Role of Pentraxin 3, Ischemia-modified albumin, and Myeloperoxidase in Predicting Acute Carbon Monoxide Poisoning Outcomes

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Abstract: Background: Carbon monoxide (CO) poisoning is a worldwide leading cause of mortality. It is well-known to be associated with delayed outcome. Among which are delayed neuropsychiatric sequelae (DNS) which are frequently attributing to direct cellular hypoxic damage, free radicals generation, postischemic reperfusion injury as well as widespread systemic inflammatory response. **Objectives:** This study aim was to assess the role of pentraxin 3 (PTX3), ischemia modified albumin (IMA) and myeloperoxidase (MPO) in predicting acute CO poisoning outcomes. **Patients and Methods:** Fifty five acutely-carbon monoxide intoxicated patients admitted to Tanta Poison Control Centre, Tanta University Emergency Hospital, Egypt and fifty five non exposed volunteers served as controls were recruited in the current study during the period from start of December 2016 to the end of November 2017. Diagnosis was confirmed by carboxyhemoglobin level (COHb%) blood level on admission. Acutely-CO intoxicated patients were further subdivided into two groups as follows: delayed neurosychiatric sequelae (DNS) (group I= 32) and non-DNS (group II= 23). Levels PTX3, IMA and MPO were measured on admission. Blood samples also underwent analysis for measurement of (Arterial blood gases (ABG), electrolytes, complete blood count, Random blood glucose, liver and renal functions. **Results:** The mean plasma PTX3, mean serum level of IMA and the median plasma MPO level were highly significantly elevated in CO-intoxicated patients compared with control group (P<0.001**, each). Moreover, the mean plasma PTX3 level and serum levels of IMA and MPO were significantly elevated in DNS-complicated group relative to non-DNS one (P=<0.05*, each). Receiver operation curve was done to evaluate the diagnostic value of these biomarkers in prediction of CO-related DNS. **Conclusion:** The studied markers (PTX3, IMA and MPO) levels on admission could be employed as useful biomarkers for predicting the acute CO poisoning outcome including development of DNS or not.

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Keywords: Carbon monoxide, delayed neuropsychiatric manifestations (DNS), pentraxin 3 (PTX3), ischemia modified albumin (IMA) and myeloperoxidase (MPO) and outcome.

1. Introduction:

Carbon monoxide (CO) is ubiquitous and potentially fatal form of poisoning worldwide (1). In Tanta poison control centre, Tanta University, Egypt, the total number of admitted acutely CO poisoned-patients were 91 (from November 2016 to the end of December 2018) according to reports from the statistical unit of Tanta University Hospitals (total number of admitted =4016). Carbon monoxide the colorless and odorless gas is the end product of incomplete combustion of carbon containing fuel (2). It has affinity to hemoglobin that exceeds oxygen by >250 times forming carboxyhemoglobin (COHb%) with subsequent decrease in oxygen-carrying capacity of blood and tissue hypoxia ensues (3, 4). Delayed neuropsychiatric manifestations (DNS) are common CO-related sequelae. They result from interactions of multiple factors including; direct cellular hypoxic damage, free radicals generation, impaired mitochondrial ATP production, post-ischemic reperfusion injury as well as widespread systemic inflammatory response that leads to brain lipid peroxidation and cerebral vascular endothelium damage (5, 6,7). Clinical features DNS include cognitive impairments, affective disorders and abnormal neurological signs (8). There is an insisting need for new promising objective methods including biochemical markers for early detection of patients at risk of CO-related DNS.

Pentraxin 3 (PTX 3) is a proinflammatory biomarker that is released in response to various ischemic and hypoxic states**.** Previous scientific reports found that PTX 3level increases in the circulation in ischemic conditions as acute myocardial infarction and unstable angina pectoris (9). Carbon monoxide in blood circulation produces platelet and neutrophil interaction and aggregation ending in release of myeloperoxidase, proteases, and reactive oxygen species. This will lead to oxidative stress, lipid peroxidation, and apoptosis (10). Ischemia-modified albumin (IMA) is formed due to changes in human serum albumin occurring during ischemic insult (11).

