



The Prognostic Value of Systemic Immune Inflammation Index in Children with Carbon Monoxide Poisoning

Karbon Monoksit Zehirlenmesi Olan Çocuklarda Sistemik İmmün İnflamasyon İndeksinin Prognostik Değeri

Emine Özdemir Kaçer

Department of Pediatrics, Faculty of Medicine, Aksaray University, Aksaray, Turkey

Abstract

Aim: Carbon monoxide (CO) is an odorless and colorless gas that forms when organic materials burn incompletely. Children are more susceptible to CO poisoning than adults because their respiratory and immune systems are still developing. The systemic immune inflammation index (SII) is a marker that reflects the balance between inflammation and immunity. In this study, we investigate the relationship between CO poisoning in children and SII.

Material and Method: We conducted a retrospective observational study involving pediatric patients (age <18 years) diagnosed with CO poisoning and treated at Aksaray University Training and Research Hospital, a tertiary medical center, from January 2018 to January 2023. We included consecutive pediatric patients (age <18 years) with CO poisoning who had available clinical and laboratory data and were treated at our hospital.

Results: The study included 393 patients with a mean age of 7.24 (± 4.67) years, of whom 184 (46.8%) were male. When comparing COHb groups, significant statistical differences emerged between the groups regarding GCS, pH levels, occurrences of dizziness, confusion, seizures, lethargy, and prognosis ($p < 0.05$). When comparing lactate groups, significant differences were observed between the groups concerning GCS, COHb levels, pH levels, occurrences of confusion, lethargy, prognosis, and LOS ($p < 0.05$). Upon evaluating the SII, no statistically significant difference was found between the groups in terms of gender, COHb levels, lactate levels, LOS, and prognosis.

Conclusion: SII cannot be considered a reliable predictor of the severity of carbon monoxide poisoning in children. Despite the evident inflammatory response triggered by exposure to carbon monoxide, the SII did not consistently correlate with the varying degrees of poisoning severity.

Keywords: Carbon monoxide poisoning, Inflammatory response, Pediatric patients, Severity assessment, Systemic immune inflammation index (SII)

Öz

Amaç: Karbon monoksit (CO), organik maddelerin eksik yanmasıyla oluşan kokusuz ve renksiz bir gazdır. Çocuklar CO zehirlenmesine yetişkinlerden daha duyarlıdır çünkü solunum ve bağışıklık sistemleri hala gelişmektedir. Sistemik immün inflamasyon indeksi (SII), inflamasyon ve bağışıklık arasındaki dengeyi yansıtan bir belirteçdir. Bu çalışmada, çocuklarda CO zehirlenmesi ile SII arasındaki ilişkiyi araştırdık.

Gereç ve Yöntem: Ocak 2018 - Ocak 2023 tarihleri arasında üçüncü basamak bir tıp merkezi olan Aksaray Üniversitesi Eğitim ve Araştırma Hastanesi'nde CO zehirlenmesi tanısı alan ve tedavi edilen çocuk hastaları (18 yaş altı) içeren retrospektif gözlemsel bir çalışma yürüttük. Klinik ve laboratuvar verileri mevcut olan ve hastanemizde tedavi edilen CO zehirlenmesi olan ardışık çocuk hastaları (yaş <18) dahil ettik.

Bulgular: Çalışmaya yaş ortalaması 7,24 ($\pm 4,67$) yıl olan ve 184'ü (%46,8) erkek olan 393 hasta dahil edildi. COHb grupları karşılaştırıldığında, GKS, pH düzeyleri, baş dönmesi, konfüzyon, nöbet, letarji ve prognoz açısından gruplar arasında anlamlı istatistiksel farklılıklar ortaya çıktı ($p < 0,05$). Laktat grupları karşılaştırıldığında, GKS, COHb seviyeleri, pH seviyeleri, konfüzyon, letarji, prognoz ve hastanede kalış süresi açısından gruplar arasında anlamlı farklılıklar gözlenmiştir ($p < 0,05$). SII değerlendirildiğinde, gruplar arasında istatistiksel olarak anlamlı bir fark bulunmamıştır.

