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ORIGINAL PAPER

Evaluation of oxidative stress level and glutathione system in patients with psoriasis in Basrah Governorate, Iraq

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ABSTRACT

Introduction and aim. Psoriasis is a persistent chronic disease with no known cause or cure. This study aimed to estimate oxidative stress and glutathione systems, and their association with factors (age, gender, disease severity, and geographical location) in psoriasis patients.

Material and methods. The study was carried out in the Al-Fayhaa and the Basrah Teaching Hospitals. The number of patients was 45 with 45 in the control group. We quantified the amounts of malondialdehyde (MDA), protein carbonyl (PC), 8-hydroxyguanosine, glutathione, glutathione reductase (GR), glutathione peroxidase (GPx), and selenium.

Results. The results showed significant differences in all variables at multiple statistical levels ($p<0.05$, $p<0.01$, $p<0.001$). The study found significant differences between two groups within the allowed concentration range. Some inter-factor fluctuations were found, and these fluctuations were noticeable in age and sex, and not significant in disease severity or location. The patients did not experience oxidative stress due to the oxidation of lipids and proteins, but rather DNA oxidation.

Conclusion. Lipid peroxidation or protein oxidation do not correlate with psoriasis. While a marker for DNA oxidation exists, it yields different results in psoriasis patients compared to healthy individuals. We observed a correlation between MDA, GR and PC, GPx, PC, and selenium, which serves as the cofactor of the GPx enzyme.

Keywords. glutathione system, Iraq, oxidative stress, psoriasis

Introduction

Psoriasis is a persistent, chronic disease for which there is no known cause or treatment. It is believed that there is a defect in the immune system that attacks itself.[1] While some studies have suggested that skin infiltration is the cause, others have indicated that intestinal infiltration is involved in stimulating the immune system.[2-4] Psoriasis is characterized by red, inflamed spots topped with white scales, which frequently cause itching and appear on the elbows, knees, chest, and scalp. It also has multiple forms.[5] Psoriasis is considered a quite common skin disease, and its prevalence varies by age, sex, geographical area, and surroundings.[6] Psoriasis is prevalent in children (0–2.1%) with an incidence of 40.8 cases per 100,000 people; its prevalence in adults (0.91–8.5%) has an incidence of 78.9-230 cases per 100,000 people.[7] In Iraq, outbreaks of psoriasis range from 0.5% to 0.7%. Psoriasis affects patients' quality of life, as most suffer from feelings of depression and shyness due to their condition.[8] Research also indicates that psoriasis frequently coexists with cardiovascular disease, diabetes, and obesity, extending beyond the skin.[9] It is believed that multiple, mostly genetic, factors exacerbate psoriasis. One of these factors is stress, having co-developed with psoriasis.[10,11] However, non-genetic factors, such as infections, bac-

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terial imbalance in the skin and intestines, lipid metabolism disorders, sex hormone imbalances, and mental illness can stimulate the onset and recurrence of psoriasis in genetically predisposed individuals.[12,13] Other environmental factors such as skin trauma, unhealthy lifestyles, and medications, can also cause psoriasis.[14] Accordingly, many theories have attempted to explain the pathophysiology of psoriasis by investigating the role of oxidation and antioxidants in the exacerbation of psoriasis.[15,16] Oxidative stress refers to an imbalance between levels of reactive oxygen species (ROS) and nitrogen free radicals on the one hand and the antioxidant defense system on the other hand.[17] Since the skin is more exposed to environmental factors, being a source of free radicals, it counters microorganisms and differentiates cells when they are at low concentrations.[18-20] When free radicals increase in the body, they participate in lipid oxidation, cell protein degradation, DNA alteration, programmed cell death, and tissue injury. All these alterations jointly trigger the initiation and intensification of psoriasis.[21,22] Therefore, to evaluate the involvement of oxidative stress in the exacerbation of psoriasis, we examined the status of lipid oxidation, cell protein degradation, DNA oxidation, as well as the effect of the glutathione antioxidant system.[23-26] Moreover, studies have held that glutathione is crucial in supporting tissue repair and regeneration, which is essential for maintaining skin elasticity, and the investigation of the associations between oxidation balance and reduction following age, sex, disease severity, and geographical location in both patients and the control group.[27,28]

Aim

Estimate oxidative stress and glutathione systems, their association with factors (age, gender, disease severity, and geographical location), and their effects on psoriasis patients.

