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ORIGINAL

Acromegaly is associated with higher frequency of female sexual dysfunction: experience of a single center

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Abstract. The aim of the study was to assess female sexual dysfunction (FSD), quality of life and depression status in female patients with acromegaly. Fifty-seven sexually active female patients with acromegaly disease (21 controlled, 36 uncontrolled) monitored by Cerrahpasa Medical School, Endocrinology and Metabolism out-patient clinic and age and body mass index-matched 46 healthy female subjects were included in the study. Sexual functions and status of depression in both patient and control groups were evaluated by using the Female Sexual Function Index Form (FSFI) and the Beck Depression Inventory (BDI), respectively. Quality of life was evaluated by using the Acromegaly Quality of Life (AcroQoL) Scale. Hormone levels were studied in the groups. The FSFI total score and desire, arousal, orgasm, and satisfaction domains in patients with acromegaly were significantly lower than in the healthy controls ($p \leq 0.0001$). There was no difference between biochemically controlled and uncontrolled patients with acromegaly with respect to FSFI scores ($p = 0.7$). AcroQoL total score in female patients with controlled acromegaly and uncontrolled acromegaly were 46.33±16.5% and 50.13±18.21%, respectively ($p = 0.53$). The difference in BDI scores between controlled and uncontrolled acromegaly patients was not significant but they were significantly higher in the control group ($p \leq 0.0001$). In the correlation analysis, a negative correlation was found between FSFI total and BDI score ($r = -0.69$, $p < 0.001$), age ($r = -0.45$, $p < 0.001$), and IGF-I ($r = -0.28$, $p = 0.006$). This study showed that sexual dysfunction and depression rates in female patients with acromegaly are higher than in healthy females.

Key words: Acromegaly, Sexual dysfunction, Quality of life, Depression

FEMALE SEXUAL DYSFUNCTION (FSD) has many dimensions and may be affected by various factors such as age, education, chronic diseases, medications, psychological and physical conditions [1]. Dysfunction of the hypothalamic-pituitary axis, hyperprolactinemia, surgical or medical castration, premature ovarian failure, old age and chronic birth control use are common causes of hormonally based FSD [2]. FSD traditionally includes disorders of desire, arousal, pain/discomfort, inhibited orgasm, and satisfaction [3, 4]. Sexual problems are highly prevalent in women. In an earlier study from Turkey, approximately 46.9 percent of women had distressing sexual problems, and FSD was observed to be significantly positively correlated with age, chronic disease, multiparity and/or menopause, and negatively correlated with education [5].

Acromegaly is characterized by chronic growth hormone (GH) and insulin-like growth factor-I (IGF-I) excess and is associated with increased morbidity and mortality [6]. The main clinical features are enlarged extremities, thickened soft tissue. Facial changes include large lips and nose, frontal skull bossing, mandibular overgrowth with prognatism, maxillary widening with teeth separation. The disease also has rheumatologic and metabolic consequences [7]. Diagnosis of acromegaly is often delayed by several years, when changes in appearances, as well as in many internal tissues, may not be reversible, even after successful

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treatment. While biochemical disease control and restoration of morbidity and mortality to normal can be achieved in most patients, patients' preferences and features relevant to individual health related quality of life (HRQoL) often are not considered [8, 9]. As a consequence of the clinical characteristics and complications of the disease, patients with acromegaly often have a severe impairment of the quality of life associated with a decreased perception of the general well-being, dissatisfaction from body image, tendency to social isolation and possibly sexual dysfunction [10]. In a recent review reported that GH and IGF-I receptors are widely expressed in many cells including cartilage, bone, liver, muscle, fat, heart, vascular system, kidney, pancreas, central nervous system and gonads. It is plausible that GH excess is associated with sexual dysfunction in both sexes and this situation could allow hypothesizing a possible multifactorial mechanism underlying sexual dysfunction in acromegaly. Additionally, it was concluded that data on sexual function in patients with acromegaly are still scant [11]. So far, there is no data related to sexual dysfunction in acromegalic females, this study was aimed to assess sexual dysfunction of the patients and the relationship between disease activity, complications, psychological status and quality of life.

