



Caustic Ingestion in Children: a Systematic Review and Meta-Analysis

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ABSTRACT

Introduction: Caustic ingestion that occurs accidentally is one of the most common problems in children.

Methods: This systematic review has been performed by searching the databases including Science Direct, ProQuest, Google Scholar, and PubMed. A strategic search was performed with keywords including caustic, corrosive, ingestion, and children, and was limited to articles in English and Persian. Data were analyzed using Comprehensive Meta-Analysis2 and PASW Statistics 18.

Results: We selected 64 articles regarding caustic ingestion with a total sample of 11,345 cases. The data analysis indicated a higher consumption in young boys (age range 2.78 (2.02) years (OR=0.53 with a 95% confidence interval of 0.49-0.57 (P=0.08)). The most common caustic substances were household cleaning agents, particularly bleaches and cleaners. Esophageal cancer and death were reported as well as digestive and respiratory complications. Invasive and expensive techniques are frequently used for diagnosis, treatment and follow up.

Conclusion: The results demonstrated that although caustic ingestion is a serious problem among children, it is a preventable and manageable issue. Therefore, appropriate efforts by families, government, factories, health team and media should be made to handle adequately this matter.

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Introduction

Caustic ingestion by children is still a serious medical and social issue.¹ Ingestion of caustic agents leads to injuries in the esophagus, pharynx, larynx, and mouth, which often lead to death or other adverse effects on the gastrointestinal and respiratory tracts.²

Ingestion of caustic agents are frequently reported in children,^{3,4} especially when children start to walk or crawl. Therefore these accidents were considered as one of the main causes of death in children less than 5 years with the peak incidence at 2 years of age.

However, these incidents also were observed in lower than one years old children.⁵ Annually, more than 40,000 cases of caustic ingestion in children are reported in England and Wales.⁶ In Galsya, with a population of half a million children under the age of 14 years, 4.8% of the annual medical service admissions were associated with caustic ingestion in children.⁷ It is still common in children of the United States, despite the declining of caustic ingestion in (5,000 to 15,000 reductions per year), with incidence of 15.8 cases in every 100,000 persons.⁸⁻¹⁰ From 2005 to 2006, 10% of the 51 children admitted

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to the department of pediatrics, Children's hospital of Tabriz, Iran, had stenosis and gastric outlet obstruction following ingestion of caustic agents.¹¹ However, prevalence of these accidents in our area is unknown. In a retrospective study conducted between 2002 and 2004, 74.7% of the 72 children admitted at the department of pediatrics, Lohman Hakim hospital of Iran, were reported to be due to accidental ingestions.¹²

There are more than 500 toxic substances at home that most of them were kept at the kitchen without considering appropriate storing points.⁵ Additionally, most of ingestions are due to consumption of household chemicals, such as detergents and bleaches.^{6,7} On the other hand, the swallowing of these agents could lead harmful health consequences and impose an economic burden for measurement, treatment, follow up and caring.^{6,11,13,14} Esophageal stricture is considered a short-term effect, but esophageal perforation, esophageal obstruction and cancer could be some of the long-term effects of ingestion of caustic agents.¹⁵⁻¹⁷

Although the ingestion of caustic materials is a simple preventable problem, but it has continued in most developing countries.^{2,9} Families, manufacturing, government and health staff have a major role in the control and management of these accidents.^{5,9,18,19} Persist and ongoing communication among these teams could reduce the rate of accidents or modify the course of the disease.^{18,20} The aim of study was to evaluate age distribution, sex ratio type of caustic agents, signs and symptoms, complications, and management of caustic ingestion in children by a systematic review and meta-analysis research method. Also, we are going to determine the maximum events according to age and sex and the adverse agents and toxic effect that utilizing appropriate preventive strategies would be effective against accidental caustic ingestion.

Materials and methods

This study was performed to review the studies on caustic ingestion in children to

determine the prevalence of age, sex ratio, and complications in children. We conducted a systematic review of papers published since 1980, in four phases. These involved planning the search strategy and performing the search, collection of articles and systematic review, evaluation of inclusion and exclusion criteria, and data analysis. These phases are described in the following sections.

