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Evaluation of Anxiety and Perceived Stress Levels in Patients with Acromegaly After the First Lockdown of the Coronavirus Disease 2019 Pandemic

ABSTRACT

Objective: The aim of this study is to examine and compare the anxiety level and stress perception of acromegaly patients with controlled and active disease in the coronavirus disease 2019 pandemic.

Methods: A total of 49 (23 females/26 males) patients applied to the outpatient clinic during the month after the first lockdown of the pandemic period were recruited in this cross-sectional study. State-Trait Anxiety Inventory (S-Anxiety for state scale, T-Anxiety for trait scale) and Perceived Stress Scale-14 were used to evaluate the event-related current state anxiety, the general tendency to anxiety, and perceived stressful situations. Patients were divided into 2 groups as active (n = 14) and well-controlled (n = 35) patient groups and compared.

Results: The active acromegaly group had significantly higher scores than well-controlled patients on all the S-Anxiety ($P = .011$), T-Anxiety ($P = .002$), and Perceived Stress Scale-14 ($P = .007$) scores after controlling for age, gender, body mass index, education years, marital and occupation status, disease duration, and disease-specific medical treatment status covariates. S-Anxiety ($P = .021$), T-Anxiety ($P = .004$), and Perceived Stress Scale-14 ($P = .009$) scores were found significantly higher in single patients than in married ones.

Conclusion: This study showed significantly increased anxiety and perceived stress levels after the first lockdown of the coronavirus disease 2019 pandemic, especially in the active and single acromegaly patients compared to the well-controlled and married ones. Psychiatric symptoms should be carefully evaluated in the follow-up of acromegaly patients. The necessary psychological support should be provided to patients by focusing on these symptoms to improve patient management, particularly in a health-related stressful situation such as the coronavirus disease 2019 pandemic.

Keywords: Acromegaly, anxiety, COVID-19 pandemic, disease activity, perceived stress

Introduction

Acromegaly is a rare disease with hypersecretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) and is almost always caused by a pituitary adenoma.[1] Both genders are affected equally, and patients are generally diagnosed in the fourth or fifth decade of their life.[2] Increased levels of GH and IGF-1 may lead to a wide range of systemic manifestations, clinical symptoms, and several complications.[3] The most common acromegaly complications include musculoskeletal disease, respiratory disease, cardiovascular disease, gastrointestinal disease, cerebrovascular disease, psychiatric disorders, and metabolic complications such as diabetes mellitus (DM), dyslipidemia, impaired glucose tolerance, and insulin resistance.[2,3]

Depression, increased anxiety, decreased self-esteem, and cognitive dysfunctions were the determined symptoms of acromegaly.[4] The occurrence of psychopathological findings in acromegaly affects both the disease prognosis and the quality of life (QoL) in the long term. Although less emphasis is placed on it, psychiatric disorders are more frequent in acromegaly than other chronic diseases. Psychiatric morbidity may accompany acromegaly, and the effects of GH/IGF-1 excess on the central nervous system could be an explanation. While psychological distress increases in the active phase of the disease, studies have shown that both surgery and medical treatment options improved the psychopathological findings.[5] On the other hand, it was reported that acromegaly patients with biochemical remission had a higher prevalence of psychopathological conditions than healthy controls.[6,7] This could be explained by the possibility of an irreversible effect of long-lasting previous GH/IGF-1 hypersecretion on mood and behavior.[8] Whether there are interactions related to disease activity in terms of psychological symptoms still needs further evaluations.

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Coronavirus disease 2019 (COVID-19) is a disease caused by the severe acute respiratory syndrome coronavirus 2, which has become a pandemic starting in China and spread rapidly. Restriction of mobility, social isolation, exposure to inadequate and conflicting information, and financial losses led to negative psychological situations, including anxiety, depression, and acute stress for all those involved. Besides, the pandemic strongly affected patients, especially those with chronic diseases. Those patients did not apply to hospitals for fear of being infected or could not reach their physician because the outpatient admissions were suspended. Although the psychiatric effects of the pandemic have been examined in normal populations and healthcare workers, few studies were conducted in those special patient groups with chronic diseases.[9-12]

This study aimed to examine and compare the anxiety level and stress perception during the COVID-19 pandemic period in acromegaly patients with controlled and active disease, whose psychiatric distress has known to affect treatment compliance and morbidity.

