INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders seen in 6-10% of reproductive-aged women including adolescents (1). Diagnosis is based on fulfilling two of three criteria: irregular menses, polycystic ovaries on ultrasound, and elevated serum androgens (2). According to overall metabolic and endocrine long-term consequences, patients with PCOS have an increased prevalence of psychiatric and physical comorbidities (3,4).

In terms of psychiatric problems, it is well established that women with PCOS suffer from impaired emotional well-being and reduced quality of life (5,6). Also, based on a review of studies from different world regions the most common mental health problems in women with PCOS were depression and anxiety (36.6%) (7,8). On the other hand, one of the most observed symptoms in the clinic, the anger, is not adequately addressed in studies although the potential role of hyperandrogenemia and high levels of testosterone in inducing anger are known (5,9,10).

In this study, we aimed to examine the relationship between anger and anxiety associated with the hyperandrogenemia. For this, we compared the anxiety-anger relationship in adolescents with PCOS and healthy control group.
Our hypotheses were:
1. Trait and state anxiety were both high among adolescents with PCOS than controls.
2. The relationships between anger types and anger control styles and anxiety levels were different in adolescents with PCOS.

**METHODS**

The research protocol for this study was approved by the Research Ethics Committee of Ufuk University School of Medicine (Ethics Approval Number: 18052016). Patients were recruited from Pediatric Endocrinology Department of the University Hospital, from among the girls who were newly diagnosed as PCOS and agreed to participate the study after informed consent between March 2015 and August 2015. Twenty eight adolescents with PCOS were recruited for the study.

Sixteen healthy, matched for age and BMI, regularly menstruating girls with no clinical signs of hirsutism served as controls. Control group were recruited from the patients who were referred to the Department of Pediatrics for respiratory tract infections, who did not have any chronic endocrinological disease and psychiatric symptoms and agreed to participate the study.

The exclusion criteria for both groups were: abnormal thyroid function, hyperprolactinaemia, congenital and adrenal hyperplasia, using medication that could be influenced sex steroids in last 3 months, and as well as any psychiatric disorders diagnosed before.

PCOS patients were physically evaluated by the child endocrinologist (ATE). In each girl in this group, a transabdominal pelvic ultrasound examination was performed. Ovaries were considered as polycystic if 12 or more cysts were present in at least one ovary. During the follicular phase of menstrual cycle, the basal plasma concentration of gonadotropins (LH, FSH), androstenedione, testosterone, 17-hydroxyprogesterone, estradiol, thyroid hormones, and dehydroepiandrosterone were measured. For psychiatric evaluation, The Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime version (KSADS-PL) were administered by the Child and Adolescent Psychiatrist (HG).

All participants were administered the State-Trait Anxiety Inventory (STAI I-II) and the Trait Anger and Anger Expressions Scale.

**The State-Trait Anxiety Inventory (STAI I-II)**

It is developed by Spielberger et al. (11). It is a 40-item self-report instrument assessing levels of situation-related (state) anxiety (20 items) or trait anxiety (20 items). State Anxiety Scale, determines what an individual feels self-renewal on certain and specific conditions. Trait Anxiety Scale indicates how the individual feels about himself / herself independently of the conditions. This inventory was translated into Turkish by Oner and Le Compte for validation and reliability study (12). Items are rated on a 4-point Likert-type scale to produce a summative score ranging from 20 to 80 with higher scores indicating higher levels of anxiety.

**The Trait Anger and Anger Expressions Scale**

This scale has 34-items and two main dimensions developed by Spielberger et al. (13). The first 10 items of the scale are the Trait Anger subscale, which questions whether the person usually feels or is angered. Trait Anger indicates high levels of anger at high scores. The second dimension, Expression Style of Anger is divided into three sub-scales. Eight of these items are related to anger outside, 8 to anger inside, and 8 to anger control. The high scores on the inside scale indicate that the anger has been suppressed. The adaptation of the scale to Turkish has been done by Özer (14). Reliability study of the scale has Cronbach’s alpha internal consistency coefficients of 0.6 and 0.92 respectively.

**Statistical Analysis**

The data were evaluated using the SPSS 18.0 package program (SPSS Inc., Chicago, IL, USA). We evaluated data for assumptions of normality by using visual and analytical methods (histograms, probability plots and Kolmogorov- Smirnov / Shapiro-Wilks test). Since the measurements were normally distributed, parametric tests (independent-samples t-test) were conducted to
compare the parameters. In addition we used Pearson’s correlation analysis (two-tailed) to determine the relationship between variables. We have chosen the error level as $\alpha=0.05$ and interpreted as "statistically significant difference" for $p$ values equal or smaller than these values.

**RESULTS**

There were no significant differences in terms of age, maternal age, paternal age, monthly income, and BMI between PCOS and control group.

Only PCOS group had been evaluated according to the anthropometric measurements and hormonal values. These values supported the diagnosis of PCOS (Table 1).