Materials and Methods

Total of 77 consecutive, sexually active women with acromegaly who were followed-up and treated at the Cerrahpasa Medical School, Endocrinology and Metabolism outpatient clinic between 1990 and 2012 were recruited into the study. Five patients refused to participate the study. Fifteen patients not meeting the inclusion criteria of the study were excluded from the study. As a result, 57 patients and age and body mass index-matched 46 healthy female subjects were included in the study.

Exclusion criteria included the following in both groups: any drug that could possibly affect sexual or psychiatric status; using oral contraceptives, a habit of heavy smoking, presence of inflammatory genital disease or vaginal discharge, presence of musculoskeletal, neurologic, inflammatory, or clinically significant chronic diseases or detection/suspicion of any of these conditions during the investigation, and pregnancy.

All women recruited into the study had a stable, heterosexual relationship and were sexually active with a normal sexually active male partner. Demographic features and a detailed medical history, which included the presence of any systemic disease, use of medication, menopausal status and cigarette use, were obtained from all subjects. Height and weight were used to calculate the body mass index (BMI). A detailed physical and gynecological examination was performed. The previous therapies of the acromegalic patients, history of surgery and radiotherapy, disease duration and status of the pituitary functions were examined.

For the assessment of sexual satisfaction, all subjects were administered the Female Sexual Function Index (FSFI), which was described by Rosen *et al*. and includes the domains of sexual desire, arousal, lubrication, orgasm, satisfaction, and pain during sexual intercourse. The overall score and subscores of sexual functional status in patients and controls were calculated, as described previously [12].

All patients and controls were evaluated in terms of possible presence of depression with the Beck Depression Inventory (BDI), and the cutoff point was accepted as 17 [13].

The AcroQoL was used to evaluate HRQoL in patients with acromegaly. The AcroQoL was recently developed by Webb *et al*. [8, 14] and is a disease-specific questionnaire. Each question has five possible answers scored 1–5, with a total maximum score of 110 and quoted as a percentage. The score of 110 reflects the best possible QoL. These scales have been validated in the Turkish language and in Turkish populations [15, 16].

During the study, diagnosis of active disease was determined by the presence of clinical findings and failure to suppress nadir GH level to less than 1 ng/mL during the oral glucose tolerance test (OGTT) and as well as high levels of IGF-I adjusted for age and gender. Acromegaly was considered to be in remission when both circulating IGF-I level was within normal age and gender-adjusted ranges and nadir GH was less than 1 ng/mL during OGTT [17]. In 3 patients on pegvisomant therapy, remission status was based on IGF-I levels only. All of the parameters were evaluated according to the activity of the disease and compared with healthy controls.

Blood was obtained to determine prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), dehydroepiandrosterone-SO_4 (DHEA-SO_4), total testosterone, free testosterone, 17α hydroxyprogestrone (17-OH P), androstenedione, estradiol (E_2), free thyroxine (FT_4) and thyrotropin (TSH), cortisol,

glucose, insulin, in the early follicular phase before 10:00 a.m. in patients with acromegaly and controls. Macroprolactin was determined who had high PRL levels. Chemiluminescence immunoassay was done to assess PRL (normal 3.4 to 23.3 ng/mL), LH (normal 2.4 to 12.6 mIU/mL), FSH (normal 3.6 to 12.5 mIU/mL), E_2 (normal 12.5-166 pg/mL), DHEA-SO_4 (normal 96 to 340 µg/dL), total testosterone (normal 254-853 ng/mL), cortisol (6.2-19.4 µg/dL), TSH (normal 0.4 to 4.0 mIU/mL) and free thyroxine (normal 0.8 and 1.9 ng/dL). Radioimmunoassay was done to assess free T (normal 0.45 to 3.17 pg/mL), 17-OH P (normal 0.15 to 1.3 ng/mL) and androstenedione (normal 0.1 to 2.9 ng/mL). IGF-I levels were evaluated after ethanol extraction with IRMA (Diagnostic System Laboratories Inc. Webster, Texas U.S.A.; normal values: 100-494 ng/mL for ages of 30-40 years, 101-303 ng/mL for ages of 40-50 years, and 78-258 ng/mL for ages of 50-70 years). Plasma GH levels were also studied with IRMA (GH; Immunotech, Marseille, France; normal value <10 ng/mL).

