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ORIGINAL ARTICLE

The effect of full blood count and cardiac biomarkers on prognosis in carbon monoxide poisoning in children

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Abstract

Aims In this study, cardiac biomarkers, blood parameters, electrocardiography (ECG), and echocardiography were investigated in children with carbon monoxide (CO) poisoning, and the diagnostic value of these parameters was investigated.

Methods The demographical, clinical, and laboratory data of children aged 0–18 years who were admitted to the pediatric emergency department due to CO poisoning between January 2019 and January 2022 were retrospectively scanned from medical records. The patients were divided into two groups as troponin-I positive and troponin-I negative.

Results There were 107 children aged 0–18 years (average age, 10.46 ± 5.77 years; 51% female) with CO poisoning. There were 13 patients with troponin-I positive myocardial injury. Troponin-I was positive in 3 patients whose carboxyhemoglobin (COHb) level was below 2% at the time of admission. In one patient, troponin-I, which was normal at admission, increased by the 24th hour of hospitalization. Hyperbaric oxygen therapy was given due to headache in one patient, although the COHb level of that patient was below 25%. An NT-proBNP level of ≥ 219.5 ng/L predicted the development of troponin-I positivity with a sensitivity of 70% and a specificity of 86.7% (AUC, 0.967 (0.58–0.994); $p = 0.017$). White blood cell (WBC), neutrophil, neutrophil-to-lymphocyte ratio (NLR), immature granulocyte (IG), and IG% levels were found to be significantly higher in the troponin-positive patient group.

Discussion and conclusion NT-proBNP has been shown to be an early diagnostic marker for myocardial dysfunction. Additionally, when cardiac markers are not available, full blood parameters may assist clinicians for patient treatment and referral.

Keywords Blood · Carbon monoxide poisoning · Carboxyhemoglobin · NT-proBNP · Pediatric emergency department · Troponin-I

Introduction

Carbon monoxide (CO) is a tasteless, odorless, colorless, non-irritant, and lighter-than-air gas that is formed due to the incomplete combustion of organic materials and fossil fuels [1]. It is also known as a silent killer, as victims die without realizing that they have been poisoned [2]. CO poisoning is seen in places which are not adequately ventilated and mostly in cold climates and winter months [3, 4]. Sometimes, CO poisoning can be seen due to the blockage of discharge pipes by heavy snow clogs [5]. An increased rate of CO poisoning has also been reported after hurricanes

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[6]. In addition, CO poisoning can occur by inhaling solvents containing methylene chloride [7].

CO reduces the oxygen-carrying capacity of hemoglobin and impairs the release of oxygen to the tissues. In addition, it shows harmful effects by binding to other heme-containing substance, such as myoglobin, guanylate cyclase, certain cytochromes, and nitric oxide synthase [8, 9]. Vital organs are affected by CO poisoning, causing short-term and long-term morbidity, even death in some cases [10, 11].

BNP is released from the ventricles to the peripheral circulation mainly by mechanical stress, alpha adrenergic agonists, endothelin1, angiotensin 2, interleukin (IL)-1β, IL-18, tumor necrosis factor (TNF)-α, and transforming growth factor (TGF)-β. It antagonizes the renin–angiotensin–aldosterone system, causing a decrease in vascular tone, natriuresis and diuresis. In addition, its antifibrotic and antihypertrophic effects have also been demonstrated in the heart [12, 13].

Cardiovascular complications caused by CO poisoning have mostly been reported as left ventricular dysfunction, arrhythmia, myocardial stunning, arrhythmias, and pulmonary edema.

A literature search performed by our team has shown that although several studies have evaluated cardiac functions of adult patients with CO poisoning, similar studies in pediatric patients are scarce [14–16]. In this study, we investigated cardiac markers, blood parameters, electrocardiography (ECG), and echocardiography in children with CO poisoning. We aimed to investigate the diagnostic values of these parameters.

Methods

Study design and patients

In this single-center, retrospective study, we enrolled children aged 0–18 years, who were admitted to the pediatric emergency department of a tertiary university hospital for CO poisoning between January 2019 and January 2022. Annually, approximately thirty-four thousand children are admitted to the pediatric emergency department of that university hospital. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee before the study.

Patients with congenital or acquired heart disease were excluded from the study.

The diagnosis of CO poisoning was made with a history of CO exposure, clinical findings and symptoms caused by CO poisoning, and blood carboxyhemoglobin (COHb) level [17]. Since COHb level may be low in patients with a long period of time between hospital admission and CO exposure, carbon monoxide poisoning was diagnosed using clinical symptoms, history, and carbon monoxide half-life in such patients [16].

