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RESEARCH

Neurosteroids, Anxiety and Quality of Life in Acromegaly

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Abstract

Objective Acromegaly reduces quality of life. Neurosteroids can impact neuropsychological status and anxiety, but their effects on anxiety in acromegaly cases and quality of life are unclear. This study aims to evaluate the relationship between neurosteroids, anxiety, and quality of life in acromegaly patients.

Design This study included 33 cases in the acromegaly group (AG) and 30 healthy subjects in the control group (CG). Beck Anxiety Inventory (BAI) and Short Form-36 (SF-36) were used to assess anxiety levels and Quality of Life (QoL), respectively. The research assessed how anxiety and quality of life scores correlate with the concentrations of growth hormone, IGF-1, and specific neurosteroids (Allopregnanolone (AP), pregnenolone (PRG), 24S-hydroxycholesterol (24OHC), dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), androsterone (ADT)).

Results AG had significantly higher BAI scores in comparison to CG. The SF-36 subdomain scores of general health, physical functioning, role limitations due to physical health, energy/fatigue, emotional well-being, social functioning, and pain were significantly lower in the AG.

Conclusion Neurosteroids may affect the quality of life and be associated with depression and anxiety levels in acromegaly.

Keywords Neurosteroids · Quality of life · Anxiety · Acromegaly

1 Introduction

Acromegaly is a medical condition characterized by an overproduction of growth hormone (GH), typically resulting from a pituitary adenoma that secretes GH. It pertains to the interplay of systemic diseases, multisystem health challenges, and fluctuations in mood states. [1, 2].

Previous studies showed increased anxiety levels in cases with pituitary adenoma, including those with acromegaly. However, the anxiety level of cases with acromegaly did not

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differ from cases with other pituitary adenomas [3, 4]. Elevated anxiety levels may reflect a diminished quality of life (QoL) in individuals with acromegaly, and research indicates that fluctuations in mood and reduced QoL in this condition do not correlate with hormone concentrations [5–7].

Neurosteroids (NS) are a group of hormones that can affect neuropsychological status, and their levels are associated with anxiety [1, 8, 9]. Allopregnanolone, an NS, is an allosteric modulator of the GABA type A receptor, and anxiety may be related to reduced endogenous allopregnanolone synthesis [10]. Many studies stated positive and negative relations between NS and anxiety, including pregnenolone sulfate, dehydroepiandrosterone, and dehydroepiandrosterone sulfate [9] Also, QoL was related to the NS levels [11].

Previously, we have shown the impact of NS on depression and cognitive functions in cases with acromegaly for the first time [1]. While the effect of NS on anxiety, in general, has been studied before, whether they affect anxiety and QoL in individuals with acromegaly or not may need more focus. In this sequel study, we aimed to evaluate and discuss the possible relationship between anxiety, QoL, and NS in cases with acromegaly.

2 Material and Methods

In this comparative cross-sectional study, 63 participants who were informed about the study volunteered to participate, and all provided sufficient data. Thirty-three cases with acromegaly composed acromegaly group (AG) and thirty age, gender, and education-matched healthy subjects. Individuals with a history of stroke, those with a current or past diagnosis of any psychiatric disorder, and those with psychiatric treatment were excluded. Also, individuals on steroid therapy were excluded, except in one case with acromegaly, who had pituitary hypocortisolism and was on physiologic replacement doses of glucocorticoid. Of the 33 cases, 26 individuals had previously transsphenoidal surgery. Among the remaining cases, three were on Octreotide-LAR (20 µg) treatment, two were receiving 60 µg of Lanreotide, 1 was on 90 µg of Lanreotide, and three were receiving 120 µg of Lanreotide. Additionally, 2 cases were being treated with cabergoline, and eight individuals received radiotherapy, specifically Gamma-knife treatment. Five patients experienced hypopituitarism and were under replacement therapy. A total of 22 cases were in remission at the time of the study. Regarding comorbidities, three individuals had diabetes, 1 had hypertension, and 3 had diabetes and hypertension. The Ethics Committee of Istanbul Training and Research Hospital approved the study protocol. All the subjects read and signed the informed consent forms before enrolling in the study.

