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https://doi.org/10.31925/farmacia.2025.6.18 **ORIGINAL ARTICLE**

CARBAMAZEPINE USERS WITH CHANGED LEVELS OF OXIDATIVE STRESS BIOMARKERS

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Abstract

Carbamazepine (CBZ) is used for various diseases, such as mood disorders, epilepsy and chronic pain. In all of these, oxidative stress (OS) is involved in its pathophysiology; however, in Brazilian context studies, there are still no concrete data on the effect of CBZ on these parameters. This study aimed to analyse OS biomarkers among CBZ users in the Brazilian Unified Health System. A cross-sectional, analytical and quantitative analysis that included CBZ users. Data were collected via questionnaires, medical record reviews and blood samples. The OS markers analysed were catalase (CAT), superoxide dismutase (SOD), thiobarbituric acid reactive substances (TBARS) and non-protein thiols (NP-SH), which were compared to healthy controls. Higher concentrations of SOD and lower concentrations of CAT and NP-SH were observed in carbamazepine users. Higher levels of TBARS were associated with brown race and polymedication or polypharmacy. Patients who were CBZ users have changes in OS biomarkers. The study investigated the difference in OS between CBZ users with epilepsy/chronic pain and mood disorders, in addition to being one of the first in Brazil. The results contribute to the body of knowledge in the field, as the literature remains inconsistent regarding OS markers in patients receiving CBZ.
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Rezumat

Scopul acestui studiu a fost analiza biomarkerilor de stres oxidativ (OS) la utilizatorii de carbamazepine (CBZ) din cadrul Sistemului Unic de Sănătate brazilian. A fost realizat un studiu transversal, analitic și cantitativ, care a inclus utilizatori de CBZ. Datele au fost colectate prin chestionare, analiza fișelor medicale și prelevare de probe de sânge. Markerii de OS analizați au fost catalaza (CAT), superoxid dismutaza (SOD), substanțele reactive la acid tiobarbituric (TBARS) și tiolii neproteici (NP-SH), iar valorile acestora au fost comparate cu cele ale unui lot de control sănătos. La utilizatorii de carbamazepină s-au observat concentrații crescute de SOD și concentrații scăzute de CAT și NP-SH. Nivelurile ridicate de TBARS au fost asociate cu apartenența la rasa brună și cu polimedicația sau polifarmacia. Pacienții care utilizează CBZ prezintă modificări ale biomarkerilor de stres oxidativ. Studiul a investigat diferențele de OS între utilizatorii de CBZ cu epilepsie/durere cronică și cei cu tulburări de dispoziție, fiind totodată unul dintre primele studii de acest tip din Brazilia.

Keywords: catalase, superoxide dismutase, malondialdehyde, thiols

Introduction

Oxidative stress (OS) is defined as an imbalance between oxidants and antioxidants, with oxidants prevailing and contributing to the cause and consequences of various diseases [1-8]. In epilepsy, OS plays an important role in the process of epileptogenesis. As a result of the epileptic seizure, reactive oxygen species (ROS) and reactive nitrogen species (RNS) are also formed, which appear to be related to subsequent neuronal death [9]. In turn, neuronal death further contributes to the progression of epileptogenesis, seizures and epilepsy [10]. The initial effects of reactive species are reactive gliosis, lipid peroxidation and damage to mitochondrial deoxyribonucleic acid (DNA). All these processes result in neurodegeneration, neurogenesis, rearrangement of neuronal circuits, hyperexcitability and decreased seizure threshold. The generation of ROS in patients with epilepsy impairs several metabolic pathways, leading to decreased glutathione (GSH) levels, reduced superoxide dismutase (SOD) activity and increased lipid peroxidation [11]. In mental diseases, such as anxiety, depression, bipolar disorder and schizophrenia, the imbalance between oxidants and antioxidants has been well described [12]. In these cases, an increase in lipid peroxidation and a decrease in catalase (CAT) levels can be observed [13].

Furthermore, despite medication treatment, there may be no change in these markers [14].

