Frequency of polycystic ovarian syndrome in women with postadolescent acne
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Introduction
Acne is generally recognized as a disorder of young adults; however, the referral of patients older than 25 years of age is increasing. Postadolescent acne is defined as the presence of acne after the age of 25 years, irrespective of the age at onset [1]. There are two forms of the disease: persistent and late onset [2]. Persistent acne represents a continuation of acne from adolescence into adult life and late-onset acne describes significant acne occurring for the first time after the age of 25 years [3].

In most studies, female postadolescent acne mainly affect the face [2,3] and notably the chin and the mandibular region [2]. The perioral region is frequently affected [4]. Important criteria of postadolescent acne are no or low response to local or systemic antibiotic treatment [2] and premenstrual flare of the lesions [5]. Most often, female postadolescent acne is mild to moderate acne [2,4], with lesions that tend to be less numerous compared with adolescent acne [6]. However, the lesions of persistent acne are usually deep-seated, tender, inflammatory papules and nodules, frequently involving the lower third of the face, jaw line, and neck. Comedonal lesions may also involve the forehead or lateral margins of the face, but they are not always prominent [3]. Two main pathological factors seem to predominate in the development of adult female acne: a peripheral hormonal factor and a chronic stimulation of innate immunity. These factors could be modulated by both genetic and external factors [6]. The hypothesis is that female acne could be a peripheral hormonal illness related to

Background
Acne vulgaris in females may appear for the first time at or persist after the age of 25 years and may be resistant to treatment despite topical and systemic therapy for a sufficient period. In this condition, acne may be a manifestation of an underlying endocrine condition such as polycystic ovarian syndrome (PCOS).

Objective
The aim of this study was to assess the frequency of PCOS in women with postadolescent acne.

Patients and methods
This case–control study included 40 female patients with postadolescent acne vulgaris and 20 acne-free female participants as a control group. Both patients and controls were subjected to full assessment of history, dermatological examination, and assay of serum total testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). Two of the following criteria were required for the diagnosis of PCOS: a clinical or a biochemical feature of hyperandrogenism and/or ratio of LH to FSH of at least 2 and/or ultrasonic findings of PCOS.

Results
The frequency of PCOS among postadolescent acne patients was 37.5 and 5% in the control group, with a statistically significant difference ($P=0.006$). There was no statistically significant difference between the acne group and the control group regarding serum levels of total testosterone, FSH, and LH ($P=0.23$, 0.14, and 0.86, respectively). However, statistically significant difference was found between both groups in the LH/FSH ratio ($P=0.033$). Also, there was a highly statistically significant difference between acne patients with PCOS and those without PCOS in the LH/FSH ratio and LH ($P<0.001$ for both).

Conclusion
All women with postadolescent acne should be considered for underlying PCOS. Hormonal profile and ultrasonography should be performed for patients with postadolescent acne despite the absence of menstrual irregularities or hirsutism.

Keywords:
Follicle stimulating hormone, luteinizing hormone, post adolescent acne, polycystic ovarian syndrome, total testosterone


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hyperactivity or abnormal activity of 5α-reductase enzyme expressed in the skin both in sebocytes and keratinocytes [6]. The development of acne lesions could be linked to an abnormal activity of one or several molecules involved in innate immunity such as Toll-like receptors or defensins inducing a chronic inflammation of some sebaceous glands. This chronic inflammation would be maintained by the development of resistant Propionibacterium acnes strains in pilosebaceous follicle [7]. Androgens stimulate sebum production, which is necessary for the development of acne. Hyperandrogenism in women can be caused by various conditions, the most prevalent of which is polycystic ovarian syndrome (PCOS) [8]. PCOS affects 5–10% of reproductive-aged women [9] and 23% of women with PCOS are apparently normal [10].

The aim of this study was to assess the frequency of PCOS in women with postadolescent acne.

Patients and methods
This case–control study included 40 female patients with postadolescent acne vulgaris and 20 healthy acne-free age-matched and sex-matched participants as a control group. They were recruited from the Outpatient Clinic of Dermatology and Andrology of Benha University Hospital in the period from February 2012 to August 2012. All the participants provided informed consents to participate in this study. The laboratory investigations were carried out at the Clinical Pathology Department of Benha University Hospital under complete aseptic conditions. The study was approved by the Research Ethics Committee of Benha Faculty of Medicine. The inclusion criteria were 20 female patients with persistent acne that began in adolescence and continued into adult life and 20 female patients with late-onset acne that appeared for the first time after the age of 25 years. Their age ranged from 25 to 45 years. The exclusion criteria included female patients with acne associated with oral contraceptive pills, female patients with pregnancy-associated and lactation-associated acne, and patients with a history of other endocrine diseases such as congenital adrenal hyperplasia, adrenal, or ovarian tumor.

