

The Potential Role of Procalcitonin Compared to C-reactive protein and Neutrophil Lymphocyte Ratio in Prediction of Severity and Outcomes of Acute Corrosive Ingestion

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Abstract

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Background: Caustic ingestion in children is considered a serious healthcare issue worldwide due to its high morbidity and mortality rates. **Aim:** The present study aimed to evaluate the potential role of procalcitonin (PCT) compared to C-reactive protein (CRP) and neutrophil lymphocyte ratio (NLR) in assessment of severity and prediction of outcomes of acute corrosive ingestion for early intervention and better prognosis. **Methods:** This prospective study was conducted on 60 patients aged from 6 months to 12 years, who were admitted to poison control center, Ain Shams University Hospitals with diagnosis of acute caustic ingestion. Demographic, clinical data and blood samples were collected from each patient, with biomarkers' assessment within 24 hours post caustic ingestion. **Results:** The majority of patients were males (70%) with median age 1.5 years. Acute and/or chronic complications occurred in 43.3% of the studied patients. Significantly higher levels of PCT, CRP and NLR were detected in complicated patients, as well patients with DROOL score ≤ 4 . Procalcitonin level >1.4 ng/mL was the most specific biomarker (94.12%) with the highest positive predictive value (90.5%) in predicting complications occurrence, whereas CRP level >9.6 mg/L was the most sensitive biomarker (100%). **Conclusion:** This study supports the role of PCT, CRP and NLR as reliable biomarkers in early predicting the severity and outcomes of corrosive ingestion in children. PCT seemed to be superior to CRP and NLR in predicting complications post caustic ingestion.

Key words

Caustic, Corrosive ingestion, Complications, Procalcitonin, C-reactive protein, Neutrophil lymphocyte ratio

Introduction

Caustic ingestion continues to be a significant problem worldwide especially in developing countries and particularly in children. Indeed, potentially catastrophic presentations and lifelong complications resulting from corrosive ingestion are one of the most challenging situations in pediatric medical practice (Advenier & Grandmaison, 2018; Di-Nardo et al., 2020).

Caustic can damage tissues in variety of mechanisms; as the properties of the ingested substance determine its physiopathologic effect on the aerodigestive tract (İsbir et al., 2022). Apart from the direct esophageal damage caused by the chemical substance; oxidative stress and related inflammatory processes also lead to further damage and increase the risk of mortality (Uyar & Kok, 2017; Rezan et al., 2020). Corrosive poisoning may be associated with acute and/or chronic serious complications as pneumonia, respiratory failure, bleeding, perforation, shock, gastrointestinal (GIT) strictures and carcinomas; esophageal strictures is one of its most dangerous and major complications in children (Caganova et al., 2017; Mantho et al., 2022).

Early identification of poor outcomes is essential for early decision making and better management plans. Prediction of the presence and severity of GIT injury post caustic ingestion is a

challenging problem; several studies have shown that clinical manifestations are not always good predictors for the degree of injury and possible outcomes occurrence (Tosca et al., 2021). Also there is a debate about performing esophagogastroduodenoscopy or computerized tomography for early caustic ingestion evaluation especially in children, owing to the associated high risks, unavailability and the need for highly qualified health professionals (Aydin et al., 2017; Kamat et al., 2019).

Thus, there is an increasing need for quantifiable, fast, and inexpensive markers that can early predict post corrosive outcomes as well as the ongoing inflammatory process. (Uyar and Kok, 2017; Rezan et al., 2020).

Although there are limited studies on the role of procalcitonin (PCT) in children with burns and no previous studies had evaluated its value in acute corrosive ingestion, there is a consensus that PCT is a new inflammatory index with a raising level in response to exacerbated inflammation, burn injuries or other various types of stress regardless the occurrence of infection (Luiz et al., 2019; Xu et al., 2021). In addition, PCT level has prognostic implications as it's found to be significantly correlated with burn severity in several studies (Martinez & Rode, 2018; Carlton et al., 2021). Both neutrophil lymphocyte ratio (NLR) and

C-reactive protein (CRP) are cost effective methods, available and important indicators for systemic inflammation, infections and burns. Therefore, this study aimed to evaluate the potential role of PCT compared to CRP and NLR in assessment of severity and prediction of outcomes of acute corrosive ingestion for early intervention and better prognosis.

Patients and Methods

This prospective cross-sectional study was conducted on children aged from 6 months to 12 years of both sex, who were admitted to poison control center of Ain Shams University Hospitals (PCC-ASUH) with established diagnosis of acute corrosive ingestion. Diagnosis was made upon history of corrosive ingestion within 24hrs, as well as clinical manifestations suggestive for corrosive ingestion.

Patients with any of the following conditions were excluded from the current study: Patients exposed to corrosive agent by routes other than ingestion, asymptomatic patients treated as outpatients and didn't need admission, patients with history of fever or concomitant trauma at time of ingestion, patients diagnosed with acute inflammatory diseases as: GIT diseases or respiratory diseases, Patients having thyroid diseases or paraneoplastic syndrome, Patients on immune-modulator therapy and patients with mixed intoxication.

