Evaluation of dynamic thiol/disulfide balance and oxidative metabolism in patients with obsessive compulsive disorder

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SUMMARY

Objective: We aimed to compare Total Oxidant Level (TOL), Total Antioxidant Level (TAL), Oxidative Stress Index (OSI), Thiol/Disulfide levels, Plasma Malondialdehyde (MDA) levels in both plasma and erythrocyte patients with OCD and healthy controls.

Method: Our study included 47 patients with OCD and 49 healthy controls. Sociodemographic data form was applied to all participants, CGI and Y-BOCS were applied to the patient group. TAL and TOL measurements were made in both plasma and erythrocytes, and Malondialdehyde (MDA) and Thiol/Disulfide measurements were made only in plasma.

Results: TAL, TOL, OSI and MDA values in the plasma of the patient and control groups were compared, no statistically significant difference was found. However, erythrocyte TAS level was lower in the patient group ($p<0.05$) and OSI level was higher ($p<0.05$) in the patient group. While no difference was observed in plasma total thiol level in the patient group compared to the controls, plasma native thiol levels were significantly higher ($p<0.001$) and plasma disulfide levels were significantly lower ($p<0.05$).

Discussion: The high level of native thiol, an antioxidant molecule in plasma, in OCD patients can be interpreted as an effort to compensate for the decreased antioxidant capacity in erythrocytes. According to these results, we think that when evaluating oxidative stress parameters in psychiatric diseases such as OCD, it is important to study the thiol/disulfide ratio as well as the total oxidant capacity of the plasma, and it would be appropriate to measure these parameters not only in the plasma but also in the erythrocyte.

Key Words: Obsessive compulsive disorder, oxidative stress, thiol, disulfide, thiol/disulfide balance

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a chronic psychiatric condition characterized by obsessions and/or compulsions, leading to significant functional impairment (1). Although genetic predisposition and neurobiological factors are believed to contribute to the etiology of OCD, its pathophysiology remains not fully elucidated (1,2). In recent years, oxidative free radical damage has been proposed as a potential etiological factor for OCD (3).

Oxidative stress arises when there's an imbalance between the production and consumption of free radicals within an organism (4). This condition results in an increased formation of free radicals, impairment of the antioxidant defense mechanism, and consequently, tissue damage (4). It's known that the brain is sensitive to alterations in oxidative metabolism and possesses limited antioxidant capacity to tolerate oxidative stress (5,6). The identification of increasing neurodegenerative changes

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in neuropsychiatric disorders has given rise to the notion that oxidative damage may be integral to the etiology of these conditions (5,6). However, data on the role of oxidative stress in the complex neurobiological underpinnings of OCD pathophysiology are both limited and inconsistent. While some studies report no difference in oxidative stress levels in OCD, others suggest an alteration favoring either antioxidants or oxidants (7-10).

Erythrocytes, or red blood cells, are among the most affected by oxidative stress in the body (5). The limited metabolism of erythrocytes makes them susceptible to effects like oxidative stress exposure (11). Therefore, evaluating erythrocyte intracellular oxidative stress parameters in such studies, alongside plasma oxidative stress parameters, could be of significant importance.

Thiols, major and frequently utilized antioxidants in plasma, play a critical role in preventing the onset of oxidative stress in cells. They achieve this functionality through their sulfhydryl (-SH) groups. Reactive oxygen species oxidize thiols in the environment, leading to the formation of disulfides. The dynamic thiol/disulfide balance is key in antioxidant protection, signal transmission, apoptosis, enzymatic activity, transcription factor regulation, and cellular signaling mechanisms (12). Evaluating the thiol/disulfide homeostasis is considered critically important in understanding the role of oxidative stress in the pathogenesis of diseases (12). Abnormal levels of thiol/disulfide balance have been demonstrated to be involved in the pathogenesis of various diseases (13,14,15). Literature does contain studies examining the relationship between the thiol/disulfide balance and certain psychiatric diseases (16,17,18). However, no study investigating the thiol/disulfide balance in adult patients diagnosed with OCD undergoing treatment has been encountered.

