RESEARCH ARTICLE

Profiling serum levels of glutathione reductase and interleukin-10 in positive and negative-PCR COVID-19 outpatients: A comparative study from southwestern Iran

Mahshid Naghashpour1 | Hamid Ghiassian2 | Sara Mobarak3 | Maryam Adelipour4 | Maghsud Piri5 | Maryam Seyedtabib6 | Sahar Golabi7

1Department of Nutrition, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran
2School of Medicine, Abadan University of Medical Sciences, Abadan, Iran
3Department of Infectious Diseases, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran
4Department of Biochemistry, School of Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
5Vice Chancellor for Health, Abadan University of Medical Sciences, Abadan, Iran
6Department of Biostatistics and Epidemiology, School of Public Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
7Department of Medical Physiology, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran

Correspondence
Sahar Golabi, Department of Medical Physiology, School of Medicine, Abadan University of Medical Sciences, Ayatollah Taleghani Blvd, Abadan, Iran.
Email: s.golabi@abadanums.ac.ir

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Abstract
Since the outbreak of COVID-19 in China, it has rapidly spread across many other countries. We evaluated antioxidant defense systems and inflammatory status related to the SARS-CoV2 infection in a population from southwestern Iran. Comorbidities and clinical symptoms of 104 subjects (comprising negative and positive-PCR COVID-19 outpatients) were assessed. Serum concentrations of glutathione reductase (GR) and interleukin-10 (IL-10) were measured using ELISA. In the positive-PCR group, follow-ups on clinical symptoms were carried out for 28 days at 7-day intervals. In the positive-PCR group, hypertension, diabetes, liver disease, chronic heart disease, and chronic kidney disease were the most common comorbidities. In the general category of symptoms, we found a significant difference between negative and positive-PCR groups, except regarding runny noses. In the pulmonary category, there was a significant difference between the two groups except in terms of chest pain. We also determined a significant difference in neurologic symptoms, except for ear pain, between negative and positive-PCR groups. We also found significantly lower levels of GR but higher levels of IL-10 in the positive-PCR group (p = 0.000 for both). In the positive-PCR group, serum levels of IL-10 (odds ratio = 0.914, p = 0.012) decreased the chances of neurological symptoms occurring over time. The antioxidant defense systems of positive-PCR outpatients failed as demonstrated by a reduction in the serum levels of GR. We also indicated a dysregulation in the immune response against COVID-19, characterized by changes in serum IL-10 levels.

KEYWORDS
COVID-19, glutathione reductase, interleukin-10, southwestern Iran

1 | INTRODUCTION
The rapid global spread of SARS-CoV2, or COVID-19, has become a difficulty for the health system, and identifying high-risk individuals has become a critical challenge.1 COVID-19 is transmitted through respiratory droplets or direct contact and respiratory tract infections. Most cases cause pneumonia, and 15% of cases lead to acute respiratory distress syndrome (ARDS).2 The SARS-CoV2 coronavirus epidemic is characterized by a high infection rate and a relatively high mortality rate. In most severe cases, the clinical manifestations of the disease—in addition to fever, cough, and other conditional symptoms—are cytokine storms, respiratory failure, and eventually death. Symptoms of COVID-19 can vary from person to person. Symptoms may also vary across different age groups.3 Immunology-based studies enlighten the possible
pathophysiological mechanisms of COVID-19 infection may be useful to establish more efficient management protocols.4

Human COVID-19 is divided into low and highly pathogenic species. However, the infection caused by this virus is not necessarily followed by recognizable symptoms. The low pathogenic COVID-19 infects the upper respiratory tract and causes mild respiratory problems such as colds. The highly pathogenic form causes more severe problems, such as acute respiratory syndrome, by infecting the lower airways.5

For laboratory diagnosis of the virus, the virus's RNA can be detected using RT-PCR from samples of the upper respiratory tract, the lower respiratory tract, and blood plasma. This test is currently the gold standard for diagnosing the virus.6,7