Concerning the treatment against epilepsy, it is carried out using drugs to prevent seizures by stabilising neuronal activity, and for mental diseases, drug treatment primarily seeks to reduce symptoms. In epilepsy, monotherapy with anticonvulsant drugs slightly changes redox homeostasis, followed by different relationships between antioxidant components [14, 15, 26].

Among the medications, CBZ stands out for its use in cases of epilepsy, mood disorders and chronic pain. The mechanisms of action of CBZ include sodium channel inhibition, enhanced neuronal plasticity, neurotrophic effects and positive regulation of gamma-aminobutyric acid (GABA) receptors [15-18]. In epilepsy, patients have a different redox state than those treated with anticonvulsants. The results showed that CBZ therapy increased nitrite levels but reduced SOD activity [14]. In a case-control study, healthy patients had higher antioxidant capacity, whereas people with epilepsy showed no increase in antioxidant capacity after CBZ treatment [19]. In a study of bipolar disorder, induced in rats, patients had increases in thiobarbituric acid reactive substances (TBARS) in the brain, and the treatment with CBZ was able to decrease TBARS [13].

Considering the above and the evidence in the literature, there are still conflicting results about the effect of CBZ on OS, especially in patients with mood disorders. In addition to the difficulty in terms of checking the influence of the disease and treatment on OS, as well as the influence of other factors on the redox balance [20-23]. With this in mind, the aim was to analyse OS biomarkers in CBZ users of the Brazilian Unified Health System.

Materials and Methods

Study design and background

This is an observational, cross-sectional, analytical and quantitative study that analyses OS biomarkers among CBZ users of the public health system in Ijuí, State of Rio Grande do Sul. The research was conducted with patients from the Colmeia Psychosocial Care Centre (CAPS, as per its Portuguese acronym) and with users of the Primary Care dispensing pharmacy of the Brazilian Unified Health System (SUS, as per its Portuguese acronym) in Ijuí, Rio Grande do Sul, Brazil. Data collection took place between January and July 2023.

Participants

Patients were identified: (a) through a CBZ withdrawal report in the city's computerised medication dispensing system; (b) through access to the CAPS medical and identification of CBZ use. Once identified, they were invited to participate in the study during their appointments at CAPS or when they picked up their medication from the SUS dispensing pharmacy in Ijuí, Brasil. Another recruitment strategy was to contact them by telephone to schedule their participation in the study; they were invited to participate, depending on their availability, at CAPS, at the Central Pharmacy, or at home.

From the reports, a population of 237 individuals was identified; after exclusions and losses, the final sample comprised 71 participants (Figure 1). It should be underlined that all possible diagnoses of CBZ use were included, such as mood disorders, epilepsies or chronic pain. The inclusion criteria for the study were: use of CBZ for at least 1 week and age > 18 years. Patients with a cancer diagnosis who were unable to collect a blood sample of 10 mL or more or who were interdicted were excluded.

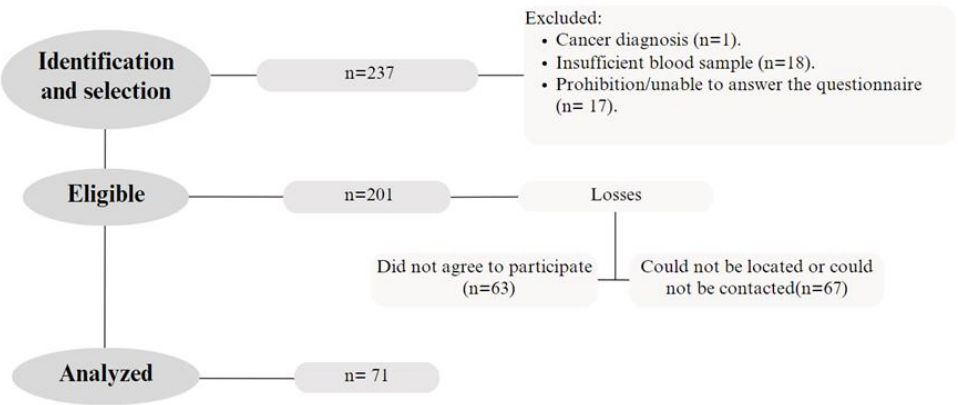

Figure 1.
Flowchart for identifying and selecting participants with carbamazepine use.