The study protocol was approved by the Ethics Committee of Cerrahpasa Medical School, Istanbul University. All the subjects read and signed the informed consent forms before enrolling in the study.

The data was statistically analyzed with SPSS 15.0 package program. Type of therapies, previous surgery, radiotherapy, medical treatment, birth and residency settlement type, education and income levels, smoking history, menstrual status, and associated complications of the patients were expressed as observation number and percentages (%). Chi-square test and Fisher's Exact test were used for categorical variables. Kruskal-Wallis test was used to compare the healthy subjects with the patients according to remission status. The variables with significance were evaluated by Mann-Whitney U test to investigate difference in the groups. The results are presented as median and interquartile range [IQR]. Independent variables affecting the questionnaires were explored with stepwise linear regression analysis. Spearman's and Pearson tests were used for correlation analysis. $p< 0.05$ was considered statistically significant.

Results

Fifty-seven sexually active female acromegalic patients with a median time of 48 months [IQR= 27-156 months] since being diagnosed were included to the study. Two groups were identified: controlled (n= 21, median age 50 [IQR= 40.5-56.5] years) and uncontrolled acromegaly (n= 36, median age 45 [IQR= 35.2-52.7] years) according to the current criteria. Duration of disease was longer in controlled female patients with acromegaly than in uncontrolled patients ($p< 0.0001$). This was because there were more newly-diagnosed patients in the uncontrolled group. Four (19%) patients in the controlled acromegaly group and 4 (11.1%) patients in the uncontrolled acromegaly group had hypopituitarism. Two patients had hypothyroidism and hypogonadism, 2 had hypocortisolism, 2 had hypogonadism, 1 had central diabetes insipidus and hypogonadism and 1 had hypocortisolism and hypogonadism. They were receiving appropriately hormone replacement therapy. Fifteen patients had received radiotherapy. The median follow-up time of the patients after radiotherapy was 70 [IQR: 24-80] months. Patient characteristics are detailed in Table 1.

There was no difference between the patients and the healthy controls in terms of age, BMI, income level, smoking habits, and menopause duration and status. Acromegalic patients had a higher prevalence diabetes mellitus (DM), hypertension and obstructive sleep apnea syndrome (OSAS) than healthy controls. Demographic data of the patients with acromegaly and healthy controls were shown in Table 2.

The factors affecting female sexual functions such as inflammatory genital disease or vaginal discharge were not found in the gynecological examination in either group.

FSD was diagnosed in 39 of 57 patients with acromegaly (68%), while only 13 of 46 healthy women (28%) were found to have FSD by FSFI. The mean total FSFI score ($p< 0.0001$) and domain scores for desire ($p< 0.0001$), arousal ($p< 0.0001$), orgasm ($p< 0.0001$), and satisfaction ($p< 0.0001$) were significantly lower in both controlled and uncontrolled female acromegalic patients than in healthy females. However, lubrication and pain domain scores were not different in the groups ($p= 0.05$, $p= 0.83$). There was no statistical difference in the mean total FSFI score and domain scores between controlled acromegalic female patients and in uncontrolled acromegalic female patients (Table 3).

The BDI score was higher in female patients with acromegaly than in healthy subjects ($p\leq 0.0001$). However, BDI scores did not vary according to disease activity in acromegalic patients (Table 3).