The SARS-CoV2 receptor is an angiotensin-converting enzyme 2 (ACE2) that is expressed by almost all human organs.3 ACE2 is a protease that, along with the angiotensin-converting enzyme (ACE), is part of the renin-angiotensin system. Downstream effects of ACE activation include vasoconstriction, oxidative stress, inflammation, and apoptosis. Downstream effects of ACE2 activation include vasodilation, angiogenesis, anti-inflammatory, antioxidant, and antiapoptotic effects. The balance between the expression and activity of ACE- ACE2 is regulated by a set of interactions between dehydroepiandrosterone (DHEA), cortisol, 25- (OH) 2-vitamin D, and glutathione (GSH). Each person can have a different balance between ACE and ACE2, which can explain differences in people’s reactions to an infection caused by a particular virus.

Reducing oxidative stress, which is secondary to an imbalance between ACE and ACE2, might be the best way to prevent and treat COVID-19. ACE2 is inactivated when bound to a virus. This inactivation of ACE2 subsequently leads to an imbalance between the numbers of angiotensin II (ANGII) and angiotensin molecules. By binding to AT1R, ANGII activates NADPH oxidases, which transport an electron from NADPH to O2, producing O·- radicals.12 The overproduction of ROS and deprivation of antioxidant mechanisms are important for virus replication and subsequent virus-associated disease. It is noteworthy that a marked increase in the blood levels of cytokines and chemokines has been observed in patients with COVID-19 infection. Cytokine storms create a pro-inflammatory environment associated with severe tissue damage and fatal outcomes in COVID-19 patients.

On the other hand, the relationship between inflammation and oxidative stress is well established.13 In a previous study, the clinical features of COVID-19 were examined in a group of patients in Shanghai. Compared to non-ICU patients, patients admitted to the ICU were found to have higher glutathione reductase than other patients (66.7 vs. 36.9).14 In another study that investigated the relationship between antioxidant defense status, malondialdehyde (MDA), and viral load in patients with hepatitis C virus (HCV) infection, it was found that oxidative stress participates in the pathogenesis of HCV infections. Fifty patients whose HCV infections were confirmed by serological and molecular markers and 40 healthy volunteers (the positive control group) were included. Patients were classified according to viral load. The levels of catalase, SOD, and glutathione peroxidase (GPx) of red blood cells and serum MDA were measured in all groups. The results showed a decrease in SOD and GP levels and an increase in MDA and catalase levels in patients with HCV when compared to the healthy control group—these differences were statistically significant, except that concerning catalase (p = 0.05, t = 19.3). Thus, the data obtained in patients infected with HCV showed a significant decrease in the level of antioxidant enzymes and a significant increase in the level of MDA as an indicator of oxidative stress.15

Another study investigated the association between viral infection and oxidative stress related to the Mayaro virus (MAYV), a tropical arbovirus. In this study, whether MAYV causes oxidative stress in host cells
was investigated by measuring ROS production, oxidative stress markers, and antioxidant defense at various time intervals after MAYV infection. The results showed that MAYV caused significant oxidative stress in HepG2-infected cells. This was demonstrated by an increase in MDA and carbonyl protein levels and a significant decrease in the ratio of reduced glutathione to oxidized glutathione (GSH/GSSG).\(^{15}\)

Inflammation is involved in COVID-19 pathology. In COVID-19 patients, the release of pro-inflammatory cytokines causes active inflammation, which damages the lungs.\(^ {17}\) The alteration of inflammatory markers in COVID-19 patients can be a good indicator to consider when finding these patients.

Studies have shown a link between inflammatory markers and the severity of COVID-19.\(^ {18}\) Interleukin-10 (IL-10) is one of the cytokines that predicts the severity of COVID-19 disease.\(^ {19}\) IL-10 is a significant component of the cytokine system that regulates and suppresses the expression of pro-inflammatory cytokines during the healing stages of infections, thereby reducing the damage caused by inflammatory cytokines. IL-10 is a central negative regulator of inflammation. Another important point about this cytokine, which is doubly important in COVID-19 studies, is the importance of IL-10 in viral immunity control. IL-10 balances pro-inflammatory signals induced by viral PAMPs (pathogen-associated molecular patterns).\(^ {20}\)

Studies that have examined the antioxidant profile of COVID-19 patients are limited. Also, previous studies have reported varied and contradictory results regarding the status of the inflammatory factor IL-10 in patients with COVID-19 of different severities. Besides this, the society of Abadan County is generally an immigrant society of different ethnicities and diverse genetic resources. It should also be noted that the antioxidant and inflammatory profile is affected by a person’s climatic conditions, region, ethnicity, nutritional patterns, and living and welfare conditions. So, their evaluation is of therapeutic, nutritional, health, and epidemiological importance.