In the first step, Springer, Science Direct, ProQuest, Google Scholar, and PubMed search randomly following the PRISMA guidelines was made for articles on caustic ingestion in children. Studies published in English or Persian from 1980 to July 14, 2013 were reviewed. The keywords used were caustic, corrosive, ingestion, and children, and by Medical Subject Headings (Mesh) for medical science databases with the cooperation of a gastroenterology pediatric subspecialist, physiologist, PhD by Research, and clinical librarian. The following search strategy was employed for PubMed:

Caustics" [Pharmacological Action] or "caustics" [MeSH Terms] or "caustics" [All Fields] or "caustic" [All Fields] or "caustics" [Pharmacological Action] or "caustics" [Mesh Terms] or "caustics" [All Fields] or "corrosive" [All Fields] and "eating" [Mesh Terms] or "eating" [All Fields] or "ingestion" [All Fields] and "child" [Mesh Terms] or "child" [All Fields] or "children" [All Fields].

- Focus question:

The focus question was established according to the PICO (population, intervention, comparison, and outcome)

Format: In patients with caustic ingestion in children

- P (population): patients with caustic ingestion in children.

- I (intervention): -

- C (comparison): Age, sex, and complications in children

- O (outcome): Patients who referred to hospital

- Inclusion criteria:

In the second phase, all eligible studies were separately surveyed by two expert appraisers to evaluate article equality, minimize bias, and

to excluded irrelevant studies (e.g., related to adults, swallowing batteries, and drug abuse, which were excluded due to low quality) based on agreement between the appraisers. Related studies were included, and then debatable articles were referred to the third appraiser. Kappa agreement rate was higher than 85%. Finally, kappa agreement was considered as inclusion criterion for the next phase.

- Exclusion criteria:

In the third phase, irrelevant studies, systematic articles, case control articles, cohort articles, clinical trial articles, animal studies, kappa agreement rate less than 84%, duplicated articles, and letters were excluded from the sample. In addition, the articles which obtained manually from the references of the previously selected articles were added to the set. Figure 1 shows the process of manuscripts' selection.

In the fourth phase, all papers were divided in two categories (quantitative and qualitative). The summary of the four phases

are shown in table 1.

The data was summarized in an extraction table using the Microsoft Office Excel software, and were then analyzed using Comprehensive Meta-Analysis (CMA) and PASW Statistics 18 and a meta-analysis was performed to obtain the measure of an overall effect (odds ratio, OR). A forest plot was used to report the results. A forest plot is made up of squares in which each square represents the sample size and the lines beside each square represent the 95% confidence interval for each study. A funnel plot was used for assessment of publication bias. The methods of handling data and statistical methods as fixed or random effects models were used for combining results of studies. The study of heterogeneity was made by I² statistical calculation. I² values of 25%, 50%, and 75% correspond to cut-of points for low, moderate, and high degrees of heterogeneity. If condition was homogeneity, fixed model was used and a heterogeneity condition was used random effects models. The level of significance used in the analysis was 5% ($\alpha=0.05$).