Material and methods

Study population

This is a case-control study that was conducted at Basrah College of Education for Pure Sciences, Department of Biochemistry, Basrah, Iraq, from March 2024 to July 2024, a ninety-participant sample was chosen; we randomly selected 45 psoriasis patients as cases and 45 healthy individuals as controls, with both groups being matched in age and sex. Psoriasis patients often visit the dermatology clinic at both Al-Faihaa Teaching Hospital and the Basrah Teaching Hospital for consultations or routine check-ups. We collected blood serum early in the morning after an eight-hour fast. All subjects gave their informed consent for inclusion before they participated in the study. The Ethics Committee approved the protocol on 7/1/2024, Issue 12, and we conducted the study in accordance with the Declaration of Helsinki.

Criteria of exclusion

Patients with liver disease, hypertension, diabetes, kidney disease, tumors, heart disease, and thyroid disease were excluded. Patients undergoing gastric bypass surgery were excluded. Patients who were younger than 13 years and older than 70 years were excluded. In addition, we excluded patients with any other type of skin disease, smoking, or other diseases. The control group also excluded any chronic disease. During morning hours in the hospital, the patients and the controls were requested to fill a questionnaire containing their demographical data., i.e., age, and gender.

Sample collection

Three milliliters of venous blood were drawn by syringe, and the blood samples were placed into tubes containing a clotting-inducing gel. Then, the tubes were left for half an hour and transferred to a 3000-rpm centrifuge for 10 minutes. The serum was divided into five sections, each placed in a Pendrov tube. The tubes were frozen at -20 °C pending analysis avoiding serum re-thawing.

Laboratory tests

We measured the concentrations of malondialdehyde ((MDA), REF:YBS-16322), protein carbonyl ((PC), REF:YBS-10911), 8-hydroxy-deoxyguanosine ((8-OHdG), LOT:202406), reduced glutathione ((GSH), REF:YBS-11265), oxidized glutathione ((GSSG), REF:YBS-12563), glutathione peroxidase ((GPx), LOT:202406), glutathione reductase ((GR), REF:YBS-11277), and SELENBP1 (REF:YBS-14855) using a human-adaptable ELISA kit provided by Shanghai Ideal Medical Technology Co., Ltd.[29] Furthermore, we measured absorbance at 450 nm. We used a BioTek (USA) 800TS microplate reader and constructed a standard curve of optical density versus concentration using dilutions specified in the flask of each kit. Then, we measured the concentrations of the obtained samples against the standard curve, which has an analysis-specific detection range.

Statistical analysis

The current study used SPSS version 25 (IBM, Armonk, NY, USA) for statistical analysis; we extracted the results using descriptive statistics such as mean, standard deviation (SD), and percentages, as well as one-way ANOVA analysis and the Kruskal-Wallis test. We applied Pearson's correlation coefficient to evaluate the correlation coefficient (r-value), and p values less than 0.05 were considered significant.

Study design

Study design is presented in Figure 1.

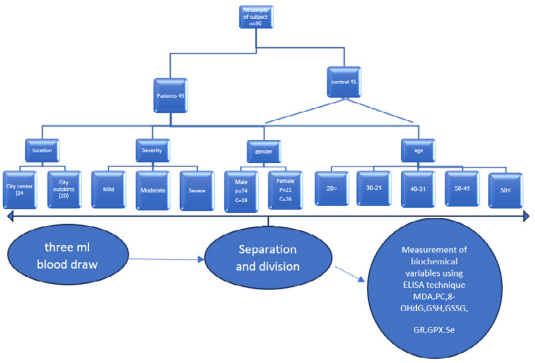

Fig. 1. Research design

Results

Table 1, which displays the demographic data and biochemical variables of the participants, indicates no statistically significant differences in the numbers of the patients and the controls, as male patients exceeded 50%. Also, the results showed more statistically significant differences in healthy people than in the patients for each variable, namely in MDA, GSSG, and GR. Moreover, the results indicated statistically significant differences in 8-OHdG and GPx in which these variables were higher in the patients than in the controls. However, these results showed no significant differences in PC, GSH, and Se levels.