As mentioned, very few studies have evaluated the oxidant/antioxidant status of patients with COVID-19 (especially in the lower grades of the disease), and contradictory results have been presented in the few studies in this field. There are also needs to evaluate the oxidant/antioxidant values to balance the level of immunity in different grades of outpatient and hospitalized patients, maintain or increase the level of antioxidants in the blood circulation in COVID-19 patients, and assess the inflammatory system as an indicator for clinical evaluation of the disease course in the target population of this study. For these reasons, this study aimed to evaluate and compare the antioxidant (serum levels of glutathione reductase) and inflammatory (IL-10) profiles of positive and negative PCR outpatients of COVID-19 referred to health centers in southwestern Khuzestan (Abadan and Khorramshahr cities).

### 2 METHODS

#### 2.1 Study design and subjects

This epidemiologic, cross-sectional study was approved by the ethics and research review committee of the Abadan University of Medical Sciences (Ethics Code: IR.ABADANUMS.REC.1399.116). A written letter of introduction was obtained from the vice-chancellor of education and research for the vice-chancellor for the health of the university to cooperate and provide the PCR results (positive or negative) of the outpatients referred to comprehensive health centers in Abadan city. Then, the study sample was selected from the statistical population of the cities of Abadan and Khorramshahr in the province of Khuzestan. The participants were taken from the population of patients who were referred to one of the comprehensive health centers of Abadan from the beginning of April 2020 to the end of July 2020 and who underwent a PCR test for COVID-19. A simple random sampling method was used. Voluntary consent was obtained from the subjects before their participation in the study. Clients who wished to participate in the study and completed the informed consent form entered the study. Inclusion criteria were as follows: all ages over 11, male and female patients, clear PCR result (positive, negative), willingness to participate in the study, and the ability to understand the relevant information and complete the informed consent form. Exclusion criteria were as follows: pregnancy and lactation in women, unclear PCR test result, undergoing a second PCR test, smoking during the test period, use of drugs that affect the oxidant-antioxidant profile and the inflammatory system, and—for the control group—not working in high-risk jobs (including health care staff, counter offices, and driving public transport).

The necessary information was given to the selected individuals via telephone conversations, and they were invited to Imam Khomeini Health Center of Abadan. In this center, the participants completed and signed the informed consent form. Comorbidities and COVID-19 symptoms were evaluated using a researcher-made questionnaire for the self-report of patients. Patients were then referred to a private health laboratory in Abadan for blood sampling. The day of referral to Imam Khomeini Health Center was considered the first day of the study for each participant. Clinical symptoms of positive-PCR outpatients were followed up on and recorded for 28 days in 1-week intervals by telephone contact.

#### 2.2 Study groups

The study groups were as follows:

1) Negative-PCR: The non-COVID-19 group comprised patients whose COVID-19 disease was not confirmed by PCR. Also, the CT results of these people were checked if available—if the person’s CT was positive despite the negative PCR test, the person was not included in the study. In addition to CT, the jobs of people whose PCR was negative were checked. If the person had a high-risk job (e.g., medical staff, bank staff), he/she was excluded from the study. The history of exposure and suspicious symptoms of individuals in this group were also accurately assessed through reporting from individuals to minimize the possibility of false results in the negative PCR test. People who reported a history of exposure or suspicious symptoms, such as
fever, coughing, and headaches in the last 2 weeks were not included in the study despite the negative PCR test result.

2) Positive-PCR: These patients were infected individuals whose PCR tests were positive for SARS-CoV2. Fifty-two participants were included in each group. However, in each group, seven serum samples were not usable because they contained insufficient volumes required for biochemical analysis.

