Hematological Parameters Predicting Complications of Caustic Ingestion:
A Retrospective Study

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Purpose: In addition to chemical burn of the alimentary tract, caustic ingestion can cause severe complications including esophageal perforation, airway edema, esophageal stricture, and death. Hematological parameters have been reported to be useful inflammatory markers predicting prognoses in various clinical situations where oxidative stress is increased. We hypothesized that hematological parameters might be useful for prediction of complications after caustic ingestion.

Methods: We performed a retrospective analysis of patients admitted to our Emergency Department after caustic ingestion. The numbers of leukocytes, neutrophils, lymphocytes, and monocytes, and the neutrophil-lymphocyte ratio were compared between uncomplicated and complicated patient groups. Receiver operating characteristic curve analysis was performed for parameters that differed between the two groups. Subgroup analysis was performed according to the substance ingested, thus acid or alkali.

Results: Thirty-seven patients were included in our study and eight had complications. Leukocyte, neutrophil counts, and the neutrophil-lymphocyte ratio of the complicated group were higher than those of the uncomplicated group. The areas under the receiver operating characteristic curves of leukocyte counts, neutrophil counts, and the neutrophil-lymphocyte ratio were 0.819, 0.832, and 0.750, respectively. The cut-off values of these parameters for prediction of complications were 12 060/μL, 9607/μL, and 2.72, respectively. In subgroup analysis, the leukocyte and neutrophil counts, and the neutrophil-lymphocyte ratio of complicated patients who had ingested alkali were higher than those of the uncomplicated group.

Conclusion: Leukocyte counts, neutrophil counts, and the neutrophil-lymphocyte ratio might serve as useful predictors of complications after ingestion of caustic substances.

Key Words: Blood cell count, Caustics, Esophagus, Wounds and injuries

Article Summary

What is already known in the previous study
Hematological parameters have been reported to be useful inflammatory markers for predicting prognoses in various clinical situations where oxidative stress is increased.

What is new in the current study
Use of leukocyte counts, neutrophil counts, and/or the neutrophil-lymphocyte ratio can be helpful in predicting the presence of complications after caustic ingestion. Higher parameters were observed in complicated cases than in uncomplicated cases.

Introduction

More than 5000 cases of caustic ingestion are reported annually in the United States. Although common body areas exposed to caustic substances include the eyes, face, and extremities; fatalities have been reported only after caustic ingestion. About 80% of all caustic ingestions occur in children and are mainly accidental. Caustic ingestions in adults are usually associated with a suicidal intent and are frequently life-threatening. The mortality caused by caustic injury has been reported to be 14% after acid ingestion and 2% after alkali ingestion. Caustic ingestion first causes chemical burning of the alimentary tract and may trigger more serious com-
lications, such as esophageal perforation, airway edema caused by laryngeal chemical burns, systematic toxicity including hemodynamic instability, acidosis, and death6). Early esophagogastroduodenoscopy (EGD) is crucial for the evaluation of caustic injury. Classification of esophageal burns via EGD is valuable prognostically, and is frequently employed for patient management in clinical settings5,6). However, early EGD is not always available, depending upon patient condition and the hospital visited. Apart from the initial chemical burn to the esophagus, oxidative stress and related inflammatory processes are known to further damage that tissue5). Several studies have evaluated laboratory data on inflammatory processes in efforts to define prognostic markers. Leukocyte counts reflected mortality from caustic ingestion in one study, but were not meaningfully correlated with occurrence of esophageal strictures in another work6,9). Leukocytosis, neutrophilia, monocytosis, and lymphocytopenia have been reported in the acute phase of clinical conditions in which oxidative stress is increased12-14). The neutrophil-lymphocyte ratio (NLR) is a useful prognostic marker in various diseases featuring inflammatory responses, such as sepsis, stroke, and appendicitis12-16). The complete blood count (CBC) is a widely used laboratory test that yields information on the hematological parameters mentioned above. However, to date, parameters other than leukocyte counts have not been investigated for their abilities to predict complications associated with caustic ingestion. Thus, we explored the utilities of hematological parameters in predicting complications of caustic ingestion.