Sample size: Sixty patients were included in the current study according to sample size determined by Community Medicine and Environmental Department, Faculty of Medicine, ASU, to achieve 80% power to detect a difference of 0.20 between a diagnostic test with an area under the Receiver Operating Characteristic curve (AUC) of 0.80 and another diagnostic test with an AUC of 0.60 using a 2 sided Z-test at a significance level of 0.050.

Ethical considerations: an official permission was taken from the general director of the PCC-ASUH. Approval was obtained from the Local Research Ethics Committee at the faculty of medicine, ASU. (Number: FMASU MS 79/2022). An informed valid consent was taken from patients' legal guardians. All personal data were kept anonymous to ensure confidentiality of records.

Study methods:

History taking and clinical examination were done for the included patients; data were collected and recorded in a special sheet including:

1. Sociodemographic data (age & sex) & Intoxication data (Manner of exposure and type, form and amount of the ingested caustic agent).
2. Clinical manifestations on admission (GIT and respiratory system manifestations).
3. Investigations:
 - a) Biomarkers under the current study:
 - Neutrophil to lymphocyte ratio was calculated from the routine laboratory records by dividing the absolute count of neutrophils over the absolute count of lymphocytes measured within 24 hrs post corrosive ingestion (Siddique et al., 2021).

- Venous blood about 5 cc was collected from each patient under aseptic precautions within the first (6-24 hrs) post corrosive ingestion (Xu et al., 2018; Sinha et al., 2021). Procalcitonin Level was measured using commercial ELISA Kit from Bioassay Technology Laboratory Company, following the manufacturer instructions (Khaleel & Al-Barzinji, 2021; Sinha et al., 2021). While serum CRP was measured with particle-enhanced immunoturbidimetric assay on a Cobas c501 device (Roche Diagnostics, Mannheim, Germany) as per manufacturer's instructions (Oncul et al., 2023).

- b) Barium study: it was done 3 – 6 weeks post corrosive ingestion to diagnose GIT stricture or stenosis.
4. Treatment lines received by the patients according to the guidelines of PCC-ASUH protocols of management.
5. Severity and outcomes: severity was assessed by DROOL score, which was used to predict esophageal injury as defined by Uygun et al. (2012); which included drooling of saliva, reluctance to eat or dysphagia or food intolerance, oropharyngeal lesions and other symptoms and sign as persistent fever, hematemesis, abdominal tenderness, and dyspnea, in addition to high TLC, which was done routinely at admission and during hospital stay. Score ≤ 4 indicates high risk of esophageal strictures, while Score > 4 indicates low risk of esophageal strictures.

Follow up of the patients was done during the hospital stay to assess occurrence of acute complications as (GIT hemorrhage, GIT perforation, stridor, aspiration pneumonia, acute chest infections, respiratory distress, pulmonary edema, shock and septicemia) and after discharge for 3-6 weeks post corrosive ingestion through regular visits at outpatient clinic to assess occurrence of chronic complications as (GIT stricture, stenosis and fibrosis). Occurrence of GIT stricture was diagnosed clinically by (persistent dysphagia, progressive emesis, development of early satiety, weight loss, chronic abdominal pain, and repeated chest infections) and confirmed radiologically using barium studies (Hay et al., 2020; Sarma et al., 2021).

Outcomes were documented according to hospital disposition {inpatient or Intensive care unit (ICU)}, hospital stay duration and the occurrence of complications; accordingly, cases were divided into complicated and non-complicated groups. Data management and Statistical analysis:

Data was collected, tabulated, revised, coded, and entered into the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations for parametric distribution and median and interquartile ranges for non-parametric distribution. Qualitative variables were presented as number and percentages.

The comparison between groups regarding qualitative data was done by using Chi-square test. The comparison between two independent groups with quantitative data and parametric distribution was done by using independent t-test while with non-parametric data; they were done by using Mann-Whitney test. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. Receiver Operating Characteristic (ROC) curve was used to compare the diagnostic performance of the laboratory tests and assess their sensitivity and specificity. The results from statistical analysis were tabulated and presented in figures and histograms for interpretation and discussion.

Results

The present study comprised 60 patients who were admitted to PCC-ASUH with established diagnosis of acute corrosive ingestion during the period from January 2022 to December 2022 according to the aforementioned inclusion and exclusion criteria.

Patients were classified according to occurrence of complications into 2 groups as follows:

1. Complicated group: Included 26 patients who developed acute complications and/or chronic complications, representing (43.3%) of the total number of patients.
2. Uncomplicated group: Included 34 patients, representing (56.7%) of the total number of patients.