Sonuç: SII, çocuklarda karbon monoksit zehirlenmesinin şiddetinin güvenilir bir göstergesi olarak kabul edilemez. Karbon monoksit maruziyetinin tetiklediği bariz inflamatuvar tepkiye rağmen SII, değişen derecelerdeki zehirlenme şiddetiyle tutarlı bir şekilde korelasyon göstermedi.

Anahtar Kelimeler: Karbon monoksit zehirlenmesi, İnflamatuvar yanıt, Pediatrik hastalar, Şiddet değerlendirmesi, Sistemik immün inflamasyon indeksi (SII)



INTRODUCTION

Carbon monoxide (CO) is an odourless, colourless gas produced by the incomplete combustion of organic matter.^[1,2] It is a major cause of illness and death worldwide, particularly in countries where people use wood and coal-burning stoves for heating without proper ventilation.^[3] In fact, CO poisoning accounts for 3.6-9.4% of all poisonings in children.^[4] Children are more susceptible to CO poisoning than adults because their respiratory and immune systems are still developing. CO has a much higher affinity for haemoglobin than oxygen, preventing oxygen from reaching the tissues and causing hypoxia.^[5] CO also interferes with cellular oxidation, binds to myoglobin and cytochromes, and damages lipids.^[6] These effects trigger an inflammatory response that can be measured by acute-phase reactants such as leukocytes, neutrophils, lymphocytes, platelets and proteins.^[7]

The Systemic Immune Inflammation Index (SII) is a marker that reflects the balance between inflammation and immunity. It is calculated from the absolute numbers of neutrophils, lymphocytes and platelets. High levels of SII indicate a strong inflammatory response in the body and are associated with several diseases, such as cardiovascular disease and infections.^[8]

CO poisoning can cause a wide range of symptoms, from mild headaches and dizziness to severe confusion and coma. It can also have long-term effects, such as cognitive impairment and respiratory problems, which can affect children's health and development.^[9,10]

In this study, we investigate the relationship between CO poisoning in children and the SII. We aim to determine whether the SII can be used as a predictor of the severity of CO poisoning.

MATERIAL AND METHOD

Study Design

We conducted a retrospective observational study of pediatric patients (age <18 years) diagnosed with CO poisoning and treated at Aksaray University Training and Research Hospital, a tertiary medical center, from January 2018 to January 2023. The study was carried out with the permission of Local Ethics Committee (Decision No: 2021/17-06).

Study Setting and Patient Cohort

Consecutive pediatric patients (age <18 years) with CO poisoning who had available clinical and laboratory data and who were treated at our hospital were included in the study. CO poisoning was defined as exposure to CO emissions and a carboxyhemoglobin (COHb) level above 5% at the time of admission to the pediatric emergency department. Patients with chronic diseases (such as chronic pulmonary, cardiac, renal, hepatic, inflammatory, hematological, rheumatic diseases, or immunosuppression), those for whom information could not be retrieved from the electronic record system, and patients older than 18 years were excluded.

Patients were divided into two groups according to their COHb levels: mild to moderate poisoning (COgroup-1) with levels between 5% and 20%, and severe poisoning (COgroup-2) with

COHb levels above 20%. In addition, patients were classified based on their blood lactate levels: mild-moderate (Lgroup-1) if lactate was less than 2.2 mmol/L, and severe poisoning (Lgroup-2) if lactate was 2.2 mmol/L or greater.

Patients were divided into three categories based on length of hospital stay (LOS): 0-24 hours, 24-72 hours, and over 72 hours. Patients were also divided into four groups according to their clinical outcome: discharge after treatment in the emergency department, admission to the hospital's pediatric service, admission to intensive care, and referral to another medical facility.

The SII was calculated using the formula $SII = \frac{(\text{platelet count} \times \text{neutrophil count})}{\text{lymphocyte count}}$.^[11] Patients' SII levels were evaluated in relation to their CO levels, lactate levels, length of hospital stay, and clinical outcomes.