Materials and Methods

Two independent investigators reviewed written and/or electronic medical records to retrieve demographic data; types of ingested caustics; CBCs obtained soon after admission to the ED; endoscopic findings within 24 h of ingestion; and complications such as esophageal perforation, mediastinitis, airway edema caused by laryngeal burns, esophageal stricture, or death. The counts of leukocytes, neutrophils, lymphocytes, and monocytes; and the NLR, were explored to determine if any feature was a useful predictive parameter. Grade 2B or higher burn in endoscopic finding was defined as a severe esophageal burn and, otherwise, a mild esophageal burn6). Included patients were divided into two groups in terms of the presence of complications: the uncomplicated and complicated groups. Hematological parameters predicting complications were the primary outcomes of the present study; such parameters were compared between the uncomplicated and complicated groups. As the type of caustic ingestion might influence the development of complications, subgroup analysis by acid or alkali ingestion was performed in the same manner.

An investigator blinded to the purpose of the study performed all data analysis, which employed SPSS version 21.0 (IBM corporation, Armonk, NY, USA) and MedCalc version 14.12.0. The demographic factors and hematological parameters of each group were subjected to descriptive analysis. Continuous data were expressed as means with standard deviation (SDs) if their distributions were normal, and as medians with interquartile ranges (IQRs) otherwise. Categorical data were expressed as numbers with percentages. After normality was analyzed, the demographic factors and hematological parameters of the two groups were compared. Student’s t-test was used to compare continuous data that were normally distributed and the Mann-Whitney U-test was employed to compare continuous data that lacked a normal distribution. Pearson’s chi-squared test and Fischer’s exact test were used to compare categorical data. Receiver operating characteristic (ROC) curves of hematological parameters that differed between the two groups were drawn to determine the statistical power of complication prediction. By using Youden’s J statistics, the optimal cut-off values of each parameter were calculated. A p value<0.05 was considered to indicate statistical significance.
Results

In the study period, 41 patients were admitted after ingestion of caustics. Four patients were excluded from final analysis because of a lack of CBC data obtained within 24 h of ingestion. Eight patients had complications; six had esophageal strictures, two died in hospital, and no one had other complications (Fig. 1). Severe metabolic acidosis and multiple organ failure were the cause of death in two died patients. Demographic variables did not differ between the two groups. The compli-

![Study flow diagram](image)

**Fig. 1.** Study flow diagram.

<table>
<thead>
<tr>
<th>Uncomplicated (29)</th>
<th>Complicated (8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n) M (14), F (15)</td>
<td>M (2), F (6)</td>
<td>0.423</td>
</tr>
<tr>
<td>Age, years, Mean ± SD 46.2 ± 21.7</td>
<td>47.9 ± 15.2</td>
<td>0.837</td>
</tr>
<tr>
<td>Height, cm, Median (IQR) 163 (156-171)</td>
<td>159 (152-163)</td>
<td>0.496</td>
</tr>
<tr>
<td>Weight, kg, Median (IQR) 61 (55-68)</td>
<td>54 (46-59)</td>
<td>0.530</td>
</tr>
<tr>
<td>Substrate (n) Acid (9), Alkali (17), Unknown* (3)</td>
<td>Acid (4), Alkali (4)</td>
<td>0.460</td>
</tr>
<tr>
<td>Endoscopic grade (n) Mild (23), Severe (6)</td>
<td>Mild (4), Severe (2), Unknown (2)</td>
<td>0.018</td>
</tr>
<tr>
<td>Leukocytes, cells/μL, Median (IQR) 10 150 (8,095-11,580)</td>
<td>17 295 (12,803-21,483)</td>
<td>0.005</td>
</tr>
<tr>
<td>Neutrophils, cells/μL, Median (IQR) 7179 (4,538-8,951)</td>
<td>13 583 (9,294-18,991)</td>
<td>0.003</td>
</tr>
<tr>
<td>Lymphocytes, cells/μL, Median (IQR) 2152 (1,509-3,693)</td>
<td>1861 (1,109-2,700)</td>
<td>0.479</td>
</tr>
<tr>
<td>Monocytes, cells/μL, Median (IQR) 583 (401-756)</td>
<td>756 (291-1,385)</td>
<td>0.414</td>
</tr>
<tr>
<td>NLR, Median (IQR) 2.59 (1.39-4.60)</td>
<td>7.39 (3.13-16.45)</td>
<td>0.032</td>
</tr>
</tbody>
</table>

SD: standard deviation, IQR: inter quartile range, NLR: neutrophil-lymphocyte ratio
* The acidity of ingested substance was uncertain in three cases.
cated group had higher numbers of leukocytes and neutrophils, and a higher NLR, than the uncomplicated group (Table 1). The areas under the ROC curves (AUCs) of leukocyte and neutrophil counts, and the NLR, used to predict complications were 0.819, 0.832, and 0.750, respectively (Table 2, Fig. 2). Pairwise comparisons of the three ROC curves revealed no differences among the AUCs. The optimal cut-off values of the leukocyte and neutrophil numbers, and the NLR, were 12,060/μL, 9607/μL, and 2.72, respectively (Table 2).

