THE POSSIBLE LINK BETWEEN EOSINOPHILIC ESOPHAGITIS AND CAUSTIC-INDUCED ESOPHAGITIS: A PROSPECTIVE STUDY IN THE POISON CONTROL CENTER OF AIN SHAMS UNIVERSITY HOSPITALS

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ABSTRACT

Background: Corrosive ingestion is a common health problem in developing countries. Previous case reports suggested possible association between caustic injury of the esophagus and eosinophilic esophagitis (EoE). **Aim of the work:** This study aimed to explore the immunological mechanisms underlying caustic-induced esophagitis, particularly the role of IgE and eosinophilic responses and thus, identify individuals who may benefit from targeted treatments, such as immunomodulatory or anti-inflammatory therapies. **Patients and methods:** This prospective study included patients with corrosive ingestion admitted to the Poison Control Center of Ain Shams University Hospitals between July and December 2022. Investigations included complete blood count, serum IgE, serum cortisol, C-reactive protein (CRP), and alpha-1 antitrypsin (AAT), with blood samples collected within 24 hours and repeated at 72 hours following ingestion. **Results:** Thirty children were enrolled and categorized into stricture and non-stricture groups. A significant rise in serum IgE, eosinophil count, AAT was observed in the second sample compared to the first. High levels of IgE, AAT and CRP were significantly associated with the development of esophageal strictures. **Conclusion:** This study concluded that elevated IgE levels following caustic ingestion, along with their association with the development of esophageal strictures, may suggest an immune based mechanism underlying caustic injury-induced strictures. Identifying this mechanism could open avenues for targeted therapeutic approaches, such as the early use of anti-IgE therapies to enhance patient outcomes and reduce the risk of long-term complications.

Keywords: *Caustic; Injury; Eosinophilic Esophagitis; Esophageal Stricture; IgE.*

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INTRODUCTION

Corossive ingestion remains a major health concern in developing countries, with serious upper gastrointestinal tract injury. It causes esophageal and gastric burns leading to acquired motility disorders or esophageal strictures. These strictures result in permanent disability and are associated with severe consequences, including feeding difficulties, growth retardation, and nutritional deficits ***(Abbasi et al., 2023)***.

Researchers have primarily focused on understanding the pathophysiology and treatment of esophageal burns caused by corrosive injury. However, the role of immune responses in the development of these injuries is not well-documented. Of particular interest, eosinophilic esophagitis (EoE), has been suggested in case reports as a potential contributor to esophageal injury following caustic ingestion ***(Kozyk et al., 2023; Predescu et al., 2024)***.

Eosinophilic esophagitis is characterized clinically by esophageal dysfunction, including dysphagia, and histologically by dense eosinophilic infiltration of the esophageal mucosa ***(Low and Dellon, 2024)***. The mechanisms underlying eosinophilic recruitment to the esophagus is most commonly triggered by dietary antigens, but other stimuli, including infections, drugs, and esophageal injury from caustic agents, have been implicated ***(Kozyk et al., 2023)***.

It is hypothesized that caustic injury may disrupt the esophageal epithelial barrier triggering pleiotropic eosinophils to migrate to esophageal mucosa initiating an immune cascade that include thymic stromal

lymphopoietin (TSLP), interleukin-5 (IL-5), and interleukin-13 (IL-13). These cytokines facilitate eosinophilic infiltration and inflammation, which may play a key role in the progression and chronicity of esophageal injury or breakdown of the esophageal mucosal barrier by the caustic material, which enables food antigens to trigger an immune response resulting in EoE ***(Votto et al., 2020; Khokhar et al., 2022; Kozyk et al., 2023)***.

Diagnosing EoE typically requires endoscopic evaluation and histological analysis of biopsy specimens. However, emerging evidence suggests that peripheral blood biomarkers, such as eosinophil counts, total IgE levels, and inflammatory markers like C-reactive protein (CRP), may offer additional diagnostic value and help assess disease activity .Endoscopic examination is an invasive procedure, and repeated evaluations to assess disease activity are challenging ***(Rodrigo-Muñoz et al., 2021)***.

THE AIM OF THE WORK

This study aimed to explore the immunological mechanisms underlying caustic-induced esophagitis, particularly the role of IgE and eosinophilic responses and thus, identify individuals who may benefit from targeted treatments, such as immunomodulatory or anti-inflammatory therapies.

PATIENTS AND METHODS

Study Design and Setting

This prospective observational study was conducted at the Poison Control Center of Ain Shams University Hospitals (PCC-ASUH). It included patients diagnosed with corrosive ingestion who were admitted during the study period.

Study population:

Inclusion criteria

Patients were eligible for inclusion if they were admitted to PCC-ASUH with a diagnosis of corrosive ingestion during the study period. The diagnosis was established based on a reported history of corrosive substance ingestion and clinical manifestations such as vomiting, hematemesis, oropharyngeal burns, lip edema, dysphagia, epigastric pain, drooling, or respiratory distress.

Exclusion criteria

The following patients were excluded from the study:

- Patients with delay time more than 24 hours.
- Asymptomatic patients
- Patients with history of allergic disease.
- Patients with known diagnosis of any gastrointestinal inflammatory condition.

Patient grouping and follow up

Patients meeting the selection criteria were followed up in the outpatient clinic for a period of three weeks. During this period, the development of esophageal strictures was assessed, defined as the presence of dysphagia confirmed by barium swallow studies. Any complications arising during the follow-up were documented, along with patient outcomes.

Study tools

Data collection

A structured data sheet was used to collect detailed information, including:

- Demographic Data: Age and sex.
- Intoxication and Clinical Data:

Type of corrosive agent (acidic or alkaline).