Previous studies exist in the literature that reports a high level of IMA in CO-poisoned patients, owing to its sensitivity to hypoxia. However, further investigations are needed to confirm this association (12).

The aim of the study was to assess the role of pentraxin 3 (PTX3), ischemia modified albumin (IMA) and myeloperoxidase (MPO) in predicting acute CO poisoning outcomes.

2. Patients and Methods:

This study was conducted on 55 acutely-CO intoxicated patients of both sexes who were admitted to the Tanta Poison Control Center (TPCC) of Tanta University Hospitals, Egypt, during the period starting from 1st of December 2016 to the 30th November 2017 following approval of the medical research ethical committee of Faculty of Medicine, Tanta University. A Written informed consent was obtained from patients or from their guardians. Diagnosis of CO poisoning was based on history of exposure, Clinical signs and symptoms (as alteration in consciousness level, syncope, seizures, shortness of breath, chest pain and palpitation… etc) and was confirmed by carboxyhemoglobin level (COHb%) blood level on admission using Rad 57 CO-Oximeter device (Massimo Set Rainbow company). All patients underwent follow up for 6 months after discharge from hospital at neuropsychiatric hospital, Tanta University, Egypt except the five cases who were died early for detection of any delayed neuropsychiatric sequelae. The diagnosis of DNS in this study was defined as delayed onset of clinical symptoms or neuropsychometric test abnormalities or both after acute carbon monoxide (CO) poisoning (13). Patients who acquired delayed neuropsychiatric manifestations (DNS) were referred to as DNS group (N=32) and those without DNS were referred to as non-DNS group (N=23). Another 55 healthy non-exposed volunteers served as control group.

Exclusion criteria:

Patients retrieved from fires, clinical evidence of chronic hypoxia as ischemic heart diseases, hypertension, diabetes mellitus and respiratory problems, smokers, pregnant, hypoalbuminemia, co-exposure to other xenobiotics, previous history of neuropsychiatric disease and head trauma.

All groups were subjected to the following: Full medical history taking: past history of surgery, medical diseases, family history and toxicological history including (source of carbon monoxide (CO), duration and place of exposure to CO, number of exposed persons, delay time before arrival to ER, symptoms of CO poisoning and pre presentation treatment including number of hyperbaric oxygen sessions).

All patients were generally examined on admission to obtain vital data (blood pressure, pulse, temperature and respiratory rate) and to detect any signs of head injury. The level of consciousness was assessed by Glasgow Coma Scale (GCS) immediately at presentation. Assessment of patient's neurological and psychological outcome was done initially after patient regain stable level of consciousness. Patients were invited for follow up visits for 6 months following discharge from hospital at neuropsychiatry hospital. Neurological examination was conducted by neuropsychiatric specialist could detect any neurologic abnormalities as gait and speech difficulties. Cognitive functioning as memory problems was evaluated using the Revised-Wechsler Memory Scale. Seven subtests are included in the test: information, orientation, mental control, logic memory, digits forward and backward, visual reproduction and associate learning. The WMS provides a total "memory quotient" (MQ) that accounts for age-related mnemonic variability (14). Psychiatric assessment was performed according to standard reference of the Diagnostic and Statistical Manual of Mental Disorders.

Estimation of plasma pentraxin (PTX3) 3 was done using ELISA technique with assay range 0.2-7.2 ng/ml (15). Estimation of serum myeloperoxidase (MPO) enzyme levels using ELISA technique pg/ml and 312–20000 pg/ml (16, 17). Both kits were supplied by Chongqing Biospescompany (Catalouge No. BYEK1108 and BYEK1165 respectively). Spectrophotometric albumin cobalt binding assay for serum ischemia-modified albumin was performed and the results were reported as absorbance units (ABSU) according to the method of (18). Blood samples also underwent analysis for measurement of (Arterial blood gases (ABG), electrolytes, complete blood count, Random blood glucose, liver and renal functions at the laboratory of Tanta university hospitals. Brain CT scan was done on arrival to the emergency room or during early hospitalization to exclude traumatic brain lesion.

