POLYCYSTIC OVARY SYNDROME AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS IN DUHOK CITY, KURDISTAN REGION OF IRAQ

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ABSTRACT

Background: PCOS is the most common endocrine disorders with a potential to cause short- and long-term comorbidities especially T2DM. The present study was conducted to determine the prevalence of PCOS among type 2 diabetic patients in Duhok City, Kurdistan Region of Iraq.

Methods: This study is an observational study conducted through cross-sectional design. Type 2 diabetic women (n = 200) at reproductive age were included. PCOS was confirmed using the clinical, hormonal and radiological findings according to Rotterdam criteria. Data of the study are determined in frequency distribution whether mean and standard deviation or frequency and percentage.

Results: The prevalence of PCOS was high (81.5%) among type 2 diabetic women. The frequency of clinical findings in the type 2 diabetic patients revealed that majority of them had clinical feature and hormonal features while 77% of them had positive ultrasound features, 49% were newly diagnosed diabetic patients and 44.5% of the patients on metformin medication.

Conclusions: PCOS is highly prevalent in type 2 diabetic patients. In-depth research is required to determine the appropriate methods to identify susceptible women including genetic studies in order to prevent or treat or limit the implications.

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Keywords: Polycystic ovary syndrome, Diabetes Mellitus, Rotterdam criteria.

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorders and most common cause of infertility in women affecting about 6-15% of women at reproductive age[1], characterized by elevated androgen hormone, menstrual irregularities, and/or small cysts on one or both ovaries[2]. PCOS often coexist with other conditions such as dysglycemia and insulin resistance, that range from impaired glucose tolerance to type 2 diabetes mellitus (T2DM)[3], hyperandrogenism[4], reproductive disturbances and oligo/anovulation[1], and women may develop or be at higher risk for several serious health conditions especially if they are overweight such as heart disease, diabetes mellitus, high blood pressure, high level of low-density lipoprotein (LDL cholesterol), sleep apnea, stroke5, and susceptible to develop anxiety, depression and chronic stress with poorer ego-resiliency[6].

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Because of complexity of PCOS, diagnosis can be challenging, there are many sets of criteria for diagnosis of PCOS such as National Institutes of Health (NIH) Criteria (Stein and Leventhal are credited in 1935), Rotterdam Criteria (European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine adopted this set of criteria in 2003), Androgen Excess Society (AES) Criteria in 2006, Evidence-Based Guidelines published in 2013 by the Endocrine Society and the 2018 International Evidence-Based Guideline[7].

All the aforementioned sets share potentials and limitations but the main principles depend on menstrual irregularity, hormonal abnormality and presence of ovarian morphology[8]. Furthermore, insulin resistance is a noticeable feature in women with PCOS, which occurs in 70-95% of women with PCOS who are overweight and 30-75% of women with PCOS who are normal or underweight[9].

Many studies present the link between glucose intolerance and PCOS. A recent study presents a direct association between the risk of T2DM in women with PCOS and the overweight/obesity status especially during early adulthood[10].

Prevalence of diabetes mellitus is expected to increase rapidly. In Iraq, it is estimated that the number of diabetics exceed 1.7 million[11]. More than 90% are T2DM which is a major cause of premature illness and death and an increased risk of cardiovascular diseases[12],[13].

Meanwhile, maintaining healthy weight leads to significant reduction of T2DM risk in women with PCOS3. Pelusi et al. (2004) concluded that women with PCOS have 5-10 folds increase risk of glucose intolerance than normal women which is not limited to a single ethnic group[14]. Long et al. (2022) states that PCOS is common in female patients with T2DM or at risk of developing T2DM mainly at childbearing age, therefore, screening and prevention of PCOS is considered very important[15].

The goal of this study is to find out how common is PCOS among women with T2DM, and ascertain the relationship between PCOS and T2DM in Duhok City, Kurdistan Region of Iraq.

METHODS

This study is an observational study conducted through cross-sectional design at Azadi Teaching Hospital in coordination with Maternity and Gynecology Teaching Hospital in Duhok City on 200 cases. The study conducted from April 15th to September 15th, 2023.