Table 1. Demographic data and biochemical variables of study participants*

p	Mean±SD		Variables	
	Patients (n=45)	Controls (n=45)		
NS	33.71±13.507	32.91±12.236	Age (years)	
NS	24 (53.3%)	19 (42.2%)	Male	Gender
NS	21 (46.6%)	26 (57.7%)	Female	
0.002	1.297±3.035	1.190±3.84	MDA (0.5–8) nmol/mL	
NS	1.467±6.663	1.520±6.06	PC (0.5–8) nmol/mL	
0.001<	8.666±54.257	8.814±43.741	8-OHdG (6.25–100) ng/L	
NS	2.334±13.154	3.280±13.586	GSH (1.25–20) µmol/L	
0.001<	67.965±537.172	109.464±630.032	GSSG (150–2400) nmol/L	
0.001<	31.010±97.197	41.595±129.395	GR (10–160) U/mL	
0.013	53.661±224.706	52.282±194.785	GPx (10–160) U/L	
NS	0.683±3.725	0.861±3.679	Se (0.5–8) ng/ml	

* NS – not significant

To reveal the effect of age on serum variables, participants were divided into five age groups, as shown in Table 2. The study revealed fluctuations in MDA and PC levels, statistically significant at p<0.01, in patients and controls aged 31–40 years and different levels in 8-OHdG in most age groups shown in the table. Similarly, differences related to GSSG were observed in individuals aged 31–50 years with the same significance as the previous levels, and a decrease in GR level was observed in patients with a difference of p<0.01 at ages (31–40) and an increase in GPx level in patients with a level of p<0.01 at ages (21–30) years. No distinction was observed between the five age groups with regard to the remaining variable.

Table 2. Levels of variables according to age (Kruskal-Wallis test)*

Variables		Mean rank		p
		Controls (n=45)	Patients (n=45)	
MDA (nmol/mL)	<20	10.17	7.50	NS
	21–30	16.04	12.11	NS
	31–40	16.08	8.27	<0.01
	41–50	10.13	6.88	NS
	>50	6.20	5.83	NS
PC (nmol/mL)	<20	11.67	6.60	NS
	21–30	11.77	16.07	NS
	31–40	8.38	17.36	<0.01
	41–50	7.69	9.31	NS
	>50	6.00	6.00	NS
8-OHdG (ng/L)	<20	11.10	4.17	<0.01
	21–30	8.62	19.0	<0.001
	31–40	9.23	16.36	0.05
	41–50	6.50	10.50	NS
	>50	3.80	7.83	<0.05
GSH (µmol/L)	<20	8.00	8.80	NS
	21–30	12.62	15.29	NS
	31–40	11.31	13.91	NS
	41–50	8.88	8.13	NS
	>50	8.00	4.33	NS
GSSG (nmol/L)	<20	7.83	8.90	NS
	21–30	16.46	11.71	NS
	31–40	16.46	7.82	<0.01
	41–50	11.44	5.56	<0.05
	>50	8.20	4.17	<0.05
GR (U/mL)	<20	8.50	8.50	NS
	21–30	17.00	11.21	NS
	31–40	16.38	7.91	<0.01
	41–50	10.50	6.50	NS
	>50	8.10	4.25	NS
GPx (U/L)	<20	7.17	9.30	NS
	21–30	8.23	16.12	<0.01
	31–40	8.50	13.27	NS
	41–50	4.00	7.14	NS
	>50	6.80	5.33	NS
Se (ng/mL)	<20	7.50	9.10	NS
	21–30	12.42	15.46	NS
	31–40	14.62	10.00	NS
	41–50	8.75	8.25	NS
	>50	6.40	5.67	NS

* NS – not significant

The results in Table 3 show significant differences between males in the two groups (p<0.01) at MDA and (p<0.05) at PC. Differences appear at 8-OHdG at a significance level (p<0.01) and at GSSG with a significant difference in favor of controls at a level (p<0.001). For GPx, differences appeared in male patients at a statistical lev-

el ($p<0.05$). No significant differences were recorded in GSH and Se in males. As for females from the two groups, no significant differences appeared in MDA, PC, GSH, GSSG, and Se. While significant differences were found at 8-OHdG at a significance level ($p<0.001$). A significant increase in GR was observed in female controls ($p<0.05$) and a significant increase in GPx in female patients ($p<0.05$).

As Table 4 shows, no statistically significant differences in all variables between female and male patients have been detected.

