

VARIATIONS OF SERUM DEHYDROEPIANDROSTERONE-SULPHATE (DHEAS) LEVEL WITH PREGNANCY, FERTILITY, ABORTION, OVARIAN RESERVE AND ENDOTHELIAL FUNCTIONS

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Abstract

Objectives. It was aimed to evaluate the relationship of Dehydroepiandrosterone-sulphate(DHEAS) level with pregnancy, fertility, abortion, ovarian reserve and endothelial functions.

Patients and Method. Ninety-six fertile women aged 20-35 years whose DHEAS levels were measured and 28 women aged 40-55 years with oligomenorrhea-amenorrhea were included in the study. The DHEAS values of the patients, which were measured at least 12 months apart, were recorded.

Results. The first measured mean DHEAS level was 208.34 ± 119.7 ug/dL and the last measured mean DHEAS level was 187.5 ± 101.7 ug/dL. Among 28 patients with oligomenorrhea-amenorrhea, the levels of DHEAS increased in 10 patients and decreased in 18 patients. Although the annual decrease in DHEAS levels was greater in those who had pregnancy than in those who had not given birth, the difference was not statistically significant ($p=0.085$). Although the initial DHEAS level in 5 patients who had an abortion was higher than in those who did not have an abortion, the difference was not statistically significant ($p=0.427$). The increase in systolic blood pressure was statistically significant in patients with decreased DHEAS levels ($p=0.03$). While the mean DHEAS level was 85.3 ± 47.3 ug/dL in menopausal patients, the DHEAS level was 82.1 ± 49.2 ug/dL in non-menopausal patients ($p=0.435$).

Conclusion. The age at which the DHEAS level reaches its peak level shows individual differences. While pregnancy slows down the decrease in DHEAS levels, abortion accelerates the decrease in DHEAS levels. A decrease in serum DHEAS levels can increase systolic blood pressure.

Keywords: Dehydroepiandrosterone-sulphate, fertility, pregnancy, abortion menopause, hypertension.

INTRODUCTION

Dehydroepiandrosterone (DHEA) is a 19-carbon steroid precursor that is primarily secreted directly from the adrenal glands (1). With tissue sulfotransferase/sulfatase activity, DHEA is rapidly converted to Dehydroepiandrosterone-sulphate (DHEAS), which has a lower clearance, a longer life, and actually lacks androgenic activity (2).

Large amounts of DHEA and its sulfate ester, DHEAS, are hidden in the adrenal glands of humans and closely related primates. Excess amounts of DHEAS are stored in the fetal adrenal glands and converted to estrogens by the placenta during pregnancy. Serum DHEAS concentrations fall to low levels soon after birth. However, the repetition level begins to rise during the adrenarche, around the average age of 7–9 years. The highest levels of DHEAS occur around the age of twenties and reach higher levels than any other hormone. Then, DHEAS levels begin to decline over the next 5 decades. Some studies have shown that this decrease in DHEAS is associated with a decrease in mental and physical abilities in aging people (3, 4).

Gender and age are the largest determinants of serum DHEAS levels. Serum DHEAS levels are approximately twice as high in men as in women and show a progressive decrease from late puberty to old age in both sexes. However, reductions in DHEAS levels have been associated with an increased risk for cardiovascular disease, suggesting hyperinsulinemic conditions such as obesity. In a study, the relationship of serum levels of DHEAS and insulin with age and body mass index (BMI) was investigated. DHEAS levels and BMI were positively related before menopause, but

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no correlation was found after menopause. Increasing BMI and insulin secretion suggest that it is not associated with decreased DHEAS in women, and it is unlikely that DHEAS is to blame in the pathogenesis of cardiovascular disease in obese women (5).

In a study on the hormonal status of cortisol and DHEAS in Tunisian elderly patients, it was observed that while cortisol levels did not change with age, DHEAS levels decreased with age in both genders. The cortisol/DHEAS ratio increasing with age is associated with an increased incidence of certain adult diseases (diabetes mellitus, atherosclerosis, dementia, and osteoporosis). Improvements can be seen in cognitive impairment, immune disorders, sexual dysfunction, and depression scores with DHEA replacement (6).