Data Collection

Data on patient demographic characteristics such as age and sex, symptoms and complaints at the time of application, Glasgow Coma Scale (GCS), LOS, clinical outcomes (discharge/hospitalisation/referral), initial laboratory results; white blood cell (WBC), platelet, neutrophil, lymphocyte, monocyte, and lactate values were retrospectively recorded from the patient's medical records.

Statistical Analysis

Statistical analyses were performed using SPSS 21.0 (IBM Inc, Chicago, IL, USA). Numerical parameters were expressed as median (min-max) or mean \pm SD, and categorical variables were expressed as frequencies and percentages (%). Kolmogorov-Smirnov test, histogram analysis and skewness/kurtosis data were used to assess the conformity of numerical variables with normal distribution. Levene's test was used to analyse the homogeneity characteristics of numerical parameters between groups. When comparing two independent groups, the independent t-test was used for parameters with normal distribution, while the Mann-Witney U test was used for parameters without normal distribution. Spearman's correlation analysis was used for correlations between numerical parameters. Binary logistic regression analysis was used to determine the predictive factors. The accuracy of binary relations and analyses in the models was confirmed by the Hosmer-Lemeshow test. Chi-squared or Fisher's exact tests were used to analyse the relationship between binary categorical groups. Significant parameters that might influence the severity of poisoning were subjected to ROC analysis and diagnostic data were presented. The type I error rate was set at 5% for the entire study, and $p < 0.05$ was considered significant.

RESULTS

In our study, a total of 457 patients with acute CO poisoning were admitted to our pediatric emergency department. After applying the exclusion criteria, 64 patients were considered ineligible, leaving a final inclusion of 393 patients. The mean age of the patients was 7.24 (± 4.67) years and 184 (46.8%) were male. The mean GCS score was 13.55 (± 1.72), while the mean COHb level was 7.92 (± 5.50). Most patients (74%) were admitted 8-24 hours

after CO exposure. Of the patients, 369 (94.1%) had COHb levels between 5% and 20%, while 24 (5.9%) had COHb levels $\geq 20\%$.

Regarding lactate levels, 324 (82.4%) patients had lactate levels below 2.2 mmol/L, while 69 (17.6%) had lactate levels of 2.2 mmol/L or higher. The most common symptom on admission was headache (41.7%), followed by dizziness (36.4%) and epileptic seizures (36.1%). Of the patients, 255 (64.9%) were discharged within the first 24 hours after treatment, while 24 (6.1%) were referred to another facility for hyperbaric oxygen requirements or other reasons. To the best of our knowledge from the medical records, no patient succumbed to the disease. Detailed demographic characteristics, laboratory findings, symptoms on admission, length of hospital stay, and follow-up data are shown in **Tables 1 and 2**.

When evaluating the COHb groups, it was observed that COgroup-1 was most frequently associated with headache (n=154; 41.7%), whereas COgroup-2 had a higher incidence of confusion (n=22; 91.7%). The mean GCS score for COgroup-1 was 13.68 (± 1.64), whereas COgroup-2 had a mean GCS score of 11.50 (± 1.67). In addition, the mean pH was 7.35 (± 0.05) for COgroup-1 and 7.28 (± 0.06) for COgroup-2. Regarding hospitalization, the majority of COgroup-1 patients were admitted to the hospital pediatric service (n=172; 46.6%), whereas most COgroup-2 patients were transferred to another medical facility (n=22; 91.7%). When the COHb groups were compared, statistically significant differences were found between the groups in terms of GCS, pH levels, incidence of dizziness, confusion, seizures, lethargy, and prognosis ($p < 0.05$). Detailed comparisons of group data based on COHb levels are shown in **Tables 3 and 4**.

