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Manifestation and Etiology of Refractory Esophageal Strictures in Children's University Hospital in Damascus

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Abstract:

Background and Objective: Pediatric esophageal strictures in general, and refractory strictures in particular are an important cause of morbidity and growth failure in children and could be a big challenge for clinicians, this study was conducted to assess the causes and characteristics of the strictures that may become refractory, and may not respond to the classic treatment in esophageal dilation.
Materials and Methods: The present study was carried out in the Pediatric Endoscopy Unit in Children's University Hospital in Damascus, from the beginning of March 2020 to the end of December 2021.
The sample size included all children ranged from 1 to 13 years with esophageal strictures who required more than five esophageal dilation and still had significant dysphagia.
Results: The number of sample was 35 cases 57,14% of them were male.
The etiologies of the esophageal strictures were as follows: corrosive ingestion 57,14% (n = 20), peptic 37,14% (n =13), anastomotic (after esophageal atresia surgical repair) 5,71%(n = 2).
Upper esophageal third was the most common site of stricture (42,85%), and 71,42% of strictures were less than 3 cm in length.
Conclusions: Corrosive-induced strictures was the most common cause of refractory esophageal strictures and the upper esophageal third was the most common site of these strictures, these strictures may not respond to the esophageal dilation alone and may need other adjuvant treatments or surgery intervention.

Keywords: Esophagus, Stricture, Refractory, Children.

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التظاهرات والسببيات المرضية لتضيقات المري المعندة في مشفى الأطفال الجامعي بدمشق

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الملخص:

خلفية البحث وهدفه: تشكل تضيقات المري عند الأطفال بشكل عام والمعندة بشكل خاص سبباً للإمراضية وفشل النمو عند الأطفال، وتحدّياً علاجياً هاماً للأطباء الممارسين، تهدف هذه الدراسة لتبيان المظاهر والأسباب الرئيسية لتضيقات المري المعندة عند الأطفال والتي قد لاتستجيب على العلاج التقليدي بجلسات التوسيع.

مواد البحث وطرائقه: أجريت هذه الدراسة بوحدة التنظير الهضمي بمشفى الأطفال الجامعي بدمشق بدءاً من آذار 2020 حتى نهاية كانون أول 2021، وقد شملت 35 طفلاً مصابين بتضيق مري خاضعين لجلسات توسيع دورية والذين خضعوا لأكثر من 5 جلسات توسيع متتابعة مع استمرار أعراض عسرة البلع لديهم.

النتائج: شملت الدّراسة 35 مريضاً لديهم تضيق مري معنّد، 57,14% منهم ذكور، شكّل تضيق المري التالي للحرق بالكاويات السبب الأشيع للتضيقات المعندة 57,14%، تلاه تضيق المري الهضمي 37,14%، ثم التضيق التالي لجراحة رتق المري (تفميم المري) 5,71%، وشكّل تضيق الثلث العلوي للمري الموقع الأشيع للتضيق 42,85%، وكان 71,42% من التضيقات طولها أقل من 3 سم.

الاستنتاج: شكّلت تضيقات المري التالية لحروق المري بالكاويات السبب الأشيع لتضيقات المري المعندة عند الأطفال، وشكّل تضيق الثلث العلوي للمري الموقع الأشيع للتضيقات المريئية المعندة، هذه التضيقات التي قد لاتستجيب للعلاج بجلسات التوسيع وحدها بحال استمرار أعراض عسرة البلع وإنما قد تحتاج لعلاجات أخرى مساعدة أو تداخلاً جراحياً.

الكلمات المفتاحية: تضيّق، المري، المعنّدة ، الأطفال

Introduction:

Esophageal strictures (ES) are anatomical lesions that can cause luminal narrowing of the esophagus[Dall'Oglio, T. L., *et la,* 2016, pp. 212-219].

These are usually diagnosed on upper endoscopy or esophagogram(Figure 1) either as an incidental finding or during the workup of dysphagia which is the most common symptom of Esophageal strictures in children[Simon M ., *et la,* 2019, pp. 1-12].

