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Predictive Value of Complete Blood Count, Venous Blood Gas Measurements, and Glucose/Potassium Ratio for Delayed Neuropsychiatric Syndrome in Children with Acute Carbon Monoxide Poisoning Due to Coal-Burning Stove

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What is already known on this topic?

- *Delayed neuropsychiatric syndrome (DNS) due to carbon monoxide (CO) poisoning includes varying levels of cognitive deficits, personality changes, movement disorders, and focal neurological deficits.*
- *In studies conducted in adult patients with CO poisoning, it was concluded that data obtained from complete blood count such as systemic immune inflammation index, neutrophil count, neutrophil/lymphocyte ratio, glucose/potassium ratio, and lactate level may be effective in predicting DNS. However, pediatric studies are very limited.*

What this study adds on this topic?

- *In children, systemic immune inflammation index, neutrophil count, and neutrophil/lymphocyte ratio measured immediately after the poisoning in the pediatric emergency department may be effective parameters in predicting the development of delayed neuropsychiatric syndrome (DNS) within 1 year.*
- *Although the sensitivity of glucose/potassium ratio in predicting DNS in children was very high, its specificity was significantly low.*

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ABSTRACT

Objective: Delayed neuropsychiatric syndrome may occur after carbon monoxide poisoning has completely healed. The literature on indicators to predict delayed neuropsychiatric syndrome in pediatric patients is limited. The aim of the study is to investigate the effectiveness of complete blood count parameters, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, systemic immune inflammation index, glucose/potassium ratio, venous blood gas parameters, and carboxyhemoglobin in predicting delayed neuropsychiatric syndrome in children with carbon monoxide poisoning due to coal-burning stove.

Materials and Methods: The patients admitted to the pediatric emergency department with acute carbon monoxide poisoning between 2014 and 2019 were analyzed. The patients were divided into 2 groups as delayed neuropsychiatric syndrome (+) and delayed neuropsychiatric syndrome (−). Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, systemic immune inflammation index (platelet count×neutrophil count/lymphocyte count), and glucose/potassium ratio were calculated.

Results: Of the 137 patients, 46 were diagnosed with delayed neuropsychiatric syndrome within 1 year of carbon monoxide poisoning. A control group was formed from 137 age- and sex-matched children. Glasgow Coma Scale < 15 was found in 11% of patients with delayed neuropsychiatric syndrome (−) and 8.7% of patients with delayed neuropsychiatric syndrome (+) (P = .773). Blood glucose, potassium, glucose/potassium ratio, platelet/lymphocyte ratio, white blood cell, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio, systemic immune inflammation index, venous partial pressure of carbon dioxide, carboxyhemoglobin, and methemoglobinemia levels were significantly different between control, delayed neuropsychiatric syndrome (+), and delayed neuropsychiatric syndrome (−) groups (P < .05). The most effective predictors for delayed neuropsychiatric syndrome were systemic immune inflammation index (area under the curve = 0.852; cut-off value > 1120; sensitivity = 89.1%; specificity = 75.8%), neutrophil (area under the curve = 0.841; cut-off value > 8000/mm3; sensitivity = 78.2%; specificity = 79.1%), and neutrophil/lymphocyte ratio (area under the curve = 0.828; cut-off value > 4; sensitivity = 78.2%; specificity = 75.5%).

Conclusion: About one-third of children with carbon monoxide poisoning due to coal-burning stove develop delayed neuropsychiatric syndrome. Systemic immune inflammation index, neutrophil count, and neutrophil/lymphocyte ratio obtained immediately after the poisoning in the pediatric emergency department may be effective predictors for delayed neuropsychiatric syndrome.

Keywords: Carbon monoxide poisoning, delayed neuropsychiatric syndrome, glucose/potassium ratio, neutrophil count, neutrophil/lymphocyte ratio

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INTRODUCTION

Carbon monoxide (CO) is an odorless, tasteless, colorless, and non-irritating gas produced by the combustion of hydrocarbons.[1] About 50 000 people are poisoned by CO annually in the United States of America (USA), and the most common cause is fire.[2] In response to a written question submitted in 2018 in the Grand National Assembly of Türkiye, it was reported that a total of 108 905 CO poisoning incidents were recorded in Turkey between 2013 and 2018.[3] The most common etiology of CO poisoning in Turkey is coal stove poisoning.[4]

