

# Attention deficit-hyperactivity disorder symptoms in women with polycystic ovary syndrome

Sabri Hergüner<sup>1</sup>, Hatice Harmancı<sup>1</sup>, and Harun Toy<sup>2</sup>

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## Abstract

**Objectives:** Several studies suggest that androgens are involved in the etiology of attention deficit-hyperactivity disorder (ADHD). In this study, we investigated the ADHD symptoms in women with polycystic ovary syndrome (PCOS), a complex endocrine, hormonal, and metabolic condition associated with hyperandrogenism.

**Methods:** Forty women between the ages of 18 and 35 years with PCOS were recruited for the study group. For comparison, 40 healthy women who had regular menses were included. Current and childhood ADHD symptoms were assessed by using the Adult ADHD Self-Report Scale and Wender-Utah Rating Scale, respectively.

**Results:** Women with PCOS had higher total Adult ADHD Self-Report Scale and total Wender-Utah Rating Scale scores than controls. According to the Wender-Utah Rating Scale, the frequency of childhood ADHD was significantly higher in PCOS group than the control. Adult ADHD Self-Report Scale: Hyperactivity–Impulsivity and Wender-Utah Rating Scale: Behavioral Problems/Impulsivity scores were significantly higher in women with PCOS. However, there were no significant differences between groups in both current and childhood inattention scores. We found no correlations between ADHD symptoms and serum hormone levels including testosterone in women with PCOS.

<sup>1</sup>Department of Child and Adolescent Psychiatry, Meram Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey

<sup>2</sup>Department of Obstetrics and Gynecology, Meram Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey

## Corresponding author:

Sabri Hergüner, Department of Child and Adolescent Psychiatry, Meram Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey.

Email: cocukergen@yahoo.com

**Conclusions:** These results suggest that women with PCOS have higher ADHD symptoms. Further studies are needed to investigate the association between PCOS and ADHD.

### **Keywords**

Polycystic ovary syndrome, prenatal androgens, attention deficit-hyperactivity disorder, testosterone, sex difference

## **Introduction**

Sexual differentiation of the brain occurs under the control of gonadal hormones, particularly androgens, during early development. Androgen levels during the prenatal development permanently influence brain regions and behaviors that show sex differences. For instance, in rhesus monkeys, treating pregnant females with androgens increases male-typical behaviors and reduces female-typical behaviors in female offspring.<sup>1,2</sup>

Attention deficit-hyperactivity disorder (ADHD) is a common neurodevelopmental disorder that affects 6–12% of school-aged children and 4–5% of adults. Males are more likely to receive the diagnosis than females, with ratios ranging from 2:1 to 9:1.<sup>3</sup> Affected females display lower rates of hyperactivity and aggression and are more likely to be diagnosed with the ADHD/Inattentive type than males.<sup>4,5</sup> The male preponderance suggest that ADHD may be influenced by prenatal androgen levels.<sup>6,7</sup>

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder of reproductive age women, affecting 6–7% of women during their childbearing years. It is characterized by hyperandrogenism, chronic oligo/anovulation, and polycystic ovaries on ultrasound.<sup>8</sup> Based on animal models, experimental evidence showed that pregnant monkeys receiving exogenous androgens gave rise to daughters with PCOS symptoms which support the role of prenatal androgens in the etiology of PCOS.<sup>9,10</sup>

Previous studies have suggested the role of androgens in the development of ADHD. The ratio of second to fourth digit length (2D:4D) is suggested as an indicator of prenatal androgen exposure.<sup>11</sup> More masculine (lower) 2D:4D ratio was found to be associated with higher ADHD symptoms.<sup>5</sup> Cattrall et al.<sup>12</sup> reported that women with PCOS also had lower 2D:4D ratio. In addition to intrauterine androgen levels, current androgen levels were shown to be related with ADHD. Children with ADHD were reported to have higher salivary levels of dehydroepiandrosterone compared with controls.<sup>13</sup>

In this study, we compared the ADHD symptoms between women with PCOS and controls. As it had been suggested that androgens are implied in the etiologies of both ADHD and PCOS, we predicted that women with PCOS would have higher ADHD scores than controls.

## Methods

### Procedure

Forty women between the ages of 18 and 35 years with a diagnosis of PCOS were recruited from the Department of Obstetrics and Gynecology, Meram Faculty of Medicine, Konya, Turkey. PCOS diagnosis was based on Rotterdam diagnostic criteria.<sup>14</sup> Exclusion criteria were use of hormone therapy to treat symptoms of PCOS within three months prior to recruitment, current use of psychotropic medications, and current psychiatric illness. For comparison, 40 healthy women between the ages of 18 and 35 years who had regular menses according to their self-report were recruited from the hospital staff. Women with a history of irregular menstrual cycles, acne, or excessive hair growth or those using oral contraceptives were excluded. All other inclusion and exclusion criteria for the PCOS group were also applied to the selection of control group. As adult ADHD is associated with overweight and obesity,<sup>15</sup> Body mass index (BMI) was measured in all subjects.

