

Clinical patterns and treatment outcomes of polycystic ovarian syndrome

SHAWQI H. ALAWDI^{1,2}, MARWAN ALHALABI^{3,4,5}, RANA AL-HALLAK⁶

¹ Department of Pharmacology, Faculty of Pharmacy, Syrian Private University (SPU), Damascus, Syria

² Department of Pharmacology, Faculty of Medicine, Thamar University, Yemen

³ Department of OBGYN, Faculty of Medicine, Damascus University, Syria

⁴ Maternity hospital of OBGYN, Damascus University, Syria

⁵ Division of Reproductive Medicine, Embryology and Genetics, Faculty of Medicine, Damascus University, Syria

⁶ Department of Biochemistry and Microbiology, Faculty of Pharmacy, Al Rasheed University, Damascus, Syria

Corresponding author: Shawqi H. Alawdi, Ph.D.

Department of Pharmacology, Faculty of Pharmacy, Syrian Private University (SPU), Damascus, Syria

Department of Pharmacology, Faculty of Medicine, Thamar University, Yemen

Phone: +963 988 606 530; E-mail: shawqialawdi@yahoo.com

Abstract: Background: Polycystic ovary syndrome (PCOS) is a common chronic endocrine disorder in women with complex and poorly understood etiologies. The present study aimed to describe the clinical features of PCOS in a sample of Syrian women as well as the risk factors, associated comorbid diseases, and patterns and efficacy of treatment.

Methods: The present study is cross-sectional observational study conducted on a sample of Syrian women diagnosed with PCOS, using self-administered questionnaire during the period between December 25, 2023 and January 18, 2024. Overall, 1666 women with PCOS were recruited through online platforms.

Results: Higher frequency of PCOS was observed in young women aged 15–25 years (63.1%) and in single ladies (76.5%). The main chief complaints experienced by patients with PCOS were hirsutism (71.25%), irregular menstrual cycle (70.95%), depressed mood (53.9%), acne (49.52%), abdominal obesity (43.88%), alopecia (38.12%), and weight gain (34.57%). The most common risk factors observed in patients with PCOS were lack of physical exercise (76.4%), unhealthy food habits (51.6%), family history (38.5%), and history of taking anabolic steroids (17.2%). Comorbid diseases were found in 11.5% of PCOS patients. These diseases were hypothyroidism (5.7%), hypertension (3.06%), dyslipidemia (1.68%), heart diseases (1.56%), and diabetes mellitus (0.78%). Most patients were treated with oral contraceptive pills (82.11%) or metformin (64.83%). The efficacy of treatment was observed as complete cure in 430 patients (25.8%) and partial response alleviating symptoms in 819 patients (49.2%), while and no benefit was found in 417 patients (25%).

Conclusions: PCOS is associated with widespread dermatological and metabolic aberrations that pose psychological burden on women and increase their risk for having comorbid diseases. Most patients with PCOS do not receive adequate therapy. Understanding the risk factors and clinical features for each patient is essential to choose the proper treatment.

Keywords: endocrinology, hirsutism, polycystic ovary syndrome, medical treatment.

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Introduction

Polycystic ovary syndrome (PCOS) is a common metabolic and endocrine disorder in reproductive-age women. Hirsutism, acne, menstrual dysfunction, infertility, and obesity often manifest as typical symptoms of PCOS and can also lead symptoms of depression [1]. Delayed diagnosis of PCOS and dissatisfaction with care are common complaints all over the world [2].

The National Institutes of Health criteria (1992), Rotterdam criteria (2003), and Androgen Excess Society criteria (2006) are three sets of criteria that have been created for the identification of PCOS. All these three subsets include chronic anovulation, polycystic ovarian morphology on transvaginal ultrasound, and clinical and/or biochemical hyperandrogenism or various combinations of these conditions [3]. The International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome (2018) transitioned from consensus-based to evidence-based criteria, still, evidence-practice gaps persisted [4]. The 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome recommend that PCOS is diagnosed when two criteria are met and other causes are excluded: (i) clinical/biochemical hyperandrogenism, (ii) ovulatory dysfunction, and (iii) polycystic ovaries on ultrasound or elevated anti-mullerian hormone (AMH) levels [5].