When we compared the scale scores, we determined that the scores of State and Trait Anxiety, Externalized Anger and Trait Anger were significantly higher (for State Anxiety $p=0.003$; for Trait Anxiety $p<0.001$; for Externalized Anger $p=0.011$; for Trait Anger $p=0.001$) and the Anger Control was significantly lower in the PCOS group ($p=0.001$) (Table 2).

According to correlation analyses; the relationships between State anxiety and anger types were different between PCOS and control group. In control group, state anxiety was positively correlated with trait anger, internalized and externalized anger ($r=0.65; r=0.62; r=0.64$ respectively and correlation is significant at the 0.01 level) while there were no relationships between the variables mentioned above in the PCOS group. On the other hand, in PCOS group state anxiety was negatively correlated with the anger control ($r=-0.57$, correlation is significant at the 0.05 level).

In terms of trait anxiety, trait anger and externalized anger were positively associated with this type of anxiety in control group ($r=0.63; r=0.71$ respectively and

### Table 1: Anthropometric Characteristics And Endocrinological Data of PCOS Group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PCOS group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>16.0±0.0</td>
<td>16.1±0.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.1±13.6</td>
<td>60.2±13.2</td>
</tr>
<tr>
<td>BMI (W/H^2)</td>
<td>22.5±5.39</td>
<td>22.30±4.89</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.6±6.87</td>
<td>164.67±6.91</td>
</tr>
<tr>
<td>Waist/Hip Ratio</td>
<td>0.72±0.07</td>
<td>-</td>
</tr>
<tr>
<td>LH/FSH</td>
<td>2.35±1.4</td>
<td>-</td>
</tr>
<tr>
<td>Prolactin</td>
<td>18.35±10.3</td>
<td>-</td>
</tr>
<tr>
<td>Testosterone (0.06-0.82) ng/ml</td>
<td>1.53±0.12</td>
<td>-</td>
</tr>
<tr>
<td>Free testosterone</td>
<td>3.14±1.21</td>
<td>-</td>
</tr>
<tr>
<td>ACTH</td>
<td>40.18±20.8</td>
<td>-</td>
</tr>
<tr>
<td>DHEA (85-368µg/dl)</td>
<td>272.5±91.6</td>
<td>-</td>
</tr>
<tr>
<td>fT4</td>
<td>1.27±0.21</td>
<td>-</td>
</tr>
<tr>
<td>TSH</td>
<td>2.64±1.1</td>
<td>-</td>
</tr>
<tr>
<td>Fasting Insulin</td>
<td>23.03±11.2</td>
<td>-</td>
</tr>
</tbody>
</table>

**BMI**: Body Mass Index, **W**: Weight, **H**: Height, **LH**: Luteinizing Hormone, **FSH**: Follicle-Stimulating Hormone, **ACTH**: Adrenocorticotropic hormone, **DHEA**: Dehydroepiandrosterone, **fT4**: Free thyroxine, **TSH**: thyroid stimulating hormone

### Table 2: Differences Between Scale Scores of Groups

<table>
<thead>
<tr>
<th>Scale Scores</th>
<th>PCOS</th>
<th>Control</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>STAI-I</td>
<td>37.0±12.4</td>
<td>24.8±5.4</td>
<td>0.003$^3$</td>
</tr>
<tr>
<td>STAI-II</td>
<td>41.7±8.7</td>
<td>31.5±2.6</td>
<td>&lt;0.0001$^2$</td>
</tr>
<tr>
<td>Internalized Anger</td>
<td>15.7±4.3</td>
<td>12.7±4.5</td>
<td>0.080</td>
</tr>
<tr>
<td>Externalized Anger</td>
<td>18.2±6.5</td>
<td>15.7±2.5</td>
<td>0.011$^3$</td>
</tr>
<tr>
<td>Anger Control</td>
<td>19.6±5.0</td>
<td>30.6±1.1</td>
<td>&lt;0.0001$^4$</td>
</tr>
<tr>
<td>Trait anger</td>
<td>22.7±7.7</td>
<td>14.0±4.4</td>
<td>0.001$^5$</td>
</tr>
</tbody>
</table>

Analyses were two tailed

1. $t(42)=-3.38$, $p=0.003$, Cohens d=1.27; $r=0.53$  
2. $t(42)=-4.19$, $p<0.0001$, Cohens d=1.58; $r=0.62$  
3. $t(42)=-2.77$, $p=0.011$, Cohens d=1.02; $r=0.45$  
4. $t(42)=-7.96$, $p<0.0001$, Cohens d=3.00; $r=0.83$  
5. $t(42)=-3.69$, $p=0.001$, Cohens d=1.37; $r=0.56$
correlations are significant at the 0.01 level). Similarly, in PCOS group, trait anxiety was positively correlated with the externalized anger (r=0.55; correlation is significant at the 0.01 level).

The most important difference from the control group in the correlation analyses is the negative relationships between anxiety types and anger control (Table 3). In PCOS group, we found that both anxiety levels were inversely correlated to anger control scores, that is, anxiety levels decreased as anger control increased. But in the control group, we did not observe such a correlation.