Methods
Two of the following criteria were required for the diagnosis of PCOS: a clinical or a biochemical feature of hyperandrogenism and/or ratio of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) of at least 2 and/or ultrasonic findings of PCOS [11,12]. Both patients and controls were subjected to the following:

Careful clinical examination
A dermatological examination was performed for all patients with a focus on the distribution and type of acne lesions (comedonal or inflammatory) and signs of hyperandrogenism, for example androgenetic alopecia and hirsutism.

Radiological investigations
Pelvic abdominal ultrasonography was performed for all patients with a diagnosis of PCOS either transabdominally or transvaginally (in married women). Either a 3.5MHz transabdominal (full bladder technique) or a 5 MHz transvaginal probe was used. The ovarian morphology was visualized carefully.

Polycystic ovarian morphology can be established in the follicular phase when at least one ovary has at least 12 follicles measuring 2–9 mm in diameter and/or the ovarian volume is greater than 7.5 cm³ in at least one ovary. The follicles are usually tightly spaced along the periphery of the ovary with increased stromal volume (the ‘pearl necklace’ sign) [13]. The transabdominal criteria for polycystic ovaries were 10 follicles identified in one plane (usually between 2 and 8mm in diameter) arranged peripherally around a dense core of stroma or increased amount of stroma [14].

Laboratory investigations
Venous blood samples (5 ml) were collected from each participant for the assay of serum total testosterone (TT), LH, and FSH by a microplate immunoenzymometric assay IEMA/ELISA. Samples were collected between 08:00 and 09:00 a.m. at the second to fifth day of the menstrual cycle of each participant under complete aseptic conditions. Samples were placed in a water bath at 37°C and centrifuged at 2000–4000 rpm for 5 min to separate the serum. Serum was stored at –20°C until analysis.

Statistical analysis
The data collected were tabulated and analyzed using the Statistical Package for Social Science (version 16; SPSS Inc., Chicago, Illinois, USA). Categorical data were presented as number and percentages, whereas quantitative data were expressed as mean ± SD and range. Fisher’s exact test was used to analyze categorical variables; the Mann–Whitney U-test was used to analyze the difference between two quantitative variables from two independent groups. The accepted level of significance in this work was set at 0.05 (P<0.05 was considered significant, whereas P<0.001 was considered highly significant).

Results
A total of 40 female patients with postadolescent acne vulgaris and 20 acne-free female control participants were included in this study. Their age ranged from 25 to 45 years, mean 35.3 ± 5.5 years for the acne group and 34.7 ± 5.9 years for the control group. The difference between the acne and the control group in terms of age...
was insignificant \((P = 0.69)\). In this study, the most common clinical form of postadolescent acne was the papulopustular type, which was found in 19 (47.5%) patients, followed by the closed comedones + papules in seven (17%) patients. The face, especially the mandibular region, and the chin were affected in 25 (62.5%) patients. Hirsutism was found in nine (22.5%) patients and four (20%) control participants. Androgenetic alopecia was found in eight (20%) patients and one (5%) control participant. Menstrual irregularities were found in five (12.5%) patients and three (15%) control participants. Comparisons between patients and controls in terms of hirsutism, androgenetic alopecia, and menstrual irregularities were insignificant \((P = 0.7, 0.25, 0.75, \text{ respectively})\).

PCOS was detected in 15 (37.5%) postadolescent acne patients and one (5%) control participant. Comparison between patient and control groups in the frequency of PCOS was statistically significant \((P = 0.006)\).

### Table 1. Comparison between the acne group and the control group regarding the hormonal profile

<table>
<thead>
<tr>
<th>Variables</th>
<th>Acne group ((N = 40))</th>
<th>Control group ((N = 20))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (ng/ml)</td>
<td>0.97 ± 0.59</td>
<td>0.75 ± 0.44</td>
<td>0.23</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>10.67 ± 8.63</td>
<td>8.29 ± 4.32</td>
<td>0.86</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>10.79 ± 6.05</td>
<td>13.15 ± 5.38</td>
<td>0.14</td>
</tr>
<tr>
<td>LH/FSH ratio</td>
<td>1.14 ± 0.93</td>
<td>0.66 ± 0.50</td>
<td>0.033*</td>
</tr>
</tbody>
</table>

The Mann–Whitney \(U\)-test was the statistical test used.

FSH, follicle-stimulating hormone; LH, luteinizing hormone; LH/FSH ratio, luteinizing hormone/follicle-stimulating hormone ratio; TT, total testosterone.