Written informed consent was obtained from all participants. Before entering the study, weight and height of all participants were measured and their BMI were calculated. All participants were then invited to complete the Wender-Utah Rating Scale (WURS) and Adult ADHD Self-Report Scale (ASRS). The study was approved by the Meram Faculty of Medicine Ethical Committee, Konya, Turkey.

### Instruments

**Data form.** An interview form developed by the investigators was used to collect data about the demographic characteristics of the participants. This form included questions including age and education level (number of years in full-time education) of the participants.

**Biochemical markers.** Blood samples of subjects with PCOS were obtained as a part of routine clinical examination during their early follicular phase (within 2–5 days after the first day of spontaneous menstrual bleeding) and serum concentrations of free testosterone, estradiol, follicle-stimulating hormone, luteinizing hormone, and progesterone were measured in fasting blood in the morning at the Chemistry Laboratory of Meram Faculty of Medicine using standard measurement assays.

**Wender-Utah Rating Scale.** The WURS is a 25-item self-report scale designed to assess childhood symptoms of ADHD retrospectively.<sup>16</sup> Items are rated on a five-point severity scale, from 0 = *not at all or slightly* to 4 = *very much*. The Turkish version of the WURS has been found to be a reliable and valid instrument for assessing childhood symptoms of ADHD in adults.<sup>17</sup> The Turkish version has five factors including (1) Irritability, (2) Depression, (3) School Problems, (4) Behavioral Problems/Impulsivity, and (5) Inattentiveness. In this

sample, WURS had excellent internal consistency (Cronbach's  $\alpha = .902$ ). The cut-off point of the WURS was determined as 36.

**Adult ADHD Self-Report Scale.** The ASRS is a self-report scale designed to measure current ADHD symptoms. It consists of 18 items based on DSM-IV criteria for ADHD that were measured on a five-point scale (0 = *never/seldom* and 4 = *very often*). The ASRS consists of two subscales, inattention and hyperactivity-impulsivity, each of them containing nine items.<sup>18</sup> Validity and reliability study of the ASRS in Turkish adult population was conducted by Doğan et al.<sup>19</sup> In this sample, ASRS had good internal consistency (Cronbach's  $\alpha = .749$ ). The cut-off score for ASRS in Turkish population was not studied.

### Statistical analyses

Data were presented as means  $\pm$  standard deviations. Kolmogorov–Smirnov test was performed to test the normal distribution of the data, and according to the results, an independent *t* test (two-tailed) or Mann-Whitney *U* test was used to compare continuous variables. Pearson's correlation analysis was performed to examine the correlations between ASRS, and WURS scores and hormone levels, age, education, and BMI. A *p*-value of less than 0.05 was considered as statistically significant. Statistical analyses were done using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

There were no significant differences in age, education, and BMI between groups. The descriptive characteristics of the groups are reported in Table 1.

Women with PCOS had significantly higher total current (ASRS) and total childhood (WURS) ADHD scores than controls. Hyperactivity-Impulsivity score of ASRS and Behavioral Problems/Impulsivity score of WURS were higher in PCOS group. There were no significant differences between groups in both ASRS and WURS inattention scores (Table 2). Based on the cut-off score of WURS, the frequency of childhood ADHD was significantly higher in PCOS group (11/40) than the control (2/40) ( $p = 0.013$ ).

Pearson correlation analysis revealed that there were no associations between ASRS, and WURS scores and hormone levels, age, and BMI (Table 3). Duration of education was negatively correlated with WURS-School Problems ( $r = -0.356$ ,  $p = 0.24$ ) and WURS-Inattentiveness ( $r = -0.338$ ,  $p = 0.33$ ).

## Discussion

We found that women with PCOS had higher total childhood and current ADHD symptoms than controls. The dopamine system is thought to play a

**Table 1.** Means ( $\pm$ SD) for age, education, and BMI by group.

	PCOS <i>n</i> = 40	Control <i>n</i> = 40	<i>p</i>
Age (years)	22.28 $\pm$ 3.68	22.33 $\pm$ 3.66	.952 <sup>a</sup>
Education (years)	13.75 $\pm$ 2.56	13.18 $\pm$ 1.89	.327 <sup>b</sup>
BMI (kg/m <sup>2</sup> )	22.07 $\pm$ 4.96	22.48 $\pm$ 3.61	.674 <sup>a</sup>
Weight (kg)	58.18 $\pm$ 12.39	59.93 $\pm$ 9.28	.477 <sup>a</sup>
Height (cm)	162.55 $\pm$ 5.35	163.43 $\pm$ 6.15	.499 <sup>a</sup>

BMI: body mass index.

<sup>a</sup>Independent *t* test.

<sup>b</sup>Mann-Whitney *U* test.

