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Anxiety and depression in adolescents with polycystic ovary syndrome and Mayer-Rokitansky-Küster-Hauser syndrome

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Abstract
Purpose. The purpose of this study was to assess self-reported depressive and anxiety symptoms in adolescents with polycystic ovary syndrome (PCOS) and those with the rare Mayer-Rokitansky-Küster-Hauser Syndrome (MRKHS), compared with healthy adolescents.

Material and methods. The participants were 49 adolescent girls, of whom 27 were patients with confirmed menstrual disorder, 22 with PCOS and 5 with MRKHS; and 22 were healthy eumenorrheic adolescents (control group) matched by age and school grade. The Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI-Gr) were used to measure depression and anxiety, respectively.

Results. The results showed that it was 1.08 times more likely for the PCOS group (p = 0.043) and 1.12 times more likely for the MRKHS group (p = 0.039) to have higher scores than healthy adolescents on the anxiety scale. The MRKHS group was 1.40 times more likely to have a higher number of depressive symptoms (p = 0.040) than the control group.

Conclusions. These findings, although based on a small sample, suggest a relationship between PCOS and MRKHS and the presence of psychological problems, such as anxiety and depressive symptoms in adolescents. This study is among the first to examine psychological difficulties in adolescents with such a rare menstrual syndrome as MRKHS.

Keywords: PCOS, MRKHS, anxiety, depression, psychopathology, menstrual disorders

Introduction
Menstruation is considered to be one of the archetypal symbols of femininity and thus constitutes a phenomenon of great significance in the nature of woman. The appearance of menstruation with normal characteristics and within the expected time period provides an indication of women’s physiological normality concerning the female nature, since the cyclical pattern that characterises female physiology is in this way being observed [1]. Menarche and menstrual cycling in adolescence are major events that establish the passage from childhood to adulthood and symbolise reproductive competence.

Several medical conditions, such as endocrine disorders or congenital abnormalities of the genital tract, lead to various kinds of disturbance in the menstrual cycle, including oligomenorrhea or primary amenorrhea (PA). Oligomenorrhea is defined as menses occurring less frequently than every 35 days (or ≤8 menstrual cycles in a year) and the commonest cause of this menstrual disorder is polycystic ovary syndrome (PCOS) [2]. PCOS is the most common endocrine disorder among women of reproductive age, with an incidence of 5–10% in the general population [3], and is characterised by androgen hypersecretion, insulin resistance and chronic anovulation [4]. Clinical manifestations of the syndrome include menstrual irregularities, hirsuitism, acne, alopecia, obesity and infertility. Treatment with oral contraceptives can help to improve the menstrual regularity and may interrupt the ‘vicious circle’, between hyperandrogenism and insulin resistance, through modulation of the hypothalamic-pituitary-gonadal regulatory system [5].

PA refers to the absence of menarche, and when PA is apparent at the age of 16 years, in the presence of
normal secondary sexual development, this may be the result of congenital abnormalities of the reproductive tract, such as those occurring in Mayer-Rokitansky-Küster-Hauser Syndrome (MRKHS). Women with MRKHS, which occurs in 1 in 5000 female births, have a 46XX genotype and a normal female phenotype, with spontaneous development of secondary sexual characteristics, as functional ovarian tissue is present. However, the syndrome is characterised by complete or partial absence of the vagina, uterus and proximal fallopian tubes, with associated renal tract anomalies in 15–40%, and anomalies of the skeletal system in 19–20% of patients [2]. The diagnosis is usually made in late adolescence with the major symptom of PA. These patients will not experience menses and pregnancy due to the absence of a functional uterus and vagina. The goal of treatment for adolescents with MRKHS is sexual function, which may be achieved by vaginal reconstruction, either by surgical creation of a neovagina [6–8] or non-surgically, using vaginal dilators [9].

As MRKHS is often diagnosed during adolescence, the psychosexual development and the identity, femininity, body image and self-esteem of the patients can be significantly impaired by receiving this type of information about their bodies [8,10]. Adolescent girls with MRKHS may also experience frustration or embarrassment because of failed attempts at intercourse or associated sexual difficulties that may affect their heterosexual relationships [11].

Very little is known about the short- and longer-term psychological impact of MRKHS in females, but several clinicians have suggested that the physical malformations, the absence of menstruation and infertility and the subsequent surgical intervention may all contribute to narcissistic damage in these patients [12].