The present study included children with median age 1.5 years. 30% were females and 70% were males, with 100% accidental exposure in all children. Table (1) shows that there was no significant difference regarding age and sex as well as the type and the form of ingested caustic agents between both groups, while most of complicated group ingested high significant larger amounts of caustic agents compared to uncomplicated group. Additionally, highly significant prolonged saliva drooling >12 hrs (84.6%), prolonged dysphagia >24 hrs (73.1%), chest crepitation (65.4%), tachypnea (23.1%), and significant severe oral lesions (34.6%) were found among complicated group compared to uncomplicated group. On the contrary, no significant difference was found between both groups regarding vomiting occurrence. Most of complicated group were admitted to ICU (69.2%) with a significantly longer hospital stay duration (1-34 days) compared to the uncomplicated group, in which all

patients were admitted to inpatient ward with maximum 7 days hospital stay duration.

Table (2) shows that respiratory complications (21.7%) was the most common acute complication occurred in this study, followed by acute GIT complications (13.3%), and the least complication was shock (1.7%). On the other hand, chronic GIT complications were developed in 13 cases (21.7%) of the studied children; 12 patients (20%) had GIT stricture/stenosis and one patient had localized tongue fibrosis.

There was a significant relation found between the biomarkers of the current study [NLR, CRP and PCT] and the incidence of complications in corrosive intoxicated children, principally the PCT and CRP levels which were highly significant; PCT levels in complicated group ranged between 0.6 and 2.2 ng/mL with mean level 1.59 ± 0.40 ng/mL, while in uncomplicated group PCT levels ranged between 0.13 and 1.69 ng/mL with mean level 0.85 ± 0.38 ng/mL as shown in table (3).

In the present study, there were 26 patients (43.3%) had DROOL score ≤ 4 , with higher risk of GIT stricture incidence; table (4) shows that there was a significant relation between the studied biomarkers (NLR, CRP and PCT) and Drool score results, particularly PCT and CRP levels. The median value of CRP, NLR, and the mean value of PCT were significantly higher in patients with DROOL score ≤ 4 compared to patients with Drool score > 4 .

Furthermore, a positive correlation was found between the studied biomarkers (NLR, CRP and PCT) and hospital stay duration of corrosive intoxicated patients under the current study as shown in figure (1).

The best cut off points for the biomarkers (NLR, CRP and PCT) in the current study to predict incidence of complications in corrosive intoxicated patients was > 2.44 , > 9.6 mg/L and > 1.4 ng/mL respectively; as shown in figure (2). Taking in concern that PCT with cutoff point > 1.4 ng/mL was the most specific biomarker (94.12%) with the highest positive predictive value (90.5%) in prediction of complications occurrence, with sensitivity 73.8%; whereas, CRP level with cutoff point > 9.6 mg/L was the most sensitive biomarker (100%), with specificity (82.35%). On contrary NLR was the least specific and sensitive biomarker in complications prediction in the current study.

Table (1): Comparison between the studied groups regarding patients' demographic and clinical characteristics. (No.= 60)

Patients' characteristics		Total number of patients=60	Uncomplicated group	Complicated group	Test value	P-value
			No. = 34	No. = 26		
Age (years)	Median (IQR)	1.5 (1.5-3.25)	2 (1.5 - 3.5)	1.5 (1.5 - 3)	-0.839#	0.401
Sex	Male	42 (70%)	26 (76.5%)	16 (61.5%)	1.564*	0.211
	Female	18 (30%)	8 (23.5%)	10 (38.5%)		
Type of caustic agent	Alkali	45 (75%)	25 (73.5%)	20 (76.9%)	0.090*	0.764
	Acid	15 (25%)	9 (26.5%)	6 (23.1%)		
Form of caustic agent	Liquid	43 (71.7%)	23 (67.6%)	20 (76.9%)	0.624*	0.429
	Solid	17 (28.3%)	11 (32.4%)	6 (23.1%)		
Amount of caustic agent	Small	30 (50%)	28 (82.4%)	2 (7.7%)	33.83*	0.000
	Average	25 (41.7%)	6 (17.6%)	19 (73.1%)		
	Large	5 (8.3%)	0 (0.0%)	5 (19.2%)		
Vomiting		45 (75%)	23 (67.6%)	22 (84.6%)	2.262*	0.133
Dysphagia/ Odynophagia	No	3 (5.0%)	1 (2.9%)	2 (7.7%)	17.391*	0.000
	Less than 24hrs	57 (95%)	25 (73.5%)	5 (19.2%)		
	More than 24hrs		8 (23.5%)	19 (73.1%)		
Drooling of saliva	No	8 (13.3%)	6 (17.6%)	2 (7.7%)	11.923*	0.003
	Less than 12hrs	52 (86.7%)	14 (41.2%)	2 (7.7%)		
	More than 12hrs		14 (41.2%)	22 (84.6%)		
Oral Lesions	No	2 (3.3%)	1 (2.9%)	1 (3.8%)	8.323*	0.016
	Mild	47 (78.3%)	31 (91.2%)	16 (61.5%)		
	Severe	11 (18.3%)	2 (5.9%)	9 (34.6%)		
Tachypnea		6 (10%)	0 (0.0%)	6 (23.1%)	8.718*	0.003
Chest crepitations		19 (31.7%)	2 (5.9%)	17 (65.4%)	26.606*	0.000
Place of admission	Inpatient	42 (70%)	34 (100.0%)	8 (30.8%)	33.626*	0.000
	ICU	18 (30%)	0 (0.0%)	18 (69.2%)		
Hospital stay duration (days)	Median (IQR)	3 (2-5)	2 (2-3)	5 (3-15)	-5.194#	0.000
	Range	1-34	1-7	1-34		

IQR: interquartile range, No: Number, hrs: hours, ICU: Intensive care unit, P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant. *: Chi-square test; #: Mann-Whitney test.