Carbon monoxide binds to hemoglobin with much greater affinity than oxygen, forming carboxyhemoglobin (COHb) and causes deterioration in oxygen transport and use.[1] Carbon monoxide causes the release of myeloperoxidase, proteases, and reactive oxygen species, and platelet and neutrophil aggregation. Ultimately, oxidative stress leads to lipid peroxidation and apoptosis. These effects are more pronounced in the central nervous system (CNS), explaining the clinical situation of nitric oxide-mediated vasodilation and oxidative damage.[5] In the acute period, the sympathetic nervous system is activated. It leads to elevated production of catecholamines such as adrenaline, noradrenaline, and dopamine.[6] Catecholamines are important because they cause an increased glucagon secretion after stress, thereby raising blood glucose concentrations.[7] An elevation in serum glucose concentrations caused by excessive catecholamine secretion also induces insulin secretion and subsequently leads to the entry of serum potassium into cells.[8]

The most common acute clinical findings in CO poisoning are headache, weakness, nausea, dizziness, difficulty concentrating or confusion, shortness of breath, and visual changes. Carbon monoxide poisoning is considered severe in patients with neurologic (seizures, syncope, transient loss of consciousness, or coma), metabolic (lactic acidosis), and cardiovascular (acute myocardial ischemia, myocardial injury, ventricular arrhythmias, and pulmonary edema) findings.[9] Delayed neuropsychiatric syndrome (DNS) may occur in patients who survive acute CO poisoning. It may occur in 3%-40% of patients with significant CO exposure. The DNS usually occurs within 20 days after the CO-poisoned patient has fully recovered. It can occur between 3 and 240 days after acute poisoning. Clinical manifestations associated with DNS may persist for a year or more. Following a short recovery period, there may be neuropsychiatric signs and symptoms such as speech and memory disorders, seizures, delirium, agnosia, ataxia, apraxia, personality changes, and mood disorders. The DNS mechanism is not fully understood. However, it is estimated that it develops due to lipid peroxidation caused by reactive oxygen molecules produced by xanthine oxidase. Xanthine oxidase is produced from xanthine dehydrogenase, which is formed by enzymes secreted by leukocytes that adhere to damaged endothelial cells.[1,9–12]

The aim of the study is to investigate the effectiveness of complete blood count (CBC) parameters, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), systemic immune inflammation index (SIII), glucose/potassium ratio (GPR), venous blood gas parameters, and COHb in predicting the development of DNS in children admitted to the emergency department due to CO poisoning.

MATERIALS AND METHODS

Study Design

This study was a retrospective case-control study in a single center. The medical records of the patients who were admitted to the pediatric emergency department due to CO poisoning between January 1, 2014, and December 31, 2019, were evaluated by the pediatric emergency specialists. The study group was formed according to the inclusion and exclusion criteria of the study. According to the medical records, after the CO poisoning was completely resolved, the medical records of those who were admitted to the pediatric neurology and/or child psychiatry outpatient clinic were separated. The medical records of these patients were evaluated retrospectively by a pediatric neurologist and a pediatric psychiatrist. Then, these patients were contacted by phone and called to the hospital for reassessment. Patients were reevaluated by the pediatric neurologist and the pediatric psychiatrist.

In our research, our hypothesis was that the risk of DNS would increase as the immunological or metabolic response increases in CO poisoning. Therefore, the difference could be seen more clearly when the change in laboratory parameters was compared as control, DNS (−) and DNS (+) groups. A control group was formed from healthy children who admit to the social pediatrics outpatient clinic of the same hospital between 2014 and 2019. The children in the control group had no known chronic disease and were asymptomatic at presentation. The control group was formed in an equal number with the number of patients and matched exactly in terms of age and gender. Same-sex and patient age ± 6 months criteria were used for matching.

Setting

This study was conducted in a pediatric emergency department of a children's hospital, where approximately 120 000 patients were admitted annually. The children's hospital is the only hospital in the region to have a pediatric neurology sub-specialty department and a pediatric psychiatry outpatient clinic.

Inclusion Criteria

Patients aged 18 years and younger who were admitted to the pediatric emergency department of our hospital between January 2014 and December 2019 with acute CO poisoning within 24 hours were included in the study. Patients who first presented to our emergency department with CO poisoning and whose first COHb level was 10% or more and patients who completed at least 1 standard treatment period in our hospital were enrolled on the study.