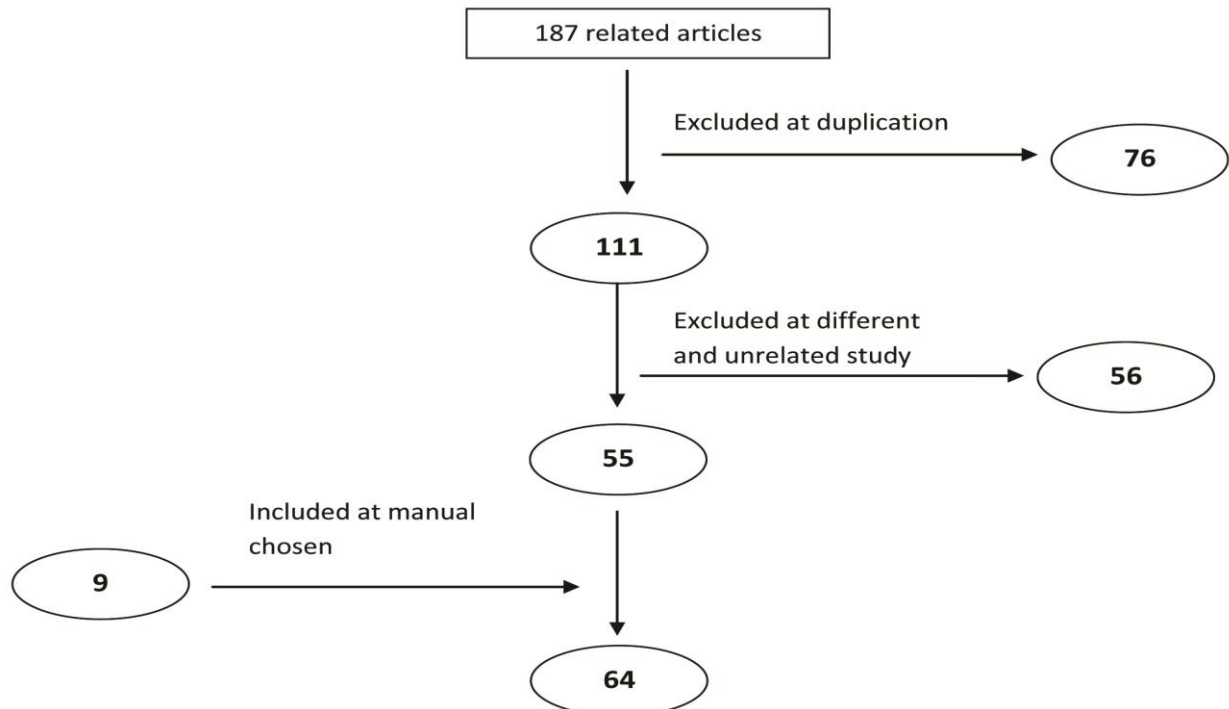


Figure 1. Summary of studies contributing to the Systematic Review

Table 1. Summary of performed process for searching strategy

Phases
Phase 1
Planning of search strategy
Electronic search from databases (Science Direct, ProQuest, Springer, Google Scholar, PubMed)
Selection of related articles based on titles
Phase 2
Collection of articles with full text
Evaluation of quality articles by two appraisers
Exclusion of unrelated studies (related to adults, battery swallowing ,drug abuse, published articles before 1980)
Assessment of articles and referring disputes to the third appraiser
Phase 3
Exclusion of unrelated studies based on the subject, Cohort studies, Case control studies, Clinical trial, Animal studies, Systematic review
Performance of manual research and inclusion of review articles references
Phase 4
Extraction of article information and statistical analysis

Results

A total of 187 studies were identified based on the exclusion and inclusion criteria. Out of them, 76 papers were excluded in Phase 2, and 56 articles in Phase 3. Further, nine manually selected articles were added in Phase 3, leading to the final sample of 64 articles from which data were extracted (Table 2).

From 64 (11,345 participants) articles that were included in our study, 52 articles were cross-sectional studies (81.5%), eight articles were case reports (12.5%), and four articles were case series (6%). Most of the studies were conducted in Turkey with 14 articles (21.8 %).

The sample of children comprised 4,632 boy (55.33%) and 3,756 girl (44.77%). With reference to distribution of gender, based on the results of different studies and the random effect model, we found that the frequency of caustic agent ingestion was more common in boys (42%, 95% CI: 0.29–0.57); however, this difference was not statistically significant. The mean age of the children with reported cases of ingestion was 2.78 (2.02) years (age range: 12 days–10 years).

The mean time of endoscopy after ingestion was 30 hours (range: 1–108 hours).

The most common caustic substance was alkaline, reported in 41.5% patients, followed by acid (30.7%), while most of the cases were exposed to household cleaning agents,

particularly bleaches and cleaners. With reference to industrial agents, the most abused agents were industrial detergents and soda.

Various factors were found to have an impact on the severity of the injuries presented. Most common were those related to the physical characteristics of agents, such as concentration, amount of ingested agent, type of agent, and interval between swallowing and referral to emergency department.

A majority of the patients were symptomatic at admission, and the most common symptoms included gastric, respiratory, and ENT-related symptoms. Vomiting, abdominal pain, dysphagia, respiratory distress, drooling, and burns of the oral cavity were the most frequently observed symptoms (Table 2).

The majority of the lesions observed in digestive, respiratory, and ENT tracts. The injuries of digestive included esophageal damage, nutritional problems, gastro-esophageal reflux, and gastric ulceration, respectively. The injuries of respiratory were aspiration pneumonia, laryngeal sore and mediastinitis. Skin sore, mouth sore, and sore throat were reported as lesions of ENT. Esophageal cancer and even death was also reported in ingested children. The summary of articles based on injuries and complications are shown in table 3.