*\(P\) value < 0.05 is considered significant.

### Table 2. Hormonal profile among acne patients those with and without polycystic ovarian syndrome

<table>
<thead>
<tr>
<th>Variables</th>
<th>No PCOS ((N = 25))</th>
<th>PCOS ((N = 15))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (ng/ml)</td>
<td>0.86 ± 0.47</td>
<td>1.13 ± 0.73</td>
<td>0.27</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>6.42 ± 3.42</td>
<td>17.77 ± 10.06</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>11.80 ± 6.66</td>
<td>9.10 ± 4.61</td>
<td>0.13</td>
</tr>
<tr>
<td>LH/FSH ratio</td>
<td>0.61 ± 0.29</td>
<td>2.04 ± 0.94</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

The Mann–Whitney \(U\)-test was the statistical test used.

FSH, follicle-stimulating hormone; LH, luteinizing hormone; LH/FSH ratio, luteinizing hormone/follicle-stimulating hormone ratio; PCOS, polycystic ovarian syndrome; TT, total testosterone.

*\(P\) value < 0.05 is considered significant.

### Table 3. Hormonal profile of the control group, patients with persistent acne, and patients with late-onset acne

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control group ((N = 20))</th>
<th>Persistent acne ((N = 20))</th>
<th>Late-onset acne ((N = 20))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (ng/ml)</td>
<td>0.75 ± 0.45</td>
<td>1.03 ± 0.68</td>
<td>0.91 ± 0.49</td>
<td>0.16</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>8.29 ± 4.32</td>
<td>9.04 ± 6.91</td>
<td>12.31 ± 9.98</td>
<td>0.21</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>13.15 ± 5.38</td>
<td>11.86 ± 7.59</td>
<td>9.72 ± 3.91</td>
<td>0.18</td>
</tr>
<tr>
<td>LH/FSH ratio</td>
<td>0.86 ± 0.50</td>
<td>0.98 ± 0.92</td>
<td>1.33 ± 1.02</td>
<td>0.039*</td>
</tr>
</tbody>
</table>

The Mann–Whitney \(U\)-test was the statistical test used.

FSH, follicle-stimulating hormone; LH, luteinizing hormone; LH/FSH ratio, luteinizing hormone/follicle-stimulating hormone ratio; TT, total testosterone.

*\(P\) value < 0.05 is considered significant.

In terms of the hormonal profile, there was no statistically significant difference between the acne group and the control group in TT, FSH, and LH \((P = 0.23, 0.14, \text{ and } 0.86, \text{ respectively})\). However, a statistically significant difference was found between both groups in the LH/FSH ratio \((P = 0.033)\) (Table 1).

There was a highly statistically significant difference between acne patients with PCOS \((N = 15)\) and those without PCOS \((N = 25)\) in the LH/FSH ratio and LH \((P < 0.001 \text{ for each})\) (Table 2).

PCOS was detected in six (30%) patients with persistent acne, nine (45%) patients with late-onset acne, and one (5%) control participant, with a statistically significant difference \((P = 0.015)\). However, there was no statistically significant difference between patients with persistent acne and late-onset acne in the frequency of PCOS \((P = 0.33)\). Comparison between patients with either persistent acne or late-onset acne and the control group in the LH/FSH ratio was statistically significant \((P = 0.039)\) (Table 3).

**Discussion**

Patients with postadolescent acne appear to represent an increasingly important population of acne sufferers. Two main clinical groups were identified: those with persistent acne and those with late-onset acne [14].

In this study, the papulopustular form of acne was found in 21 (52.5%) postadolescent patients. This finding is in agreement with that of Goulden et al. [15], Dumont-Wallon and Dréno [16], and Benchikh and Ouhajjou [17].

In this study, the face, especially the mandibular region, and the chin were affected in 25 (62.5%) patients. This finding was in agreement with that of Benchikh and Ouhajjou [17], who found that the mandible was involved in 98 (57.9%) patients.

In this study, there was no significant difference in the frequency of clinical manifestations of hyperandrogenism including hirsutism, androgenetic alopecia, and menstrual irregularities between patients and controls. This, however, was not in agreement with the result of Goulden et al. [15], who found a significantly higher percentage (37%) of postadolescent acne women with features of hyperandrogenism compared with controls. Also, Maneschi...
et al. [18] reported significantly higher percentage (70%) of mild and heterogeneous clinical features of hyperandrogenism in women with adult acne (late onset or persistent) and Vexiau et al. [19] reported features of hyperandrogenism in 86% of patients with persistent acne. Seirafi et al. [1] found that there was no significant difference in menstrual irregularities between women with adult-onset acne and hirsutism and women with adult-onset acne without hirsutism. These contradictory results suggest the role of factors other than hormonal factors in the pathogenesis of postadolescent acne.