In our research, our primary objective was to evaluate oxidative stress parameters, specifically in the context of the thiol-disulfide balance, in adult patients diagnosed with OCD who were undergoing pharmacological treatment. In addition, besides samples taken from plasma, we aimed to assess parameters related to the oxidative system in erythrocytes, given their capacity to reflect cellular-level changes. Thus, in both patients with OCD and healthy controls, we sought to compare levels of Total Oxidant Level (TOL), Total Antioxidant Level (TAL), Oxidative Stress Index (OSI), Thiol/Disulfide levels, and Plasma Malondialdehyde (MDA) levels in both plasma and erythrocytes. Furthermore, we hypothesized a potential relationship between the severity of obsessive-compulsive symptoms, levels of functionality, and the balance of thiol/disulfide along with oxidative markers. We believe that our study will contribute to the literature by providing data related to the thiol/disulfide balance and oxidative system parameters in both plasma and erythrocytes within the context of OCD.

METHOD

Our study sample comprised patients diagnosed with OCD and healthy controls who were matched with the patient group in terms of age and gender.

Based on the power analysis conducted, to compare the patient and control groups with a confidence level of 95% (alpha=0.05) and a power of 80% (beta=0.80), the required minimum sample size per group was calculated to be 41, assuming an effect size of 0.63.

Participants included in our study were aged between 18 and 65, had at least basic literacy, did not have any known chronic physical illnesses as verified by medical records and self-report, had no substance use disorders, and did not exhibit medical conditions such as rheumatological diseases, neurological diseases, severe obesity, pregnancy, vascular diseases, or history of traumatic brain injury. Moreover, participants who had been taking xanthine oxidase inhibitors (e.g., allopurinol, folic acid) or agents with antioxidant properties (e.g., vitamin E, vitamin C, N-acetyl cysteine) were excluded.

Between December 2020 and June 2021, 62 patients who presented to the outpatient clinic of a university hospital's psychiatry department and were diagnosed with OCD by a psychiatric specialist/assistant according to DSM-5 were evaluated for participation in the study (19). Eight patients were excluded due to incomplete survey responses, and seven were excluded due to the presence of concurrent psychiatric or chronic metabolic diseases determined after psychiatric assessment. Ultimately, 47 patients diagnosed with OCD with-

out co-morbid psychiatric conditions were included in the study. All these patients were undergoing treatment with drugs from the Selective Serotonin Reuptake Inhibitor (SSRI) group. All the patients included in the study had been under pharmacotherapy for at least two years, but had recently presented to the outpatient clinic due to exacerbated OCD symptoms. The healthy control group consisted of 49 health workers from our hospital, none of whom had any psychiatric illnesses.

Ethical approval for this research was obtained from İnönü University Faculty of Medicine, Medical Ethics Committee with the decision number 19.02.2019/ 81. Informed consent was duly obtained from all participants.

Procedure

In our study, all participants were administered a Socio-demographic data form. Participants in the patient group were additionally assessed using the Clinical Global Impression Scale (CGI) and the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). These evaluations were conducted by an interviewer, taking approximately 30-45 minutes. Subsequently, blood samples were collected from all participants.

Measurment Tools

Sociodemographic Data Form: A semi-structured interview schedule created by the researchers conducting the study, the Sociodemographic Data Form queries information regarding age, gender, marital status, education, smoking habits, and past substance use history (not currently using).

Clinical Global Impression Scale (CGI): The Clinical Global Impression Scale (CGI) is used to evaluate clinical progression across all psychiatric disorders (20). The scale comprises three sub-dimensions and sheds light on symptom improvements and severity. It's a semi-structured scale filled out during the interview. The first two sub-dimensions are in a seven-point Likert scale format, revealing overall improvement and severity of the disease. The last sub-dimension reveals the efficacy index, based on a four-point Likert scale.

Yale-Brown Obsessive Compulsive Scale (Y-BOCS): Y-BOCS is a scale developed to grade the quality and severity of OCD symptoms (21,22). Administered by the interviewer, it consists of 19 items; however, only the first ten items are used to determine the total score. The first five items assess obsessions, while items 6 to 10 evaluate compulsions. Each item is scored between 0 and 4, with total scores ranging from 0 to 40. The scale's validity and reliability in Turkish were studied by Karamustafalıoğlu et al. in 1993 (23).