DISCUSSION

This present study aims to report an exploration of anger and anxiety in the adolescent girls with PCOS and indicate the associations between anger and anxiety types in this group compared to the healthy controls.

Overall, PCOS patients showed significantly more pronounced emotional distress, anxiety, and anger (5,7,8,15) and our findings strongly supported these results on PCOS emotional outcomes in adolescents except for internalized anger. In addition, our study indicated that, both state anxiety and trait anxiety were negatively associated with anger control in adolescents with PCOS, while there were no such associations in healthy controls. This is an interesting and relatively new finding (5,16,17).

Anxiety and anger are often linked together but the role of anger in the development, maintenance, and treatment of anxiety is still unclear, vice versa (18). The possible relationship between anxiety and anger seems to depend on 3 main theoretical model: (1) Childhood traumas: Unpredictable parenting induces anxiety in children that in turn triggers aggressive behavior and anger.

(2) Chronic Anxiety: Prolonged periods of anxiety deplete children’s capacity to inhibit impulses and trigger the aggression.

(3) Daily stress: Minor daily stressors give rise to anxiety while cognitive perseveration maintains anxious moods and increasing the children to have aggression (18). These theoretical models are compatible with our results in the healthy control group which the state anxiety and trait anxiety are positively correlated with anger types. On the other hand, in adolescents with PCOS trait anxiety is only associated with the externalized anger and anxiety types are mainly and negatively associated with anger control. These could be a consequence of chronic hyperandrogenemia. As known, testosterone is released in response to perceived challenges of social status, often followed by an increase in aggressive behaviors and physiological activation. Both endogenous and exogenous testosterone appear to modulate amygdala response to fear and anger expression (19). Additionally, studies demonstrated that endogenous testosterone levels are associated with prefrontal cortex and amygdala functional connectivity in response to affective social stimuli (20). Alteration in medial prefrontal cortex (mPFC) activities could be possible neurobiological mechanisms underlying the relationship between endogenous testosterone levels and anger (21). The dorsal aspect of the mPFC (22) is correlated with parasympathetic activity, and the mPFC generally serve as a final common pathway linking affect with autonomic system response (23) via the parasympathetic branch of the autonomic nervous system that myelinated vagus nerve which exerts inhibitory

<table>
<thead>
<tr>
<th></th>
<th>PCOS State Anxiety</th>
<th>PCOS Trait Anxiety</th>
<th>Control State Anxiety</th>
<th>Control Trait Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trait Anger</td>
<td>0.39</td>
<td>0.51</td>
<td>0.65**</td>
<td>0.63**</td>
</tr>
<tr>
<td>Internal Anger</td>
<td>0.31</td>
<td>0.40</td>
<td>0.62**</td>
<td>0.42</td>
</tr>
<tr>
<td>External Anger</td>
<td>0.42</td>
<td>0.55**</td>
<td>0.64**</td>
<td>0.71**</td>
</tr>
<tr>
<td>Anger Control</td>
<td>-0.57*</td>
<td>-0.61*</td>
<td>0.13</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.05 level (two-tailed), **Correlation is significant at the 0.01 level (two-tailed)
control of both behavior and cardiac activity (24). Chronic stimulation of the vagus nerve also reduces HPA axis reactivity and corticotrophin releasing hormone (25,26). Atypical regulation of these systems are associated with many psychiatric disorders including major depressive disorder and generalized anxiety disorder (27) like among women with PCOS (28). Although it is not possible to evaluate causality in a cross-sectional study like the present one, in the light of our results and results of other studies mentioned above, it can be speculated that chronic hyperandrogenemia could be related to anger control problems and these problems could be an etiologic risk factor for anxiety symptoms in adolescents with PCOS. Also our results demonstrated that chronic hyperandrogenemia may be related with the externalized anger than internalized. This difference could be important for treatment approaches in adolescents with PCOS and should be evaluated in larger samples.

Our results must be evaluated in light of certain limitations. Firstly, due to a cross-sectional design, it is not possible to comment on causality. Secondly, although the high effect size results, the sample size of groups were small, which limits the generalizability of the study findings. Thirdly, only PCOS adolescents’ hormonal levels were evaluated. By working with the healthy control groups' hormonal levels and analyzing the correlation between testosterone level and anger-anxiety scores, more information could have been obtained. And finally the data for anger and anxiety were collected by self-reports. The physical tests like heart rate variability, respiratory sinus arrhythmia and electrodermal activity would reveal different possible associations.

CONCLUSION
To our knowledge, this is the first study that examines the anger-anxiety relationship in adolescents with PCOS. In the light of recent studies and our results, we demonstrated that there was a unique relationship between anxiety and anger in adolescents with PCOS than healthy controls. This could be a consequence of hyperandrogenemia and early lifestyle modification, medical and psychiatric treatment could prevent adolescents PCOS from development of anxiety.

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REFERENCES


