Prevalence of polycystic ovary syndrome in women with acne vulgaris

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Authors' contributions

This work was carried out in collaboration between all authors. Author KT designed the study, wrote the protocol , performed the statisticl analysis, wrote the first draft of the manuscript , managed the analyses of the study and managed the literature searches. Author AHR was supervisor professor. Author JK was assistant supervisor professor. All authors read and approved the final manuscript.

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ABSTRACT

Background: Acne is one of the most common dermatological conditions encountered in day to day practice. Many recent studies have reported a strong association between acne and underlying systemic endocrine disorders, more particularly Polycystic ovarian syndrome
Objective: To study the association between acne and polycystic ovarian syndrome, in women presenting with adult onset acne and its associated factors with regard to the clinical findings.
Study design: This was a cross –sectional study.
Place and Duration of Study: Department of dermatology at Tishreen university Hospital , Lattakia ,Syria , from January 2018 to February 2019
Methodology: Total of 150 female patients aged 18-43 years, with various degree of acne did not receive hormonal treatment, including hormonal contraceptive and antiandrogen therapy, for at least 3 months prior to study. Each participant was evaluated by complete medical history, detailed dermatological examination , abdominal ultrasound examination, and hormonal assays. The presence of PCOS was assessed using Rotterdam criteria 2003.
Results: The final analysis had included 150 women with acne . The proportion with mild, moderate , severe and very severe acne was 56%, 30%, 11% and 3% respectively. The prevalence of PCOS was 34% .PCOS had shown no statistically significant association with severity of acne or total testosterone concentration (p value >0.05).The factors which have shown statistically significant association were late onset acne above 25 years, irregularity of menstrual cycle , presence of Hirsutism, higher BMI and higher waist circumference .
Conclusion: : PCOS is a common disorder among women with acne vulgaris. However it is not related to the severity of acne. Presence of menstrual disturbance, hirsutism , obesity are strong risk factors for PCOS. Early diagnoses and treatment can avoid the possible complications.

Keywords: Acne vulgaris ,Polycystic ovary syndrome, PCOS.

1. INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units, characterized by comedones, papules, pustules, nodules, and often scars. It affects primarily the face, neck, upper trunk, and upper arms.

Acne Vulgaris remain one of the most common dermatological condition affecting the adolescents and young adults and is usually resolved by the mid-twenties, and it is of multifactorial etiology[1-2].

Even though considered as disease of teenage it may continue into the 30s and 40s in a minor proportion of the affected subjects[3].

Acne is a common manifestation of hyperandrogenemia. Numerous factors contribute to the development of acne. Androgenic stimulation of sebaceous glands is one of the important factors in its development[4].The amount of excess sebum production correlates with the severity of acne. Increased sensitivity to androgenic hormones has also been reported to be a contributing factor. The enzyme 5-alpha reductase converts testosterone to the more potent androgen dihydrotestosterone within the sebaceous glands[5].

Acne by itself is a serious cosmetic disorder, as well as also be a sign of an underlying disease[6].In females, the most common cause of hyperandrogenemia is the polycystic ovary syndrome (PCOS).

Polycystic ovarian (PCOS) syndrome is a common endocrinopathy of women of reproductive age(15-45years)[7]. It is a disorder of androgen excess, with an estimated prevalence of 5 to 10% among general population [8-9].

Excess of ovarian androgens can lead to wide range of symptoms such as acne, hirsutism, insulin resistance, obesity and cardiovascular disease[10].

According to Rotterdam criteria 2003, PCOS is a syndrome of ovarian dysfunction, hyperandrogenism (clinical or biochemical) and polycystic ovary morphology on pelvic ultrasound (transabdominal or transvaginal). There should be two features out of three to be considered while diagnosing the disease [11].

In our country, the current study is carried out first time and this research will help to establish frequency of PCOS syndrome in acne patients. If found significant, we can start screening every female presenting with acne for PCOS syndrome so that early detection will lead to early intervention and thus improved quality of life.

2. MATERIAL AND METHODS

This study was a cross-sectional study, carried out in department of dermatology, at Tishreen university Hospital , Lattakia ,Syria , from January 2018 to February 2019 over a period of 12 months. The study population included women above 18 years of age presenting to dermatology outpatient department with features suggesting of acne and were confirmed with Acne vulgaris after clinical examination. A total of 150 women who were diagnosed with acne were recruited by purposive sampling into the study.