Regarding PCOS, many aspects of the syndrome, including irregular or absent menstrual periods, infertility, the associated changes in appearance and possible disturbances in sexual attitudes may cause significant emotional distress and influence the identity and sense of femininity in patients [13]. The health-related quality of life of adolescent patients with PCOS has been found to be impaired [14].

Studies concerning the psychosocial aspects of adolescent patients with PCOS have focused mainly on the quality of life and the sexual behaviour of participants. To the knowledge of the authors, there are no reports of empirical studies on the psychological aspects of MRKHS in female adolescents, before vaginal reconstruction. This study includes preliminary prospective findings on psychological aspects of mood, i.e., depression and anxiety, in adolescent females with MRKHS.

The purpose of this study was to examine the psychological functioning of adolescent patients with PCOS and MRKHS by comparing the self-reported depressive and anxiety feelings of these patients with a non-patient (control) group of female adolescents. It was hypothesised that (a) adolescents who suffer from PCOS and MRKHS, with the leading symptoms of oligomenorrhea and PA respectively, would report significantly higher scores for depressive and anxiety symptoms in comparison to eumenorrheic adolescents, namely those with regular menstruation, and (b) patients with MRKHS, given the greater severity of the disorder, would report significantly higher scores than those with PCOS.

Methods
Participants
The study included 27 adolescent girls, who sought medical help for menstrual disorders, amenorrhea or oligomenorrhea, at a major University Department of Obstetrics and Gynaecology in Athens, Greece. All these patients underwent physical, hormonal and biochemical examination and ultrasound scan of the genital tract. On the basis of the clinical evaluation, they were divided into two groups, one consisting of 22 patients with oligomenorrhea due to PCOS, diagnosed according to the European Society of Human Reproduction and Endocrinology diagnostic criteria [15] and the other of 5 patients with PA, diagnosed as having MRKHS. All 27 patients were examined with quantitative self-administered questionnaires before starting treatment, with either oral contraceptives (for patients with PCOS) or vaginal reconstruction (for patients with MRKHS).

The entry criteria for both groups were as follows: chronological age <= 20 years, incident cases, no treatment in the past, and with <= 8 menstrual cycles during the last year or absence of menstrual cycling. The control group consisted of a convenience sample of 22 eumenorrheic females, recruited from Athens high schools and colleges, matched individually by age with the patients with PCOS, and with a normal menstrual cycle. Exclusion criteria for the control subjects included any known medical condition, irregular periods, hormonal disturbances or endocrine disorders and use of oral contraceptives. The characteristics of the participants are summarised in Tables I and II.

Procedures
The participants were informed of the anonymity and confidentiality of their data and responses. They all, and when the participant was under 18 years of age, their parents, signed written consent forms before entering the study. The study was approved by the Hospital Ethics Committee. The patients underwent psychological evaluation with the completion of self-report questionnaires, before the beginning of
treatment with oral contraceptives or surgical creation of a neovagina, depending on the clinical condition. Of a total of 25 incoming patients with PCOS, who fulfilled the entry criteria, 22 agreed to participate in the study (88%), while all 5 incidence cases (100%) with MRKHS agreed to participate.

Instruments

The following measures were used to evaluate, respectively, the mood, anxiety and stressful life events of the participants:

(a) *The Beck Depression Inventory (BDI)* [16], which is a widely used questionnaire and is the depression rating scale that is most often used with adolescents [17]. BDI consists of 16 items, designed to assess the cognitive, behavioural, affective and somatic components of depression, and the severity of self-reported depressive symptoms. The Greek BDI version was used, which has been standardised in a Greek population sample, providing satisfactory information on the reliability and validity of the instrument [18].

(b) *The State-Trait Anxiety Inventory (STAI)* [19,20], which is used extensively to assess global anxiety that varies across situations (state anxiety) and anxiety that is stable across time and situations (trait anxiety). The STAI is composed of two separate self-report scales, the S-Anxiety and the T-Anxiety, each of which consists of 20 statements. The Greek version of the STAI (STAI-Gr) [21] was used, which has provided data on satisfactory test–retest reliability and discriminant validity.