2.1 Psychological Assessment

Beck Anxiety Inventory (BAI) is a self-report measure of anxiety with 21 items. The sum of the scores was used to evaluate the presence and severity of anxiety [12, 13].

36-Item Short Form Survey (SF-36) was used to evaluate health-related QoL (HRQoL). Questions about the perceptions of the cases on health-related concepts, including physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to emotional problems, emotional well-being, social functioning, vitality (energy/fatigue), and general health are included in the survey [14, 15].

As we previously depicted, the median scores on Beck Depression Inventory (BDI) were higher in AG [16 [IQR: 9.5–22.5]] than in CG [3 [IQR: 1–9.3]] ($p < 0.001$) [1].

2.2 Laboratory Evaluation

Individuals with IGF-I levels that align with the age and gender-adjusted standards, and who recorded a nadir GH of less than 1 ng/mL during the oral glucose tolerance evaluation, were recognized as having their acromegaly adequately controlled. Serum levels of allopregnanolone (AP), pregnenolone (PRG), 24S-hydroxycholesterol (24OHC), dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEAS), androsterone (ADT) were used to correlate with the scores on anxiety and QoL. Our earlier publication outlined the techniques employed in the laboratory analysis [1].

2.3 Statistics

The data were analyzed with the Jamovi version 2.3.19.0 (30). The Chi-square test was used for categorical variables. Sample distribution was evaluated with the Kolmogorov–Smirnov test. Continuous variables with normal distribution were compared by using the Student's test. Continuous variables with non-normal distributions were compared by using the Mann–Whitney U test. Pearson's correlation coefficient was used for the calculation of associations between variables. p values under 0.05 were considered statistically significant. Possible relationships between some scales were examined by a mediation analysis model based on correlation analyses. Mediation analysis of the model was performed with the jAMM module on Jamovi [16] with Bootstrapping. The bootstrapping method was chosen to robustly evaluate the mediators' effects to reduce type 1 errors and to check for possible mediator effects of depression. The assessment of mediator

variables utilized 1000 bootstrap samples for statistical analysis. The statistical significance of the variables was assessed with a confidence interval of 95% employed for determining significance (Fig. 1, 2).

3 Results

The mean age was 47.8 ± 11.8 years in AG and 45.4 ± 11.7 years in CG (p = 0.5). The female/male ratio was 23/10 in AG and 22/8 in CG (p = 0.8).

3.1 Laboratory Evaluation

Cases of acromegaly had higher levels of GH and IGF-1 (p = 0.02 and p = 0.04, respectively) and lower levels of 24OHC and DHEA (p = 0.002 and p = 0.007, respectively) compared to the control group. Levels of GH, IGF1, and NS are presented in Table 1.

3.2 Psychological Assessment

The median BAI scores were significantly higher in AG than in CG (p < 0.001) (Table 2). The scores on BAI were not correlated with GH, IGF-1, or disease duration (p = 0.63, p = 0.90, p = 0.35). The levels of anxiety experienced by individuals with acromegaly showed no significant variation when considering the presence or absence of hypopituitarism, the type of medical interventions received, the administration of radiotherapy, or the existence of other comorbid conditions (p = 0.71, p = 0.74, p = 0.28, p = 0.52).