Hyperandrogenism is assessed by step-wise testing of total testosterone and calculated testosterone, before testing of dehydroepiandrosterone sulfate and androstendione [5]. Ovulatory status is ascertained by relying on menstrual cycle regularity after exclusion of other causes of anovulation and/or androgen excess [6]. Oligoamenorrhea occurs as menstrual cycles are less than 21 or more than 35 days with only four to nine periods in a year while amenorrhea is the absence of menses for 3 consecutive cycles or 6 months in a previously menstruating woman [7]. Hyperandrogenism and ovulatory dysfunction must be present to diagnose PCOS in adolescents [5]. Polycystic ovarian morphology is diagnosed by transvaginal ultrasonography (≥ 20 follicles or an ovarian volume ≥ 10 ml in at least 1 ovary) or transabdominal ultrasonography (≥ 10 follicles or an ovarian volume ≥ 10 ml in at least one ovary) [5, 8, 9]. Both ultrasonography and anti-mullerian hormone levels are not required for diagnosis with the presence of irregular menstruation and hyperandrogenism [5].

The present study aimed to describe the clinical features of polycystic ovary syndrome in a sample of Syrian women as well as the risk factors, associated comorbid diseases, and patterns of treatment.

Methods

Study design and setting

The present study is cross-sectional observational study conducted during the period between December 25, 2023 and January 18, 2024 in Syria. The participants were recruited from several media platforms including, Facebook, WhatsApp, X (formerly Twitter), Instagram, Telegram, and WeChat. Participation in the study was voluntarily, and completion of the survey was interpreted as a consent to participate in the study. Anonymity was kept to ensure privacy. Overall, 1892 women with PCOS above responded to the online request and participated in the survey. In total, 1666 women completed the online survey, and 226 women were excluded due to missing data.

Inclusion and exclusion criteria

The study population comprised women diagnosed with PCOS aged 15–55 years who responded to the online survey. Incomplete surveys and those for respondents aged less than 15 years or more than 55 years were excluded from the study.

Survey development

The survey was based on previously published online PCOS-related surveys. The questions were designed to collect information regarding socio-demographic characteristics, risk factors, diagnosis of PCOS and its associated comorbidities including infertility, diabetes, hypothyroidism, dyslipidemia, hypertension, and heart diseases. The questions regarding symptoms of PCOS included frequency of menses, mood disturbances, infertility, and signs of hyperandrogenism such as hirsutism, alopecia, profound acne, and excessive weight gain. The collected data also included of pharmacological management of PCOS.

Data analysis

The data obtained were analyzed using SPSS 26 (IBM Corporation, New York, USA). The categorical variables were presented as the number of cases and the percentage and the relationships between them were analyzed by chi square (χ^2) analysis. Descriptive analysis was also conducted to explore perceptions about PCOS in general. Statistical significance was set at $p \leq 0.05$.

Results

The initial sample size was 1892 women with polycystic ovarian syndrome (PCOS) who completed the survey. However, 226 women were excluded from the study due to missing data. A total of 1666 women diagnosed with PCOS were included in the present study.

The patients' age ranged between 15 and 55 years, and most cases (95.5%) of PCOS patients aged 15–35 years. Higher frequency of PCOS was observed in young women aged 15–25 years (63.1%) and in single ladies (76.5%). In the other hand, 24.1% of the patients had overweight while 61.4% had ideal body weight. The demographic characteristics of the patients are presented in Table 1.

The most common risk factors observed among patients with PCOS were the lack of physical exercise (76.4%) and unhealthy food habits (51.6%). Family history was also reported in 38.5% of respondent women. Additionally, history of taking anabolic steroids was observed in 17.2% of PCOS patients, and the presence of other comorbid diseases was found in 11.5% of the patients. Risk factors are presented in Table 2.

Most PCOS patients (98.08%) were diagnosed by ultrasonography alone or in combination with biochemical investigations (27.19%) or pelvic physical examination, Fig. 1.

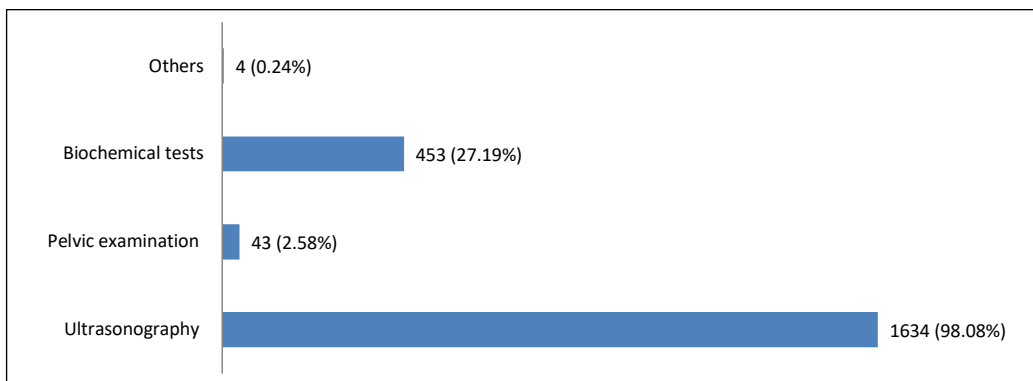
The most common chief complaints experienced by PCOS patients were hirsutism (71.25%) and irregular menstrual cycle (70.95%). Large numbers of patients also experienced depressed mood (53.9%), acne (49.52%), abdominal obesity (43.88%), excessive hair loss (38.12%), and rapid weight gain (34.57%). Additionally, sleep apnea (9%) and infertility (8.16%) were less common chief complaints in PCOS patients, Fig. 2.