2.3 Clinical assessments

In Imam Khomeini Health Center of Abadan, an expert colleague recorded participants’ comorbidities using a researcher-made questionnaire for self-reporting. Hypertension, diabetes, cancer, liver disease, chronic lung disease, chronic neurological disease, chronic kidney disease, chronic heart disease, and AIDS/HIV were questioned. COVID-19 clinical signs were assessed in four categories as (1) General (fever, fatigue, night sweating, shivering, runny nose, and sore throat), (2) pulmonary (chest pain, dry cough, and breath shortness), (3) gastrointestinal (nausea, vomiting, anorexia, diarrhea, constipation, and bloating), and (4) neurologic (myalgia, ear pain, joint pain, taste/odor disorder, and headache). Moreover, clinical symptoms of the positive-PCR group were followed for 28 days at weekly intervals.

2.4 Laboratory examination of blood samples

About 5 ml of blood was taken with a collection tube from each person in each group. Blood samples were transferred to a tube without anticoagulant for serum isolation and tests for glutathione reductase and IL-10. Serum samples were separated by 2000 rpm/20 min centrifugation. To measure serum levels of desired variables, a calorimetry method was employed using a kit and a spectrophotometric device. The GR and IL-10 kits were made by Zellbio.

To measure the levels of glutathione reductase in serum, samples and standards were first prepared. Then, 50 μl of the sample/standard was added to the test tubes for each previously labeled sample/standard. In the next step, 50 μl of R4 was added. Then, 1 ml of chromogen solution was added to the test tube. The resulting mixture was heated in a boiling water bath for 1 h. The tubes were then allowed to cool in an ice bath and then centrifuged for 10 min at 3000–4000 rpm. In the next step, 200 μl of the pink supernatant was removed by pipette. The supernatant was poured into a microplate, and the sample absorbance was read at 535 nm using an ELISA reader.

To measure serum levels of IL-10, after preparing the reagents, samples, and standards, we added 40 μl of the sample, plus 10 μl of the interleukin 10 antibodies, to the respective wells. We then added 50 μl of the standards to the respective wells. Also, 50 μl of streptavidin-HRP was added to all wells. The wells were then incubated at 37°C for one hour.

After that, washing was performed, and 100 μl of chromogen solution was added. The mixture was incubated for 10 min at 37°C. Then, 50 μl of stop solution was added, and the adsorption was read at 450 nm using an ELISA reader. Using standard concentrations and read absorptions, the standard curve was plotted, and then the concentration of interleukin 10 in each sample was calculated.

2.5 Statistical analysis

Using the Kolmogorov–Smirnov test, the normality of the data was checked. The results were demonstrated as mean ± standard deviation (SD) for quantitative and number (percent) for qualitative variables. An independent sample t-test was used to compare quantitative data, and the Chi-square was used to compare the qualitative data between the study groups. The generalized estimating equations (GEE) technique model was used with AR (1) correlation to analyze a longitudinal data set with two measurements (serum levels of GR and IL-10) on a positive-PCR group (45 subjects) for each of the four dichotomous outcome variables (general, pulmonary, gastrointestinal, and neurologic symptoms), separately. The odds ratio (OR) and confidence interval values (95% CI) for OR were reported for each model. Statistical analysis was performed using SPSS software (SPSS Inc.) version 21. The significance level was considered 0.05.

3 RESULTS AND DISCUSSION

3.1 Comorbidities and clinical symptoms

The results of the comparison of comorbidities and clinical signs between positive and negative-PCR groups are presented in Table 1. In the studied comorbidities, significant differences were not observed between positive and negative groups, which was expected due to the presence of PCR-positive patients in the early (asymptomatic/mild, moderate) stages of the disease. In line with our observations, Yang et al. found that underlying diseases may be risk factors for severe patients compared with non-severe patients.

Our results are also consistent with those of other studies showing that underlying diseases are associated with a poor prognosis and a higher chance of worsening disease and death. In the positive-PCR group, hypertension, diabetes, liver disease, chronic heart disease, and chronic kidney disease were the most common comorbidities (18.9%, 11.3%, 9.4%, 7.5%, and 5.7%, respectively). Yang et al. in a systematic review and meta-analysis, also found that the most prevalent comorbidities in 1576 infected patients were hypertension and diabetes, which is in line with our results. Like us, Guan et al. reported that the most prevalent comorbidity in their study population (1590 cases of COVID-19) was hypertension, followed by diabetes.