Material and Methods

Study Design and Patients

The first COVID-19 case was reported on March 11, 2020, in Turkey. Afterward, strict precautionary measures were applied, and the first lockdown was initiated by the government between March 11, 2020, and June 01, 2020. Of the 53 patients who applied to the endocrinology outpatient clinic during the month after the first lockdown of the pandemic period when the normalization process started, 49 (23 females and 26 males) patients were recruited in this observational and cross-sectional study. Four patients were not included in the study according to exclusion criteria such as using psychiatric drugs, a history of psychiatric disease, and being unable to understand questions on scales. None of the patients included in the study had a COVID-19 infection previously. Participants were divided into 2 groups: the active group consisted of 14 (28.6%) patients, and the well-controlled group consisted of 35 (71.4%) patients. According to the last guideline, patients with high IGF-1 levels adjusted to age and gender and GH levels higher than 1 ng/mL were accepted for the active disease group, and patients with normalized IGF-1 levels adjusted to age and gender were accepted for the well-controlled disease group.[8] Patients whose biochemical control was achieved by surgical or medical therapies were accepted for the well-controlled group.

Sociodemographic and descriptive data including age, gender, education duration, marital status, occupational and clinical appointment status during the pandemic period, disease history, and clinical and laboratory findings were compared in groups. Patients who could not attend their scheduled appointments during the pandemic period for any reason were considered in the group of postponed appointments due to the pandemic. Diabetes mellitus, hypertension, coronary artery disease, obstructive sleep apnea syndrome, and hypopituitarism due to lack of any of the pituitary hormones were determined as comorbidities. Therapy with 2 long-acting available somatostatin receptor ligands (octreotide and lanreotide) was accepted as the disease-specific treatment. The levels of IGF1 were adjusted as IGF1/upper limit of the normal range × 100 for all patients.

This study was approved by Bakırköy Dr. Sadi Konuk Training and Research Hospital ethics committee unit on June 22, 2020, with the protocol number 2020/271. Signed informed consent was obtained from all cases. Procedures were performed according to the ethical standards in the Helsinki Declaration.

State and Trait Anxiety Inventory

State-Trait Anxiety Inventory is a self-report scale with 40 items developed to measure the presence and severity of anxiety in current and general level by Spielberger et al[13] in 1970. State-Trait Anxiety Inventory has 2 subscales: the State Anxiety Scale (S-Anxiety) for the situation or event-related current state of anxiety and the Trait Anxiety Scale (T-Anxiety) for the general tendency to anxiety. Each of them is a 20-item self-report questionnaire with a 4-point Likert-type scale to produce a score ranging from 20 to 80. An increase in scores indicates an increase in anxiety levels. The validation study of the STAI scale for the Turkish population was performed by Oner and Le Compte.[14] We described a cutoff level of >39 as a high-anxiety category and ≤39 as a low-anxiety category in both STAI scales in this study, as shown previously.[15]

Perceived Stress Scale

Perceived Stress Scale-14 is a self-report questionnaire developed to measure perceived stressful situations and self-sufficiency in personal life by Cohen et al.[16] Perceived Stress Scale-14 is a 14-item questionnaire with a 5-point Likert-type scale varying between "never (0)" and "very often (4)." The scale produces scores ranging from 0 to 56. A high score indicates an excessive perception of stress. The validity and reliability of PSS for the Turkish population were demonstrated previously.[17] As shown in the literature, we described a cutoff level of >25 as the high PSS level and ≤25 as the low PSS level in this study.[18]

Statistical Analysis

Statistical Package for the Social Sciences Version 20.0 (IBM Corp.; Armonk, NY, USA) program was performed in analyzing the data obtained from the study. A normal distribution of data was confirmed with the Kolmogorov Smirnov test. Student's *t* and Mann–Whitney *U* tests were performed for comparisons between 2 groups, and descriptive statistical methods (mean, standard deviation, median, minimum–maximum) were applied according to the distribution of variables. A chi-square test was performed to compare categorical variables, and the Pearson correlation analysis was applied to evaluate the relationship between variables. A multivariate analysis of covariance (MANCOVA) was used to evaluate whether the scores of STAI and PSS were related to acromegaly disease activity while correcting for possible factors affecting the psychopathological situation. The Box–Cox transformation was applied for variables with non-normal distribution. Leneve's test was performed to assess the equality of variances. All psychopathological dimensions that were thought to be clinically significant in the patients with acromegaly were counted as covariates such as age, gender, education duration, marital status, occupation status in the pandemic period, body mass index, disease duration, comorbidities status, and acromegaly disease-specific medical treatment status. The statistical significance level was set as <.05.