Electrocardiographic recording was done for every patient on admission then repeated for those with initial abnormalities in ECG using a **CardiMax FCP-7101**ECG machine **(FUKUDA DENSHI©, Japan)**, at 10 mm⁄mV and 25 mm⁄ s paper speed. All ECGs were coded and analyzed manually by a cardiology specialist who was unaware of other patient data.

Statistical analysis

The data were processed and analyzed using IBM SPSS software package version 21.0. Significance was adopted at $p < 0.05$, highly significant if < 0.01 and non significant if > 0.05 for all tests **(19).**

3. Results:

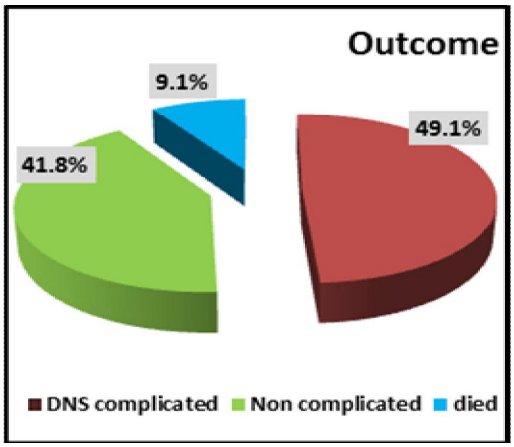

Figure (1): Outcome of the studied acutely carbon monoxide-poisoned patients (n=55).

Figure (1) showed that, 27 patients acquired delayed neuropsychological sequelae (DNS) referred to as DNS group and23 patients didn't develop any complications (Non-DNS group) representing 49.1% and 41.8% respectively of total studied. Five patients died representing (9.1%) of the studied patients. Memory disturbances were the commonest recorded DNS complications following acute carbon monoxide (CO) poisoning (12.7%) as assessed by Wechsler Memory Scale, followed by affective disorders (10.9%), while the least recorded complication was gait disturbances and speech difficulties (5.5%, each).

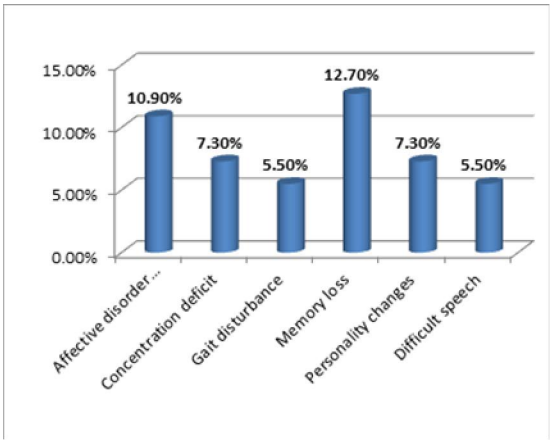

Figure (2): Distribution of delayed neuropsychiatric sequelae-complicated patients (n=27).