The control group consisted of healthy patients recruited in the city where the study was carried out. After reading and signing the free and informed consent form (FICF), blood was collected, and then the sociodemographic questionnaire was completed. This group was matched for gender and age, and individuals without disease and not receiving continuous medication were selected. For approximately every two CBZ users in the same

age range, one control was matched; a total of 30 controls were matched.

Data collection and study variables

Data were collected after signing a free and informed consent form, using a structured questionnaire with evaluative questions on socioeconomic factors, adverse effects and anxiety levels; venous blood was also collected at this time. Data collection was conducted by the study's proponent and previously trained staff. Furthermore, the participants' medical records were reviewed to confirm the diagnosis and document the medications used.

The participants' anxiety was evaluated using the Beck Anxiety Inventory, which identifies 21 anxiety symptoms experienced over the last week. Each symptom can be scored from 0 to 3, with 3 being the most severe. At the end, the total score ranges from 0 to 63 (higher scores indicate greater anxiety). Accordingly, the general classification of the score is: minimal anxiety (0 - 7), mild anxiety (8 - 15), moderate anxiety (16 - 25) and severe anxiety (26 - 63) [24]. For data analysis, patients were stratified into low anxiety (score up to 15) and moderate/high anxiety (above 15 points).

Body mass index (BMI) was calculated as weight in kilograms divided by height squared [25]. The poly-medication was defined as the use of five or more concomitant medications [15, 26].

The study variables were: gender, age, education, BMI, polymedication, adverse effects, anxiety level, CAT, SOD, NP-SH and TBARS.

Oxidative stress biomarkers

As for analysing OS biomarkers, a tube (EDTA) was used for blood collection to obtain erythrocytes or red blood cells (RBC). The whole blood samples were centrifuged for 15 minutes at 2500 rpm. Next, the erythrocytes were washed twice in 0.9% Sodium Chloride (NaCl) and recovered by centrifugation. The techniques carried out were: SOD, CAT, NP-SH and TBARS, which are described below:

CAT technique

CAT activity in red blood cells was measured by the Aebi method, through the addition of RBC to a cuvette with 50 mM phosphate buffer (pH 7.0), and the reaction starts with the addition of hydrogen peroxide (H_2O_2) 0.5 mM (pH 7.0), freshly prepared. The rate of H_2O_2 decomposition was measured by a spectrophotometer at 240 nanometers (nm). Accordingly, CAT activity was expressed in μmol H_2O_2/min/mL of RBC [27].

SOD technique

SOD activity was analysed using the method described by McCord and Fridovich, which is based on SOD's ability to inhibit the auto-oxidation of adrenaline to adrenochrome. The test was performed with a dilute RBC solution, using three volumes, and was read in a spectrophotometer at 480 nm. SOD activity was expressed in μSOD/mL haemoglobin [28].

Non-protein thiol technique

The non-protein thiol groups of red blood cells, which allow indirect assessment of glutathione (GSH) levels, were determined after haemolysis of RBCs with 10% Triton. 20% trichloroacetic acid (TCA) was added to the mixture, which was then centrifuged at 4000 rpm for 10 min. The supernatant was used as a sample. Next, 2-nitrobenzoic acid (NTD) was added, and the absorbance was measured immediately at 412 nm using a spectrophotometer. For the GSH standard curve, concentrations of 25, 50, 75 and 100% were used [29].

TBARS technique

The TBARS assay used the RBC. Subsequently, the preparation was performed in the presence of 10 mM butylated hydroxytoluene (BHT) and 20% TCA. For homogenization, samples were vortexed and centrifuged at 4000 rpm for 5 minutes. Therefore, the sample consisted of supernatant. A standard curve was prepared using different concentrations and volumes of distilled water, 0.03 mM malondialdehyde (MDA), 10% phosphoric acid (H3PO4) and 0.6% thiobarbituric acid (TBA). The tubes were placed in a water bath at 95°C for 60 minutes, and the absorbance was measured immediately in a spectrophotometer at 532 nm [30].