Data analysis

Demographic, laboratory, and clinical data of the patients were obtained from the medical records. Full blood count, blood gas analysis, troponin-I, NT-proBNP, creatine kinase (CK), CK-MB, albumin, aspartate transaminase (AST), alanine transaminase (ALT), electrocardiography, and echocardiography were performed. While laboratory studies were performed in all patients at the time of admission, ECG and echocardiography were performed in patients with an elevated troponin-I level.

Myocardial damage was defined as a troponin-I value above 0.02 (µg/L). The patients diagnosed with CO poisoning were divided into 2 groups as those with troponin-I value above 0.02 (µg/L), which represented the troponin-positive group with myocardial damage, and those with a troponin-I value less than 0.02 (µg/L), which represented the troponin-negative group without myocardial damage.

Indications for hyperbaric oxygen therapy included a COHb level of 25% or greater, presence of neurological symptoms such as unconsciousness, confusion, headache, seizure, and evidence of myocardial ischemia [16].

The level of consciousness was assessed with the Glasgow coma score [18].

Troponin-I analysis

Serum troponin-I levels were measured via a one-step enzyme immunoassay using a Roche Cobas 8000 automatic analyzer (with an analytical range of 0.01–0.02 µg/L).

NT-proBNP analysis

Serum NT-proBNP levels were determined by using the AQT90 FLEX analyzer (Radiometer Medical, Copenhagen, Denmark); the cut-off value was set at 133 ng/L.

Electrocardiography and echocardiography

Electrocardiography (ECG) was performed at the time of admission, while echocardiography was performed in patients with troponin elevation within 1 h of the presentation at the latest. In addition, ECG and echocardiography were re-evaluated at discharge. ECGs and echocardiographic studies of the patients were evaluated by a pediatric cardiologist.

Table 1 Comparison of demographic and laboratory data of children with carbon monoxide poisoning according to troponin-I

	Troponin-I negative ($n=94$)	Troponin-I positive ($n=13$)	p
Age (year)	8.56 ± 4.56	7.48 ± 4.24	0.33
Sex (female/male)	49/45	6/7	0.77
GCS	13.9 ± 0.62	12.15 ± 1.99	< 0.001
pH	7.36 ± 0.04	7.28 ± 0.09	0.010
pCO_2 (mmHg)	42.49 ± 8.07	43.13 ± 6.55	0.788
HCO_3 (mmol/L)	22.76 ± 2.73	19.24 ± 4.44	0.015
COHb (%)	14.28 ± 9.96	17.05 ± 13.48	0.379
Lactate (mmol/L)	2.33 ± 1.07	4.70 ± 3.50	0.032
WBC ($\times 10^9$/L)	10.26 ± 4.09	15.33 ± 4.41	< 0.001
Neutrophil ($\times 10^9$/L)	5.60 ± 3.08	11.32 ± 4.78	< 0.001
Lymphocyte ($\times 10^9$/L)	3.64 ± 2.30	3.02 ± 2.31	0.356
Monocyte ($\times 10^9$/L)	0.67 ± 0.36	0.85 ± 0.48	0.102
NLR	2.89 ± 7.81	5.70 ± 3.84	0.041
LMR	5.68 ± 2.24	4.12 ± 2.79	0.064
IG%	0.259 ± 0.139	0.678 ± 0.382	0.001
IG ($\times 10^9$/L)	28.44 ± 22.97	108.57 ± 75.12	0.002
Hb (g/dL)	12.78 ± 1.27	12.64 ± 1.25	0.697
PLT ($\times 10^9$/L)	293.91 ± 79.19	321.64 ± 65.91	0.217
INR	1.59 ± 2.32	1.11 ± 0.09	0.652
Albumin (g/L)	4.54 ± 0.27	4.46 ± 0.35	0.401
AST (U/L)	26.28 ± 7.09	38.36 ± 24.61	0.091
ALT (U/L)	15.10 ± 5.85	15.14 ± 5.03	0.979

Statistics: Mann–Whitney *U* test; chi-square test

Abbreviations: *pCO_2*, carbon dioxide partial pressure; *HCO_3*, bicarbonate; *COHb*, carboxyhemoglobin; *WBC*, white blood cell count; *NLR*, neutrophil-to-lymphocyte ratio; *LMR*, lymphocyte-to-monocyte ratio; *IG*, immature granulocyte; *Hb*, hemoglobin; *PLT*, platelet; *INR*, international normalized ratio; *AST*, serum aspartate transaminase; *ALT*, alanine transaminase

Statistical analysis

Statistical Package for Social Sciences for Windows 22 software was used for statistical analysis. Study variables were presented as number (n) and percentage (%) and mean ± standard deviation. The normality of the distribution of the study variables was tested using the Kolmogorov–Smirnov test. Normally distributed numerical parameters were evaluated with one-way analysis of variance or Student's t test. Kruskal–Wallis or Mann–Whitney U test was used for numerical variables without a normal distribution. The relationship between the variables was analyzed by Pearson correlation analysis. Receiver operating characteristic (ROC) curve analysis was performed to find an estimated optimal cut-off point. A p value less than 0.05 was considered statistically significant.

