Research Article

Role of Carboxyhemoglobin as a predictor of delayed neuropsychiatric syndrome of acute carbon monoxide poisoning in Minia poisoning control center- Egypt.

Hala M Ahmed[*], **Rehab H A Younis***, **Mostafa M Asem Mohammed Zaki***, **Hala G Nafea Ibrahim****.**

* Forensic Medicine & Toxicology Department, Faculty of Medicine, Minia University, Egypt.
** Resident doctor at Clinical Toxicology unit, Minia University Hospital, Egypt.

Abstract
Introduction: Carbon monoxide **(CO)** is a colorless, odorless, tasteless, nonirritating gas in low concentrations. **Methods:** The study evaluated 118 case diagnosed as acute CO poisoning and admitted to Minia University Hospital Poison Control Center during the period from 1"st January, 2019 to 31th June, 2021. The studied patients were classified into 2 groups: group1 patients with DNS and group 2 patients without DNS. **Results:** there was a significant increase in COHb level and a significant decrease in PH and HCO3 levels in cases with DNS than cases without DNS. **Conclusions:** we suggest that COHb level may be a rapid and good predictor for DNS development.

Keywords
Carbon monoxide **(CO)**, carboxyhemoglobin **(COHb)**, delayed neuropsychiatric syndrome**(DNS).**

Introduction
CO poisoning has a global cumulative incidence and fatality rate of 137 cases per million and 4.6 deaths per million, respectively. During the last 25 years, the global incidence has remained steady, although mortality and the percentage of patients who died have decreased by 36% and 40%, respectively **(Kandis et al., 2009).**

Carbon monoxide is rapidly absorbed by the endothelium of the lungs. The degrees of oxygenation and, to a lesser extent, minute ventilation are directly linked to elimination. CO has a half-life of almost 250 to 320 minutes when a patient is breathing room air, despite the fact that breathing high-flow oxygen through a nonrebreathing face mask takes about 90 minutes and breathing 100 percent hyperbaric oxygen takes over 30 minutes *(Clardy et al., 2015).*

Almost all systems are involved in the clinical presentation, as well as a wide range of symptoms. Children and the elderly, patients with respiratory and cardiovascular diseases, those living in high-altitude areas, smokers, and people with higher CO Concentrations are all at greater risk to the toxicity to a significant degree **(Weaver, 2009).**

DNS (delayed neurological sequelae) is a serious problem and matter. DNS can occur in up to 40% of patients with acute CO poisoning between 2 to 40 days after main symptoms completely resolved **(Oh & Choi, 2015).**

Pathophysiology of CO toxicity and consequent DNS is very complicated and still unsuccessfully understood. A recognized main pathophysiological mechanism in CO toxicity is hypoxic stress. Though, impaired oxygen transport to the cells and tissue hypoxia does not entirely clarify the involvement of cerebral damages. CO may alter the tissues in the brain precisely, and inflammatory reactions and cell construction changes are convoluted to the pathophysiological sequalae **(Park et al., 2014).**

Diagnosis of CO poisoning remains a clinical one: the regular description needs a history of current CO exposure, the existence of symptoms related to CO poisoning, and determination of a high carboxyhemoglobin level **(Hampson et al., 2012).**

Even though past studies have evaluated the association between the COHb level and the

severity of CO toxicity, no conclusive relationships have been detected **(Cervellin et al., 2014).**

The COHb level in healthy, non-smoker is fewer than 2 %, and the level in smokers is fewer than 15 %. At 10 % COHb levels, no prominent symptoms are detected. Neurological symptoms are detected like vomiting, headache and faintness with COHb levels more than 10 %. Tachypnea and tachycardia, syncopal attacks, motor weakness, paralysis and confusion are detected with COHb level of 30–50 %. COHb levels above 50 % are thought to be lethal, and life threatening condition **(Farraj et al., 2015).**

Patients and methods

This current study is a clinical retrospective and prospective study that was conducted on 118 adult patients diagnosed as acute carbon monoxide poisoning according to history, clinical manifestations and blood carboxyhemoglobin (COHb) level. The patients of the study were selected from the cases admitted to Minia University Hospital Poison Control Center during the period from 1st January, 2019 to 31th June, 31th, 2021 and were prospectively cross-sectional studied. A written consent was taken from the patients or from their relatives including their agreement to participate in this study.

Patients:
Inclusion criteria:
Patients diagnosed as acute carbon monoxide poisoning according to (history, clinical presentation at the time of admission and improvement on oxygen therapy).
Exclusion criteria:
- Patients with Previous diagnosis of a neuropsychiatric disease.
- Patients with previous history of head trauma.
- Concurrent toxicity with another poison.
- Patients refuse to participate in this study.
Methods
The work sheet was assessed to contain main four parts which are detailed history of the patient, complete clinical examination including general and systemic evaluation, laboratory investigations including CBC (HB, WBC), ABG (PH,HCO3) and COHb level, and out-come of the patient.