**Table 2.** Means ( $\pm$ SD) for total WURS and ASRS scales and subscale scores by group.

	PCOS <i>n</i> = 40	Control <i>n</i> = 40	<i>p</i>
ASRS: Inattention	13.30 $\pm$ 5.78	11.58 $\pm$ 3.46	.110 <sup>a</sup>
ASRS: Hyperactivity-Impulsivity	15.28 $\pm$ 6.02	12.03 $\pm$ 4.67	.009 <sup>a</sup>
ASRS: Total	28.58 $\pm$ 10.80	23.35 $\pm$ 6.85	.012 <sup>a</sup>
WURS: Inattentiveness	6.18 $\pm$ 4.57	5.18 $\pm$ 2.88	.245 <sup>a</sup>
WURS: School Problems	2.30 $\pm$ 2.80	1.15 $\pm$ 1.64	.059 <sup>b</sup>
WURS: Depression	5.50 $\pm$ 4.77	4.10 $\pm$ 2.59	.508 <sup>b</sup>
WURS: Irritability	8.00 $\pm$ 7.09	5.08 $\pm$ 4.18	.093 <sup>b</sup>
WURS: Behavioral Problems/Impulsivity	4.13 $\pm$ 4.22	2.28 $\pm$ 2.62	.048 <sup>b</sup>
WURS: Total	25.85 $\pm$ 20.09	17.88 $\pm$ 9.04	.025 <sup>a</sup>

ASRS: Adult ADHD Self-Report Scale; WURS: Wender-Utah Rating Scale.

<sup>a</sup>Independent *t* test.

<sup>b</sup>Mann-Whitney *U* test.

**Table 3.** Correlation between ASRS and WURS scores and hormone levels, age, and BMI.<sup>a</sup>

	fT	E2	FSH	LH	P	BMI	Age
ASRS: Total	.094	.155	.012	-.084	.033	-.045	-.034
WURS: Total	-.099	-.136	-.203	-.065	.166	-.046	-.208

ASRS: Adult ADHD Self-Report Scale; WURS: Wender-Utah Rating Scale; fT: free testosterone; E2: estradiol; FSH: follicle-stimulating hormone; LH: luteinizing hormone; P: progesterone; BMI: body mass index.

<sup>a</sup>Correlation coefficients.

central role in the neurobiology of ADHD.<sup>20</sup> Androgens are known to modulate dopamine activity in the mesolimbic system and to influence the development of dopamine neurons in the prefrontal cortex.<sup>21,22</sup> King et al.<sup>23</sup> reported that exposure to elevated androgen levels in early development led to decreased dopamine innervation in the frontal cortex and enhanced expression of ADHD-like behaviors in rats. Our findings support that high androgen levels may alter dopaminergic neurotransmission and increase the risk for ADHD.

In our study, childhood (WURS) Behavioral Problems/Impulsivity and current (ASRS) Hyperactivity-Impulsivity scores were higher in PCOS group. Pasterski et al.<sup>24</sup> found that girls with congenital adrenal hyperplasia, a disorder in which androgens are elevated prenatally, were reported by their mothers to be significantly more active and aggressive than their unaffected sisters. Öner et al.<sup>25</sup> also reported that girls with congenital adrenal hyperplasia had higher externalization scores on Child Behavior Checklist. These results suggest that androgen exposure may have an effect on hyperactivity and impulsivity in women with PCOS.

We found no significant differences between groups in both current and childhood inattention scores. Several studies confirmed that parents and teachers of children with ADHD are more likely to rate boys as being more hyperactive than girls, and girls to be more inattentive than boys.<sup>26,27</sup> Chance et al.<sup>28</sup> reported that testosterone levels were associated with aggression but not with cognitive ability. We can suggest that androgens do not exert a direct influence on inattention.

Positive relationship between testosterone and aggression was reported in children with disruptive behaviors.<sup>29</sup> However, there was a lack of association between impulsivity/aggression and serum androgen levels in adults.<sup>30,31</sup> In this study, we found no relation between serum testosterone levels and ADHD symptoms in women with PCOS. It may be that androgen effect on ADHD symptoms occur at an early stage of brain development. It should also be borne in mind that peripheral testosterone levels may not be correlated with actual levels of testosterone in the brain.

This study must be considered with its limitations. Our major limitation was subjects in the control group recruited according to their self-reports for PCOS rather than a clinical examination. Second limitation was all measures were based purely on self-report. Also, the use of WURS for childhood ADHD symptoms might lead to inaccurate recall. The ASRS and WURS are useful tools for screening but do not have the ability to make a clinical diagnosis. Finally, the main hypothesis of this study, which was the involvement of prenatal androgen exposure in the development of ADHD and PCOS, was not directly tested. These limitations suggest that results of this study should be viewed as very preliminary.

In conclusion, the present study found that women with PCOS had significantly higher hyperactivity-impulsivity but not inattention scores than controls.

These results suggest that androgen exposure may be involved in the development of ADHD symptoms. Further studies are needed to investigate the association between PCOS and ADHD.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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