Ethical aspects

This paper was approved by the Research Ethics Committee of the Regional University of the Northwest of the State of Rio Grande do Sul, Brazil, under the Protocol No. 6.011.881, dated December 27, 2022.

Statistical analysis

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA), version 23.0. The figures were generated using GraphPad Prism 10.2.0. Data normality was tested using the Kolmogorov-Smirnov test. Continuous data were described as mean ± standard deviation (SD) or median (interquartile range), and categorical data as absolute and relative frequencies. As for checking the association between two or more qualitative variables, Pearson's Chi-square hypothesis test was used. For quantitative variables, a mean-comparison test was used. For non-parametric, independent-samples comparisons, the Mann-Whitney test was used (variables SOD, CAT and NP-SH). Lastly, for parametric analysis, Student's T-test were applied (variable TBARS). Multivariate analyses were conducted in R using Principal Component Analysis with Biplot and in SPSS using a Generalised Linear Model. For all tests, the 5% significance level was used.

Results and Discussion

The mean age of CBZ users was 48.92 ± 15.2 years; most were male and married. Regarding education, 46.5% had incomplete primary education. The control group (CG) comprised 30 volunteers, with a mean age of 46.37 ± 14.5 years (Table I).

Table I

Demographic variables of carbamazepine users from the Brazilian Unified Health System in the city of Ijuí, Rio Grande do Sul, Brazil. 2023. (n = 101)

Variable		Carbamazepine	Control group	P
Age[#]		48.92 ± 15.2	46.37 ± 14.5	0.430[a]
BMI[#]		29.9 ± 7.81	27.2 ± 3.6	0.101[a]
Gender	Female	31 (43.6 %)	13 (43.3%)	0.976[b]
	Male	40 (56.3%)	17 (56.6%)	
Marital Status	Married	35 (49.3%)	20 (66.7)	0.218[b]
	Single	29 (40.8%)	10 (33.3%)	
	Divorced	4 (5.6%)	0 (0%)	
	Widowed	3 (4.3%)	0 (0%)	

BMI (Body Mass Index); # (mean ± standard deviation); p* (p > 0.05); a (t-test for independent samples); b (Pearson's Chi-square); Carbamazepin (n = 71); Control group (n = 30).

Among the OS biomarkers analysed, CBZ users had lower levels of CAT and NP-SH than the control group and higher levels of SOD, as shown in Figure 2. It was observed that participants who identified as white had lower TBARS levels than those who identified as brown. Furthermore, polymedicated patients had higher levels of TBARS (19.32 ± 9.70) than non-polymedicated patients (15.04 ± 7.29), as displayed in Table II. Considering the patients' diagnoses, it was found that participants with mood disorders had higher levels of CAT (p = 0.017). In the other variables, there were no differences between the groups.