Figure (2). In the current study, the highest prevalence of CO poisoning was noticed in the age group (18-28 years) without significant gender variations in the rate of exposure. The commonest source of exposure to CO gas was defective gas water heater at bathrooms, followed by defective gas stove in kitchens. Those who develop DNS were exposed to CO gas for significantly longer median duration than Non-DNS group (5 and 3 hrs respectively) (P=<0.05*) (Table 1). Disturbed consciousness level was the commonest presenting symptom of all studied CO-poisoned patients. The mean heart and respiratory rates was highly significantly-increased in CO-intoxicated patients compared with control group (P=<0.001**, each) (Table 2). The median Glasgow Coma Scale (GCS) of DNS group was significantly-lowered than Non-DNS one (11 and 15 respectively) (P=<0.05*) (Table 3). The mean oxygen saturation was highly significantly-reduced in DNS group (91%±8%) compared with non-DNS one (97%±2%) (P= <0.001**). The mean carboxyhemoglobin (COHb%) was significantly-elevated in DNS group (15%±10%) compared with Non-DNS one (8%±5%) (P=<0.05*) (Table 4). The mean plasma pentraxin 3 (PTX3) level was highly significantly elevated in CO-intoxicated patients compared with control group (6.3±4 and 1.6±1 ng/ml respectively). The mean serum ischemia-modified albumin (IMA) level was highly significantly-elevated in CO-intoxicated patients compared with control group (1.52±0.6 and 0.81±1.29 ABSU respectively). The median serum myeloperoxidase enzyme (MPO) level was significantly elevated in CO-intoxicated patients compared with control group (19839 and 3145 pg/ml respectively) (P=<0.001**, each) (Table 5). Moreover, the mean plasma level of PTX 3 was significantly increased in DNS group (6.2±3 ng/ml) relative to Non-DNS one (4.5±2.4 ng/ml). The mean serum level of IMA was significantly increased in DNS group relative to Non-DNS group (1.5±0.4 and 1.2±0.3 ABSU respectively). The mean serum level of MPO was significantly increased in DNS-group compared with Non-DNS group (26235.6 and 14695.3pg/ml respectively) (P=<0.05*, each) (Table 6). There was a significant negative correlation between PTX 3, IMA and MPO levels and level of consciousness as assessed by GCS. Moreover, a strong significant positive correlation exists between COHb% level and plasma PTX 3, IMA and MPO levels. A moderate significant positive correlation existed between plasma PTX 3 and serum MPO levels, and the duration of exposure to CO gas (P= <0.05*, each). However, there was no statistically significant correlation between the studied markers and either delay time to reach emergency department or number of hyperbarric oxygen sessions. Furthermore, serum ischemia-modified albumin (IMA) levels had recorded a weak insignificant positive correlation with duration of exposure to carbon monoxide (CO) gas (P= >0.05, each) (Table 7). Analysis of receiver operating characteristics (ROC) curves of PTX 3, IMA and MPO as predictors of delayed neuropsychological

sequelae (DNS) in cases of acute CO poisoning showed that, IMA had the highest area under the curve (AUC = 0.760), followed by MPO (AUC =0.712) then PTX 3 (area under the curve (AUC) = 0.669). The AUCs of IMA, MPO and PTX 3 were significant (compared with an AUC = 0.5). As regards PTX 3, it had a sensitivity of 66.7% (was able to detect 66.7% of DNS-complicated patients and a specificity of 65.2% % (was able to detect 65.2% of cases that were non DNS-complicated) at a cut off value > 4.9 ng/ml (Figure 3). For MPO, it had a sensitivity of 55.6% (was able to detect 55.6 %% of DNS-complicated cases) and a specificity of 95.5 % (was able to detect 95.5%% of cases that were non-complicated) at a cut off value 20744 pg/ml (Figure 4). As regards IMA, it had a sensitivity of 59.4% (was able to detect 59.4 %% of DNS-complicated cases) and a specificity of 73.9% % (was able to detect 73.9%% of non-complicated cases at a cut off value ≥1.34 ABSU (Figure 5). The positive predictive value of PTX 3, IMA and MPO were (69.2, 76 and 93.8 respectively). Whereas, the negative predictive value of the former biomarkers were (62.5, 68 and 64.7 respectively) (Table 8). It is noteworthy that, ST segment depression myocardial ischemia was only recorded in DNS group (33.3%) indicating ischemic insults to both brain and myocardium. The mean number of hyperbaric oxygen sessions registered a highly significant increase in DNS group of patients (3±2.3) compared with non-DNS one (1±1) (P=<0.001**) (Table 9).

Table (1): Distribution of duration of exposure (hours) to carbon monoxide gas according to the outcome:

Duration (hours) of exposure to CO gas	Outcome		Tests of significance	
	Non- DNS group (N = 23)	DNS group (N = 27)	Z	P-value
Minimum	1	1	-2.396	0.017*
Maximum	12	15		
Median	3	5		
Interquartile range	1 - 4	3 - 8		
Mean ranks	20.2	30.0		

Z_{MW}: Mann-Whitney test * Significance at p-value<0.05
DNS: Delayed neurological sequelae N: number CO: Carbon monoxide.

