Journal of Medicine in Scientific Research

Volume 5 | Issue 1 Article 8

Subject Area:

Prevalence, phenotypic distribution, and clinical characteristics of polycystic ovary syndrome in Egyptian women with type 1 diabetes mellitus

Ayat I. Ghanem
National Institute of Diabetes and Endocrinology (NIDE), ayatghanem@yahoo.com

Dina H. Abd Elmonem
Al-Azhar University

Eman M. Aly
Al-Azhar University

Fatma K. Hammad
Al-Azhar University

Recommended Citation

Ghanem, Ayat I.; Abd Elmonem, Dina H.; Aly, Eman M.; and Hammad, Fatma K. (2022) "Prevalence, phenotypic distribution, and clinical characteristics of polycystic ovary syndrome in Egyptian women with type 1 diabetes mellitus," *Journal of Medicine in Scientific Research*: Vol. 5: Iss. 1, Article 8.
DOI: https://doi.org/10.4103/jmisr.jmisr_39_21

Original Article

Prevalence, phenotypic distribution, and clinical characteristics of polycystic ovary syndrome in Egyptian women with type 1 diabetes mellitus

Dina H. Abd Elmonem[a], Fatma K. Hammad[a], Ayat I. Ghanem[b], Eman M. Aly[a]

[a]Department of Internal Medicine and Department of Endocrinology and Metabolism, Faculty of Medicine for Girls, Al-Azhar University
[b]Department of Clinical and Chemical Pathology, National Institute of Diabetes and Endocrinology (NIDE), Cairo, Egypt

Abstract

Background

Type 1 diabetes mellitus (T1DM) has shown a steady increase in prevalence in most parts of the world. Polycystic ovary syndrome (PCOS) frequently occurs in 15–20% of women in their reproductive age. It is associated with subfertility, ovulatory dysfunction, dysregulated androgen biosynthesis, and increased risk of insulin resistance. This study aims to assess the prevalence, phenotypic distribution, and clinical characteristics of PCOS in a sample of Egyptian women with T1DM.

Patients and methods

A total of 100 Egyptian women in their reproductive age (18–42 years old) previously diagnosed as having T1DM were recruited in the study. They were screened for symptoms and signs of PCOS by clinical, laboratory, and radiological investigations.

Results

Overall, 28% of our women with T1DM had PCOS and 61% had metabolic syndrome. Frank PCOS was the most common PCOS phenotype (47%). When women with T1DM with and without PCOS were compared, BMI, waist circumference, systolic blood pressure, and fasting blood sugar were statistically higher in the PCOS group, whereas high-density lipoprotein cholesterol was statistically lower ($P < 0.05$). Follicular-stimulating hormone (FSH) and sex hormone-binding globulin were also statistically lower and luteinizing hormone (LH), LH/FSH ratio, and total testosterone (TT) were statistically higher ($P < 0.01$) in the PCOS than in the non-PCOS group. In women with T1DM, LH, LH/FSH ratio, and TT were positively correlated with BMI and waist circumference, whereas LH/FSH ratio and TT were negatively correlated with high-density lipoprotein cholesterol.

Conclusion

The prevalence of PCOS among women with T1DM in our sample of Egyptian patients revealed that PCOS and its associated traits are common findings. Thus, current T1DM management guidelines should include screening tests for PCOS and androgen excess as these patients have a high incidence of metabolic syndrome.

Keywords: Metabolic syndrome, phenotypes, polycystic ovary syndrome, type 1 diabetes mellitus

Introduction

Type 1 diabetes mellitus (T1DM) is a heterogeneous disorder characterized by pancreatic beta cell destruction, leading to total insulin deficiency. It represents about 5–10% of the total cases of diabetes worldwide [1]. Polycystic ovary syndrome (PCOS) is a heterogeneous condition characterized by hyperandrogenism and chronic anovulation. Approximately 6–20% of females in the reproductive age are affected, depending on the diagnostic criteria [2]. Numerous studies conducted on various continents

Access this article online

Quick Response Code:

Website: www.jmsr.eg.net

DOI: 10.4103/jmisr.jmisr_39_21

Correspondence to: Ayat I. Ghanem, MD, 5 Amin El Rafeey, Dokki, Giza 3750330, Egypt.
Tel: +20 122 215 2816;
E-mail: ayatghanem@yahoo.com

Submitted: 01-Jun-2021 **Revised:** 30-Jul-2021 **Accepted:** 13-Sep-2021 **Published:** 08-Apr-2022

How to cite this article: Abd Elmonem DH, Hammad FK, Ghanem AI, Aly EM. Prevalence, phenotypic distribution, and clinical characteristics of polycystic ovary syndrome in Egyptian women with type 1 diabetes mellitus. J Med Sci Res 2022;5:51-8.

have investigated the prevalence of PCOS. However, the prevalence varies according to different diagnostic criteria and ethnic groups [3]. Although there are many PCOS definitions, the Rotterdam consensus is the most commonly used. It needs two of the following: oligo/anovulation, clinical and/or biochemical hyperandrogenism, and/or ultrasound (US)-confirmed polycystic ovaries (PCO) [4]. Additionally, The Rotterdam and AE-PCOS Society guidelines distinguish at least three distinct clinical phenotypes: Frank PCOS (oligomenorrhea, hyperandrogenism, and PCO), ovulatory PCOS (hyperandrogenism, PCO, and regular menstrual cycles), and non-PCO-PCOS (oligomenorrhea, hyperandrogenism, and normal ovaries). A fourth phenotype is also recognized, mild or normo-androgenic PCOS, which is defined by PCO, oligomenorrhea, and normal androgens [5]. PCOS may present with menstrual disturbance, infertility, features of hyperandrogenemia (Hirsutism and acne), and signs of metabolic disturbances like insulin resistance and dyslipidemia [6].