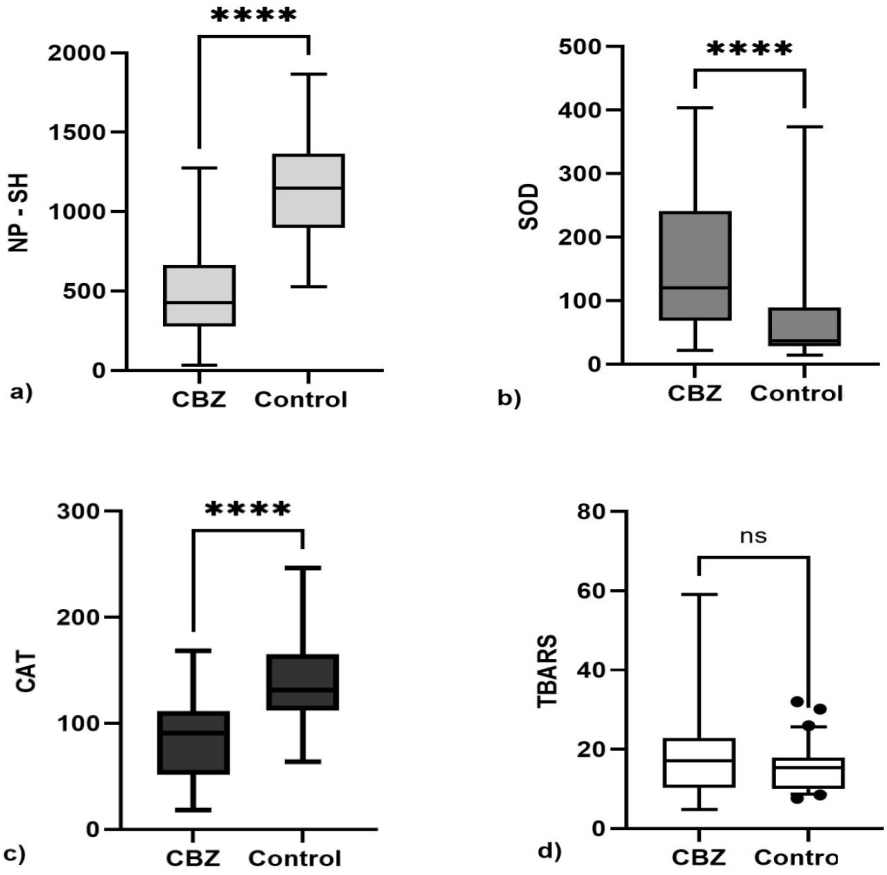

Figure 2.

Oxidative stress biomarkers in Carbamazepine (CBZ) users when compared to healthy patients (Control group). a) Non-Protein Thiols (NP-SH) (nmol NP-SH/mL erythrocytes); Median (CBZ 401.4; Control 1,148.7). b) Super-oxide Dismutase (SOD) (µSOD/mL haemoglobin); Median (CBZ 120.1; Control 37.2). c) Catalase (CAT) (mmol/ H_2O_2/mL red blood cells); Median (CBZ 90.6; Control 131.1). d) Thiobarbituric Acid Reactive Substances (TBARS) (nmol MDA/mL erythrocytes); Mean (CBZ 17.3; Control 16.3). A, B and C (Mann-Whitney U test for non-parametric samples presented as Median). D (Student's T-test for independent samples presented as Mean) **** (p < 0.05), Ns (not significant)

Table II

Thiobarbituric acid reactive substances (TBARS), catalase, superoxide dismutase and non-protein thiols from carbamazepine users in the Brazilian Unified Health System in the city of Ijuí, Rio Grande do Sul, Brazil, 2023 (n = 71)

Variables		TBARS & (Mean ± SD)	NP-SH#	SOD#	CAT#
Gender	Female	17.41 ± 10.23	467.5	158.1	90.5
	Male	17.33 ± 7.74	370.4	119.3	93.8
	p	0.971	0.471	0.822	0.986
Race	White	16.57 ± 7.38	370.4	129.2	80.9
	Brown	25.15 ± 19.51	464.5	50.4	108.1
	p	**0.036***	0.516	0.143	0.09
BMI	≤ 25	16.17 ± 6.99	457.5	98.6	105
	≥ 25	17.87 ± 9.54	390.5	161.9	72.1
	p	0.513	0.476	0.933	0.176
Polymedication	Yes	19.32 ± 9.70	357.8	146.1	96.4
	No	15.04 ± 7.29	435.1	99	77.1
	p	**0.047***	0.265	0.947	0.517
Anxiety	Low	17.10 ± 7.23	414.9	110.7	81.6
	Moderate/high	17.78 ± 11.09	390.5	159.1	98.5
	p	0.759	0,708	0,233	0,606
Medical diagnosis (ICD) - medical record	Mood disorders	18.61 ± 10.52	426.3	147.1	97.9
	Epilepsies/seizures/chronic pain	16.37 ± 6.53	302.3	102.1	72.1
	p	0.374	0.205	0.303	**0.017***
Number		70	66	65	70