Symptoms reported before and after admission to PCC-ASUH.

Clinical findings from general and systemic examinations, including gastrointestinal, cardiovascular, and respiratory systems, performed upon admission and during hospitalization.

Investigations:

Laboratory Tests

Two venous blood samples were collected from each patient: one within 24 hours of admission and the second 72 hours after ingestion, at 9:00 AM each time. Each blood sample was divided into two parts: one anticoagulated with EDTA for complete blood count (CBC) analysis and the other placed in a dry centrifuge tube, allowed to clot, and centrifuged for serum separation. Serum samples were analyzed for IgE, cortisol, C-reactive protein (CRP), and alpha-1 antitrypsin (AAT).

Chemicals and Reagents:

CBC: Performed using a Sysmex XN-1000 automated hematology analyzer, with confirmation by blood film examination.

Serum IgE: Measured by immunoassay using the Human IgE Simple Step ELISA® Kit (ab195216) and BioTek ELISA reader.

Serum Cortisol: Assessed via immunoassay using the AccuDiag™ Cortisol ELISA Kit and BioTek ELISA reader.

CRP: Measured semi-quantitatively using the Spinreact CRP-Latex Slide Agglutination test.

AAT: Determined using an immunoturbidimetric method with the K-assay Alpha-1 Antitrypsin ELISA Kit (KAI-001).

Radiological Investigations:

A barium swallow study was performed to confirm the presence of strictures, identified as esophageal irregularities characterized by eccentric narrowing, indicative of asymmetric scarring ***(Rossero et al., 2024)***.

Ethical Considerations

Ethical approval was obtained from the Ain Shams University Ethical Committee (*Approval number: FMASU R 96/2022*). Written informed consent was obtained from all patients or their legal guardians, ensuring confidentiality and anonymity of participant data.

Data Management and statistical tools

Sample Size Calculation

The sample size was calculated using PASS software (version 11), with a power of 80%, alpha error of 5%, and reference to prior research ***(Kim et al., 2015)***, which reported an AUROC of 0.819 for predicting complications from leukocyte count. A minimum sample size of 30 patients was deemed sufficient.

Statistical Analysis:

Data were collected, reviewed, and analyzed using IBM SPSS Statistics (version 23).Quantitative data were presented as means and standard deviations for parametric data or as medians and interquartile ranges (IQRs) for non-parametric data. Qualitative data were presented as frequencies and percentages Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also qualitative variables were presented as number and percentages. The comparison between groups with qualitative data was done by using Chi-square test. The comparison between two independent groups with quantitative data and parametric distribution were done by using Independent t-test. While with non-parametric distribution was done using Mann-Whitney test. Also, the comparison between two paired groups with quantitative data and parametric distribution were done by using paired t-test while with non-parametric distribution was done using Wilcoxon Rank test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of <0.05.

RESULTS

This prospective study was conducted at the PCC-ASUH during the period from July 2022 till December 2022. Thirty children aged ≤ 5 years with corrosive ingestion were enrolled in the study according to the inclusion and exclusion criteria**.** The selected patients were followed at the outpatient clinic for three weeks and were divided according to presence or absence of stricture into; stricture group included 12 cases and non-stricture group included 18 cases.

The baseline characteristics of studied patients are listed in **Table (1)**. There was a significant difference between both groups as regards vomiting and dysphagia. Hematemesis occurred in 58.3% of stricture group while none of non-stricture group suffered from hematemesis and this difference was highly significant.

Table (2) shows the laboratory parameters of the studied patients were compared between two time points: the first sample, collected within 24 hours of corrosive ingestion, and the second sample, collected at 72 hours. A significant rise in serum IgE and AAT levels was observed in the second sample compared to the first. Additionally, eosinophil count, lymphocyte count, monocytes significantly increased in the second sample. Although CRP levels increased in the second sample, this rise was not statistically significant. When comparing biomarkers between the stricture and non-stricture groups at the two time points as shown in tables 3 and 4; certain parameters stood out. High levels of AAT and CRP measured within the first 24 hours were significantly associated with the development of strictures, as these

markers were significantly higher in the stricture group compared to the non-stricture group. However, no significant differences were observed between the two groups for other parameters measured at this time point. At 72 hours, serum IgE and cortisol levels were significantly higher in the stricture group compared to the non-stricture group. CRP levels continued to rise at 72 hours and remained significantly higher in the stricture group compared to the non-stricture group. Additionally, metamyelocytes and band forms were elevated in the stricture group at at 72 hours, while no significant differences were found in TLC or segmental neutrophils between the two groups.

Table (1): Demographic data and clinical characteristics of the patients groups.

Parameter		Overall patients No:30	Non-stricture No. = 18	Stricture No. = 12	Test value	P-value	Sig.
Age (years)	Mean ± SD	2.56 ± 1.15	2.14± 0.16	2.62± 0.2	-9.41¢	0.364	NS
Sex	Female	13 (43.3%)	9 (50.0%)	4 (33.3%)	0.814*	0.367	NS
	Male	17 (56.7%)	9 (50.0%)	8 (66.7%)			
Type of corrosive	Acid	12 (40.0%)	7 (38.9%)	5 (41.7%)	0.023*	0.879	NS
	Alkali	18 (60.0%)	11 (61.1%)	7 (58.3%)			
Vomiting	No	12 (40.0%)	10 (55.6%)	2 (16.7%)	4.537*	0.033	S
	Yes	18 (60.0%)	8 (44.4%)	10 (83.3%)			
Hematemesis	No	23 (76.7%)	18 (100.0%)	5 (41.7%)	13.696*	<0.001	HS
	Yes	7 (23.3%)	0 (0.0%)	7 (58.3%)			
Dysphagia	No	13 (43.3%)	11 (61.1%)	2 (16.7%)	5.792*	0.016	S
	Yes	17 (56.7%)	7 (38.9%)	10 (83.3%)			
Respiratory distress	No	26 (86.7%)	17 (94.4%)	9 (75.0%)	2.356*	0.125	NS
	Yes	4 (13.3%)	1 (5.6%)	3 (25.0%)			
Shock	No	26 (86.7%)	17 (94.4%)	9 (75.0%)	2.356*	0.125	NS
	Yes	4 (13.3%)	1 (5.6%)	3 (25.0%)			
Hospital stay duration (days)	Median (IQR)	4 (3 – 7)	3.5 (3 – 4)	7 (4 – 10)	-2.916≠	0.004	NS
	Range	2 – 17	2 – 10	3 – 17			
Site of admission	Inpatient wards	20 (66.7%)	16 (88.9%)	4 (33.3%)	9.067*	0.002	HS
	Intensive care unit	10 (33.3%)	2 (11.1%)	8 (66.7%)			

