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Oxidative stress and anti-oxidant status in children with sepsis

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Abstract

Background Sepsis is a life-threating cause in childhood ages. The recognition and treatment early are significant for decreasing mortality. Sepsis has many factors and various biomarkers function in the pathogenesis, the stress indicators oxidants increased and antioxidants decreased. The objective of our study was to investigate the levels of thiol disulfides with and without sepsis in a pediatric intensive care unit (PICU).

Materials and methods A cohort study was conducted between October 2022 and March 2023 at the PICU, comprising 64 with sepsis and 62 children without sepsis. Blood samples from sepsis and the control group were collected and centrifuged. Subsequently, the samples were stored at -80 °C until the day of the experiment. Once the requisite number of patients had been enrolled, the thiol-disulfide values in the collected samples were analysed in accordance with the ELISA kit method.

Results The research parameters investigated, namely total oxidant status, plasma 8-OHdG, total-native thiol and native/total thiol percent ratio, were found to be considerably elevated in the sepsis group in comparison to the control ($p < 0.05$). Furthermore, the oxidative stress parameters investigated (total antioxidant status, paraoxonase 1 activity, disulfide, disulfide/native thiol percent ratio, disulfide/total thiol percent ratio) were found to be significantly lower in the sepsis group than in control ($p < 0.05$).

Conclusions In our study as well, we detected all antioxidant parameters are low and oxidant parameters are statistically significantly higher in sepsis. Our study posits that thiol-disulfide levels have the potential to serve as a diagnostic tool in conjunction with traditional established biomarkers of inflammation in critically ill children in the PICU who are being treated for sepsis.

Clinical trial registration Not applicable.

Keywords Sepsis, Pediatric, Intensive care, Oxidant, Antioxidant

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Introduction

Sepsis is characterised by a systemic inflammatory response syndrome associated with immune system abnormalities, microcirculation disorders and end-organ failure induced by infection. Septic shock and associated organ dysfunction syndromes are caused to increased mortality/morbidity in children's age [1, 2]. Early recognition and treatment are key to reducing mortality from pediatric sepsis. Despite the development of treatment options for sepsis and septic shock, mortality rates of 5–40% are still reported [3]. Severe diseases, such as sepsis, are crucial in pediatric ages and must be treated in pediatric intensive care units. (PICU) [4]. Sepsis is characterised by a range of variable features, including systemic inflammation, disruption to the immune system, irregularities in microcirculation and the malfunctioning of organs. The sepsis severity is contingent upon the progression to severe sepsis and shock. The presence of a systemic inflammatory response syndrome (SIRS) in children with a suspected or proven infection is defined as sepsis. In order to diagnose SIRS, it is sufficient to observe the presence of at least two of the following criteria: fever or hypothermia, tachycardia, tachypnoea, and an elevated leukocyte count (at least one of which must be accompanied by an abnormal body temperature or leukocyte count) [5].

The development of cellular and metabolic processes in organisms depends on the oxidants and antioxidants being in a specific equilibrium [6]. The elevation of oxidative stress (OS) levels results in cellular injury due to the heightened presence of endogenous or exogenous oxidants, namely reactive oxygen species (ROS) [7]. The oxidants in question induce damage to lipids, proteins and DNA within cells, which ultimately results in cell death. A growing body of evidence from recent studies suggests that the levels of ROS are elevated in sepsis patients [8]. Moreover, it has been observed that the antioxidant potential may be diminished in the initial stages of sepsis in comparison to that observed in healthy individuals. However, following the administration of sepsis therapy, the levels of these antioxidants have been shown to return to normal or even elevated levels [6, 8].

The plasma thiol contains potent antioxidants that are capable of eliminating free radicals within the physiological environment. Plasma levels of these compounds are among the most reliable indicators of an individual's antioxidant status. In physiological conditions, and in the absence of disease, a certain equilibrium exists between the thiols and the disulfides. This balance is thanks to the protective role of redox homeostasis in cellular metabolism. This is a metabolic process known as dynamic thiol/disulfide homeostasis. If this redox homeostasis proceeds to increase free radicals, OS ensues. This condition has been linked to the onset of various pathological processes [9, 10].