Upon subgroup analysis, hematological parameters did not differ between the complicated and uncomplicated group if acid had been ingested. After alkali ingestion, however, the complicated group had larger numbers of leukocytes and neutrophils, and a higher NLR, than the uncomplicated group (Table 3). The AUCs of leukocyte and neutrophil counts, and the NLR, for predicting complications after alkali ingestion were 0.956, 0.956, and 0.838, respectively, and pairwise comparisons of the three ROC curves revealed no difference among the AUCs. The optimal cut-off values of leukocyte and neutrophil numbers, and the NLR, were 11,400/μL, 7718/μL, and 4.77, respectively.

**Discussion**

Acids and alkalis injure tissues in different ways. Acids induce coagulation necrosis accompanied by eschar formation. This protects the tissue from further injury by inhibiting acid penetration and limits the depth of the injury. On the other hand, alkalis induce liquefactive necrosis and saponification after contact with body tissues, and thus penetrate deeper into the tissues. When the difference in injury mechanisms is considered, esophageal injury would be expected to be more serious after alkali ingestion, but this is not always true in clinical situations. In one study, strong acid ingestion was associated with more serious problems (a longer hospital stay, more systemic complications) than alkali ingestion. As both strong acids and alkalis can penetrate esophageal tissues rapidly, both can create full-thickness esophageal injuries.

Oxidative stress is the principle mechanism of pathophysiology in most toxin-caused diseases. Likewise, esophageal injury is complicated by oxidative stress, with subsequent lipid peroxidation, after initial chemical burning upon caustic ingestion. Increased levels of free radicals, and decreased antioxidant capacities, have been reported after caustic esophageal injury. When the production of free radicals exceeds the antioxidant capacity, the CBC changes, triggered by oxidative stress. For example, all of leukocytosis, neutrophilia, monocytosis, and lymphocytopenia have been reported in previous studies on the acute inflammatory response to oxidative stress.

Although, in theory, the differential leukocyte count might be a useful marker of caustic injury, only leukocyte counts per se were evaluated. A leukocyte count over 20000/mm³ was found to be an independent predic-

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**Table 2.** ROC curve analysis of hematological parameters predicting complications.

<table>
<thead>
<tr>
<th></th>
<th>AUC (95% CI)</th>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytes</td>
<td>0.819 (0.658-0.926)</td>
<td>12,060 cells/μL</td>
<td>88%</td>
<td>83%</td>
<td>58%</td>
<td>96%</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>0.832 (0.673-0.934)</td>
<td>9,607 cells/μL</td>
<td>75%</td>
<td>90%</td>
<td>67%</td>
<td>93%</td>
</tr>
<tr>
<td>NLR</td>
<td>0.750 (0.581-0.877)</td>
<td>2.72</td>
<td>88%</td>
<td>55%</td>
<td>35%</td>
<td>94%</td>
</tr>
</tbody>
</table>

AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value, NLR: neutrophil-lymphocyte ratio ratio.
tor of death, with an odds ratio of 6.0, in a previous retrospective study. However, another retrospective work on caustic ingestion by pediatric patients found that the leukocyte count did not predict an esophageal burn of grade 2B or greater, or development of esophageal stricture. Neutrophil counts correlated with clinical observations on the inflammatory process, but such counts were not investigated in cases of caustic injury. In our present study, both leukocyte and neutrophil counts were higher in the complicated group, and the diagnostic utilities of these counts for prediction of complications were good. However, neither monocyte nor lymphocyte counts differed between the uncomplicated and complicated groups of our present study.

The NLR is a relatively simple and low-cost inflammatory marker compared to other inflammatory markers such as the C-reactive protein level. The NLR is a widely used marker of inflammatory processes and significant prognostic utilities thereof have been reported in various clinical circumstances including cardiovascular disorders, sepsis, stroke, rheumatoid disease, acute appendicitis, and cancer. However, to date, NLR has not been investigated as a marker of caustic ingestion. In our present study, the NLR was higher in complicated than uncomplicated patients and was of fair diagnostic utility for prediction of complications.

Although all three parameters afforded good diagnostic powers in this context, their powers were not strong enough for using in clinical situation. Especially because of low prevalence of complicated cases, positive predictive value was relatively low. And we do not yet know which parameter is the most reliable. Prospective studies with large cases are required to confirm and compare the diagnostic powers of the three parameters.