It has been reported that DHEA replacement stimulates ovulation in women with chronic an ovulation with low DHEAS levels. Additional DHEA treatment to be given during ovarian stimulation may be a new method to maximize the ovarian response (7).

The aim of this study is to compare the change in the levels of DHEAS, which is a marker of adrenal aging, in women who gave birth to those who did not give birth, to investigate the relationship of DHEAS levels with fertility and abortion, and to show whether it can be used as a marker for menopause. In addition, it is to evaluate its relationship with flow mediated dilatation (FMD), which is one of the parameters showing endothelial function.

MATERIAL AND METHOD

This study is an analytical study conducted with ethical approval from the Ethics Committee of Yüzüncü Yıl University Faculty of Medicine and is a retrospective study (ethics approval date and number: 04.10.2022/298). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study included 96 fertile women aged 20-35 years whose DHEAS levels were measured and 28 women aged 40-55 years with oligomenorrhea-amenorrhea, whose DHEAS levels were measured in the same years, who applied to the Internal Medicine and Endocrinology Polyclinic of Yüzüncü Yıl University Faculty of Medicine between 2019-2021 were included in the study.

Among fertile women aged 20-35 years whose DHEAS levels were measured between 2019-2021, DHEAS levels were measured again by calling those whose phone numbers could be reached from the

hospital records. The number of patients who could be reached by telephone and who followed our call was 92. Later, four more patients over 35 years of age participated in the study and the total number of patients was 96. It was asked whether the women were married, if they were married, how many births they had, abortion history, menstrual cycle, age at menarche and menopause status. Venous blood samples were taken in the morning and sent to the biochemistry laboratory for re-measurement of the serum DHEAS level.

The study protocol was explained to the patients who were called to the outpatient clinic and their written informed consent was obtained. Patients who did not give consent were excluded from the study. Flow mediated dilatation (FMD) measurements were performed by the cardiology department, whose height, weight and blood pressure were measured. A high resolution ultrasound (Vivid 3, General Electric) 7 MHz probe was used to view the brachial artery longitudinally, 5-10 cm above the antecubital pit with the brachial artery method. The brachial artery diameter was measured initially, and then the cuff was placed in the upper arm proximal to the location of the ultrasound imaging of the artery. The blood pressure cuff was inflated to 250 mmHg and waited for 5 minutes. The brachial artery diameter was measured at the end of diastole, 30 and 60 seconds after the cuff deflating. After 15 minutes, the brachial artery diameter was measured again 3-4 minutes after sublingual nitroglycerin administration. The Flow Mediated Dilatation (FMD) value was calculated with the formula (8).

$$\text{FMD} = \frac{\text{Arterial diameter change}}{\text{basal artery diameter}} (\%)$$

The number of women aged 40-55 with oligomenorrhea-amenorrhea, whose DHEAS levels was measured between 2019 and 2021 were 28. Patients were asked whether they had menstruation and, when it was understood that they had entered menopause, when the symptoms began. Two ml of blood samples taken from the patients were placed in standard blood count tubes containing ethylene diaminetetracetic acid (EDTA). Serum DHEAS levels were studied with the chemiluminescence enzyme immunometric method using original kits in the Immulite 2000 device of the Diagnostic Products Corporation (DPC) company at Yüzüncü Yıl University Faculty of Medicine Biochemistry Laboratory.

Statistical analysis

The data from the study were uploaded to

the SPSS (Version 22.0, Inc. Illinois, Chicago, USA) program for analysis with the significant difference test for two means and the chi-square test used. Data are presented as arithmetic mean \pm standard deviation, number of subjects (n) and percentage on tables with level of error 0.05. $P < 0.05$ was accepted as significant.

RESULTS

The number of fertile patients included in our study was 96. Mean age was 27.7 ± 6.15 years, mean age at menarche was 13 ± 1.18 years. The mean DHEAS measured for the first time was 208.34 ± 119.7 $\mu\text{g/dL}$, and the mean DHEAS measured for the last time was 187.5 ± 101.7 $\mu\text{g/dL}$. The number of patients with increased DHEAS levels was 35 (36.5%), and the number of patients with decreased DHEAS levels was 61 (63.5%). Demographic findings and mean DHEAS values of the patients in the fertile patient group are given in Table 1.

