

PalArch's Journal of Archaeology
of Egypt / Egyptology

**CORRELATION OF NEUTROPHIL TO LYMPHOCYTE RATIO
ENDOSCOPIC GRADE OF INJURY IN CAUSATIC INJURIES**

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Correlation Of Neutrophil To Lymphocyte Ratio Endoscopic Grade Of Injury In Causatic Injuries Jamshid Siddique, Maryum Altaf , Sadia Khan -Palarch's Journal Of Archaeology Of Egypt/Egyptology 17(8), 613-621. ISSN 1567-214x

Keywords Neutrophil to Lymphocyte Ratio, Endoscopy, Caustic injury.

ABSTRACT

In the early period, caustic ingestion may be the cause of superficial edema, erosions, erythema, ulcerations and necrosis that eventually leads to perforation. The main finding for further management of caustic ingestion is endoscopic degree of injuries. The purpose of our study is to find correlation of neutrophil to lymphocyte ratio and endoscopic grade of injury in caustic injuries. A cross sectional study based on 148 cases was conducted at Department of Gastroenterology, DHQ Gujranwala over a period of six months from 22-05-2019 to 22-09-2019. Endoscopy for all cases have been performed by a senior consultant having more than 5 years of experience. The blood sample of 5 cc have been taken from all cases for NLR analysis. The mean age of the patients was 33.61 ± 8.247 years. 47.3 % (n=70) were male whereas 52.7 % (n=78) were females. Frequency of grade 0 was 16.5% (n=25), grade 1 was 25.7 % (n=38), grade 2 was 9.5 % (n=14), grade 3 was 10.8 % (n=16), grade 3a was 23.6% (n=35), grade 4 was 0.7% (n=1). Value of correlation $r = 0.828$ (p-value < 0.005). There is strong correlation of neutrophil to lymphocyte ratio and endoscopic grade of injury. Neutrophil to lymphocyte ratio increased as endoscopic grade of injury was high. Higher the NLR values indicates the widespread and severe involvement of caustic ingestion.

INTRODUCTION:

The major cause of morbidity and mortality is the ingestion of caustic substances, especially in low- income and middle-income countries.¹ Corrosive injuries were may cause by a widespread variety of chemical agents comprising of organic acids, minerals, alkali, denaturants, oxidizing agents, hydrocarbons and other chemicals. Even though the mechanism, the timing, and the severity of the injury may fluctuate, all these substances result in damage to living tissue on contact.² Damage to the upper respiratory and digestive tract may be caused by caustic ingestion of acid or alkaline substances.³ Initial clinical presentation resulting from caustic ingestion may consist of oropharyngeal pain, stridor and dysphagia.^{3,4} A multidisciplinary approach that includes emergency care physicians, anesthesiologists, surgeons, radiologists, gastroenterologists, and psychiatrists is required for emergency management of caustic injuries.⁵

The standard of care for emergency patient is endoscopy which is used to evaluate the patient condition after caustic ingestion.⁶ An endoscopic degree of injuries is the chief finding for further managing of caustic ingestions however, if endoscopy cannot be executed immediately, clinicians choose on treatment plan and follow-up objectives according to the signs and symptoms of the patient.⁷ In the pathophysiology of vascular disease, inflammation also plays an important role. We consider the associations between the neutrophil–lymphocyte ratio (NLR; an indicator of inflammation) and vascular disease and also its associated risk factors in this review.⁸ The important measure of systemic inflammation is neutrophil-lymphocyte ratio (NLR) method which is cost effective and readily accessible.⁸ In various diseases such as cancer, inflammatory disorders, hypertension, diabetes, obesity, hyperlipidemia and vascular diseases it used as an inflammatory marker. Deprived survival rate and increased morbidity are associated with elevated NLR levels in numerous chronic conditions. In addition, elevated NLR levels have been associated with poor survival of patients undergoing coronary bypass surgery. NLR can be significant predictor of overall and disease-specific survival of patients showed by cancer survival studies^{7,8}

A study reported that correlation between grade of injury and NLR was 0.43, p-value < 0.001.⁷