The inclusion criteria were age of the subject between 18 to 43 years of age and clinically diagnosed as acne. The study has excluded all antenatal women, lactating mothers and women diagnosed with other Acneiform lesions like. Women on certain drug treatments like oral contraceptive pills, ovarian stimulating drus and oral hypoglycemic agents like metformin were excluded from the study.

Each participant was evaluated by complete medical history, detailed dermatological examination and abdominal ultrasound examination, and hormonal assays.

The history included the onset of acne (before or after 25 years of age), family history of persistent acne, recent or frequent use of cosmetics, drug history

(topical steroids, systemic drug therapy or use of contraceptives), menstrual history, marital status, and history of infertility.
The dermatological examination was conducted by visual inspection, with the aid of magnifying lens. Type of lesions whether noninflammatory or inflammatory , the distribution of acne lesions was assessed and assessment of acne severity and grading it into mild, moderate, severe or very severe by GAGS .
The total severity score is derived from summation of six regional sub scores. Each is derived by multiplying the factors- 2 for forehead, 2 for each check, 1 for nose, 1 for chin, 3 for both chest and back by the most heavily weighted lesion within each region (1 for ≥ one comedone, 2 for ≥ one papule,3 for ≥ one pustule, and 4 for ≥ one nodule). The regional factors were derived from consideration of surface area and distribution and density of pilosebaceous units.(Table 1)

Table 1. The Global Acne Grading System

Location	Factor X Grade (0-4) = local score	
Forehead	2	[Global score = 0 = None 1-18 = Mild 19-30 = Moderate 31-38 = Severe > 39 = Very severe]
Right cheek	2	
Left cheek	2	
Nose	1	
Chin	1	
Chest & upper back	3	

Grade 0, No lesions; 1 ≥ One comedone; 2 ≥ One papule; 3 ≥ One pustule; 4 ≥ One nodule.
Other cutaneous manifestations of hyperandrogenemia like androgenic alopecia, acanthosis nigricans and hirsutism were also noted.
the waist circumference and body mass index are obtained for all patients.
A trans abdominal ultrasound was done for all patients using the criteria that fulfill sufficient specificity and sensitivity to define the PCO. These criteria include the presence of 12 or more ovarian follicles measuring (2–9 mm) in diameter and increased ovarian volume more than (10 cm3) [12].

Hormonal assay included measurement of serum level of total testosterone.

The presence of polycystic ovarian syndrome was confirmed, if the patient satisfies Rotterdam criteria[11].

Data analysis

Data was analyzed by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Presence of PCOS was considered as primary outcome variable.
The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. Chi square test was used to test statistical significance. P value <0.05 was considered statistically significant.
Data analysis was done by IBM SPSS version 23 was used for statistical analysis[13].

3. RESULTS

A total of 150 females with acne vulgaris were enrolled in the study; their ages ranged from 18 to 43 years with a mean of 25.1 ± 6.2 (SD). Eighty-one patients (54%) were below the age of 25 years and 69 patients (46%) were above the age of 25 years.
Major proportion (58%) of study participants were unmarried. Irregular menstrual cycle was reported 36% of the study population.
As per the WHO criteria, only 20% of the participants had BMI in normal weight range. The proportion of women, who were overweight and obese were 40% and 32% in the study population. Waist circumference was high (>88 cm) among 44,7% of the study subjects. The proportion of women having various degrees of hirsutism was 73.3%. Alopecia was present in 25.3%. The proportion of women with acanthosis nigricans 42% in the study population (Table 2).

Among the study population, Eighty-four patients (56%) had mild acne, 45 patients (30%) had moderate acne, 17 patients

(11%) had severe acne, and 4 patients (3%) had very severe acne .

The proportion of women having PCOS was 34% in the current study (Fig 1).

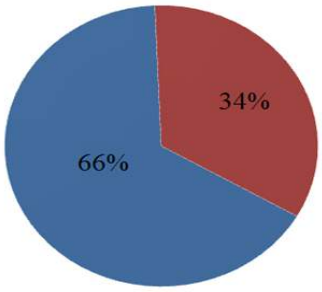

Fig .1. Prevalence of PCOS in study population (N=150)

Table 2. Baseline characteristics of the study population (N=150).