Ninety-six patients had DHEAS measured at least 12 months apart. The mean time between two

DHEAS measurements was 41.3 ± 15.5 months. The mean decrease in DHEAS was 26.4 ± 90.4 $\mu\text{g/dL}$ and the annual change in DHEAS was 8.6 ± 28.1 $\mu\text{g/dL}$.

The number of patients with oligomenorrhea-amenorrhea was 28, and the number of patients with regular menstruation was 67. Among 28 patients with oligomenorrhea-amenorrhea, the levels of DHEAS increased in 10 patients and decreased in 18 patients. The DHEAS levels of 67 patients who had regular menstruation increased in 25 patients and decreased in 42 patients.

Of the 96 patients, 62 were single and 34 were married. Of the 34 married patients, 28 had children, and 6 had no children. Five of the married women had a history of abortion.

The characteristics of patients with decreased and increased DHEAS levels are given in Table 2. The initial DHEAS values of patients with decreased serum DHEAS levels were found to be statistically significantly higher than those of patients with increased DHEAS levels. (250.3 ± 15.9 $\mu\text{g/dL}$ vs. 151.4 ± 14 $\mu\text{g/dL}$, $p < 0.001$). There was no statistically

Table 1. Demographic findings and mean DHEAS values of the patients in the fertile patient group (n=96)

	Mean \pm SD	Minimum	Maximum
Age	27.79 \pm 6.15	20.0	58.0
Age at menarche	13.09 \pm 1.18	11.0	18.0
Height (cm)	158.50 \pm 8.47	110	173
Weight (kg)	61.45 \pm 12.40	30.0	97.0
Systolic blood pressure (mmHg)	105.00 \pm 12.10	80.0	130.0
Diastolic blood pressure (mmHg)	68.83 \pm 9.94	50.0	90.0
First measured DHEAS value (mg/dL)	208.34 \pm 119.68	5.0	539.1
Last measured DHEAS value (mg/dL)	187.54 \pm 101.69	15.0	476.1
DHEAS decrease amount (mg/dL)	26.44 \pm 90.42	-221.0	418.0
Time between two measured DHEAS (months)	41.30 \pm 15.5	12	109
Annual change in DHEAS (%)	8.63 \pm 28.12	-85.55	100.32

DHEAS: Dehydroepiandrosterone-sulphate, N: number of patients, Mean \pm SD: Mean \pm standard deviation.

Table 2. Characteristics and statistical analyzes of patients with increased and decreased DHEAS levels in the fertile age group

	Patients with increased DHEAS levels (n=35) Mean \pm SD	Patients with decreased DHEAS levels (n=61) Mean \pm SD	P value
Age	26.69 \pm 4.9	28.36 \pm 6.75	0.215
Age at menarche	13.26 \pm 1.34	13 \pm 1.1	0.124
Systolic blood pressure (mmHg)	106.25 \pm 13.38	104.38 \pm 11.5	0.132
Diastolic blood pressure (mmHg)	69.84 \pm 10.04	68.6 \pm 9.71	0.245
First measured DHEAS value (mg/dL)	151.43 \pm 83.29	250.31 \pm 124.46	<0.001
Last measured DHEAS value (mg/dL)	208.34 \pm 98.37	175.61 \pm 102.43	0.113
Change in DHEAS (mg/dL)	56.91 \pm 54.08	-74.7 \pm 70.67	0.092
Annual change in DHEAS (mg/dL)	17.58 \pm 17.704	23.67 \pm 21.08	0.162
Percentage change in DHEAS (%)	74.93 \pm 128.43	- 30.24 \pm 20.89	0.094
Annual percentage change in DHEAS (%)	24.87 \pm 50.3	-9.92 \pm 7.9	0.085
FMD (%)	27.92 \pm 6.57	-25.59 \pm 11.58	0.098

DHEAS: Dehydroepiandrosterone-sulphate, FMD: flow mediated dilatation, n: number of patients, Mean \pm SD: Mean \pm standard deviation, %: percentage.

significant difference in other measured parameters between patients with decreased and increased DHEAS levels.