Table 1 Characteristics of controlled and uncontrolled female patients with acromegaly

Variables	Controlled Female Acromegaly n=21	Uncontrolled Female Acromegaly n=36	*p*
Age	50 [40.5-56.5]	45 [35.2-52.7]	0.23
Body mass index (kg/m^2)	31.6 [28.9-35.9]	28.8 [26-35]	0.09
Duration of diagnosis (month)	144 [48-192]	36 [21.7-93]	**<0.0001**
Mean GH (ng/mL)	0.69 [0.31-0.97]	3.1 [1.58-5.84]	**<0.0001**
Mean IGF-I (ng/mL)	328 [227-387]	643 [534-885]	**0.01**
Treatment of acromegaly			
Previous surgery (n,%)	19 (90.5)	26 (72.2)	0.10
Radiotherapy (RT) (n,%)	9 (42.86)	6 (16.7)	**0.03**
Conventionally RT	5 (55.6)	0 (0)	
GKR	4 (44.4)	5 (83.3)	
Combine-RT	0 (0)	1 (16.7)	
Medical treatment (n,%)			0.77
SA	9 (42.9)	14 (38.8)	
SA+DA	5 (23.8)	8 (22.2)	
SA+DA+PEG	0 (0)	1 (2.8)	
DA	0 (0)	1 (2.8)	
SA+PEG	0 (0)	2 (5.6)	
None	7 (33.3)	10 (27.8)	

Data was expressed as median and IQR. GKR, Gammaknife radiosurgery; SA, Somatostatin analog; DA, Dopamin agonist; PEG, pegvisomant
Bold letters represent $p< 0.05$ and were considered statistically significant.

Table 2 Demographic data of the female patients with acromegaly and healthy controls

Variable	Controlled acromegaly n=21	Uncontrolled acromegaly n=36	Healthy female controls n=46	*p*
Birth settlement type (n,%)				**0.04**
Rural area	16 (76.2)	28 (77.8)	21 (45.7)	
Urban area	5 (23.8)	8 (22.2)	25 (54.3)	
Residency settlement type (n,%)				**0.04**
Rural area	3 (14.3)	4 (11.1)	0 (0)	
Urban area	18 (85.7)	32 (88.9)	46 (100)	
Education status (n,%)				**<0.0001**
Literate	7 (33.3)	8 (22.2)	0 (0)	
Primary school	11 (52.4)	22 (61.1)	17 (37)	
Middle school	1 (4.8)	1 (2.8)	0 (0)	
High school	2 (9.5)	3 (8.3)	20 (43.5)	
University	0 (0)	2 (5.6)	9 (19.6)	
Income level ($/month) (n,%)				0.46
< 500	11 (52.4)	10 (27.8)	14 (30.4)	
500-<1000	7 (33.3)	19 (52.8)	21 (45.7)	
1000-2500	3 (14.3)	7 (19.4)	8 (17.4)	
> 2500	0 (0)	0 (0)	3 (6.5)	
Smoking history (n,%)				0.22
Present	20 (95.2)	28 (77.8)	38 (82.6)	
Absent	1 (4.8)	8 (22.2)	8 (17.4)	
Associated complications (n,%)				
Hypertension	10 (47.6)	18 (50)	5 (10.9)	**<0.0001**
Diabetes mellitus	8 (38.1)	11 (30.6)	6 (13)	**0.04**
Sleep apnea syndrome	4 (19)	9 (25)	0 (0)	**0.02**
Hypopituitarism	4 (19)	4 (11.1)	0 (0)	**0.01**
Menstruation status (n,%)				0.58
Menstrual cycyle (+)	11 (47.6)	23 (63.9)	30 (65.2)	
Menopause	10 (52.4)	13 (36.1)	16 (34.8)	
Menopause duration (month)	120 (84-156)	72 (27-114)	120 (36-171)	0.25
Systolic blood pressure (mmHg)	120 (110–145)	130 (120–150)	120 (110–130)	0.19
Diastolic blood pressure (mmHg)	70 (60-80)	80 (70-90)	70 (60-80)	**0.02**

Bold letters represent $p< 0.05$ and were considered statistically significant.

Table 3 Female Sexual Function Index (FSFI), Beck Depression Inventory (BDI) questionnaire scores of the controlled and uncontrolled female patients with acromegaly and healthy female controls

Variable	Controlled acromegaly n=21	Uncontrolled acromegaly n=36	Healthy female controls n=46	*p*
BDI	18 [14-25]	17.5 [11-22]	9 [4-15]	**<0.0001**
FSFI total%	19.1 [16.9-23.3]	20.65 [13.2-23.7]	25.5 [21.7-30.8]	**<0.0001**

Data was expressed as median and IQR. Bold letters represent $p< 0.05$ and were considered statistically significant.