The subdomain scores of the SF-36 associated with general health, physical capabilities, role restrictions stemming from physical health, energy levels and fatigue, emotional wellness, social interactions, and pain were significantly diminished in the AG relative to the CG (p < 0.001). There

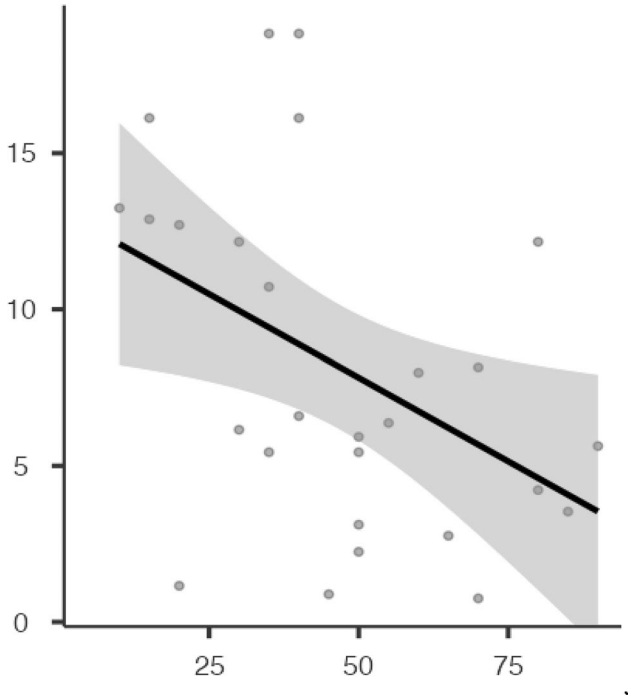

Fig. 1 Correlation matrix for relation of DHEA with the scores on vitality

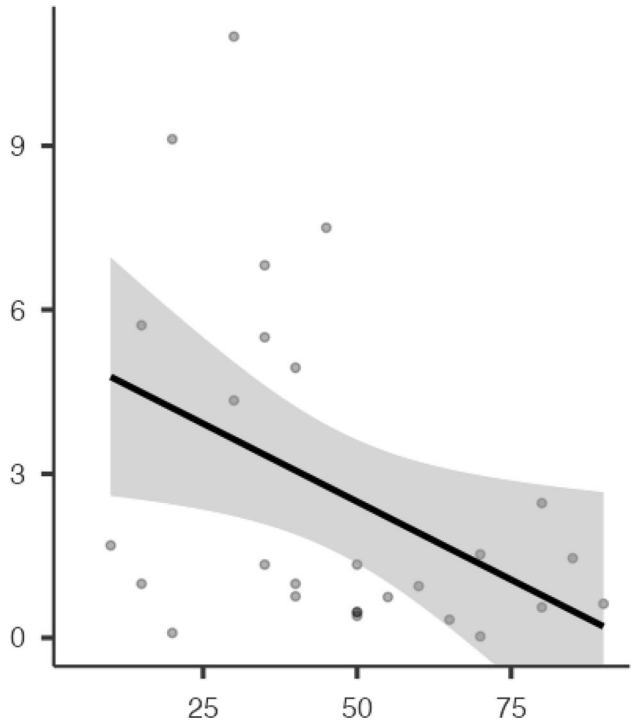

Fig. 2 Correlation matrix for relation of DHEAS with the scores on vitality

Table 1 GH, IGF-1 and neurosteroid levels of the two groups

	Acromegaly (n = 33)	Control group (n = 30)	*P*
GH (ng/ml)	0.5 [0.137–1.69]	0.09 [107–130]	0.02*
IGF-1 (ng/ml)	151 [113–278]	115.9 [0.0600–0.180]	0.04*
ADT (ng/ml)	17.4 [6.71–27.4]	16.1 [1.92–19.1]	0.174
AP (ng/ml)	31.6 [9.95–67.4]	22.2 [5.54–32.4]	0.181
OHC24 (ng/ml)	8.7 [6.82–15.6]	44.3 [20.2–131]	**0.002***
PRG (ng/ml)	5.32 [4.56–5.78]	5.06 [4.56–5.66]	0.540
DHEA (ng/ml)	6.37 [3.88–12.4]	9.48 [7.96–21.9]	**0.007***
DHEAS (ng/ml)	1.34 [0.590–4.64]	1.68 [0.980–2.36]	0.666