Measurement and Calculation of Variables Biochemical Analysis

Blood samples were taken from both the patient and control groups after 12 hours of fasting from the antecubital vein. Blood drawn into anticoagulant full blood tubes was centrifuged at 3,000 rpm for six minutes to collect serum. The erythrocyte pack's bottom phase was washed twice with saline, obtaining erythrocyte packets. Both plasma and erythrocyte packs were stored in storage tubes at -80°C until analysis. On the analysis day, samples were thawed, and measurements of MDA, TAL, TOL, total thiol, and native thiol were taken, and OSI was calculated.

Measurement of Total Antioxidant Level (TAL): TAL is a method that measures the intracellular and extracellular total antioxidant capacity of the body. The measurement of total antioxidant status was performed with a commercial kit (RelAssay Diagnostic, Turkey). This method relies on the principle that antioxidants in the sample convert ABTS radicals from a deep blue-green color to a colorless ABTS state (24). As specified in the kit, in an ELISA device set to 25 °C, 500 μL of reagent 1 (measurement buffer) and 30 μL of serum were mixed, and the absorbance was measured at 660 nm. This mixture was incubated with 75 μL of reagent 2 (colored ABTS solution) for 10 minutes, and subsequently, the absorbance was measured again at 660 nm to calculate TAL levels.

Measurement of Total Oxidant Level (TOL): TOL represents the cumulative value of oxidative stress in the body. The total oxidant level measurement was performed with a commercial kit (RelAssay

Diagnostic, Turkey). This method is based on the color difference resulting from the interaction between ferrous ion-chelator complexes being oxidized to ferric ions by the oxidants in the sample and a chromogenic substance in an acidic environment (25). As specified in the kit, in an ELISA device set to 25 °C, 500 μL of reagent 1 (measurement buffer) and 75 μL of serum were mixed, and the absorbance was measured at 530 nm. This mixture was incubated with 25 μL of reagent 2 (prochromogen solution) for 10 minutes, and subsequently, the absorbance was measured again at 660 nm to calculate TOL levels.

Calculation of Oxidative Stress Index (OSI): The Oxidative Stress Index (OSI) was determined using the Total Oxidant Status (TOL)/Total Antioxidant Status (TAL) formula (26).

Measurement of Plasma Malondialdehyde (MDA): Level MDA level was measured in plasma. MDA, one of the final products of lipid peroxidation, serves as an indirect indicator of oxidation. MDA measurement was conducted according to the method of Uchiyama et al. (27). MDA levels were measured by reading the color change resulting from the supernatant's reaction with thiobarbituric acid at 95 °C in the n-butanol phase using a spectrophotometer at 535 and 520 nm.

Measurement of Thiol/Disulfide Levels: Thiol-disulfide was evaluated from serum samples. The thiol-disulfide level (native thiol (-SH) – disulfide (-S-S-)) was determined using a commercial kit (RelAssay Diagnostics, Mega Med, Gaziantep, Turkey). The commercial kit method initially involves the conversion of disulfide bonds in serum samples to functional thiol groups with sodium borohydride (NaBH4). Subsequently, a method using formaldehyde and reductive sodium borohydride prevents the reduction of 5,5'- dithiobis-(2-nitrobenzoic) acid (DTNB) (28). This method inhibits potential disulfide bond formation. Sulfite amounts were calculated as natural thiol/total thiol, disulfide/total thiol, and disulfide/natural thiol percentages.

The dynamic thiol/disulfide balance and the oxidation end product MDA were only measured in plasma, while parameters reflecting total oxidant and antioxidant statuses, namely TAL, TOL, and OSI, were compared both in plasma and erythrocytes.

Statistical Analyses

Data obtained in the study was analyzed using SPSS 22.0 (Statistical Package for the Social Sciences). Data were presented as mean (standard deviation) and number (percentage). The Kolmogorov-Smirnov test was used for testing normal distribution. For data that followed a normal distribution, parametric tests were applied, whereas non-parametric tests were used for data that did not conform to a normal distribution. The chi-square test was applied for the comparison of categorical sociodemographic data between groups. The t-test was used for the comparison of numerical data between two groups. Correlations between data, which exhibited a normal distribution, were determined using the Pearson Correlation Coefficient test. A significance level of $p<0.05$ was established for evaluations.