Results
This study was conducted on 118 patients diagnosed as acute CO poisoning. The studied patients were classified according to the development of delayed neurological sequelae (DNS) into 2 groups:
Group I: included 93 patients who were diagnosed as acute carbon monoxide poisoning without development of DNS.
Group II: included 25 patients who were diagnosed as acute CO poisoning and developed DNS.
:

Table (1): Sociodemographic variables among patients with DNS and without DNS.

		DNS		P value
		Without DNS	**With DNS**	
		N=93	**N=25**	
Age	*Median* *IQR*	22 (17-30)	19 (15-29)	0.192
Gender [C]	*Male* *Female*	46(49.5%) 47(50.5%)	17(68%) 8(32%)	0.117
Marital state [F]	*Single* *Married* *Divorced*	54(58.1%) 38(40.9%) 1(1.1%)	15(60%) 9(36%) 1(4%)	0.474
Mode of poisoning [F]	*Accidental* *Homicidal* *Suicidal*	93(100%) 0(0%) 0(0%)	25(100%) 0(0%) 0(0%)	1

- *Mann Whitney test for non-parametric quantitative data between the two groups*
- *Chi square test (C) or Fisher's exact test (F) for qualitative data between the two groups*
- *Significant level at P value < 0.05*

Role of Carboxyhemoglobin as a predictor of delayed
                                   neuropsychiatric syndrome of acute carbon monoxide poisoning

Sociodemographic variables
As regarding age, median age of patients without DNS and patients with DNS were (22, 29) respectively. There was no significant difference between the two groups. As regarding gender in non DNS group females (50.5%) were higher than males (49.5%) while in DNS group it was found that males (68%) were higher than females (32%), there was no statistically significant difference between them. There was no statistically significant difference between DNS and non DNS group as regarding marital status. As regarding mood of poisoning; only the accidental mode was found in all cases (93 cases without DNS and 25 cases with DNS), there was insignificant difference between patients with DNS and patients without DNS as shown in table (1).

Table (2): Comparison of laboratory parameters according to DNS status.

| | | DNS | | P value |
| | | Without DNS | With DNS | |
		N=93	N=25	
HB	*Range* *Mean ± SD*	(10-16) 12.4±1.2	(10-15) 12.5±1.4	0.646
WBC	*Median* *IQR*	4.5 (3.5-5.6)	5 (4-9)	0.140
PH	*Range* *Mean ± SD*	(7.3-7.5) 7.4±0.04	(7-7.5) 7.3±0.1	0.017*
HCO₃	*Range* *Mean ± SD*	(3.5-23) 19±2.6	(7.3-24) 15.4±3.7	<0.001*
COHB	*Median* *IQR*	17.3 (12-22)	28.6 (24.4-35)	<0.001*

- *Chi square test (C) or Fisher's exact test (F) for qualitative data between the two groups*
- **: Significant level at P value < 0.05*

As regards, (table2), there was a significant increase, as regarding laboratory data, in COHb level and a significant decrease in PH and HCO3 levels in cases with DNS than cases without DNS. Otherwise there were no statistically significant differences in HB and WBS levels between the two groups.

Discussion
CO is a colorless, odorless, tasteless, and nonirritating gas that makes it hard to be detected by individuals who are exposed. CO is widely recognized as the "silent killer" since it has no sensory warning features and is responsible for a high percentage of the unintentional poisonings and deaths recorded each year all over the world *(Sikary et al., 2017).*

This study is aimed at evaluating the adequacy of COHb level for predicting delayed neuropsychological sequelae after CO poisoning.

In the present study, as regarding the sociodemographic data, the age of CO poisoning cases were found to be higher in adult group than in children and old age and the median age of patients didn't develop DNS was higher than patients developed DNS but there was no statistically significant difference between the two groups.

As regarding laboratory data, the results showed that blood carboxyhemoglobin (COHb) level in patients with DNS show significant increase than patients without DNS.

These results are in accordance with **Pepe et al., 2011** who found that carboxyhemoglobin levels were statistically significant higher in patients who develop DNS than who didn't develop DNS.

This may be explained as COHb formation has been theorized to be fatally hazardous in CO Poisoning patients. Also it has been linked to an elevated risk of neurological impairment and has been linked to clinical prognosis in previous investigations that higher levels cause

significant tissue anoxia and subsequent acidosis **(Ku et al., 2010).**

These results were in contrast to **Doğan et al., 2020** who determined the risk factors and incidence of DNS in CO poisoning through a retrospective study between 2015 and 2016 and it was recorded that there was no significant relationship between the two groups.