*P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant *: Chi-square test; ≠: Mann-Whitney test ¢:Student t test*

Table (2): Comparison between first and second samples of all patients regarding the studied laboratory parameters.

Laboratory parameters		All Patients 1st sample	All Patients 2nd sample	Difference Mean ± S.E	Test value	P-value	Sig.
IgE (IU/ml)	Median (IQR)	23.25 (16.7 – 34)	31.05 (20 – 97.4)	19.04 ± 6.93	-3.990≠	0.000	HS
	Range	4.4 – 141.6	4.7 – 190				
Cortisol (ug/dl)	Median (IQR)	19.75 (12 – 28)	17.95 (11 – 22)	-3.88 ± 2.15	-1.975≠	0.048	S
	Range	6.2 – 65.9	4.8 – 52.2				
Alpha1 antitrypsin (mg/dl)	Mean ± SD	169.70 ± 38.78	205.77 ± 45.05	36.07 ± 4.62	7.800•	0.000	HS
	Range	112 – 250	127 – 280				
C-reactive protein (mg/L)	Median (IQR)	9 (0 – 24)	15 (6 – 32)	8.20 ± 5.23	-1.341≠	0.180	NS
	Range	0 – 96	0 – 96				
Total leucocytic count (number/mm3)	Median (IQR) Range	10375 (8200 – 13950) 3700 – 27800	8100 (6200 – 11100) 3600 – 12500	-2985.33 ± 894.48	-3.735≠	0.000	HS
Segmental (%)	Median (IQR) Range	49 (37 – 59) 21 – 75	41 (34 – 51) 1 – 67	-9.57 ± 3.21	-2.717≠	0.007	HS
Band (%)	Median (IQR)	19 (8 – 24)	14 (8 – 18)	-3.67 ± 2.19	-2.049≠	0.041	S
	Range	0 – 41	1 – 42				
Eosinophil (%)	Median (IQR)	0 (0 – 1)	1 (0 – 4)	1.45 ± 0.43	-2.988≠	0.003	HS
	Range	0 – 5	0 – 10				
Basophil (%)	Median (IQR)	0 (0 – 0)	0 (0 – 0)	0.10 ± 0.15	-0.604≠	0.546	NS
	Range	0 – 2	0 – 3				
Lymphocytes (%)	Median (IQR)	25 (13 – 36)	33.5 (27 – 41)	10.37 ± 2.63	-3.921≠	0.000	HS
	Range	3 – 55	8 – 67				
Monocyte (%)	Median (IQR)	5 (3 – 7)	7 (4 – 8)	1.03 ± 0.61	-2.017≠	0.044	S
	Range	0 – 18	0 – 11				
Metamelocytes (%)	Median (IQR) Range	0 (0 – 2) 0 – 5	0.5 (0 – 1) 0 – 5	-0.10 ± 0.35	-0.315≠	0.753	NS

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant •: Paired t-test; ≠: Wilcoxon Ranks test.

Table (3): Comparison between stricture group and non-stricture group regarding studied laboratory parameters measured within 24 hours post corrosive ingestion.

1st sample within 24 hours		Non- stricture No. = 18	Stricture No. = 12	Test value	P-value	Sig.
IgE (IU/ml)	Median (IQR)	22.5 (16.7 – 25)	30.85 (17.45 – 105.3)	-1.821≠	0.069	NS
	Range	4.4 – 88.5	11.4 – 141.6			
Cortisol (ug/dl)	Median (IQR)	15 (9.8 – 27.3)	24.7 (17.65 – 31.45)	-1.546≠	0.122	NS
	Range	6.4 – 65.9	6.2 – 41.5			
Alpha1 antitrypsin (mg/dl)	Mean ± SD	150.78 ± 25.83	198.08 ± 38.32	-4.051•	0.000	HS
	Range	112 – 218	140 – 250			
C-reactive protein (mg/L)	Median (IQR)	0 (0 – 12)	24 (12 – 48)	-2.838≠	0.005	HS
	Range	0 – 48	0 – 96			
Total leucocytic count (number/mm^3)	Median (IQR)	10050 (8200 – 12900)	10475 (9025 – 16700)	-0.932≠	0.352	NS
	Range	3700 – 16000	5700 – 27800			
Segmental (%)	Median (IQR)	48.5 (37 – 56)	52 (37 – 66.5)	-0.614≠	0.539	NS
	Range	25 – 73	21 – 75			
Band (%)	Median (IQR)	12.5 (4 – 23)	21 (16.5 – 25.5)	-1.568≠	0.117	NS
	Range	0 – 41	8 – 39			
Eosinophil (%)	Median (IQR)	0 (0 – 1)	0 (0 – 1.5)	-1.066≠	0.287	NS
	Range	0 – 2	0 – 5			
Basophil (%)	Median (IQR)	0 (0 – 0)	0 (0 – 0)	-0.430≠	0.667	NS
	Range	0 – 2	0 – 2			
Lymphocytes (%)	Median (IQR)	26.5 (15 – 41)	19.5 (9.5 – 29)	-1.717≠	0.086	NS
	Range	4 – 55	3 – 33			
Monocyte (%)	Median (IQR)	5 (2 – 6)	3.5 (3 – 7)	-0.150≠	0.881	NS
	Range	0 – 10	1 – 18			
Metamyelocyte(%)	Median (IQR)	0 (0 – 1)	1 (0 – 2)	-1.063≠	0.288	NS
	Range	0 – 5	0 – 5			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant •: Independent t-test; ≠: Mann-Whitney test