Ethical approval

This study was approved by the ethics committee of the Kahramanmaraş Sutcu Imam University before its start (No.: 2022/09–04).

Results

There were 107 children aged 0–18 years with CO poisoning (average age 10.46 ± 5.77 years; 51% female). The source of CO poisoning was an improperly planned ventilation system of an indoor heating system or its accidental malfunction in all patients. There were 13 patients with troponin-positive myocardial injury and 94 troponin-negative patients. There was no significant difference between the patient groups in terms of gender distribution and mean age (Table 1). Glasgow coma scale of the patients was lower in the troponin-positive group (Table 1). Three troponin-I positive patients had a carboxyhemoglobin (COHb) level below 2% at the time of admission. A patient with a normal admission troponin-I level had an increased troponin-I level at the 24th hour of hospitalization. Eight patients were administered hyperbaric oxygen therapy. Hyperbaric oxygen therapy was given due to headache in one patient, although the COHb level of that patient was below 25%. It was applied to the other 7 patients because their COHb level was above 25%. None of our patients was intubated. None of our patients was connected to a mechanical ventilator, and no vasoactive

Table 2 Comparison of cardiac biomarkers of children with carbon monoxide poisoning according to troponin-I

	Troponin-I negative ($n=94$)	Troponin-I positive ($n=13$)	p
NT-proBNP 0 h (ng/L)	113.63 ± 154.24	2317.01 ± 3583.79	0.005
NT-proBNP 6 h (ng/L)	177.40 ± 249.94	3750.60 ± 4117.46	0.003
NT-proBNP 12 h (ng/L)	118.67 ± 137.04	2983.36 ± 3773.64	0.031
NT-proBNP 24 h (ng/L)	120.16 ± 134.38	1942.60 ± 3053.46	0.092
CK 0 h (U/L)	115.73 ± 44.62	232.14 ± 193.13	0.043
CK 6 h (U/L)	103.42 ± 47.49	271.55 ± 190.78	0.030
CK 12 h (U/L)	91.30 ± 28.15	546.84 ± 1053.39	0.162
CK 24 h (U/L)	107.34 ± 42.11	455.30 ± 1007.90	0.419
CK-MB 0 h (µg/L)	3.11 ± 2.24	21.45 ± 28.18	0.030
CK-MB 6 h (µg/L)	3.82 ± 1.60	30.29 ± 45.83	0.085
CK-MB 12 h (µg/L)	1.75 ± 1.85	19.94 ± 29.60	0.047
CK-MB 24 h (µg/L)	1.88 ± 1.76	9.51 ± 17.05	0.300

Statistics: Mann–Whitney *U* test

h hour, *NT-proBNP* NT-pro–brain natriuretic peptide, *CK* creatine kinase

drug was given to any patient. Sixteen patients were treated in hospital.

Comparison of cardiac biomarkers by troponin-I status in children with CO poisoning was presented in Table 2. A comparison of the laboratory data of troponin-positive and troponin-negative patients revealed that the NT-proBNP values at admission, the 6th hour, and the 12th hour were significantly higher in the troponin-positive group ($p=0.005$, $p=0.003$, and $p=0.031$, respectively). There was no significant difference between the two groups regarding the NT-proBNP value measured at the 24th hour ($p=0.092$). Using a ROC curve analysis, we found that the best cut-off point of NT-proBNP to predict troponin positivity in patients with CO poisoning was ≥ 219.5 ng/L. Accordingly, we determined that a NT-proBNP level of ≥ 219.5 ng/L predicted troponin positivity with a sensitivity of 70% and a specificity

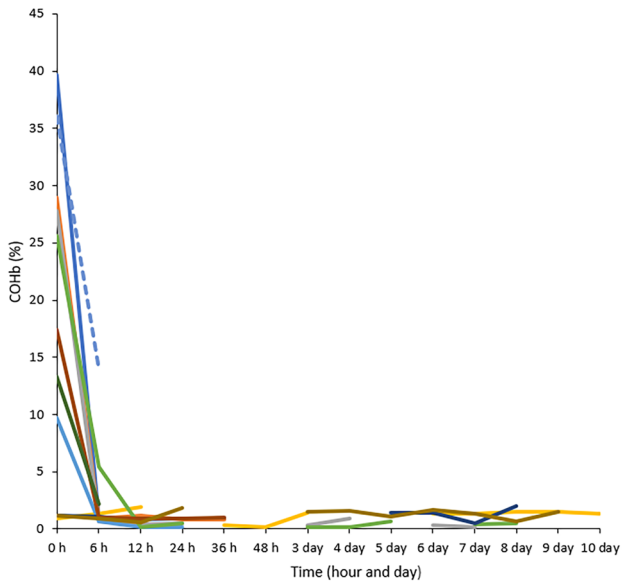

Fig. 1 Graphical representation of COHb levels of in troponin-positive in children with CO poisoning