The objective of our study was to assess the potential of thiol/disulfide levels as a tool for the diagnosis of sepsis in patients in the PICU. Additionally, the levels of oxidant and antioxidant parameters in septic patients were also investigated in our case-control study.

Methods

A cohort study was conducted between October 2022 and March 2023 at the PICU, comprising 64 with sepsis and 62 children without sepsis. In this heterogeneous cohort of admissions, comprising patients with a range of conditions including sepsis, multiple traumas, pneumonia, congenital metabolic diseases, status epilepticus, and genetic disorders, we conducted a comprehensive evaluation of their clinical and laboratory features during their stay in the PICU.

The patients included in the study as a sepsis group (SG) were receiving treatment for sepsis or septic shock at the time of the study in the PICU. The patients included in the control group (CG) were treated for other aetiologies without evidence of sepsis. In our study, SG and CG patients were selected and matched in terms of age, gender, length of stay, comorbidity, PRISM III scoring, initial respiratory support, initiation of inotropic agents and mortality.

Patients were included in the sepsis group with the presence of at least two criteria. The study population comprised all patients who met the clinical and laboratory criteria for pediatric sepsis, with or without microbial culture growth. Patients aged between 0 and 18 years old, with malnutrition, malignancy, or systemic hematological diseases, were excluded from the study.

The demographics, past histories, comorbidities, length of stay, the Pediatric Risk of Mortality Score III (PRISM III), initiation of mechanical ventilation, laboratories (included at inflammation markers, lactate, albumin, etc.), use of inotropic drugs, morbidities, and mortalities were evaluated. These data were detected in their electronic and archive files.

Increased C-reactive protein (CRP) level and white blood cell (WBC) count are indicative of infection in sepsis. Also, high lactate levels are used as an adult sepsis criterion, too. But, albumin levels are decreased levels in sepsis and infection as a negative acute phase response indicator. These laboratory findings are generally used in infections and sepsis. In our study, these laboratory findings were used to support the accuracy of thiol/disulfide levels and to identify sepsis patients. When the data obtained from our own study were evaluated, the effect size was calculated as 2.08. Accordingly, the power of the study was found to be 99.98%.

Blood samples were obtained from the selected patients within 48 to 72 h of meeting the inclusion criteria, after which they were subjected to centrifugation. Subsequently, the plasma and serum samples were stored at -80 °C until the day of the experiment. Once the requisite number of patients had been enrolled, the thiol-disulfite values in the collected blood samples were analysed in accordance with the ELISA kit method. The laboratory analyses of the blood samples taken were performed in accordance with the following methodology and absorbance measurements were performed using a UV-VIS Spectrophotometer.

Measurement of 8-OHdG levels

Immediately following the collection of heparinised blood samples (2–3 ml), these were subjected to centrifugation at 3000 rpm (1512 g) for a period of 15 min at room temperature. This was done in order to facilitate the analysis of 8-OHdG. Subsequently, the plasma was stored in microtubes at − 80 °C until analysis. The 8-OHdG concentration in plasma samples was determined using a commercially available ELISA kit (NWK-8-OHdG02; Northwest Life Science Specialties, LLC, WA, USA). The intra-assay coefficient of variation for the 8-OHdG assays was calculated to be 5.9%. The plasma 8-OHdG concentrations were expressed in ng/ml. Calibration, curve fitting, and data analysis were conducted in accordance with the manufacturer's instructions [11].

Measurement of paraoxonase 1 (PON1) activity

Paraoxon was used as a substrate and the color absorption of paraoxon at 412 nm at 37 °C was measured. The PON1 activity was measured by reading the absorbances with a spectrophotometer (Genesys 10 UV Scanning UV/VIS Spectrophotometer; Shimadzu) using kits (Rel Assay Diagnostics kit; Mega Tıp). PON1 activity was measured as basal activity and the results were expressed in units per liter (U/L) [12].

