Neutrophil to Lymphocyte Ratio As A Predictor of Endoscopic Damage in Caustic Injuries

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Abstract

Objective: To assess the ingestion of caustic substances is a medical emergency and esophagogastroduodenoscopy (EGD) is helpful in diagnosis, prognostication and management. Here, we investigated the NLR of patients, to assess the correlation of neutrophil lymphocyte ratio (NLR) with degree of caustic injury and to evaluate whether NLR can predict the degree of caustic endoscopic injury.

Method: This cross sectional study was carried out on 180 patients in gastroenterology department of DHQ teaching hospital, Gujranwala from 1st Jan 2021 to 31 Dec 2021. The endoscopy was performed and CBC was sent for analysis of NLR. The esophageal and stomach mucosal injury was graded by Zargar's classification and divided into low grade and high grade. Independent sample t test was used for comparison between mean NLR versus low and high grade injury.

Results: Patients with high grade damage has remarkably higher values of NLR as compared to low grade. For prediction of grade of damage, ROC analysis was used and AUC (area under curve) value was 0.838 (95% CI (0.783-0.894, p<0.001) and if we take NLR cut-off value as 3.5, the sensitivity will be 96.0% and specificity 63.3%, if we take cut-off value as 4.5, the sensitivity will be 93.1% and specificity 48.1% and if we take cut-off value as 5.5, the sensitivity will be 75.2% and specificity 35.4%.

Conclusion: Neutrophil to lymphocyte ratio can predict degree of gastroesophageal injury in patients with caustic ingestion.

Keywords: Caustic injury, NLR, Zargar classification

Introduction

The ingestion of caustic substances is a medical emergency causing serious injuries to gastrointestinal tract[1]. Caustic substances ingestion (CSI) is usually accidental in children while intentionally in adults, and

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injuries tend to be severe.[1,3] Most of caustic ingestions are seen in female gender and younger age group.[11] Caustic substances with high and low pH are responsible for most of gastroesophageal injuries including mucosal swelling, exudates, redness, ulcerations and visceral perforation in acute setting.[2,3] Late sequelae include strictures in the esophagus and stomach, pyloric channel deformities and narrowing, mucosal metaplasia and carcinoma.[3] The depth of damage depends on many factors like socioeconomic status, intend of intake, physical consistency, concentration of the substance, ingested volume, contact time, and pH.[4-6] Endoscopy is used for assessment of gastroesophageal mucosal damage.[6-8] Endoscopy has role not only in diagnosis of mucosal damage due to corrosive but also helpful in making plan for management and prognostication[6]. In general, EGD

is performed as early as possible usually with 1 to 2 days after corrosive ingestion[9] and Zargar's classification (annexure attached) is routinely used to grade gastro-esophageal injury.[6] EGD is usually avoided in patients with unstable hemodynamic status, respiratory distress, and suspected visceral perforation.[3] Patients with low grade corrosive injury 0, I and IIA usually have no long term complication while patients with high grade injury IIB and III may develop strictures, fistulas and carci-noma.[10,12] Increase in morbidity, mortality, systemic complications and death was seen with every increase in grade of caustic injury.[3]

Patients with corrosive ingestion when present in medi-cal emergency, initial management start with securing of airway and stabilization of hemodynamic status and surgical evaluation.[6] Blood tests and X-rays are done to assess any complication. Patients are treated with an injectable acid suppressive therapy (proton pump inhi-bitors) and are kept nil per oral till their condition is stabilized and endoscopy done and their extent of injury is graded.[14-16] Complicated patient with corrosive inges-tion are transferred to intensive care unit (ICU) for fur-ther management.[6]

Negative endoscopy rate is 60 to 80 % in patients with corrosive substance ingestion[10,13] and yet many studies have been done for prediction of gastroesophageal damage in patients with corrosive ingestion at admission. EGD is inevitable for determination of gastroesophageal damage in patients with corrosive ingestion, because of questionable reliability of history obtained from patients and attendants.

The complete blood count (CBC) is cost effective, easily available and widely used blood test.[13] Routine blood test like CBC is used for assistance in diagnosis of diffe-rent anemia, infections and blood disorders, it has been recently investigated that NLR which is easily available from routine CBC is a marker of inflammation and high value is associated with bad prognosis[19] and increased illness in different diseases.[17] Normal NLR values in an adult health population are between 0.78 and 3.53.[20]

In a study conducted by Seyit Uyar and Mehmet Kok on relationship of NLR and endoscopic damage in corrosive ingestion has found that patients with gastroesophageal injuries induced by corrosive has higher NLR value (p<0.001) and found cut off value of NLR higher than 8.71 has acceptable diagnostic value with sensitivity of 90% and specificity of 91.7% for the discrimination of low and high grade damage (grade 0, 1, 2A vs. 2B 3, 4).[18]

The objective of this article was to determine signifi-cance of NLR values of patients in predicting severity of caustic gastroesophageal injury.