Table 3. Level of variables in the study community according to gander (Kruskal-Wallis test)*

Variables		Mean rank		p
		Controls (n=45)	Patients (n=45)	
MDA (nmol/mL)	Male	30.47	19.61	<0.008
	Female	27.13	20.12	NS
PC (nmol/mL)	Male	18.55	27.70	<0.025
	Female	22.79	25.50	NS
8-OHdG (ng/L)	Male	16.89	28.82	<0.003
	Female	16.23	33.62	<0.001
GSH (µmol/L)	Male	25.18	23.20	NS
	Female	22.15	26.29	NS
GSSG (nmol/L)	Male	33.92	17.27	<0.000
	Female	27.12	20.14	NS
GR (U/mL)	Male	32.47	18.25	<0.001
	Female	27.60	19.55	<0.045
GPx (U/L)	Male	15.15	23.71	<0.033
	Female	16.41	27.66	<0.003
Se (ng/mL)	Male	22.79	24.82	NS
	Female	25.23	22.48	NS

* NS – not significant

Table 4. Levels of variables according to gender*

p	Mean±SD		Variables
	Female (n=21)	Male (n=24)	
NS	1.403±2.988	1.236±3.070	MDA (nmol/ml)
NS	1.483±6.726	1.480±6.616	PC (nmol/ml)
NS	10.875±55.246	6.677±53.515	8-OHdG (ng/L)
NS	2.403±13.659	2.250±12.776	GSH (µmol/l)
NS	56.695±555.510	73.302±523.418	GSSG (nmol/L)
NS	25.840±98.731	34.809±96.047	GR (U/ml)
NS	52.506±244.115	51.146±211.535	GPx (U/L)

* NS – not significant

In Table 5, the patient groups were divided according to how severe the disease is per the topical spread of psoriasis. Thus, the patients were subdivided into three groups; mild, moderate, and severe. No statistically significant differences have been noticed between the three groups in any variable.

In Table 6, the patient groups were subdivided into two groups following their places of residence (urban or suburban) and the questions answered by the patients. No significant differences regarding geographical location were noticed among the groups.

Table 5. Levels of variables according to disease severity*

Variables		Mean±SD	p	Variables		Mean±SD	p
MDA (nmol/mL)	Mild	0.707±2.494	NS	GSSG (nmol/L)	Mild	72.594±544.779	NS
	Moderate	1.349±2.874			Moderate	56.075±538.146	
	Severe	1.349±3.328			Severe	76.270±533.947	
PC (nmol/mL)	Mild	1.570±6.246	NS	GR (U/mL)	Mild	20.325±85.206	NS
	Moderate	1.313±7.250			Moderate	28.321±95.802	
	Severe	1.467±6.386			Severe	35.295±102.182	
8-OHdG (ng/L)	Mild	11.204±50.713	NS	GPx (U/L)	Mild	56.259±232.324	NS
	Moderate	7.446±52.713			Moderate	43.768±223.716	
	Severe	8.119±56.822			Severe	60.524±223.143	
GSH (µmol/L)	Mild	2.984±13.928	NS	Se (ng/mL)	Mild	0.417±3.926	NS
	Moderate	1.567±13.289			Moderate	0.885±3.655	
	Severe	2.576±12.801			Severe	0.599±3.708	

* NS – not significant

Table 6. Levels of variables according location*

p	Mean±SD		Variables
	City outskirts (n=20)	City center (n=24)	
NS	1.301±3.004	1.317±3.056	MDA (nmol/mL)
NS	1.311±6.786	1.582±6.578	PC (nmol/mL)
NS	10.593±53.984	7.247±54.444	8-OHdG (ng/L)
NS	2.446±12.849	2.274±13.365	GSH (µmol/L)
NS	64.366±530.545	71.094±541.742	GSSG (nmol/L)
NS	28.747±93.131	32.063 ±100.001	GR (U/mL)
NS	64.934±918.585	45.284±222.259	GPx (U/L)
NS	0.881±3.599	0.504±3.812	Se (ng/mL)

* NS – not significant

The study found a positive age-gender correlation at MDA, GSSG, and GR. Also, the study revealed a negative correlation at 8-OHdG and GPx with age and a positive correlation between 8-OHdG and disease severity. Table 7 shows significant differences in the correlation coefficient for other variables.