Measurement of total oxidant status (TOS)

Serum TOS levels were measured using spectrophotometrically (Genesys 10 UV Scanning UV/VIS Spectrophotometer; Shimadzu) at 530 nm using kits (Rel Assay Diagnostics kit; Mega Tıp, Gaziantep, Turkey) developed by Erel [13].

Measurement of total antioxidant status (TAS)

Serum TAS levels were measured spectrophotometrically (Genesys 10 UV Scanning UV/VIS Spectrophotometer; Shimadzu, Kyoto, Japan) at 660 nm using kits (Rel Assay Diagnostics kit, Mega Tıp, Gaziantep, Turkey) developed by Erel [14].

Oxidative stress index (OSI)

OSI, which is an indicator of oxidative stress, was expressed as the percentage of the ratio of TOS levels to TAS levels [15]. Specifically, OSI (arbitrary unit) = TOS (μmol H_2O_2 Eq/L) / TAS (mmol Trolox Eq/L).

Total and native thiol measurement and disulfide calculation

The total thiol and native thiol measurements were conducted using the modified Ellman method, as described by Erel et al. [13]. The disulfide level was calculated using the following formula: [(total thiol-native thiol)/2]. The results for disulfide/native thiol, disulfide/total thiol, and native thiol/total thiol were obtained by proportioning the total thiol level, native thiol level, and disulfide to each other. The resulting data were expressed as percentages and subjected to comparative analysis [10].

Ethics approval and consent to participate

Prior to the commencement of the study, the requisite ethical approval was obtained from the Harran University Clinical Research Ethics Committee (HRÜ/22.21.16). The study was conducted in accordance with the principles set forth in the Declaration of Helsinki. A signed informed consent form was obtained from the families or legal guardians of all patients included in the study. In addition, consent was obtained from the patients themselves over the age of 16. Clinical trial number: Not applicable.

Statistical analysis

The statistical analysis was conducted using the IBM® SPSS® 26 software (SPSS Inc., Chicago, IL, USA) for Windows 22.0. The normality of the variables was assessed using analytical methods, specifically the Kolmogorov-Smirnov test. Descriptive analyses were presented as mean and standard deviation. Descriptive statistics were employed to ascertain the frequency and percentage values of the categorical variables pertaining to sociodemographic and clinical information. The independent two-sample t-test was employed for the comparison of groups, given that the values in question were normally distributed. In the case of non-normally distributed enzyme levels, the non-parametric Mann-Whitney U test and the Wilcoxon rank-sum test were employed to ascertain the significance of the observed differences between variables. The data are presented with mean values ± standard deviation (SD). A p-value of less than 0.05 was considered to be statistically significant.

Results

The study cohort comprised 64 children in the SG and 62 children in the CG, all of whom were treated in the PICU between November 2022 and January 2023. The patients,

Table 1 Demographic, prognostic, and statistical analysis results of sepsis and control groups

	Sepsis group ($n=64$)	Control group ($n=62$)	*P* values
Age (month) (mean ± SD)	42.18 ± 56.79	38.11 ± 46.64	0.322
Gender	**Boy/Girl**	**Boy/Girl**	0.191
	24(37.5%) 40(62.5%)	32(51.6%) 30(48.4%)	
Comorbidity	**Yes/No**	**Yes/No**	0.128
	40(62.5%) 24(37.5%)	40(64.5%) 22(35.5%)	
Lenght of stay (day) (mean ± SD)	30.90 ± 41.60	29.03 ± 53.93	0.350
PRISM III score (mean ± SD)	31.30 ± 31.77	12.45 ± 12.03	0.001
Respiratory support	**n(%)**	**n(%)**	0.001
room air	0	8 (12.9%)	
HFNC	2 (3.1%)	4 (6.5%)	
BIPAP	10 (15.6%)	18 (29%)	
invasive MV	52 (81.3%)	32 (51.6%)	
Inotropic treatment	**Yes/No**	**Yes/No**	0.001
	54(84.4%) 10(15.6%)	6(9.7%) 56(90.3%)	
Mortality	**Alive/Exitus**	**Alive/Exitus**	0.007
	36(56.3%) 28(43.7%)	54(87.1%) 8(12.9%)	