The current study designed to see correlation of neutrophil to lymphocyte ratio endoscopic grade of injury in caustic injuries in our local population. As no local data is, publish yet and international data is lacking in this regard, only one study was found in which significant positive correlation was found between neutrophil to lymphocyte ratio endoscopic grade of injury in caustic injuries. Therefore, if we also found positive significant correlation then in future we will also use NLR as non-invasive procedure to know the severity of esophageal injuries. Preliminary identification of caustic esophageal injury and grading of the extent or severity thereof can direct proper management. To find correlation of neutrophil to lymphocyte ratio and endoscopic grade of injury in caustic injuries is objective of current study.

METHODOLOGY:

At Department of Gastroenterology, DHQ Gujranwala, this cross sectional study was conducted which comprised of 148 cases that are recruited through Non-probability consecutive sampling.

By using 5% Type-I error and 10% type-II error sample size was calculated and correlation between grade of injury and NLR was 0.43.⁷ All cases recruited aged 18-60 years of either gender having Caustic injuries. Patients with Cardiovascular diseases, known malignancies and pregnant females were excluded from the study. Endoscopy for all cases was performed by a senior consultant having more than 5 years of experience. Blood sample of 5 cc was taken from all cases and deliver to hospital laboratory for NLR analysis. By dividing absolute neutrophil count by the absolute lymphocyte count, NLR was obtained. Endoscopic classification of caustic injuries

was presented in Table 1.⁹

| Grade | Features |
|----------|--|
| Grade 0 | Normal |
| Grade 1 | Superficial mucosal edema and erythema |
| Grade 2 | Mucosal and submucosal ulcerations |
| Grade 2A | Superficial ulcerations, erosions, exudates |
| Grade 2B | Deep discrete or circumferential ulcerations |
| Grade 3 | Transmural ulcerations with necrosis |
| Grade 3A | Focal necrosis |
| Grade 3B | Extensive necrosis |
| Grade 4 | Perforations |

Table 1: Endoscopic Classification of Caustic Injuries

Grade of injury and NLR was calculated as per operational definition. A self-structured questionnaire was used to collect data. From each case necessary demographic information such as name, age and address was taken. Quantitative data like age, NRL was presented as mean \pm S.D. Age, Gender, BMI and duration group was presented in form of frequency and percentage. Association has been assessed between grades of injury and demographic variables (age, gender, BMI and duration group). Spearman's rank correlation coefficient was calculated for grade of injury and NLR. Data was consider statistically significant if p-value is less than 0.05. All data was analyzed using Statistical Package for social sciences (SPSS version 22).

Results**Table 1: Demographic Data of Patients**

| Variables | Total, 148 n (%) | GRADE 0 (n= 25) | GRADE 1 (n= 38) | GRADE 2 (2, 2a, 2b) (n= 32) | GRADE 3 (3, 3a, 3b) (n= 52) | GRADE 4 (n= 1) | p-value |
|----------------------------|------------------------|-----------------------|-----------------------|--------------------------------------|--------------------------------------|----------------------|---------|
| Age | | | | | | | |
| 18-40 yrs. | 115(77.7) | 17(68) | 30(78.9) | 22(68.8) | 45(86.5) | 1(100) | 0.042 |
| 41-60 yrs. | 33(22.3) | 8(32) | 8(21.1) | 10(31.3) | 7(13.5) | 0(0) | |
| Gender | | | | | | | |
| Male | 70(47.3) | 13(52) | 21(55.3) | 17(53.1) | 18(34.6) | 1(100) | 0.000 |
| Female | 78(52.7) | 12(48) | 17(44.7) | 15(46.9) | 34(65.4) | 0(0) | |
| BMI | | | | | | | |
| 17-22 kg/m ² | 44(29.7) | 10(40) | 11(28.9) | 9(28.1) | 14(26.9) | 0(0) | 0.676 |
| >22 kg/m ² | 104(70.3) | 15(60) | 27(71.1) | 23(71.9) | 38(73.1) | 1(100) | |
| Duration Group | | | | | | | |
| ≤24 hours | 103(69.6) | 24(96) | 32(84.2) | 19(59.4) | 28(53.8) | 0(0) | 0.000 |
| >24 hours | 45(30.4) | 1(4) | 6(15.2) | 13(40.6) | 24(46.2) | 1(100) | |