(c) *The Stressful Life Events Schedule*. In this instrument life events are grouped into the following 11 classes: family discord, accidents, illness, school, entrance (e.g., pregnancy), exit, (bereavements), threatened exit (departures from home), family mobility (migration), financial, changes in social relationships and legal. The participants were asked whether any of the above 11 classes have occurred in the last 12 months. The negative impact of events within a class was rated on a four-point scale. Summation of events scores and impact scores gave the total number of classes in which there had been an event and for how many there had been substantial impact [22–25].

Statistical analysis

The association of PCOS and MRKHS with depression and anxiety was examined using logistic regression models. Conditional logistic regression was used to compare the PCOS group with the control group, adjusted for the potentially confounding variables of chronological age, socio-economic status and stressful life events together. Logistic regression was also conducted to compare the MRKHS group with the control group; and the PCOS group with the MRKHS group, with adjustments for the same confounding variables separately, because of the small sample size of the MRKHS group. The effects are reported as odds ratios (Ors) with 95% confidence intervals (CIs) using the menstrual disorders as the respective predictor variables.

Results

The demographic and clinical data for the PCOS, MRKHS and control groups are presented in Tables I and II. The mean ages of the girls in the groups were 16.95, 18.00 and 17.04 years, respectively. Menstrual
functioning was expressed by the number of menstrual cycles during the past 12 months, which indicates the severity of menstrual cycle abnormality. The educational level of the parents was used for the categorisation of the socio-economic status of the participants.

Scores that demonstrate an indicator of clinical depression, based on the cut-off scores of the Greek version of BDI, were recorded by 40% of the patients with MRKHS. Specifically, according to the cut-off scores of the Greek version of BDI, 20% reported mild depression and 20% moderate depression, whereas the respective percentages for mild depression were 27.3% for the patients with PCOS and 9.1% for the controls (Table III).

The PCOS syndrome group had higher scores than the control group on the state-anxiety scale of STAI-Gr (OR = 1.08, p < 0.05), after adjustment for the potentially confounding variables of chronological age, socio-economic status and stressful life events together. In other words it was 1.08 times more likely for the PCOS group to have higher scores than the control group on STAI-Gr (Table IV).

The MRKHS group also presented higher scores than the control group on the state-anxiety scale of STAI-Gr (p < 0.05). Specifically, it was 1.12 times more likely for the MRKHS group to have higher scores on STAI-Gr than the control group, after adjustment for stressful life events (OR = 1.12) and 1.11 times more likely after adjustment for chronological age (OR = 1.11). The association was not significant when the scores of the MRKHS group were adjusted for socio-economic status (Table IV).

The MRKHS compared with the control group also had significantly higher scores on BDI after adjustment for stressful life events (OR = 1.19) and socio-economic status (OR = 1.40, p < 0.05), but this significance disappeared after adjustment for chronological age (Table V). The association between the PCOS group and depression (BDI scores) was not statistically significant (Table V). Comparison between the PCOS and the MRKHS groups revealed no significant difference between the two groups in their STAI-Gr and BDI scores.

**Discussion**

The results demonstrate that adolescents who suffer from MRKHS and those with PCOS experience greater state anxiety than healthy adolescent control subjects, that is, anxiety related to a current unpleasant emotional state or condition, but not trait anxiety, which relates to more stable personality

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### Table III. Descriptive results based on the cut-off scores of the Greek version of BDI in all three groups.

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<th>Beck Depression Inventory (BDI)</th>
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<td>Groups</td>
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<td>PCOS</td>
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<td>MRKHS</td>
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<td>Controls</td>
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### Table IV. Comparisons between anxiety scores (STAI-Gr) in a) the PCOS and control groups and b) the MRKHS and control groups.

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<th>State-Trait Anxiety Inventory (STAI-Gr)</th>
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<td>Control</td>
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<td>PCOS</td>
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<td>MRKHS</td>
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aAdjusted for all variables of chronological age, socio-economic status and stressful life events, using conditional logistic regression analyses.

bAdjusted for stressful life events.

cAdjusted for chronological age.

dAdjusted for socio-economic status, using logistic regression analyses.

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### Table V. Comparisons between depression scores (BDI) in (a) the MRKHS and control groups and (b) the PCOS and control groups.