Results

This study was conducted on 49 patients (23 females/26 males) with acromegaly with a mean age of 49.8 ± 9.6 years. In the study group, the mean S-Anxiety level was 44.47 ± 11.6, the T-Anxiety level was 45.57 ± 8.1, and the mean PSS-14 level was 24.22 ± 8.79 in all patients group. Comparison of sociodemographic and clinical characteristics

Table 1. Sociodemographic and Clinical Characteristics of Patients with Active and Well-Controlled Acromegaly

	All patients with Acromegaly	Acromegaly Disease Phase*	
	Total (n = 49)	Active (n = 14)	Controlled (n = 35)
Gender (n, %)			
Female	23 (46.9)	4 (28.6)	19 (54.3)
Male	26 (53.1)	10 (71.4)	16 (45.7)
Age (years)		47.78 ± 10	50.57 ± 9.5
BMI (kg/m^2)		29.88 ± 5.3	31.20 ± 3.7
Education duration (years)		7.14 ± 3.6	5.49 ± 4.3
Marital status (n, %)			
Married	41 (83.7)	13 (92.6)	28 (80)
Single	8 (6.3)	1 (7.1)	7 (20)
Occupation status in the pandemic period (n, %)			
Working	7 (14.3)	4 (28.6)	3 (8.6)
Working from home	3 (6.1)	1 (7.1)	2 (5.7)
Not working	39 (79.6)	9 (64.3)	30 (85.7)
Smoking (n, %)	18 (36.7)	6 (42.9)	12 (35.3)
Alcohol usage (n, %)	2 (4.1)	1 (7.1)	1 (2.9)
Postponed appointment due to pandemic (yes/no) (n)	33/16	10/4	23/12
Estimated time until diagnosis (years)*		1 (0-6)	1 (0-7)
Disease duration (years)*		4 (0.4-25)	3 (1-22)
Co-morbidities (n, %)	40 (81.6)	9 (64.3)	31 (88.6)
Hypopituitarism (n, %)	7 (14.3)	0	7 (14.6)
Acromegaly-specific medical treatment (yes/no) (n)	24/25	13/1	11/24

Data were given as mean ± standard deviation or *median (minimum–maximum) according to distribution.
BMI, body mass index; check the manuscript for the co-morbidities and acromegaly-specific medical treatments.
*There was no significant difference in all comparisons between acromegaly patient groups.

of active and well-controlled patients with acromegaly was summarized in Table 1. The mean of the adjusted IGF-1 levels at the time of diagnosis was 296.16 ± 68.4 units in the active acromegaly group and 253.93 ± 85.2 units in the well-controlled patient group ($P > .05$). The mean of the adjusted last IGF-1 level was found to be significantly higher in active patients (176.57 ± 67.15 units) compared to controls (86.25 ± 27.54 units) ($P < .001$). There was no significant relationship between adjusted IGF-1 levels and neuropsychiatric test scores.

When the MANCOVA method was performed for the active and well-controlled acromegaly patient groups, the active acromegaly group had significantly higher scores on all the S-Anxiety ($P = .011$), T-Anxiety ($P = .002$), and PSS-14 ($P = .007$) after controlling for age, gender, BMI, education years, marital and occupation status, disease duration, and disease-specific medical treatment status covariates (Table 2). S-Anxiety ($P = .021$), T-Anxiety ($P = .004$), and PSS-14 ($P = .009$) scores were found significantly higher in single patients than in married ones after controlling for age, gender, BMI, education years, occupation status, disease phase (active or well-controlled), disease duration, and disease-specific medical treatment status covariates (Table 3).

There were 30 (61.2%) patients in the high S-Anxiety category, 39 (79.6%) patients in the high T-Anxiety category, and 22 (44.9%) patients in the high PSS category for all acromegaly patients. Categorical comparison of S-Anxiety, T-Anxiety, and PSS levels in active and well-controlled acromegaly patients was summarized in Table 4.

In correlation analysis, there was a positive and strong correlation between PSS-14 levels and S-Anxiety and T-Anxiety ($r = 0.796$, $P < .001$; $r = 0.778$, $P < .001$, respectively). There were no significant correlations between other parameters.