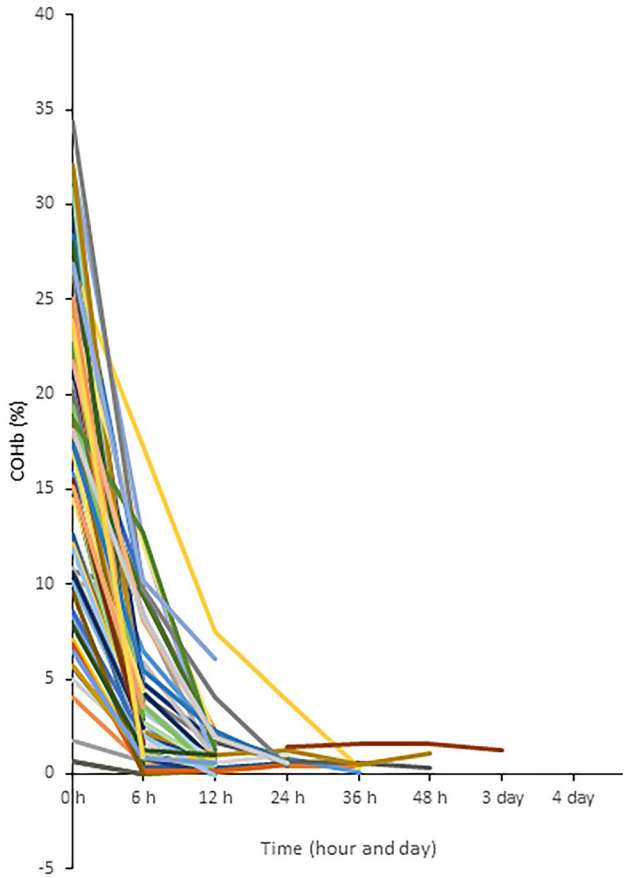

Fig. 2 Graphical representation of COHb levels of in troponin-negative in children with CO poisoning

of 86.7% (AUC, 0.967 (0.58–0.994); $p=0.017$). An analysis of the CK values showed that the CK values were significantly higher in the troponin-positive group at admission and the 6th hour ($p=0.043$, $p=0.030$, respectively). There was no statistically significant difference between the groups with respect to the CK values at the 12th and 24th hours ($p=0.162$, $p=0.419$, respectively). In addition, although CK-MB values at admission and at the 12th hour were significantly higher in the troponin-positive patient group ($p=0.030$, $p=0.047$, respectively), there was no significant difference between the groups in terms of CK-MB values at the 6th and 24th hours ($p=0.085$, $p=0.300$, respectively).

A comparison by the blood gas analysis performed at admission revealed that the pH and bicarbonate (HCO_3) values were significantly lower in the troponin-positive patient group ($p=0.010$, $p=0.015$, respectively). There was no significant difference between the groups in terms of pCO2 and COHb levels ($p=0.788$, $p=0.379$, respectively) (Table 1). COHb levels of patients with CO poisoning with and without myocardial injury were presented in Figs. 1 and 2.

Lactate, white blood cell (WBC), neutrophil, neutrophil-to-lymphocyte ratio (NLR), immature granulocyte (IG), and IG% levels were found to be significantly higher in the troponin-positive patient group ($p=0.032$, $p<0.001$, $p<0.001$, $p=0.041$, $p=0.002$, $p=0.001$, respectively) (Table 1). There was no statistically significant difference between the two groups in terms of lymphocyte, monocyte, lymphocyte-to-monocyte ratio (LMR), hemoglobin (Hb), platelet (PLT), international normalized ratio (INR), albumin, aspartate aminotransaminase (AST), and alanine aminotransaminase (ALT) values ($p=0.356$, $p=0.102$, $p=0.064$, $p=0.697$, $p=0.217$, $p=0.652$, $p=0.401$, $p=0.091$, $p=0.979$, respectively) (Table 1).