While DHEAS levels decreased by 53.7 µg/dl in 28 women with a history of pregnancy, a decrease of 15.7 µg/dl was found in those who did not have a child. The difference was statistically significant ($p=0.046$). Although the annual decrease in DHEAS levels in pregnant women was higher than in non-childbearing women, the difference was not statistically significant (16.0 µg/dL vs. 5.8 µg/dL/year, $p=0.085$). Among the patients whose DHEAS level decreased, the decrease in DHEAS was higher in those who became pregnant, but the difference was not statistically significant (81.8 µg/dL vs. 71.3 µg/dL, $p=0.557$). When the patients who had abortions were excluded, the mean decrease in DHEAS levels was 64.6 µg/dL in those with a history of pregnancy. There was a statistically significant but negative correlation between the number of live births and the amount of decrease in DHEAS levels and the annual decrease in DHEAS levels in the patient group with decreased DHEAS levels ($p=0.025$ $kk=-0.487$ and $p=0.009$ $kk=-0.554$, respectively). There was a statistically significant difference and a positive correlation between the number of abortions and the amount of decrease in DHEAS levels and the annual decrease in DHEAS levels in the patient group with decreased DHEAS levels ($p=0.001$ $kk=0.729$ and $p=0.001$ $kk=0.650$, respectively). The mean age was higher in patients with a history of pregnancy than in patients without a history of pregnancy, which was statistically significant (31.7 vs. 26.2 years, $p=0.001$).

Although the initial DHEAS level was higher in 5 patients who had abortion than in patients who did not have abortion, the difference was not statistically significant ($p=0.427$). However, the annual change in DHEAS level and the amount of decrease in DHEAS level were found to be significantly higher ($p=0.038$ and $p=0.049$, respectively). The number of abortions was statistically significantly and positively correlated with the amount of decrease in DHEAS level and the annual decrease in DHEAS level ($p=0.002$ $kk=0.569$ and $p=0.005$ $kk=0.482$, respectively).

The frequency of oligomenorrhea-amenorrhea did not change in patients with increased DHEAS levels compared to patients with decreased DHEAS levels ($p=0.883$). There was no statistically significant difference between the first DHEAS level, the last DHEAS level, the amount of decrease in DHEAS and the annual decrease in DHEAS between patients with oligomenorrhea-amenorrhea and patients with

regular menstrual cycles ($p=0.432$, $p=0.135$, $p=0.305$, $p=0.148$, respectively).

The weight status of patients with increased DHEAS levels was found to be statistically significantly but negatively correlated with the first and last measurements of DHEAS levels, as well as the percentage increase in DHEAS levels and the annual percentage increase ($p=0.001$ $kk=-0.681$, $p=0.004$ $kk=-0.589$, $p=0.006$ $kk=-0.567$, $p=0.007$ $kk=-0.818$, respectively). The height status of patients with increased DHEAS levels was found to be statistically significantly but negatively correlated with the percentage increase in DHEAS and the annual percentage increase ($p<0.001$ $kk=-0.762$ and $p<0.001$ $kk=-0.817$, respectively). Height was statistically significantly and positively correlated with age at menarche ($p=0.02$ $kk=0.345$). In the same group, the body mass index (BMI) values of the patients were statistically significantly and positively correlated with the percent increase in DHEAS and the percent annual increase ($p=0.002$ $kk=0.733$ and $p<0.001$ $kk=0.792$, respectively).