Parameter	Number	Percentage
Age group		
< 25 year	81	54%
≥ 25 years	69	46%
Menstrual cycle		
Regular	96	64%
Irregular	54	36%
BMI		
Under weight	12	8%
Normal weight	30	20%
Over weight	60	40%
Obese(>30)	48	32%
Waist Circumference		
High (>88 cm)	67	44.7%
Low (≤ 88 cm)	83	55.3%
Hirsutism		
Present	110	73.3%
Absent	40	26.7%
Alopecia		
Present	38	25.3%
Absent	112	74.7%
Acanthosis nigricans		
Present	63	42%
Absent	87	58%
Severity of acne (as per gags)		
Grade-1	84	%56
Grade-2	45	%30
Grade-3	17	%11
Grade-4	4	%3

Abbreviations used in table 1 :BMI (body mass index), gags(global acne grading system)

With regard to the age of presentation (before or after 25 years), 36 acne patients (70.5%) with PCOS, 33 acne patients (33.3%) without PCOS had age of presentation above 25 years and the difference was statistically significant (*P* <.05).

In this study, the most common clinical form of acne with PCOS was the papulopustular type (inflammatory), which was found in 42 (82.35%) patients, followed by the closed comedones+ papules (un inflammatory) in nine (17.65%) patients. The face, especially the mandibular region, and the chin (U zone regin) were affected in 39 (76.47%) patients acne with PCOS.

Among the 51 people with PCOS group, 25 (49%) women had regular menstrual cycle, and 26 (51%) women had irregular menstrual cycle. Among the 99 people without PCOS group, 71 (71.7%) women had regular menstrual cycle, and 28 (28.3%) women had irregular menstrual cycle. The difference in the proportion of PCOS group and menstrual cycle status was statistically significant (*P* = .01).

Among the 51 people with PCOS group 11 (21.5%) participants were had BMI below 25, 15 (29.4%) participants were had BMI 25 to 30, and 25(49.1%) participants were had BMI above 30.

Among the 99 people without PCOS group, 31 (31.3%) participants were had BMI below 25, 45 (45.5%) participants were had BMI 25 to 30, and 23 (23.2%) participants were had BMI above 30. The difference in the proportion of PCOS group and BMI was statistically significant (*P* =.016).

Among the 51 people with PCOS group, 30 (58.8%) participants had high (> 88cm) waist circumference, and this proportion was only 37.4% among women without PCOS the difference in the proportion of PCOS group and waist circumference

status was statistically significant (*P* = 0.001).

Table 3. factors affecting PCOS in study population (n=150).

Parameter	PCOS (N=51)	NO PCOS (N=99)	Chi square value	P value
Age group				
< 25 years	15(29.5%)	66(66.6%)	18.807	0.001
≥25 years	36(70.5%)	33(33.3%)		
Menstrual cycle			6.57	0.01
Regular	25(49%)	71(71.7%)		
Irregular	26(51%)	28(28.3%)		
BMI			10.31	0.0161
Below 25	11(21.5%)	31(31.3%)		
25 to 30	15(29.4%)	45(45.5%)		
above 30	25(49.1%)	23(23.2%)		
Waist Circumference			5.43	0.0197
>88 cm	30(58.8%)	37(37.4%)		
≤ 88 cm	21(41.2%)	62(62.6%)		
Severity of acne				
Mild	25(49.1%)	59(59.6%)	3.84	0.277
Moderate	15(29.4%)	30(30.3%)		
Severe	9(17.6%)	8(8%)		
Very severe	2(3.9%)	2(2.1%)		
Hirsutism			3.95	0.046
Present	43(84.3%)	67(67.7%)		
Absent	8(15.7%)	32(32.3%)		
Androgenic alopecia			3.29	0.036
Present	18(35.3%)	20(20.2%)		
Absent	33(64.7%)	79(79.8%)		
Acanthosis nigricans			4.51	0.033
Present	28(55%)	35(35.3%)		
Absent	23(45%)	64(64.6%)		

Abbreviations used in table 2: BMI (body mass index).

There was no statistically significant difference regarding acne severity (*P*>0.05) between acne patients with PCOS and acne patients without PCOS. (Table 3).