We assessed and reported clinical symptoms in four categories. In the general category, we found a significant difference between
negative and positive-PCR groups, except regarding the runny nose symptom. In the pulmonary category, there was a significant difference between the two groups except in terms of chest pain. Gastrointestinal symptoms were assessed only in the positive-PCR group. Diarrhea, nausea, blowing, constipation, and vomiting were the most common gastrointestinal symptoms (35.8%, 20.8%, 15.1%, 9.4%, and 5.7%, respectively). We also detected a significant difference in neurologic symptoms, except for ear pain, between negative and positive PCR groups. Odor disorder was not assessed in the negative-PCR group.

### Table 1

| Variable category | Variables                          | Positive PCR group (n = 52) | Negative PCR group (n = 52) | p    |
|-------------------|-----------------------------------|-----------------------------|-----------------------------|------|
| Serum biomarkers  | GR (u/L)                          | 23.3 ± 14.6                 | 44.2 ± 26.8                 | 0.000|
|                   | IL-10 (ng/ml)                     | 23.8 ± 8.1                  | 20.7 ± 5.4                  | 0.000|
| Comorbidities     | Hypertension (%)                  | 10 (18.9%)                  | 5 (9.4%)                    | 0.132|
|                   | Diabetes (%)                      | 6 (11.3%)                   | 4 (7.5%)                    | 0.371|
|                   | Cancer (any) (%)                  | 2 (3.8%)                    | 0 (0%)                      | 0.248|
|                   | Liver disease (%)                 | 5 (9.4%)                    | 3 (5.7%)                    | 0.358|
|                   | Chronic lung disease (%)          | 2 (3.8%)                    | 0 (0%)                      | 0.248|
|                   | Chronic neurological disease (%)  | 2 (3.8%)                    | 1 (1.9%)                    | 0.493|
|                   | Chronic kidney disease (%)        | 3 (5.7%)                    | 4 (7.5%)                    | 0.500|
|                   | Chronic heart disease (%)         | 4 (7.5%)                    | 2 (3.8%)                    | 0.348|
|                   | AIDS/HIV (%)                      | 2 (3.8%)                    | 0 (0%)                      | 0.248|
| General symptoms  | Fever (%)                         | 12 (22.6%)                  | 3 (5.7%)                    | 0.012|
|                   | Fatigue (%)                       | 32 (60.4%)                  | 5 (9.4%)                    | 0.000|
|                   | Night sweating (%)                | 25 (47.2%)                  | 3 (5.7%)                    | 0.000|
|                   | Shivering (%)                     | 5 (9.4%)                    | 0 (0%)                      | 0.028|
|                   | Runny nose (%)                    | 4 (7.5%)                    | 1 (1.9%)                    | 0.181|
|                   | Sore throat (%)                   | 14 (26.4%)                  | 4 (7.5%)                    | 0.009|
| Pulmonary symptoms| Chest pain (%)                    | 5 (9.4%)                    | 1 (1.9%)                    | 0.103|
|                   | Dry cough (%)                     | 23 (43.4%)                  | 9 (17%)                     | 0.003|
|                   | Breath shortness (%)              | 14 (26.4%)                  | 4 (7.5%)                    | 0.009|
| Gastrointestinal symptoms | Nausea (%)                      | 11 (20.8%)                  | –                            | –    |
|                   | Vomiting (%)                      | 3 (5.7%)                    | –                            | –    |
|                   | Diarrhea (%)                      | 19 (35.8%)                  | –                            | –    |
|                   | Constipation (%)                  | 5 (9.4%)                    | –                            | –    |
|                   | Blowing (%)                       | 8 (15.1%)                   | –                            | –    |
| Neurologic symptoms| Myalgia (%)                      | 11 (20.8%)                  | 1 (1.9%)                    | 0.002|
|                   | Joint pain (%)                    | 13 (24.5%)                  | 2 (3.8%)                    | 0.002|
|                   | Ear pain (%)                      | 5 (9.4%)                    | 1 (1.9%)                    | 0.103|
|                   | Taste disorder (%)                | 26 (49.1%)                  | 0 (0%)                      | 0.000|
|                   | Odor disorder (%)                 | 33 (62.3%)                  | –                            | –    |
|                   | Headache (%)                      | 18 (34%)                    | 6 (11.3%)                   | 0.005|