PCOS has been described as a significant nonmodifiable risk factor associated with T2DM [7]. A few preliminary studies have found an elevated incidence of PCOS and androgen excess in women with T1DM. PCOS in T1DM may be affected to some degree by the same metabolic correlations associated with insulin resistance that are commonly seen in the general population of patients with PCOS without T1DM [8]. Insulin resistance can also occur in a significant number of patients with T1DM. However, regardless of diabetic control, glycated hemoglobin (HbA1c), or BMI, ovarian hyperandrogenism, and PCOS are common in teenage and adult women with T1DM. Investigations of the pathways underlying PCOS in nondiabetic women have shown a strong correlation between insulin levels and ovarian hyperandrogenism [9]. The root mechanism of hyperandrogenism in type I diabetes women is unknown. However, several studies have shown that in nondiabetic women with PCOS, insulin significantly increases ovarian steroidogenesis in a manner that is greater than that seen in normal women [10]; moreover, combining luteinizing hormone (LH) and insulin stimulation at normal concentrations can increase androgen biosynthesis in PCOS ovarian tissue [9].

Patients and methods

This study was carried out between 2018 and 2020. A total of 100 Egyptian women in their reproductive age previously diagnosed as having T1DM were recruited from the gynecology, obstetrics, and endocrinology outpatient clinics of the National Institute of Diabetes and Endocrinology (NIDE), Cairo, Egypt. All patients gave written informed consent before participation, which was approved by the ethics committee of Al-Azhar University, Faculty of Medicine for Girls, Cairo, Egypt.

Inclusion criteria: Egyptian women with T1DM aged between 18 and 42 years diagnosed according to the criteria of the American Diabetes Association were included [11]. According to the Rotterdam criteria for the diagnosis of PCOS, they were divided into two groups (PCOS and non-PCOS women with T1DM) [12].

Exclusion criteria: patients with T2DM and other types of diabetes, known history of any major medical conditions (cardiac-hepatic-renal diseases), patients on hormonal contraception, and other causes of excess androgen secretion were excluded.

All patients were subjected to medical history taking, including diabetes onset and duration, current insulin doses, a well-recorded medical history of very low c-peptide levels, and positive autoantibodies in the patient's documentation. A history of menstrual irregularities, fertility, Hirsutism, acne, and acanthosis nigricans was obtained. The examination included anthropometric measurements: BMI (weight in kilograms/height in square meters) and waist circumference (the midpoint between the lowest rib and the iliac crest). Hypertension prevalence was described as a systolic or diastolic blood pressure of 140 or 90 mmHg, respectively, and/or current therapy with a blood pressure-lowering medication(s) prescribed for the treatment of high blood pressure. Signs of hyperandrogenism (Hirsutism, acne, androgenic alopecia, and virilization) were documented. For patients with a history of increased hair growth, the degree was evaluated using a modified Ferriman–Gallway score [13]; modified Ferriman–Gallway score more than or equal to 8 defines Hirsutism.

Sample collection and laboratory analysis

From all of the patients, venous blood of 5 ml was withdrawn and divided into two sample tubes after 12–14 h of overnight fasting. The first 3 ml was put in a serum separator tube for blood chemistry and left to clot. Using centrifugation, serum was rapidly separated at 3000 rpm for 10 min. It was assessed for fasting blood sugar (FBG) and lipid profile [total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c)] using Cobas c311 analyzer for clinical chemistry (supplied by Roche Diagnostics, Mannheim, Germany). The second 2 ml was placed in a separate EDTA vacutainer for HbA1c analysis using D-10 HPLC ion-exchange chromatography (USA, supplied by Bio-Rad, Afak El Mostakbal Company, Cairo, Egypt). The hormonal profile was assessed for women with regular menses on the second day of menstruation. For nonmenstruating women, blood samples were taken at any time in the cycle. Overall, 3 ml of venous blood was drawn from each woman and left in a serum separator tube to clot. By centrifugation, the serum was rapidly separated for 10 min at 3000 rpm. It was tested for serum follicular-stimulating hormone (FSH), LH), total testosterone (TT), and sex hormone-binding globulin (SHBG), using Cobas e601 analyzer ELECSYS for immunoassay (ECLA) (supplied by Roche Diagnostics). LH/FSH ratio and free androgen index [FAI = TT (ng/dl)/SHBG (nmol/l)×100] were calculated.