Table 2. Classification of characteristics of agents, clinical findings, methods of diagnostic and therapeutic, and complications

Subgroup
Type of ingested agents
Household chemicals
Industrial chemicals
Effective factors in presentation of clinical symptoms and complications
The demographic characteristics of the individual
The physical properties of agents
The physical properties of the individual
The manners of consume of agents
Clinical symptoms
Gastrointestinal problems
Respiratory problems
ENT problems
Cardiovascular problems
Neurological problems
Psychological problems
Techniques of diagnosis
Invasive
Non-invasive
Methods of therapeutics
Supportive therapies
Medical therapies
Surgical therapies
Complications
Gastrointestinal complications
Respiratory complications
Renal complications
Hepatic complications
Cardiovascular complications

Table 3. The summary of articles based on injuries and complications

Authors	Location	Injuries	Complications
Mamede R. et al ¹	Brazil	-	Gastrointestinal-death
Turner A. et al ²	England	Gastrointestinal- psychological	-
Lee HJ. et al ³	Korea	Gastrointestinal- respiratory- psychological	-
Bicakci U. et al ⁴	Turkey	Psychological	Gastrointestinal
Stiff G. et al ⁶	Wales	Gastrointestinal- psychological	Respiratory-renal-cardiovascular
Manenti F. et al ⁷	England	-	Gastrointestinal- respiratory
Sawalha AF. et al ⁸	Palestine	Gastrointestinal- psychological – cardiovascular	-
Ekpe EE. et al ⁹	Nigeria	-	Gastrointestinal-death
Arévalo-Silva C. et al ¹⁰	-	Gastrointestinal- respiratory	Gastrointestinal
Temiz A. et al ¹⁵	Turkey	Gastrointestinal- respiratory- psychological	Gastrointestinal- cardiovascular
Mamede RCM. et al ¹⁶	Brazil	-	Gastrointestinal-death
Previtera C. et al ¹⁷	Italy	Gastrointestinal- respiratory- psychological -ENT	Gastrointestinal
Casasnovas AB. et al ¹⁸	Spain	Gastrointestinal- respiratory- psychological	-
Otçu S. et al ²¹	Turkey	-	-
Doğan Y. et al ²²	Turkey	-	Gastrointestinal
Ciftci AO. et al ²³	Turkey	Psychological	-
Pearn J. et al ²⁴	Australia	ENT- psychological	-
Broto J. et al ²⁵	Spain	-	Gastrointestinal

Table 3. The summary of articles based on injuries and complications (continued)