Figure(1): Esophagogram of esophagus show lower esophagus stricture.

Post-esophageal atresia anastomotic strictures and postcorrosive esophagitis are the most frequent types of cicatricial esophageal stricture. Congenital esophageal stenosis has been reported to be a rare but typical disease in children; other pediatric conditions are peptic, eosinophilic esophagitis and dystrophic recessive epidermolysis bullosa strictures[Shah JN,. *et la,* 2006, pp. 63(1):164–7][Youn BJ., *et la,* 2010, pp. 203-210].

The incidence of the non- congenital strictures varies between countries. In developing countries, caustic injuries are more frequent while prevalence of peptic strictures has decreased; due to the extensive use of proton pump inhibitors (PPIs) which is important as medical therapy to provide local control of esophagus inflammation in dosage 1-2 mg/kg especialy in peptic and corrosive esophagitis or long-gap esophageal atresia anastomosis strictures[Zouari, M, H,. *et la,* 2014, pp. 22–25][Tam PK., 2003, pp. 1712-1715].

Improvements in endoscopes and accessories have supported an increase in the number of patients who are conservatively treated with endoscopic dilations (ED) rather than surgical treatment.

Esophageal dilation by wire-guided bougie (Savary-Giliard bougies) or through-the-scope balloon dilators under general anesthesia is the first step in the treatment of symptomatic benign esophageal strictures[Siersema. PD., 2019, pp. 70(5):1000–12].

Rodriguez-Baez and Andersen showed that balloon dilators are most useful when it is desirable to minimize esophageal trauma and when the strictures are short. Savary-Gilliard dilators are useful for strictures resistant to balloon dilation and for long strictures that require carefully controlled and graded dilation. Different treatments have been proposed for subtypes of ES, but their effectiveness remains controversial.[Siersema PD, 2009] [Gurfinkel A., *et la,* 2015].

Both Savary-Giliard bougies and balloon dilators are equally effective and safe in achieving adequate dilation[Gurfinkel A., *et la,* 2015].

ED therapy was arranged for patients with dysphagia scores of greater than 2 or 2 with acute weight loss. The dysphagia scores were based on the study by Parthipun *et al.* Dysphagia scores were classified into five grades according to the swallowing ability: 0, normal diet; 1, ability to swallow a semi-solid diet; 2, ability to swallow a soft diet; 3, ability to swallow liquids only, and 4 complete dysphagia[Dehghani S. M., *et la,* 2019, pp. 7-11].Table 1.

Table(1): Dysphagia scoring system

Dysphagia scores	Degree of dysphagia
0	Able to eat normal diet/no dysphagia
1	Able to swallow some solid foods
2	Able to swallow only semi-solid foods
3	Able to swallow liquids only
4	Unable to swallow anything

The goal of treatment is to improve degree of dysphagia until relieve dysphagia symptoms from mechanical stenosis, reduce the risk of pulmonary

aspiration, and prevent recurrence of stricture [Cakmak M., *et la*, 2016, pp. 179–184] [Al Sarkhy. A., *et la*, 2018, pp. 787–791].

The incidence of refractory strictures is poorly reported due to the variety in definitions used in literature. Regarded as a consensus among experts, the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) has set the following definition for a refractory esophageal stricture: an anatomical restriction without endoscopic inflammation that results in dysphagia after a minimum of five dilatation procedures at maximally 4-week intervals[Ismail. N., *et la*, 2021, pp. 48-57] [Vandenplas Y., 2017, pp. 211-215].

In practice, what this means is that a stricture should only be considered refractory once non- congenital and neuromuscular causes have been excluded, the patient has had a number of sequential dilatations at short intervals and has optimised treatment for the underlying cause, the need for further dilations is determined based on the symptoms[Vandenplas Y., 2017, pp. 211-215][Berenson GA, 1994].

Due to the importance of refractory esophageal stricture in children, this study was conducted to assess the causes and characteristics of the strictures that may become refractory.