Ovarian US imaging (transvaginal US) was performed using a MEDISON SONACE X-4-EXP with a vaginal probe frequency

of 7.5 MHz, and an abdominal probe frequency of 3.5 MHz was used in transabdominal US in women who were unable to use a vaginal approach. Sonographic PCO disease is described by the presence of more than or equal to 12 follicles of 2–9 mm in diameter in either or both ovaries or by an ovarian volume more than 10 cm^3. Just one ovary matching any of these criteria is sufficient to diagnose PCO [14].

Additionally, all patients were assessed for three or more of the following five criteria for metabolic syndrome, as defined by the NCEP ATP III [15]: waist circumference more than 40 inches (102 cm) or 35 inches (88 cm) for men and women, respectively; blood pressure more than 130/85 mmHg or on medication for previously diagnosed hypertension; fasting triglyceride level greater than 150 mg/dl; HDL-c level less than 40 mg/dl (men) or 50 mg/dl (women) or specific treatment for this lipid abnormality; and FBG more than or equal to 100 or specific treatment for hyperglycemia.

Statistical analysis

Data were analyzed using SPSS 20.0 (SPSS Inc., Chicago, Illinois, USA). Mean ± SD or median and range were used to summarize numerical data. In the case of normal data distribution, independent *t* test was used for comparisons. If not normal, comparisons were made using Mann–Whitney *U* test. Categorical data were presented as frequencies (%). Comparisons of categorical data were performed by χ^2 test. Pearson's or Spearman's correlation coefficient test (*r*) was used for correlation analysis. *P* values less than or equal to 0.05 were considered statistically significant.

Results

This study was conducted on 100 Egyptian women in their reproductive age (18–42 years old) previously diagnosed as having T1DM. According to the Rotterdam criteria for PCOS diagnosis, 28 (28%) women with T1DM in the analyzed sample had PCOS and 61 (61%) had metabolic syndrome according to the NCEP ATP III definition.

Table 1 shows the prevalence of PCOS, metabolic syndrome, and hyperandrogenic characteristics in all women with T1DM ($N = 100$).

The phenotypic distribution criteria of PCOS in women with T1DM ($N = 28$) revealed that Frank PCOS, ovulatory PCOS, non-PCO-PCOS, and norm-androgenic PCOS were 13 (47%), eight (28%), three (11%), and four (14%), respectively. Comparisons between women with T1DM with and without PCOS regarding clinical, biochemical, and hormonal characteristics are described in Table 2. Regarding age, duration of diabetes, and diastolic blood pressure, no statistically significant differences were observed between the two groups ($P > 0.05$). The BMI, waist circumference, and systolic blood pressure were statistically higher in PCOS than in non-PCOS ($P < 0.01$, $P < 0.01$, and $P = 0.05$, respectively). Moreover, FBG was statistically higher and HDL-c was statistically lower in PCOS than non-PCOS ($P = 0.01$ and $P < 0.01$), respectively, whereas no statistically significant differences were noted between the two groups regarding HbA1c, total cholesterol, triglycerides, and LDL-c ($P > 0.05$). The hormonal profiles of PCOS regarding FSH and SHBG were statistically lower, whereas LH, LH/FSH ratio, and TT were statistically higher than non-PCOS ($P < 0.01$), with no statistically significant differences between the two groups regarding FAI.

Furthermore, when we compared the two groups in terms of metabolic syndrome, clinical findings of PCOS, and US abnormalities, we found that there was no significant difference

Table 1: Prevalence of polycystic ovary syndrome, metabolic syndrome, and hyperandrogenic characteristics in all women with type 1 diabetes mellitus (*n*=100)

Parameters	*n* (%)
PCOS	28 (28)
MS	61 (61)
Irregular menses	31 (31)
Hirsutism	18 (18)
Acne	17 (17)
Acanthosis nigricans	25 (25)

MS, metabolic syndrome; PCOS, polycystic ovary syndrome.

Table 2: Comparisons between women with type 1 diabetes mellitus with and without polycystic ovary syndrome regarding clinical, biochemical, and hormonal characteristics

Parameters	Mean±SD		*P*
	PCOS (*n*=28)	Non-PCOS (*n*=72)	
Age (year)	31.96±7.91	30.02±7.64	0.26
Duration (years)	10.0±8.2	12.0±9.0	0.54
BMI (kg/m^2)	30.87±5.74	25.66±6.23	<0.01*
Waist circumference (cm)	104.25±9.05	93.44±12.63	<0.01*
Systolic BP (mmHg)	131.60±20.50	123.37±15.51	0.05*
Diastolic BP (mmHg)	83.21±9.15	82.04±13.55	0.67
FBG (mg/dl)	148.89±17.42	136.77±22.04	0.01*
HbA1c (%)	9.00±1.80	9.08±1.95	0.84
Cholesterol (mg/dl)	223.28±96.20	217.49±60.59	0.72
TG (mg/dl)	173.07±78.57	138.48±122.38	0.16
HDL-c (mg/dl)	44.46±11.59	52.12±8.03	<0.01*
LDL-c (mg/dl)	101.78±37.63	93.11±20.40	0.14
FSH (mU/ml)	4.87±0.92	5.87±1.11	<0.01*
LH (mU/ml)	11.17±4.39	6.36±1.09	<0.01*
LH/FSH ratio	2.3±0.8	1.2±0.3	<0.01*
TT (ng/dl)	68.57±25.08	32.30±8.43	<0.01*
SHBG (nmol/l)	47.55±10.26	92.14±23.35	<0.01*
FAI	2.58±0.67	2.43±0.75	0.34

BP, blood pressure; FAI, free androgen index; FBG, fasting blood sugar; FSH, follicle-stimulating hormone; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; LH, luteinizing hormone; PCOS, polycystic ovary syndrome; SHBG, sex hormone-binding globulin; TG, triglycerides; TT, total testosterone. *Statistically significant.

in metabolic syndrome criteria ($P = 0.4$), but menstrual irregularity, Hirsutism, acne, acanthosis nigricans, and US abnormalities' criteria were significantly higher in the PCOS group than the non-PCOS group ($P < 0.01$), as shown in Table 3.