Table 4 Hormone levels in female patients with acromegaly and female healthy controls

Variable	Controlled acromegaly n=21	Uncontrolled acromegaly n=36	Healthy female controls n=46	*p*
Glucose	101 [80-118]	92 [82-99]	81 [73-89]	**0.004**
Insulin	7.5 [4.3-9.4]	9.1 [6-16.2]	8.6 [3.8-13]	0.35
Free T4	1.2 [1.1-1.3]	1.3 [1.2-1.4]	1.25 [1.1-1.3]	0.15
TSH	1.35 [0.7-3.2]	1.5 [0.95-1.8]	2.07 [1.3-3.2]	**0.02**
Estradiol	21.8 [6.8-33]	21.6 [8.9-36]	30.7 [16.7-43]	**0.02**
FSH	10.6 [5-25]	7.9 [4.7-46.6]	8.9 [6.4-38.4]	0.06
LH	4.8 [2.5-9.9]	4.3 [2.5-20.8]	7.9 [5.25-20]	**0.02**
PRL	8.1 [3.8-10.8]	8.9 [4.5-15]	9.8 [6.9-13.8]	0.18
DHEA-SO_4	105 [36.4-146.6]	112 [76.6-167.5]	177 [115-252]	**0.003**
Androstenedione	0.99 [0.68-1.1]	1.17 [0.8-1.7]	1.43 [0.86-1.66]	**0.035**
T. Testosterone	0.17 [0.1-0.2]	0.15 [0.11-0.24]	0.23 [0.15-0.31]	0.06
F. Testosterone	1 [0.6-1.4]	1 [0.8-1.6]	1.2 [0.8-1.6]	0.38
17OH Progesterone	0.4 [0.3-0.6]	0.48 [0.36-0.68]	0.47 [0.34-0.63]	0.74
Cortisol	11.5 [8.8-14.7]	13 [9.7-16]	16 [12.5-18.5]	**0.002**
GH	0.69 [0.31-0.97]	3.1 [1.58-5.84]	0.38 [0.2-1]	**<0.0001**
IGF-I	328 [227-387]	643 [534-885]	336 [281-369]	**<0.0001**

Data was expressed as median and IQR. Bold letters represent $p< 0.05$ and were considered statistically significant.

Median AcroQoL total score was 46.6% (IQR= 35.8-59) in the acromegalic female patients. But there was no significant difference in AcroQoL total scores between controlled and uncontrolled acromegalic female patients ($p= 0.53$).

Hormone levels in female patients with acromegaly and female healthy controls are shown in Table 4. GH and IGF-I levels were high in uncontrolled acromegalic patients than in controlled acromegalic patients and healthy controls ($p< 0.0001$, $p< 0.0001$, respectively). TSH, E_2, LH, androstenedione, DHEA-SO_4, cortisol levels were lower in the acromegalic patients than in healthy controls. Other than for GH and IGF-I levels, there was no difference in hormone levels between uncontrolled patients and controlled patients.

In the correlation analysis, a negative correlation was found between FSFI total and BDI score ($r= -0.69$, $p< 0.001$), age ($r= -0.45$, $p< 0.001$), IGF-I ($r= -0.28$, $p= 0.006$). There was a positive correlation between FSFI total score and E_2 level ($r= 0.31$, $p= 0.003$). Additionally, a moderately positive correlation was found between FSFI total and AcroQoL total score ($r= 0.45$, $p< 0.001$). In a regression analysis, the FSFI total score was associated with educational level ($\beta= 0.31$, $p= 0.01$), age ($\beta= -0.37$, $p< 0.001$) and IGF-I level ($\beta= -0.42$, $p= 0.001$ F= 17.5, adjusted R square: 0.518) (Fig. 1).

