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The Correlation Between Serum Uric Acid Level and Certain Clinical Variables in Antisocial Personality Disorder Patients

Antisosyal Kişilik Bozukluğu Tanılı Hastalarda Serum Ürik Asit Seviyesi ve Klinik Değişkenler Arasındaki İlişki

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ABSTRACT

Objectives: In this study, we aimed to compare serum uric acid levels in patients diagnosed with antisocial personality disorder with a healthy control group, and also to investigate the relationship between serum uric acid levels and impulsivity and aggressive attitudes.

Methods: The study was conducted with 126 individuals (69 with antisocial personality disorder, 57 controls). The Sociodemographic Data Form, the Barratt Impulsivity Scale (BIS-11), and the Buss–Durkee-Hostility Inventory (BDHI) were applied to all participants. Venous blood samples were collected from all participants to measure serum uric acid levels.

Results: It was determined that both the BIS-11 and the BDHI sub-dimensions, and the total scores of the antisocial personality disorder patients were higher when compared to the healthy control group. The serum uric acid levels of the patient group were significantly higher when compared to those of the control group. Furthermore, there was a significant positive correlation between serum uric acid level and Barratt Impulsivity Scale–11 ($r = 0.635$, $P < .001$) and Buss–Durkee Hostility Inventory ($r = 0.572$, $P < .001$) scores.

Conclusion: In our study, it was found that serum uric acid levels were higher in patients with antisocial personality disorder, which is characterized by impulsivity and aggressive behavior, when compared to the control group. The findings of the present study suggest that purinergic dysfunction may also play a role in the etiopathogenesis of the disease. Further studies are required to determine whether this was a cause or an outcome.

Keywords: Antisocial personality, uric acid, impulsivity, aggression

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ÖZ

Amaç: Bu çalışmada, Antisosyal Kişilik Bozukluğu (ASKB) tanısı olan hastalarda serum ürik asit seviyelerini sağlıklı kontrol grubu ile karşılaştırmak ayrıca serum ürik asit düzeylerinin dürtüsellik ve saldırgan tutumlar ile ilişkisini araştırmayı amaçladık.

Yöntemler: Çalışmaya 69 ASKB, 57 sağlıklı kontrol olmak üzere 126 kişi dahil edildi. Bütün katılımcılara sosyodemografik veri formu, Barratt Dürtüsellik Ölçeği (BIS-11), Buss-Durkee Hostilite Ölçeği (BDHÖ) uygulandı. Tüm katılımcılardan venöz kan örneği alındı ve serum ürik asit değerleri ölçüldü. Analizler SPSS 22 paket programında değerlendirildi.

Bulgular: ASKB tanılı bireylerin hem BIS- 11 hem de BDHÖ alt boyutları ve toplam puanı sağlıklı kontrol grubundan yüksek bulundu. Hasta grubun serum ürik asit seviyesi kontrol grubundan anlamlı şekilde yüksek saptandı. Ayrıca serum ürik asit ile BIS-11 ($r = 0,635$, $P < ,001$) ve BDHÖ ($r = 0,572$, $P < ,001$) ölçek puanı arasında pozitif yönde anlamlı korelasyon olduğu görüldü.

Sonuç: Çalışmamızda, dürtüselliğin ve saldırgan davranışların ön planda olduğu ASKB hastalarında, kontrol grubuna göre serum ürik asit seviyelerinin yüksek olduğu bulunmuştur. Bulgularımız, hastalığın etiyopatogenezinde, purinerjik disfonksiyonun da bir rolü olabileceğini işaret etmektedir. Bu durumun sebep mi yoksa sonuç mu olduğunu belirleyebilmek için daha fazla sayıda araştırmaya ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Antisosyal kişilik, dürtüsellik, saldırganlık, ürik asit

INTRODUCTION

Antisocial personality disorder (ASPD) is a psychological disorder characterized by behavioral disorders before the age of 18 and by clinical symptoms such as criminal acts, deception, irresponsibility, and impulsivity after the age of 18. ASPD is a treatment-resistant chronic disease that leads to unrest in the patient's environment and negatively affects familial and professional life.[1]