Authors	Location	Injuries	Complications
Ein S H. et al ²⁶	Canada	-	Respiratory-death
Ryan F. et al ²⁷	England	Gastrointestinal	-
Ferguson MK. et al ²⁸	America	Gastrointestinal- respiratory- psychological	Gastrointestinal
Riffat F. et al ²⁹	Australia	Gastrointestinal- psychological	Gastrointestinal
Contini S. et al ³⁰	Italy	Gastrointestinal- respiratory- psychological -ENT	Gastrointestinal
Youn BJ. et al ³¹	Korea	Gastrointestinal- psychological	Gastrointestinal- respiratory
Arici M. et al ³²	Turkey	Gastrointestinal- psychological	-
Melek M. et al ³³	Turkey	Gastrointestinal- respiratory- psychological	Gastrointestinal
Bychkova OV. et al ³⁴	Belarus	Psychological	Gastrointestinal-respiratory
Reith DM. et al ³⁵	Australia	-	Cardiovascular
Kane TD. et al ³⁶	America	Gastrointestinal	Gastrointestinal- respiratory
Pintus C. et al ³⁷	-	-	-
Huang YC. et al ³⁸	Taiwan	Gastrointestinal	Gastrointestinal
Babl FE. et al ³⁹	America	Gastrointestinal- respiratory- psychological	-
Betalli P. et al ⁴⁰	Italy	Gastrointestinal- respiratory- psychological - cardiovascular- ENT	Gastrointestinal
Thirlwall A. et al ⁴¹	England	Gastrointestinal- psychological	Gastrointestinal
Thomas MO. et al ⁴²	Nigeria	Gastrointestinal	Gastrointestinal
Karnak I. et al ⁴³	Turkey	-	Gastrointestinal
Turna C. et al ⁴⁴	Turkey	Gastrointestinal- respiratory- psychological	Gastrointestinal- respiratory
Janoušek P. et al ⁴⁵	Czech	Gastrointestinal	Gastrointestinal
Saetti R. et al ⁴⁶	Italy	-	Gastrointestinal
Stone MM. et al ⁴⁷	America	-	Gastrointestinal- respiratory
Gerzic ZB. et al ⁴⁸	Yugoslavia	Psychological	-
Ceylan H. et al ⁴⁹	Turkey	Gastrointestinal- respiratory- psychological	Gastrointestinal
Kukkady A. et al ⁵⁰	New Zealand	Gastrointestinal	Gastrointestinal
Chen TY. et al ⁵¹	Taiwan	Gastrointestinal-respiratory-psychological- cardiovascular	Gastrointestinal-death
Shukla RM. et al ⁵²	India	Psychological	-
Turner A. et al ⁵³	Australia	-	-
Ozcan C. et al ⁵⁴	Turkey	-	Gastrointestinal
Rigo GP. et al ⁵⁵	Italy	-	Gastrointestinal-death
Brown RA. et al ⁵⁶	South Africa	Psychological	Gastrointestinal
Baskın D. et al ⁵⁷	Turkey	Gastrointestinal- psychological	Gastrointestinal
Brun JG. et al ⁵⁸	-	-	-
Tiryaki T. et al ⁵⁹	Turkey	-	Gastrointestinal
Gupta SK. et al ⁶⁰	India	Gastrointestinal-respiratory- psychological	-
Uhlen S. et al ⁶¹	America	Psychological	Gastrointestinal
Heran MK. et al ⁶²	Canada	Gastrointestinal	Gastrointestinal
Rosseneu S. et al ⁶³	England	-	Gastrointestinal
Lin YC. et al ⁶⁴	Taiwan	Gastrointestinal	Gastrointestinal
Atabek C. et al ⁶⁵	Turkey	-	Gastrointestinal
Wiseman HM. et al ⁶⁶	England	Gastrointestinal- respiratory- psychological	Hepatic – renal
Mehreghan F. et al ⁶⁷	Iran	Respiratory- psychological- neurological	Gastrointestinal-respiratory-death
Azadeghan M. et al ⁶⁸	Iran	Gastrointestinal- respiratory- psychological	-
Rafeey M. et al ⁶⁹	Iran	Gastrointestinal- psychological	Gastrointestinal-death
Talebyan A. et al ⁷⁰	Iran	Respiratory- psychological- neurological	-
Osar SH. et al ⁷¹	Iran	Respiratory- psychological- neurological- gastrointestinal-ENT- cardiovascular	-

Our review revealed that physical examination and invasive techniques were carried out for detection and evaluation of digestive tract lesions. Endoscopy was frequently performed in addition to other diagnostic methods, such as esophagoscopy and barium swallows.

Therapeutic protocols included medical, surgical, and conservative treatments, respectively. Serum therapy, antibiotics, systemic steroids, Anti-acid, H₂ blockers, protein pump inhibitors, and topical injection of Mitomycin and steroid were used. The most common surgical methods included esophageal dilatation and esophageal

replacement. Implantation of a stent and catheter in the esophagus were also mentioned in some of the articles. On selecting for the meta-analysis the 64 articles that showed the caustic ingestion in children, the Forest plot stated OR=0.53 (Figure 2) with a 95% confidence interval (95% CI) of 0.49-0.57 (P=0.08) for boys and OR=0.38 (Figure. 2) with a 95% confidence interval (95% CI) of 0.35-0.42 (P<0.001) for girls. Therefore, the caustic ingestion was more common in boys compared to girls. The studies were non-homogeneous (I²=83.68% and P<0.001 for boys & I²=82.44% and P<0.001 for girls), so for estimate risk was used from random results.