Female patients at reproductive age (18 - 49 years according to World Health Organization definition) that meet criteria of T2DM (FBS ≥ 126 mg/dl, RBS ≥ 200 mg/dl, HbA1c ≥ 6.5% according to American Diabetes Association criteria) and PCOS (Clinical, hormonal, radiological findings according to Rotterdam criteria, presence of two of three of the following criteria: presence of menstrual irregularity as oligo-anovulation, clinical/biochemical signs of hyperandrogenism (LH: 10-20 mIU/ml, FSH: 4-8 mIU/ml, Prolactin: more than 20 mIU/ml, Ratio of LH:FSH is 2:1) and polycystic ovaries seen on ultrasonography antral follicular excess on ultrasound with ≥12 follicles from 2 mm to 9 mm per ovary and/or ovarian volume ≥10 ml in at least one ovary)) are included in the study. While pregnant women and patients with other diseases that result in excess androgen (e.g., Cushing's syndrome, hyperprolactinemia, thyroid dysfunction, and tumors), congenital adrenal hyperplasia, malabsorptive disorder, eating disorder, post-menopause, a history of bariatric surgery, liver, renal disease and missing data in patient charts were excluded. Data collection from medical records are mined including age,

height, weight, body mass index (BMI), any menstrual disturbance (oligomenorrhea/primary or secondary amenorrhea), hirsutism, acne, male alopecia, or infertility (primary or secondary) are just a few of the variables that were collected, hormonal test profile and ultrasonography.

Data of the study are determined in frequency distribution whether mean and standard deviation or frequency and percentage. The statistical calculation performed by Statistical Package for Social Sciences version 27.0 (SPSS; IBM; USA).

All scientific and ethical consideration have been taken into consideration, the study obtained the approval of Scientific Committee at College of Medicine, University of Duhok and Research Ethics Committee at Duhok Directorate General of Health. Before patients' interview each patient were informed about the aim of the study and the confidentiality of their data as well as their rights to refuse or participate in the present study were confirmed, then all subjects gave oral and written consent prior to participation in the study.

RESULTS

The sociodemographic characteristics of the 200 study subjects shows that most common age group were 35 - 44 years old; married with 1-3 children (Table: 01).

Table 01: Sociodemographic characteristics of the study sample (diabetic patients)

Characteristic	No.	%
18 - 24	15	7.5
25 - 34	6<4	32.0
35 - 44	100	50.0
45 - 49	21	10.5
Duhok	174	87.0
Shekhan	13	6.5
Zakho	5	2.5
Semel	4	2.0
Bardarash	3	1.5
Amedi	1	0.5
Married	179	89.5
Single	21	10.5
Nullipara	43	21.5
1 - 3	76	38.0
4 - 6	55	27.5
7 - 11	26	13.0
Total	**200**	**100.0**

The mean age of the study population was 36, the mean number of children was 3, the mean BMI was 31 (kg/m2) and the mean glycemic index was 7 (Table: 02).

Table 02: Descriptive statistics of the study 200 type 2 diabetic patients

Characteristic	No.	Minimum	Maximum	Mean	Standard Deviation
Age (years)	200	18	51	36.29	7.18
No. of children	200	0	11	3.20	2.62
LH (mIU/ml)	197	1.00	66.70	16.01	10.48
FSH (mIU/ml)	197	2.00	64.00	8.49	4.86
Prolactin (mIU/ml)	192	1.70	49.00	25.59	8.86
BMI (kg/m^2)	200	17.7	44.1	31.09	4.54
HbA1c (%)	200	4.89	12.90	7.19	1.03

The frequency of clinical findings in the type 2 diabetic patients revealed that majority of them had clinical feature and hormonal features while 77% of them had positive ultrasound features, 81.5 % had positive diagnosis of PCOS according to Rotterdam criteria, 49% were newly diagnosed diabetic patients and 44.5% of the patients on metformin medication (Table: 03).

Table 03: Clinical characteristics of the study sample (diabetic patients)

Characteristic		No.	%
Clinical features	Positive	195	97.5
	Negative	5	2.5
US features	Positive	154	77.0
	Negative	46	23.0
Hormone	Positive, hormone done	194	97.0
	Negative, hormone not done	6	3.0
PCOS diagnosis	Positive	163	81.5
	Negative	37	18.5
DM	Old	81	40.5
	New	119	59.5
Medication	Metformin	89	44.5
	Clomiphene	0	0.0
	Letrozole	4	2.0
	Metformin+Clomiphene	17	8.5
	Metformin+Letrozole	13	6.5
	None	77	38.5

A significant relation between PCOS diagnosis and the age, marital status, number of children and medications had been found (p=0.003, 0.016, 0.012, 0.026 respectively) (Table: 04) (Figure: 01, 02, 03).