RESULTS

The statistical analysis of descriptive data related to the sociodemographic characteristics of the participants included in the study is presented in Table 1.

Table 1: Comparison of the data related to the descriptive statistics of the participants' sociodemographic characteristics

		Patients (n:47)	Control (n:49)	p
Age (Mean±SD)		31.10±12.08	29.61±7.27	0.463
Gender (n/%)	Male	23 (%48.9)	24 (%49)	0.998
	Female	24 (%51.1)	25 (%51)	
Marital Status	Married	14(%29.8)	21(%42.9)	0.130
	Single	28 (%59.6)	27(%55.1)	
	Divorced	5 (%10.6)	1(%2)	
Smoking	Yes	16(%34)	10(%20.4)	0.133
	No	31(%66)	39(79.6)	
Educational Status	Primary Education	8(%17)	0 (%0)	**0.006**
	High School	10(%21.3)	8(%16.3)	
	University	27(%57.4)	41(%83.7)	
	Other	2(%4.3)	0(%0)	
Residental Status	Country	2(%4.3)	1(%2)	0.154
	City	43(%91.5)	48(%98)	
	Other	2(%4.3)	0(%0)	
Occupational Status	Employee	13(%27.7)	28(%57.1)	**0.004**
	Unemployee	34(%72.3)	21(%42.9)	
Having a child	Yes	14(%29.8)	15(%30.6)	0.930
	No	33(%70.2)	34(%70.4)	
Substance Use History	Yes	1(%2.1)	0(%0)	0.305
	No	46 (%97.9)	49(%100)	

Mean±SD: Mean=Standart Deviation, Chi-square test, significant p value <0.05

Table 2. Minimum, maximum and mean scores of participants in Patient group from the Y-BOCS and CGI

	Min-Max.	Mean±SD
Y-BOCS-Obsession	1-20	13.04±4.27
Y-BOCS-Compulsion	1-20	9.89±4.74
Y-BOCS-Total	6-40	22.93±8.42
CGI	5-14	8.70±2.04

Min-Max: Minimum-Maximum, Mean±SD: Mean±Standart Deviation, Yale-Brown Obsession- Compulsion Scale (Y-BOCS), Clinical Global Impression Scale (CGI)

The mean score for the Y-BOCS obsession subscale of the patient group is 13.04±4.27, and for the Y-BOCS compulsion subscale, it's 9.89±4.74. The overall mean score for Y-BOCS is 22.93±8.42. The average score patients obtained from CGI is 8.70±2.04 (Table 2).

When comparing the patient and control groups in terms of plasma TAL, TOL, OSI, and MDA values, no statistically significant difference was observed ($p>0.05$). It was determined that the OSI level in erythrocytes, one of the oxidative stress markers, was higher in the patient group compared to the control group ($p<0.05$). Among the antioxidant markers, it was found that the erythrocyte TAL level in patients was lower than that in the control group ($p<0.05$) (Table 3).

Upon examining data related to plasma thiol-disulfide levels, while no significant difference was observed between patient and control groups regarding total thiol levels, which is an antioxidant marker, it was determined that the native thiol level in plasma was higher in the patient group ($p<0.001$). The plasma disulfide level, an oxidative stress marker, was found to be lower in patients compared to the control group ($p<0.05$). Consequently, in this study, the ratio of disulfide/total thiol and disulfide/native thiol, which are oxidative stress markers, was significantly lower in the patient group compared to the healthy controls, while the native thiol/thiol ratio, an antioxidant marker, was found to be significantly higher ($p<0.05$) (Table 3). It was determined that the plasma TAL level measured in the patient group was inversely weakly correlated with the Y-BOCS subscales and total score ($p<0.05$). A positive weak correlation was observed between the plasma TOL level and the illness duration ($p<0.05$) (Table 4).