Materials and Methods:

The present study was carried out in the Pediatric Endoscopy Unit in Children's University Hospital in Damascus, from the beginning of March 2020 to the end of December 2021.

A review of medical records was made for all patients diagnosed with refractory esophageal strictures presented to the Pediatric Endoscopy Unit. The sample size included all children ranged from 1 to 13 years with refractory esophageal strictures. All had significant dysphagia and required more than five esophageal dilation sessions on a regular basis without endoscopic inflammation.

Patients with motility disorders (achalasia) or neuromuscular causes , less than five esophageal dilation sessions, no regular interval between dilation sessions and association of dysphagia with esophageal inflammation have been excluded from the study.

Data were gathered on patients' sex, age, esophageal stricture etiologies, and location of stricture (including upper esophageal third, middle third, and lower third), and length of stricture.

The length of the stricture was measured by radiologic studies. A length of three centimeters was used as a threshold value for classifying the stricture2 (<3 cm, short stricture; ≥3 cm, long stricture).

Statistical Analysis:

Descriptive statistics were calculated as frequency counts and percentages for categorical variables and median with interquartile range (IQR) for continuous variables. All analyses were performed using SPSS 26 software (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp).

Results:

The number of sample was 35 cases; The mean age was 5.1 ± 3.9 years (1-13 years), 57,14% (n = 20) of them were male(Figure 2).

The etiologies of the esophageal strictures were as follows: corrosive ingestion 57,14% (n = 20), peptic 37,14% (n =13) and Post-esophageal atresia anastomotic strictures 5,71%(n = 2); (Table 2, Figure 3).

Strictures locations were as follows: upper esophageal third (proximal); 15(42,85%), middle esophageal third; 6(17,14%) and lower esophageal third (distal); 14(40%).

All anastomotic strictures were located in the upper esophageal third whereas all peptic strictures were confined to the lower esophageal third.

Corrosive-induced strictures characteristically involved all 3 segments of the esophagus; (Table 3, Figure 4).

All peptic and anastomotic strictures were less than 3 cm in length, whereas 10(28,57%) of the corrosive induced strictures were between 3 and 6 cm in length(Table 3,Figure 5).

Discussion:

Esophageal strictures in children have multiple etiologies such as congenital anomalies, anastomic strictures (after esophageal atresia surgical repair), eosinophilic esophagitis, gastro-esophageal reflux disease (peptic strictures) and caustic ingestion

following ingestion of acids or alkali[Shah JN,. *et la*, 2006, pp. 63(1):164–7].

The aquired injuries can induce edema, and finally lead to stricture formation through stimulating the proliferation of fibrotic tissue and accumulation of collagen that subsequently impede the passage of ingested material from the mouth to the stomach[Youn BJ., *et la,* 2010, pp. 203-210].

Esophageal dilation is the first step in the treatment of esophageal strictures, different dilators are now available; for example, reusable dilators that are applied over the wire such as semirigid Savary-Giliard bougies and disposable balloon dilators have been used. Balloon dilators pass over a guide wire or through the channel of the endoscope. All of these dilators are available in different lengths and diameters[Dall'Oglio, T. L., *et la,* 2016, pp. 212-219][Tam PK., 2003, pp. 1712-1715]. There is no difference in clinical outcomes between wire-guided bougie and through-the-scope balloon dilators[Cakmak M., *et la*, 2016, pp. 179–184]

Most strictures can be treated successfully with endoscopic dilation with only a few complications. Nonetheless, approximately one third of patients develop recurrent symptoms after dilation within the first year. The majority of these patients are managed with repeat dilations, depending on their complexity[Ismail. N., *et la*, 2021, pp. 48-57].

Normal food intake without dysphagia is the only achievable target of conservative treatment because there are no treatments that can achieve a true normal esophagus with normal motility at the level of the esophageal stenosis[Dall'Oglio, T. L., *et la,* 2016, pp. 212-219][Vandenplas. Y., 2017, pp. 211-215].