Table 04: Characteristics of the study sample (n = 200) by PCOS diagnosis

Characteristic		Positive (n=163)		Negative (n=37)		Total		*P* value*
		No.	%	No.	%	No.	%	
Age (years)	18 – 24	15	100.0	0	0.0	15	100	**0.003**
	25 – 34	58	90.6	6	9.4	64	100	
	35 – 44	77	77.0	23	23.0	100	100	
	45 – 49	13	61.9	8	38.1	21	100	
Marital status	Married	142	79.3	37	20.7	179	100	**0.016**
	Single	21	100.0	0	0.0	21	100	
No. of children	Nullipara	41	95.3	2	4.7	43	100	**0.012**
	1 – 3	63	82.9	13	17.1	76	100	
	4 – 6	42	76.4	13	23.6	55	100	
	7 – 11	17	65.4	9	34.6	26	100	
DM	Old	61	75.3	20	24.7	81	100	0.063
	New	102	85.7	17	14.3	119	100	
Medications	Metformin	70	78.7	19	21.3	89	100	**0.026**
	Letrozole	4	100.0	0	0.0	4	100	
	Metformin+Clomiphene	12	70.6	5	29.4	17	100	
	Metformin+Letrozole	8	61.5	5	38.5	13	100	
	None	69	89.6	8	10.4	77	100	

* Based on Chi square or Fisher's exact test.

A statistically significant higher level of LH in those with positive PCOS diagnosis compared to negative diagnosis of PCOS (p=<0.001) (Table: 05).