Discussion

In this study, we evaluated the anxiety and perceived stress of patients with acromegaly after the first lockdown of the COVID-19 pandemic and revealed that anxiety and perceived stress scores were significantly higher in active disease than in controlled disease after controlling for confounding covariates.

Most current studies have mainly focused on the clinical features and epidemiology of COVID-19 due to the course and the spread rate of the disease being unknown. The psychopathological effects related to COVID-19 were largely neglected. Wang et al[19] reported significantly higher depression and anxiety levels in health workers who have a high risk according to their working environment. A study revealed that the healthcare workers had high levels of S-Anxiety, T-Anxiety, and hopelessness levels and were more affected psychologically in the COVID-19 pandemic period than non-healthcare workers in the Turkish population.[9] Although these studies consisted of healthcare professionals, they point out that pandemics can cause anxiety and psychological distress in individuals who especially have chronic disorders. Acromegaly, particularly when considering its comorbidities, may be considered a risky chronic disease for COVID-19 patients. All scores of S-Anxiety, T-Anxiety, and PSS-14 were significantly higher in our acromegaly patients, especially in patients with the active disease after the first lockdown of the COVID-19 pandemic. Although there was no control group in our study, the frequency of our patients in the high-anxiety and perceived stress category was higher than the frequency of individuals in the high-anxiety and perceived stress category in other studies conducted with the S-Anxiety, T-Anxiety, or PSS scales for Turkish population.[20,21]

Affective disorders (predominantly depression and anxiety), decreased self-esteem, and cognitive impairment were previously reported as factors influencing QoL in acromegaly patients.[3,5]

Table 2. Comparison of STAI-S, STAI-T, and PSS-14 Levels of Patients with Active and Controlled Acromegaly

	Patient Group (n = 49)		Comparison*	
	Acromegaly Disease Phase			
	Active (n = 14)	Well-Controlled (n = 35)	*F*	*P*
S-Anxiety	48 ± 10.8	43.06 ± 11.78	7.295	.011
T-Anxiety	48.57 ± 7.76	44.37 ± 8.03	10.066	.003
PSS-14	27.07 ± 9.68	23.09 ± 8.28	8.397	.007

Data were given as mean ± standard deviation.
*Multiple analysis of covariance (MANCOVA); S-Anxiety, State Anxiety Scale; T-Anxiety, Trait Anxiety Scale; PSS: Perceived Stress Scale.

Table 3. Comparison of STAI-S, STAI-T, and PSS-14 Levels of Acromegaly Patients According to Marital Status

	Patient Group (n = 49)		Comparison*	
	Marital Status			
	Single (n = 8)	Married (n = 41)	*F*	*P*
S-Anxiety	48.9 ± 13.9	43.6 ± 11.1	5.846	.021
T-Anxiety	49.3 ±9.3	45.6 ± 8.1	9.536	.004
PSS-14	26.6 ± 11.3	24.2 ± 8.7	7.692	.009

Data were given as mean ± standard deviation.
*Multiple analysis of covariance (MANCOVA); S-Anxiety, State Anxiety Scale; T-Anxiety, Trait Anxiety Scale; PSS, Perceived Stress Scale.

Table 4. Categorical Comparison of S-Anxiety, T-Anxiety, and PSS-14 in Patients with Active and Controlled Acromegaly

	Acromegaly Disease Phase (n = 49)		
	Active (n = 14)	Well-Controlled (n = 35)	*P*
S-Anxiety			N.S.
Low anxiety (≤39 point) (n, %)	3 (21.4)	16 (45.7)	
High anxiety (>39 point) (n, %)	11 (78.6)	19 (54.3)	
T-Anxiety			N.S.
Low anxiety (≤39 point) (n, %)	1 (7.1)	9 (25.7)	
High anxiety (>39 point) (n, %)	13 (92.9)	26 (74.3)	
PSS-14			N.S.
Low PSS (≤25 point)	6 (42.9)	21 (60)	
High PSS (>25 point)	8 (57.1)	14 (40)	

S-Anxiety, State Anxiety Scale; T-Anxiety, Trait Anxiety Scale; PSS, Perceived Stress Scale; N.S., not significant.

