

Many essential limitations need to be considered. For instance, the numbers of patients and controls were relatively small, and the present study was explicitly created to assess the levels of adipokines (β-Trophin, E-Trophin and Metrnl) in women with PCOS based on their BMI and show the relationship between adipokines and anthropometric, reproductive and metabolic parameters. Notwithstanding these limitations, further experimental parameters are needed to examine the correlations between these adipokines and anthropometric, reproductive and metabolic parameters more closely in larger sample sizes.

Conclusions

The most prominent findings from this study are that reproductive and metabolic characteristics statistically change as the degree of adiposity increases. Furthermore, β-Trophin and E-Trophin levels significantly increased, while Metrnl levels decreased as the degree of adiposity increased in women with PCOS. There is a statistical association between β-Trophin, E-Trophin and Metrnl and both reproductive and metabolic characteristics. Consequently, the results from this study suggest that β-Trophin, E-Trophin and Metrnl significantly reflect the abnormalities in reproductive and metabolic characteristics and could be used to detect the severity of reproductive and metabolic abnormalities and their complications in PCOS.

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Оцінка рівня адипокінів (бетатрофіну, ендотрофіну та білка, подібного до метеорину) та їхній взаємозв'язок із репродуктивними й метаболічними порушеннями в жінок із синдромом полікістозних яєчників залежно від індексу маси тіла

Мета роботи — вивчити порушення репродуктивної та метаболічної функції, а також рівні адипокінів (бетатрофіну, ендотрофіну та білка, подібного до метеорину) у жінок із синдромом полікістозних яєчників (СПКЯ) залежно від їхнього індексу маси тіла (ІМТ).

Матеріали та методи. У дослідженні взяли участь 160 жінок, обстежених на кафедрі хімії Наукового коледжу Університету Аль-Мустансирія, яких розподілили на чотири групи: 40 жінок із ожирінням і СПКЯ, 40 жінок із надмірною масою тіла та СПКЯ, 40 жінок із нормальною масою тіла та СПКЯ, а також 40 здорових жінок без СПКЯ. Усім жінкам проведено обстеження, яке передбачало визначення антропометричних, репродуктивних і метаболічних показників та рівня адипокінів.

Результати та обговорення. Рівні бетатрофіну й ендотрофіну були статистично значуще підвищені в жінок із СПКЯ порівняно зі здоровими жінками, тоді як рівень білка, подібного до метеорину, був значуще зниженим. Із підвищенням ступеня ожиріння в підгрупах СПКЯ рівень бетатрофіну та ендотрофіну зростав, а білка, подібного до метеорину, — знижувався. Установлено прямий зв'язок між бетатрофіном і ендотрофіном та індексом маси тіла, інсуліном і моделлю оцінки гомеостазу–

інсулінорезистентності у жінок із надмірною масою тіла й ожирінням і СПКЯ. Натомість білок, подібний до метеорину, мав зворотний зв'язок із зазначеними показниками в підгрупах.

Висновки. Отримані результати свідчать про те, що контроль маси тіла суттєво впливає на порушення системи адипокінів, пов'язані з ожирінням і його ускладненнями при СПКЯ.

Ключові слова: адипокіни, ожиріння, синдром полікістозних яєчників.

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