Considering the correlation between the hormonal profile in all women with T1DM ($N = 100$) with the anthropometric and metabolic parameters, FSH was negatively correlated with BMI and waist circumference ($P < 0.05$), whereas LH and LH/FSH ratio were positively correlated with BMI and waist circumference ($P < 0.05$). Moreover, a significant negative correlation was noted between LH/FSH ratio with HDL-c ($P = 0.03$). Besides, TT showed a positive correlation with BMI, waist circumference, and FBG ($P < 0.05$), and it showed a negative correlation with HDL-c ($r=-0.225$; $P = 0.02$). SHBG showed a significant positive correlation with waist circumference ($P = 0.03$). FAI was not correlated with other parameters ($P > 0.05$), as mentioned in Table 4.

Moreover, no statistically significant correlation was found between the hormonal profile of patients with T1DM with PCOS ($N = 28$) and the anthropometric and metabolic parameters ($P > 0.05$), as shown in Table 5.

Discussion

T1DM is a progressive autoimmune disease that impairs natural reproductive activity during life in a variety of ways. Despite advancements in diabetes treatment, teenage girls and young women with T1DM continue to experience regular reproductive system disturbances [16]. Despite the fact that PCOS is often associated with insulin-resistant conditions such as T2DM, numerous studies have shown that patients with T1DM may often encounter insulin resistance, especially obese individuals who exhibit a high degree of hyperandrogenic disorders [17]. In the current study, we aimed to assess the prevalence, phenotypic distribution, and clinical characteristics of PCOS in a sample of Egyptian women with T1DM.

Table 3: Clinical findings and ultrasound abnormalities in polycystic ovary syndrome and non-polycystic ovary syndrome cases with type 1 diabetes mellitus

Parameters	PCOS ($n=28$) [n (%)]	Non-PCOS ($n=72$) [n (%)]	P
MS			
Yes	18 (64.4)	40 (55.6)	0.40
No	10 (35.7)	32 (44.4)	
Menstrual irregularity			
Yes	20 (71.4)	12 (16.7)	<0.01*
No	8 (28.6)	60 (83.3)	
Hirsutism			
Yes	18 (67.9)	0 (0.0)	<0.01*
No	10 (32.1)	72 (100)	
Acne			
Yes	9 (32.1)	8 (11.1)	0.01*
No	19 (67.9)	64 (88.9)	
Acanthosis nigricans			
Yes	12 (42.9)	14 (19.4)	0.01*
No	16 (57.1)	58 (80.6)	
US abnormalities			
Yes	25 (89.3)	5 (6.9)	<0.01*
No	3 (10.7)	67 (93.0)	

MS, metabolic syndrome; PCOS, polycystic ovary syndrome; US, ultrasonography. *Statistically significant

The main finding in our study is that the prevalence of PCOS among Egyptian women with T1DM represents 28 (28%) of the total 100 patients with T1DM. In agreement with our result, a systematic review and meta-analysis in 2016 demonstrated that in women with T1DM, the prevalence of PCOS and its associated trait was 24% in nine primary studies including 475 adolescent or adult women with T1DM [8], but a lower prevalence (7.4%) of PCOS was detected among Italian T1DM adolescents [18] and higher (52%) was identified in Japanese women with T1DM [19]. The relationship between PCOS and T1DM is complex. Insulin deficiency, hyperglycemia with glucose toxicity, and exogenous systemic hyperinsulinism, caused by supraphysiological doses of subcutaneous insulin and insulin resistance, may result in decreased gonadotropin levels due to decreased gonadotropin-releasing hormone secretion, thus favoring the occurrence of PCOS in patients with T1DM [20]. Irregular menstruation is one of the PCOS diagnostic criteria, but 30% of women with PCOS may have normal menstruation [21]. In our study, 31% of our patients had menstrual irregularities (oligomenorrhea or amenorrhea). In agreement, Schweiger *et al.* [22] investigated 181 T1DM women and reported a 35% prevalence of menstrual irregularities. Overall, 18% of our women with T1DM complained of excessive hair growth and 17% complained of acne. Codner *et al.*[23] investigated 42 women with T1DM and reported that 29 and 17% had Hirsutism and acne, respectively, whereas Zachurzok *et al.* [24] found that the prevalence of Hirsutism was 6% among adolescent women with T1DM. This could be explained by the fact that clinical and laboratory findings of hyperandrogenism evolve slowly during the second decade of life. According to the NCEP ATP III criteria, the prevalence of metabolic syndrome in our study was 61%. Depending on the diagnostic criteria used, ~50% of patients with T1DM are currently obese or overweight and between 8 and 40% meet the metabolic syndrome criteria [25].