Discussion

Our study showed that FSFI total score and desire, arousal, orgasm, and satisfaction domains in female patients with acromegaly were significantly lower than in the healthy controls. FSD was associated with BDI and AcroQoL scores, age, and IGF-I level. BDI score was higher in female patients with acromegaly compared to healthy controls. However, there was no significant difference between biochemically controlled and uncontrolled patients with acromegaly with respect to FSFI and BDI scores. Regardless of the disease activity, female acromegalic patients had severely impaired QoL.

Female sexual dysfunction is a common problem having detrimental effects on women's QoL. It is

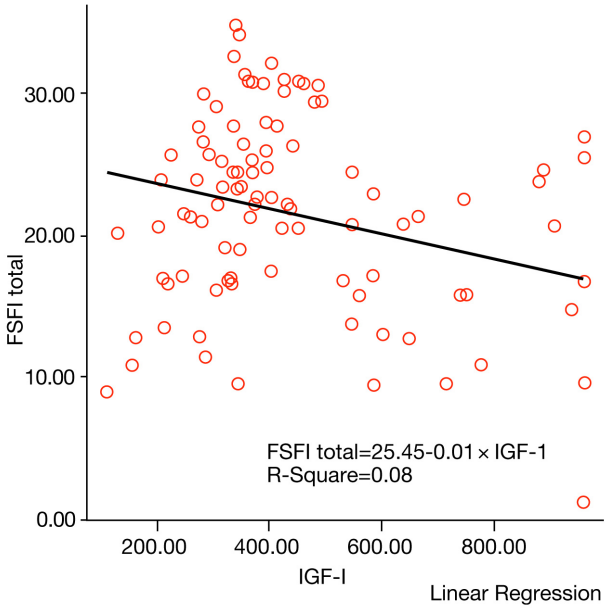

Fig. 1 A negative correlation was shown between FSFI total score and IGF-I

defined as disorders of sexual desire, arousal, orgasm and sexual pain which lead to personal distress [3]. The etiology of FSD is frequently multifactorial, it is related to male partner, general physical and mental well-being, age, education, menopause, gynecological problems, chronic diseases, medications and hormonal problems [2, 19]. Sexual function in men and women with acromegaly is scantily studied, it is not clear whether they are dependent directly GH effect or consequences of acromegaly. It can be hypothesized that the disease activity of the patients, therapies, related complications, psychological status, and QoL could play an important role on the sexual functions in acromegaly. The data in our study reveal that FSFI total and subdomains scores in female patients with acromegaly were significantly lower than in the healthy controls. Although the FSFI total score was not different between controlled and uncontrolled acromegaly patients, regression analysis showed that the FSFI total score was associated with IGF-I levels. Because although there are strict cure criterias for the treatment of acromegaly, GH and IGF-I levels remain high compared with healthy controls. While patients were considered cured on biochemically, some co-morbidities are not fully restored by treatment, could affect sexual functions of patients with acromegaly.

The first phase of female sexual function is desire, which means a mental state created by external and internal stimuli characterized by wanting to partake in sexual activity. Data from the PRESIDE study suggest rates of distressingly low sexual desire in the general population of 10% [20]. Generally, desire may be affected by psychological and emotional factors, hormone deficiencies and medical or surgical intervention [3, 4]. Physiological factors such as age, pregnancy, and menopause can also have an impact on sexual desire. In our study, the most affected domains were desire and arousal. Low sexual desire were found in 46 of 57 patients (80%) with acromegaly. Desire could be affected by the depressive mood of the patients and impaired QoL. Sexual hormones interact with neurotransmitters in the central nervous system, where the equilibrium between excitatory and inhibitory factors can control sexual functioning [21]. Although testosterone levels were not different in the groups, low estradiol, androstenedione, DHEA-SO_4 levels might affect the desire domain of the FSFI.

Sexual arousal disorder may be expressed as a lack of subjective excitement, genital lubrication/swelling or other somatic responses [22]. Although lubrication scores were not different in the groups, low arousal scores were found in 51 of 57 patients (89.5%) with acromegaly in our study. The cause of orgasmic difficulties is likely multifactorial and can be different for each woman. According to our data, orgasm and satisfaction scores in the patients with acromegaly were significantly lower compared to those in healthy controls and they were correlated with AcroQoL total score. Sexual pain disorders can be classified as dyspareunia and vaginismus [23]. In our study, the subjects presenting with inflammatory genital disease or vaginal discharge were excluded from the study after gynecological examination. We did not find any difference in the pain scores of FSFI between the groups.