Table (4): Comparison between stricture group and non-stricture group regarding studied laboratory parameters measured at 72 hours post corrosive ingestion.

2nd sample at 72 hours		Non- stricture No. = 18	Stricture No. = 12	Test value	P-value	Sig.
IgE (IU/ml)	Median (IQR)	26 (16.2 – 53)	95.55 (31.05 – 132.65)	-2.710≠	0.007	HS
	Range	4.7 – 107.6	10.8 – 190			
Cortisol (ug/dl)	Median (IQR)	16.45 (12 – 21)	19.35 (8.1 – 23.7)	-4.520≠	0.000	HS
	Range	5 – 52.2	4.8 – 28			
Alpha1 antitrypsin (mg/dl)	Mean ± SD	182.28 ± 38.81	241.00 ± 27.67	-0.318•	0.751	NS
	Range	127 – 259	187 – 280			
C-reactive protein (mg/L)	Median (IQR)	6 (6 – 24)	24 (18 – 48)	-2.533≠	0.011	S
	Range	0 – 96	6 – 96			
Total leucocytic count (number/mm^3)	Median (IQR)	7900 (6200 – 11100)	8750 (6050 – 10550)	-0.297≠	0.767	NS
	Range	3600 – 12500	4350 – 12000			
Segmental (%)	Median (IQR)	41 (38 – 52)	40.5 (30 – 48.5)	-0.360≠	0.719	NS
	Range	7 – 67	1 – 60			
Band (%)	Median (IQR)	11.5 (7 – 15)	18 (13.5 – 26)	-2.631≠	0.009	HS
	Range	1 – 19	6 – 42			
Eosinophil (%)	Median (IQR)	1 (0 – 2)	2 (0 – 8)	-0.756≠	0.449	NS
	Range	0 – 5	0 – 10			
Basophil (%)	Median (IQR)	0 (0 – 0)	0 (0 – 1)	-1.174≠	0.240	NS
	Range	0 – 1	0 – 3			
Lymphocytes (%)	Median (IQR)	35 (30 – 44)	31.5 (23 – 36.5)	-1.675≠	0.094	NS
	Range	22 – 67	8 – 65			
Monocyte (%)	Median (IQR)	7 (4 – 8)	6.5 (3.5 – 8)	-0.021≠	0.983	NS
	Range	0 – 8	1 – 11			
Metamyelocyte(%)	Median (IQR)	0 (0 – 1)	1 (0.5 – 3)	-2.575≠	0.010	S
	Range	0 – 3	0 – 5			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant •: Independent t-test; ≠: Mann-Whitney t.

DISCUSSION

Caustic injury which affects mainly the esophageal tissue is one of the serious emergencies encountered in the emergency ward. Esophageal stricture is a frequent complication of corrosive ingestion and can be challenging to manage in some cases ***(Manto et al., 2022)***.

Given the need for effective medical interventions to prevent or mitigate this complication and considering reports suggesting a possible association between caustic injury and eosinophilic esophagitis, this study aimed to explore the immunological mechanisms underlying caustic-induced esophagitis, particularly the role of IgE and eosinophilic responses and thus, identify individuals who may benefit from targeted treatments, such as immunomodulatory or anti-inflammatory therapies.

This study investigated patients with corrosive ingestion admitted to the PCC-ASUH between July 2022 and December 2022.

Thirty children aged less than 5 years with corrosive ingestion were enrolled in the study and they were matching the inclusion criteria and were stratified according to the presence or absence of esophageal strictures.

Patients with strictures were more likely to experience vomiting, hematemesis, and dysphagia compared to those without strictures. ***Uygun and Bayram (2020)*** indicated that experiencing prolonged dysphagia and drooling for 12 to 24 hours could be a predictor of esophageal scar formation. Similarly, ***Gharib et al. (2016)*** observed that symptoms such as hematemesis, vomiting, dysphagia, and drooling following caustic ingestion were linked to a higher likelihood of complications and the development of esophageal stricture.

Interestingly, although statistically non-significant, but the number of male patients in the current study who developed esophageal strictures were double the number of females (8 versus 4), while there was equal distribution between both sex in the non-stricture group (9 of each sex). ***Davis and Rothenberg (2016)*** and ***Dhar et al. (2022)*** reported that EoE is seen more in males than in females, and this is the case in our patients group with esophageal stricture.

In the current study, laboratory investigations were done for patients within 24 hours of admission and repeated after 72 hours. Comparing the findings of the two specimens, IgE levels, were found to be significantly higher in the 2nd sample taken after 72 hours compared to the 1st sample. High levels of IgE are reportedly present in immune-mediated reactions ***(Ramirez et al., 2018)***. Accordingly, patients in the current study started to have a recognizable immune reaction 72 hours after caustic injury as indicated by rising level.