Table 1. Demographics and laboratory findings of the study population

	Mean	SD	Median	25%	75%
Age (years)	7.24	4.67	6.00	3.00	10.00
GCS ¹	13.55	1.72	14.00	12.00	15.00
WBC ² (10 ³ / μ L)	12.16	37.45	9.24	7.41	11.77
Lymphocyte (10 ³ / μ L)	2.42	1.23	2.18	1.63	3.01
Monocyte (10 ³ / μ L)	0.62	0.56	0.55	0.41	0.70
Neutrophil (10 ³ / μ L)	6.82	5.05	6.19	4.82	7.67
Platelet (10 ³ / μ L)	255.94	92.41	244.00	197.00	296.00
pH	7.35	0.05	7.35	7.32	7.36
COHb ³ (%)	7.92	5.50	5.00	5.00	8.00
SII ⁴	982.47	2459.66	699.39	430.42	1071.23

¹Glasgow Coma Scale, ²White Blood Cell, ³Carboxyhemoglobin, ⁴Systemic Immune-Inflammation Index

Table 2. Demographics, symptoms, and prognosis of the study population.

	Count	Column N %
Gender		
Female	209	53.2%
Male	184	46.8%
Application Time		
0-8 Hours	73	18.6%
8-24 Hours	291	74.0%
>24 Hours	29	7.4%
Lactate (mmol/L)		
<2.2	324	82.4%
>2.2	69	17.6%
Headache		
No	318	
Yes	75	
Nausea-Vomiting		
No	318	80.9%
Yes	75	19.1%
Weakness		
No	266	67.7%
Yes	127	32.3%
Dizziness		
No	250	
Yes	143	
Syncope		
No	283	72.0%
Yes	110	28.0%
Confusion		
No	253	
Yes	140	
Seizure		
No	251	63.9%
Yes	142	36.1%
Lethargy		
No	266	67.7%
Yes	127	32.3%
Length of Hospital Stay		
0-24 Hours	256	65.1%
24-72 Hours	122	31.0%
>72 Hours	15	3.8%
Follow-Up		
Discharge after treatment in the E.D.*	88	22.4%
Pediatric service	173	44.0%
Intensive care unit	108	27.5%
Referral	24	6.1%

*Emergency Department

Table 3. Comparisons of COHb groups' demographics and laboratory findings.

	COgroup-1					COgroup-2					p value
	Mean	SD	Median	25%	75%	Mean	SD	Median	25%	75%	
Age (years)	7,23	4,65	6,00	3,00	10,00	7,42	4,99	6,50	3,00	10,00	0,911
GCS ¹	13,68	1,64	15,00	13,00	15,00	11,50	1,67	11,00	11,00	12,50	<0,001
WBC ² (10 ³ / μ L)	12,33	38,63	9,24	7,42	11,77	9,66	4,01	9,07	6,76	12,14	0,567
Lymphocyte (10 ³ / μ L)	2,42	1,24	2,15	1,58	3,05	2,43	1,07	2,29	1,79	3,00	0,707
Monocyte (10 ³ / μ L)	0,63	0,57	0,55	0,41	0,70	0,53	0,22	0,47	0,39	0,63	0,166
Neutrophil (10 ³ / μ L)	6,83	5,15	6,19	4,82	7,67	6,69	3,10	6,15	4,88	7,65	0,993
Platelet (10 ³ / μ L)	255,98	93,02	245,00	197,00	296,00	255,21	84,30	233,50	206,50	294,50	0,909
pH	7,35	0,05	7,36	7,33	7,36	7,28	0,06	7,28	7,23	7,32	<0,001
SII ³	985,73	2526,68	704,56	430,86	1071,23	932,44	981,63	589,89	337,19	1041,69	0,687

¹Glasgow Coma Scale, ²White Blood Cell, ³Systemic Immune-Inflammation Index

Table 4. Comparisons of COHb groups' demographics, symptoms, and prognosis of the study population.