Exclusion Criteria

Those with chronic diseases (such as neurological, diseases, psychiatric diseases, diabetes, immunodeficiency, cancer, hematological diseases, etc.), with a history of neurological or psychiatric diseases, pregnancy, who use immunosuppressant drugs, who died due to poisoning, who were poisoned due to multiple substances, and who refused treatment were excluded from the study.

Measurements

The following data were collected retrospectively from medical records: age, sex, duration of CO exposure, source of CO

poisoning, Glasgow Coma Scale score at presentation, clinical findings, laboratory results at first admission, radiological examinations, and treatment types. During the first admission, peripheral CBC (hemoglobin, red blood cell, platelet count, white blood cell [WBC]), basic serum biochemistry, and venous blood gas analysis (pH, partial pressure of carbon dioxide [pCO_2], bicarbonate, COHb, methemoglobinemia [metHb], lactate) results were evaluated. The PLR, NLR, and SIII (platelet count × neutrophil count/lymphocyte count) were calculated.

Diagnostic Procedures

Venous blood samples were taken within the first 15 minutes after admission. Whenever possible, blood is sampled first from the non-dominant extremity, according to department quality rules. The vena cephalica is preferred primarily on the forearm in the pediatric emergency department. Blood samples are sent to the emergency room laboratory without waiting. The blood gas is analyzed immediately, and the result is available within 5 minutes (ABL80FLEX-BASIC®, France). The COHb and lactate were measured in venous blood gas analysis. Hemogram results are available within 15 minutes and biochemistry results are available within half an hour (Beckman Coulter®, ABD; Abbott Arcitect C16000, ABD).

Acute Carbon Monoxide Poisoning Treatment Protocol in the Pediatric Emergency Department

In the pediatric emergency department, all patients routinely receive 100% oxygen support at a flow rate of 10 L/min with a nonrebreathing oxygen mask. Indications for hyperbaric oxygen (HBO) therapy are the presence of any neurological deficit including unconsciousness and seizure, severe metabolic acidosis (pH < 7.25), evidence of end-organ ischemia (e.g., electrocardiogram changes, chest pain, or altered mental status), and a COHb level more than 25%. If symptoms do not improve after 1 session of HBO, a maximum of 5 HBO sessions are administered over the next 48 hours. The HBO was applied with 100% oxygen at 2.5 atmospheres pressure for 2 hours (HiperTech MULTIPLACE, Turkey).[2,9,10]

Delayed Neuropsychiatric Syndrome Diagnosis

The DNS is defined as those who did not have any previous neurological, psychiatric, or metabolic disease, who presented to the pediatric emergency department due to CO poisoning and were discharged from the hospital, and who developed a new neurological or psychiatric complaint after complete recovery within 1 year after CO intoxication. The main symptoms of DNS, are seizure, speech disorder, psychosis, psychoneurosis, strial syndrome, motor and sensory deficit, spinal cord, and peripheral nerve deficiency. However, the diagnostic criteria of DNS are not yet clear. The clinical judgment of the physician is still very important in diagnosis.[13] The DNS (+) patients were collected from hospital records according to the International Classification of Diseases (ICD-10) code, retrospectively. The final clinical status of the patients was evaluated clinically by a child neurologist and a child psychiatrist. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, DSM-5 November 2016-Turkish Adaptation was used in the psychiatric evaluation.[14]

Statistical Analyses

Normality analysis was performed using the Kolmogorov–Smirnov test for continuous data. Continuous data that does not show normal distribution were expressed as median and quartile range (interquartile range [IQR]; 25th percentile-75th percentile); categorical data were expressed as numbers (n) and percentages (%). Mann–Whitney *U*-test was used for comparing the continuous data of the 2 independent groups. In independent groups, when the number of groups is more than 2, Kruskal–Wallis test was used for the continuous data. Mann–Whitney *U* test and Bonferroni correction were used as a post hoc test for Kruskal–Wallis analysis. We analyzed the categorical data by chi-square or Fischer's exact test, whichever is appropriate. The receiver operating characteristic curve (ROC) analysis to predict DNS, area under the curve (AUC) was detected. The diagnostic accuracy was regarded as excellent for AUC values between 0.9 and 1, good for AUC values between 0.8 and 0.9, fair for AUC values between 0.7 and 0.8, poor for AUC values between 0.6 and 0.7, and failed for AUC values between 0.5 and 0.6. When the AUC values were statistically significant according to the ROC analysis, sensitivity and specificity values were determined according to the cut-off points. Cut-off points in ROC analysis were determined by Youden index (Youden's J statistic). The IBM Statistical Package for the Social Sciences Statistics for Windows 22.0 (IBM Corp, Armonk, NY, USA) and MedCalc (MedCalc Software Ltd, Belgium) were used in the analysis. A *P* value below .05 was accepted as significant.