Both caustic injury and EoE are characterized by esophageal inflammation and tissue remodeling resulting in fibrosis and esophageal strictures ***(Medina et al., 2021; Broderick et al., 2023)***. Our findings support the hypothesis that an immune-mediated response, particularly involving IgE, is involved in caustic-induced esophagitis. Similarly, previous studies have demonstrated elevated serum IgE levels in patients with EoE ***(Dellon et al., 2012)***.

Elevated IgE levels may serve as an early indicator of a heightened immune response, reflecting a potential role in esophageal remodeling and stricture formation ***(Khokhar et al., 2022)***. This aligns with the hypothesis that caustic injuries may trigger IgE mediated inflammatory condition and linking eosinophilic inflammation to esophageal stricture formation even in non-EoE conditions ***(Straumann et al. 2016)***.

The present study also revealed that IgE levels within 24 hours were slightly higher in the stricture group compared to the non-stricture group. Although this difference was not statistically significant, yet in the second sample taken at 72 hours, IgE levels were significantly higher in the stricture group compared to the non-stricture group. Accordingly, this study suggests a correlation between IgE levels and the severity of esophageal injury.

This finding is of particular importance as it suggests a possible dose-response relationship between the immune response and esophageal injury. A stronger immune response, as indicated by higher IgE levels, may result in

increased inflammation, ultimately leading to more severe esophageal injury ***(Dellon et al., 2012; Simon et al., 2014)***.

In the same aspect, the eosinophil count was also checked. It was found a significantly higher eosinophil count in the 2nd sample taken at 72 hours compared to the 1st sample within 24 hours. Eosinophils are known to increase in cases of allergic reactions ***(Sharma et al., 2019)***. The change in eosinophil percentages between the first and second samples highlights the dynamic inflammatory response following caustic injury. However, no statistically significant difference was detected between stricture group and non-stricture group for both samples.

Taraghikhah et al. (2020) recorded a relation between the increase in serum eosinophil count and the occurrence of EoE, however, they concluded that the increase was inadequate to provide utility in diagnosing EoE. Other studies reported an association between the degree of eosinophilic infiltration in the esophagus and the severity of esophageal injury in EoE ***(Dhar et al., 2022; Dellon et al., 2014)***.

Furthermore, although eosinophilic infiltration of the esophageal mucosa is the hallmark of eosinophilic esophagitis (EOE), there have been reports of cases without esophageal eosinophilia. ***Straumann et al. (2016)*** identified patients with EOE-like symptoms that were responsive to corticosteroids, but without tissue eosinophilia.

Fujiwara et al. (2020) suggest an explanation that proton pump inhibitor treatment in EOE patients, a treatment for caustic patients as well, may mask both the endoscopic and histologic signs of the condition.

However, the absence of a significant increase in eosinophils in patients with strictures in the present study raises questions about the precise role of eosinophils in these cases and their relationship to severity of the injury and development of strictures.

Serum AAT levels and CRP were higher in second sample compared to first sample while cortisol level was significantly higher in the first sample compared to second sample taken at 72 hours .

Cortisol is known to increase in acute phase response to inflammation and injury ***(Janciauskiene et al., 2018)***.

The increase in cortisol levels reflects a stress response to the caustic-induced esophageal injury, as it is a known stress hormone that plays a role in regulating inflammation ***(Sapolsky et al., 2000)***.

The observed increase in AAT levels is an indicative of an acute phase response, as AAT is a well-established acute phase reactant produced by the liver in response to inflammation that regulates inflammatory processes by inhibiting enzymes like kallikrein 5 (KLK5) and proteinase-activated receptor 2 (PAR2), which are implicated in epithelial barrier dysfunction and inflammation. This elevation may reflect the body's attempt to counteract increased protease activity and maintain tissue integrity and CRP is a known marker of inflammation and has been associated with various inflammatory conditions ***(Pepys and Hirschfield, 2003; McCarthy et al., 2014)***. This finding suggests the presence of a systemic inflammatory response in caustic-induced esophagitis.

In this study also revealed that AAT and CRP were significantly higher in the stricture group than in the non-stricture group at 24 hours while at 72 hours, cortisol and CRP were significantly higher in stricture group compared to non-stricture group. Similar Findings were reported in other studies where ***Saleh et al. (2024)*** recorded an increase in CRP in patients with corrosive ingestion. ***Oreby and El-Sarnagawy (2017)*** also reported an increase in CRP in their study and correlated its high level to poor outcome in patients with corrosive ingestion.

Metamyelocytes and band counts were significantly higher in the stricture group when compared to non-stricture group in the second sample taken at 72 hours These findings are consistent with previous studies that have reported left shift in patients with severe corrosive injuries Metamyelocytes and band cells; the precursors for mature neutrophils; are immature white blood cells that are released into the bloodstream during acute infections and ongoing inflammatory

process ***(Mare et al., 2015; Park, 2014; Bongers et al., 2021)***.

These findings further support the involvement of an immune-mediated response in the pathogenesis of caustic-induced esophagitis.

The findings of the current study have several clinical implications. The increased serum levels of cortisol, AAT, and CRP along with elevated counts of metamyelocytes and band cells support the presence of a systemic inflammatory response in the pathogenesis of caustic-induced esophagitis. This response was more pronounced in patients who developed esophageal strictures. Furthermore, the significant changes in the laboratory parameters over time also indicate that disease progression.

The increased serum IgE levels, CRP as well as increase of eosinophilic count over time and a correlation between IgE levels and severity of esophageal injury suggest a possible immune-mediated mechanism probably involving IgE and raise the possibility that a subset of patients with caustic injury may develop an EoE-like inflammatory profile, predisposing them to long-term esophageal remodeling. This awareness can help clinicians to tailor treatment strategies, such as the use of corticosteroids either swallowed topical or intralesional injection, to manage the immune-mediated response and potentially mitigate esophageal injury in selected patients.