*PRISM III: Pediatric Risk of Mortality Scores III, HFNC: High Flow Nasal Cannulas Oxygen Therapy, BIPAP: Bi-level Positive Airway Pressure Therapy, MV: Mechanical Ventilation

*Data are presented with mean values ± standard deviation (SD)

Table 2 Laboratory results and statistical comparisons of two (sepsis and control) groups

Laboratory analysis	Sepsis group (mean ± SD)	Control group (mean ± SD)	*P* values
Hemoglobin (Hb) (g/dL)	9.79 ± 1.84	10.70 ± 1.64	0.043
Hematocrit (Htc) (%)	29.10 ± 5.02	31.46 ± 4.41	0.053
White blood cell (WBC) (10^3/uL)	15015.62 ± 10721.03	9998.70 ± 5488.61	0.023
Platelets (Plt) (10^3/uL)	244687.50 ± 167366.78	331612.90 ± 198169.23	0.064
C-reactive protein (CRP) (mg/L)	105.99 ± 59.64	9.64 ± 15.08	0.001
pH	7.35 ± 0.09	7.36 ± 0.09	0.758
pCO2 (mmHg)	45.05 ± 13.53	46.04 ± 15.09	0.785
HCO3 (mmol/L)	24.38 ± 6.41	24.22 ± 5.03	0.915
Lactate (mmol/L)	1.89 ± 1.26	1.40 ± 0.73	0.065
Albumin (g/L)	29.22 ± 6.17	36.51 ± 5.96	0.001

* Data are presented with mean values ± standard deviation (SD)

*The increased levels of WBC and CRP levels were shown to be related to sepsis

*The decreased levels of albumin levels were shown to be related to sepsis

both SG and CG, included in our study's descriptive features (age, gender, comorbidity) and their length of stay in PICU, mortality rates, PRISM III scores, first respiratory supports, and the status of initiating inotropic treatment were shown in detailed Table 1. Additionally, the mortality rates of SG (48.3%) were much than CG (17.9%). Although the matching of age, gender, comorbidity and length of stay were not statistically significant ($p > 0.05$); PRISM III scores, type of respiratory supports, initiating of inotropic treatment, and mortality were significant ($p < 0.05$). These statistical analysis results of sepsis and control groups are shown in Table 1.

The WBC and CRP are increased in sepsis as a positive indicator of infection. High lactate levels are also utilized as an adult sepsis criteria. In our study, WBC and CRP were higher in SG compared to CG. But, albumin levels which is decreased levels in sepsis and infection as a negative acute phase response indicator. We detected in study, the albumin levels were lower in SG than in CG. A comparison of the hemoglobin, WBC, CRP, and albumin levels revealed a notable statistical discrepancy between the two groups ($p < 0.05$). In contrast, no notable discrepancy was observed in the levels of hemotocrite, platelets, pH, pCO_2 and lactate ($p > 0.05$). The analysis results of the these laboratory tests on the study day of the SC and CG are also shown in Table 2.

When our SG patients were examined, the source of sepsis was respiratory 40 (62.5%) and bloodstream infection 24 (37.5%), and microbial growth was detected in the blood culture of 48 (75%) of these patients. Microbial growth types were 34 (53.1%) gram-negative, 10 (15.6%) gram-positive bacterial, and 4 (6.3%) fungi, respectively.