Patients with ASPD are less likely to prevent an action they enjoy.[2] These patients exhibit impulsive behaviors that are inadequate and unplanned for the environment, often with undesirable consequences, harming the patient or others.[3] Impulsivity is manifested as impatience, novelty, and excitement-seeking, risk-taking behavior, and the inability to calculate the possibility of harm. Impulsivity is the main component of several psychiatric disorders, including bipolar disorder, attention deficit hyperactivity disorder, substance abuse, and antisocial personality disorder.[4,5] Aggressive behaviors that cause verbal, physical, or indirect harm and could be observed in several psychiatric disorders are also a general behavioral pattern in ASPD cases.[1,6] Previous studies have suggested that impulsivity and aggressive behavior have a physiological foundation, and were increasingly interested in the investigation of biomarkers associated with this condition.[7] Serum uric acid level is a promising candidate for such research. Uric acid, the end-product of purine metabolism, functions as an endogenous antioxidant and neuroprotectant.[8]

It is known that serum uric acid levels increase under chronic psychological stress.[9] Although it has not been directly associated with impulsivity, uric acid has been studied in several psychiatric disorders characterized by impulsivity. In a study on pathological gambling addiction, where impulsivity is prevalent, it was determined that serum uric acid levels were higher in the patient group when compared to healthy individuals.[10] In a study conducted in the forensic psychiatry service that hosts violent offenders, it was demonstrated that the uric acid levels of aggressive individuals were higher.[11] Based on this evidence, we were curious about the correlation between clinical variables and serum uric acid levels in ASPD, in which aggression and impulsivity are prevalent. The hypothesis of this study is that high serum uric acid levels are associated with impulsivity and aggressive behaviors in individuals with ASPD. We believe that identifying a biomarker that may be associated with impulsivity and aggression in ASPD will contribute to the literature.

METHODS

The approval of the Firat University Ethics Committee (Date: February 25, 2021, Number: 2021-19384) was obtained for the research study, and the study was conducted in accordance with the Helsinki Declaration. Eighty-seven ASPD patients who were admitted in the psychiatry outpatient clinic at Firat University and treated in the outpatient or inpatient clinics and 57 volunteering hospital staff without prior psychiatric treatment and a history of systemic disease were included in the study. Since ASPD is more prevalent in the male population, only male patients were included in the study. Patients under drug treatment for an autoimmune disorder, liver disorder, gout, hypertension, hypercholesterolemia, diabetes, or thyroid disorder, patients with cancer, and patients who were taking corticosteroids or anti-inflammatory drugs were excluded from the study. In addition, patients with psychiatric diseases other than adjustment disorder and those using psychiatric drugs were not included in the study. Ten participants did not volunteer to participate in the study afterward, 8 individuals were excluded from the study due to missing responses in the scale. Our study group included 69 patients and 57 healthy male control group members with similar sociodemographic characteristics and body mass index. The interviews were conducted in the psychiatry outpatient clinic, and lasted at least 30 minutes based on the DSM-5. Written informed consent forms were obtained from all cases before the analysis.

Data Collection Instruments

The sociodemographic data form included demographic information such as age, marital status, educational status, place of

residence, employment, alcohol/substance use, smoking, and the presence of a physical wound (self-inflicted). The height and weight measurements of all participants were taken with the same scale at the hospital.

Buss–Durkee Hostility Inventory: The Buss–Durkee Hostility Inventory (BDHI) was developed to determine the aggression potential of individuals. It is a 34-point Likert-type self-report inventory where each item is scored between 1 and 5. Its sub-dimensions include physical aggression, verbal aggression, anger, hostility, and indirect aggression. Furthermore, the total aggression level is calculated based on the total score; a high score indicates a high aggression potential. The validity and reliability of the scale were confirmed.[12,13]

Barratt Impulsiveness Scale-11: The Barratt Impulsiveness scale-11 (BIS-11) is a 30-item self-report scale employed to determine impulsivity. It includes 3 subscales: (1) attentional (cognitive instability, and attention); (2) non-planning (cognitive complexity and self-control); and (3) motor (motor and perseverance). It was reported that a high total score depicts high impulsivity. It was developed by Patton et al. and Turkish validity and reliability were studied by Güleç et al.[14,15]

Analysis of the Serum Uric Acid Levels

Samples of 5 cm^3 fasting venous blood were obtained from the antecubital vein and collected into biochemistry tubes for analysis from all participants, and were examined in the biochemistry laboratory. The samples were studied within half an hour, using the Siemens Advia 2400 device (Siemens Healthcare, Erlangen, Germany), and the patients' results were uploaded to the patient registry system within 2 hours. The uric acid reference range was 3.4-7 in the device.