Table (2): Comparison between acutely carbon monoxide-intoxicated patients and control group according to their vital measurements:

Vital parameters	Groups		Tests of significance	
	CO-poisoned Patients N (55)	Control N (55)	t	p-value
Systolic blood pressure (mmHg)			0.904	0.368
Minimum	90	100		
Maximum	150	140		
Mean	113	115		
Standard Deviation	13	10		
Diastolic blood pressure (mmHg)			t	p-value
Minimum	50	60	1.463	0.147
Maximum	100	85		
Mean	68	71		
Standard Deviation	12	8		
Heart rate (beat/minute)			t	p-value
Minimum	62	60	-10.144	<0.001**
Maximum	153	96		
Mean	105	75		
Standard Deviation	20	9		
Respiratory rate (cycle/minute)			t	p-value
Minimum	5	14	-6.633	<0.001**
Maximum	34	24		
Mean	21	16		
Standard Deviation	5	2.5		
Temperature (^{o}C)			t	p-value
Minimum	36	36	-0.920	0.360
Maximum	38	37.5		
Mean	36.9	36.8		
Standard Deviation	0.7	0.4		

t: Independent sample T test.*Significant at p-value<0.05. CO: carbon monoxide. **Highly significant atp-value <0.001.

Table (3): Comparison of Glasgow Coma Scale between DNS and non-DNS groups:

Glasgow Coma Scale (GCS)		Outcome		Tests of significance	
		Non-DNS group (N = 23)	DNS group (N = 27)	Z_{MW}	p-value
	Minimum	3	3	-2.595	0.009*
	Maximum	15	15		
	Median	15	11		
	Interquartile range	13 - 15	8 - 15		

Z_{MW}: Mann-Whitney test,* Significance at p-value<0.05. DNS: Delayed neurological sequelae N: number.

Table (4): Comparison of oxygen saturation and carboxyhemoglobin between DNS and non-DNS groups:

		Outcome		Tests of significance	
		Non-DNS Group (N = 23)	DNS Group (N = 27)	t	p-value
	The reference range of Oxygen saturation (95-100%)				
	Minimum	90	76	= 4.004	<0.001**
	Maximum	100	100		
	Mean	97	91		
	Standard Deviation	2	8		
	The reference range of COHb% *Nonsmokers: Up to 3% * Smokers: Up to 10%				
	Minimum	1	12	t	p-value
	Maximum	20	33	3.576	0.001*
	Mean	8	15		
	Standard Deviation	5	10		

T: Independent sample T test. DNS: Delayed neurological sequelae, N: number ** Highly significant at p-value<0.001.

Table (5): Comparison of serum Pentraxin 3, Ischemia-modified albumin and myeloperoxidase levels between acute CO-intoxicated patients & controls:

The studied biomarkers		Group		Tests of significance	
		CO-intoxicated patients (N = 55)	Control (N = 55)	t	p-value
Plasma Pentraxin 3 (PTX3)	Minimum	0.6	0.3	t=8.474	<0.001**
	Maximum	17.2	4.2		
	Mean	6.3	1.6		
	Standard Deviation	4	1		
Serum ischemia-modified albumin (IMA)	Minimum	0.65	0.01	t=3.678	<0.001**
	Maximum	3.78	6.3		
	Mean	1.52	0.81		
	Standard Deviation	0.60	1.29		
Serum myeloperoxidase (MPO)	Minimum	1582	313	$Z_{MW=}$-7.978	<0.001**
	Maximum	69123	12369		
	Median	19839	3145		
	Interquartile range	10964 - 32944	793 - 6214		

t= Independent samples T test; Z_{MW}: Mann-Whitney test; CO: carbon monoxide.
*** significant at p<0.05. ** Highly significant at <0.001.**

Table (6): Comparison of levels of pentraxin 3, ischemia-modified albumin and myeloperoxidase between DNS and non-DNS groups:

The studied Biomarkers		Outcome		Tests of significance	
		Non-DNS group (N = 23)	DNS group (N = 27)	t	p-value
Pentraxin 3 (PTX 3)	Minimum	0.6	0.8	-2.176	0.034*
	Maximum	8.6	11.9		
	Mean	4.5	6.2		
	Standard Deviation	2.4	3.0		
Ischemia-modified albumin (IMA)	Minimum	0.7	0.8	3.576	0.001*
	Maximum	1.7	2.3		
	Mean	1.2	1.5		
	Standard Deviation	0.3	0.4		
Myeloperoxidase Enzyme (MPO)	Minimum	1582.0	2356.0	-3.306	0.002*
	Maximum	22629.0	59188.0		
	Mean	14695.3	26235.6		
	Standard Deviation	6283.8	16809.8		

T: Independent sample T test. DNS: Delayed neurological sequelae N: number * Significant at p-value<0.05.