RESULTS

General Characteristics of Patients with Acute Carbon Monoxide Poisoning and Control Group

A total of 183 children were diagnosed with CO poisoning in the pediatric emergency department of our hospital between 2014 and 2019. A total of 137 patients were included in the study. The control group was formed from 137 healthy children without acute illness (Figure 1). The coal-burning stove was the cause in all cases included in the study. All patients were admitted to the pediatric emergency department within 1 hour after the signs of poisoning appeared. A total of 137 patients were divided into 2 groups as DNS (+) and DNS (−). A total of 46 cases (33.5%) were diagnosed with DNS within 1 year after CO poisoning (Table 1).

Clinical Features of Acute Carbon Monoxide Poisoning and Delayed Neuropsychiatric Syndrome

Fifty-eight patients (42.3%) were symptomatic when they were admitted to the pediatric emergency department. Vomiting was the most common symptom (23 patients, 16.8%) in the pediatric emergency department. Among the DNS-related symptoms, the most common was personality change (23 patients, 50%) (Table 2). Glasgow Coma Scale score < 15 was found in 10 (11%) patients with DNS (−) and 4 (8.7%) patients with DNS (+) ($P = .773$). When the duration of DNS-related symptoms after CO poisoning was evaluated in 46 patients, 27 patients (58.7%) had symptoms within the first month after discharge from the pediatric emergency department (6 headaches, 16 personality changes, 5 depressions), 13 patients (28.3%) had symptoms between the 1st and 2nd month (3 headaches, 7 behavior changes, 3 depressions), and 5 patients (10.9%) had symptoms between the 2nd and 3rd month (1 headache, 3 depressions, 1 vertigo). In 1 case, afebrile convulsion (2.1%) was observed in the 5th month after poisoning. Electroencephalogram and magnetic resonance imaging (MRI) were normal. It did not recur for a year. He did not need antiepileptic drug therapy. Magnetic resonance imaging was performed in 27 cases due