Table 3. Comparison of the participants' TAL, TOS, OSI, MDA, Total Thiol, and Native Thiol levels in plasma and erythrocytes between groups

	Patients (n=47) Mean±SD**	Control (n=49) Mean±SD	T	p
TAL-Erythrocyte	0.35±0.02	0.36±0.02	**2.096**	**0.045**
TOL-Erythrocyte	5.71±0.93	5.80±0.86	-0.503	0.616
OSI-Erythrocyte	16.73±2.90	14.97±2.73	**3.073**	**0.032**
MDA-Plasma	2.80±0.42	2.84±0.47	0.740	0.461
TOL-Plasma	1.18±0.90	1.32±0.86	-0.995	0.322
TAL-Plasma	0.62±0.17	0.66±0.14	-1.778	0.079
OSI-Plasma	2.73±1.87	2.57±1.80	0.434	0.680
Plasma-Total Thiol	305.03±32.33	294.67±35.12	1.632	0.106
Plasma-Native Thiol	231.04±30.46	208.31±28.30	**8.367**	**0.000**
Plasma-Disulfide	37.29±15.39	47.12±18.94	**-2.784**	**0.006**
Native Thiol/ Total Thiol	0.75±0.09	0.69±0.11	**3.558**	**0.001**
Disulfide/Total Thiol	0.12±0.04	0.15±0.05	**-3.558**	**0.001**
Disulfide/Native Thiol	0.16±0.08	0.27±0.25	**-2.651**	**0.009**

Mean±SD: Mean±Standart Deviation, Independent sample t test, significant p value <0.01, TAL: Total Antioxidant Level Serrysel, TOL: Total Oxidant Level,OSI: Oxidative Stress Index, MDA: Malondialdehyde

DISCUSSION

One of the significant findings of our research is that in patients diagnosed with OCD, compared to controls, the ratio of reduced thiol (native thiol/total thiol), which is an indicator of the antioxidant system, is high. In contrast, the thiol oxidation-reduction ratio (disulfide/native thiol) and oxidized thiol ratio (disulfide/total thiol), indicators of the oxidative system, are low. To our knowledge, based on the literature review, there is no research examining thiol-disulfide levels in adult OCD patients. In a study conducted only in the child and adolescent group, it was reported that, contrary to our data, the plasma oxidized thiol ratio and thiol oxidation-reduction ratios were significantly higher in the OCD patient group not taking pharmacological treatment than in the control group (29). One possible reason for this difference may be that the patients included in our study were using pharmacological treatments. Another possible reason might be that, during childhood when the disease starts, disulfide levels trend higher due to an increase in oxidative stress, whereas in adulthood, possibly due to the chronic nature of the illness, a potential compensatory mechanism might lead to a decrease in plasma disulfide levels and an increase in native thiol levels.

In the adult period, there are studies examining the thiol/disulfide balance in psychiatric disorders other than OCD. Based on the results of studies conducted in patients diagnosed with Schizophrenia, Heroin Use Disorder, and Anxiety

Table 4. Correlation of the patients' levels of TAL, TOL, OSI, MDA, Total Thiol and Native Thiol in erythrocytes and plasma and CGI, Y-BOCS, illness duration