Table (7): Correlation analysis between the studied markers and some parameters:

		Pentraxin 3	Ischemia-modified albumin	Myeloperoxidase enzyme
Number of hyperbarric oxygen sessions	r	0.068	-0.339	0.120
	p	0.624	0.011	0.383
Prehospital period	r	0.181	0.202	-0.003
	p	0.186	0.139	0.982
Duration of exposure	r	0.397	0.065	0.453
	p	0.003*	0.637	0.001*
Glasgow Coma Scale (GCS)	r	-0.566	-0.306	-0.537
	p	<0.001**	0.023*	<0.001**
Carboxyhaemoglobin level	r	0.780	0.644	0.602
	p	<0.001**	<0.001**	<0.001**

r: Correlation coefficient.*Significant at p <0.05.* Highly significant at <0.001.**

Table (8): Prediction of outcome (non-DNS or DNS-complicated) using pentraxin 3, ischemia-modified albumin and myeloperoxidase levels:

	Pentraxin 3 (PTX3)	Ischemia-modified albumin (IMA)	Myeloperoxidase Enzyme (MPO)
AUC	0.669	0.76	0.712
SE	0.077	0.071	0.077
95% CI	0.522 - 0.796	0.618 - 0.869	0.566 - 0.831
p	0.029*	<0.001**	< 0.006*
Cut off	> 4.9 ng/ml	≥1.34 (ABSU)	> 20744 Pg/ml
sensitivity	66.7%	59.4%	55.6%
specificity	65.2%	73.9%	95.7%
PPV	69.2%	76.0%	93.8%
NPV	62.5%	68.0%	64.7%

*Significant at p <0.05. * Highly significant at <0.001**. ABSU: Absorbance unit.
AUC: area under the curve; SE: standard error; CI: confidence interval
PPV: Positive predictive value NPV: Negative predictive value

Table (9): Comparison between non-DNS and DNS groups as regards number of hyperbaric oxygen sessions:

Number of hyperbaric oxygen sessions		Outcome		Tests of significance	
		Non-DNS group (N = 23)	DNS-group (N = 27)	Test statistic	p-value
	Minimum	0	0.0	t=-4.355	<0.001**
	Maximum	3	7.0		
	Mean	1	3.0		
	Standard Deviation	1	2.3		

Independent samples T test. N: number * Significance at p-value<0.05
DNS: Delayed neurological sequelae **Highly significant at <0.001.

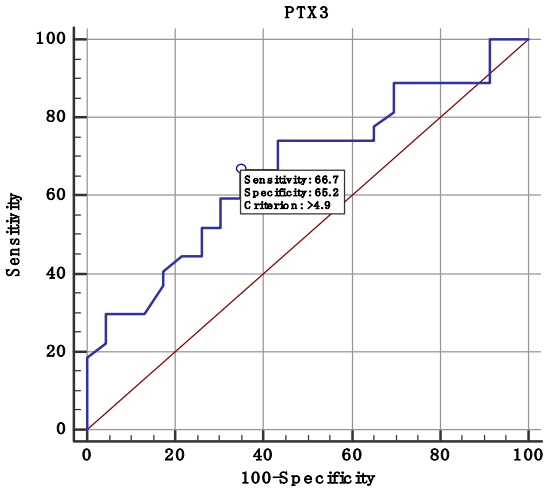

Figure (3): ROC curve of plasma pentraxin 3 level (peak value) for predicting major outcome of acute carbon monoxidepoisoned patients.