Among patients, FMD measurements were not correlated with any data, including systolic and diastolic blood pressure measurements. In those with decreased DHEAS levels, systolic blood pressure and the amount of decrease in DHEAS level and the amount of annual DHEAS level decrease were statistically significantly and positively correlated ($p=0.02$ $kk=0.251$ and $p=0.031$ $kk=0.284$, respectively). No such statistical significance and correlation were observed in those with increased DHEAS levels ($p=0.131$ $kk=0.251$ and $p=0.232$ $kk=0.284$, respectively). On the other hand, the diameters of the brachial artery in the FMD measurements in those with increased DHEAS levels were statistically significantly and positively correlated ($p=0.021$ $kk=0.488$). There was no significant correlation in those with decreased DHEAS levels ($p=0.341$ $kk=0.792$). 28 individuals aged 40-55 years were included in the menopause group (mean age 43 ± 2.3 years). None of the patients whose DHEAS levels were measured between 2019 and 2021 had no menopausal status at the time of the first DHEAS level measurement. Up to the study date, 10 women had developed menopause and one woman had given birth. While the mean DHEAS level was 85.3 ± 47.3 µg/dL in menopausal patients, the DHEAS level was 82.1 ± 49.2 µg/dL in non-menopausal patients, and there was no statistically significant difference between the two groups ($p=0.435$). There was no statistically significant difference between the mean DHEAS levels of patients

with or without a history of pregnancy, with or without abortion and with or without curettage ($p=0.324$, $p=0.426$, $p=0.128$, respectively).

DISCUSSION

The level of DHEAS tends to decline rapidly during the first year of life and remains at this level for up to five years after falling to minimum levels. It starts to increase significantly after an average of 6-7 years, and this increase reaches its maximum levels at the age of 24 for women and at the age of 30 for men. Then it tends to decrease rapidly. However, this decline is more moderate after the age of 50-60 (9).

Since the DHEAS level draws a parabola, it is characterized by an increase in a certain age range, and a decrease in a certain age range. In our study, DHEAS levels tended to decrease in some patients and increase in some patients.

In a study by Mazat *et al.* (10), they found that DHEAS levels were higher in men than women, decreased with age, and there was a negative correlation between DHEAS levels and mortality in men. They found an annual decrease of 2.3% in men and 3.9% in women in DHEAS levels in 290 cases followed for 8 years; however, they found an increase in DHEAS levels in only 30% of the cases. In our patient group, we found an increase in DHEAS levels in 36.5% of our patients and a decrease in 63.5% of them. Considering that the DHEAS level peaks around the age of 30 and then declines, it would be expected that the patient group with decreased DHEAS levels would be older, and the patient group with increased DHEAS levels would be younger. However, in our study, there was no age difference between patients whose DHEAS levels increased or decreased. This indicated that the age at which the DHEAS level reached its peak values showed a heterogeneous distribution in our study group. In our study, we observed a 9.9% decrease in DHEAS levels. In the study of Mazat *et al.* (10), individuals over the age of 65 were included in the study. The fact that the younger patient group was followed in our study may be a reason for the higher decrease in DHEAS levels. Davison *et al.* (9) found that DHEAS levels decreased rapidly with age in women aged 18-75 years, and this decrease was faster at early ages.

DHEAS levels in pregnant women are significantly lower than in non-pregnant women (11). Post-pregnancy data is unclear. In our study, the decrease in DHEAS levels in those with a history of pregnancy was significantly higher than in those who

were not pregnant. The reason for this may be that the mean age of pregnant patients is higher than that of non-pregnant patients (31.6 years *vs.* 26.1 years, $p=0.001$). Another reason may be that the decreased levels of DHEAS during pregnancy, as a result of conversion to estrogen in the placenta, do not increase after birth. The fact that the annual decrease in DHEAS levels is higher in those with decreased DHEAS levels, although it is not statistically significant, and the annual increase in those with increased DHEAS levels is less in those who become pregnant, which may suggest that pregnancy accelerates adrenal aging (9.6 $\mu\text{g/dL}$ *vs.* 19.2 $\mu\text{g/dL}$, $p=0.118$). However, when patients with abortion history were excluded, the annual decrease in DHEAS levels in women who gave birth were similar to those who did not give birth (decrease in serum DHEAS level 64.5 $\mu\text{g/dL}$, annual decrease in serum DHEAS level 18.6 $\mu\text{g/dL}$ /year in those who gave birth, decrease in serum DHEAS level 71.2 $\mu\text{g/dL}$, annual decrease in serum DHEAS level 64.6 $\mu\text{g/dL}$ / year in those who did not give birth). Excluding abortions, the number of pregnancies and the decrease in DHEAS levels and the annual decrease in DHEAS levels were negatively correlated. Although the number of patients is limited, we can say that live birth slows down the decrease in DHEAS levels, whereas abortion accelerates the decrease in DHEAS levels.