Statistical Analysis

The analyses were conducted with the SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, Ill, USA) version 22 software. Descriptive study data are presented in counts and percentages for the categorical data, and in mean ± standard deviation (mean ± SD) and median interquartile range (25-75 percentiles) for the continuous data. Chi-square analysis (Pearson chi-square) was employed to compare categorical variables between the groups. The normal distribution of continuous variables was determined with the Kolmogorov–Smirnov test. The comparison of paired groups was conducted with Student's *t*-test for variables with normal distribution, and with the Mann–Whitney U-test for variables that did not exhibit normal distribution. The correlations between the continuous variables with normal distribution were determined with the Pearson correlation test, and Spearman's correlation test was employed for the variables without normal distribution. The statistical significance level was accepted as $P < .05$ in the analyses.

RESULTS

The study was conducted with 126 participants, including 69 male ASPD patients and 57 male healthy individuals in the control group. The mean age of the patient group was 34.8 ± 11.2 years and the mean age of the control group was 34.1 ± 6.3 years.

The rate of unmarried individuals (39.1%) in the patient group was significantly higher when compared to the rate of unmarried individuals (17.5%) in the control group ($P = .008$). The rate of education at middle school level and below in the ASPD group (63.8%) was significantly higher when compared to the rate of education at middle school level and below (14.0%) in the control group ($P < .001$). The rate of low-income individuals in the patient group (53.6%) was significantly higher when compared to that in the control group (28.1%) ($P = .004$). In the ASPD group, 29% of the patients had comorbid psychiatric diseases, while none had a comorbid psychiatric disease in the control group ($P < .001$). While 40.6% of the patients underwent previous psychiatric treatment, none of the controls underwent previous psychiatric treatment ($P < .001$). The rate of psychiatric illness in the family history of the patient group (53.6%) was significantly higher when compared to the control group (14%) ($P < .001$). Self-mutilation was observed in 68.1% of ASPD patients, while no one exhibited this behavior in the control group ($P < .001$). The rate of attempted suicide was 49.3% in the patient group, while there was no suicide attempt in the control group ($P < .001$). The rate of smoking in the patient group (82.6%) was significantly higher when compared to the control group (10.5%) ($P < .001$). While 60.9% of the ASPD patients consumed alcohol or other substance, no one in the control group did ($P < .001$) (Table 1).

The uric acid levels, BIS-11 sub-dimension and total scores, and BDHI total scores of the individuals diagnosed with ASPD were significantly higher when compared to the control group (Table 2, Figure 1).

It was observed that there was a significant positive correlation between uric acid level and BIS-11 and BDHI scale scores. Furthermore, a significant positive correlation was determined between BIS-11 and BDHI scale scores ($P < .01$, $r = 0.794$) (Table 3 and Figure 2).

DISCUSSION

In the present study, it was determined that serum uric acid levels were higher in ASPD patients when compared to healthy controls. There was also a positive correlation between uric acid levels and impulsivity and aggression scores in the patient group.

Since most personality disorder patients were males, based on the sociodemographic data, only male individuals were assigned to the healthy control group.

It is known that individuals with ASPD are significantly impulsive and that these individuals cannot delay their behavior.[6,16] Similar to the study conducted by Lijffijt et al[17] on ASPD patients, we determined that the BIS-11 scale total and sub-dimension scores of the patient group were higher when compared to those of the control group. It has also been evidenced that ASPD patients exhibit aggressive behavior toward themselves as well as others,[17,18] and we determined that the Buss–Durkee scores of the patient group were higher in each subscale when compared to the control group.