Table (2): Acute and chronic complications which occurred to the complicated group in the current study. (No.=26)

Complications		Number	Percentage	
		26	43.3%	
Acute complications	Respiratory complications		13	21.7%
	Upper respiratory tract edema/ stridor		2	3.3%
	Respiratory distress		4	6.7%
	Chest infection	Acute bronchitis	11	18.3%
		Aspiration pneumonia	1	1.7%
	GIT complications		8	13.3%
	GIT hemorrhage		8	13.3%
	GIT perforation		0	0.0%
	Other acute complications			
	Septicemia		5	8.3%
	Shock		1	1.7%
Total number of acute complicated patients		17	28.3%	
Chronic complications	GIT Stricture/stenosis		12	20%
	Tongue fibrosis		1	1.7%
	Total number of chronic complicated patients		13	21.7%

GIT: Gastrointestinal tract, No: Number

Table (3): Comparison between the studied groups regarding the studied biomarkers [NLR, CRP and PCT]. (No.=60)

Biomarkers		Uncomplicated group	Complicated group	Test value	P-value
		No. = 34	No. = 26		
NLR	Median (IQR)	1.38 (0.7 – 2.22)	2.36 (1.27 – 3.46)	-2.417 \neq	0.016
	Range	0.25 – 6.3	0.54 – 18.6		
CRP (mg/L)	Median (IQR)	4.1 (1.7 – 9.2)	42.55 (20.5 – 60)	-5.671 \neq	0.000
	Range	0.6 – 68.7	9.8 – 145.8		
PCT (ng/mL)	Mean \pm SD	0.85 \pm 0.38	1.59 \pm 0.40	-7.264 \bullet	0.000
	Range	0.13 – 1.69	0.6 – 2.2		

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, \bullet : Independent t-test, \neq : Mann-Whitney test. NLR: neutrophil lymphocyte ratio, CRP: C-reactive protein, PCT: procalcitonin, SD: standard deviation, IQR: interquartile range, No: Number.

Table (4): Comparison between patients with DROOL score \leq 4 and patients with DROOL score $>$ 4 regarding the studied biomarkers [NLR, CRP and PCT]. (No.=60)

Biomarkers		DROOL score \leq 4	DROOL score $>$ 4	Test value	P-value
		No. = 26	No. = 34		
NLR	Median (IQR)	2.18 (1.27 – 3.4)	1.38 (0.69 – 2.44)	-2.238 \neq	0.025
	Range	0.54 – 18.6	0.25 – 6.3		
CRP (mg/L)	Median (IQR)	42.55 (20.6 – 60)	4.1 (1.7 – 9.2)	-5.812 \neq	0.000
	Range	9.6 – 145.8	0.6 – 68.7		
PCT (ng/mL)	Mean \pm SD	1.62 \pm 0.36	0.84 \pm 0.37	8.094 \bullet	0.000
	Range	0.84 – 2.2	0.13 – 1.69		

P-value >0.05: Non-significant; P-value <0.05: Significant; P-value < 0.01: Highly significant, \bullet : Independent t-test, \neq : Mann-Whitney test, CRP: C-reactive protein, NLR: neutrophil lymphocyte ratio, PCT: procalcitonin, No: Number, IQR: interquartile range, SD: Standard deviation.

