Introduction:

Caustic material ingestion continues to be a challenging issue across the globe especially in low-to-middle income countries (LMIC). It can lead to significant injury to any part of the alimentary tract, but most commonly the upper tract, including the oropharyngeal cavity, larynx, esophagus, and stomach [1]. The aim of this article was to review the epidemiology, prevention and management of caustic material ingestion in pediatric population comparing LMIC with high-income countries (HIC).

Methods:

We conducted a detailed English literature review using PubMed database by using the following key words: "(caustic or corrosive) AND ingestion AND (pediatric OR paediatric)". Our search retrieved 253 citations; all abstracts were screened by authors to ensure relevance; a total of 52 articles were selected for inclusion into our work and the remaining results were excluded because they were irrelevant to our study.

Epidemiology:

Epidemiologic studies showed that corrosive injury is more common in LMIC, but still seen in HIC. In US alone, a recent report showed that there about 5,000 to 15,000 corrosive ingestions reported per year [2-4]. Whereas in England and Wales, there are more than 40,000 cases are reported annually [5]. On the other hand, the number of cases in LMIC are largely unreported and the epidemiologic studies are scarce, but limited data available supports the large scale of the problem, which is a major public health issue. The shortage of information about prevention, management and outcome of these relatively common accidents in pediatric population in LMIC makes it social and healthcare challenge. Most cases worldwide involve children (68%) as a result of unintentional, accidental ingestion of caustic substances, in contrast to adults in which they are mostly suicidal and usually more severe [6, 7]. Most of the pediatric caustic ingestion (86–90%) occur within the home environment or its surroundings [8]. The accidental ingestion of corrosive substances is declining in high-income countries (HIC), but unfortunately not in LMIC [7, 9, 10]. Alkaline materials accounts for most caustic ingestions in HIC whereas injuries from acid are more prevalent in some LMIC [11]. Alkaline material ingestion leads to more proximal injury; primarily in oropharyngeal and esophageal. They tend to cause a more severe damage due to their liquefactive necrosis pattern. In contrast, acidic injury are usually less severe due to their coagulative necrosis effect and they tend to affect the stomach and spare the esophagus [12].

In a review published by the WHO [13], they found that most ingestions in children in a number of centres in LMIC in Africa and Eastern Asia were due to lack of parental knowledge of the risk of corrosive substances kept in and around the house, and crowded living conditions in poor neighborhoods, combined with the natural curiosity of children. They have also found that the strongest predisposing factor for these injuries is the lack of any preventive measures. The most frequently injured children were those who are less than 5 years (80%), and boys were the majority (70%). The most commonly reported corrosive material was caustic soda (sodium hydroxide [NaOH] crystals), followed by kerosene, sodium hypochlorite and household chemicals. The vast majority of caustic ingestion victims reported in this study (73%) underwent gastrostomy tube insertion, as compared with 11% of severe injuries reported in an Italian (HIC) multicenter observational study [14]. Another challenge for caustic ingestion victims in LMIC, is that they usually present late, and as result of the lack of parental knowledge the long time needed to reach the emergency department, also these victims are frequently treated by home remedies or by unexperienced health.

Prevention:

Prevention has a significant role in reducing the occurrence of corrosive ingestion especially in pediatric population, but unfortunately this goal is far from being reached in LMIC. Preventive measures have dramatically reduced the incidence of caustic injuries in many countries. Unfortunately, it is still a goal that needs to be met by many LMIC [15]. Therefore, collaboration to mitigate this grave public health problem is essential. In some countries, they have introduced new legislations to ban domestic retail of sodium hydroxide-based cleaning agents [16] or limiting concentration of strong bases in domestic preparations. These rules have significantly reduced the occurrence and severity of injuries in these countries. Legislated safety requirements may include clear package labelling, listing dangerous ingredients and information on first aid in case of ingestion or skin contact, as well as poison help-line telephone numbers. Public Health education programmes can further decrease the epidemic of caustic-related injuries, which occur mostly in LMIC [15]. Childproof bottle tops and spray-bottle safety catches should be manufacturing norms for the domestic market, and preferably in agricultural and industrial applications as well [17].

Management:

The mainstay of diagnosis of caustic ingestion is considered flexible upper gastrointestinal endoscopy, CT scan and endoscopic ultrasound [18], but lack of resources and availability of these services severely limits the LMIC physician in diagnosing and assessing the extent of damage. Delayed presentation and management of corrosive ingestion can result in stricture formation and other late sequelae and have been found to be strong predictors of future esophageal replacement [19]. This issue requires different management strategies for patients presenting at early or late stage, and this especially crucial in LMIC, where late presentations are common, as in one study from Nigeria where 75% of the cases presented late [3]. After initial survey, medical management involves intensive fluid and electrolyte treatment, administration of broad-spectrum antibiotics, and close follow-up [12].

Although steroid use in caustic esophageal strictures is still a controversial topic, some randomized clinical trials have showed that intralesional steroid injection leads to greater esophageal stricture dilatation in the treatment group compared with the control group [15, 20-23]. Local injection of steroids or Mitomycin C is a reasonable step with acceptable risks. Systemic steroids, on the other hand should be cautioned against in the developing world. There is conflicting evidence on their efficacy and a meta-analysis suggesting there is no overall benefit to systemic steroids [24]. Additionally there are reports of perforation of the esophagus and the overall side effects of systemic steroids that mask the severity of the patient. This is particularly pertinent in the developing world where access to adequate monitoring of patients and access to trained intensivists is a challenge. Systemic steroids should be approached with extreme caution unless all the pieces to care for the potential complications are in place.