Table 1. Demographic characteristics of women with PCOS (n = 1666).

Characteristic	Frequency (n)	Percent (%)
<i>Age (years)</i>		
15–25	1052	63.1
26–35	540	32.4
36–45	61	3.7
46–55	13	0.8
<i>Body mass index</i>		
<18.5 = underweight	75	4.5
18.5–24.9 = ideal weight	1023	61.4
25–29.9 = overweight	402	24.1
30–34.9 = obesity class 1	122	7.3
35–39.9 = obesity class 2	36	2.2
>40 = extreme obesity class 3	8	0.5
<i>Marital status</i>		
Single	1274	76.5
Married	392	23.5

Table 2. Risk factors for PCOS (n = 1666).

Characteristic	Frequency (n)	Percent (%)
Family history	642	38.5
History of anabolic steroids	286	17.2
Unhealthy food habits	860	51.6
Lack of physical exercise	1272	76.4
Comorbidities	191	11.5

**Fig. 1.** Diagnosis of PCOS (n = 1666).

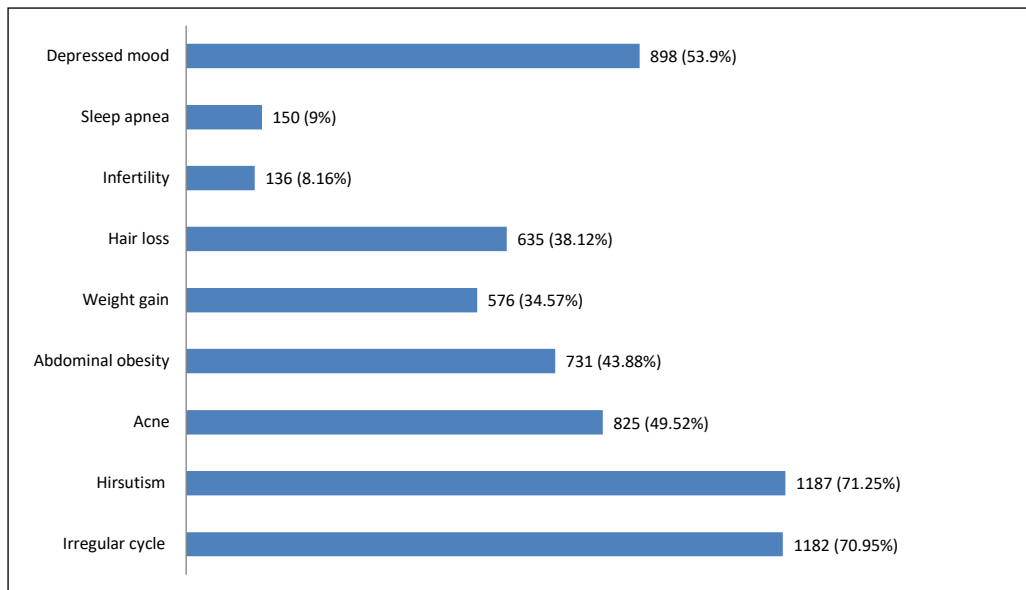


Fig. 2. Symptoms associated with PCOS (n = 1666).