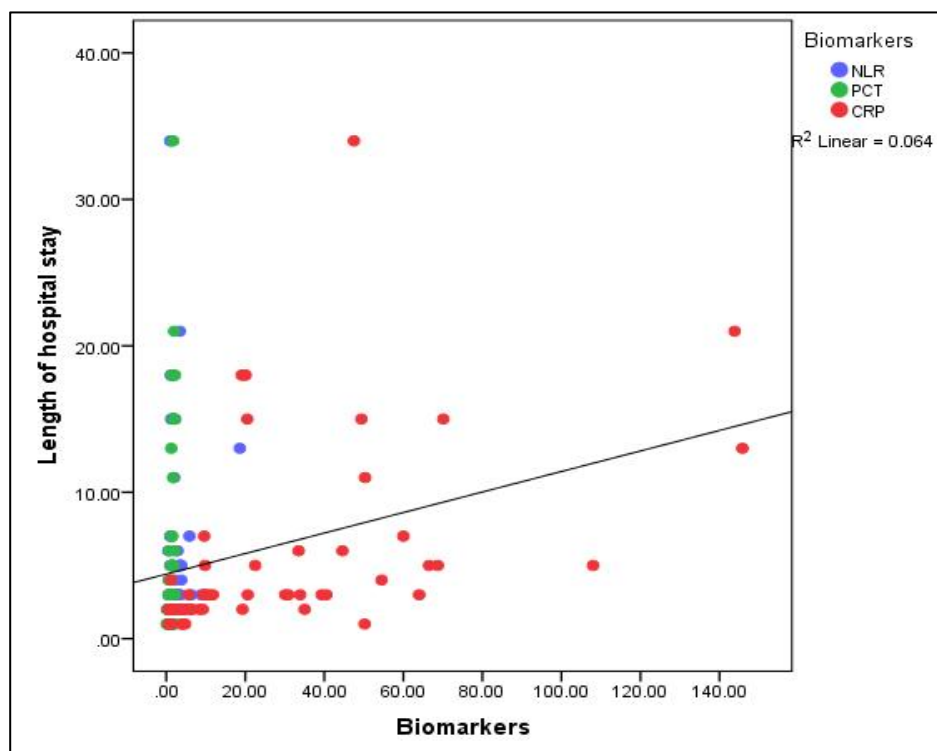


Figure (1): Correlation between studied biomarkers (NLR, CRP and PCT) and hospital stay duration of corrosive intoxicated patients in the current study

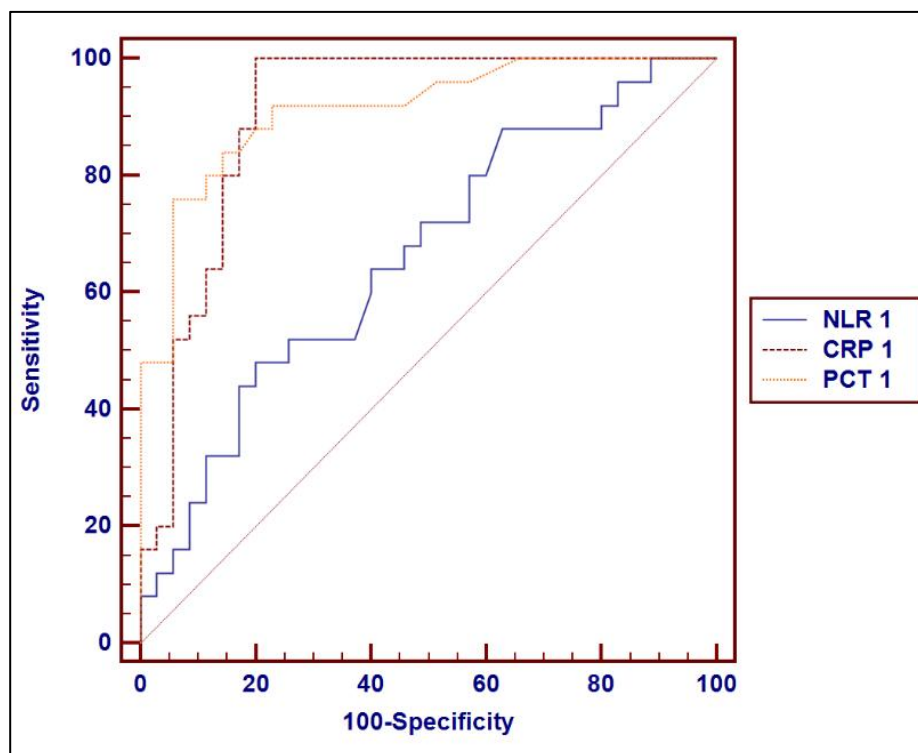


Figure (2): Receiver operating characteristic (ROC) curve of the studied biomarkers (NLR, CRP and PCT) for predicting the incidence of complications in corrosive intoxicated patients in the current study.

Discussion

Caustic ingestion is a serious health concern with potentially devastating short- and long-term consequences. Thus, predication of severity and outcomes of caustic ingestion is emphasized to stop the development of injury and prevent the progression of complications (De Lusong et al., 2017; ELHelaly et al., 2022). The current study aimed to evaluate the potential role of PCT compared to CRP and NLR in assessment of severity and prediction of outcomes of acute corrosive ingestion for early intervention and better prognosis.

Conjointly with our study, several studies had reported that children younger than 5 years are the highest risk group for caustic ingestion, with peak incidence around 2 years, owing to the fact of children curiosity at this age, poor discrimination of harmful objects along with the common habit of keeping caustic agents in beverage bottles (Di-Nardo et al., 2020; Al-Mousa et al., 2021). As well, Goussard et al., (2019) and Yalçın & Aygün, (2019) stated that boys at this age peak are usually more hyperactive with more boisterous behavior than girls, making them more vulnerable to poisoning.