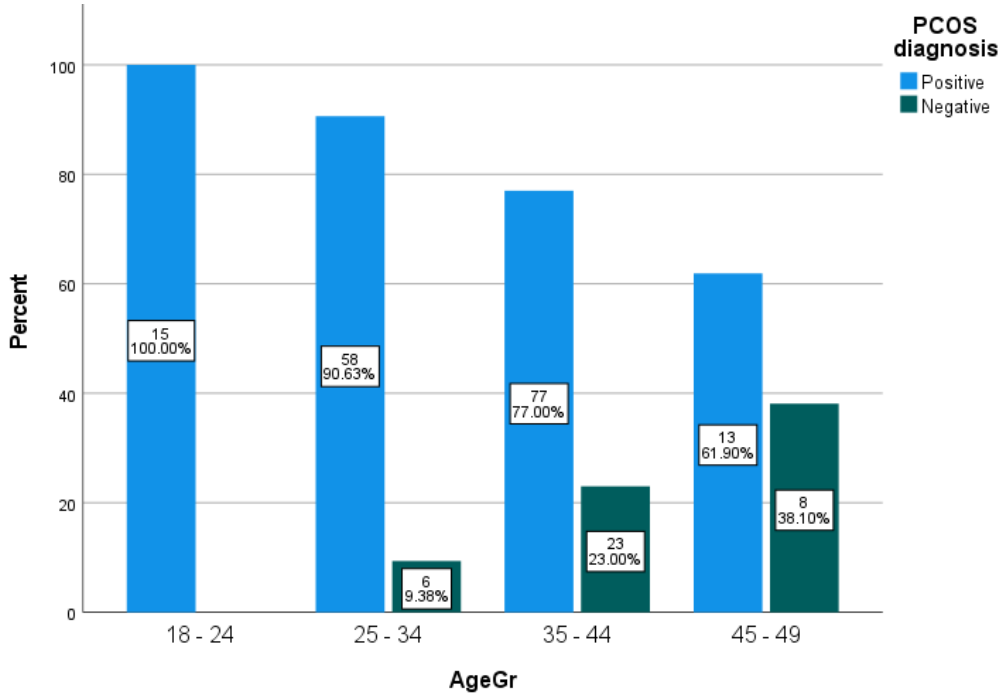

Figure 01: Significant relationship between age group and PCOS diagnosis

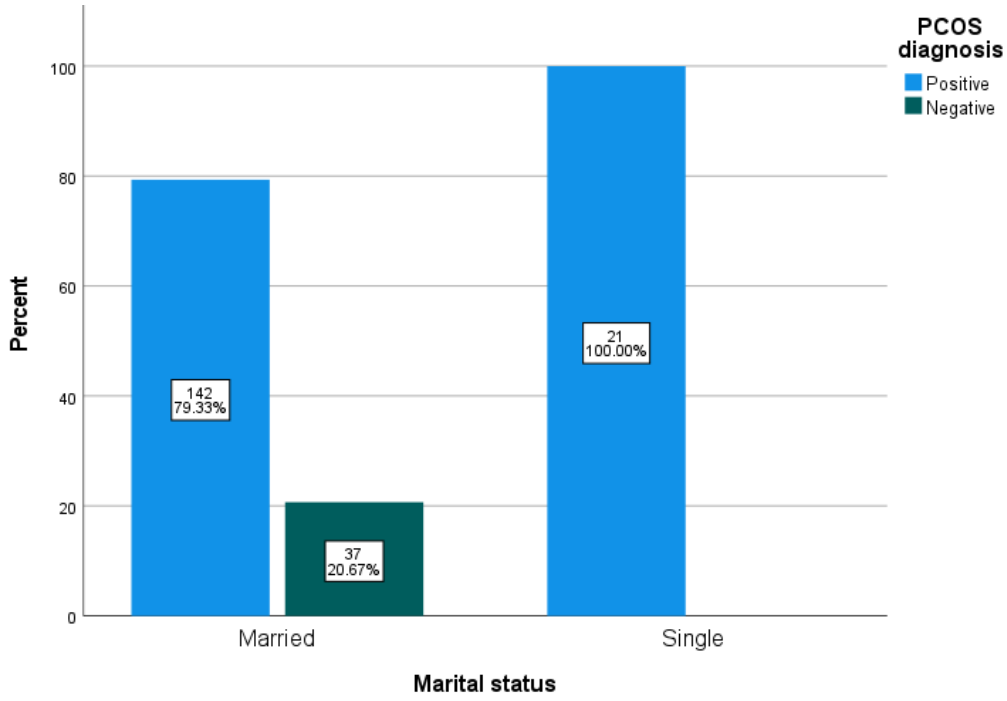

Figure 02: Significant relationship between marital status and PCOS diagnosis

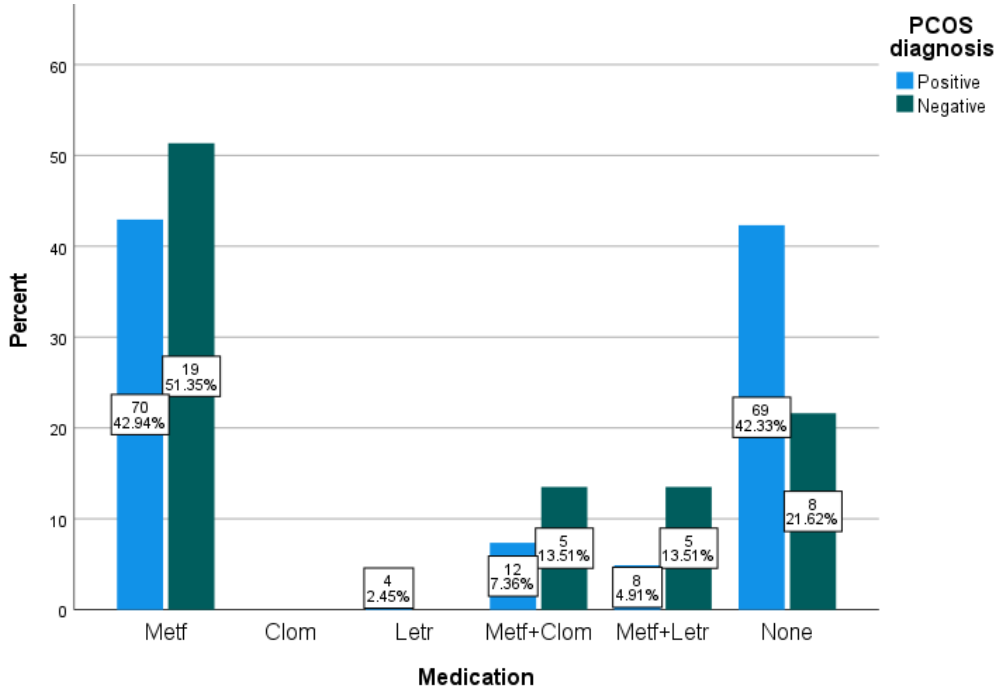

Figure 03: Significant relationship between medication and PCOS diagnosis

Table 05: Comparison of means between diabetic patients with PCOS, and diabetic patients without PCOS

Item	PCOS diagnosis								P value*
	Positive (n = 163)				Negative (n = 37)				
	Min.	Max.	Mean	SD	Min.	Max.	Mean	SD	
LH (mIU/ml)	1.00	66.70	17.28	10.99	2.00	23.91	10.31	4.63	< **0.001**
FSH (mIU/ml)	2.02	64.00	8.38	5.03	2.00	22.30	8.96	4.00	0.522
Prolactin (mIU/ml)	1.70	49.00	25.95	9.02	6.60	39.00	23.88	7.98	0.218
HbA1c (%)	4.89	10.30	7.08	0.86	5.90	12.90	7.68	1.49	**0.022**
BMI (kg/m2)	17.7	44.1	31.0	4.7	25.0	38.1	31.7	3.8	0.394

SD: Standard Deviation.