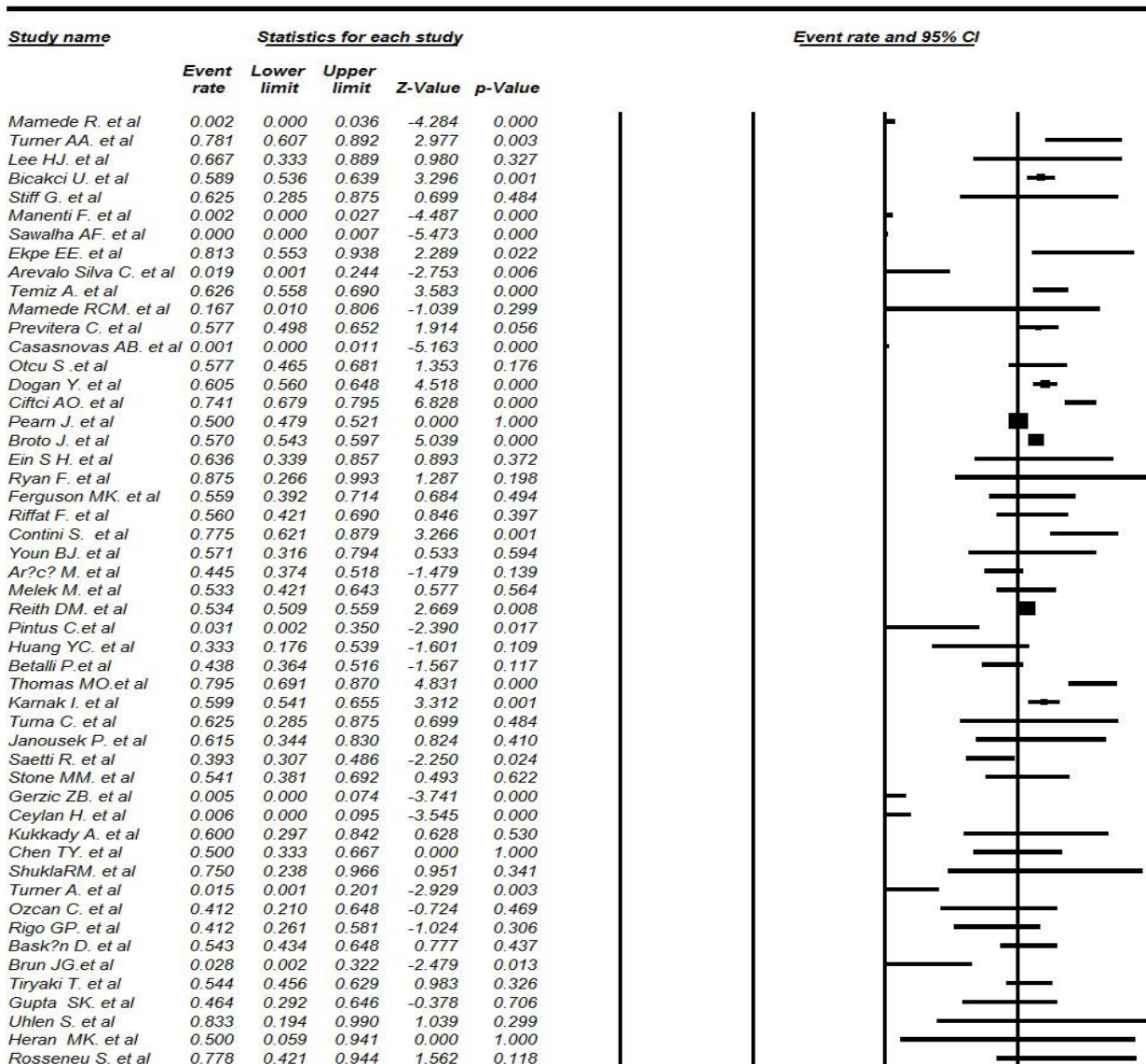


Figure 2. Meta-analysis for boys and girls

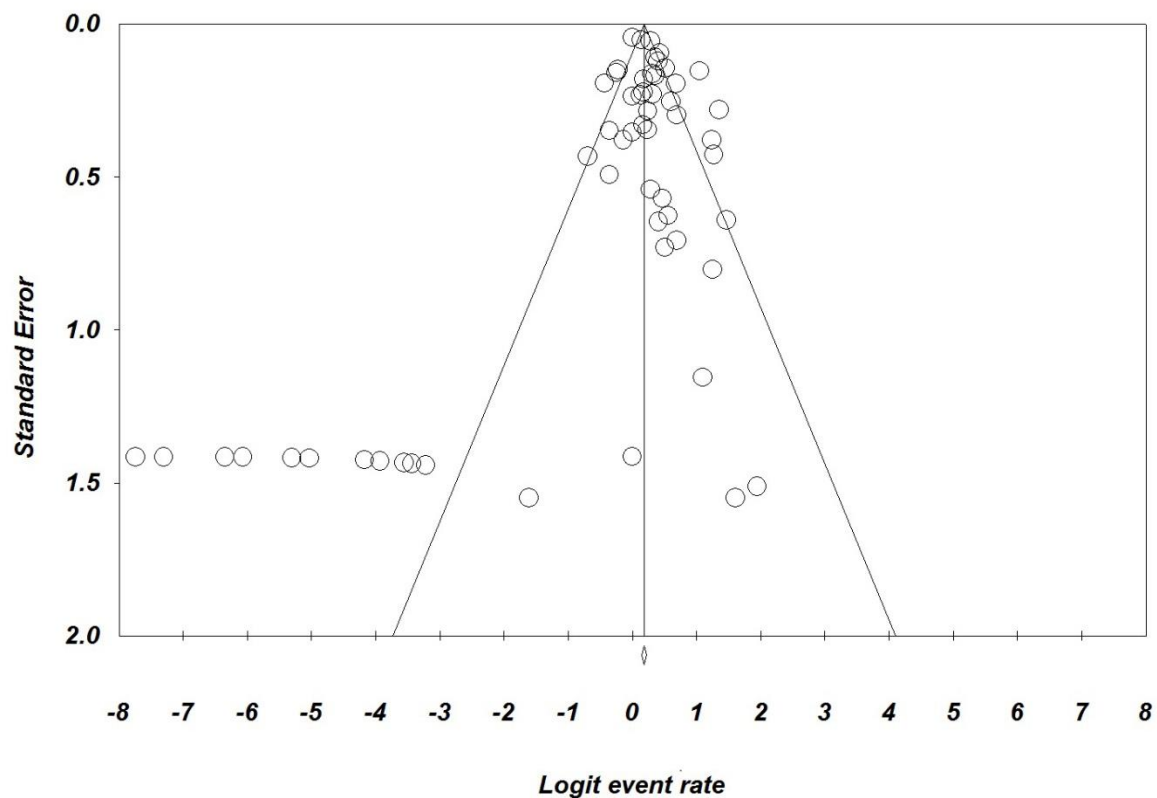


Figure 3. Funnel plot of standard error by logit event rate for boys and girls

The extracted data are shown in the funnel plot to evaluate the publication bias for sample size and effect size (Figure 3). Regarding the funnel plot view, it may be noted that the publication bias in the process of search and selection in the present study was at an acceptable level (Table 1).

Discussion

The goal of this systematic review was to evaluate previous literature and examine the age distribution, sex ratio, and the types of ingested agents, symptoms and signs, management, and the impact of chemical factors on the complications caused by the ingestion of caustic agents in children because of highlighting on primary preventive programs. The widespread use, easy availability, low costs of cleaners and detergents especially in Asia¹⁷ as well as other products have led to an increase in the

occurrence of swallowing of agents among children.

In term of demographic characteristics, we found that the group at the highest risk for accidental caustic ingestion comprised children of preschool ages (mean age = 1.74 (3.38) years), and mostly boys were involved in such incidents. In a study by Seluck Otcu in Turkey, 58% of the children who ingested caustic substances were boys, and 42% were girls, with a mean age of 3.6 (2.8) years.²¹ Other related studies had similar results.^{22,23,72} Children, especially boys, have well-developed skills and are curious to examine substances and drink them. However, they lack the knowledge of the portability of substances. This implies that boys in preschool stage (3–4 years) need more attention and caring by parents to avoid such ingestion incidents. Moreover, parents' behaviors are affected further by culture.^{5,23} It is

recommended to consider these points by families:

- The large amounts of detergent must not be kept at the home, especially at kitchen.
- Chemical substances should be placed on the locked cabinet and the upper shelves and were immediately put in its place after utilization.
- Chemical materials should be kept in the labeled containers with tight door.
- Chemicals substances should not be stored in food containers.
- When a drug is given as a medicine, it not be mentioned as candy.