The majority of patients (75%) in the current study ingested alkaline caustic agents, this was in accordance with several studied, which proposed that acidic agents usually cause severe immediate pain after ingestion and are rapidly expelled, while alkaline agents have almost imperceptible taste and odor with an easy swallowing, in addition to the wide spread and availability of alkaline agents in homes (Agbara et al., 2019; Acehan et al., 2021). Nevertheless, no significant

relation was found between complications occurrence and the type of caustic agents in the present study, which agreed with studies done by Elawady et al. (2017); Mohammadi et al. (2022) and Sharif et al. (2022). Conversely, Ghonem & El Sharaby, (2018); Alser et al. (2019) and Di-Nardo et al. (2020) reported that alkalis ingestion was associated with higher incidence of complications, higher probability of esophageal stricture and worse endoscopic score compared to acids. Le Naoures et al. (2017) explicated this conflict between studied, that at high volumes or concentrations, both acids and alkalis can cause deep and severe tissue damage; in addition to other factors which can affect the degree of tissue injury post caustic ingestion as physical form, viscosity of corrosives, presence or absence of food in stomach, manner of exposure, duration of contact and titratable acid or alkali reserve (Di-Nardo et al., 2020 and Acehan et al., 2021).

Most of the ingested caustic agents in the present study were in liquid form (71.7%), without any significant difference was found between the studied groups. The same was reported by Mahmoud et al. (2019), who attributed this to the wide daily usage of liquid caustics at homes more than solid form, beside their easy ingestion. As regard the amount of the ingested caustic agents, most of complicated patients ingested high significant larger amounts of caustic agents than the uncomplicated patients; Similarly, Chirica et al. (2017) suggested that a larger amount of ingested caustic substance was related to the severity of GIT damage.

In the current study, the presence of initial signs and symptoms on admission was found to be significantly higher in the complicated group as compared to the uncomplicated group. Correspondingly, Bonnici et al. (2014) and Uygun & Bayram, (2020) reported that prolonged dysphagia and drooling for 12-24 hrs can predict esophageal scar formation. Also Gharib et al. (2016) found that presence of hematemesis, vomiting, dysphagia and drooling after caustic ingestion, was associated with increased risk of complications and esophageal stricture. As well, saliva drooling and dysphagia were found to be strongly related to increased morbidity and mortality post caustic ingestion by Sagar et al. (2016) and Mantho et al. (2022). However, Controversy exists regarding the predictive value of symptoms and signs following caustic ingestion; several studies reported that clinical manifestations are variable, non-reliable predictors for the degree and depth of injury and do not necessarily correlate with severity and outcomes of corrosive poisoning (Bharath-Kumar et al., 2019; Rezan et al., 2020 and Patel, 2021).

The present study showed that most of complicated patients were admitted to ICU with significantly longer hospital stay duration compared to uncomplicated patients. This was in accordance with Chen et al. (2021), who mentioned that average length of hospital stay was significantly longer in severe group compared with mild group of corrosive poisoning in their studies.

Respiratory complications were the most common acute complications occurred, followed by acute GIT complications. Correspondingly, Challine et al. (2022) reported that pulmonary complications were the most frequent acute adverse events in their study. On contrary, Acehan et al. (2021) rendered the low airway and pulmonary complication rate in their study to the highly protective pharyngeal-glottic mechanism in adult patients compared to children. Chest infections were the most common acute respiratory complication (20%) in this study; which was explained by Agarwal et al. (2020), who attributed the higher incidence of chest infection post corrosive ingestion to the risk of aspiration and opportunistic lung infections, secondary to the reduced immune status and malnutrition.

Regarding chronic GIT complications, 12 patients (20%) developed esophageal stricture/stenosis in this study and one patient (1.7%) developed localized tongue fibrosis. This was in line with results of Mahmoud et al. (2019), who found that most common post-corrosive complication in their study was GIT stricture (18.5%). Patient complicated with tongue fibrosis in the current study, presented at time of admission with severe oral lesions post ingestion of sodium hydroxide in a solid form, which was equivalent to Niedzielski et al. (2020), who mentioned that solid caustic agents often injure the oropharynx more than the distal parts of GIT. Tongue fibrosis and leukoplakia are considered the most common premalignant tongue lesions (Tong et al., 2016). Hence, patients with post-corrosive injuries should be kept in long term follow-up due to significantly increased risk of carcinoma (Sarma et al., 2021).

In the current study, complicated patients had a significantly higher NLR (median value 2.36) than uncomplicated patients (median value 1.38). In addition, NLR was significantly higher in the more severe patients with DROOL score ≤ 4 compared to less severe patients with DROOL score > 4 , indicating its correlation with a higher risk of GIT strictures incidence. In accordance with these results, Lionte et al. (2021) reported a significantly higher NLR in severely poisoned caustic patients, who developed complications over the course of hospitalization; adding on, it was a good prognostic value for predicting the need for ICU hospitalization in their study. Also Rezan et al., (2020), postulated that high levels of NLR indicated severe caustic damage, extensive involvement, and the likelihood of developing late complications along with acute outcomes.

Neutrophil lymphocyte ratio is considered a robust inflammatory parameter, owing to the possibility of implementing its parameter simply by using the already available subtype counts of white blood cells to evaluate inflammatory conditions (Fuss et al., 2018; Lattanzi et al., 2018). NLR combines two independent markers of inflammation; neutrophilia reflects inflammation, whereas lymphocytopenia reflects poor general health and physiologic stress (Kim et al., 2015; Ghonem & El Sharaby, 2018). Gurağaç & Demirel, (2016) clarified the beneficial role of NLR in prediction of inflammatory process even when leucocyte count is within the normal range. These data could explain the significant elevation of NLR in complicated patients in the present study.