The higher DHEAS level in abortion patients can be explained by the higher DHEAS level in patients with Polycystic Ovary Syndrome (PCOS). There are publications showing that high DHEAS levels are associated with anovulation and infertility (12-15). In another study, serum DHEAS levels, it were measured under basal conditions in 32 infertile patients known to be ovulatory, 37 women with oligomenorrhea, and 52 patients with hirsutism. Serum DHEAS levels were found to be high in only 18% of infertile women with regular ovulation, 34% of oligomenorrhic patients, and 60% of women with hirsutism (16). One hundred nineteen euprolactinemic anovulatory infertile patients evaluated for ovulation induction with clomiphene citrate were studied to determine the prevalence of increased adrenal androgen secretion in this group. Although elevated DHEAS levels were detected in 50% of these patients, increased adrenal androgen secretion was also demonstrated. In conclusion, it has been suggested that while high DHEAS levels do not explain the increased adrenal androgen secretion in the vast majority of patients, serum DHEAS levels are frequently elevated in anovulatory infertile patients (17). In our study, the decrease in serum DHEAS levels

and the high annual decrease in abortion patients may be a sign of accelerated adrenal aging. The correlation between the number of abortions and the amount of decrease in DHEAS levels also supports this. However, the fact that the number of patients who had abortion was only 5 is not enough to draw a reliable conclusion.

In our study, no significant difference was found between the first DHEAS level, the last measured DHEAS level, the amount of decrease in DHEAS level, and the annual decrease in DHEAS level between women with oligomenorrhea-amenorrhea and those with regular menstruation. Again, contrary to what is expected between the oligomenorrhea-amenorrhea group and those with regular menstruation, more pregnancies were detected in the oligomenorrhea-amenorrhoea group, four patients who had no children in the regular menstruation group had a short marriage period (between 1 month and 8 months) and three patients had PCOS has been effective. While amenorrhea was present in approximately 20% of patients with PCOS, regular ovulatory function was observed in 5-10% of cases. In some recent studies, cases with ovulation functions that are regulated later in the reproductive age have been reported (18, 19). In the meantime, an important point that should not be forgotten is that regular menstrual cycles in the past do not rule out the diagnosis of PCOS.

In our study, we found that in those with increased DHEAS levels, the percentage of increase and the annual increase were negatively correlated with height and weight. The correlation was strongest with height, and therefore, when BMI was calculated, there was a positive correlation with the percentage increase in DHEAS. All the patients in our study were over the age of 20, and considering the age of menarche, it is thought that the epiphyseal plates are closed. It is known that androgens and estrogens accelerate the maturation of epiphyseal plaques, and hypogonadal individuals are taller than normal. The fact that the relationship between height and the amount of change in DHEAS level continued after the age of 20 in our study suggests that the adrenarche continues after puberty at an individual-specific rate. In our study, height was also correlated with age of menarche, consistent with previous studies (20, 21). It is known that seeing menarche at an earlier age causes a shorter adult height. After menarche, an average of 4-6 cm of height growth occurs. It has been reported that prepubertal lengthening increases, postpubertal elongation decreases, and adult height is not affected in cases of early adrenarche (22). According to the results of our study, we can say that in individuals with a high

rate of increase in adrenal androgens, the epiphyses close earlier and the adult height is short. On the other hand, there was no difference in height and weight between those with decreased or increased DHEAS levels in our study. However, since the age distribution of both groups is similar, we can think that those with decreased DHEAS levels rise to peak DHEAS levels earlier, so their epiphyses should close faster and remain short in stature. These data may indicate that the rate of increase in DHEAS levels is more effective in height growth than the age at which the DHEAS level reaches its peak value. The growth process ends long before DHEAS reaches its peak. It would be appropriate to investigate the effects of the rate of increase of DHEAS levels on growth at younger ages.