The effect of serum uric acid on impulsivity was evidenced with the Lesch–Nyhan syndrome.[19] Individuals with this syndrome exhibit an enzyme deficiency that leads to uric acid accumulation, and impulsive behavior is dominant in the clinical manifestation of the Lesch–Nyhan syndrome. There are studies in the literature that have reported a positive correlation between impulsivity and uric acid levels in animals.[20]

The majority of the patient group included individuals with a lower education level when compared to the healthy control group. This finding was consistent with previous study findings as well. It is known that individuals diagnosed with ASPD could not complete

Table 1. Comparison of the Sociodemographic Data of the Patient and Control Groups

	Patient (n = 69)	Control (n = 57)	Total (n = 126)	
	n (%)	n (%)	n (%)	*P**
Age, mean ± SS	34.8 ± 11.2	34.1 ± 6.3	34.5 ± 9.3	.650**
Marital status				
Unmarried	27 (39.1)	10 (17.5)	37 (29.4)	**.008**
Married	42 (60.9)	47 (82.5)	89 (70.6)	
Education level				
Middle school or lower	44 (63.8)	8 (14.0)	52 (41.3)	**<.001**
High school or higher	25 (36.2)	49 (86.0)	74 (58.7)	
Place of residence				
Village/town	25 (36.2)	12 (21.1)	37 (29.4)	.063
Urban	44 (63.8)	45 (78.9)	89 (70.6)	
Income level				
Low	37 (53.6)	16 (28.1)	53 (42.1)	**.004**
Medium	32 (46.4)	41 (71.9)	73 (57.9)	
Employment				
Employed	34 (49.3)	32 (56.1)	66 (52.4)	.443
Unemployed	35 (50.7)	25 (43.9)	60 (47.6)	
Comorbid organic disease				
Yes	1 (1.4)	3 (5.3)	4 (3.2)	.328
No	68 (98.6)	54 (94.7)	122 (96.8)	
Comorbid psychiatric disease				
Yes	20 (29.0)	0 (0.0)	20 (15.9)	**<.001**
No	49 (71.0)	57 (100.0)	106 (84.1)	
Prior psychiatric treatment				
Yes	28 (40.6)	0 (0.0)	28 (22.2)	**<.001**
No	41 (59.4)	57 (100.0)	98 (77.8)	
Psychiatric disorder history in the family				
Yes	37 (53.6)	8 (14.0)	45 (35.7)	**<.001**
No	32 (46.4)	49 (86.0)	81 (64.3)	
Self-mutilation				
Yes	47 (68.1)	0 (0.0)	47 (37.3)	**<.001**
No	22 (31.9)	57 (100.0)	79 (62.7)	
Suicide history				
Yes	34 (49.3)	0 (0.0)	34 (27.0)	**<.001**
No	35 (50.7)	57 (100.0)	92 (73.0)	
Smoking				
Yes	57 (82.6)	6 (10.5)	63 (50.0)	**<.001**
No	12 (17.4)	51 (89.5)	63 (50.0)	
Alcohol/substance consumption				
Yes	42 (60.9)	0 (0.0)	42 (33.3)	**<.001**
No	27 (39.1)	57 (100)	84 (66.7)	

*Chi-square analysis; **Student's *t*-test.
The statistical significance level in the analyses was accepted as $P < .05$.
SD, standard deviation.

their education due to behavioral disorders and impulsivity.[21] In the personality disorder group, smoking, alcohol and substance abuse rates were higher when compared to the control group. This was consistent with the literature and the diagnostic criteria for ASPD.[21] Moreover, similar to other studies,[22-24] most individuals in the ASPD group had self-inflicted cuts on their bodies and 49.3% had a history of suicide attempt.

It was also reported that uric acid levels were indicated as high in certain psychiatric diseases that could be accompanied by aggression and impulsivity symptoms.[25-27] Acutely increased uric acid levels are also known to induce locomotor activity and impulsivity in rats.[28] High urinary uric acid levels in adolescents have been associated with aggressive behavior.[29] In a study conducted by Ran et al.[30] it was reported that serum uric acid levels were elevated higher than controls in patients of depression accompanied by impulsivity. In another study, serum uric acid levels in major depressive disorder (MDD) patients with suicide risk (245.01 ± 55.44 µmol/L) (MDD) patients without suicide risk (274.17 ± 72.65 µmol/L), and healthy controls (271.42 ± 55.25 µmol/L) were significantly lower. In conclusion, it was stated that low serum uric level may be associated with suicide risk in MDD patients.[31] In 2016, researchers studied impulsivity and serum uric acid levels in individuals with substance use disorder and found that the serum uric

Table 2. Comparison of Patient and Control Group Uric Acid Levels and Scale Scores