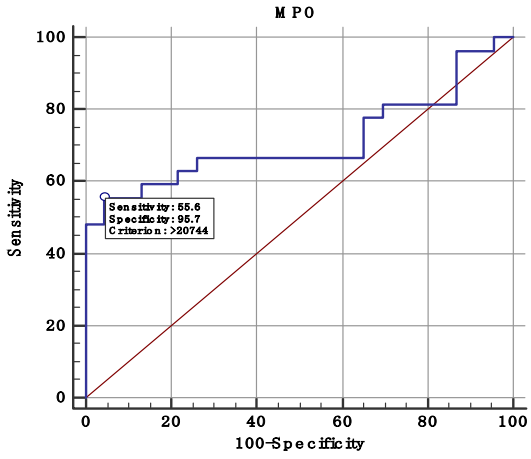

Figure (4): ROC curve of serum myeloperoxidase enzyme level (peak value) for predicting major outcome of acute carbon monoxide poisoned patients.

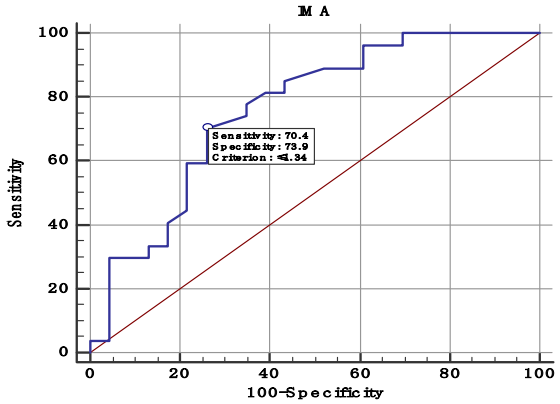

Figure (5): ROC curve of plasma ischemia-modified albumin level (peak value) for predicting major outcome of acute carbon monoxidepoisoned patients

4. Discussion:

Acute carbon monoxide (CO) poisoning is one of the leading causes of morbidity and mortality and a significant health issue in developing and developed countries as well. Delayed neuropsychiatric manifestations (DNS) after acute CO poisoning are not uncommon sequelae. The current study revealed that, 49.1% of cases developed DNS and memory disturbances were the commonest observed complications (12.7%). This agreed with (20, 21*),* who reported that 46% and 47.5% of the studied CO intoxicated patients developed DNS and in disagreement with (22, 23) who reported 16.5% and 22% respectively of cases developed DNS. Acute CO poisoning-related DNS could be attributed to CO-induced hypoxia that is followed by reoxygenation injury to the brain leading to increase production of partially reduced oxygen species. Reduced oxygen species could oxidize essential proteins and nucleic acids and produce brain lipid peroxidation resulting in typical reperfusion injury. Cerebral vascular autoregulation, accumulation of toxic metabolites and oxidative free radical-mediated damage are also contributing factors (24, 25). Prevalence of CO intoxication in young age (18-28 years) in the current