Complicated patients in the present study had significantly higher CRP levels (median level 42.55 mg/L) than uncomplicated patients (median level 4.1 mg/L). Moreover, a significant relation was found between CRP levels and Drool score results; the median value of CRP was significantly higher in patients with DROOL score ≤ 4 (42.55 mg/L) compared to patients with Drool score > 4 (4.1 mg/L), indicating a higher risk of GIT stricture incidence. Equivalently, Eweda et al., (2023) considered CRP a reliable marker in predicting severity and outcome of caustic ingestion, with significantly higher levels of CRP in patients admitted to ICU 24 hrs post caustic ingestion. Di-Nardo et al. (2020) and Mantho et al. (2022) found that CRP level was related to a higher risk of stricture formation post corrosive ingestion in their studies. Arunachalam & Rammohan (2016) and Chirica et al. (2022) considered the elevated levels of CRP as one of the predictors of mortality and poor outcomes in corrosive patients.

C-reactive protein (CRP) is a useful parameter for monitoring inflammation and tissue injury. It was demonstrated by Lionte et al. (2021) a significantly higher CRP levels in caustics' poisoned patients compared to patients intoxicated with other combination of poisons, chemicals, pesticides, and plant toxins.

Elevated PCT levels were found in caustic poisoned patients in the current study and there was a high significant relation between PCT level and occurrence of complications; complicated patients had significantly higher PCT levels (mean level 1.59

ng/mL) compared to uncomplicated patients (mean level 0.85 ng/mL). Additionally, patients with Drool Score ≤ 4 had higher mean level of PCT (1.62 ng/mL) compared to patients with Drool Score >4 (0.84 ng/mL), indicating the correlation of this biomarker with severity prediction and higher risk of GIT strictures post caustic ingestion in the current study.

Corresponding to these results, Samsudin & Vasikaran, (2017), Kundes & Kement (2019) and Xu et al. (2021) reported that patients with more extensive burn injuries had a higher PCT level, which was presumably related to the stronger inflammatory response caused by more severe burn injuries. This prognostic power of PCT for burn patients had also been reported by Cabral et al. (2017) and Carlton et al. (2021), as the magnitude and duration of PCT elevation were correlating with injury severity and outcome. Tan et al. (2021) found that PCT levels could serve as a prognostic marker for mortality in the first 48 hrs post burn injuries. As well, Jasem et al. (2017) and Sinha et al. (2021) reported that rising trend of serum PCT values was associated with poor prognosis of burn patients; PCT level ≥ 2 ng/mL during hospitalization indicated poor prognosis with sensitivity 100% and specificity of 80.56% and the likelihood of death was increased by 4.5 times.

Procalcitonin is considered an acute-phase protein and an inflammatory marker with high specificity and sensitivity. Recently, it was found that PCT level might be affected by non-infective factors as tissue hypoperfusion injury and systemic inflammatory response, which commonly occur after major burns (Seoane et al., 2014; Tan et al., 2021). The same was stated by Samsudin & Vasikaran, (2017) & Xu et al. (2021) that burn injuries are one of the non-infectious causes that may induce PCT rising levels.

To the best of authors' knowledge, no other studies had evaluated the value of PCT as a predictor of patients' outcome in acute corrosive ingestion. However, Serum PCT was already used to predict severity, infections, sepsis, and mortality in burn patients in several studies.

Keeping with our findings, the studied biomarkers (NLR, CRP and PCT) were significantly correlated with the duration of hospital stay of patients under the current study, which intense their role in predicting the negative outcomes of corrosive intoxicated children. This was in accordance with other previous studies by Rosanova et al. (2015); Uyar & Kok, (2017) and Eweda et al., (2023).

Conjointly, Uyar & Kok, (2017) and Siddique et al. (2021), had correlated NLR with the endoscopic grades of injury of corrosive ingestion in their studies, and reported that patients with NLR values of 8.71 and above at time of admission, should be hospitalized for a longer period with closer observation and further evaluation compared to those with lower values, which is considered a valuable finding for emergency departments, since endoscopy is not readily available.

The present study found that the best cut off point for the studied biomarkers (NLR, CRP and PCT) to predict incidence of complications in corrosive

intoxicated patients was >2.44 , >9.6 mg/L and >1.4 ng/mL, with AUC 0.68, 0.930 and 0.906 respectively.

Neutrophil lymphocyte ratio was the least specific (80%) and sensitive (50%) biomarker with in predicting the occurrence of complications compared to CRP and PCT levels, coinciding with data reported by Kim et al. (2015), who revealed that NLR was a fair but not a good predictor for corrosive toxicity complications. Also Fuss et al. (2018) highlighted that depending on NLR solely in outcomes prediction could be associated with false negative or positive results and unfavorable consequences for management plans.