	Patient	Control	
	Median (IQR)	Median (IQR)	*P**
Uric acid	5.9 (5.0-6.7)	4.3 (3.7-5.4)	**<.001**
BSI-SF-11-motor	27.0 (23.0-31.0)	12.0 (11.0-16.0)	**<.001**
BSI-SF-11-attentional	21.0 (17.0-23.0)	11.0 (9.0-12.0)	**<.001**
BSI-SF-11-non-planning	28.0 (23.0-31.0)	13.0 (12.0-14.0)	**<.001**
BSI-SF-11 total	76.0 (65.0-82.0)	36.0 (32.0-41.0)	**<.001**
BDHI-physical aggression	29.0 (23.0-33.0)	11.0 (9.0-13.0)	**<.001**
BDHI-verbal aggression	18.0 (16.0-21.0)	9.0 (8.0-10.0)	**<.001**
BDHI-anger	26.0 (23.0-28.0)	10.0 (9.0-12.0)	**<.001**
BDHI-hostility	25.0 (22.0-30.0)	7.0 (5.0-9.0)	**<.001**
BDHI total	98.0 (85.0-108.0)	35.0 (34.0-41.0)	**<.001**

*Mann–Whitney U-test was employed. IQR, Interquartile range.
The statistical significance level in the analyses was accepted as $P < .05$.
BIS-11, Barratt Impulsivity Scale; BDHI, Buss–Durke Hostility Inventory.

