



# BMJ Open Esophagogastroduodenoscopy in paediatrics: does abiding by the international guidelines lead to appropriate management? A cross-sectional study

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## ABSTRACT

**Objectives** Esophagogastroduodenoscopy (EGD) is one of the most practiced procedures in paediatric gastroenterology. As with all other procedures, it is guided and controlled by specific guidelines developed and approved internationally. The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the American Society for Gastrointestinal Endoscopy (ASGE) guidelines are two of the most followed guidelines in paediatric gastroenterology. This study aimed to determine how optimal patient condition management is when following international paediatric gastroenterology guidelines and to correlate the appropriateness of EGD and other variables with positive or negative findings on EGD.

**Design** A cross-sectional retrospective cohort of all first-time diagnostic upper endoscopies was conducted between 1 January 2016 and 1 February 2020, in Prince Hamzah Hospital in Jordan.

**Participants** Paediatric patients between 9 months and 14 years of age with indications for EGD.

**Results** Overall, 529 diagnostic EGDs were performed during the study period. *Helicobacter pylori*-associated gastritis was the most common final diagnosis in 247 patients (47%). Furthermore, 488 (92%) EGDs were deemed appropriate, while 41 (7.7%) were considered inappropriate. Finally, 74.0% of all biopsies performed had positive contributive findings.

**Conclusions** Abiding by international guidelines in paediatric gastroenterology can optimise care for paediatric patients. General paediatricians are urged to follow guidelines rigorously when referring patients to minimise inappropriate procedures.

## BACKGROUND

Esophagogastroduodenoscopy (EGD) and colonoscopy are essential diagnostic and therapeutic tools and thus pivotal procedures in adult and paediatric gastroenterology. EGD and colonoscopy have evolved over the last 30 years due to advancements in endoscopists' training and the equipment used in

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Our sample size was large, with 529 procedures analysed.
- ⇒ We included a sample that was representative of the Jordanian population, as our service is the only referral gastroenterology service in the Jordanian Ministry of Health.
- ⇒ The pathologist who studied the histopathology samples was blinded to the presenting symptoms.
- ⇒ It is a retrospective study on electronic files, and some data may have been missed.
- ⇒ A limited number of studies are available on the surrounding region that can be used as a reference for comparison.

these procedures. Many societies concerned with paediatrics and gastroenterology have established comprehensive guidelines for the indication and timely conduction of paediatric upper and lower endoscopies to minimise the overuse of these procedures and maximise appropriateness when the decision is taken to conduct them.<sup>1-5</sup>

In children, the most commonly encountered indications for EGD and colonoscopy are symptoms and signs of organic pathologies, such as (but not restricted to) haematemesis, refractory iron deficiency anaemia, weight loss and so on; these indications are considered to avoid these procedures in cases of functional disorders. The number of performed endoscopies in units in developing countries is on the rise, and the leading concern is that EGD is overused even in paediatrics.<sup>3</sup> Though EGD in children is relatively safe, it still has a small but definite risk.<sup>6,7</sup> Therefore, the appropriateness of endoscopy in children is an important subject. Several

guidelines for the 'appropriateness' and 'inappropriateness' of EGD in paediatrics have been established by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN), The European Society for Gastrointestinal Endoscopy (ESGE) and the North American Society of Paediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN).<sup>1,48</sup>

This study was conducted in the only paediatric gastroenterology service in the Jordanian Ministry of Health. This unit receives referrals from peripheral and central Jordanian healthcare centres. In most cases, the decision to perform upper and lower endoscopies is taken by the paediatric gastroenterologists working in the unit. However, some referred patients, mainly from remote areas, undergo the designated procedure and are sent back to their caregivers to complete their management plan unless their condition requires continued care at our centre.

The applicability of international paediatric gastroenterology guidelines has never been studied in Jordan. Therefore, this study aimed to determine how optimal patient management in a third-world country is when performed by following international paediatric gastroenterology guidelines. The second aim of this research was to correlate the appropriateness of EGD and other variables with positive or negative findings on EGD, such as *Helicobacter pylori* gastritis, coeliac disease and reflux esophagitis.