A benign refractory or recurrent stricture in children occurs in case of an anatomic restriction because of cicatricial luminal compromise or fibrosis that results in dysphagia after dilation sessions in the absence of endoscopic evidence of inflammation. There is consensus that this may occur as the result of either an inability to successfully remediate the anatomic problem to obtain age-appropriate feeding possibilities after a maximum of five dilation sessions[Berenson. GA ., *et la,* 1994,pp 18:250-2][Lévesque. D., *et la* ,2013 ,pp. 382-387].

In Zein study, esophageal strictures are commonly a result of peptic esophagitis, ingestion of caustics, or injury at the site of a surgical anastomosis[Zein. NN., *et la,* 1995, pp. 596-598.

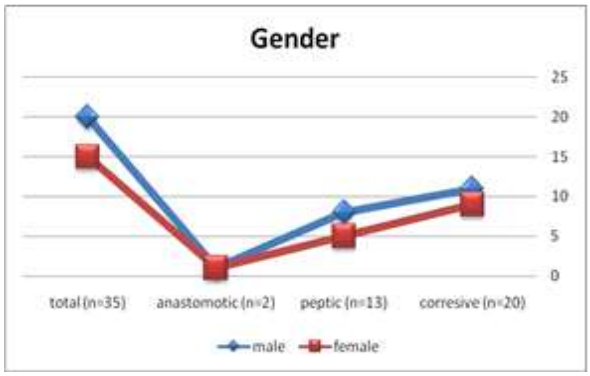
Table(2): The Etiology of 35 pediatric patients with refractory esophageal strictures

Etiology	n = 35 (100%)
Corrosive	20(57,14%)
Peptic	13(37,14%)
Anastomotic	2(5,71%)

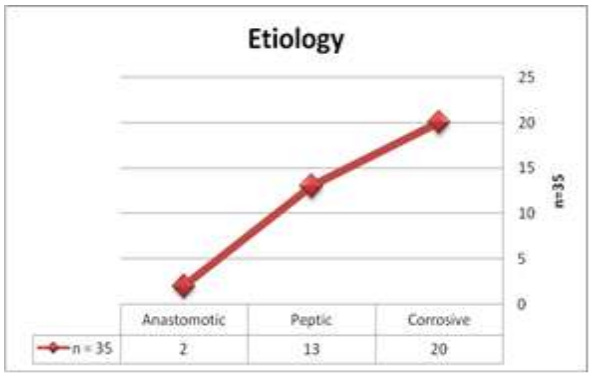
Table (3): Characteristics of 35 pediatric patients with refractory esophageal strictures

	Corrosive (n = 20)	**Peptic** (n = 13)	**Anastomotic** (n = 2)	**Total** (n = 35)
Gender (M:F)	11:9	8:5	1:1	20:15
Site of S Upper third Middle third Lower third	13(37,14%) 6(17,14%) 1(2,85%)	13(37,14%)	2(5,71%)	15(42,85%) 6(17,14%) 14(40%)
Length of S <3 cm ≥3 cm	10(28,57%) 10(28,57%)	13(37,14%)	2(5,71%)	25(71,42%) 10(28,57%)

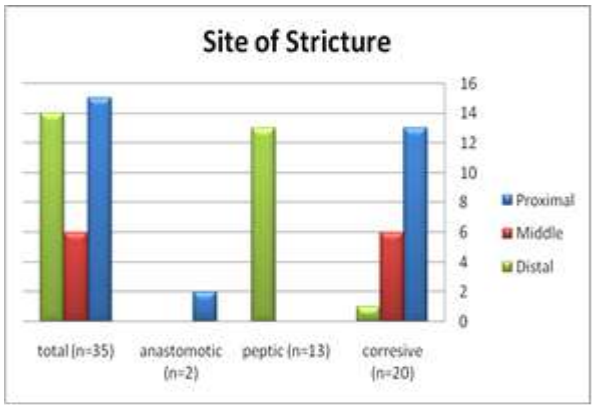
M; Male. F; Female. S; stricture.