EGD has been regarded as a cornerstone of initial evaluation after caustic ingestion, because classification of burns is important in management and prognosis. Patients of grade 0 or 1 do not develop esophageal strictures and can be safely discharged to home after symptoms are relieved; a normal diet can be taken. Previous studies found that esophageal strictures can develop in as much as 71% of patients with grade 2B burns and 100% of patients with grade 3 burns. Despite the importance of early EGD in prognosis and management, EGD may not always be available. The hospital may not have the equipment or the patient’s condition may contraindicate

<table>
<thead>
<tr>
<th>Acid Ingestion (n=13)</th>
<th>Alkali Ingestion (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated (n=9)</td>
<td>Complicated (n=4)</td>
</tr>
<tr>
<td>Leukocytes*, cells/µL</td>
<td>11100 (9,775-13,905)</td>
</tr>
<tr>
<td>Neutrophils*, cells/µL</td>
<td>7758 (5,624-9,313)</td>
</tr>
<tr>
<td>Lymphocytes*, cells/µL</td>
<td>2852 (1,054-4,129)</td>
</tr>
<tr>
<td>Monocytes*, cells/µL</td>
<td>615 (431-824)</td>
</tr>
<tr>
<td>NLR*</td>
<td>2.59 (1.60-6.35)</td>
</tr>
<tr>
<td>p value</td>
<td>0.148</td>
</tr>
<tr>
<td>Uncomplicated (n=17)</td>
<td>Complicated (n=4)</td>
</tr>
<tr>
<td>Leukocytes*, cells/µL</td>
<td>8520 (7,480-10,870)</td>
</tr>
<tr>
<td>Neutrophils*, cells/µL</td>
<td>16 955 (6,731-19,504)</td>
</tr>
<tr>
<td>Lymphocytes*, cells/µL</td>
<td>2487 (1,702-3,870)</td>
</tr>
<tr>
<td>Monocytes*, cells/µL</td>
<td>581 (372-756)</td>
</tr>
<tr>
<td>NLR*</td>
<td>2.40 (1.13-3.85)</td>
</tr>
<tr>
<td>p value</td>
<td>0.199</td>
</tr>
</tbody>
</table>

NLR: neutrophil-lymphocyte ratio

* These parameters are expressed with median (with interquartile range).
EGD. For example, EGD is contraindicated in certain clinical conditions including esophageal perforation, and epiglottic or supraglottic burns with edema. Some investigators claimed that EGD should not be performed on all patients with caustic ingestion, because 10~30% of such ingestions did not induce any gastrointestinal injury. Thus, hematological parameters may be valuable as prognostic markers by virtue of their simplicity and ease of calculation.

A chemical esophageal burn is a local injury caused by direct contact with caustics. The injury is complicated by generation of reactive oxygen species and lipid peroxidation attributable to that injury and subsequent stricture formation. As leukocyte counts reflect systematic inflammatory processes, early hematological parameters may not be useful predictors of the severity of esophageal burns, which are associated with a localized pathology. In our present study, 6 of 29 patients (20.7%) in the uncomplicated group and 2 of 8 (25%) in the complicated group had severe esophageal burns in the endoscopic evaluation. We examined the prognostic utilities of five hematological parameters in the context of esophageal burn severity; none predicted severity, in agreement with data of a previous study in which leukocyte counts did not predict esophageal burns of grade 2B or greater.

Our study had several limitations. First, this was a retrospective single-center work and the results cannot be generalized. Moreover, complicated cases were relatively few in number, and the significance of parameters associated with each complication could not be assessed. Second, although CBC data were obtained within 24 h after ingestion, variation in the time interval between caustic ingestion and blood testing may have affected the results. Third, although hematologic parameters might be influenced by underlying medical conditions, we did not analyze their effect. Lastly, although esophageal injury may be affected by several factors including pH, the quantity and/or concentration of caustic, and the intentionality of ingestion, we could not consider such factors due to the scarce information from medical records. Notwithstanding these limitations, this is the first study to evaluate various hematological parameters in terms of predicting development of complications after caustic ingestion. Further prospective multicenter studies with larger numbers of cases are needed to confirm the predictive abilities of the parameters herein identified.

**Conclusion**

We found that patients developing complications after caustic ingestion had higher leukocyte and neutrophil counts, and NLRs. Similar findings were made in the subset of patients who ingested alkali. Leukocyte counts, neutrophil counts, and the NLR measured within 24 h after caustic ingestion might be useful markers predicting esophageal stricture or mortality.

**REFERENCES**