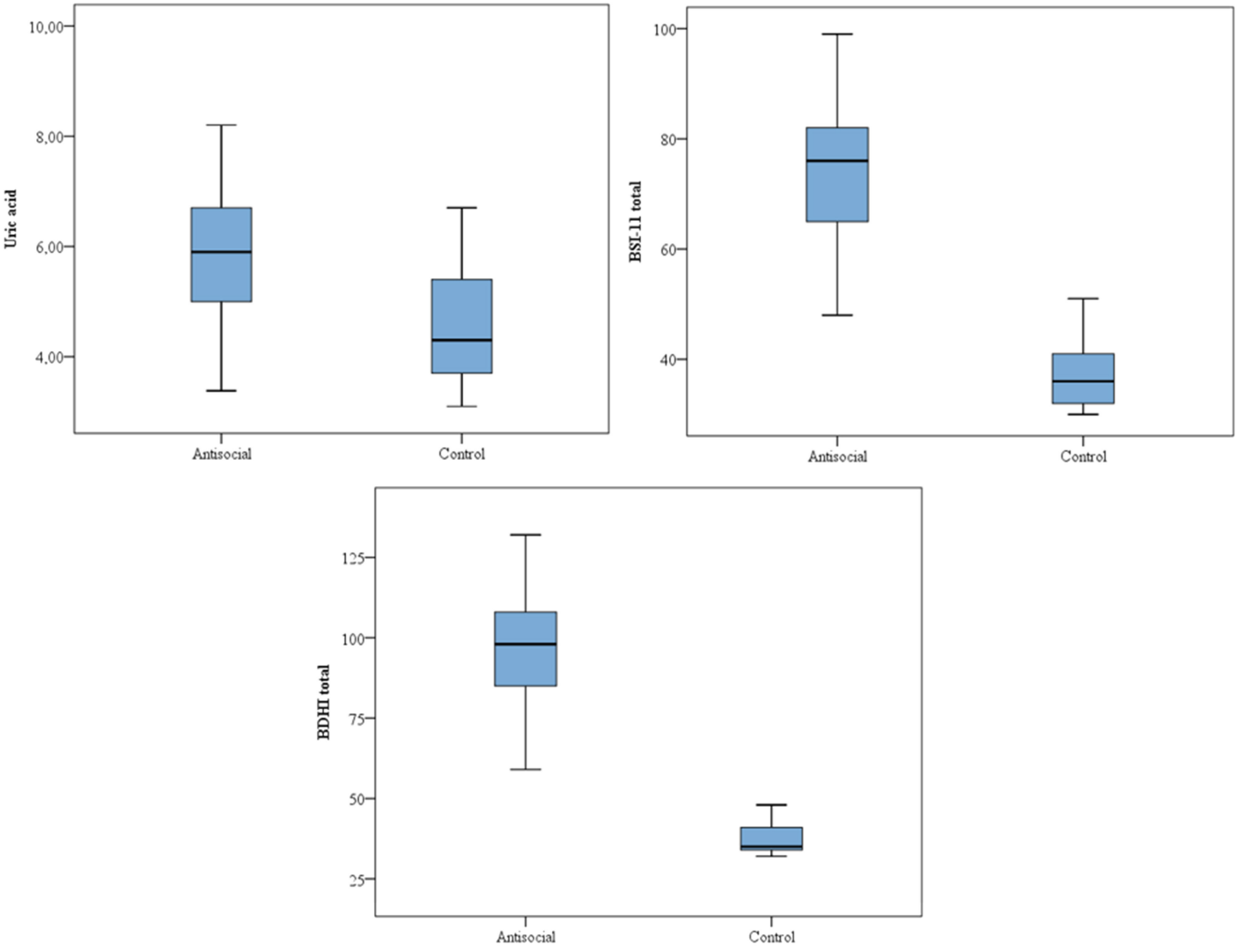

Figure 1. Comparison of uric acid levels and scale scores between the patient and control groups.

acid level in the patient group was significantly higher than in the control group.[32]Studies that investigated the correlation between the physiology of the purinergic system and mood disorders demonstrated that elevated uric acid levels affected intracellular signaling pathways, increasing the incidence of hallucinations, suicidal ideation, and mania.[26,27] This could explain the uric acid–impulsivity–mood disorder cycle. In the present study, it was determined that individuals with high impulsivity also had high serum uric acid levels and there was a positive correlation between these 2 variables, consistent with the literature.

Table 3. The Correlation Between Patient Group Uric Acid Levels and Scale Scores

		Uric Acid	BIS-11-Motor	BIS-11-Attention	BIS-11-Non-planning	BIS-11 Total	BDHI-Physical Aggression	BDHI—Verbal Aggression	BDHI-Anger	BDHI-Anger
BIS-11-motor	*r*	.627								
	P	.000								
BIS-11- attention	*r*	.575	.884							
	P	.000	.000							
BIS-11- non-planning	*r*	.602	.904	.893						
	P	.000	.000	.000						
BIS-11 total	*r*	.635	.968	.948	.962					
	P	.000	.000	.000	.000					
BDHI- physical aggression	*r*	.559	.784	.719	.759	.771				
	P	.000	.000	.000	.000	.000				
BDHI- verbal aggression	*r*	.562	.763	.699	.705	.736	.797			
	P	.000	.000	.000	.000	.000	.000			
BDHI- anger	*r*	.566	.792	.734	.768	.778	.865	.859		
	P	.000	.000	.000	.000	.000	.000	.000		
BDHI- hostility	*r*	.506	.799	.758	.757	.779	.808	.810	.863	
	P	.000	.000	.000	.000	.000	.000	.000	.000	
BDHI total	*r*	.572	.815	.748	.776	.794	.933	.895	.947	.917
	P	.000	.000	.000	.000	.000	.000	.000	.000	.000

The statistical significance level in the analyses was accepted as $P < .05$.
BIS-11, Barratt Impulsivity Scale; BDHI, Buss–Durke Hostility Inventory.