Limited studies had determined a cutoff point for CRP level as a predictor for severity and outcomes of acute corrosive ingestion. In the current study, C-reactive protein was the most sensitive biomarker (100%) in predicting the occurrence of complications with a relative low cost; however, it had a low specificity (82.35%) compared to PCT. The low CRP specificity will show many false positive results if it is used alone as a biomarker; hence, Lawang et al. (2019) recommended its usage should always be associated with other clinical biomarkers as PCT, to increase its specificity in diagnosis and to assess changes in therapeutic approaches.

Procalcitonin was the most specific biomarker (94.12%), with the highest positive predictive value (90.5%), with sensitivity 73.8% in prediction of complications occurrence post caustic ingestion in the present study. Equivalently, Huang et al. (2022) reported that PCT is an inflammation marker with high specificity and sensitivity in guiding early clinical diagnosis and prediction of prognosis in burn patients. This was in accordance with several studies reported that PCT was more sensitive and specific in pediatrics and adults than CRP (Samsudin & Vasikaran, 2017; Eschborn & Weitkamp, 2019; Permatasari et al., 2021).

Conclusion

The current study concluded that PCT, CRP and NLR could predict severity and outcomes of acute corrosive ingestion in children. Procalcitonin seemed to be superior to CRP and NLR as a predicting biomarker with the highest specificity and the highest positive predictive value.

Recommendations

Preventive measures will always remain the main recommendation, stringent legislation is necessary for developing countries to limit unrestricted access to dangerous corrosive agents. The present study suggested a better assessment of outcome after corrosive ingestion by adding PCT, CRP and NLR to the routine investigations of patients with acute caustic ingestion for early prediction of esophageal injury and deciding management plans as well. Combining scoring systems as DROOL score with the measured biomarkers can be reliable and valuable in predicting poor outcomes post caustic ingestion. Correlating the studied biomarkers with the endoscopic grades of GIT injury post caustic ingestion is recommended for further evaluation of the biomarkers' role in emergency settings.

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الدور المحتمل للبروكالسيبتونين مقارنة ببروتين سي التفاعلي ونسبة الخلايا المتعادلة والخلايا اللمفاوية في التنبؤ بخطورة و نتائج التسمم الحاد بتناول المواد الكاوية

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الملخص العربي

الخلفية العلمية: يعتبر تناول المواد الكاوية في الأطفال مشكلة صحية خطيرة علي النطاق العالمي نتيجة لإرتفاع معدلات المرض والوفاة التي تصاحبها. **الهدف:** تحدف الدراسة الحاليه الى تقييم الدور المحتمل للبروكالسيبتونين مقارنة بدور بروتين سي التفاعلي ونسبة الخلايا المتعادلة والخلايا اللمفاوية في التنبؤ بخطورة ونتائج التسمم الحاد بتناول المواد الكاوية من أجل التدخل المبكر والحصول علي أفضل نتائج. **الطريقة:** أجريت تلك الدراسة المستقبلية علي 60 مريضاً من الجنسين من عمر 6 اشهر الي 12 عاماً، الذين قد تم حجزهم في مركز علاج التسمم بمستشفيات جامعة عين شمس أثر تناول مواد كاوية. وتم جمع البيانات الديموغرافية والاكلينيكية وسحب عينات الدم من كل مريض مع فحص المؤشرات الحيوية في خلال 24 ساعة عقب تناول المواد الكاوية. **النتائج:** كانت اغلبية المرضى من الذكور (70%) بمتوسط عمر سنة ونصف وبلغت نسبة حدوث المضاعفات الحادة و/او المزممة 43.3% في المرضى الخاضعين للدراسة. وقد وجدت مستويات مرتفعة من البروكالسيبتونين، بروتين سي التفاعلي ونسبة الخلايا المتعادلة والخلايا اللمفاوية في المرضى ذي المضاعفات وايضاً في المرضى الذين حصلوا علي ≥ 4 بمعيار DROOL. ارتفاع البروكالسيبتونين لمستوي اعلي من 1.4 نانوغرام/مل كان أكثر مؤشحيوي ذو نسبة نوعية (94.12%) ونسبة تنبؤ إيجابي (90.5%) في التنبؤ بحدوث المضاعفات. بينما كان بروتين سي التفاعلي هو أكثر مؤشر ذو حساسية عند مستوي أعلي من 9.6 ملغرام/لتر . **الإستنتاج:** تدعم تلك الدراسة دور البروكالسيبتونين، بروتين سي التفاعلي ونسبة الخلايا المتعادلة والخلايا اللمفاوية كمؤشرات حيوية فعالة في التنبؤ المبكر بخطورة و نتائج تناول المواد الكاوية في الأطفال. فقد بدى أن البروكالسيبتونين أفضل من بروتين سي التفاعلي ونسبة الخلايا المتعادلة والخلايا اللمفاوية في التنبؤ بمضاعفات التسمم بتناول المواد الكاوية. **التوصيات:** توصي تلك الدراسة بالاهتمام بترصد البيانات المعملية للتنبؤ بخطورة تناول المواد الكاوية و تجنب حدوث المضاعفات في وقت مبكر.