* Based on unpaired (independent) t-test.

DISCUSSION

PCOS is a common hormonal disorder with a potential to cause short- and long-term comorbidities[2],[16].

The present study is conclusive with all the previous research that described the relation between PCOS and diabetes mellitus in which diabetic women had PCOS more frequently than healthy women. In reference to the age, a significant relation between the presence of PCOS and reproductive age has been established across all age group especially 35 to 44 years old. This is comparable to Hsu (2013) and Falcetta et al. (2021) findings that aging is associated with metabolic disturbances and clinical and biochemical hyperandrogenism[17],[18].

The present study also determined that married diabetic women are more susceptible to PCOS, in this regard, Choudhary et al. (2017) finds that the overall prevalence of PCOS were higher among unmarried women[19].

The prevalence of PCOS among diabetic women was 81.5% in this study population according to Rotterdam score, among them 77% of them had positive ultrasound features, 49% were newly diagnosed diabetic patients and 44.5% of the patients were already on metformin medication.

The association between the risk of T2DM in women with PCOS and the overweight/obesity status especially during early adulthood is an established fact[10].

Additionally, PCOS women have 5-10 folds increase risk of glucose intolerance than normal women14. Data by World Health Organization estimate that 8-13% of women at reproductive age are suffering from PCOS and around 70% of them remain undiagnosed causing anovulation and infertility[20].

Our study revealed that the mean age was 36 years old, the mean number of children was 3, the mean BMI was 31 (kg/m2) and the mean glycemic index was 7%.

Meanwhile, Deswal et al. (2020) yielded 27 surveys with a pooled mean prevalence of 21.27%21. The prevalence concluded in this study is considered relatively high compared to the aforementioned facts and the main reasons can be summarized as: small size of sample (this can be considered as a limitation of the study), the fact that the study targeted diabetic women and most of them had visited the hospital already complaining of menstrual abnormality and/or infertility.

In conclusion, the prevalence of PCOS among women with T2DM involved in this study was found to be relatively high. Moreover, the frequency of clinical findings revealed that majority of women with PCOS had clinical feature and hormonal features while 77% of them had positive ultrasound features, 81.5 % had positive diagnosis of PCOS according to Rotterdam criteria. Finally, even though, plenty of studies documented the relation between PCOS and diabetes mellitus, further in-depth research are required to determine the appropriate methods to identify susceptible women including genetic studies in order to prevent or treat or limit the implications.

CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

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پوختە

نەخوشییا فرەکیسکێن هێلکەدانێ دناڤ نەخوشێن شەکرێ ژ جورێ دووێ ل پارێزگەها دهوک/هەرێما کوردستانێ – عیراق

پێشەکی و ئارمانج: نەخوشیا فرەکیسکێن هێلکەدانی ئیک ژ بەربەلاڤترین تیێکچونێن ئندوکراینی یە کو شیانێن هەیی ببیتە ئەگەرێ نەخوشیێن کورتخایەن و دریژخایەن ب تایبەتی نەخوشیا شەکرێ ژ جورێ دووێ, ئەف ڤەکولینە بۆ دیارکرنا بەلاڤبونا نەخوشیا فرەکیسکێن هێلکەدانێ دناڤ نەخوشێن شەکرێ ژ جورێ دووێ هاتیە ئەنجامدان ل پاریزگەها دهوکێ/ هەرێما کوردستان – عیراق.

ڕێکێن ڤەکولینێ: ئەف ڤەکولینە ڤەکولینەکا چاڤدیرییە کو ب ڕێکا کرووس_سیکشن دیزاین هاتیە کرن، ئافرەتێن نەخوشیا شەکرێ هەی ژ جورێ دووێ (ژمارا وان =۲۰۰) د ژیێ زاوزیێ دا ب خوڤە دگریت. فرەکیسکێن هێلکەدانێ دهیتە پشتراستکرن ب کارئینانا (پشکنینا کلینیکی و پشکنینا هورمونی و سونەرێ لدیڤ پیڤەرێن ڕوتەردام هاتینەکرن. زانیاریێن ڤەکولینێ د دابەشکرنا فرینکوێنسی دا دیاردکەن چ لادانی ستاندارد یان تێکرا بن یان فریکوێنسی و ریژا سەدی.