Table 7. Pearson correlation coefficient for biochemical variables and other relevant variables

Location		Severe		Gender		Age		Variables
p	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	
NS	0.200-	NS	0.258	0.012	0.258	0.002	0.311	MDA (nmol/mL)
NS	0.071	NS	0.063-	NS	0.155-	NS	0.199-	PC (nmol/mL)
NS	0.026-	0.044	0.289	0.000	0.522-	0.000	0.519-	8-OHdG (ng/L)
NS	0.110-	NS	0.175-	NS	0.100	NS	0.077	GSH (µmol/L)
NS	0.082-	NS	0.057-	0.000	0.360	0.000	0.461	GSSG (nmol/L)
NS	0.110-	NS	0.194	0.002	0.316	0.000	0.407	GR (U/mL)
NS	0.095-	NS	0.050-	NS	0.157-	0.013	0.272-	GPx (U/L)
NS	0.155-	NS	0.082-	NS	0.065	NS	0.030-	Se (ng/mL)

* NS – not significant

Table 8 indicates a direct correlation between MDA-GR, PC-GPx, and PC-Se. Additionally, the correlation between (8-OHdG) and antioxidants from the glutathione system showed no significant differences.

Table 8. Pearson correlation coefficient for oxidative stress and antioxidant levels of the glutathione system*

Se		GPX		GR		GSSG		GSH		Variables
p	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	
NS	0.151	NS	0.043-	0.045	0.208	NS	0.178	NS	0.062	MDA
0.042	0.210	0.026	0.246	NS	0.143-	NS	0.023-	NS	0.055	PC
NS	0.120	NS	0.165	NS	0.021-	NS	0.015	NS	0.017	8-OHdG

* NS – not significant

Figures 2 to 4 show us that there is a positive relationship in the glutathione system.