Figure(2): Gender of children with esophageal strictures.



Figure(3): Etiology of refractory esophageal strictures.



Figure(4): Refractory esophageal strictures site.

Pieczarkowski et al in Poland and Bittencourt *et al* in Brazil reported the most common causes of esophageal stricture were postoperative stenosis, but stenosis due to caustic ingestion had many dilation sessions and inappropriate response to this sessions (refractory)[Pieczarkowski. S., 2016][Sadeghi. H *et la.*, 2020].

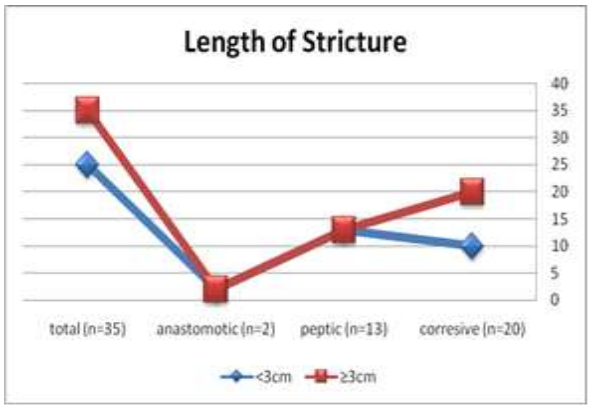


Figure (5): Refractory esophageal strictures length.

Gurfinkel A, *et la* found that the long-term success rate of dilation of ES depends primarily up on the etiology of the stenosis. Certain disorders, such as congenital ES, eosinophilic esophagitis, foreign body ingestion, and peptic, had the best long-term results, compared to other etiology, especially caustic ingestion[Gurfinkel A., *et la,* 2015].

In Eskander study, Caustic ingestion and the development of refractory esophageal strictures remain a major health problem in the pediatric age group, and this was similar to our study.

In the previous study endoscopic management requires several repeated sessions of dilatation for a long period up to 2–3 years[Eskander. A. E., *et la,* 2018, pp. 4932–4938].

Divarci et al found in their study on 20 children with refractory esophageal stricture that the types of esophageal strictures were corrosive esophageal strictures in 14 patients, anastomotic strictures in 5 patients, and congenital esophageal stricture in 1 patient. The length of the stricture was long in 10 patients[Divarci. E., *et la,* 2017].

Esophageal dilation in children is a safe procedure with a high rate of long-term success. Long-term success of dilation among children with esophageal strictures depends primarily on the etiology of stenosis and less on the method of dilation[Thomson. M., *et la,* 2017].

In our study caustic esophageal strictures were the most common cause of refractory esophageal strictures, these strictures are not easy to be dilated ,that usually related to the extent and depth of fibrotic reaction within the esophageal wall.

In many cases, the management is challenging and dilation is unsatisfactory as restenosis following scar formation remains the main problem.

Repeated dilatation procedures may cause repeated trauma to the mucosa leading to increase fibroblast proliferation and collagen deposition, thus worsening of the stricture[Divarci. E., *et la,* 2017].

However, a small percentage of patients progress to refractory strictures. The benign recalcitrant or refractory esophageal strictures are difficult to manage both medically and endoscopically as they do not respond to conventional treatment with proton pump inhibitors and esophageal dilations. Patients with refractory esophageal strictures are at a high risk of developing debilitating malnutrition and morbidity due to severe dysphagia[Ya-Wu Zhang., *et la,* 2021].

Also, this can be a financial burden on the healthcare industry due to several sessions of treatment[Boregowda. U ., *et la,* 2021].

In this article, we discuss the classification of esophageal strictures in children and knowledge which much of them can become refractory and may need adjuvant treatments to relieve dysphagic symptoms.

Conclusion:

In our study, Corrosive-induced stricture was the most common cause of refractory esophageal stricture. It was realized that the upper esophageal third was the most common site of stricture, and 28,57% of these strictures were long (≥3 cm in length).

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