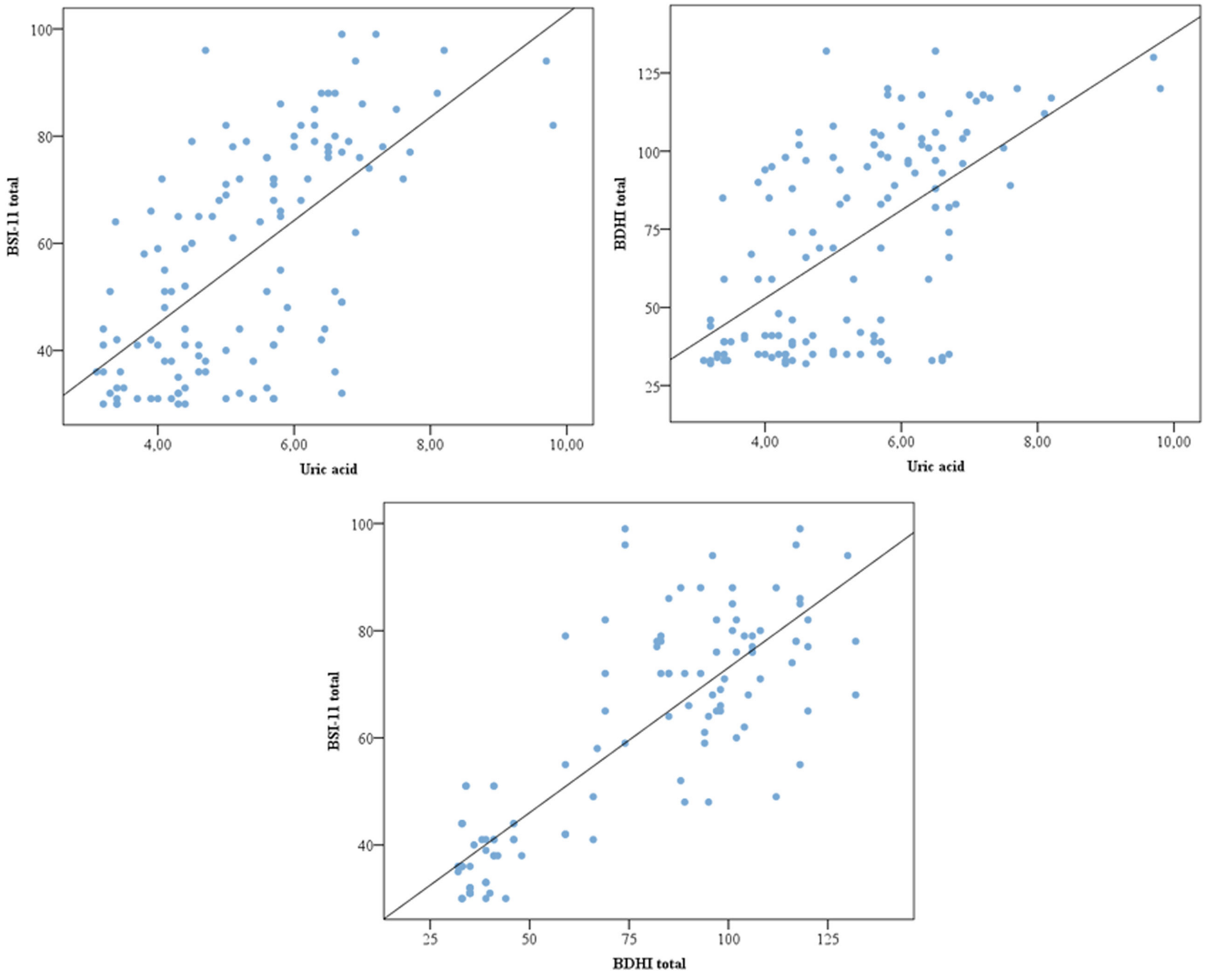

Figure 2. The correlation between uric acid levels and scale scores.

The literature review did not reveal a study where serum uric acid levels were investigated in ASPD patients. It could be stated that this was the first study conducted with this patient group. Since serum uric acid measurement is inexpensive and feasible, it can be considered as a biomarker that should be examined in clinical areas. However, the fact that our study was cross-sectional, the sample size was small, the study group included only male patients, and serum uric acid levels in the reference range in the patient and healthy control group could be considered as the important limitations of our study. Although people with psychiatric comorbidities other than adjustment disorder were not included in the study, the effect of alcohol and substance use on uric acid level was not examined, and the control and patient groups were not sociodemographically similar, which can be counted among the limitations of our study.

CONCLUSION

The study findings demonstrated that serum uric acid levels were higher in patients with ASPD when compared to the typical population. In the present study, it was determined that serum uric acid levels were higher in ASPD patients when compared to healthy controls, and a positive correlation between uric acid levels and impulsivity and aggression scores was demonstrated in the patient group. We think that the serum uric acid level is a parameter that should be examined in similar disease groups accompanied by impulsivity.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Fırat University (Date: February 25, 2021, Number: 2021-19384).

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

Peer Review: Externally peer-reviewed.

Author Contributions: Concept – S.Y.; Design – A.K., S.Y..; Supervision – S.K., K.U.; Resources – S.Y.; Data Collection and/or Processing – A.K.; Analysis and/or Interpretation – O.K.; Literature Search – S.Y., S.K.; Writing Manuscript – S.Y., A.K., S.K, K.U.; Critical Review – O.K., S.K., K.U.

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