In a study by Yen *et al.* (23), they showed that oral DHEA reduced weight gain in genetically obese mice without any change in the amount they ate. In many studies conducted in recent years, the anti-obesity effect of DHEA has been proven. For example, in a study by Nawata *et al.* (24), after 3 months of a diet containing 0.3% DHEA in castrated male Zucker rats with obesity, there was a significant decrease in weight gain in the DHEA group compared to the DHEA-administered and non-castrated rats. In another study, it was reported that there was a decrease in weight gain with the addition of DHEA to the diet in obese female Zucker rats, and this decrease may have occurred due to the decrease in energy metabolism of DHEA (25). There are publications showing that DHEA achieves its anti-obesity effect by reducing calorie intake. However, there are also publications showing that it has no effect on food intake (24). In our study, no relationship could be established between weight and DHEAS level in patients with decreased DHEAS levels, while it was observed that weight was negatively correlated with the initial level and rate of increase of DHEAS in patients with increased DHEAS levels. This may be an indication of the anti-obesity effect of DHEAS.

The ability of the endothelium to sense the current and the hemodynamic forces associated with the flow and convert them into biochemical signals to secrete endothelial mediators has not yet been fully resolved. Activation of ion channels and intracellular calcium homeostasis are involved in the acute response of the endothelium to mechanical stimulation. It has been shown that the endothelial response to hemodynamic stimuli is impaired in hypertension and a decrease in flow-induced endothelial-derived vasodilation in hypertensive rats (17). However, in our study, no relationship was found between blood

pressure and FMD patients. The fact that the patient group was selected from the young population and there was only one patient diagnosed with hypertension may have played a role in the inability to find a relationship between FMD and blood pressure.

In those whose DHEAS level decreased, the amount of decrease in systolic blood pressure and of decrease in DHEAS level were found to be correlated. This means that those with lower DHEAS levels have higher blood pressure. It has been reported that DHEA replacement causes improvements in endothelial functions (26). As DHEAS level decreases with age, the incidence of hypertension increases with age. In a study by Matulevicius *et al.* (27), they obtained study results showing that there is a rapid decrease in DHEAS levels with aging, especially after the age of 55. No relationship has been reported between DHEAS levels and blood pressure. The effects of DHEA replacement on blood pressure have also not been studied. In our study, no correlation was found between DHEAS levels and blood pressure, but a correlation was found between the decrease in DHEAS levels and the aforementioned group. Peak values of DHEAS levels may differ from person to person. DHEAS levels have important roles in the vascular bed. We can conclude that the endothelium has a DHEAS memory in normal individuals, and that vascular tone increases according to the rate of decrease in DHEAS levels. On the other hand, we can think that zona reticularis, which atrophies with age, causes an increase in mineralocorticoid and glucocorticoid levels that retain water and salt. Considering that only one of our patients was diagnosed with hypertension and all measured blood pressure values were within normal limits, we can say that the relationship between DHEAS level and systolic blood pressure existed long before the development of hypertension. A decrease in DHEAS levels may be one of the causes of essential hypertension. There is a need for studies covering more advanced age groups, including hypertension patients who support this situation.

No relationship could be established between DHEAS levels and menopause in patients considered to be in the menopausal group. Adrenal aging was not associated with ovarian reserve in our patient group. However, due to the small number of patients, it may not be accurate to reach a definite conclusion.

In conclusion, the results we obtained in this study, which evaluated the relationship between serum DHEAS levels and fertility, pregnancy, abortion, ovarian reserve and endothelial functions, are as follows: The age at which the serum DHEAS level

reaches its highest level shows individual differences; those with lower serum DHEAS levels are taller; Pregnancy slows the decrease in serum DHEAS levels; Abortion accelerates the decrease in DHEAS levels; Endogenous DHEAS has an anti-obesity effect. A decrease in serum DHEAS level may increase systolic blood pressure, but serum DHEAS levels are not an indicator of ovarian reserve. As a result, there is a need for new literature studies that are multicenter and include a large number of patients to support the results we obtained in our study.

Conflict of interest

The authors declare that they have no conflict of interest.

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