On the other hand **Hafez & El-Sarnagawy, 2020** and **Moon & Kim 2014** also found a lack of correlation between COHb level and DNS.

This may explained by the fact that COHb level just illustrate the COHb binding ratio. As a consequence, when CO absorption is interrupted, it lowers over time and more efficiently as a result of oxygen supply in the ambulance. As a result, COHb levels after emergency admission are not directly related to the degree of systemic tissue injury as seen in the results of a study done by **Kudo et al., 2014** which failed to demonstrate a significant relationship between COHb levels and the development of DNS, on the contrary they found that the group that did not develop DNS had a higher COHb level.

Conclusion

Development of DNS after acute CO poisoning is a major and dangerous problem. Clinicians must study possible factors that might be needed to predict prognosis. The present study suggest that COHb level may be a rapid and good predictor for DNS development.

References

1. Cervellin, G., Comelli, I., Rastelli, G., Picanza, A., & Lippi, G. (2014). Initial blood lactate correlates with carboxyhemoglobin and clinical severity in carbon monoxide poisoned patients. Clinical biochemistry, 47(18), 298-301.
2. Clardy, P., Manaker, S., Perry, H., & ZET, A. (2015). Carbon monoxide poisoning. Uptodate, ed. P. TW. Vol. Uptodate. 2015, Uptodate: Waltham MA.
3. Doğan, F. S., Güneysel, Ö., Gökdağ, E., Güneş, M., & Sümen, S. G. (2020). Demographic characteristics and delayed neurological sequelae risk factors in carbon monoxide poisoning. The American journal of emergency medicine,
4. 38(12), 2552-2556.
5. Farraj, A. K., Hazari, M. S., & Costa, D. L. (2015). Pulmonary Toxicology. Mammalian Toxicology, 519-538.
6. Hafez, A. S., & El-Sarnagawy, G. N. (2020). S-100β in predicting the need of hyperbaric oxygen in CO-induced delayed neurological sequels. Human & experimental toxicology, 39(5), 614-623.
7. Hampson, N. B., Piantadosi, C. A., Thom, S. R., & Weaver, L. K. (2012). Practice recommendations in the diagnosis, management, and prevention of carbon monoxide poisoning. American journal of respiratory and critical care medicine, 186(11), 1095–1101
8. Kandis, H., Katirci, Y., & Karapola, BS (2009). Carbon monoxide poisoning. Journal of Düzce Faculty of Medicine, 11 (3), 54-60.
9. Ku, H. L., Yang, K. C., Lee, Y. C., Lee, M. B., & Chou, Y. H. (2010). Predictors of carbon monoxide poisoning-induced delayed neuropsychological sequelae. General hospital psychiatry, 32(3), 310-314.
10. Kudo, K., Otsuka, K., Yagi, J., Sanjo, K., Koizumi, N., Koeda, A., ... & Sakai, A. (2014). Predictors for delayed encephalopathy following acute carbon monoxide poisoning. BMC emergency medicine, 14(1), 1-7.
11. Moon, G. J., & Kim, G. T. (2014). Acute carbon monoxide poisoning: Prognostic factors for delayed neuropsychiatric sequelae. Journal of the Korean Society of Emergency Medicine, 25(3), 268-276.
12. Oh, S., & Choi, S. C. (2015). Acute carbon monoxide poisoning and delayed neurological sequelae: a potential neuroprotection bundle therapy. Neural regeneration research, 10(1), 36.
13. Park, E. J., Min, Y. G., Kim, G. W., Cho, J. P., Maeng, W. J., & Choi, S. C. (2014). Pathophysiology of brain injuries in acute carbon monoxide poisoning: a novel hypothesis. Medical hypotheses, 83(2), 186-189.
14. Pepe, G., Castelli, M., Nazerian, P., Vanni, S., Del Panta, M., Gambassi & Grifoni, S. (2011). Delayed neuropsychological sequelae after carbon monoxide poisoning: predictive risk factors in the Emergency

Department. A retrospective study. Scandinavian journal of trauma, resuscitation and emergency medicine, 19(1),1-8.

15. Sikary, A. K., Dixit, S., & Murty, O. P. (2017). Fatal carbon monoxide poisoning: A lesson from a retrospective study at All India Institute of Medical Sciences, New Delhi. Journal of family medicine and primary care, 6(4), 791–794.

16. Weaver, L. K. (2009). Carbon monoxide poisoning. New England Journal of Medicine, 360(12), 1217-1225.

Role of Carboxyhemoglobin as a predictor of delayed neuropsychiatric syndrome of acute carbon monoxide poisoning