The phenotypic distribution criteria of PCOS among patients with T1DM with PCOS revealed that frank PCOS, ovulatory PCOS, non-PCO-PCOS, and norm-androgenic PCOS were 47, 28, 11, and 14%, respectively. In comparison with our results, Fauser *et al.*[26] studied 88 female patients with PCOS, where 65% of them were classified as frank PCOS, 12% as ovulatory, 10% as non-PCO-PCOS, and 13% as normo-androgenic PCOS. Other studies reported that ovulatory PCOS is the most prevalent phenotype of PCOS in type 1 diabetes [20,23].

A comparison of the PCOS group and the non-PCOS group among our patients with T1DM revealed that there was no

significant difference between the two groups in terms of age and duration of diabetes. This is in line with a study published in 2013 [24]. The PCOS group had a significant higher BMI than the non-PCOS group. A similar result was reported among 102 women with T1DM in Saudi Arabia [27]. However, another study among Japanese women revealed no significant difference between the two groups in BMI [19]. Moreover, waist circumference was higher in the PCOS

Table 4: Correlation between the hormonal profile with the anthropometric and metabolic parameters in all women with type 1 diabetes mellitus (*n*=100)

Parameters	FSH (mU/ml)		LH (mU/ml)		LH/FSH ratio	
	r	*P*	*r*	*P*	*r*	*P*
Age (year)	−0.02	0.81	0.03	0.74	0.03	0.80
Duration (years)	0.20	0.07	−0.18	0.06	0.003	0.206
BMI (kg/m^2)	−0.250	0.01*	0.210	0.04*	0.267	0.01*
Waist circumference (cm)	−0.329	<0.01*	0.427	0.01*	0.327	<0.001*
FBG (mg/dl)	−0.06	0.66	0.15	0.15	0.17	0.09
HbA1c (%)	0.01	0.89	−0.01	0.95	−0.01	0.89
TG (mg/dl)	−0.16	0.12	0.80	0.45	0.12	0.22
HDL-c (mg/dl)	0.14	0.15	−0.16	0.10	−0.215	0.03*
	TT (ng/dl)		SHBG (nmol/l)		FAI	
	r	*P*	*r*	*P*	*r*	*P*
Age (year)	0.01	0.89	0.12	0.25	0.50	0.63
Duration (years)	−0.20	0.06	0.06	0.57	−0.18	0.07
BMI (kg/m^2)	0.22	0.03*	0.15	0.13	−0.02	0.81
Waist circumference (cm)	0.296	<0.01*	0.225	0.03*	0.09	0.38
FBG (mg/dl)	0.209	0.04*	0.03	0.80	0.11	0.20
HbA1c (%)	−0.02	0.86	0.01	0.88	0.00	0.99
TG (mg/dl)	0.14	0.17	0.02	0.86	0.19	0.06
HDL-c (mg/dl)	−0.225	0.02*	0.00	0.99	−0.03	0.77

FAI, free androgen index; FBG, fasting blood sugar; FSH, follicle-stimulating hormone; HbA1c, glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; LH, luteinizing hormone; SHBG, sex hormone-binding globulin; TG, triglycerides; TT, total testosterone. *Statistically significant

Table 5: Correlation between the hormonal profile and the anthropometric and metabolic parameters in all women with type 1 diabetes mellitus with polycystic ovary syndrome (*n*=28)

Parameters	FSH (mU/ml)		LH (mU/ml)		LH/FSH ratio	
	r	*P*	*r*	*P*	*r*	*P*
Age (year)	0.144	0.464	−0.172	0.383	−0.243	0.213
Duration (years)	−0.114	0.563	−0.311	0.107	−0.264	0.175
BMI (kg/m^2)	−0.003	0.989	−0.178	0.365	−0.205	0.294
Waist circumference (cm)	−0.004	0.984	−0.129	0.512	−0.129	0.514
FBG (mg/dl)	−0.133	0.500	−0.159	0.420	−0.102	0.605
HbA1c (%)	−0.051	0.801	−0.042	0.836	−0.018	0.928
TG (mg/dl)	−0.044	0.822	−0.049	0.804	−0.026	0.896
HDL-c (mg/dl)	0.004	0.982	0.143	0.469	0.150	0.446
	TT (ng/dl)		SHBG (nmol/l)		FAI	
	r	*P*	*r*	*P*	*r*	*P*
Age (year)	−0.323	0.093	0.213	0.275	−0.095	0.632
Duration (years)	−0.362	0.058	0.136	0.489	−0.225	0.249
BMI (kg/m^2)	0.220	0.06	0.15	0.13	−0.02	0.81
Waist circumference (cm)	0.296	0.07	0.225	0.03	0.09	0.38
FBG (mg/dl)	−0.176	0.371	−0.081	0.683	−0.148	0.45
HbA1c (%)	0.000	1.000	0.020	0.920	0.189	0.345
TG (mg/dl)	−0.045	0.820	0.083	0.673	−0.020	0.920
HDL-c (mg/dl)	0.139	0.480	0.126	0.524	−0.073	0.710

FAI, free androgen index; FBG, fasting blood sugar; FSH, follicle-stimulating hormone; HbA1c, glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; LH, luteinizing hormone; SHBG, sex hormone-binding globulin; TG, triglycerides; TT, total testosterone.

group compared with the non-PCOS group, which agreed with Amato *et al*. [28], but Busiah *et al*. [20], reported no significant difference in waist circumference between female patients with T1DM with and without PCOS. Excess androgen and insulin resistance can be responsible for the progression of all metabolic syndrome symptoms associated with PCOS [29].