	CO group-1		CO group-2		p value
	n	%	n	%	
Gender					0,345
Female	194	52,6%	15	62,5%	
Male	175	47,4%	9	37,5%	
Application Time					0,501*
0-8 Hours	68	18,4%	5	20,8%	
8-24 Hours	275	74,5%	16	66,7%	
>24 Hours	26	7,0%	3	12,5%	
Headache					0,995
No	215	58,3%	14	58,3%	
Yes	154	41,7%	10	41,7%	
Nausea-Vomiting					0,791*
No	299	81,0%	19	79,2%	
Yes	70	19,0%	5	20,8%	
Weakness					0,429
No	248	67,2%	18	75,0%	
Yes	121	32,8%	6	25,0%	
Dizziness					0,038
No	230	62,3%	20	83,3%	
Yes	139	37,7%	4	16,7%	
Syncope					0,547
No	267	72,4%	16	66,7%	
Yes	102	27,6%	8	33,3%	
Confusion					<0,001
No	251	68,0%	2	8,3%	
Yes	118	32,0%	22	91,7%	
Seizure					<0,001
No	246	66,7%	5	20,8%	
Yes	123	33,3%	19	79,2%	
Lethargy					<0,001
No	261	70,7%	5	20,8%	
Yes	108	29,3%	19	79,2%	
Length of Hospital Stay					0,248*
0-24 Hours	237	64,2%	19	79,2%	
24-72 Hours	118	32,0%	4	16,7%	
>72 Hours	14	3,8%	1	4,2%	
Follow-Up					<0,001*
Discharge after treatment in the E.D.**	88	23,8%	0	0,0%	
Pediatric service	172	46,6%	1	4,2%	
Intensive care unit	107	29,0%	1	4,2%	
Referral	2	0,5%	22	91,7%	

* Fisher's exact test p value and all others Pearson Chi-square test **Emergency Department

Evaluation of the lactate groups showed that the mean GCS scores for Lgroup-1 and Lgroup-2 were 13.88 (± 1.51) and 11.99 (± 1.79) respectively. Lgroup-2 had a higher mean COHb value compared to Lgroup-1, with values of 10.86 (± 8.02) and 7.29 (± 4.57), respectively. In addition, the mean pH was 7.36 (± 0.05) in L-group-1 and 7.29 (± 0.04) in L-group-2. In terms of symptoms, headache was the most common presentation in L-group-1 (n=133; 41%), whereas confusion was the predominant symptom in L-group-2 (n=34; 49.3%). Regarding hospitalization, the majority of L-group-1 patients were admitted to the hospital's pediatric service (n=159; 49.1%), whereas the majority of L-group-2 patients were admitted to the intensive care unit (n=40; 58%). When comparing the lactate groups, statistically significant differences were observed between the groups for GCS, COHb, pH, confusion, lethargy, prognosis, and LOS ($p < 0.05$). Detailed comparisons of the data between the lactate groups are shown in **Tables 5** and **6**.

When evaluating the SII, we found no statistically significant difference between groups in terms of gender, COHb levels, lactate levels, LOS, and prognosis. A comprehensive comparison of group data based on SII is presented in **Table 7**.

There were no patient deaths for which records were available.

DISCUSSION

To the best of our knowledge, this study is the first to investigate the relationship between CO poisoning and SII in children in the Central Anatolian region. Contrary to initial expectations, our comprehensive analysis of the relationship between CO poisoning and the SII revealed that the SII is not reliable enough to accurately predict the severity of CO poisoning in children. While CO exposure does induce an inflammatory response, the magnitude of this response does not consistently correlate with the severity of poisoning symptoms.

Table 5. Comparisons of lactate groups' demographics and laboratory findings.

	L group-1					L group-2					p value
	Mean	SD	Median	25%	75%	Mean	SD	Median	25%	75%	
Age (years)	7,30	4,69	6,00	3,00	10,00	6,96	4,61	6,00	3,00	9,00	0,600
GCS ¹	13,88	1,51	15,00	13,00	15,00	11,99	1,79	12,00	11,00	13,00	<0,001
WBC ² (10 ³ /μL)	12,49	41,11	9,19	7,42	11,69	10,62	7,34	9,48	7,35	12,22	0,686
Lymphocyte (10 ³ /μL)	2,43	1,23	2,22	1,63	3,00	2,40	1,23	2,12	1,42	3,07	0,829
Monocyte (10 ³ /μL)	0,59	0,39	0,55	0,41	0,70	0,77	1,02	0,55	0,42	0,76	0,689
Neutrophil (10 ³ /μL)	6,96	5,41	6,24	5,04	7,83	6,15	2,66	5,75	4,49	7,11	0,106
Platelet (10 ³ /μL)	255,68	93,48	244,50	196,00	296,50	257,14	87,87	241,00	203,00	286,00	0,895
pH	7,36	0,05	7,36	7,34	7,36	7,29	0,04	7,31	7,28	7,31	<0,001
SII ³	1012,91	2693,44	706,90	433,67	1026,24	839,58	625,77	675,38	401,16	1124,41	0,564
COHb ⁴	7,29	4,57	5,00	5,00	7,50	10,86	8,02	5,00	5,00	15,00	<0,001