In the present study, the frequency of PCOS in women with postadolescent acne was 15 (37.5%) patients compared with one (5%) participant in the control group, with a statistically significant difference. Most previous studies [1,11,12,20–25] carried out on acne patients did not discriminate between patients of adolescent or postadolescent acne and reported a higher frequency of PCOS and polycystic ovaries compared with the control group. Begum et al. [12] detected PCOS in 11 (27.5%) female patients with acne (their age ranged from 15 to 40 years) and one (3.3%) control participant, with a statistically significant difference. Timpatanapong and Rojanasakul [11] reported PCOS in 37.3% of female patients with acne and none in the control group. Seirafi et al. [1] showed that the frequency of PCOS in women with acne was 40%. Pescirico et al. [20] detected polycystic ovaries (by pelvic ultrasound imaging) in 45.4% of the patients (their age ranged from 14 to 45 years) and in 17.1% of the controls. The study was carried out on 119 women with acne (excluding those with obesity, hirsutism, and menstrual disturbance) and 35 normal women as a control group. The results of the previous study indicated that polycystic ovaries were common in women with acne and not necessarily associated with menstrual disorders, obesity, or hirsutism. Maluki [21] found that 63 (51.2%) patients with resistant acne (their age ranged from 17 to 40 years) have PCOS in comparison with eight (6.2%) control participants, with a highly statistically significant difference. Betti et al. [22] reported that 24 (52.2%) patients with postadolescent acne (late-onset or persistent acne) had polycystic ovaries detected by ultrasound scanning. In the study of Zandi et al. [23] on 118 women with acne, the estimated frequency of polycystic ovaries by ultrasonography was 48 and 60.2% PCOS on the basis of NIH diagnostic criteria. Bunker et al. [24] reported that 83% of women with acne had PCOS compared with 19% in the control group. The high percentage of PCOS reported in the previous studies was because of the wide age range of acne patients, not just postadolescent acne patients. However, Walton et al. [25] reported that in two (5.5%) acne patients, polycystic ovaries could be observed. However, they did not report the frequency of the syndrome, but only focused on polycystic ovaries.

PCOS was detected in six (30%) patients with persistent acne and nine (45%) patients with late-onset acne, with no statistically significant difference ($P = 0.33$). To our knowledge, this is the first published study to compare the frequency of PCOS among patients with persistent and late-onset acne.

The present study found no statistically significant difference between the acne group and the control group in serum levels of TT, FSH, and LH. However, a statistically significant difference was found between both groups in the LH/FSH ratio.

Generally, the absence of significant difference in serum TT in postadolescent acne patients compared with controls was in agreement with the result of Williams and Layton [3], who reported that free testosterone and sex hormone-binding globulin were elevated, without a statistically significant difference. This indicates that the contribution of the systemic hormones versus the contribution of the skin’s own ability to produce hormones may be important in the formation of acne [2]. These findings thus suggest that end-organ hypersensitivity and not testosterone level may be the central factor in the pathogenesis of the disease. However, Begum et al. [12] and Rahman et al. [26] found that the mean serum testosterone level was higher in acne patients than in controls, with a statistically significant difference. This difference may be because of the wide age range (15–40 and 13–45 years, respectively) and different methods used to determine serum TT.

The results of the present study are in agreement with those of Timpatanapong and Rojanasakul [11] and Begum et al. [12], who reported no statistically significant difference in serum levels of LH and FSH of patients with acne in comparison with the control group.

In the present study, there was a high statistically significant difference between acne patients with PCOS ($N = 15$) and those without PCOS ($N = 25$) in the LH/FSH ratio and LH ($P < 0.001$, $< 0.001$). These results were in agreement with the study of Betti et al. [22] and Bunker et al. [24], who found that adult women with acne and PCOS had higher values of LH and LH/FSH ratio than those without ovarian abnormalities. Zandi et al. [23] reported that only the LH/FSH ratio differed significantly between acne patients with PCOS and those without PCOS.

**Conclusion**

All women with postadolescent acne should be considered for underlying PCOS. The papulopustular form of acne was the most prominent form in postadolescent acne and the face, especially the mandibular region, and the chin were the most affected sites. There was no statistically significant difference in the frequency of associated hirsutism, androgenetic alopecia, and menstrual irregularities between postadolescent acne patients and controls. Further studies are needed to detect other causes of postadolescent acne and to compare the frequency of PCOS in females with postadolescent acne and those with adolescent acne.

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**Conflicts of interest**

There are no conflicts of interest.
References