*The results were shown as mean ± standard deviation (SD) for quantitative and number (percent) for qualitative data. Independent sample T and chi-square tests were applied to compare study groups.*
3.2 | Biochemical assays

In this study, GR values were examined to evaluate how antioxidant values are affected in COVID-19 outpatients. We also profiled serum levels of IL-10 to assess inflammatory status among our study population. Fifty-two outpatients diagnosed as positive for SARS CoV2 RT-PCR, as well as a control group (diagnosed as negative for SARS CoV2 RT-PCR) of 52 healthy individuals (matched to the positive group in terms of sex and age) were included in the study. Forty-five individuals’ serum GR and IL-10 values were determined. The results of the comparison between the groups’ GR and IL-10 values are presented in Table 1.

We found significantly lower levels of GR in the positive-PCR group ($p = 0.000$). Also, the serum levels of IL-10 were significantly higher in the positive-PCR group ($p = 0.000$). A common denominator in all conditions associated with COVID-19 appears to be the impairment of redox homeostasis, which is responsible for ROS accumulation. So, the antioxidant system could be critical in extinguishing the exacerbated inflammation that triggers organ failure caused by COVID-19.

GR is an enzyme that catalyzes the reduction of glutathione disulfide (GSSG) to the sulfhydryl form of glutathione (GSH), which is a critical molecule in resisting oxidative stress and maintaining the reducing environment of the cell. Karkhanei et al.25 measured the levels of glutathione, total antioxidant capacity, and total oxidant status in the serum of patients with COVID-19. A total of 96 individuals with and without COVID-19 were enrolled and divided into an infected group and a healthy (control) group. The researchers found elevated levels of oxidative stress and reduced antioxidant status in the patient group,25 in line with our results—we also reported a significant decrease in serum levels of GR, an antioxidant enzyme, in the patient group.

In another study, Muhammad et al.26 recruited 50 COVID-19 symptomatic patients and 21 healthy individuals as controls in northwest Nigeria. Levels of antioxidant trace elements (Se, Zn, Mg, Cu, and Cr), 8-isoprostaglandin F2 alpha, and malondialdehyde in the plasma and erythrocyte activity of glutathione, glutathione peroxidase, superoxide dismutase, and catalase were determined. The researchers concluded that COVID-19 patients are prone to depleted levels of antioxidant substances,26 which is in line with our results.

Increased levels of inflammatory cytokines and excessive activation of T lymphocytes, macrophages, and endothelial cells called “cytokine storm” were observed in COVID-19 cases. Interferon-gamma (IFN-$\gamma$), interleukin 6 (IL-6), tumor necrosis factor-alpha (TNF-$\alpha$), IL-10, IL-1, IL-5, IL-8, IL-10, and granulocyte-macrophage colony-stimulating factor (GM-CSF) were reported to be the main mediators behind cytokine storm.4 Lu et al.27 reported a unique feature of cytokine storms in COVID-19 patients (i.e., the dramatic elevation of IL-10), which supports the results obtained in our study. This elevation is thought to be a negative feedback mechanism to suppress inflammation. Inefficient viral clearance at any stage is a hallmark of COVID-19. Disease severity is associated with increases in peripheral blood cytokines, among which IL-10 increases particularly early and independently of patient age, which is not seen in active SARS-CoV infections. The known multi-faceted immune regulatory role of IL-10—both in protecting the lung from injury and in defense against infections, as well as its potential cellular source—should be considered. Although the absence of an IL-10 response in SARS is thought to contribute to early deterioration, it is expected that IL-10 protects the lungs from early immune-mediated damage and interferes with viral clearance in COVID-19.28 Also, in experimental Rhesus Macaques, serum IL-10 levels were elevated about 16-fold as early as on the first day after SARS-CoV-2 infection.29