Data was expressed as median and interquartile range

Statistically significant *p* values are shown in a bold format

IGF-1 insulin-like growth factor, *ADT* androsterone, *AP* allopregnanolone, *DHEA* dehydroepiandrosterone, *DHEAS* dehydroepiandrosterone sulfate, *PRG* pregnenolone, *24-OHC* 24-(S)hydroxycholesterol

Table 2 Difference between the acromegaly and the control groups for psychological variables

	Acromegaly group (n = 33)	Control group (n = 30)	*P*
BAI	9 [4.00–19.0]	2.5 [0.00–5.75]	**< 0.001**
General Health	55 [35.0–70.0]	75 [65.0–80.0]	**< 0.001**
Physical functioning	70 [50.0–90.0]	100 [96.3–100]	**< 0.001**
Role limitations due to physical health	25 [0.00–100]	100 [100–100]	**< 0.001**
Emotional problems	33.3 [0.00- 100]	100 [100–100]	**< 0.001**
Vitality	45 [30.0–60.0]	60 [55.0–65.0]	**0.02**
Emotional well-being	60 [48.0–72.0]	64 [57.0–72.0]	0.3
Social functioning	50 [37.5–75.0]	93.8 [71.3–100]	**< 0.001**
Bodily pain	55 [32.5–75.5]	100 [77.5–100]	**< 0.001**

The results are presented as median and interquartile range

BAI beck anxiety inventory

p-values in bold were statistically significant

was no statistically significant difference between AG and CG for emotional well-being (p = 0.3). Detailed data is presented in Table 2. Again, none of the domain scores of SF-36 differed between the cases with acromegaly when they were stratified by presence and absence of remission, radiotherapy, hypopituitarism, additional comorbidities, and medical therapy (data not shown here).

Statistically significant positive correlations were calculated between BDI and BAI scores (r = 0.6, p < 0.001). There was a negative correlation between BAI and SF-36 domain scores of vitality, social functioning, emotional well-being, and general health (r = − 0.4, p = 0.010; r = − 0.4, p = 0.008; r = − 0.4, p = 0.017, and r = − 0.4, p = 0.008). The SF-36 domains of emotional well-being, vitality, social functioning, and general health were also negatively correlated with the scores on BDI (r = − 0.5, p < 0.001 r = − 0.6, p < 0.625; r = − 0.5, p < 0.001; r = − 0.5, p < 0.01).

According to correlation analysis, a model evaluating the mediator role of depression levels in the effect of anxiety on subscales of SF-36 was developed. In correlation analyses, general health, vitality, emotional well-being, and social functioning have significant relations with BDI and BAI scores (p < 0.05). These results stated that each health in general, vitality, emotional well-being, and social functioning could be the dependent variable for different mediation models. Anxiety was selected as the predictor, and depression level was chosen as the mediator for all four mediation models. The mediation analysis stated that depression may have a mediating role in the relationship between general health, vitality, social functioning, and anxiety (p < 0.05). However, depression did not show a mediating effect in this relationship between emotional well-being and anxiety (p > 0.05).

The BAI scores in both groups did not correlate with any neurosteroid levels (Data not shown here). In AG, of the SF-36 domains, the scores on vitality were negatively correlated with DHEA (r = − 0.4, p = 0.014) and DHEAS levels (r = − 0.4, p = 0.02). The correlation of NSs with SF-36 subdomains in each group is summarized in Table 3.

Table 3 Correlations of the neurosteroid levels with the scores on depression and SF-36 subdomains in each group

Acromegaly (n = 33)	Control group (n = 30)
• DHEA	• ADT
Vitality (r = − 0.465, p = 0.014)**	Physical functioning (r = − 0.5, p = 0.015)**
Emotional well-being (r = − 0.3, p = 0.05)*	Role limitations due to physical health problems (r = − 0.5, p = 0.02)**
General health (r = − 0.3, p = 0.08)*	• 24OHC
• DHEAS	Role limitations due to physical health problems (r = 0.4, p = 0.04)**
Vitality (r = − 0.443, p = 0.02)**	• PRG
General health (r = − 0.3, p = 0.06)*	Social functioning (r = 0.3, p = 0.078)*