1Glasgow Coma Scale, 2 White Blood Cell, 3 Systemic Immune-Inflammation Index, 4Carboxyhemoglobin

Table 6. Comparisons of lactate groups' demographics, symptoms, and prognosis of the study population.

	Lgroup-1		Lgroup-2		p value
	n	%	n	%	
Gender					0,653
Female	174	53,7%	35	50,7%	
Male	150	46,3%	34	49,3%	
Application Time					0,646
0-8 Hours	58	17,9%	15	21,7%	
8-24 Hours	243	75,0%	48	69,6%	
>24 Hours	23	7,1%	6	8,7%	
Headache					0,553
No	191	59,0%	38	55,1%	
Yes	133	41,0%	31	44,9%	
Nausea-Vomiting					0,103
No	267	82,4%	51	73,9%	
Yes	57	17,6%	18	26,1%	
Weakness					0,629
No	221	68,2%	45	65,2%	
Yes	103	31,8%	24	34,8%	
Dizziness					0,159
No	201	62,0%	49	71,0%	
Yes	123	38,0%	20	29,0%	
Syncope					0,698
No	232	71,6%	51	73,9%	
Yes	92	28,4%	18	26,1%	
Confusion					0,009
No	218	67,3%	35	50,7%	
Yes	106	32,7%	34	49,3%	
Seizure					0,051
No	214	66,0%	37	53,6%	
Yes	110	34,0%	32	46,4%	
Lethargy					0,006
No	229	70,7%	37	53,6%	
Yes	95	29,3%	32	46,4%	
Length of Hospital Stay					0,002*
0-24 Hours	221	68,2%	35	50,7%	
24-72 Hours	95	29,3%	27	39,1%	
>72 Hours	8	2,5%	7	10,1%	
Follow-Up					<0,001*
Discharge after treatment in the E.D.**	87	26,9%	1	1,4%	
Pediatric service	159	49,1%	14	20,3%	
Intensive care unit	68	21,0%	40	58,0%	
Referral	10	3,1%	14	20,3%	

* Fisher's exact test p value and all others Pearson Chi-square test **Emergency Department

Among the key diagnostic and prognostic indicators for carbon monoxide poisoning, CO level stands out as one of the most important. Our results showed that patients with higher CO levels had lower GCS scores and blood pH levels, accompanied by an increased prevalence of symptoms such as dizziness, confusion, seizures, and lethargy. In addition, the need for additional interventions such as hyperbaric oxygen treatment became more apparent as CO levels escalated. These observations are consistent with the existing literature.

Another important prognostic parameter in CO poisoning is the lactate level. In our study, patients with elevated lactate levels had lower GCS scores, lower blood pH levels, and higher COHb levels. In addition, these patients had a higher incidence of confusion and lethargy. As a result, these patients had longer stays in intensive care and longer hospital stays.

Although significant differences were observed between the subgroups categorized by COHb and lactate levels, no corresponding differences were observed in SII levels. Although the SII has recently gained popularity as an index that holistically captures the balance between a patient's immune response and inflammatory state, it did not show sufficient predictive power in determining the severity of poisoning in patients presenting with CO poisoning.

Limitations: This study has certain limitations. Firstly, it has the inherent limitations of a retrospective study and it was not possible to include all patients in the analysis. Second, the single-center design and limited patient population prevent direct extrapolation of the results to all patient groups. Thirdly, the ability of the SII to predict mortality could not be assessed because there were no deaths among the patients. Finally, complete access to data on patients referred to other hospitals was not possible.