ئەنجام: ریژا بەلاڤبوونا فرەکیسکێن هێلکەدانێ (81.5%) بۆ دناف ئافرەتێن نەخوشیا شەکری ژ جورێ دووێ هەی، فریکوێنسیا پشکنینێت کلینیکی دناف نەخوشیا شەکرێ ژ جورێ دووێ دەرکەت کو پتریا وان تایبەتمەندین کلینیکی و یێن هورموناتن هەبوون ددەمەکی دا (77%) ژ وان د سونەری دا ئەرێنی دەرکەفتن. ریژا (81.5%) ژ وان پوزەتیف دەرکەتن کو فرەکیسکێن هێلکەدانێ هەبوون لدیڤ پیڤەرێن ڕوتەروام (49%) ژ نوی هاتینە دەستنیشانکرن کو نەخوشیا شەکرێ هەی. و (44.5%) ژ نەخوشان دەرمانێ میتفورمین بکاردئینا.

دەرئەنجام: فرەکیسکێن هلکەدانێ زۆر بەلاڤە دناف ئافرەتێن نەخوشێن شەکرێ ژ جورێ دووێ هەی. گرنکە ڤەکولینێن زێدەتر بهێنە کرن بو دیارکرنا ریکا گونجای بو دیارکرنا ئافرەتێن ئامادە بۆ قێ جۆرێ نەخوشیێ وەك ڤەکولینێن چینی ب مەرەما نەهیلان یان چارەسەرکرن یان دانانا سنورەکی بو توشبوونێ.

الخلاصة

متلازمة تكيس المبايض بين النساء المصابين بمرض السكري من النوع الثاني في محافظة دهوك، إقليم كردستان – العراق

الخلفية والأهداف: متلازمة تكيس المبايض هي أكثر اضطرابات الغدد الصماء شيوعا مع إمكانية التسبب في اضطرابات قصيرة وطويلة الأجل خصوصا النوع الثاني من مرض السكرى. أجريت الدراسة الحالية لمعرفة مدى انتشار متلازمة تكيس المبايض بين مرضى السكري من النوع الثاني في محافظة دهوك، أقليم كردستان العراق.

طرق البحث: هذه دراسة مقطعية أجريت في المراكز التي تقدم علاج غسيل الكلى في محافظة دهوك، أقليم كردستان العراق. تم تضمين ما مجموعه 171 حالة مسجلة تم تشخيصها على أنها فشل كلوي مزمن تتطلب علاج غسيل الكلى.

هذه الدراسة أجريت من خلال التصميم المقطعي، تم تضمين النساء المصابات بالنوع الثاني من مرض السكري (عددهن = 200) في سن الإنجاب. تم تأكيد متلازمة تكيس المبايض باستخدام الفحص السريري و الفحوصات الهرمونية والسونار وفقا لمعايير روتردام. تم تحديد بيانات الدراسة في التوزيع التكراري سواء المتوسط والانحراف المعياري أو التردد والنسبة المئوية.

النتائج: كان انتشار متلازمة تكيس المبايض مرتفعا (81.5٪) بين النساء المصابات بالسكري من النوع الثاني. كشف تواتر النتائج السريرية في مرضى السكري من النوع الثاني أن معظمهم لديهن ميزات سريرية وميزات هرمونية بينما كان لدى (77٪) منهم ميزات إيجابية بالموجات فوق الصوتية، و(81.5٪) لديهم تشخيص إيجابي لمتلازمة تكيس المبايض وفقا لمعايير روتردام، و(49٪) تم تشخيصهم حديثا بمرضى السكري النوع الثاني و(44.5٪) من المرضى الذين يتناولون دواء الميتفورمين.

الاستنتاجات: متلازمة تكيس المبايض منتشرة بشكل كبير عند النساء المصابات بمرضى السكري من النوع الثاني. ويلزم إجراء بحوث متعمقة لتحديد الطرق المناسبة لتحديد النساء المعرضات للإصابة بما في ذلك الدراسات الجينية من أجل منع الآثار المترتبة عليها أو علاجها أو الحد منها.