*Tendency

**Statistically significant

ADT androsterone, *AP* Allopregnanolone, *DHEA* dehydroepiandrosterone, *DHEAS* dehydroepiandrosterone sulfate, *PRG* pregnenolone, *24OHC* 24(S)-Hydroxycholesterol

4 Discussion

This study found elevated anxiety levels in individuals with acromegaly, suggesting a heightened prevalence of mood and anxiety disturbances relative to the general population. The scores of depression and anxiety were interrelated. Also, scores on subdomains of SF-36 were lower, meaning the quality of life may also be disturbed in acromegaly. As depression levels rose, numerous subdomain scores related to quality of life experienced a decline. Additionally, heightened anxiety corresponded with reductions in specific domains of quality of life in cases with acromegaly. Furthermore, individuals in the acromegaly cohort exhibited a decline in vitality scores, which assess overall energy and fatigue, as levels of DHEA and DHEAS increased.

Increased anxiety in acromegaly is a controversial topic since some argue in favor of increased anxiety levels in acromegaly cases, whereas others argue against it [5, 7, 17–19]. In this cohort, cases with acromegaly had higher scores on both depression and anxiety scores, meaning depression and anxiety levels were higher in cases with acromegaly compared to those in healthy controls. Neither depression nor anxiety was related to actual hormone levels, disease duration, remission status, medical treatment, history of radiotherapy, and hypopituitarism. The findings indicate that variables beyond those directly linked to the disease may also contribute to heightened levels of depressive mood and anxiety among these individuals. In individuals diagnosed with acromegaly, there existed a correlation between depression and anxiety, potentially due to the influence of a mood disturbence on the patients' anxiety levels. This study concluded that there was no discernible association between anxiety and the neurosteroids we investigated in patients with acromegaly, although our earlier work established a connection between DHEA levels and depressive symptoms [20].

The condition of acromegaly influences not just emotional states but also the QoL experienced by individuals [5, 6, 21–23]. The impact of acromegaly on QoL may arise from both the characteristics of the disease itself and the accompanying mood-related challenges. Consistent with earlier findings, this investigation revealed that all dimensions of the SF-36, with the exception of emotional well-being, exhibited diminished scores in individuals diagnosed with acromegaly. Lower scores in physical function suggest a decline in physical activity capabilities, while reduced pain scores indicate that those with acromegaly may experience heightened pain sensitivity. Additionally, decreased role limitation scores due to health issues imply that these individuals may struggle with work and daily life. Lower social functioning scores reflect disruptions in social activities, while diminished vitality scores suggest feelings of exhaustion. Lastly, lower general health perception scores reveal a sense of hopelessness regarding their overall health status. In this research, higher BDI scores were linked to role limitations from emotional difficulties, as well as lower vitality, social functioning, and general health scores, with additional negative correlations observed between vitality, social functioning, and BAI scores. The relationship between quality of life and the presence of depression and anxiety in individuals with acromegaly has been previously established [6, 24]. The present research found a positive relationship between BDI and BAI. This suggests that levels of depression and anxiety may independently affect quality of life, or their interconnectedness might lead to overlapping influences. Therefore, we conducted a multiple regression analysis that revealed depression as the key predictor of reduced QoL in individuals with acromegaly. Additional analysis demonstrated that depression plays a significant role in influencing the connection between anxiety levels and aspects such as general health, vitality, and social functioning. The findings from both regression and mediation analyses indicate that depression has a more substantial impact on QoL —particularly in specific domains—compared to anxiety.

The impact on quality of life may not be fully understood through mood-related aspects alone. Might factors associated with the illness or its therapeutic interventions have contributed to the outcome? Consistent with earlier findings, our research similarly revealed no relationship between SF-36 domain scores and factors such as remission status, history of radiotherapy, hypopituitarism, comorbid conditions, or medical interventions [5, 6, 24].