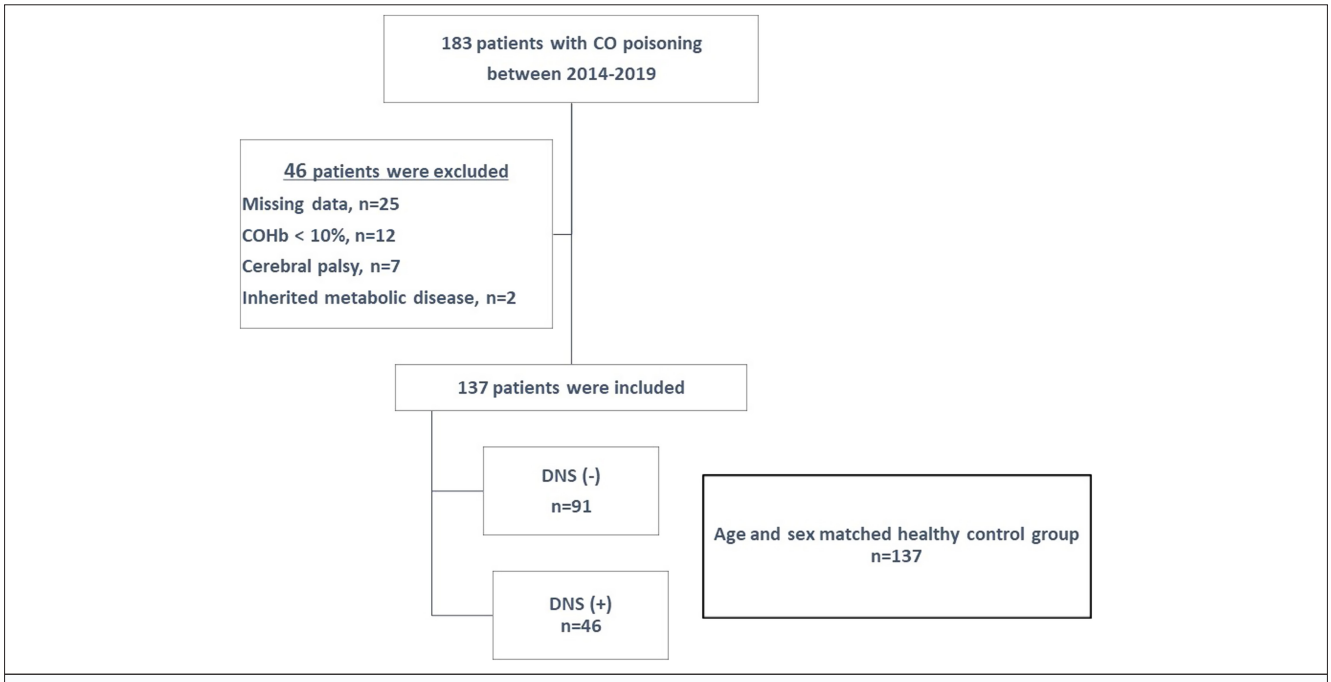

Figure 1. Flow chart of the study.

to DNS-related findings, and no pathology was detected in any of them. All cases were asymptomatic at the end of 1 year after poisoning. At the end of 1 year, none of the patients were using medication for DNS-related symptoms.

Comparison of Laboratory Results of Delayed Neuropsychiatric Syndrome (+), Delayed Neuropsychiatric Syndrome (−) and Control Groups

When we compare DNS (−), DNS (+), and control groups in terms of laboratory test results, there were significant differences in blood glucose, potassium, GPR, PLR, WBC count, absolute neutrophil count, absolute lymphocyte count, NLR, SIII, venous pCO_2, COHb, and metHb ($P < .05$) (Tables 3 and 4). The ROC analysis was performed to predict DNS. The AUC values of SIII (AUC = 0.852; cut-off value >1120; sensitivity = 89.1%; specificity = 75.8%), absolute neutrophil count (AUC = 0.841; cut-off value >8000/mm^3; sensitivity = 78.2%; specificity = 79.1%), and NLR (AUC = 0.828; cut-off value >4; sensitivity = 78.2%; specificity = 75.5%) were above 0.800 (Table 5, Figure 2).

Table 1. Comparison of Patients, Control Group, DNS (+) and DNS (−) Groups in Terms of Age and Sex

	All Patients (n = 137)	Control Group (n = 137)	*P*	DNS (−) Patients (n = 91)	DNS (+) Patients (n = 46)	*P*
Age, median (IQR)	11 (6-15)	11 (6-15)	>0.999[1]	11 (6-13)	11 (7.5-15)	.197[1]
Male, n (%)	66 (48.2)	66 (48.2)	>0.999[2]	38 (41.8)	28 (60.9)	**.034**[2]

DNS, delayed neuropsychiatric syndrome; IQR, interquartile range.
[1]Mann–Whitney *U* test.
[2]Chi-square test.
$P < .05$ is statistically significant.

Table 2. The Admission Symptoms of Children Diagnosed with Stove-Induced CO Poisoning in the Emergency Department and DNS-Related Symptoms Within the First Year After CO Poisoning

Symptoms Associated with Acute CO Poisoning in PED, n = 137	n (%)	DNS-Related Symptoms Within the First Year After CO Poisoning, n = 46	n (%)
Headache	8 (5.8)	Headache	10 (21.7)
Headache and vomiting	2 (1.5)	Vertigo	1 (2.2)
Nausea	11 (8)	Personality change	23 (50)
Vomiting	21 (15.3)	Depression	11 (23.9)
Afebrile convulsion	3 (2.2)	Afebrile convulsion	1 (2.2)
Transient loss of consciousness	13 (9.5)		
No complaints	79 (57.7)		

CO, carbon monoxide; DNS, delayed neuropsychiatric syndrome; PED, pediatric emergency department.