Clinicians must consider monitoring closely male atopic patients who suffered caustic injury as they are more prone to develop IgE mediated diseases such as EoE ***(Greuter et al., 2020; Sarma et al., 2021; Davis and Rothenberg, 2016)***.

In addition, using milk as an antidote or a diluent whose effectiveness was never proven might trigger the allergic reaction in the exposed areas of the injured esophagus and increase the risk of developing EoE in susceptible individuals ***(Contini and Scarpignato, 2013; Kaymak et al., 2022; Dhar et al., 2022)***.

Accordingly, the use of milk and other foods consumed by caustic injured patients might need to be re-evaluated.

Although this study did not confirm EoE as an underlying mechanism of caustic-induced esophageal injury due to the lack of histopathological assessment, it emphasizes the importance of monitoring serum IgE levels as a marker of disease severity. This could help guide personalized treatment strategies that address both the severity and the immune nature of the disease.

Elevated IgE and eosinophilia in the context of caustic esophagitis raise the possibility of progression to EoE, particularly in atopic individuals. Chronic mucosal damage from caustic injury may predispose patients to allergic sensitization, leading to the development of EoE over time ***(Votto et al., 2020)***.

Chronic esophageal inflammation, whether caused by caustic injury or immune-mediated mechanisms, is a recognized risk factor for esophageal carcinoma. ***Uchida et al. (2024)*** analyzed the risk of Barrett's esophagus in patients with EoE, noting that Barrett's esophagus, a precursor to esophageal adenocarcinoma, was more prevalent in EoE cases. Their findings suggest that Barrett's esophagus could serve as a mediator for the increased cancer risk in these patients.

In the same aspect, evidence from ***Muller et al. (2020)*** indicates that Barrett's esophagus may also develop as a long-term consequence of caustic-induced injury.

Furthermore, the findings lay the groundwork for future research to explore the relationship between caustic injury and EoE using endoscopic and histopathological evaluations, as well as the potential role of anti-IgE medications in specific patient populations.

Limitatations of the study

This study has several limitations. The sample size was relatively small, and microscopic evaluation of esophageal tissue was not performed, limiting the ability to confirm the role of EoE.

Future studies with larger cohorts and histopathological assessments are needed to validate these findings.

Additionally, long-term outcomes of caustic-induced esophagitis were not evaluated, which could provide further insights into the potential link between EoE and esophageal injury.

CONCLUSION

This study highlights the potential utility of non-invasive biomarkers, particularly IgE, eosinophilic count, CRP and AAT in understanding the relationship between caustic injury and EoE-like esophagitis. The findings provide a foundation for further investigation into targeted interventions aimed at reducing inflammation and preventing esophageal stricture formation

Data availability:

The datasets generated and analyzed during the current study are available from the corresponding author upon request.

Conflicts of Interest None declared.

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REFERENCES

1. **Abbasi, H.; Aftab, W.; Shahid, S. et al. (2023):** Original article. *Life Sci.,4(1):164-168*. DOI:10.37185/LnS.1.1.287
2. **Bongers, S. H.; Chen, N.; Van Grinsven, E. et al. (2021):** Kinetics of neutrophil subsets in acute, subacute, and chronic inflammation. *Front. Immunol., 12: 674079.* DOI:10.3389/fimmu.2021.674079
3. **Broderick, R. C. and Ravi, K. (2023):** Management of caustic injury and esophageal stricture. In the AFS textbook of foregut disease, *pp. 375-384. Cham: Springer International Publishing.*
4. **Chirica, M.; Bonavina, L.; Kelly, M. D. et al. (2015):** Caustic ingestion. *Lancet, 386(10000):1720–1731.*
5. **Contini, S. and Scarpignato, C. (2013):** Caustic injury of the upper gastrointestinal tract: A comprehensive review. *World J. Gastroenterol.,19(25):3918–3930.* DOI:10.3748/wjg.v19.i25.3918
6. **Davis, B. P. and Rothenberg, M. E. (2016):** Mechanisms of disease of eosinophilic esophagitis. *Ann. Rev. Pathol. Mech. Dis.,11: 365–393.*
7. **Dellon, E. S.; Speck, O.; Woodward, K., et al. (2012):** Diagnostic utility of peripheral eosinophil and IgE levels for diagnosis of eosinophilic esophagitis. *Amer. J. Gastroenterol.,107: S10.*
8. **Dellon, E. S.; Kim, H. P.; Sperry, S. L. et al. (2014):** A phenotypic analysis shows that eosinophilic esophagitis is a progressive fibrostenotic disease. *Gastrointest. Endo., 79(4): 577–585.*
9. **Dhara, A.; Haboubi, H. N.; Attwood, S. E. et al. (2022):** British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. *Gut., 71(8): 1459–1487.* DOI:10.1136/gutjnl-2022-327326
10. **Fujiwara, Y. (2020):** Symptom-based diagnostic approach for eosinophilic esophagitis. *J. Gastroenterol., 55(9): 833–845.* DOI: 10.1007/s00535-020-01701-y
11. **Gharib, B.; Mohammadpour, M.; Yaghmaie, B. et al. (2016):** Caustic agent ingestion by a 1.5-year-old boy. *Acta Medica Iranica, 54(7): 465-470.*
12. **Greuter, T.; Hirano, I. and Dellon, E. S. (2020):** Emerging therapies for eosinophilic esophagitis. *J. Allerg. Clin. Immunol., 145(1), 38–45.* DOI:10.1016/j.jaci.2019.10.027.
13. **Janciauskiene, S.; Wrenger, S.; Immenschuh, S. et al. (2018):** The multifaceted effects of alpha1-antitrypsin on neutrophil functions. Front. Pharmacol., 9: 341. DOI: 10.3389/fphar.2018.00341
14. **Kaymak, T.; Hruz, P. and Niess, J. H. (2022):** Immune system and microbiome in the esophagus: Implications for understanding inflammatory diseases. *FEBS J., 289: 4758–4772.* DOI: 10.1111/febs.16103
15. **Khokhar, D.; Marella, S.; Idelman, G. et al. (2022):** Eosinophilic esophagitis: Immune mechanisms and therapeutic targets. *Clin. Exp. Allerg.,52(10):1142–1156.* DOI: 10. 1111/cea.14196
16. **Kim, J. H.; Park, J. M. and Kim, M. J. (2015):** Hematological parameters predicting complications of caustic ingestion: A retrospective study. Journal of the *Kore. Soci. Emerg. Med.,26(6): 591–597.*
17. **Kozyk, M.; Strubchevska, K.; Kravchenko, Y. et al. (2023):** Eosinophilic esophagitis in the setting of prior caustic ingestion. *Cureus, 15(2): e35536.* DOI: 10.7759/cureus.3553
18. **Le Naouris, P.l Hamy, A.l Lerolle, N. et al. (2017):** Risk factors for symptomatic esophageal stricture after caustic ingestion: A retrospective cohort study. *Dis. Esophagus, 30(6):1–6.* DOI:10.1093/dote/dox029
19. **Low, E. E. and Dellon, E. S. (2024):** Emerging insights into the epidemiology, pathophysiology, diagnostic and therapeutic aspects of eosinophilic oesophagitis and other eosinophilic gastrointestinal diseases.