In contrast to COVID-19, blood levels of IL-10 in symptomatic SARS patients, including severe cases, did not differ from the blood of the control group. The lack of an increase in IL-10 in SARS-CoV infection has been suggested to contribute to early immune-mediated lung damage30 and, more recently, to a higher frequency of the fatal aggravation of lung injuries in SARS patients when compared to COVID-19 patients.31

3.3 | Possible association between basal serum levels of estimated biomarkers and the progression of symptoms during the clinical course of the disease

The relationships of serum levels of GR and IL-10 with the progression of symptoms during the clinical course of the disease are presented in Table 2. In terms of the general, pulmonary, and gastrointestinal categories of symptoms, we did not see any relationships between any of the examined parameters and the chances of symptoms occurring. In the neurologic category, there was a significant relationship between serum levels of IL-10 and the chances of symptoms occurring over time. Thus, serum levels of IL-10 ($OR = 0.914, p = 0.012$) had a

| Table 2 | Odds ratio (OR) and 95% confidence interval (95% CI) estimated by GEE analysis with AR (1) model to determine the clinical symptoms’ progression and the associations with serum levels of GR, and IL-10 among positive PCR outpatients |
|----------|-----------------------------------------------|
| Parameters | Clinical symptoms category$^a$ | General | Pulmonary | Gastrointestinal | Neurologic |
| | OR (95% CI) | $p$ | OR (95% CI) | $p$ | OR (95% CI) | $p$ | OR (95% CI) | $p$ |
| GR | 1.024 (0.997–1.051) | 0.081 | 1.031 (0.993–1.070) | 0.111 | 1.006 (0.947–1.039) | 0.722 | 0.994 (0.961–1.028) | 0.739 |
| IL-10 | 0.969 (0.899–1.044) | 0.410 | 1.031 (0.956–1.112) | 0.423 | 0.952 (0.895–1.013) | 0.119 | 0.914 (0.852–0.981) | 0.012 |

$^a$Dependent variables.
decreasing effect on the outcomes and the chance of occurrence of neurological symptoms. In line with our observation, Zhao et al. demonstrated that the early production of inhibitory mediators, including IL-10 and IL-1RA, were significantly associated with disease severity. They also reported that a combination of CCL5, IL-1 receptor antagonist (IL-1RA), and IL-10 at week one might predict the patient’s outcomes. They enrolled a total of 71 patients with laboratory-confirmed COVID-19 and 18 healthy volunteers.32

4 | CONCLUSION

In the infected systems of the viral agents, there are significant changes to cellular homeostasis. These changes are caused mainly by high levels of oxidative stress biomarkers and depletion of the antioxidant defense system. We investigated the failure of the antioxidant defense system in positive-PCR COVID-19 outpatients and confirmed it by demonstrating a reduction in the serum levels of GR, an antioxidant enzyme. We also indicated a dysregulation in the immune response against COVID-19, characterized by changes in serum IL-10 levels. As we investigated and demonstrated this change in the early stages of the SARS-CoV2 infection, the serum levels of this cytokine can be used as a predictor for quickly diagnosing patients with a high risk of disease deterioration.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Sahar Golabi contributed to conceptualization, project administration, methodology, and writing the original draft. Mahshid Naghashpour contributed to the methodology and writing the original draft. Maryam Adelipour, Hamid Ghiassian, Sara Mobarak, and Maghsud Piri contributed to the data collection, and investigation. Maryam Seyedtabib contributed to data analysis. Sahar Golabi contributed to funding acquisition, formal analysis, supervision, writing, review & editing.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

ORCID

Mahshid Naghashpour https://orcid.org/0000-0003-3616-6881
Sara Mobarak https://orcid.org/0000-0002-4530-1080
Maryam Adelipour https://orcid.org/0000-0002-5670-3595
Maghsud Piri https://orcid.org/0000-0002-9057-1506

Maryam Seyedtabib https://orcid.org/0000-0003-1599-9374
Sahar Golabi https://orcid.org/0000-0002-1210-7222

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