The current study revealed that all oxidative stress parameters, including TOS, OSI, 8-OHdG levels, native thiol, total thiol, and the native thiol/total thiol percent ratio, were significantly elevated in the SG group compared to the CG group ($p < 0.05$). Furthermore, the antioxidant parameters (TAS, PON1), disulfide, disulfide/native thiol percentage ratio (%), disulfide/total thiol percentage ratio (%)) were found to be significantly lower in SG than in CG ($p < 0.05$). The laboratory values and statistically analysis comparisons of the oxidant and antioxidant parameters examined in our study are shown in Table 3.

Discussion

This study makes a significant contribution to the literature on pediatric sepsis by elucidating the potential diagnostic role of thiol-disulfide homeostasis in critically ill children. A key strength of our research is the relatively large sample size (64 sepsis, 62 control) and its conduction in a PICU, setting it apart from prior studies that

Table 3 The laboratory values and comparisons of the oxidant and antioxidant parameters

	Sepsis group	Control group	*P* values
TAS (mmol Trolox equiv./L)	4.28 ± 0.66	6.56 ± 0.89	0.032
TOS (μmol H2O2 equiv./L)	51.33 ± 12.46	37.30 ± 9.24	0.019
OSI (arbitrary unit)	0.12 ± 0.05	0.06 ± 0.02	0.023
PON1 (U/L)	10.21 ± 5.17	21.75 ± 10.11	0.042
Plasma 8-OHdG levels (ng/ml)	4.03 ± 1.49	1.56 ± 1.51	0.039
Native thiol (mmol/L)	492.72 ± 56.39	388.41 ± 43.57	0.022
Disulphide (mmol/L)	11.99 ± 5.43	13.48 ± 7.01	0.041
Total thiol (mmol/L)	516.71 ± 53.90	415.37 ± 46.13	0.035
Disulphide/native thiol percent ratio (%)	2.43 ± 1.28	3.47 ± 1.76	0.011
Disulphide/total thiol percent ratio (%)	2.32 ± 1.13	3.24 ± 1.37	0.015
Native thiol/total thiol percent ratio (%)	95.35 ± 6.40	93.50 ± 5.88	0.017

*TAS: Total Antioxidant Status, TOS: Total Oxidant Status, OSI: Oxidative Stress Index, PON1: Paraoxonase 1 Activity Measurement

* Data are presented with mean values ± standard deviation (SD)

often involve smaller cohorts or different patient populations. Unlike traditional approaches that primarily focus on inflammatory biomarkers, our study provides a comprehensive evaluation of oxidative stress and antioxidant defense mechanisms, emphasizing the disruption of thiol-disulfide balance in pediatric sepsis. One of the most innovative aspects of this study is its focus on thiol-disulfide homeostasis as a novel biomarker, which has been relatively underexplored in the pediatric sepsis setting. By utilizing a systematic biochemical approach, we offer new insights into the role of oxidative stress in sepsis pathophysiology. The findings demonstrate a significant increase in oxidative stress markers and a concomitant decline in antioxidant parameters, reinforcing the hypothesis that thiol-disulfide homeostasis plays a crucial role in sepsis. By integrating these biochemical markers into the clinical framework, our study underscores their potential utility in improving the early diagnosis and prognostic assessment of sepsis in critically ill children. This study's originality lies in its novel biomarker approach, large-scale application in a PICU setting, and comprehensive evaluation of oxidative stress parameters, thereby laying the groundwork for future clinical applications and potential therapeutic strategies.

Sepsis is a severe disease in which many factors are involved and various biomarkers function in the pathogenesis. In this situation, the stress indicators oxidants increased and antioxidants decreased. Nevertheless, there are very few studies in the literature on sepsis and antioxidants and they are mostly studies in adult patients [4, 7, 16]. The role of thiol/disulfide homeostasis as a critical marker of oxidative stress is increasingly recognised and studied in a range of disorders.