		TOL-Erythrocytes	TAL-Erythrocytes	OSI-Erythrocytes	Plasma-MDA	TOL-Plasma	TAL-Plasma	OSI-Plasma	Plasma-Total Thiol	Plasma-Native Thiol	Plasma-Disulfide	Native Thiol/Total Thiol	Disulfide/Total Thiol	Disulfide/Native Thiol
CGI	R	-0,009	0,018	-0,070	-0,090	0,154	-0,232	0,210	-0,079	-0,195	0,110	-0,153	0,153	0,190
	P	0,953	0,907	0,642	0,549	0,302	0,117	0,157	0,597	0,189	0,463	0,304	0,304	0,201
Y-BOCS-obsession	R	0,224	0,252	-0,088	-0,113	0,071	**-0,444(**)**	0,274	0,027	-0,214	0,240	-0,270	0,271	0,284
	P	0,130	0,088	0,554	0,451	0,638	**0,002**	0,063	0,856	0,148	0,104	0,066	0,066	0,053
Y-BOCS-compulsion	R	0,242	0,197	0,078	-0,114	0,031	**-0,302(*)**	0,109	-0,068	-0,160	0,087	-0,119	0,119	0,122
	P	0,101	0,184	0,602	0,444	0,838	**0,039**	0,466	0,652	0,283	0,560	0,425	0,425	0,413
Y-BOCS-Total	R	0,246	0,237	-0,007	-0,118	0,053	**-0,388(**)**	0,197	-0,023	-0,188	0,162	-0,194	0,194	0,204
	P	0,096	0,108	0,963	0,430	0,724	**0,007**	0,183	0,877	0,205	0,276	0,191	0,191	0,170
Illness Duration (year)	R	0,071	0,145	-0,157	0,042	**0,316(*)**	-0,117	0,221	-0,126	-0,175	0,041	-0,094	0,094	0,057
	P	0,636	0,331	0,292	0,779	**0,030**	0,433	0,135	0,397	0,238	0,786	0,531	0,531	0,702

Pearson correlation test ,** p<0.01 * p<0.05, Yale-Brown Obsession-Compulsion Scale (Y-BOCS), Clinical Global Impression Scale (CGI), TAL: Total Antioxidant Level, TOL: Total Oxidant Level,OSI: Oxidative Stress Index, MDA: Malondialdehyde,

Disorder, an increase in oxidative parameters is generally reported when examining the thiol/disulfide balance (17,18,30-33). In a study conducted in bipolar disorder, antioxidant parameters were found to be higher in patients in the manic phase compared to patients in remission and healthy controls (16). Another study reported high antioxidant markers regardless of the clinical stage of the disease (34). In a study with a sample consisting of patients diagnosed with bipolar disorder and unipolar depression, plasma oxidative stress parameters were found to be significantly higher in both patient groups (35). In a study conducted in depression patients not taking pharmacological treatment, antioxidant parameters related to plasma thiol disulfide hemostasis were found to be high, and oxidative stress parameters were low compared to the control group (36). In summary, the literature shows conflicting data regarding the thiol/disulfide balance in psychiatric disorders. Possible reasons for these conflicting results might be that the studies were conducted during different stages of the diseases, medication use that might affect the thiol/disulfide balance, and/or the presence of accompanying psychiatric or physical illnesses. The results of our study can be interpreted as indicating a shift towards the reducing side, the native thiol, of the thiol/disulfide balance as a compensatory mechanism to offset increased oxidative stress in OCD. In conclusion, when considering other oxidative stress pathways along with dynamic thiol/disulfide homeostasis, it's conceivable that there might be a more complex interaction related to oxidative stress in OCD.

In patients diagnosed with OCD, the TAL level inside the red blood cells was found to be lower and the OSI value higher compared to the control group. No difference was found between the patient and control groups in terms of TOL value. Therefore, these results indicate that the high OSI, which is the TOL/TAL ratio, originates from a decrease in the total antioxidant capacity, i.e., TAL level. When studies evaluating psychotropic drug use, smoking, and patients with psychiatric diagnoses other than OCD are examined, there are studies reporting that antioxidant parameters in materials obtained from plasma are higher, oxidative stress parameters are lower, or there is no difference between variables compared to healthy controls (37,38). In children and adolescents with OCD who do not receive medical treatment and do not have a comorbid disease, plasma antioxidant markers were found to be lower and oxidation markers higher compared to controls (39).

In our study, we observed no difference in the oxidative system indicators in plasma. When comparing the results of previous studies, it can be inferred that the discrepancy between the results might be due to different measurement techniques, the type of material examined (red blood cells,

plasma, serum, etc.), the use of psychotropics, different age groups, sampling at different stages of the disease, different ethnic origins, lifestyle, and dietary features. While the general consensus in the literature suggests that the plasma antioxidant capacity is low in OCD (37), (40), we could not observe this result in the plasma of patients diagnosed with OCD. However, we did identify significant differences in the oxidative stress parameters inside the red blood cells. When evaluating these different findings related to oxidative values in plasma and red blood cells in OCD patients together, it can be interpreted that changes in oxidative stress markers might start within the red blood cells. Considering the interaction of red blood cells with metabolism throughout the body, and even in the brain, it can be suggested that this situation might be related to neurophysiological changes in OCD.