Table 3. Comparison of CBC and Biochemistry Results Among DNS (+), DNS (–), and the Control Groups

		25 Percentile	Median	75 Percentile	*P*[1]
Red blood cell (×10⁴/mm³)	Control	4.3	4.5	5.0	.860
	DNS (+)	4.3	4.7	5.2	
	DNS (–)	4.4	4.7	5.1	
Hemoglobin (g/dL)	Control	12.2	12.0	13.0	.485
	DNS (+)	11.4	12.5	13.2	
	DNS (–)	12.1	13.0	13.8	
Hematocrit (%)	Control	36.1	36.0	42.5	.216
	DNS (+)	33.5	36.6	39.1	
	DNS (–)	35.2	36.8	40.0	
Platelets (×10³/mm³)	Control	258	283	328	.647
	DNS (+)	244	284	392	
	DNS (–)	253	302	368	
White blood cell (×10³/mm³)	Control	6.5	7.0	9.0	**<.001***
	DNS (+)	11.0	12.6	16.4	
	DNS (–)	8.1	10.3	12.4	
Lymphocyte (×10³/mm³)	Control	2.5	3.0	3.90	**<.001****
	DNS (+)	1.2	1.5	2.2	
	DNS (–)	1.6	2.4	3.8	
Neutrophil (×10³/mm³)	Control	3.6	4.5	5.2	**<.001****
	DNS (+)	8.8	10.4	12.7	
	DNS (–)	5.0	6.3	8.3	
Neutrophil/lymphocyte ratio	Control	1.2	1.4	1.6	**<.001****
	DNS (+)	4.8	6.5	9.3	
	DNS (–)	1.3	2.5	4.3	
Platelet/lymphocyte ratio	Control	74.9	101.3	118.0	**<.001****
	DNS (+)	144.6	182.1	257.9	
	DNS (–)	91.9	112.2	163.0	
Systemic immune inflammation index	Control	350.1	396.7	485.0	**<.001****
	DNS (+)	1353.1	2038.3	2781.8	
	DNS (–)	523	766.1	1120.4	
Glucose (mg/dL)	Control	74.7	84.0	90.2	**<.001****
	DNS (+)	119.0	128.5	141.0	
	DNS (–)	87.0	96.0	129.0	
Potassium (mmol/L)	Control	4.3	4.5	4.6	**<.001***
	DNS (+)	3.9	4.1	4.2	
	DNS (–)	4.1	4.2	4.4	
Glucose/potassium ratio	Control	19.0	21.1	27.0	**<.001****
	DNS (+)	30.1	31.4	35.6	
	DNS (–)	20.4	22.0	31.0	

CBC, complete blood count; DNS, delayed neuropsychiatric syndrome.
*Control group is significantly different from DNS (+) and (–) group.
**DNS (+) group is significantly different from the control group and DNS (–) group.
[1]Kruskal–Wallis test.
$P < .05$ is statistically significant.

DISCUSSION

In our study, DNS emerged within 1 year in approximately one-third of the children admitted to the emergency department due to coal-burning stove-induced CO poisoning. The most common symptom was personality change, and all DNS symptoms disappeared within 1 year of poisoning. The SIII, absolute neutrophil count, and NLR measured at the time of admission to the pediatric emergency department due to CO poisoning were found to have good performance in predicting future DNS. The fast results and low cost of these tests increase their usefulness.

Studies on the prediction of DNS by parameters obtained from CBC have been predominantly conducted in adult patients. Pediatric studies on this subject are very limited.

The DNS is a group of neuropsychological disorders that appear days or weeks after the symptoms of acute CO poisoning have disappeared. Neurological sequelae arising after CO poisoning are at least partially reversible.[15] However, there are also studies showing that cognitive and neurological deficits continue in patients and that DNS cannot be reversed. The risk of neurological sequelae is higher in those aged 36 years

Table 4. Comparison of Venous Blood Gas Results Between DNS (+) and DNS (–) Patient Groups

	DNS (–) n = 91	DNS (+) n = 46	P[1]
pH, median (IQR)	7.35 (7.32-7.39)	7.37 (7.34-7.40)	.331
pCO_2, median (IQR)	41.4 (38-45.5)	39.3 (34.2-43.8)	**.041**
HCO_3, median (IQR)	22.6 (21.5-24)	22.5 (21.7-23.6)	.837
COHb, median (IQR)	17.6 (14-23.7)	22 (21.7-23.6)	**<.001**
MetHb, median (IQR)	0.3 (0.3-0.8)	0.7 (0.3-1)	**.009**
Lactate, median (IQR)	1.9 (1.6-2.4)	1.9 (1.5-2.4)	.980

COHb, carboxy hemoglobin; DNS, delayed neuropsychiatric syndrome; HCO_3, bicarbonate; MetHb, methemoglobinemia; pCO_2, partial pressure of carbon dioxide;
[1]Mann–Whitney *U* test.
P < .05 is statistically significant.