Table 1, depicts the demographic data of patients; mean age of patients was 33.61 ± 8.247 years. Out of 148 patients, 115(77.7%) were in age group 18-40 years, whereas 33(22.3%) were from age group 41-60 years. Majority of patients of aged 18-40 years were from grade 3(3, 3a, 3b). 70 (47.3%) were males and 78 (52.7%) were females. Majority of males were from grade 1; 21 (55.3%) 44(29.7%) were from BMI group 17-22 kg/m² and 104 (70.3%) were from BMI group > 22 kg/m². Majority of patients from 17-22 kg/m² BMI group were from grade 3 and no patient was from grade 4. 103 (69.6%) were having duration group ≤ 24 hours whereas only 45 (30.4%) were having duration group of greater than 24 hours. On the average NLR was 5.14 ± 1.83 . Age, gender and duration group was significantly associated with grades of injury (p-value < 0.05).

Table 2 Correlation between the grade of injury and NLR

| | N | R | p-value |
|-----------------------|----------|----------|----------------|
| Grades vs. NLR | 148 | 0.828 | 0.000 |

Table 2 represents the correlation between grades of injury and NLR. Spearsman rank correlation shows the strong positive correlation between grades of injury and NLR ($r= 0.828$). And NLR was significantly associated with endoscopic grading of caustic injuries ($p\text{-value}=0.000$).

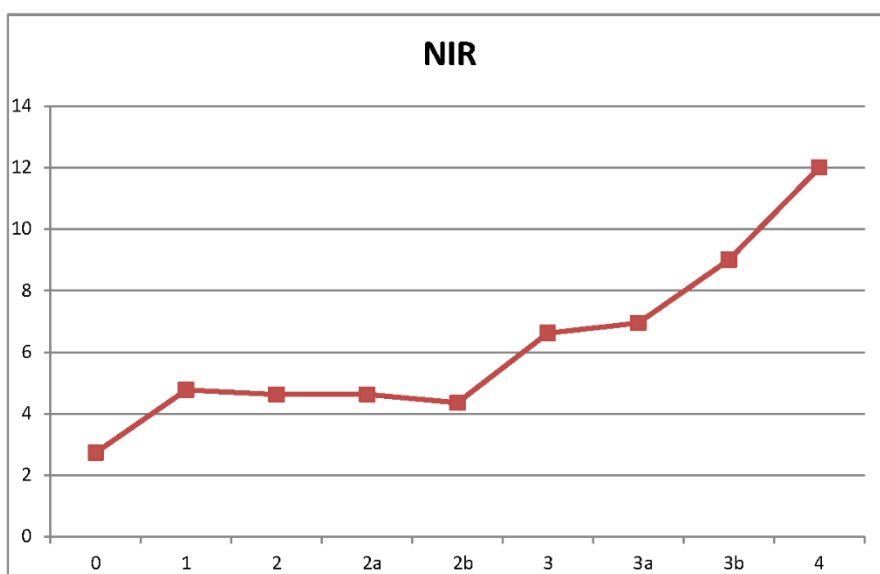


Figure 1: NLR and Grades of injury

Figure 1 shows the increasing trend of NLR in comparison to Grades of injury, as the grades changes from 0 onwards the value of NLR increases.