<table>
<thead>
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<th>Beck Depression Inventory (BDI)</th>
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<td>PCOS</td>
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aAdjusted for stressful life events.
bAdjusted for socio-economic status.
cAdjusted for chronological age, using logistic regression analyses.

dAdjusted for all variables of chronological age, socio-economic status and stressful life events, using conditional logistic regression analyses.
traits. State anxiety is characterised by subjective feelings of tension, apprehension, nervousness and worry, and by activation or arousal of the autonomic nervous system. Scores on the state anxiety scale usually increase in response to psychological stress and/or physical danger [20]. In addition, the adolescents with MRKHS experienced more depressive symptoms in comparison to eumenorrheic adolescents. In particular, scores in 40% of the amenorrheic adolescents indicate clinical depression.

It can be assumed that both MRKHS and PCOS in adolescence, as medical conditions that obstruct the development and normal physiology of the female reproductive system, would be associated with increased psychological stress and emotional difficulties. Such difficulties may be explained by the sense of being different from peers, with feelings of inadequacy and fears associated with sexuality and loss of femininity and reproductive ability.

Research on MRKHS has shown that patients report anxiety about the disorder, especially in terms of its role in their relationships with the opposite sex [26]. These patients may also become depressed, questioning themselves over their gender and doubting their ability to fulfill the female role as adults in the future. They report that infertility is the most difficult part of the condition for young women to accept [27,28].

Other studies on MRKHS suggest that the impact of the initial diagnosis is considerable and that the emotional reactions of patients include shock, denial, anger, fear, sadness and anxiety [11,29]. However, the findings of the present study are not related to the initial psychological reaction to diagnosis, but to the implications of medical condition itself, as psychological assessment was conducted at least 3 months after diagnosis.

Despite the initial positive psychological outcome after surgical correction of vaginal aplasia, with sexual rehabilitation [8,30,31], there are reports that patients remained depressed and sad about infertility many years after the operation [32].

As far as PCOS is concerned, it has been argued that adolescent patients may experience psychological distress because of the clinical manifestations of the syndrome and because of the aspect of having a chronic illness [33]. Studies have reported lower self-esteem and lower health related quality of life in adolescent patients with PCOS and it has been suggested that concerns about future fertility may affect psychological well being and health related behaviour, including sexual behaviour, in these adolescents [14,34,35]. Although high rates of mood disorders have been identified in adult women with PCOS [36–38], there have been no similar findings from studies with adolescent patients. This observation is consistent with the findings of the present study.

In contrast, the patients with MRKHS reported a higher rate of depressive symptoms than eumenorrheic adolescents. The greater severity of the features of MRKHS, in comparison to those of PCOS, may be the reason for this difference in depressive scores.

Finally, it has been argued that chronic medical illnesses in general during the critical life period of adolescence may have negative effects on the psychosexual development of adolescents, possibly giving rise to psychological and emotional disturbances [39]. Thus, these adolescents may be more vulnerable to anxiety and depression.

Among the limitations of this study is the small sample size, especially in the MRKHS group, which limits the generalisability of the reported results. The 40% rate of depression in the group of adolescents with MRKHS represents 2/5 patients and is thus susceptible to confounding variables and the vagaries of chance. In the MRKHS group, there were statistical associations that became insignificant after adjustment for potentially confounding variables, due to the very small sample size. Similarly, there were no significant differences in the scores of STAI-G and BDI between the two study groups, also possibly due to the small sample size. It should also be noted that due to relative large number of variables tested (models fitted), results are subjected to Type I error.

Nevertheless, the very low incidence of MRKHS (1/5000) and the lack of similar prospective studies about the mood and anxiety of these adolescent patients emphasise the value of these present preliminary results, which support the need for further investigation of the psychosocial characteristics of this rare group of adolescents. For the study patients with MRKHS a 6-month follow-up evaluation, after surgical creation of a neovagina is in progress, but not yet complete.

In conclusion, the findings reported here in regard to the evaluation of the association of PCOS and MRKHS with psychological difficulties in adolescence suggest a relationship between PCOS and MRKHS and both depression and anxiety disturbances. Investigation of this relationship is continuing in an ongoing study, in order to replicate and ensure the validity of the present results. However, larger scale studies on these issues are needed to confirm these findings and to heighten clinical awareness of the possible psychological ramifications of these reproductive disorders in a particularly vulnerable population.

Undoubtedly, the management of menstrual disorders in adolescence constitutes a complex multidisciplinary issue. Incorporation of a biopsychosocial approach to gynecologic practice could be extremely useful in the management of PCOS and MRKHS in adolescence, to ensure the prevention of possible psychological problems in the patients [40,41].
Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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