The biochemical serum levels and effects, whether normal or abnormal, play a significant role in identifying the progression of diseases [9]. The thiol/disulfide as an antioxidant parameter have been studied in gestational diabetes mellitus, acute myocardial infarctions, and primary hypertension in adults [16, 17, 18]. Furthermore, as in our own study, Ayar G et al. examined the thiol/disulfide homeostasis in children with sepsis [4]. A reduction in total thiol, native thiol and disulfide levels, and native thiol/total thiol ratio was observed in patients with sepsis. The findings suggest that antioxidant balance is disrupted in sepsis and other critically ill patients, as evidenced by previous literature [6, 8, 20]. In our study, we also identified TOS, OSI, and plasma 8-OHdG levels as potential OS indicators. Additionally, we observed a notable elevation in native thiol, total thiol, and the native thiol/total thiol percent ratio in SG relative to CG. Furthermore, the antioxidant stress parameters TAS, PON1, disulfide, disulfide/native thiol percent ratio, and disulfide/total thiol percent ratio in SG were found to be significantly lower than in CG.

In Turkey, another adult study of septic patients about thiol and disulfide levels was done by Yıldız [21]. He evaluated thiol and disulfide levels and compared with acute phase reactants. It was observed that the thiol-disulfide balance was disrupted in cases of septic shock and sepsis. The levels of native thiol, total thiol, and dynamic disulfide were found to be diminished in patients with septic shock and sepsis. Conversely, the levels of native thiol, total thiol, and dynamic disulfide bond were elevated in the group of patients who survived [21]. These results were similar to studies with sepsis patients of Lorente L and et al., Kumar S and et al. studies [6, 8, 20].

A multicenter study was conducted to evaluate the antioxidant capacity in adult patients with sepsis and to compare this with the survival status of the patients. The researchers identified a correlation between total antioxidant levels and mortality in patients with severe sepsis. Consequently, they proposed that an antioxidant capacity could serve as an indicator to predict the course of severe sepsis [20]. The results of our study demonstrated that the levels of antioxidant stress markers in the sepsis patient group were statistically significantly lower than those observed in the control group. Additionally, the mortality rate in the sepsis patient group was found to be 2.7 times higher. Moreover, a recent study conducted by Lorente L [6]. examining antioxidant capacity in septic patients during the initial seven-day period following the onset of sepsis identified a correlation between the severity of sepsis and mortality [6]. In contrast to the aforementioned studies, Karapetsa M and colleagues investigated the total antioxidant capacity as a potential indicator of severe sepsis on the initial day of septic shock. However, they did not identify a statistically significant difference

between the antioxidant balance of the survivor and non-survivor groups [22].

The reflection of the hyperinflammation process observed in pediatric sepsis patients on oxidative stress parameters is a subject of interest. A prospective observational study was conducted on this subject, examining 42 healthy children with sepsis and a control group. Oxidative stress and inflammatory activity biomarkers were determined in the serum samples of the included patients. Patients suffering from non-severe and severe sepsis exhibited higher levels of plasma antioxidant capacity, lower erythrocyte thiol index, lower superoxide dismutase and catalase activities, higher glutathione peroxidase activity, and higher plasma F_2-isoprostanes concentration than the control group. Patients with severe sepsis demonstrated higher NF-kappaB activation in comparison to those with non-severe sepsis. Despite observing alterations in certain biomarkers among patients with unfavourable clinical prognoses, the investigated biomarkers failed to demonstrate correlation with clinical estimators of outcome [23]. In another study published in 2017, 33 sepsis diagnosed and 30 healthy control children were included in the study and the effects of paraoxonase (PON), stimulated paraoxonase (SPON), arylesterase (ARE), ceruloplasmin (CLP), myeloperoxidase (MPO), and catalase (CAT) levels on sepsis prognosis were investigated. The examinations of the included patients were taken at the time of admission, at the 48th hour, and on the 7th day and compared. Lower ARE, lower CLP, lower MPO, and higher CAT levels were determined in the sepsis group compared to the control group. There was no difference between the groups in terms of PON and MPO levels. In this study, it was determined that ARE, CLP, CAT, and MPO levels were different between pediatric patients with sepsis and healthy controls. ARE level may be a strong biomarker for sepsis in critically ill patients in intensive care units [24]. Similarly, in our study, when comparing sepsis and non-sepsis patient groups in the PICU, it was found that all antioxidant parameters were low and oxidant parameters were statistically significantly higher in sepsis. Although various oxidant and antioxidant parameters have been studied, studies with larger patient populations and long-term follow-up are needed for clearer results.