In our study, when we examined the plasma MDA levels, which are an index of lipid peroxidation, we found no significant difference between the patient and control groups. In a study conducted with patients diagnosed with schizophrenia, it has been reported that, consistent with our results, there was no significant difference between the patient and healthy control groups in terms of plasma MDA levels (41). However, there are also studies reporting that the plasma MDA level in patients diagnosed with OCD is higher than the healthy control group (3,41). The lack of difference in plasma MDA levels in our study can be seen as a consistent result, given that while we detected differences in other oxidative stress parameters at the erythrocyte level, we did not detect any at the plasma level.

In our research, we also examined the relationship between the oxidation markers we evaluated and the average scores taken from Y-BOCS, CGI, and the duration of the disease. We found a statistically significant weak inverse relationship between the severity of obsessive-compulsive symptoms and plasma TAL level and a weak same-direction relationship between the duration of the disease and the TOL level. Selek et al. interpreted the shift in oxidative balance towards the antioxidant side in OCD patients as a rebound phenomenon or an indicator of chronicity (37). Additionally, in the same study, it was suggested that long-term exposure to the disease might have increased antioxidant mechanisms or, alternatively, the treatment might have activated antioxidant mechanisms. According to our results, the decrease in TAL levels as obsessive-compulsive symptom severity increases and the increase in TOL levels as the duration of the disease increases supports the inference that oxidative balance might be more affected by chronicity rather than disease severity.

One of the strengths of our study is that it is the first to evaluate the thiol/disulfide balance along with oxidative stress parameters such as MDA, TAL, TOL, OSI in adult patients diagnosed with OCD receiving pharmacological treatment. Another strength is our examination of oxidative stress parameters at both plasma and erythrocyte levels to reduce inconsistency related to the examined material. A main limitation of our study is its cross-sectional nature. Participants were ensured not to use antioxidant agents, and factors affecting the oxidative system were tried to be excluded by ensuring they don't have neurological, genetic, or chronic medical diseases. However, significant limitations include not excluding the effects of psychotropic drugs used by patients, nutrition, exercise status, and Body Mass Index. Although the inclusion of smokers is also a limitation of our study, the fact that there is no significant difference in smoking rates between the groups can be considered an advantage. In the study, patients from the OCD group who applied to our outpatient clinic were included; hence, the results from community screening studies might differ. As a homogeneous patient group was chosen in our study, the potential effects of other psychiatric comorbidities on the results could not be investigated.

CONCLUSION

We believe that our study's significance lies in it being the first study to investigate the Thiol/Disulfide level in adult patients with OCD (Obsessive-Compulsive Disorder). Unlike other reported systemic diseases, the dynamic thiol/disulfide homeostasis in patients diagnosed with OCD may be related to mechanisms such as increased anti-oxidative compensations in response to oxidative stress. Since our study is cross-sectional, even

though a cause-and-effect relationship cannot be clarified, it might be suggested that underlying possible mechanisms be longitudinally researched in future studies.

When evaluating the results of our study, we found that the plasma TAL and TOL values in patients with OCD were not different from the control group. However, we determined that the erythrocyte TAL level was lower in the OCD patient group, while the OSI ratio was higher. Looking at the literature, in OCD, plasma oxidative stress markers usually show high oxidant levels and low antioxidant levels (40). Contrary to the general opinion when we examined the thiol-disulfide parameters, we determined that the antioxidants were high. The high level of native thiol, an antioxidant molecule in plasma, in patients with OCD, can be interpreted as an effort to compensate for the decreasing antioxidant capacity within erythrocytes. In light of these results, we believe that when evaluating oxidative stress parameters in psychiatric diseases like OCD, in addition to plasma total oxidant capacity, studying the thiol/disulfide balance is crucial. Moreover, it could be said that measuring these parameters not only in plasma but also within erythrocytes would be appropriate.

Conflicts of interest: The authors declare that they have no conflict of interest.

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