Upper gastrointestinal endoscopy can be used for assessment of the extent of injury after caustic ingestion. However, the patient's clinical manifestations do not always reflect the severity of the endoscopic findings and the long-term outcome [25]. Immediate laparotomy and surgical resection of the affected gastric or esophageal segment might be required in some cases, especially in case of perforation or bleeding, and again this can be difficult to achieve in remote and poorly-developed centres in LMIC. The mainstay treatment of caustic esophageal strictures is graded endoscopic dilatation [26]. However, sometimes esophageal dilatation is not feasible or fails to provide an adequate esophageal caliber, and in this case esophageal segmental resection or replacement may be considered depending on the length of the stenotic segment(s). Over the last years, the indications for esophageal replacement have changed. While the majority of the surgeries were

performed for caustic esophageal injury near the time of presentation, during the past decade patients undergoing early surgery for caustic injury have dropped to 36% [15, 19]. Indeed, a series from Jordan included all caustic ingestions over a 19-year period and 19/83 went on to stricture but all were able to be managed with dilations alone [27]. Esophageal replacement can by performed using a variety of organs including colon, small bowel and stomach. Of the available options, many authors consider the stomach as the most reliable replacement for the affected esophageal segment (including the authors of this review) [28]. This is because of its sufficient length, liberal blood supply and need for only a single anastomosis [29]. Unfortunately, the stomach may not be a suitable conduit as it is often affected along with the esophagus by the ingested caustic material [30]. When all factors are combined together, the most commonly used esophageal substitutes are colon, stomach, then jejunum [31] though the preference is always for the stomach if it is suitable. A case series of 11 children with upper aerodigestive caustic injury reported by Ein, Sigmund [32] showed that gastric tube replacement has fairly good results, although some anastomosis-related complications including leak occurred. Colonic interposition has been used as a conduit for esophageal replacement since the early 1900s [33]. The left or right colon may be used and in either case, the transverse colon is always required [28]. The advantages of the use of colon as a conduit are numerous include the substantial length, especially the right colon which closely simulates that of the native esophagus. In addition, the colon is resistant to acid and causes less reflux especially when using the right colon which includes the valve of Bauhim [34]. The disadvantages of the colonic interposition include that the colon conduit may lengthen and become redundant over time that may necessitate surgical revision [35]. In addition, the colon may have or can develop native pathology and that loss of absorptive capacity of the colon may result in diarrhea [36]. Colonic reconstruction continues to be a high-risk surgical procedure, with a high rate of mortality and morbidity, despite of improvements in the perioperative management [34]. Small bowel can be also used as a conduit for esophageal reconstruction, most commonly, the jejunum. The jejunum is very effective in patients requiring the replacement of a relatively short segment of the esophagus though technically challenging [37]. Proponents of the use of jejunum as a conduit recommend it because it has a reliable blood supply, and it usually lack intrinsic pathology in contrast to the colon [38] All too commonly, jejunal conduits may not be long enough to reach the hypopharynx and the fatty mesentery may also inhibit the surgeon's ability to pull up the conduit [39] though a fatty mesentery is less common in children.

Esophageal intraluminal stenting has been used to decrease the chance of stricture formation in patients with caustic esophageal injuries [40]. Stenting is mostly used after two or more unsuccessful endoscopic esophageal dilatation [41]. In a small uncontrolled case series of caustic esophageal injury, Atabek, C., *et al.* [42] trialled intraluminal polytetrafluoroethylene (PTFE) esophageal stenting; they showed that stenting can be an effective treatment option to prevent stricture formation and to reduce the need for esophageal replacement. In contrast to esophageal strictures, surgery is the mainstay of treatment of corrosive-induced gastric injuries with good long-term outcomes [43, 44]. While endoscopic balloon dilatation can be successful in treating mild cases of gastric injury with minimal fibrosis, it has high complication and failure rates [45]. When combined with intralesional steroid injection, the success rate of balloon dilatation is considerably higher [46]. Several factors play a role in choosing the appropriate surgical procedure for corrosive-induced gastric injuries. They include the general condition of the patient, the extent of the injury, and the surgeon's preference [47]. Surgical options for treatment of corrosive-induced pyloric strictures include Finney or Heineke Mikulicz pyloroplasty, Y-V advancement antropyloroplasty and Billroth I gastrectomy with gastrojejunostomy [48-50].

Nutritional support, for instance using either nasogastric tube or jejunostomy, especially in LMIC countries is of paramount importance, and this is because management strategies in these countries are influenced by malnutrition and poor clinical conditions [51].

Long term outcomes in the developing world are lacking. Industrialized nations have reported a protracted course of stricture formation in up to 49% of patients [52]. We can only extrapolate that this number would be even higher in centers in the developing world with more limited resources and experience with these conditions. As discussed earlier, colonic interpositions often require revision as the patient grows and the colon becomes redundant in the chest [35]. In general, neither gastric pull up nor jejunal interposition requires revision as often as patients undergoing colonic interposition. Many of these patients will develop symptomatic reflux requiring acid suppression and or an anti-reflux procedure. Regardless of how much of the native esophagus remains *in situ*, the esophagus that remains must be monitored for dysplastic changes as they have a more than 1000 fold increase in malignancy after a caustic ingestion [15].

Conclusion:

Caustic ingestions represent another condition where prevention is key. Once a child suffers an injury, rapid careful evaluation of the injury with flexible endoscopy and a patient course of observation and dilations, if needed will often avoid esophageal replacement surgery. When necessary, stomach is the best first option (although often unsuitable due to the injury), followed by colon and finally jejunum.

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