Table 7. Comparisons of group data and prognosis based on SII

	SII					p value
	Mean	SD	Median	25%	75%	
Length of Hospital Stay						0,563
0-24 Hours	896,91	784,30	712,05	457,49	1082,94	
24-72 Hours	1179,78	4300,71	638,72	400,75	990,75	
>72 Hours	923,23	691,76	739,02	362,21	1260,12	
Lactate (mmol/L)						0,564
<2.2	1012,91	2693,44	706,90	433,67	1026,24	
>2.2	839,58	625,77	675,38	401,16	1124,41	
Follow-Up						0,941
Discharge after treatment in the E.D.*	883,42	724,11	712,61	478,61	1053,01	
Pediatric service	1102,01	3606,18	685,41	414,82	1025,02	
Intensive care unit	862,45	739,04	698,22	446,98	1090,82	
Referral	1024,15	1059,14	589,89	391,06	1258,97	
COHb**						0,687
COgroup-1	985,73	2526,68	704,56	430,86	1071,23	
COgroup-2	932,44	981,63	589,89	337,19	1041,69	
Gender						0,878
Female	835,81	622,53	684,04	430,86	1071,23	
Male	1149,07	3530,79	708,49	425,77	1074,28	

*Emergency Department **Carboxyhemoglobin

CONCLUSION

In conclusion, based on the results of this study, the SII cannot be considered a reliable predictor of the severity of carbon monoxide poisoning in children. Despite the apparent inflammatory response induced by carbon monoxide exposure, the SII did not consistently correlate with different degrees of poisoning severity. Further research, preferably using prospective and multicentre approaches, is needed to elucidate the complex dynamics between SII and the severity of carbon monoxide poisoning.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Local Ethics Committee (Decision No: 2021/17-06).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Piantadosi CA. Carbon monoxide poisoning. *Undersea Hyperb Med.* 2004;31(1):167-77.
2. Ghosh RE, Close R, McCann LJ, Crabbe H, Garwood K, Hansell AL, Leonardi G. Analysis of hospital admissions due to accidental non-fire-related carbon monoxide poisoning in England, between 2001 and 2010. *J Public Health (Oxf).* 2016;38(1):76-83.
3. Uysalol M, Uysalol E, Saracoglu G, Kayaoglu S. A retrospective analysis of pediatric patients admitted to the pediatric emergency service for carbon monoxide intoxication. *Balkan Med J.* 2011;28(3).
4. Marchi AG, Renier S, Messi G, Barbone F. Childhood poisoning: a population study in Trieste, Italy, 1975-1994. *J Clin Epidemiol.* 1998;51(8):687-95.
5. Lee FY, Chen WK, Lin CL, Kao CH. Carbon monoxide poisoning and subsequent cardiovascular disease risk: a nationwide population-based cohort study. *Medicine (Baltimore).* 2015;94(10):e624.
6. Roderique JD, Josef CS, Feldman MJ, Spiess BD. A modern literature review of carbon monoxide poisoning theories, therapies, and potential targets for therapy advancement. *Toxicology.* 2015;334:45-58.
7. Celik B, Nalcacioglu H, Ozcatal M, Altuner Torun Y. Role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in identifying complicated appendicitis in the pediatric emergency department. *Ulus Travma Acil Cerrahi Derg.* 2019;25(3):222-228.
8. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res.* 2014;20(23):6212-22.
9. Kinoshita H, Türkan H, Vucinic S, Naqvi S, Bedair R, Rezaee R, Tsatsakis A. Carbon monoxide poisoning. *Toxicol Rep.* 2020;7:169-173.
10. Hampson NB, Piantadosi CA, Thom SR, Weaver LK. Practice recommendations in the diagnosis, management, and prevention of carbon monoxide poisoning. *Am J Respir Crit Care Med.* 2012 Dec 1;186(11):1095-101.

11. Pollmächer T, Hinze-Selch D, Mullington J. Effects of clozapine on plasma cytokine and soluble cytokine receptor levels. *J Clin Psychopharmacol.* 1996;16(5):403-9.