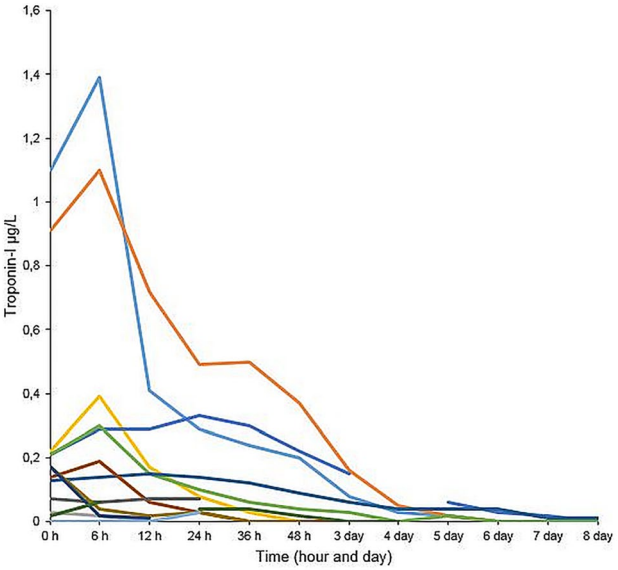

Fig. 3 Graphical representation of the course of troponin-I in troponin-positive in children with CO poisoning

Table 3 shows the data on the day on which the troponin-I, NT-proBNP, CK, and CK-MB values started to increase, for how many days they remained high, in how many days they reached the maximum level, and their maximum blood levels. In addition, the courses of troponin-I and NT-proBNP levels in troponin-positive patients were graphically presented in Figs. 3 and 4.

Table 3 Evaluation of cardiac markers in children with carbon monoxide poisoning

	Mean	Median	SD	Range
The day on which the troponin-I level started to increase	1.1	1	0.316	1–2
How many days the troponin-I level remained high	3.2	3	2.044	1–7
The day on which the troponin-I level reached at its maximum value	1.11	1	0.557	0–2
Maximum value of troponin-I (µg/L)	0.212	0.065	0.329	0.03–1.1
The day on which the NT-proBNP level started to increase	1	1	0.00	1–1
How many days the NT-proBNP level remained high	6.33	6.5	3.724	2–12
The day on which the NT-proBNP level reached at its maximum value	1.33	1	0.516	1–2
Maximum value of NT-proBNP (ng/L)	6365	7615	4872.05	205–11,700
The day on which day the CK level started to increase	1	1	0.632	0–2
How many days the CK level remained high	2	2	1.871	0–5
The day on which the CK level reached at its maximum value	1	1	0.632	0–2
Maximum value of CK (U/L)	985.83	466.5	1412.92	154–3850
The day on which the CK-MB level started to increase	1	1	0.577	0–2
How many days the CK-MB level remained high	3.17	2.5	2.483	1–8
The day on which the CK-MB level reached its maximum value	1.17	1	0.408	1–2
Maximum value of CK-MB (µg/L)	49.33	16.5	56.246	9–130

Statistics: frequencies

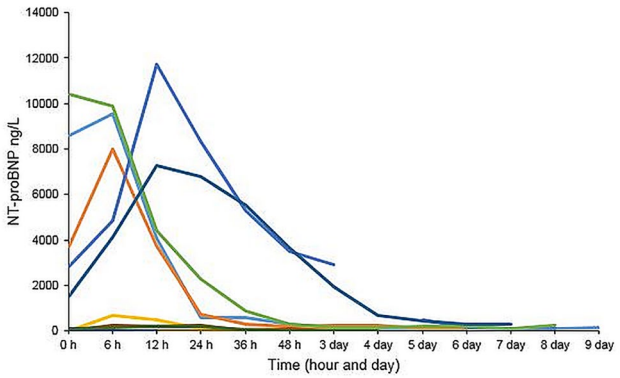

Fig. 4 Graphical representation of the course of NT-proBNP in troponin-positive in children with CO poisoning

There was no statistically significant difference between the ECG findings at the time of admission and after recovery (at discharge) in the troponin-positive patients (Table 3). When the patients were evaluated according to their echocardiography findings, we found statistically significant differences in left ventricular end-systolic diameter (LVSD) z-score, ejection fraction (EF), and fractioning shortening (FS) values at admission compared to those measured after recovery ($p = 0.026$, $p = 0.047$, $p = 0.047$, respectively). There was no statistically significant difference between the interventricular septum (IVS) z-score, the left ventricular end-diastolic dimension (LVDd) z-score, and the left ventricular posterior wall (LVPW) z-score values measured at admission and 1 week later (Table 4).