Thiobarbituric Acid Reactive Substances (TBARS) (nmol MDA/mL erythrocytes). Non-Protein Thiols (NP-SH) (nmol NP-SH/mL erythrocytes). Catalase (CAT) (mmol/H_2O_2/mL red blood cells). Superoxide Dismutase (SOD) (SOD/mL haemoglobin). Standard Deviation (SD). Body Mass Index (BMI) *($p \geq 0.05$). Number: the number of patients analysed for each variable differs, as some participants did not have enough blood for all analyses (due to difficulties in blood collection). # (Data presented as Median - Mann-Whitney U test for non-parametric samples). & (Data presented as Mean - Student's T-test for independent samples).

As for checking whether the confounding variables "hypertension", "dyslipidaemia" and "diabetes" could actually be the cause of OS in the patients surveyed, multivariate analysis was conducted. As observed in the test, among patients using carbamazepine, the variables hypertension", "dyslipidaemia" and "diabetes" influenced the OS biomarkers in the carbamazepine group. Among the biomarkers, SOD had the most significant influence on the outcome. The opposite behaviour was observed for the variables "NP-SH", "TBARS", "CAT" and "SOD" when comparing the control and carbamazepine groups, thereby reinforcing the difference between these two groups, already highlighted in the univariate analysis (Figure 3). By including the data in the Generalised Linear Model (GLM), considering the adjustment covariates: diabetes, dyslipidaemia and hypertension, the independent variable group (CG x CBZ), and the dependent variables: NP-SH, CAT and SOD. The CBZ group showed lower levels of NP-SH ($p \leq 0.001$) and SOD ($p \leq 0.001$), but there was no difference in CAT levels in this model, only demonstrating higher CAT levels in diabetics ($p \leq 0.014$).

Given this result, we also conducted a secondary analysis excluding all patients with diabetes, dyslipidaemia, or hypertension. This resulted in a sample of 30 CG (healthy patients) and 39 CBZ users (without diabetes, dyslipidaemia and hypertension). Using the Mann-Whitney U test, we observed that CBZ users had lower levels of CAT ($p \leq 0.001$) and NP-SH ($p \leq 0.001$), and higher levels of SOD ($p \leq 0.001$) than CG.

CBZ users had lower NP-SH levels than healthy patients. One of the main functions of the thiol groups is the donation of electrons, which is of paramount importance to avoid oxidative damage [4]. However, in epilepsy, there seems to be a decrease in glutathione activity, according to an animal model of induced epilepsy, as well as reduced amounts of thiols in humans [11, 31]. Conversely, it seems that CBZ cannot reverse this decrease in glutathione in epileptics [11], *i.e.*, data are still contradictory, since CBZ use in healthy rats did not show any significant change in glutathione activity when compared to the group of normal control rats, with brain samples [11]; whereas, in rat livers, CBZ decreases glutathione levels [32]. Results similar to ours found reduced levels of NP-SH [33], while another study with epileptics using CBZ found no difference when compared to the CG [34]. Such divergences and the paucity of human studies on this topic underscore the importance of the current research.

Lower levels of CAT are related to various diseases [35], such as epilepsy, bipolar disorder or anxiety [11, 13, 31]. The isolated use of CBZ does not change CAT activity in animals [11], nor can it reverse damage caused by the disease [13]; however, in the case of CBZ poisoning, there may be less activity of CAT [36]. As a result, the lower activity observed in our study appears to be related to participants' underlying

diseases, as CBZ was unable to reverse this decrease. Nevertheless, these results should be interpreted with caution and replicated in future studies, as we did not include an untreated control group.