Aliment. Pharmacol. Therap., 59(3): 22–340.

20. **Mantho, P.; Engbang, J.; Awono, C. et al. (2022):** Caustic esophageal strictures in children: Diagnosis, treatment and evolution in the city of Douala. *J. Surg. Res.,5(3): 486-493.*
21. **Mare, T. A.; Treacher, D. F.; Shankar-Hari, M. et al. (2015):** The diagnostic and prognostic significance of monitoring blood levels of immature neutrophils in patients with systemic inflammation. *Crit. Care, 19(1):57.* DOI:10.1186/s13054-015-0778-z
22. **McCarthy, C.; Saldova, R.; Wormald, M. R. et al. (2014):** The role and importance of glycosylation of acute phase proteins with focus on alpha-1 antitrypsin in acute and chronic inflammatory conditions. *J. Proteome Res.,13(7):3131–3143.* DOI:10.1021/pr500146y
23. **Medina, A. L.; Troendle, D. M. ; Park, J. Y. et al. (2021):** Eosinophilic esophagitis, Barrett's esophagus and esophageal neoplasms in the pediatric patient: a narrative review. *Trans. Gastroenterol. Hepatol.,6:32.*
24. **Methasate, A. and Lohsiriwat, V. (2018):** Role of endoscopy in caustic injury of the esophagus. *World J. Gastroint. Endo.,10(10): 274–282.* DOI:10.4253/wjge.v10.i10.274
25. **Millar, A. J. W.; Numanoglu, A. and Cox, S. (2020):** Caustic injuries of the esophagus. In Puri, P. (Ed.), Pediatric Surgery, pp. 128–1. Springer. DOI:10.1007/978-3-642-38482-0_128-1
26. **Oreby, M. M. and El-Sarnagawy, G. N. (2017):** Correlation of clinical manifestations and C-reactive protein level to patients' outcome in acute corrosive poisoning. *Mansoura J. Forensic Med. Clin. Toxicol.,25(1): 47–57.*
27. **Park, K. S. (2014):** Evaluation and management of caustic injuries from ingestion of acid or alkaline substances. *Clin. Endo.,47(4): 301–307.* DOI:10.5946/ce.47.4.301
28. **Pepys, M. B. and Hirschfield, G. M. (2003):** C-reactive protein: A critical update. *J. Clin. Invest.,111(12):1805–1812.* DOI:10. 1172/JCI18921
29. **Predescu, D. ; Achim, F.; Constantinoiu, S. et al. (2024):** From caustic stenosis to esophageal cancer, a challenging evolution -Narrative review. *Chirurg., 119: 515-532.*
30. **Ramirez, G. A.; Yacoub, M. R.; Ripa, M. et al. (2018):** Eosinophils from physiology to disease: A comprehensive review. *Biomed. Res. Inter.,28: 9095275.* DOI:10.1155/2018/9095275
31. **Rodrigo-Muñoz, J. M.; Gil-Martínez, M.; Sastre, B. and Del Pozo, V. (2021):** Emerging evidence for pleiotropism of eosinophils. *Inter. J. Molec. Sci., 22(13): 7075.*
32. **Rossero Salazar, D. H.; Honnlee, L.; Nguyen, P. H. et al. (2024):** Spatial relationships of oropharyngeal structures during respiration, chewing, and swallowing. *Anat. Record.* DOI: 10.1002/ar.25605
33. **Saleh, B. A.; Abdel Salam, M. E.; Abou Anza, R. E. et al. (2024):** The potential role of procalcitonin compared to C-reactive protein and neutrophil Lymphocyte ratio in prediction of severity and outcomes of acute corrosive ingestion. *Ain Shams J. Forensic Med. Clin. Toxicol.,42(1):35-46.* DOI:10.21608/ajfm.2024.333818
34. **Sapolsky, R. M.; Romero, L. M. and Munck, A. U. (2000):** How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr. Rev.,21(1): 55–89.*
35. **Sarma, M. S.; Tripathi, P. R. and Arora, S. (2021):** Corrosive upper gastrointestinal strictures in children: Difficulties and dilemmas. *World J. Clin. Pediatr.,10(6): 124–136.* DOI:10.5409/wjcp.v10.i6.124
36. **Sharma, M.; Khaitan, T.; Raman, S. et al. (2019):** Determination of serum IgE and eosinophils as a diagnostic indicator in allergic rhinitis. *Ind. J. Otolaryngol., Head Neck Surg.,71(Suppl 3): 1957–1961.* DOI:10.1007/s12070-018-1383-7
37. **Simon, D.; Straumann, A. and Simon, H. U. (2014):** Eosinophilic esophagitis and allergy. *Digest. Dis.,32: 30–33.* DOI: 10. 1159/000357006
38. **Straumann, A.;Blanchard, C.; Radonjic-Hoesli, S. et al. (2016):** A new eosinophilic esophagitis (EoE)-like disease without tissue eosinophilia found in EoE families. *Allergy, 71(6): 889–900.* DOI:10.1111/all.12879.
39. **Taraghikhah, N.; Ashtari, S.; Asri, N. et al. (2020):** An updated overview of spectrum of gluten-related disorders: Clinical and diagnostic aspects. *BMC Gastroenterol.,20:1-12.*
40. **Uchida, A. M.; Schuman, S. S.; Pyne, A. et al. (2024):** Risk of cancer diagnosis in patients with eosinophilic esophagitis using a nationwide Swedish population cohort.