Among the 51 people with PCOS group, 43 (84.3%) were had hirsutism. Among the 99 people without PCOS group, 67 (67.6%) were had hirsutism. The difference in the proportion of PCOS group and hirsutism status was statistically significant (*P* =.046).

Among the 51 people with PCOS group, 28 (55%) were had acanthosis nigricans . Among the 99 people without PCOS group, 35 (35.4%) were had acanthosis nigricans.The difference in the proportion of PCOS group was statistically significant. (P =.033) (Table 3).

Fig .2. Dermatological signs of PCOS.

Among the 51 people with PCOS group, 18(35.3%) were had androgenic alopecia. Among the 99 people without PCOS group, 20(20.2%) were had androgenic alopecia .The difference in the proportion of PCOS group and alopecia was statistically significant(*P* =.036).

There was no statistically significant difference regarding the mean of total testosterone (*P* >.05) between acne patients with PCOS and acne patients without PCOS.

4. DISCUSSION

Considering the increasing reports of systemic endocrine defects and a strong association of Acne vulgaris with polycystic ovarian syndrome, the present study was conducted among women with adult onset acne to explore this association.

Studies from different parts of the world showed variable association between acne vulgaris and PCOS. (Table 4) But no such study has been conducted in Syria to determine the frequency of PCOS in acne patients.

Regarding the age of presentation, 36 acne patients with PCOS (70.5%) of age more than 25 years and 15 patients (29.5%) of age less than 25 years in comparison to acne patients without PCOS and the difference was statistically significant (P<.05), so late onset acne have high incidence of PCOS as had been shown by an other study[14].

In our study 150 females having acne were enrolled. Majority of the patients were 18-25 years old. The mean age of patients was 25.1 ± 6.2 years, while minimum recorded age was 18 years and maximum was 43 years. The results of this observation are similar to the study done in Iran by Zandi et al.[15] where mean age of respondents was 22.1 ± 4.2 years. It is also comparable with the study done in Dhaka Bangladesh, by Begum et al.[16] where the mean age was 23.8±5.7 years, and an Australian study in which it came out to be 23.6±6.06 years.[16] The possible explanation for this finding is that acne appears at time of puberty and adolescence, when androgen dependent increase in sebaceous gland activity occurs leading to seborrhea and comedone formation [17].

In our study, the estimated frequency of PCOS in acne patients was 34%, which is comparable to other studies done in different parts of the world. Fraser *et al*.[18] reported PCOS in 45.37% patients of acne in Australia. Study done by Maluki, in Iraq, on resistant acne cases also showed comparable results, 51.2% patients had PCOS compared with 6.2% in control group.[19]

Zandi *et al.*[[15] in 2010 carried out a study in 118 Iranian acne patients and 60.2% (71) patients were diagnosed as PCOS cases based on NIH criteria, in which only hyperandrogenism and oligomenorrhea are noted. Around 54% of the patients complained of hirsutism and 37% of them suffered from menstrual disturbances[15].

Ultrasonography is not included in NIH criteria. We used the more recent Rotterdam criteria, in which ultrasonography is added. In spite of including another diagnostic modality, our patients had lower prevalence of PCOS. The possible explanation of this finding might be due to difference in ethnicity and genetic makeup.

In Dhaka, Begum *et al.*[16] found that 11 (27.5%) out of 40 women with acne had PCOS compared with 3.3% in control

group. The frequency of PCOS is much lower than our study 27.5% vs. 34%.[16] Similarly in Thailand, Timpatanapong et al.[6] reported lower prevalence of PCOS in acne patients. PCOS was found in 19 out of 51 acne patients (37.3%) and none of the control group had PCOS.[6]

However, various studies showed increased frequency of PCOS when diagnosed mainly by sonography method.. In a study by Zandi et al.[15] PCOS was diagnosed in 48.3% (57) patients out of 118 acne patients by sonography method. This can be explained by the difference in ethnic origin, operator's observation, resolution ultrasound of machines and the day of menstrual cycle at which ultrasound was done. Begum et al.[16] reported comparable ultrasonic prevalence of PCO in Bangladeshi females where 20% of acne patients had polycystic ovarian picture on ultrasound.

Table 4. Comparison of data reporting association of acne and PCOS.