An analysis of the correlation between cardiac markers and laboratory data showed a weak negative correlation between blood pH value and troponin-I and CK-MB and a moderately strong negative correlation between blood pH and CK ($r, -0.276$, $p = 0.015$; $r, -0.378$, $p = 0.001$; $r, -0.465$, $p < 0.001$, respectively) (Table 4). There was no significant correlation between blood pH value and NT-proBNP ($r, -0.069$, $p = 0.663$). There was no significant correlation between blood pCO_2, COHb, NLR, and lymphocyte levels and cardiac markers (Table 4). We found a weak negative correlation between blood HCO_3 value and troponin-I, CK-MB, and a moderately strong negative correlation between blood HCO_3 and CK ($r, -0.265$, $p = 0.020$; $r, -0.364$, $p = 0.001$; $r, -0.432$, $p < 0.001$, respectively). There was no significant correlation between blood HCO_3 level and NT-proBNP (Table 5). There was a weak positive correlation between blood lactate level and troponin-I, CK-MB, and a moderately strong positive correlation between blood lactate and CK (r, 0.335, $p = 0.004$; r, 0.319, $p = 0.007$; r, 0.518, $p < 0.001$, respectively). We found a weak positive correlation between white blood cell count and NT-proBNP, CK, and CK-MB (r, 0.287, $p = 0.037$; r, 0.279, $p = 0.012$; r, 0.314, p, 0.003, respectively). There was no significant correlation between troponin-I and WBC. We found a moderately positive correlation between monocyte count and NT-proBNP and a weak positive correlation between monocyte count and CK and CK-MB (r, 0.422, $p = 0.002$; r, 0.331, $p = 0.003$; r, 0.308, p, 0.004, respectively). We found a statistically significant, albeit weak, negative correlation between lymphocyte-to-monocyte ratio and troponin-I,

Table 4 Comparison of the ECG and echocardiographic findings of children with CO poisoning at the time of admission and after recovering (control)

ECG findings			
	At the time of admission	Control	*p*
Heart rates (beats/min)	113.77 ± 26.71	95.67 ± 22.03	0.110
PR interval (sec)	0.127 ± 0.009	0.128 ± 0.010	0.984
QRS duration (sec)	0.069 ± 0.011	0.065 ± 0.008	0.440
QTc interval (sec)	0.404 ± 0.019	0.409 ± 0.017	0.535
Echocardiographic findings			
	At the time of admission	Control	*p*
IVS Zs	0.232 ± 0.333	0.656 ± 0.429	0.054
LV EDD Zs	0.288 ± 0.829	−0.018 ± 0.486	0.464
LV PW Zs	0.363 ± 0.512	0.658 ± 0.229	0.248
LV ESD Zs	0.154 ± 0.673	−0.760 ± 0.653	0.026
LV EF (%)	68.90 ± 4.15	74.00 ± 4.47	0.047
LV FS (%)	38.40 ± 3.56	42.60 ± 3.36	0.047

Statistics: independent student *t* test

IVS interventricular septum, *LV* left ventricle, *EDD* end-diastolic diameter, *ESD* end-systolic diameter, *Zs* z-score, *PW* posterior wall, *FS* fractioning shortening

Table 5 Evaluation of the correlation between cardiac markers and laboratory data of children with carbon monoxide poisoning

		Troponin-I	NT-proBNP	CK	CK-MB
pH	*r*	−0.276	−0.069	−0.465	−0.378
	p	0.015	0.663	< 0.001	0.001
pCO_2	*r*	−0.051	−0.126	−0.052	−0.044
	p	0.662	0.428	0.670	0.706
HCO_3	*r*	−0.265	−0.120	−0.432	−0.364
	p	0.020	0.450	< 0.001	0.001
COHb	*r*	−0.160	−0.301	0.002	−0.160
	p	0.164	0.053	0.986	0.165
Lactate	*R*	0.335	0.224	0.518	0.319
	p	0.004	0.166	< 0.001	0.007
WBC	*r*	0.201	0.287	0.279	0.314
	p	0.061	0.037	0.012	0.003
Neutrophil	*r*	0.309	0.293	0.332	0.373
	p	0.003	0.033	0.002	< 0.001
Lymphocyte	*r*	−0.131	−0.029	−0.059	−0.045
	p	0.224	0.835	0.601	0.679
Monocyte	*r*	0.190	0.422	0.331	0.308
	p	0.077	0.002	0.003	0.004
NLR	*r*	0.075	0.209	0.153	0.059
	p	0.488	0.133	0.173	0.582
LMR	*r*	−0.272	−0.276	−0.303	0.254
	p	0.010	0.045	0.006	0.017
IG%	*r*	0.432	0.582	0.511	0.497
	p	< 0.001	< 0.001	< 0.001	< 0.001
IG	*r*	0.409	0.539	0.562	0.516
	p	< 0.001	< 0.001	< 0.001	< 0.001
Hb	*r*	−0.051	−0.358	−0.070	−0.115
	p	0.637	0.009	0.535	0.287
AST	*r*	0.774	0.830	0.589	0.779
	p	< 0.001	< 0.001	< 0.001	< 0.001
ALT	*r*	0.189	0.345	0.192	0.219
	p	0.080	0.011	0.087	0.042