Regarding biochemical parameters between the two groups, the PCOS group showed a significantly higher FBS than the non-PCOS group. In agreement with our result, Li and Li [30] concluded higher FBG in Chinese women with PCOS compared with those without PCOS. However, Kim and Choi [31], found no significant difference in FBG between PCOS and non-PCOS cases. On the contrary, HbA1c showed no significant difference between the two groups, which agrees with similar studies [27]. An atherogenic lipid profile is very common in patients with PCOS. Most often, it is represented by hypertriglyceridemia, low HDL-c, and high LDL-c. In our study, the PCOS group had higher total cholesterol, triglyceride, and LDL levels than the non-PCOS group, despite the fact that there was no statistically significant difference between the two groups ($P > 0.05$), which could be attributed to some patients' use of antihyperlipidemic medications. However, HDL-c was significantly lower in the PCOS group than the non-PCOS group, in agreement with a similar result by Braham *et al*. [27].

Regarding hormonal profile, the PCOS group showed significantly lower FSH compared with the non-PCOS group. In accordance with our results, two studies reported that FSH level was lower in T1DM with PCOS than without PCOS [19,24]. The hypothalamic-pituitary-ovarian axis has been significantly disrupted in PCOS. The most obvious neuroendocrine characteristic controlling irregular ovarian follicle production in PCOS is increased LH pulsatility in terms of frequency and amplitude, with comparatively low FSH secretion. Increased LH pulse frequency stimulates androgen activity in theca cells, whereas decreased FSH levels inhibit follicle maturation and thus ovulation. LH level and LH/FSH ratio were significantly higher in the PCOS group than the non-PCOS group, which agreed with Zachurzok *et al*. [24]. However, Arina *et al*. [19] found no statistically significant difference in LH and LH/FSH ratio between T1DM with PCOS and T1DM without PCOS. Moreover, our results showed higher TT level and lower SHBG in the PCOS group compared with the non-PCOS group. These results were matched by Busiah *et al.* [20] and Zachurzok *et al*. [24]. On the contrary, a study conducted by Amato *et al*. [28] showed there was no significant difference regarding SHBG between the two groups. PCOS women have 40% lower insulin sensitivity than normal, as well as insulin resistance and reduced insulin responsiveness. Compensatory hyperinsulinemia stimulates ovarian androgen synthesis and secretion by theca cells, thus decreasing SHBG, resulting in a rise in free androgen levels and worsening of PCOS symptoms [32]. FAI was higher in PCOS than in the non-PCOS group, with no statistically significant difference. It may contribute to that some cases of PCOS are not hyperandrogenic. A similar study [24] done on nine female patients with T1DM with PCOS and 38 female patients with T1DM without PCOS reported that FAI was significantly higher in the PCOS group.

Concerning comparison between PCOS and Non-PCOS T1DM groups regarding clinical findings of PCOS and US abnormalities, the PCOS group had a higher prevalence of metabolic syndrome than the non-PCOS group (64 vs. 56%, respectively). Ehrmann *et al*. [33] reported 43% of 368 female patients with PCOS had metabolic syndrome. Moreover, menstrual dysfunction was more prevalent in the POSC group (71 vs. 17%). Braham *et al*. [27] reported 37.5% of patients with T1DM with PCOS had irregular menses, whereas 24.4% of female patients with T1DM without PCOS had irregular menses. In terms of Hirsutism, 68% of the PCOS group had been diagnosed, compared with no cases in the non-PCOS group, which agreed with other studies that found Hirsutism prevalence rates of 89 and 80% in obese and lean PCOS cases, respectively [34]. In the PCOS group, acne and acanthosis nigricans were more prevalent than in the non-PCOS group. In accordance, Codner *et al*. [23] found that there was a higher prevalence of acne among T1DM with PCOS than without PCOS. However, a study [27] in 2017 reported no difference between the two groups in acne prevalence in females with T1DM. Finally, US abnormalities (increased ovarian volume or thickness, detectable cysts in one or both ovaries) were more prevalent in PCOS than in non-PCOS cases.