- The phone number of emergency department and poisoning control center should be recorded in notebook at home.^{5-9,24,25} In this present review, we found that most accidents were due to alkaline agents, such as bleach products, oven cleaners, and soda.

These products are often used to clean the house; however, they can cause various types of poisoning.⁸ In a study conducted in Australia, 76% of the accidents were reported to have occurred at home, where 74% were caused by alkaline, 6% by acidic agents, and 20% were caused by contamination with other agents.⁷²

Parents should avoid storing such substances in everyday, unmarked drinking bottles, especially in containers that are known to hold edible substances. It was reported in Iran and Turkey that in most cases such caustic agents had been stored in accessible places in the house and in containers without labels.^{1,15,26} Most of the studies emphasized the impact of educating parents by multimedia for raising their awareness and self-efficacy in their care of children.^{26,73}

The present study revealed that the most common signs and symptoms of caustic ingestion were related to digestive, respiratory, and ENT tracts. In a study conducted in Turkey, it was found that gastrointestinal symptoms were predominant during admission. In addition, respiratory symptoms were observed in 13% of the cases.⁷²

In order to detect lesions and evaluate the severity of the damage, physical examination, non-invasive techniques, and invasive technique especially endoscopy was used for nearly all patients. Ferguson et al., believed that the first step in the treatment of these patients is physical examination.²⁸ In this present review, the mean of initiating time of the endoscopic examination was 30 hours. In different studies, endoscopy was offered within 24-48 hours.^{18,72} Managing and following of patients result in the early diagnosis of complications and the application of continues therapeutic recommendations and health care.²⁹ The increasing of parent awareness toward preliminary canings after agent swallowing and the handling of health and caring centers on proper admission, management and care could be helpful about this episode.³⁰⁻³²

Esophageal damage, gastro-esophageal reflux, and gastric ulceration, respectively were common injuries of corrosive substance ingestion in children. The injuries of respiratory system were aspiration pneumonia and laryngeal sore. Malignant transformation was reported during long-term follow-ups. In the study conducted in Turkey, Esophageal stricture observed in 24.2% (16 patients) by endoscopy.⁷⁴ In another study in South Korea, esophageal stricture was identified as the most common long-term complication.⁷² Similarly, mortality and esophageal cancer were observed in a study conducted in Brazil.¹⁶ Thus, it is clear that although ingestion of caustic substances is relatively rare, its effects are debilitating.²⁷

In the present study, we found those medical therapies such as oral antibiotics, systemic steroids, and H2 blockers; surgical therapy, such as esophageal dilatation; and conservative treatments were used. These findings were similar to other studies.^{18,30,33,34,75,76}

Assessment of involvement of other organs and recovery through massage could help to prevent secondary problems. In our study, medical therapies such as oral antibiotics, systemic steroids and H₂ blockers, surgical

therapies such as esophageal dilatation and conservative treatments were utilized to limit the severity of inflammation and infection.⁹

Rajinder *et al.*, reported similar results in New York.³⁶ Although the benefit of each treatment have not been determined by investigators, therapeutic methods should be able to develop as the child growth.⁹

The major advantage of the present study was the use of an appropriate number of authentic studies. This advantage, along with the large sample size across all the selected studies, enabled us to use the funnel plot to assess publication bias. However, a limitation in this study was the poor accessibility of European and American papers because of problem sanctions on Iran. Finally, we recommend that more case control or clinical trial studies should be performed to provide guidelines and protocols.

Conclusion

This study implies the role of families, manufacturers, media, health care systems, and government in these accidents. Appropriate storage and usage of these hazardous substances is strongly recommended for parents. Producing materials with formulation and packaging agents in factories are essential factors. Moreover, the media and educational programs can raise public awareness. Thus, the primary prevention and reduction of undesirable health effects of accidental ingestion of caustic substances is practical and simple.

Also, we recommend that continues management and caring health programs should be applied because of the effects range from an asymptomatic state to intractable complications. With reference to treatment strategies, thus, comprehensive and continues treatment should be carried out in all cases of caustic ingestion; consist of medical therapies such as oral antibiotics, systemic steroids and H2 blockers, surgical therapies such as esophageal dilatation and conservative

treatments were utilized to limit the severity of inflammation and infection.

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Ethical issues

None to be declared.

Conflict of interest

The authors declare no conflict of interest in this study.

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