In the evaluation of SG and CG demographics; PRISM III scores, type of respiratory supports, initiating of inotropic treatment, and mortality were statistically significant. However, the length of stay was not found to be statistically significant, given that the patients included in the study had been admitted to the PICU prior to the commencement of the study, and the treatment process could vary considerably between patients.

In the definition of adult septic shock, the criterion of sepsis and hypotension despite fluid support was previously used. In accordance with the revised criteria, the administration of vasopressors and the monitoring of serum lactate levels above 2 mmol/L are advised in order to maintain a mean arterial pressure value of 65 mmHg or above, despite the implementation of adequate fluid resuscitation [25, 26]. However, as it is known, lactate level is also used clinically as a holistic indicator of oxygenation and perfusion adequacy and microcirculatory dysfunction [27]. In our study among the non-sepsis patients included, there usually were multiple organ traumas, postcardiac arrest, and postoperative surgery patients. Therefore, lactate levels were not significantly higher in SG than CG, as is shown in Table 2.

The findings of our study indicate that thiol-disulfide balance can be considered as an important biomarker in patients diagnosed with sepsis in the PICU. The findings support the role of oxidative stress in sepsis pathogenesis and suggest that thiol-disulfide homeostasis can be used as a potential indicator in the early diagnosis and prognosis follow-up of sepsis. Our study has taken an important step towards understanding the effects of oxidative stress in this patient group by revealing that thiol-disulfide homeostasis shows significant changes in pediatric patients with sepsis. Further studies with larger patient groups are needed to confirm these findings and integrate them into clinical practice. Thiol-disulfide balance is an important indicator of oxidative stress and may change in inflammatory processes such as sepsis. We believe that our study can make a new contribution to the literature by examining the clinical use potential of this biomarker in terms of sepsis diagnosis in pediatric patients. Thiol-disulfide balance may be associated with sepsis in adult patients, but studies investigating changes in PICU patients are limited. This is an important factor that makes our study original.

There are limitations due to the lack of single-center and intermittent control samples. Furthermore, the fact that tests with infection indicators such as procalcitonin and sedimentation, were not studied in the patients included in the study. Pediatric sepsis patients in our region are the ones who reveal the sepsis/septic shock clinic and laboratory data very clearly due to the delays in admission times. It is beyond question that oxidant and antioxidant parameters are reliable, given that the condition of the patients at the time of admission is serious and unambiguous.

Conclusions

Early recognition and treatment of sepsis is important for reducing mortality. Oxidative stress parameters increased and antioxidants decreased due to the pathophysiology of sepsis. In our study, we detected that all antioxidant parameters are low and oxidant parameters are statistically significantly higher in sepsis patients.

Our study demonstrates that thiol-disulfide homeostasis shows significant changes in pediatric patients with sepsis, thus taking an important step towards understanding the effects of oxidative stress in this patient group. Further studies with larger patient groups are needed to confirm these findings and integrate them into clinical practice.

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Author contributions
H.F.A. conceived the idea and was involved in clinical care of the patients. H.F.A. and M.A. collected the samples and performed statistical analyzes of the data. S.O. examined the samples. H.F.A., M.A., S.O. wrote the first draft of the manuscript which was critically revised by all the authors. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Harran University Clinical Research Ethics Committee (HRÜ/22.21.16) approval was obtained by before the study began for the study. A signed informed consent form was obtained from the families or legal guardians of all patients included in the study. In addition, consent was obtained from the patients themselves over the age of 16.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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