DISCUSSION:

Caustic injuries may progress to irretrievable catastrophic complications. The gold standard for evaluation of caustic ingestions is endoscopy, but its application takes time. Generally endoscopy is recommended in the initial 12-48 hours afterwards caustic ingestion and is reliable for up to 96 hours after the injury.¹⁰

Esophageal and gastric superficial edema, erythema, erosions, ulcerations, necrosis and ultimately perforation in the initial period may be caused by caustic ingestion.¹¹ Patients presenting with perforation have to be diagnosed without any wastage of time, as direct surgical intervention may be requisited.¹⁰

Patients has mean age of 33.61 ± 8.247 years. Out of 148 patients, 115(77.7%) were in 18-40 years of age group whereas 33(22.3%) were in 41-60 years. There were 70(47.3 %) males and 78(52.7 %) were females. A study conducted on Ingestion of caustic substances plus its complications in 2001 showed the 89.3% incidence of esophagitis, Stenosis was mild in 17.6% of cases, moderate in 59.3% and severe in 23%. The incidence rate of Caustic injuries was 80.8% in women and 62.5% in men. Caustic injuries were more common in 11-20 years that is 94.9%. these findings were similar to the current study.¹²

The majority (68 %) of cases globally involve children because of unintended, accidental ingestion of caustic substances. The residue of cases stated are adults with psychiatric turbulences, some after suicide attempts, or alcoholics.¹³

A total 18% to 46% of all caustic ingestions are associated with esophageal burns in children. This figures may be higher in adults who often utilize greater amounts of the caustic substance as account of a suicidal attempts.^{14,15} Ingestion of cleaning constituents account for more than 200,000 annually contacts reported to the United States poison control center. The 10% of adults presenting with caustic ingestions decease and 1-2% of ingestions results in stricture formation. Children younger than 5 years' account for about 80% of caustic ingestion cases that normally occur accidentally.¹⁶

In the current study the endoscopic grading of caustic injuries showed majority of the patients were in Grade I, 38 (25.7%), Grade III, 35(23.6%), and Grade 0, 25(16.5%). In a study conducted by C Cabral in 2012 on upper tract causative injuries reported that mainstream of the patients have Grade 0, Grade IIIb and Grade IIa stages. 158 (50%) patients had mild injuries entitled for no operative management and 84 (27%) patients had severe injuries. They conclude that Emergency endoscopic grading of caustic injuries is the key factor that conditions outcome subsequently caustic ingestion.¹⁷

On endoscopy, the degree of injury determined is the main finding for patient management and forecasting of complications. Usually, grade 0 and 1 lesions do not progress to sequelae and morbidity and mortality surge as the degree of injury increases. Patients with grade 1 or 2A injury permitted to oral intake initially and were normally discharge within days with antacid therapy. Patients with grade 2 or 3 injury however, are more severe cases and may require keen observation and may have longer stay in hospital.¹⁰

NLR greater than 8.71 was a significantly decent diagnostic marker for the distinction of mild and severe caustic injuries (grade 0, 1, 2 vs. 3, 4) [$p < 0.001$]. In Emergency Departments, this is a valuable finding for primary physicians to be able to plan further management of the patient. However, the integer of patients reported with severe injuries (n=10) and $NLR > 8.71$ (n=18) was low. Since, caustic injuries are generally seen in developing countries and endoscopy is not readily available and emergency endoscopic grading is the core factor reflecting patient survival and functional outcome.¹²

In a study directed by Cabral *et al.*, majority of patients with mild injuries (grade I-IIIa) were managed with help of medical treatment (10/158 patients underwent surgery), while most of the patients with severe injuries (grade IIIb-IV) were managed through surgical intervention (78/84 patients underwent surgery).¹⁷

In current study it was determine that there was strong correlation between grade of injury and neutrophil to lymphocyte ratio [$r = 0.828$ (p- value < 0.05)], which shows that NLR value increased as grade of injury was high. These findings were not similar to the study Uyar S, they reported that there was a weak correlation between NLR and grade of injury ($r= 0.43$, p-value <0.001).⁷

In a study by Havanond *c at el.*, reported the relationship between WBC count and Grade of injuries and predictability of WBC count for Caustic injuries.¹⁸ But there was not more studies conducted on NLR and Caustic injuries.

CONCLUSION:

In current study, we concluded that there is a strong correlation of neutrophil to lymphocyte ratio and endoscopic grade of injury. These are strongly associated with each other. Neutrophil to lymphocyte ratio increased as endoscopic grade of injury was high. Higher NLR values exhibited extensive and severe envelopment of caustic ingestion.

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