However, studies in the literature are controversial about the interactions of disease activity and psychological symptoms in acromegaly. Paisley et al[22] showed that while QoL deteriorated in active acromegaly patients, a significant improvement in psychological distress and QoL was achieved in well-controlled patients with the different treatment modalities. Crespo et al[23] found that both S-Anxiety and T-Anxiety scores were significantly higher in well-controlled acromegaly patients than in healthy subjects. Our study showed that the active acromegaly group had significantly higher scores on all the S-Anxiety, T-Anxiety, and PSS-14 scales consistent with these studies. One of the possible reasons for general psychiatric symptoms in acromegaly could be irreversible disfiguring alterations, especially in facial appearance, in the disease course. Body image distortion may increase perceived stress and deteriorate social relations and anxiety.[6] The other plausible reason could be the global enlargement of the grey matter in the brain of acromegaly patients and exposure to GH/IGF-1 excess, particularly long duration before treatment.[7] The third possible reason could be the stress caused by the direct effect of the treatments or being in a life-long treatment process.[8]

Diabetes mellitus, hypertension, obesity, and cardiovascular disease are possible risk factors for severe COVID-19 patients. Some of these patient groups were previously assessed regarding the psychological effects of the pandemic period. Alessi et al[24] reported that patients with type 1 and type 2 DM showed significant psychological distress, especially in patients with type 2 DM. It was also reported that patients with obesity had increased psychological distress and impaired QoL in the pandemic period.[25] These comorbidities are also frequently seen in acromegaly patients and increase the fear of being infected. On the other hand, in our study, comorbidities did not affect the test scores, and no significant difference was observed between the active and well-controlled acromegaly patients regarding comorbidities.

Other factors affecting psychological distress in acromegaly were assessed in the literature. The negative effects of age, female gender, BMI, and disease duration on psychiatric findings were defined previously.[26] Contrary to these studies, we did not find any significant difference in neuropsychiatric test scores regarding BMI, age, gender, and disease duration. Also, marital status could be effective on anxiety and depression in stressful situations, but studies were controversial for the COVID-19 pandemic. Smith et al[27] showed that being single was associated with poor mental health in the COVID-19 pandemic. In 1 of the 2 studies from Turkey, the S-Anxiety level was detected higher in married health workers than the control group; the other study has shown no predictive effect of marital status on anxiety.[9,28] Our study showed significantly higher levels of anxiety and perceived stress scores in single acromegaly patients than married ones.

To our knowledge, this is the first study evaluating the association between perceived stress score and disease phases in acromegaly patients. In a few studies, PSS was used during the COVID-19 pandemic period for reflecting the current perceived stress level.[29] A study from Turkey showed that PSS-14 scores were higher among medical students in the clinic than medical students in the pre-clinic course.[30] In our patient group, the PSS-14 score was significantly higher in active patients than in well-controlled ones. Accordingly, we have shown that disease activity significantly affects the perceived stress, but we

did not find any correlation between PSS and other variables. Unlike our anxiety results, most of the active acromegaly patients were in the high PSS category, while most well-controlled patients were in the low PSS category. This finding indicated that disease activity might have different effects on perceived stress. Further larger studies with control groups are needed to understand the importance of these results which did not reach statistical significance.

This study has some limitations. The most prominent limitation of our study is the absence of a control group, but we assessed the active acromegaly patients and compared them to well-controlled patients. The cross-sectional design limits randomization and a small number of the patient group was another limitation. However, acromegaly is a rare disease to attain a large sample size, and we wanted to reach most of the patients followed in our center without extending the duration after the first lockdown of COVID-19 pandemic.

In conclusion, our findings indicated the increased perceived stress and anxiety levels during the first lockdown period, especially in the active acromegaly patients, already tend to psychiatric distress. Additionally, it has been determined that marital status may also be effective for anxiety level and stress perception in acromegaly patients in situations that cause social isolation such as the lockdown of the COVID-19 pandemic. Psychiatric symptoms should be carefully evaluated in the follow-up of acromegaly patients, and the necessary psychological support should be provided to patients to improve patient management, morbidity, and QoL, particularly in a health-related stressful situation as the COVID-19 pandemic. Future studies are needed to include prospective and longitudinal measurements of anxiety, perceived stress, and comprehensive psychological and QoL assessments to predict the long-time psychopathological results of COVID-19 pandemic in acromegaly patients.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital on June 22, 2020 (approval No: 2020/271).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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