Sexual dysfunction is common among individuals with chronic illnesses and is associated with distress and reduced QoL. Several studies showed that QoL is severely affected in acromegalic patients, even in those patients with controlled disease [24-28]. In our study, the median AcroQoL total score seems quite low compared to other studies. There was no difference in the AcroQoL scores between controlled and uncontrolled groups. We thought that the patients with acromegaly have to cope with both lengthy treatment and its complications. A positive correlation was observed between AcroQoL total score and FSFI scores.

Little research is available on the psychological features of acromegaly, despite their importance in this chronic and debilitating condition [29, 30]. Recent studies suggest that depressive disorders are frequently associated with and/or follow the development of pituitary tumors [31]. One study showed that 36% of the patients with long term cure of acromegaly had elevated scores for anxiety and depression according to the Hospital Anxiety and Depression Scale (HADS) [32]. An increase in physical well-being was noted in the acromegalic patients who had been cured [33], but they still had a high prevalence of psychological distress, especially anxiety disorders and major depression [34]. In our study, the percent of the acromegalic female patients and healthy controls with depression was 63%, and 15%, respectively, according to the BDI. An inverse correlation was observed between BDI scores and AcroQoL total score, FSFI scores. These results suggest that depressive mood remains in the controlled acromegalic patients and associated with QoL and sexual dysfunction. A recent study showed that patients with acromegaly use ineffective coping strategies [35].

Many patients with acromegaly have had untreated disease for several years prior to diagnosis and a spectrum of morbidities such as metabolic abnormalities, hypertension, DM and OSAS are apparent [36]. However, the literature of FSD and DM give conflicting results, unlike the sexual dysfunction in males with DM. In general, both type I and type II DM are reported to adversely affect FSD [37, 38]. Onem K *et al*. showed that OSAS is associated with a significant decrease in female sexual function [39]. In our study, these co-morbidities are thought to affect FSD in patients with acromegaly.

Aging and menopausal transition has a negative influence on sexuality [1]. Estrogen plays an important role in maintaining the integrity of the vaginal tissues. Alterations in mood, sleep, and cognitive functioning are common as well. These changes may contribute to lower self-esteem, poorer self-image, and diminished sexual responsiveness and sexual desire [40]. Dennerstein *et al*. reported that a reduction in serum estradiol correlated with reduced sexual desire and sexual responsivity similarly to our result [41]. Our results showed that FSD was associated with the presence of older age. Although the number of menopausal women and menopause duration in the groups were similar, estradiol, LH, DHEA-SO_4, androstenedione levels and FSFI scores in acromegalic females were lower than in healthy controls. This difference may be due to radiotherapy in the patient group.

As well as biological and psychological factors, sociocultural factors also influence FSD. These include lower educational attainment, income level, societal taboos and conflict with religious [1]. Laumann *et al*. showed that women with a lower educational level run more risk of experiencing sexual problems [42]. Recently, Llaneza *et al*. reported that sexual functions were positively correlated to female education [43]. Cayan *et al.* demonstrated that significantly higher prevalence of FSD in the patients with lower educational level, unemployment status [5]. We thought that low education status affects sexual function of the patients with acromegaly in this study.

The small number of the patients in the groups is a limiting factor in this study because of participation of a single center. Additionally, male partner sexual status was not evaluated using the International Index of Erectile Function (IIEF) scale. Erectile functions of the partners were asked and the women whose partner had suspicious erectile dysfunction were not included in the study.

In conclusion, this study shows that regardless of the disease activity, in acromegalic females, sexual dysfunction and depression rates are higher than in healthy females. Female acromegalic patients had severely impaired QoL, even if remission had been attained.

Appendix

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Declaration of Interest

The authors declare no conflicts of interest that could be perceived as prejudicing the impartiality of the research reported.

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