Considering the correlation between hormonal profile and anthropometric and metabolic parameters among all patients, FSH was negatively correlated and LH and LH/FSH ratio was positively correlated. Among Chinese women, the LH and LH/FSH ratio was significantly associated with visceral obesity and increased weight [35]. This can be clarified by the fact that being overweight results in increased endogenous estrogen output by mesenchyme adipose tissue, which could potentially act centrally to decrease FSH. Moreover, a negative correlation between LH/FSH ratio and TT with HDL-c was observed as increased androgens connected with dyslipidemia owing to higher fibrinogen and increased plasminogen activator inhibitor-1 [36]. In agreement, Zachurzok *et al*. [24] studied 47 female patients who had T1DM and found a negative correlation between TT and HDL among their cases. However, Arshad *et al*. [37] reported a negative correlation between TT and LH/FSH ratio with HDL-c in 2019, but Pirwany *et al.* [38] found no correlation. Furthermore, a positive correlation between TT with BMI, waist circumference, and FBG was reported. Similar results identified this correlation [39], as hyperandrogenemia decreases insulin-stimulated glucose uptake in peripheral tissues, leading to insulin resistance and eventually dysglycemia. Considering the correlation between hormonal profile and the anthropometric and metabolic parameters among patients with T1DM with PCOS, no statistically significant correlation was noted ($P > 0.05$). The insufficient correlation results may be attributed to the

small number of female patients who had T1DM with PCOS. Alnakash and Al-Tae'e [40] studied 107 female patients with PCOS and found no relation between BMI and LH, FSH, and LH/FSH ratio.

Conclusion

The current study showed a 28% prevalence of PCOS in Egyptian women with T1DM. The most common PCOS phenotype is frank PCOS (47%). Moreover, 61% had metabolic syndrome criteria. This means that in women with T1DM, PCOS and its related traits are common findings. Hence, PCOS and androgen excess screening should be incorporated into the current T1DM guidelines, which shows a high prevalence of metabolic syndrome among those diabetic females. The limitations in our study included the sample size, which was relatively small, so future large-scale studies with larger sample sizes in various ethnic groups are needed to identify managements for these T1DM adolescent women, such as insulin sensitizers, which could decrease the mean insulin dose, especially during puberty, when insulin resistance may exacerbate their diabetic control and androgenic symptoms, thereby improving their quality of life.

Acknowledgements

The authors would like to express their deep appreciation to the National Institute of Diabetes and Endocrinology for its cooperation in the study.

Financial support and sponsorship

National institute of diabetes and endocrinology.

Conflicts of interest

There are no conflicts of interest.

References

1. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Epidemiology of type 1 diabetes. Endocrinol Metab Clin North Am 2010; 39:481–497.
2. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. J Endocr Soc 2019; 3:1545–1573.
3. Ding T, Hardiman PJ, Petersen I, Wang FF, Qu F, Baio G. The prevalence of polycystic ovary syndrome in reproductive-aged women of different ethnicity: a systematic review and meta-analysis. Oncotarget 2017; 8:96351–96358.
4. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, *et al*. Position statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an androgen excess society guideline. J Clin Endocrinol Metab 2006; 91:4237–4245.
5. Moghetti P, Tosi F, Bonin C, Di Sarra D, Fiers T, Kaufman J, *et al*. Divergences in insulin resistance between the different phenotypes of the polycystic ovary syndrome. J Clin Endocrinol Metab 2013; 98:E628–E637.
6. Ramanand SJ, Ghongane BB, Ramanand JB, Patwardhan MH, Ghanghas RR, Jain SS. Clinical characteristics of polycystic ovary syndrome in Indian women. Indian J Endocrinol Metab 2013; 17:138–145.
7. Gambineri A, Patton L, Altieri P, Pagotto U, Pizzi C, Manzoli L, Pasquali R. Polycystic ovary syndrome is a risk factor for type 2 diabetes results from a long-term perspective study. Diabetes 2012; 61:2369–2374.
8. Escobar-Morreale HF, Roldán-Martín MB. Type 1 diabetes and polycystic ovary syndrome: systematic review and meta-analysis. Diabetes Care 2016; 39:639–648.
9. Tibuni-Sanders S, Nader S. PCOS and hyperandrogenism in type 1 diabetes. Open J Obstetr Gynecol 2012; 2:76–80.
10. Bolli GB. Physiological insulin replacement in type 1 diabetes mellitus. Exp Clin Endocrinol Diab 2001; 109:S317–S332.
11. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes. Diabetes Care 2020; 43(Supplement 1):S14–S31.
12. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19:41–47.
13. Aswini R, Jayapalan S. Modified Ferriman–Gallwey scorein hirsutism and its association with metabolic syndrome. Int J Trichol 2017; 9:7–13.
14. Balen AH, Laven JS, Tan SL, Dewailly D. Ultrasound assessment of the polycystic ovary: international consensus definitions. Hum Reprod Update 2003; 9:505–514.
15. Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb 2005; 12:295–300.
16. Codner E, Merino PM, Tena-Sempere M. Female reproduction and type 1 diabetes: from mechanisms to clinical findings. Hum Reprod Update 2012; 18:568–585.
17. Escobar-Morreale HF, Roldán-Martín MB, Barrio R, Alonso M, Sancho J, de la Calle H, García-Robles R. High prevalence of the polycystic ovary syndrome and hirsutism in women with type 1 diabetes mellitus. J Clin Endocrinol Metab 2000; 85:4182–4187.
18. Bizzarri C, Benevento D, Ravà L, Patera IP, Schiaffini R, Ciampalini P, *et al*. Ovarian hyperandrogenism in adolescents and young women with type I diabetes is primarily related to birth weight and body mass index. Fertil Steril 2011; 96:1497–1502.
19. Arina M, So N, Masamitsu T, Takuma K, Hiroshi N, Hiraku K, *et al*. Ovarian morphology and prevalence of polycystic ovary syndrome in Japanese women with type 1 diabetes mellitus. J Diabetes Investig 2013; 4:326–329.
20. Busiah K, Colmenares A, Bidet M, Tubiana-Rufi N, Levy-Marchal C, Delcroix C, *et al*. High prevalence of polycystic ovary syndrome in type 1 diabetes mellitus adolescents: is there a difference depending on the NIH and Rotterdam criteria?. Hormone Res Paed 2017; 87:333–341.
21. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clin Epidemiol 2014; 6:1.
22. Schweiger BM, Snell-Bergeon JK, Roman R, McFann K, Klingensmith GJ. Menarche delay and menstrual irregularities persist in adolescents with type 1 diabetes. Reprod Biol Endocrinol 2011; 9:61.
23. Codner E, Soto N, Lopez P, Trejo L, Avila A, Eyzaguirre FC, *et al*. Diagnostic criteria for polycystic ovary syndrome and ovarian morphology in women with type 1 diabetes mellitus. J Clin Endocrinol Metab 2006; 91:2250–2256.
24. Zachurzok A, Deja G, Gawlik A, Drosdzol-Cop A, Małecka-Tendera E. Hyperandrogenism in adolescent girls with type 1 diabetes mellitus treated with intensive and continuous subcutaneous insulin therapy. Endokrynol Pol 2013; 64:121–128.
25. Chillarón JJ, Flores Le-Roux JA, Benaiges D, Pedro-Botet J. Type 1 diabetes, metabolic syndrome and cardiovascular risk. Metabolism 2014; 63:181–187.
26. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, *et al*. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril 2012; 97:28–38.
27. Braham R, Robert AA, Musallam MA, Alanazi A, Swedan NB, Al Dawish MA. Reproductive disturbances among Saudi adolescent girls and young women with type 1 diabetes mellitus. World J Diabetes 2017; 8:475–483.
28. Amato MC, Guarnotta V, Ciresi A, Modica R, Pantò F, Giordano C. No phenotypic differences for polycystic ovary syndrome (PCOS) between women with and without type 1 diabetes mellitus. J Clin Endocrinol Metab 2014; 99:203–211.
29. Popovic V, Korbonits M. *Metabolic syndrome consequent to endocrine disorders*. 1st Ed. S. Karger; Basel, Switzerland: 2018. DOI: 10.1159/