Study	Total of acne patients	PCOS in acne patients	% of PCOS
Zandi *et al.*[15]	118	71	60.2 %
Maluki [19]	123	63	51.2 %
Timpatanapong *et al.* [6]	51	19	37.3 %
Raja SA et al [23]	100	30	30%
Begum et al [16]	40	11	27.5 %
Jabeen *et al* [20]	200	92	46%
Bliede *et al* (Present study)	150	51	34%

There was no statistically significant difference regarding acne severity between acne patients with PCOS and acne patients without PCOS ; this means that PCOS can result in acne but not necessarily severe. The results of this observation are similar to the study Jabeen et al [20].

PCOS had shown no statistically significant association with marital status and the mean of total testosteron.

The factors which have shown statistically significant association were the apperance of acne older than 25 years of age at onset , higher BMI of the women, Higher waist circumference, menstrual disturbance, presence of Hirsutism. (Table 2)

The proportion of women with BMI more than 30 was more in PCOS group as compared to Non PCOS group (49.1% vs 23.2%, *P* value 0.016), which was statistically significant. this is very similar to a study, performed by Sharquie et al[21] In the presentstudy although obesity in acne patients with PCOS is an important feature it is not a criterion for the diagnosis of PCOS and the absence of obesity according to BMI does not exclude the diagnosis of PCOS.

The proportion of women with waist circumference more than 88 cm was also higher among PCOS women, as compared to non PCOS women (58.8% vs 37.4%, *P* value 0.019), which was also a statistically significant difference between two groups; this means that waist circumference correlates with PCOS more than the BMI and it reflects central obesity and an increased risk of metabolic problems, these results are similar to what had been obtained by other studies[22]

Higher proportion of women in PCOS group had Hirsutism, as compared to women in non PCOS group (84.3% vs 67.7%, *P*=.04), and the difference was highly significant (*P* <.04) and indicates that hirsutism is an important indicator of hyperandrogenemia and an important criterion to the diagnosis of PCOS as had been shown by Sharquie et al.[21] In a study by Raja SA *et al*, [23] a bout 93% of

patients with PCOS complained of hirsutism.

in addition to other studies[11],[14] Because hirsutism is very common in patients with PCOS and an important criterion to the diagnosis of PCOS we should look for hirsutism accurately because some women remove coarse hairs by epilation and by many other means and some patients are shameful of telling that they have hirsutism; also many women in our region cover their chins which may be heavily involved by coarse terminal hairs.

Acanthosis nigricans is a major problem among obese Individuals, In the present study acanthosis nigricans was present in 28 acne patients with PCOS (55%) in comparison to 35 acne patients without PCOS (35.3%), and the difference was highly significant (*P* <.03); this is very similar to a study performed by Sharquie et al.[21]

Androgenetic alopecia was found in 18 acne patients with PCOS (35,3%) in comparison to 20 acne patients without PCOS (20.2%) and the difference was statistically significant (*P* <.05). Sharquie et al.[21] found that androgenetic alopecia is increased in patients with PCOS but it did not reach a significant level. In the present study, although androgenetic alopecia reached a significant level it was not a common sign of PCOS like hirsutism, and menstrual disturbances.

Menstrual disturbances were present in 26 acne patients with PCOS (51%) in comparison to 28acne patients without PCOS (28.3%), and the difference was statistically significant (*P* <.05). About 25 acne patients with PCOS (49%) had regular menstrual cycles, so not all patients with PCOS have menstrual disturbance and this was also proved by other studies.[24]

Thus, our study highlights the association between acne and polycystic ovarian syndrome. Patients with acne, if screened for PCOS, may have a better quality of life due to early detection of the disease.

Hence presence of obesity, higher waist circumference and other cutaneous markers of hyperandrogenism should raise a strong suspicion towards presence of underlying PCOS among women with Acne. These women shall subjected appropriate diagnostic evaluation to diagnose PCOS in time and treat them effectively to prevent long term physical and psychological consequences of this systemic endocrine dysfunction.

4. CONCLUSION

On the basis of these findings we conclude that PCOS is present in almost third of our female acne patients. However, no relationship was found between PCOS and acne severity. It is therefore, suggested that female patients with should be screened for PCOS by history, examination and if necessary, pelvic ultrasonography and hormonal assays. Early diagnoses and treatment can avoid the possible complications.

CONSENT

As per international standard or university standard, patient's written consent has been
collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical permission has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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