United Euro. Gastroenterol. J. 12(10):1378-1387.

41. **Uygun, I.; Aydogdu, B.; Okur, M. et al. (2012):** Clinico epidemiological study of caustic substance ingestion accidents in children in Anatolia: The DROOL score as a new prognostic tool. *Acta Chirurgica Belgica, 112(5):346-354.*
42. **Vijay Kumar, T. R.; Anil Kumar, G.; Nandeesh, H. P. et al. (2019):** Clinico-endoscopic profile and outcome of corrosive ingestion: A single center experience from a tertiary care hospital in Southern India. Surg. *Gastroenterol. Oncol., 24(4): 191–196.* DOI:10.21614/s
43. **Votto, M.; Marseglia, G.L.; De Filippo, M. et al. (2020):** Early life risk factors in pediatric EoE: could we prevent this modern disease? *Front. Pediatr., 8:263.*

الرابط المحتمل بين التهاب المرئ اليوزيني والتهاب المرئ الناتج عن المواد الكاويه: دراسة مستقبلية بمركزعلاج التسمم بمستشفيات جامعه عين شمس

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الملخص العربى

المقدمة: تناول المواد الكاوية هو مشكلة صحية شائعة في البلدان النامية. أشارت تقارير الحالات السابقة إلى وجود ارتباط محتمل بين إصابة المريء بالمواد الكاوية والتهاب المريء اليوزيني .هدفت هذه الدراسة إلى استكشاف الآليات المناعية الكامنة وراء التهاب المريء الناتج عن الإصابة بالمواد الكاوية، مع التركيز بشكل خاص على دور الغلوبولين المناعيهـ واستجابات اليوزينيات، لتحديد الأفراد الذين قد يستفيدون من علاجات موجهة، مثل العلاجات المناعية أو المضادة للالتهابات

الهدف من الدراسة: هدفت هذه الدراسه الي استكشاف الاليات المناعيه الكامنه وراء التهاب المرئ الناتج عن المواد الكاوية خاصة دور استجابه الغلوبولين المناعي هاء واليوزينات ،وبالتالي تحديد الافراد الذين قد يستفيدوا من علاجات .موجهه مثل علاجات مناعيه او مضادات الالتهاب.

الطرق المستخدمة: شملت هذه الدراسة المستقبلية مرضى تناولوا مواد كاوية وتم إدخالهم إلى مركز السموم الاكلينكي بمستشفيات جامعة عين شمس خلال الفترة من يوليو إلى ديسمبر ٢٠٢٢. وشملت الفحوصات تعداد الدم الكامل، مستويات الغلوبولين المناعي هـ ، الكورتيزول في الدم، بروتين سي التفاعلي، وألفا-١ أنتيتريبسين، مع جمع عينات الدم خلال أول ٢٤ ساعة ثم بعد ٧٢ ساعة من الابتلاع.

النتائج: تم تسجيل ثلاثين طفلًا في الدراسة وتم تصنيفهم إلى مجموعتين: مجموعة المصابين بضيق المريء ومجموعة غير المصابين. لوحظت زيادة كبيرة في مستويات الغلوبولين المناعي هـ ، وعدد اليوزينيات ومستويات وألفا-١ أنتيتريبسين في العينة الثانية مقارنة بالأولى. ارتبطت المستويات المرتفعة من الغلوبولين المناعي هـ ، و بروتين سي التفاعلي، وألفا-١ أنتيتريبسين بشكل كبير بحدوث ضيق المريء.

الخلاصة: خلصت الدراسة إلى أن المستويات المرتفعة من الغلوبولين المناعي هـ بعد تناول المواد الكاوية، بالإضافة إلى ارتباطها بتطور تضيق المريء، قد تشير إلى وجود آلية مناعية كامنة وراء تضيق المريء الناتج عن الإصابة بالمواد الكاوية. قد يساعد تحديد هذه الآلية في فتح آفاق جديدة للعلاجات الموجهة، مثل الاستخدام المبكر للعلاجات المضادة لـ الغلوبولين المناعي هـ لتحسين نتائج المرضى وتقليل خطر حدوث مضاعفات طويلة الأمد.