Statistics: Pearson correlation

NT-proBNP NT-pro-brain natriuretic peptide, *CK* creatine kinase, *pCO_2* carbon dioxide partial pressure, *HCO_3* bicarbonate, *COHb* carboxyhemoglobin, *WBC* white blood cell count, *NLR* neutrophil-to-lymphocyte ratio, *LMR* lymphocyte-to-monocyte ratio, *IG* immature granulocyte, *Hb* hemoglobin, *PLT* platelet, *INR* international normalized ratio, *AST* serum aspartate transaminase, *ALT*, alanine transaminase

NT-proBNP, and CK and a negative correlation between lymphocyte-to-monocyte ratio and CK-MB ($r, -0.272$, $p = 0.010$; $r, -0.276$, $p = 0.045$; $r, -0.303$, p, 0.006; r, 0.254, $p = 0.017$, respectively). We found a moderately strong positive correlation between blood IG, IG% values, and cardiac markers (Table 5). While there was a weak negative correlation between hemoglobin and NT-proBNP, there was no significant correlation between troponin, CK, and CK-MB (Table 4). We found a highly significant positive correlation between AST and troponin-I, NT-proBNP, and CK-MB. We found a moderately strong positive correlation between CK and AST. We also found a weak positive correlation between ALT level and NT-proBNP and CK-MB. There was no statistically significant correlation between troponin and CK levels and ALT (Table 5).

Discussion

In our study, we investigated CO poisoning in children. We defined the troponin-positive patients as the group with myocardial damage. In a retrospective study on adults, conducted by Kim et al. the authors reported that cardiomyopathy developed in one of every eight patients with CO poisoning [19]. Similarly, in this pediatric study, we found that approximately one of every 8 patients had myocardial damage due to CO poisoning.

A comparison by blood gas analysis showed that pH (7.28 ± 0.09) and HCO3 (19.24 ± 4.44 mmol/L) values were significantly lower and lactate (4.70 ± 3.50 mmol/L) values significantly higher in the group with myocardial damage. In an experimental animal study of Simonsen et al. lactate was found higher and pH lower in the group with severe CO poisoning [20]. A literature search performed by our team revealed no information of the HCO3 values in patients with CO poisoning. Low pH, low HCO3, and high lactate levels all indicated metabolic acidosis in our patients. Metabolic acidosis, on the other hand, has been reported to negatively affect the prognosis of CO poisoning [10, 21, 22]. In addition, it was found that pH and HCO3 values were negatively correlated with troponin-I, CK, and CK-MB, whereas lactate value was positively correlated with those myocardial injury markers. On the other hand, no correlation was found between pCO2 and COHb levels and troponin-I, NT-proBNP, CK, and CK-MB values.

In this study, no significant difference was found between the study groups in terms of pCO2 and COHb levels. The half-life of COHb is between 250 and 320 min while breathing room air, about 90 min while breathing high-flow oxygen, and 30 min while breathing 100% hyperbaric oxygen [23]. Most of the time, oxygen therapy and hydration for patients with CO poisoning are started on the road to hospital or at the event scene, before blood samples are taken, and before patients reach the hospital. COHb can decrease to its normal blood range during ambulance transport because of its half-life, and the oxygen therapy started during transport. Therefore, a normal or less than 2% COHb value does not exclude severe CO poisoning [24, 25]. Moreover, clinical symptoms and COHb level are not necessarily correlated [9]. This was confirmed by the fact that three of our patients with normal COHb values had troponin-positive myocardial damage, and a patient with a COHb below than 25% received hyperbaric oxygen therapy for headache.

In previous studies, it has been suggested that troponin value may be normal at admission; thus, it should be measured serially in order to show myocardial damage [12, 26]. In the current study, the increase in troponin-I by 24th hour, which was normal at the beginning in one of our patients, supports this hypothesis. Therefore, we think that patients presenting to the emergency department with CO poisoning should be followed up for at least 24 h and cardiac markers should be re-checked before discharge.