Material and Methods

The study was designed as cross sectional with non-probability convenience sampling and conducted in Gastroenterology Department of DHQ hospital Gujran-wala for 12 months last year.

The sample size of 180 was calculated by using 'WHO software for Sample Size Determination in Health Studies' considering 95% confidence level with 5% margin of error and taking reported high grade injury rate as 86.4% in caustic ingestion cases.[18] Patients of either gender between ages of 15 to 60 years presenting with caustic intake and willing for endoscopy were included in this study. Patients with atherosclerotic cardiovascular disease, cerebrovascular disease, auto-immune disease, malignancy or active infection; and on drugs like antiplatelet, anticoagulant or immunosupp-ressive evaluated by history and physical examinations (investigations as required) were excluded from this study. Patients in which endoscopy were contraindicated due to instability of hemodynamic and respiratory status, and suspected perforations were excluded. Patients were also excluded if endoscopy cannot be done within first 24 hour and CBC cannot be done within first 24 hour. After an informed written consent a detailed history of presenting symptoms, past history, drug and personal history and physical examination and appropriate inves-tigations were taken and recorded on proforma. The CBC was done within first 24 hour for analysis of NLR. The endoscopy was performed and the esophageal and sto-mach mucosal injury was graded by Zargar's classifi-cation within first 24 hour.

The data was collected and interpreted through SPSS version 22. Quantitative variables like age, neutrophil to lymphocyte ratio were presented as mean±SD. Qua-litative variables like gender, injured or non-injured, severity of caustic injury grade were presented in form of frequencies and percentages. Chi-square test was applied to ascertain correlation of grade of injury with gender, suicide attempt and corrosive substance used. Independent sample t-test was applied to compare the mean age and neutrophil to lymphocyte ratio between low and high grade damage. ROC analysis was applied to determine the area under curve and cut-off value for NLR for the prediction of the grade of damage. A p-

value ≤ 0.05 was considered significant.

Results

Total 180 patients were included, majority the patients were female (76.1%). High grade injury was observed in 101 (56.1%) patients. Suicidal attempt was present in 151(83.9%) patients. Acid substance was used by 144 (80.0%) patients. The mean age of the patients was 23.3 ± 7.1 with age range from 14 to 60 years. Chi-squares test revealed no significant association of gender and corrosive substance used with grade of injury while significant association was observed between suicidal attempt and grade of injury (Tab 1).

Table 1: *Relationship of grade of injury with gender, suicide attempt and corrosive substance used for suicide*

Variables	Category		Grade of injury		p-value
			Low	High	
Gender	Male	n	22	21	0.271
		%	27.8%	20.80%	
	Female	n	57	80	
		%	72.7%	79.2%	
Suicidal attempt	Yes	n	61	90	0.031*
		%	77.2%	89.1%	
	No	n	18	11	
		%	22.8%	10.9%	
Substance	Acid	n	59	85	0.115
		%	74.7%	84.2%	
	Alkali	n	20	16	
		%	25.3%	15.8%	
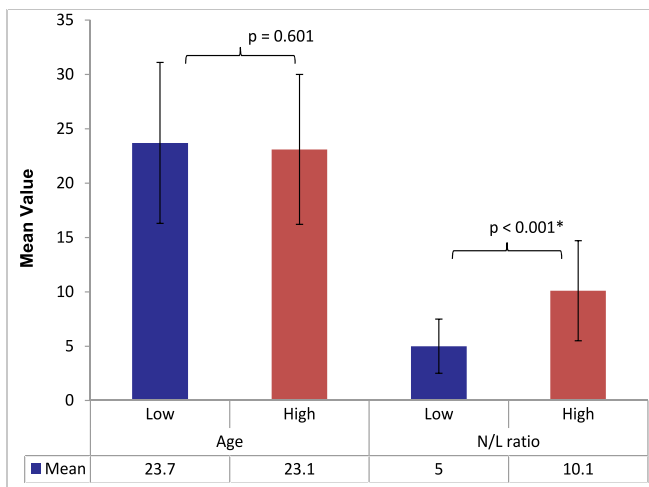
Figure 1: *Comparison of age and NLR between low and high grade injury*

Independent sample t test showed that there was no considerable variance in age between low and high grade injured patients. Significant difference was found in N/L ratio between low- and high-grade injuries. N/L ratio was higher in high grade injury as compared to low grade injury (fig 1).