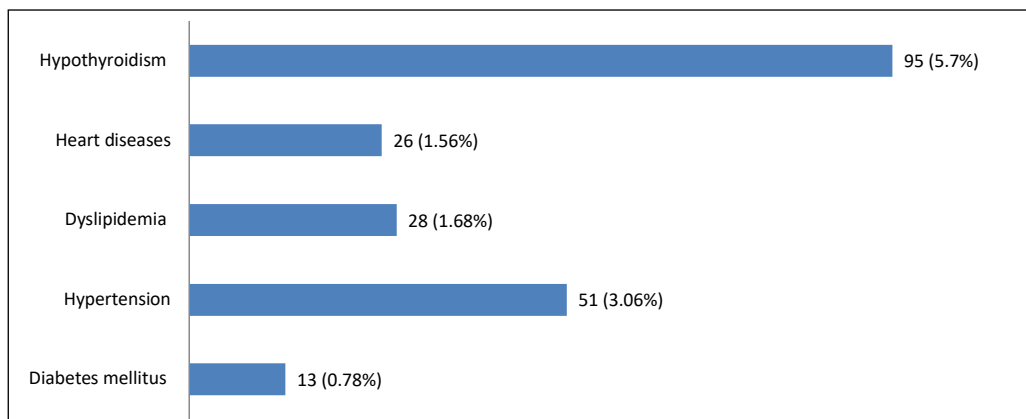


Fig. 3. Comorbid diseases in patients with PCOS (n = 1666).

Out of 1666 patients with PCOS, 191 patients (11.5%) had one or more comorbid chronic diseases. These diseases were hypothyroidism (5.7%), hypertension (3.06%), dyslipidemia (1.68%), heart diseases (1.56%), and diabetes mellitus (0.78%), Fig. 3.

A total of 2645 drugs were prescribed for the 1666 patients with PCOS (average 1.59 drugs per patient). Most patients were treated with oral contraceptive pills (82.11%) or metformin (64.83%). Less frequently, patients were treated with androgen antagonists, spironolactone (9.18%) or cyproterone (2.64%). The efficacy of treatment was reported as complete cure in 430 patients (25.8%) and partial response alleviating symptoms in 819 patients (49.2%), while and no benefit was observed in 417 patients (25%). Results are represented in Table 3 and Fig. 4.

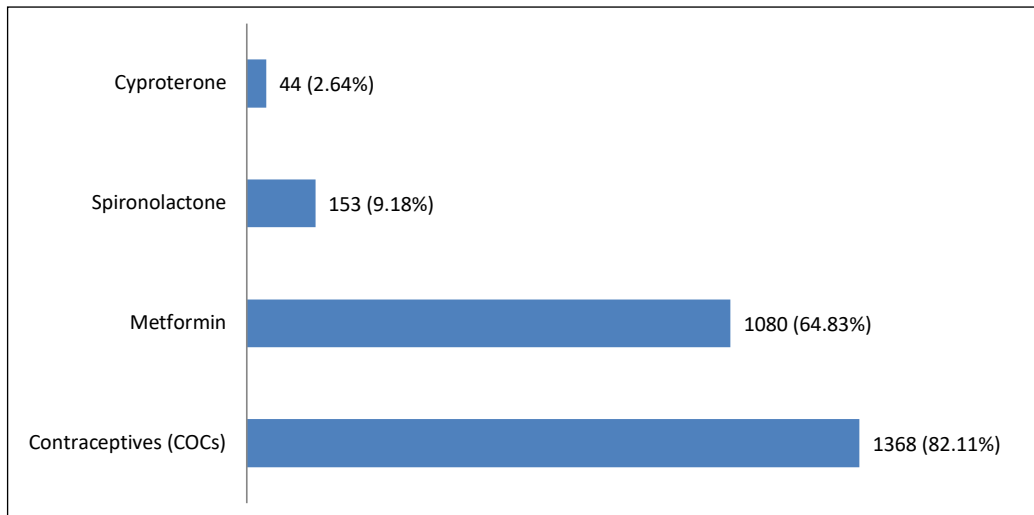


Fig. 4. Patterns of medical treatment of PCOS (n = 1666).

Table 3. Patterns of medical treatment of PCOS (n = 1666).

	Complete cure	Partial response (alleviated symptoms)	No response	Total	p-value
Contraceptives	175 (33.6%)	244 (46.8%)	102 (19.6%)	521 (31.3%)	
Metformin	65 (25.7%)	121 (47.5%)	69 (27.1%)	255 (15.3%)	
Androgen antagonists	7 (30.4%)	12 (52.2%)	4 (17.4%)	23 (1.4%)	
Contraceptives + metformin	154 (22.2%)	341 (49.2%)	198 (28.6%)	693 (41.6%)	
Contraceptives + androgen antagonists	13 (31%)	23 (54.8%)	6 (14.3%)	42 (2.5%)	
Metformin + androgen antagonists	3 (20%)	9 (60%)	3 (20%)	15 (0.9%)	
Contraceptives + metformin + androgen antagonists	13 (11.1%)	69 (59%)	35 (29.9%)	117 (7%)	
Total	430 (25.8%)	816 (49.2%)	417 (25%)	1666 (100%)	0.000

Discussion

The present study investigated the clinical features of polycystic ovary syndrome (PCOS) and the patterns of pharmacological treatment in a sample of Syrian women. The risk factors and the associated comorbid diseases with PCOS were also included. The study presented data of 1666 diagnosed cases of PCOS in women aged 15–45 years. The study highlighted an important widespread health problem affecting several millions of women in the world and represents the most common endocrine disease in reproductive-age women [10]. PCOS also significantly increases the propensity of several associated comorbid metabolic, cardiovascular, psychological, and even infectious diseases including COVID-19 [11].