study could be related to the highest activity and maximal performance of this age group in every community according to (26). Gas water heater settled in bathrooms was the commonest source of CO exposure in the current study. This agreed with many results in the literature (21, 27, 28). This is because gas water heaters are commonly-used cost-effective method for heating water at homes, especially badly-vented place as bathrooms and kitchens especially if inadequately- installed device. This results in incomplete combustion of hydrocarbon gases used for gas geysers operation with production of CO gas (1). It is mention worthy that those who were exposed to CO for longer periods, developed DNS more frequently than those with shorter duration. This may be explained on the basis that, CO may lead to loss of consciousness and muscle weakness making the victim unable to escape the danger and hence more prolonged exposure (29). In the current work, the mean pulse and respiratory rates were highly significantly-increased in CO-poisoned patients compared with their controls**.** This came in agreement with (30) and disagreed with (23) who reported no significant increase in the median heart rate of in carbon monoxide (CO)-poisoned patients compared with control group. Carbon monoxide produces cellular hypoxia and decreased cardiac systolic function that lead to early compensatory tachycardia and tachypnea (31). The current study revealed that, the median Glasgow Coma Scale (GCS) and the mean oxygen saturation of DNS group were significantly-reduced than Non-DNS group and there was a significant negative correlation between the studied markers (pentraxin 3 (PTX3), ischemia-modified albumin (IMA) and myeloperoxidase (MPO) levels) and level of consciousness as assessed by GCS. However, the mean carboxyhemoglbin (COHb%) level of DNS group were significantly-elevated than Non-DNS one owing to more significant prolonged duration of exposure and hence more COHb burden. The mean plasma PTX3and serum MPO level were highly significantly-elevated in CO-intoxicated patients compared with control group and in DNS than Non-DNS group. This may be attributed to the fact that, CO leads to systemic inflammation through hypoxia or free radical and oxidative stress-mediated mechanisms**.** Therefore, platelet and neutrophil interaction and aggregation occur with neutrophil activation which degranulate with release of various inflammatory markers of which are pentraxin 3 and myeloperoxidase (35, 37). Pentraxin 3 expression in various inflammatory and ischemic conditions similar to that produced by CO from activated endothelial cells, dendritic cells and macrophages**.** The activated leucocytes is thought to be the sources of free radicals that leads to lipid peroxidation, formation of peroxynitrite and oxidation of various proteins and nucleic acid, the mechanisms that are postulated in the literature in the development of DNS associated with CO poisoning (24,32,33)**.** Therefore it is suggested that PTX3 is increased in CO-related-DNS. The mean serum IMA level was highly significantly-elevated in CO-intoxicated patients compared with control group and in DNS than Non-DNS group. These findings match many reports in the literature (34, 35, 36), who noticed significantly higher IMA levels in acutely CO-intoxicated patients relative to their controls. Furthermore, (23) reported highly significant elevation of IMA levels in DNS relative to Non-DNS group and the control groups. This could be ascribed to the fact that, its level rises in response to various hypoxic and many ischemic conditions. Tissue hypoxia and oxidative stress-related to CO poisoning may lead to alteration in N-terminus of human serum albumin resulting in IMA formation. Therefore it is expected to rise in CO poisoning with tissue hypoxia (23,36). The significantly higher mean serum level of MPO of DNS group than Non- DNS group could be explained by findings from (32). Inthier animal models, they found that MPO increases perivascular increase in the brain concentrations of MPO mediating DNS. Myeloperoxidase enzyme catalyses the formation of nitrotyrosine which produces vascular oxidative stress and brain lipid peroxidation. The products of lipid peroxidation interacts with myelin basic proteins producing alteration in its structure mediating CO-mediated immunologic response that causes functional neurologic deficits. To our knowledge, there are few studies in the literature have been focused on clinical role of pentraxin 3, ischemia-modified albumin and myeloperoxidase in prediction of acute CO poisoning-related outcome. Therefore, our study focused on this issue.

The current study revealed that, clinical data variables associated with development of delayed neurological sequelae (DNS) after acute carbon monoxide (CO) include decreased consciousness level and prolonged CO duration of exposure. In addition, laboratory parameters variables associated with development of delayed neurological sequelae after acute CO poisoning include; elevated carboxyhemoglobin level on admission, decreased oxygen saturation and high admission levels of pentraxin 3, ischemia-modified albumin and myeloperoxidase enzyme. Analysis of receiver operating characteristics (ROC) curves of the three studied biomarkers (pentraxin 3, ischemia-modified albumin and myeloperoxidase) levels on admission suggested that they could be employed as useful biomarkers for predicting the acute CO poisoning-related outcome including development of delayed neuropsychological sequelae or not.

Conclusion:

Delayed neurolopsychological sequelae were common complications in the studied acute CO-intoxicated cases and memory disturbances were the most frequently-observed one. Follow up of acutely-CO intoxicated cases would be beneficial in early detection of CO-related DNS. The studied markers (Pentraxin 3, ischemia-modified albumin and myeloperoxidase) levels could be employed as useful biomarkers for predicting the acute CO poisoning outcome including development of DNS or not. This study revealed that clinical data variables associated with development of DNS after acute CO poisoning include decreased consciousness level and prolonged CO duration of exposure. In addition, laboratory parameters variables associated with development of delayed neurological sequelae after acute carbon monoxide poisoning include; elevated carboxyhemoglobin level on admission, decreased oxygen saturation and high admission levels of pentraxin 3, ischemia-modified albumin and myeloperoxidase enzyme.

Limitations:

The present study limitations include small sample size; exclusion of some cases from follow up due to death, variable delay time to reach poison control centre where sampling for the markers is done so the exact onset of DNS cannot be assessed in relation to the measured levels of markers and patients were non compliant for follow up visits for a more prolonged periods of time more than 6 months.

Conflict of interest

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