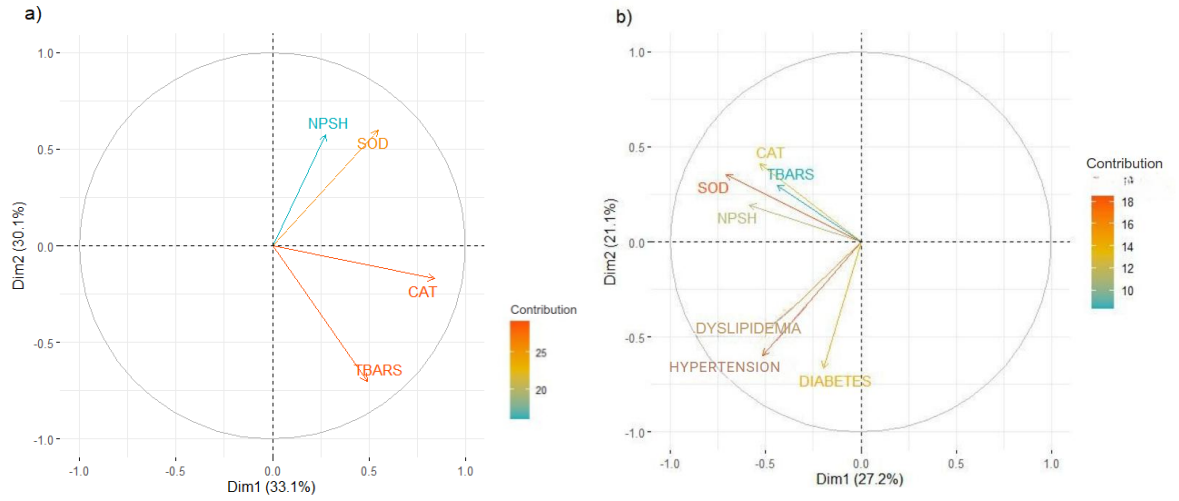

Figure 3.
Multivariate analysis.
a) Control Group; b) Carbamazepine Group (CBZ)
(NP-SH) Non-Protein Thiols (nmol NP-SH/mL erythrocytes); Superoxide Dismutase (SOD) (SOD/mL haemoglobin); Catalase (CAT) (mmol/H_2O_2/mL red blood cells); Thiobarbituric Acid Reactive Species (TBARS) (nmol MDA/mL erythrocytes); * ($p < 0.05$). Ns (not significant)

Regarding SOD, there seems to be less activity of this enzyme in patients with generalised anxiety disorder and epilepsy [11, 37]. In healthy rat models, CBZ was found to decrease SOD activity in the liver but not in the brain [11, 32, 38]. In turn, in sick patients, data are controversial, since CBZ therapy in epileptics was able to reduce SOD activity in a study held in Serbia [14]; however, in Italian children, after treatment, no change was observed [39]. Given the divergence in the literature, the increase in SOD in the patients in the current study may reflect the body's attempt to combat ROS, as this enzyme plays a key role in inactivating superoxide ions [4]. In addition to this hypothesis, it can be suggested that the generation of OS by CBZ, related to metabolites formed by pharmacokinetic metabolism, generates active intermediates that generate free radicals (Lu; Utrecht, 2008), thereby increasing the body's demand for SOD.

Malondialdehyde (MDA) is a significant marker of lipid peroxide formation in cell membranes. This is a component of thiobarbituric acid reactive substances (TBARS) and is the end product of lipid peroxidation [40]. Regarding TBARS, there was no difference between the control group and CBZ users. Contrary to this result, animal studies have shown that lipid peroxidation levels are increased in models with epilepsy or mania; however, the samples analysed consisted of the brains and livers of the animals [11, 13], differing from the current study. Furthermore, patients with generalised anxiety disorder have higher levels of MDA, which is also correlated with higher scores on the depression scale [37]. In humans, patients undergoing treatment for drug dependence, after CBZ use, had no change in MDA [41]. In epileptics, lipid peroxidation was higher in those treated with CBZ [42]; whereas, in the acute mania model, CBZ was able to reverse the increase in MDA [13].