In this study, NT-proBNP value was higher in the myocardial damage group at admission, and the elevation continued at the 6th and 12th hours. Moon et al. in a retrospective study conducted with adult patients with CO poisoning, showed that high NT-proBNP values at admission are a marker for poor prognosis and are important in identifying patients who may have a poor long-term neurological prognosis [27]. In another study conducted in adult patients with CO poisoning, NT-proBNP > 100 pg/mL at admission was found to be a significant marker in predicting left ventricular dysfunction [28]. In our previous studies, we reported the prognostic value of proBNP in various poisonings such as snake bites and scorpion bites [29, 30]. We also showed that it was predictive of cardiac involvement in children with COVID-19 at the time of admission [31]. In this study, we found that a NT-proBNP cut-off value of ≥ 219.5 ng/L predicted troponin positivity, i.e., myocardial injury, with sensitivity of 70% and a specificity of 86.7% in pediatric patients with CO poisoning. Similar to our findings, Turan et al. reported that NT-proBNP was predictive of myocardial injury in children with CO poisoning [32]. In addition, in a study by Abdel Aziz et al. it was stated that troponin-I did not differ in patients with mild, moderate, or severe CO poisoning and that NT-proBNP was more valuable than troponin-I in demonstrating myocardial damage [33].

In a retrospective study in adults, Lee et al. looked for a cut-off value for creatinine kinase for the prediction of delayed neurological sequelae. They suggested that a creatine kinase concentration of > 1603 U/L was an independent risk factor for delayed neurological sequelae [34]. Tekşam et al. found elevated CK-MB values at admission in 11 of 16 patients with myocardial injury after CO poisoning [35]. In our study, CK and CK-MB were also higher in the group with myocardial damage at admission.

CO causes tissue hypoxia and immunological, inflammatory damage at the cellular level. This causes neutrophil activation, lymphocyte proliferation, mitochondrial dysfunction, lipid peroxidation, oxidative stress, inflammation, and apoptosis [1, 36]. In a study, WBC, CK, and AST were found to be higher in patients with CO poisoning and a worse prognosis [22]. We also reached similar results in our study. Han et al. reported that NLR was predictive for myocardial injury in patients with CO poisoning [37]. In a study by Akcan Yildiz in pediatric patients with CO poisoning, it was reported that a high leukocyte count was useful in predicting prognosis and directing treatment [38]. In a study by Moon et al. with adults with CO poisoning, it was shown that both admission neutrophil count and NLR were predictive of troponin-I elevation when used together with clinical parameters in patients without troponin-I elevation or ischemic ECG changes at admission [26]. In our study, the cost-effective WBC, neutrophil, NLR, IG, and IG% levels were found to be higher in the troponin-positive group with myocardial damage; furthermore, neutrophil count, IG, and IG% were positively correlated with troponin-I, CK, CK-MB, and proBNP. Therefore, full blood count parameters, which can be measured with low-cost and almost everywhere, can guide a clinician about treatment and referral when measuring troponin-I is not an option.

There is scarce evidence on hepatic injury due to CO poisoning. In their retrospective study with 894 adult patients, Kim et al. reported that 1.6% of patients had hepatic injury and 14.3% had subclinical hepatitis-related injury [23]. In our study with 107 pediatric patients, hepatic damage was not detected in the group with and without myocardial damage. However, a weak positive correlation was detected between ALT and NT-proBNP. In various previous studies, a positive correlation was found between ALT and NT-proBNP; it was suggested that increased NT-proBNP and ALT showed deterioration in cardiac functions, and it was stated that ALT increased in relation to oxidative stress [39, 40]. In a study of Jung et al. with adult patients, AST was found to be higher in patients with poor neurological prognosis [22]. The high positive correlation between AST and cardiac markers in our study may be significant in terms of poor prognosis.

There was no significant difference between the ECG findings of our patients with myocardial injury at the time of admission and after recovery. When the patients were evaluated according to their echocardiographic findings, LVEF and LVFS values were significantly lower at the time of admission compared to the control values after recovery. In a study conducted by Teksam et al. in pediatric patients with CO poisoning, it was reported that normal ECG findings did not exclude myocardial damage [35]. Therefore, it seems more important to study the cardiac markers of the patients. In a retrospective study of Kim et al. that enrolled patients with CO poisoning, LV EF was lower in the cardiomyopathy group [19]. Park et al. suggested that left ventricular systolic dysfunction was found in the echocardiography of adult patients with CO poisoning and was associated with a poor prognosis [24]. Similarly, in our study, lower LVEF and LVFS values seen in the troponin-positive group at admission suggested that systolic dysfunction also developed.

The main limitations of our study are its retrospective, single-center design as well as the small number of patients. In addition, it did not include the clinical outcomes of patients, such as neurological deficits. There is a need for well-designed large-scale prospective studies on this subject.

Conclusion

In our study, we are of the opinion that NT-proBNP is a diagnostic marker recognizing myocardial dysfunction at an early stage, and the cut-off value we determined will help clinicians to decide on treatment in children with CO poisoning. In settings where cardiac markers are not available, we hope that full blood count parameters, which are low-cost and can be studied everywhere, will guide patient treatment and referral.

Data availability Available on request.

Declarations

Conflict of interest The authors declare no competing interests.

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