Subsequently, what additional factors could have impacted the quality of life? In order to gain a deeper insight into the fundamental pathophysiology, we investigated the correlation between QoL metrics and NSs. In prior research, we demonstrated that NS had a role in the depressive perception in cases with acromegaly [5, 6, 24]. This research further revealed that both DHEA and DHEAS correlated with diminished energy levels and negative perceptions of overall health among individuals afflicted with acromegaly. Indeed, DHEA has been recognized for its capacity to enhance both emotional well-being and physical performance [25] In our prior investigation, we demonstrated a link between DHEA levels and depressive mood in acromegaly [25]. Additionally, the detrimental influence of DHEA on the QoL in patients suffering from acromegaly could also be attributed to the factor of depression. In healthy individuals, various NS exhibited associations with distinct domains of QoL. The disparate hormonal dynamics between patients with acromegaly and their healthy counterparts may have resulted in differing effects of NS.

This research is subject to specific constraints, with the primary limitation being its reliance on a cross-sectional design. Secondly, the challenges associated with managing a rare disease have constrained the size the sample population.

Lastly, NSs can be secreted and function locally. The plasma levels may not reflect local NS concentrations. A direct method of demonstrating local levels and autocrine or paracrine actions of NSs in the CNS may be through tissue samples. Additionally, regarding statistics, small sample sizes can be added to the limitations for conducting mediation analysis. Additionally, employing ELISA as a method of assessment may have introduced some constraints to a certain extent.

In conclusion, there are specific alterations in the status of mood and anxiety in cases with acromegaly. In acromegaly, it is evident that depression, rather than anxiety, emerged as a more influential factor in diminishing the overall QoL. Changes in the NS balance due to acromegaly could potentially influence these alterations.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Conflict of Interest The authors declare no competing interests.