When comparing the epileptic group and the group with mood disorders, the only difference found was lower levels of CAT in the first group mentioned; the complexity of both diseases can justify such similarities in the redox state. In epilepsy, OS targets mitochondrial DNA and lipid peroxidation, which affect adenosine triphosphate (ATP) depletion and further contribute to excessive production of ROS/RNS [43]. Consequently, individuals with epilepsy have lower antioxidant capacity than healthy individuals [19], and anticonvulsant treatment does not rebalance redox homeostasis, as it elicits few changes in antioxidant components [14]. In anxiety, the oxidant status is higher [44], as this population shows a decrease in serum sulfhydryl levels and an increase in lipid hydroperoxide and 8-hydroxy-2'-deoxyguanosine (8-OHdG) [45-47]. In depression and associated disorders, OS plays an important role in the pathophysiology of the disease [47], as demonstrated in a meta-analysis that evaluates 8-hydroxy-2'-deoxy-guanosine (8-OHdG) and F2-isoprostanes (F2-isoPs), which have higher levels in patients with this disease [48].

Contrary to our results, which found no differences between OS markers and anxiety symptoms, in Australia, in an elderly population, F2-isoprostane levels (OS marker) were associated with negative mood, anger

and hostility [49]. It is noteworthy that, in addition to the distinct population, with healthy older adults who did not use anxiety medications, the OS markers evaluated also differed, as well as the anxiety questionnaire applied. These variables may explain the differences found.

The participants' gender did not influence the OS markers in the current study; however, it is worth underlining that OS may be associated with gender and age, with lower levels of MDA in women [23]. Before menopause, women appear to have lower OS levels, which may be due to oestrogen's antioxidant properties and antioxidant enzyme activity [21]. In this study, women were not stratified by menopause status, as this was not the study's primary aim. In the current study, no association was found between higher BMI and OS variables, which may be related to the reduced sample size and the complexity unveiled by the participants. Nevertheless, obesity is a risk factor for redox imbalance and is associated with the subsequent development of various comorbidities [20]. Regarding race, higher levels of lipid peroxidation were observed in brown individuals, consistent with other studies [22, 50]. Research suggests that African Americans exhibit overexpression of NADPH oxidase, interleukins, endothelial nitric oxide synthase and inducible nitric oxide synthase [51].

Participants using five or more medications had higher levels of TBARS. Such an association was not investigated in a previous study, but two possible hypotheses were raised. First, polymedicated patients have polymorbidity [52]. Therefore, it requires several medications. Thus, the increase in lipid peroxidation may be related to diseases, since for many it has been established that OS is related to pathophysiology [1-8]. On the other hand, the concomitant use of drugs by people who predominantly suffer from hepatic metabolism can overload the liver, in addition to CBZ itself, which is extensively metabolised by it [15], and can also generate excessive production of reactive species. However, because the other OS variables analysed were not associated with polymedication, the need for further research on this topic warrants emphasis.

This paper has some limitations, such as not having a control group with untreated mood disorders, due to the difficulty in locating such participants with this characteristic. Furthermore, an important limitation of the present study is the absence of a comparator group of epileptic patients who are still untreated or are treated with another anticonvulsant known to have minimal impact on oxidative stress, such as lamotrigine or levetiracetam. The inclusion of such a group would have allowed greater robustness in interpreting the findings by enabling distinction between oxidative alterations potentially induced by carbamazepine and those inherent to disease pathophysiology. However, establishing an active control group was not feasible, as these medications are not included on the municipality's essential medicines list. Thus, although the comparison with healthy individuals provides relevant information about the overall effect of carbamazepine, it is not possible to entirely exclude the influence of epilepsy related factors as determinants of the observed oxidative stress markers. Another limitation was participant attrition, primarily due to difficulties in data collection, which reduced the population size, and incomplete medical records led to the loss of important information, making it impossible to define key characteristics of the disease, such as the aetiology of epilepsy.

Conclusions

This study identified changes in OS markers among CBZ users, with lower levels of NP-SH and CAT and higher levels of SOD. Furthermore, higher amounts of TBARS were found in brown and polymedicated people. The study has the distinction of investigating the difference in OS between CBZ users with epilepsy/chronic pain and mood disorders, in addition to being one of the first in Brazil. The results contribute to the body of knowledge in the field, as the literature remains inconsistent regarding OS markers in patients receiving CBZ.

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Conflict of interest

The authors declare no conflict of interest.

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