isbn.978-3-318-06335-6.
30. Li W, Li Q. Dysregulation of glucose metabolism even in Chinese PCOS women with normal glucose tolerance. Endocr J 2012; 59:765–770.
31. Kim JJ, Choi YM. Dyslipidemia in women with polycystic ovary syndrome. Obstet Gynecol Sci 2013; 56:137–142.
32. Stener-Victorin E, Maliqueo M, Soligo M, Protto V, Manni L, Jerlhag E, *et al*. Changes in HbA1c and circulating and adipose tissue androgen levels in overweight-obese women with polycystic ovary syndrome in response to electroacupuncture. Obes Sci Pract 2016; 2:426–435.
33. Ehrmann DA, Liljenquist DR, Kasza K, Azziz R, Legro RS, Ghazzi MN. Prevalence and predictors of the metabolic syndrome in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2006; 91:48–53.
34. Saxena P, Prakash A, Nigam A, Mishra A. Polycystic ovary syndrome: is obesity a sine qua non? A clinical, hormonal, and metabolic assessment in relation to body mass index. Indian J Endocrinol Metab 2012; 16:996–999.
35. Zhao L, Zhu C, Chen Y, Chen C, Cheng J, Xia F, *et al*. LH/FSH ratio is associated with visceral adipose dysfunction in Chinese women older than 55. Front Endocrinol (Lausanne) 2018; 9:419.
36. Beata B, Duleba AJ, Spaczynski RZ, Pawelczyk L. Lipids in polycystic ovary syndrome: role of hyperinsulinemia and effects of metformin. Am J Obstet Gynecol 2006; 194:1266–1272.
37. Arshad FA, Mehmood R, Kausar N, Bibi A, Khan MA, Hussain S, Perveen S. Assessment and association between lipid and hormonal profile in nonpregnant females having polycystic ovarian syndrome. Endocrinol Metab Syndr 2019; 8:297.
38. Pirwany IR, Fleming R, Greer IA, Packard CJ, Sattar N. Lipids and lipoprotein subfractions in women with PCOS: relationship to metabolic and endocrine parameters. Clin Endocrinol (Oxf) 2001; 54:447–453.
39. Patel SM, Ratcliffe SJ, Reilly MP, Weinstein R, Bhasin S, Blackman MR, *et al*. Higher serum testosterone concentration in older women is associated with insulin resistance, metabolic syndrome, and cardiovascular disease. J Clin Endocrinol Metab 2009; 94:4776–4784.
40. Alnakash AH, Al-Tae'e NK. Polycystic ovarian syndrome: the correlation between the LH/FSH ratio and disease manifestations. Middle East Fert Soc J 2007; 12:35–40.