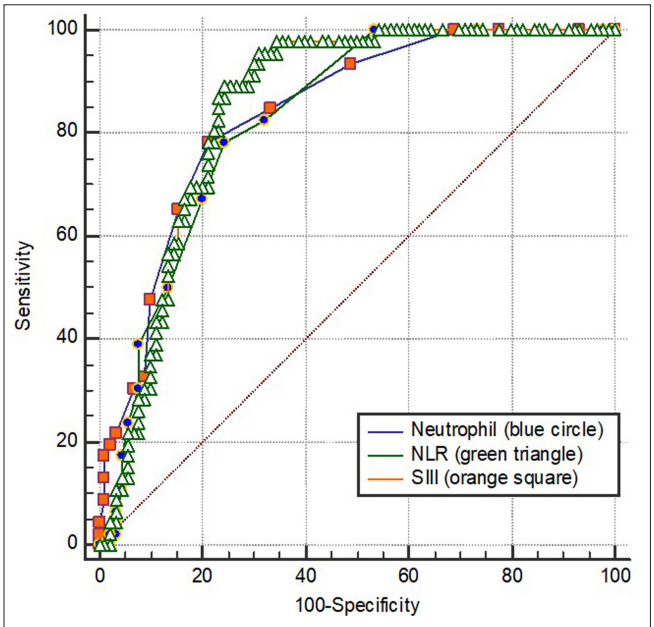

Figure 2. The ROC curves of neutrophil, NLR, and SIII for DNS prediction in children with CO poisoning due to coal-burning stove admitted to the emergency department. CO, carbon monoxide; DNS, delayed neuropsychiatric syndrome; NLR, neutrophil/lymphocyte ratio; ROC, receiver operating characteristic; SIII, systemic immune inflammation index.

or older and exposed to CO for more than 24 hours.[10] In our study, about one-third of children were diagnosed with DNS due to coal-burning stove-induced CO poisoning. Consistent with the literature,[1,10] the most common DNS-related symptom in our study was personality change. All of the DNS-related symptoms completely disappeared within a year after the poisoning. No obvious pathology was detected in the MRI results. In our study group, we observed that DNS associated with coal stove-induced CO poisoning in children generally follows a benign process. However, we cannot definitively state that DNS is a benign disorder in pediatric patients due to the single-center nature of our study and the limited number of patients.

Carbon monoxide causes tissue hypoxia, anaerobic glycolysis, and lactate production. Baseline high lactate level (>2.1 mmol/L) was an independent risk factor associated with acute serious complications and the need for intensive medical treatment in adults.[16] The DNS group was associated with significantly higher lactate concentration than that in the non-DNS group in studies in adult patients.[17] However, the results of the studies on the relationship between lactate level and clinical severity in acute CO poisoning in children are not clear.[10,18] In some studies, lactate levels in CO poisonings were not statistically significant for the severe course in the acute phase in pediatric population.[18] In another study, serum lactate level was higher in patients with neurological findings due to acute CO poisoning (59.1% vs. 78.1%).[19] The number of studies examining the relationship between baseline lactate level and DNS development in children is very limited.[10,18] In our study, lactate level was not different between DNS (+) and DNS (–) groups. Considering that the definition of high lactate level is 2 mmol/L or more, the median lactate values of the patients in the DNS (+) and DNS (–) groups were <2 mmol/L.[17] The reason for this result may be that patients admit to the emergency department in a short time after the poisoning occurs and they are not exposed to CO for a long time.