The results of the present study showed higher frequency of PCOS in young women aged 15–25 years. Similar to results were reported from Qatar [12], and India [13]. These results could be attributed to the incomplete maturation of the hypothalamic-pituitary-ovarian (HPO) axis during the period of transition from puberty to adulthood. Complete maturation of HPO axis is usually occurs during the first 5 years after menarche. Additionally, online recruitment of the study population could also explain the higher frequency among younger and single women who respond better to online surveys.

In the present study, lack of physical exercise, unhealthy food habits, family history, and history of taking anabolic steroids were observed as risk factors for PCOS. These results were in accordance with several previously reported results. Multiple meta-analyses and systematic reviews reported the beneficial effect of exercise for PCOS symptom management [14–16]. These data could be explained by the fact that physical exercise improves insulin resistance which is implicated with hyperandrogenism that underlies many PCOS symptoms. Additionally, unhealthy food habits including high-calorie diet, lack of dietary fiber, and excessive intake of saturated fatty acids were also found to be associated with PCOS [17]. Moreover, positive family history was reported as the most informative risk factor for the development PCOS [18]. Furthermore, history of anabolic steroids use was found as a risk factor for PCOS in the present study. The detrimental effects of anabolic-androgenic steroids on PCOS could be attributed to disturbing the hypothalamic-pituitary-ovarian axis or by their intrinsic androgenic activity [19]. It has been found that doping with anabolic-androgenic steroids is common among both male and female athletes and represents a growing public health problem [20].

The most common symptoms experienced by PCOS patients in the present study were hirsutism (71.25%) and irregular menstrual cycle (70.95%). These results are similar to other studies that reported hirsutism in 70–80% and irregular menstrual cycle in 75–85% of PCOS patients [21, 22]. Large numbers of patients also experienced depressed mood (53.9%), which go in line with results of a systematic review and meta-analysis [23]. Moreover, other common symptoms observed in the present study included acne (49.52%), abdominal obesity (43.88%), excessive hair loss (38.12%), and weight gain (34.57%). These symptoms are manifestations for the hyperandrogenism that is associated with PCOS and could be attributed to the underlying hormonal disturbances in HPO axis.

Notably, hypothyroidism was the most common comorbid disorder observed with PCOS in the present study. Hypothyroidism was associated with rise in thyrotropin-releasing hormone (TRH) which leads to increased prolactin and thyroid stimulating hormone (TSH). Prolactin inhibits ovulation by increasing the ratio of luteinizing hormone (LH) to follicle stimulating hormone (FSH). TSH also spills over FSH receptors and contributes in PCOS [24]. Other comorbid

diseases observed in the present study were hypertension (3.06%), dyslipidemia (1.68%), heart diseases (1.56%), and diabetes mellitus (0.78%). Previous studies demonstrated that all cardiovascular diseases including hypertension, dyslipidemia, obesity, insulin resistance, diabetes, and metabolic syndrome are elevated in patients with PCOS [25–28].

Oral contraceptives and metformin were observed as the two drugs most commonly prescribed in patients with PCOS. Less frequently, patients were treated with androgen antagonists, spironolactone or cyproterone. The overall efficacy of treatment of PCOS was reported as complete cure (25.8%), partial response (49.2%), and no benefit (25%). This reflects concerns of long-term metabolic risks of PCOS in these patients. The lack of consensus on the ideal treatment for this condition could contribute to the inadequate therapy outcomes. This suggests that further prospective research into the comparative effectiveness of the various options for PCOS treatment may be warranted [29].

Conclusions

PCOS is associated with widespread dermatological and metabolic aberrations that pose psychological burden on women and increase their risk for having comorbid diseases. Most patients with PCOS do not receive adequate therapy. Understanding the risk factors and clinical features for each patient is essential to choose the proper treatment.

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Conflict of interest

None declared.

Author contributions

S.H.A., M.H., and R.A. conceived and designed the study, conducted the study. S.H.A. analyzed data, and wrote the initial draft of the submitted manuscript. M.H. and R.A. reviewed the manuscript. All authors have critically reviewed and approved the final draft of the manuscript and are responsible for the content and similarity index of the manuscript.

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