References

1. Hatipoglu E, Hacioglu Y, Polat Y, Arslan HF, Oner S, Ekmekci OB, et al. Do neurosteroids have impact on depression and cognitive functions in cases with acromegaly? Growth Hormone IGF Res. 2022. https://doi.org/10.1016/j.ghir.2022.101496.
2. Broersen LHA, Zamanipoor Najafabadi AH, Pereira AM, Dekkers OM, Van Furth WR, Biermasz NR. Improvement in symptoms and health-related quality of life in acromegaly patients: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2021;106:577–87. https://doi.org/10.1210/clinem/dgaa868.
3. Van Der Klaauw AA, Kars M, Biermasz NR, Roelfsema F, Dekkers OM, Corssmit EP, et al. Disease-specific impairments in quality of life during long-term follow-up of patients with different pituitary adenomas. Clin Endocrinol (Oxf). 2008;69:775–84.
4. Sievers C, Ising M, Pfister H, Dimopoulou C, Schneider HJ, Roemmler J, et al. Personality in patients with pituitary adenomas is characterized by increased anxiety-related traits: comparison of 70 acromegalic patients with patients with non-functioning pituitary adenomas and age-and gender-matched controls. Eur J Endocrinol. 2009;160:367–73.
5. Kyriakakis N, Lynch J, Gilbey SG, Webb SM, Murray RD. Impaired quality of life in patients with treated acromegaly despite long-term biochemically stable disease: results from a 5-years prospective study. Clin Endocrinol (Oxf). 2017;86:806–15.
6. Geraedts VJ, Dimopoulou C, Auer M, Schopohl J, Stalla GK, Sievers C. Health outcomes in acromegaly: depression and anxiety are promising targets for improving reduced quality of life. Front Endocrinol (Lausanne). 2015;5:229.
7. Kan EK, Atmaca A, Sarisoy G, Ecemis GC, Gokosmanoglu F. Personality traits in acromegalic patients: comparison with patients with non-functioning adenomas and healthy controls. Growth Hormon IGF Res. 2022;62: 101439.
8. Schüle C, Nothdurfter C, Rupprecht R. The role of allopregnanolone in depression and anxiety. Prog Neurobiol. 2014;113:79–87.
9. Longone P, Rupprecht R, Manieri GA, Bernardi G, Romeo E, Pasini A. The complex roles of neurosteroids in depression and anxiety disorders. Neurochem Int. 2008;52:596–601.
10. Chen S, Gao L, Li X, Ye Y. Allopregnanolone in mood disorders: mechanism and therapeutic development. Pharmacol Res. 2021;169: 105682.
11. Chen C-Y, Wu C-C, Huang Y-C, Hung C-F, Wang L-J. Gender differences in the relationships among neurosteroid serum levels, cognitive function, and quality of life. Neuropsychiatr Dis Treat. 2018;14:2389.
12. Ulusoy M. Beck Anksiyete Envanteri (1993) geçerlik ve güvenirlik çalışması. Prof.Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi
13. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56:893–7. https://doi.org/10.1037/0022-006X.56.6.893.
14. Ware JE Jr, Sherbourne CD, Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care. 1992;30:473–83. https://doi.org/10.1097/00005650-199206000-00002.
15. Koçyiğit H, Aydemir Ö, Ölmez N, Memiş A. Reliability and validity of the turkish version of short form-36 (SF-36). İlaç Ve Tedavi Dergisi. 1999;12:102–6.
16. Gallucci M. jAMM: jamovi Advanced Mediation Models 2020.
17. Sievers C, Dimopoulou C, Pfister H, Lieb R, Steffin B, Roemmler J, et al. Prevalence of mental disorders in acromegaly: a cross-sectional study in 81 acromegalic patients. Clin Endocrinol (Oxf). 2009;71:691–701.
18. Imran SA, Tiemensma J, Kaiser SM, Vallis M, Doucette S, Abidi E, et al. Morphometric changes correlate with poor psychological outcomes in patients with acromegaly. Eur J Endocrinol. 2016;174:41–50.
19. Pereira AM, Tiemensma J, Romijn JA, Biermasz NR. Cognitive impairment and psychopathology in patients with pituitary diseases. Neth J Med. 2012;70:255–60.
20. Peixoto C, Grande AJ, Mallmann MB, Nardi AE, Cardoso A, Veras AB. Dehydroepiandrosterone (DHEA) for depression: a Systematic review and meta-analysis. CNS Neurol Disord Drug Targets. 2018;17:706–11. https://doi.org/10.2174/1871527317666180817153914.

21. Guo X, Wang K, Yu S, Gao L, Wang Z, Zhu H, et al. Quality of life and its determinants in patients with treated acromegaly: a cross-sectional nationwide study in China. J Clin Endocrinol Metab. 2021;106:211–25.
22. Rowles SV, Prieto L, Badia X, Shalet SM, Webb SM, Trainer PJ. Quality of life (QOL) in patients with acromegaly is severely impaired: use of a novel measure of QOL: acromegaly quality of life questionnaire. J Clin Endocrinol Metab. 2005;90:3337–41.
23. Szcześniak DM, Jawiarczyk-Przybyłowska A, Matusiak Ł, Bolanowska A, Maciaszek J, Siemińska M, et al. Is there any difference in acromegaly and other chronic disease in quality of life and psychiatric morbidity? Endokrynol Pol. 2017;68:524–32.
24. Geraedts VJ, Andela CD, Stalla GK, Pereira AM, van Furth WR, Sievers C, et al. Predictors of quality of life in acromegaly: No consensus on biochemical parameters. Front Endocrinol (Lausanne). 2017. https://doi.org/10.3389/fendo.2017.00040.
25. Kritz-Silverstein D, Von Mühlen D, Laughlin GA, Bettencourt R. Effects of dehydroepiandrosterone supplementation on cognitive function and quality of life: The DHEA and well-ness (DAWN) trial. J Am Geriatr Soc. 2008;56:1292–8. https://doi.org/10.1111/j.1532-5415.2008.01768.x.