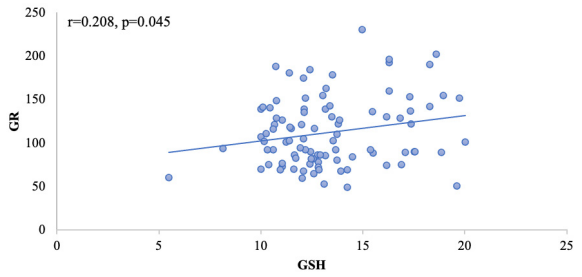

Fig. 2. Correlation between GSH and GR in psoriasis patients

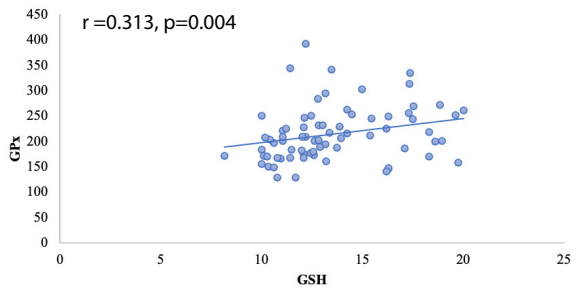

Fig. 3. Correlation between GSH and GPx in psoriasis patients

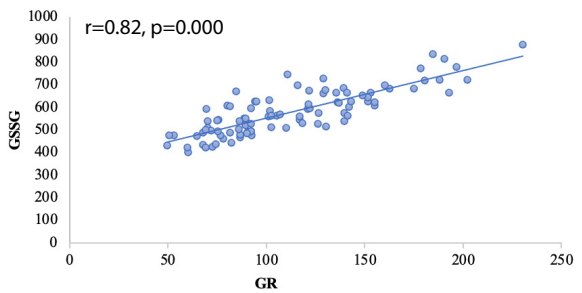

Fig. 4. Correlation between GSSG and GR in psoriasis patients

Discussion

MDA is one of the final oxidation products of unsaturated fats in cells. As free radicals trigger MDA production, it is a sign of oxidative stress.[30] The apparent results showed that psoriasis patients do not suffer from high fat oxidation, and these results were consistent with another study.[31] A positive association was observed between (MDA-GR) and age. The GR enzyme is important in renewing reduced glutathione in the detoxification of peroxides. Obviously there is a balance between antioxidants and oxidation as patients were found to have not suffered from fat oxidation. Hence, this study is consistent with another study.[32] Also, there is a gradual increase in PC in patients as it increases at 31–40 year-old patients, which indicates statistically significant differences. In other words, psoriasis patients suffer from protein oxidation. A previous study conducted in Basrah, Iraq reported similar findings with this study, having indicated a positive association between (PC-PX) and (PC-Se).[33] Likewise, other studies have confirmed that the presence of GPx reduces the amount of protein carbonyl compounds treated with oxidative stress-generating factors.[34] There are four main forms of GPx, with GPx1 depends mainly on selenium.[35] In the same view, results showed that PC was positively associated with both GPX and Se. Additionally, the results revealed significant differences as an increase in 8-OHdG in patients. This is one of the dominant forms of DNA in mitochondria and is considered a sign of oxidative stress that causes DNA damage.[36] It is also a good biomarker for assessing the risk of developing various types of cancer.[37] A previous study that agrees with the results of the current study that showed that the level of 8-OHdG can be considered a useful biomarker for early detection of psoriasis.[38] Another study conducted at the University of Basra evaluated 8-OHdG in saliva and found it to be a suitable sample for diagnosing and identifying many diseases.[39] The results showed that the level of 8-OHdG in female patients is higher than in males. The control group included more males than females, prompting us to consider the impact of female hormones on the level of oxidation, as noted in a study.[40] It also found no correlation between 8-OHdG and glutathione antioxidants, supporting another study.[41] A meta-analysis of 298 original articles found that several polymorphisms in genes encoding markers or enzymes related to redox homeostasis influence the interaction between psoriasis and oxidative stress.[31] The study demonstrated increased levels of oxidized DNA/RNA molecules in the serum of patients with exacerbated psoriasis vulgaris. Sex, the presence of metabolic syndrome, or cigarette smoking minimally influenced the results. In the psoriatic blood cells' DNA, the authors observed longer telomeres compared to healthy controls, particularly in females. The psoriasis cases exhibited marginal clinical importance due to the marginally higher global DNA methylation in their DNA compared to the controls.[42] UV radiation also leads to DNA damage, generating immune-stimulatory DNA motifs, such as 8-hydroxyguanosine.[43] Furthermore, we noticed a positive correlation between GSH-GR and GSH-GPx, and according to the

mechanism of glutathione's action in the body, it is certain that there is a positive correlation between them.[44] The results show that the glutathione system is effective in psoriasis patients, despite the apparently significant differences. The results agree with a study of the glutathione system on psoriasis patients, but they are within the limits of measurement, i.e., they do not threaten the patient with glutathione system dysfunction-associated diseases.[45,46] What is questionable is that in most chronic diseases, oxidative stress values increase with increasing severity of the disease.[47] However, in psoriasis, we observed stability and relatively negligible fluctuations in the level of the variables in relation to the severity of the disease, which prompts us to expect stability in the oxidation system and antioxidants in psoriasis patients. The study also found that the participants' geographical locations had no significant effect on the relevant variables, which could be attributed to the lack of different eating styles in both groups and that most rural residents living near urban communities have embraced city-like norms. We recommend continuing this research to confirm the importance of the studied variables, as 8-OHdG may be a risk indicator for psoriasis patients, and the results may appear different depending on the measurement method, as the accuracy of the results cannot be completely confirmed.

Study limitations

Even though we eliminated numerous samples due to their unsuitability for analysis or delays in storage, we cannot ensure the validity of all the samples under study. This is because data from the patient and control groups, as well as from the researcher, play a crucial role. We also employed several research measurements specific to ELISA, and given exposure to poor storage and transportation conditions, may have yielded varying results.

Conclusion

To some extent, psoriasis patients suffer from oxidative stress. Moreover, psoriasis is not related to lipid peroxidation or protein oxidation. While there is a marker for DNA oxidation, it has different results in psoriasis patients than in healthy individuals. We observed a correlation between MDA-GR and PC-GPx, as well as a correlation between PC and selenium, which serves as the cofactor of the GPx enzyme. However, we found no correlation between the glutathione system and DNA oxidation, indicating that the glutathione system does not influence the latter. The results of the analyses showed no significant differences as far as disease severity and geographical location are concerned.

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Declarations

Funding

The study was funded by Department of Chemistry, College of Education for Pure Sciences, University of Basrah.

Author contributions

Conceptualization, A.A. and S.S.; Methodology, A.A.; Software, A.A.; Validation, A.A. and S.S.; Formal Analysis, A.A.; Investigation, S.S.; Data Curation, A.A.; Writing – Original Draft Preparation, S.S.; Writing – Review & Editing, A.A.; Visualization, A.A.; Supervision, S.S.; Project Administration, A.A.; Funding Acquisition, S.S.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability

The data that support the findings of this study are available from Hassan A.A. but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Hassan A.A.

Ethics approval

The Ethics Committee approved the protocol on 7/1/2024, Issue 12, and we conducted the study in accordance with the Declaration of Helsinki.

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