If we take NLR cut-off value as 3.5, the sensitivity will be 96.0% and specificity 63.3%, if we take cut-off value as 4.5, the sensitivity will be 93.1% and specificity 48.1% and if we take cut-off value as 5.5, the sensitivity will be 75.2% and specificity 35.4%. ROC analysis was used for the anticipation of the grade of damages as low vs. high and AUC (area under curve) value was 0.838 (95% CI (0.783-0.894, p<0.001) (Tab 2)

Table 2: *ROC analysis and sensitivity and specificity of NLR in prediction of grade of injury*

Area under curve	p-value	95% Confidence Interval	
		Lower	Upper
0.838	< 0.001	0.783	0.894
Grade	**Cut-off value**	**Sensitivity**	**Specificity**
Low vs. High	3.5	96.0%	63.3%
	4.5	93.1%	48.1%
	5.5	75.2%	35.4%

Discussion

Corrosive substances ingestion can lead to irreversible devastating complications. Endoscopy is recommended for evaluation of degree of injury by corrosive ingestions and usually done in the first 1 to 2 days after ingestion. Zargar classification is used to grade injury, patients with low grade of injury (I and IIA) usually don't develop complications and are discharged on same day while patients with high grade of injury (IIB and III) usually develop complications and stay longer in hospital. In this study, total 180 patients were included and high grade injury was observed in 101 (56.1%) patients.

Studies on inflammatory markers like neutrophil to lymphocyte ratio have done in different diseases such as atherosclerotic cardiovascular diseases, inflammatory diseases and tumors[17,19,21], but are limited in corrosive substances injuries. In this study, NLR values of patients with low and high grade injury were studied and significant difference was found in NLR values between low- and high-grade injuries. NLR was higher in high grade injury as compared to low grade injury. High levels of NLR indicate severe caustic damage, extensive involvement, and the likelihood of developing complications with high sensitivity. A low NLR may be directive in

deciding a hospital discharge.

Sung Jan et al have conducted a study on NLR values of patients with nonmetastatic head and neck cancer and found that high NLR values were associated with poor survival[21].

Jing et al have conducted a study on prognostic value of NLR in patients with lung cancer and found that elevated NLR values were associated with poor survival[22].

Uyar S and Kok M have made a retrospective evaluation of 190 patients presented in University of Health Sciences Antalya Training and Research Hospital, Turkey with diagnosis of caustic ingestions. The purpose of this article was to establish the link between degree of corrosive damage and inflammatory markers such as white blood cells (WBC), C-reactive protein (CRP) and NLR and to evaluate predictability of NLR for severity of injuries. NLR was remarkably high in patients with mucosal damage than patients without it (p=0.010), whereas WBC and CRP not. NLR was also remarkably high in patients with both esophagus and gastric injuries compared to patients without organ damage (p<0.001). NLR, WBC and CRP were weakly correlated to the grade of involvement. Higher NLR value revealed higher degree of corrosive damage. NLR also appears to more definitive marker to distinguish between lower and higher degree of damage.[18]

Karalla et al have conducted a retrospective study in Turkey on 133 patients admitted due to corrosive ingestions , and revealed that patients in Group I have NLR and WBC values were statistically important and lower than patients in Group II (p<0,05). Patients with Zargar grade 0, 1 and 2A corrosive injury were included in Group1, whereas 2B, 3A and 3B corrosive injury included in Group 2.[10]

Ghonem and El Sharaby included 44 patients with corrosive ingestion presented in medical emergency, Tanta University. They used leucocyte parameters to assess acute complication due corrosive ingestions, and they found that NLR is good predictor of acute complications and cut off value >2.42 has 63.64% sensitivity and 100% specificity.[8]

Conclusion

Neutrophil to lymphocyte ratio can predict degree of gastroesophageal injury in patients with caustic ingestion.

Annexure I

Zargar classification and its corresponding endoscopic description

Zargar classification	Description
Grade 0	Normal mucosa
Grade I	Edema and hyperemia of the mucosa
Grade IIA	Superficial ulcerations
Grade IIB	Deep or Circumferential ulcerations
Grade IIIA	Transmural ulcerations with focal necrosis
Grade IIIB	Transmural ulcerations with extensive necrosis
Grade IV	Perforation

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Authors Contribution

NA: Conceptualization of Project

NA: Data Collection

RKF: Literature Search

NA: Statistical Analysis

MM: Drafting, Revision

NA, MAN: Writing of Manuscript