Table 5. Predicting DNS with ROC Analysis in Children Admitted to the Emergency Department due to Stove-Induced Carbon Monoxide Poisoning

	Cut-Off Value	AUC	P	Sensitivity	Specificity
Alanine aminotransferase, (U/L)	≤15	0.633	**.007**	65.2	59.3
Glucose (mg/dL)	>102	0.766	**<.001**	97.8	62.6
Potassium (mmol/L)	≤4.1	0.737	**<.001**	73.9	61.5
Glucose/potassium ratio	>24.4	0.796	**<.001**	100	61.5
pCO_2 (mmHg)	≤36.6	0.607	**.209**	43.5	78
COHb (%)	>18.4	0.726	**.002**	100	56
MetHb (%)	>0.3	0.635	**.045**	71.7	52.7
Platelet/lymphocyte ratio	>126.8	0.747	**<.001**	89.1	62.6
White blood cell ($\times10^3/mm^3$)	>10,000	0.720	**.003**	82.6	51.6
Neutrophil ($\times10^3/mm^3$)	>8000	0.841	**<.001**	78.2	79.1
Lymphocyte ($\times10^3/mm^3$)	≤1000	0.709	**<.001**	47.8	81.3
Neutrophil/lymphocyte ratio	>4	0.828	**<.001**	78.2	75.5
SIII	>1120	0.852	**<.001**	89.1	75.8

AUC, area under the curve; COHb, carboxyhemoglobin; MetHb, methemoglobinemia; ROC, receiver operating characteristic; SIII, systemic immune inflammation index.
P < .05 is statistically significant.

White blood cell count and its subtypes are markers of systemic inflammation, and neutrophils are pivotal players in innate immune responses.[20] Lymphocytopenia reflects the elevated release of catecholamines and corticosteroids due to acute brain lesions.[21] Several investigators suggested that variables derived from routine blood count parameters, that is, PLR, NLR, and SIII could serve as a simple indicator of immune function. Increased NLR and PLR may be poor prognostic markers when compared to healthy controls in the patient group.[11,21,22] Studies have shown that CO exposure triggers aggregation of platelets–neutrophils and also activation of neutrophils in the bloodstream. Perivascular oxidative stress associated with immune-mediated neurological sequelae also occurs with myeloperoxidase released by neutrophils.[23] The NLR and SIII have diagnostic accuracy for DNS in adult patients.[11] Low NLR and PLR levels are associated with higher COHb levels in children with CO poisoning in admission to the pediatric emergency department. In addition, low PLR level was reported to be associated with high lactate level.[24] We found that high SIII, neutrophil count, and NLR values measured at the time of admission to the emergency department in children predicted DNS (+) due to CO poisoning at a good level. Studies in the literature on the predictive power of CBC parameters for DNS were generally performed in adult patients. Since our study was conducted in pediatric patients, it makes an additional contribution to the literature.

In CO poisoning, an increase in sympathetic activity and subsequent high catecholamine levels occur. High catecholamine levels increase glucose and decrease serum potassium levels. Studies have reported that GPR is more effective than glucose in predicting long-term brain damage.[13,25,26] In our study, serum glucose and GPR had similar efficacy in predicting DNS (+). When we compared glucose and GPR with SIII, neutrophil count, and NLR, the predictive power of hemogram parameters was found to be higher. Although the sensitivity of glucose and GPR values was higher than SIII, neutrophil count, and NLR, their specificity was lower.

The most important limitation of our study is the experience of a single center and the limited number of patients. Second, the patients included in the study were not exposed to CO for a long time, and they were admitted to the emergency department as soon as possible after the symptoms appeared. Third, the diagnostic criteria of DNS are not yet clear. Therefore, our study group may have a higher number of DNS patients, or some patients may not have consulted a doctor even though they had symptoms. However, there are also strengths of our study. To the best of our knowledge, studies to predict DNS have generally been performed in the adult patient population, and studies in children are limited. Finally, the analysis of venous blood gas and basic biochemical tests along with CBC parameters within the same pediatric group strengthened the study.

CONCLUSION

About one-third of children with coal-burning stove-induced CO poisoning develop DNS within 1-year period. The SIII, neutrophil count, and NLR measured immediately after poisoning in the pediatric emergency department may be effective parameters in predicting the development of DNS within 1 year. They can be used as easily accessible, fast, and low-cost prognostic tools in clinical areas. Although the sensitivity of GPR in predicting DNS is very high, its specificity is significantly low.

Data Availability Statement: Data from this study can be requested from the corresponding author.

Peer-review: Externally peer-reviewed.

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