### EGD procedure

All diagnostic EGDs were performed by one of the two gastroenterologists (SB and MB) at the Prince Hamza Hospital in the operation room of the endoscopy unit. Patients were sedated with propofol with or without midazolam by an anesthesiologist. Children below the age of 2 years underwent EGD in the operating room under general anaesthesia.<sup>6</sup> Biopsies were obtained from macroscopically abnormal areas or according to the presenting symptoms, considering the ESPGHAN and NASPGHAN guidelines for sight and the number of biopsies for every specific pathology.

When *H. pylori* gastritis was suspected either due to the presence of the *H. pylori* antigen in the stool or a macroscopic appearance of the gastric mucosa suggestive of *H. pylori* gastritis, a rapid urease test (campylobacter-like organism test) was performed. No early or late complications were encountered during the study period.

The biopsy samples were studied by a pathologist blinded to the presenting symptoms. In some cases, the pathologist would discuss the case with the gastroenterologist before reaching a final diagnosis.

## MATERIALS AND METHODS

This was a cross-sectional, retrospective study of all first-time diagnostic upper endoscopies performed in paediatric patients between 9 months and 14 years of age. These procedures were performed between 1 January

2016 and 1 February 2020. All diagnostic procedures were included, whether performed by the gastroenterologists at our centre or by gastroenterologists at peripheral centres. The exclusion criteria comprised patients who were above the age of 13 years at the time of the procedure, repeated follow-up endoscopies, incomplete procedures (not passing the distal part of the esophagus), therapeutic procedures and patients who did not have at least one follow-up visit after the first EGD.

The procedure was labelled appropriate when the patient's health benefits (relief of symptoms and improved quality of life) exceeded the expected health risks (pain, discomfort, time and cost) by an acceptably wide margin.<sup>9</sup> In this cohort, EGD was considered appropriate when the indication to perform the EGD was in coherence with the ESPGHAN, ESGE and NASPGHAN guidelines or if the patient presented with alarming signs. Meanwhile, it was considered inappropriate when the indications were uncomplicated gastro-esophageal reflux and functional gastrointestinal (GI) pathology.

Electronic files on 529 EGDs were studied retrospectively. A parent or a care provider signed the consent forms before each procedure, allowing us to use the data from these files. Missing data were retrieved at the first follow-up, and we did not use any questionnaires. The demographics, indications, laboratory results and microscopic and macroscopic findings were analysed.

### Patient and public involvement statement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

### Statistics

Statistical analyses were performed using statistical software programmes (SPSS V.20.0, SPSS, Chicago, IL, USA). Data were analysed using a two-tailed  $\chi^2$  test; the ORs and 95% CIs were calculated. A p value < 0.05 was considered significant. Multivariate analysis was performed on selected signs and symptoms, predicting a positive contributive yield (change) on the initial diagnosis or subsequent therapeutic plan.

## RESULTS

### Demographics

A total of 529 diagnostic EGDs were performed during the study period. The median age of the children undergoing these procedures was 4 years; 40% of the patients were in the 9–11-year-age group. Females predominated the study population at 52.9%. The available weight and length/height data showed that approximately 23% of the children were under the fifth centile for weight, and 20% were under the fifth centile for length/height. Failure to thrive was present at the time of diagnosis in 32% of the children. Furthermore, 26.5% of the children had different comorbidities; the most common were familial Mediterranean fever (FMF) and diabetes mellitus (7.3% vs 4.3%, table 1).

**Table 1** Characteristics of the study population and histological findings

		Histological findings						
		N (%)	Oesophagus (96)		Stomach (422)		Duodenum (347)	
			Reflux esophagitis N (%)	Eosinophilic esophagitis N (%)	<i>H. pylori</i> gastritis N (%)	Gastritis N (%)	Duodenitis N (%)	Coeliac disease N (%)
Sex	Male	249 (47.1)	19 (20)	3 (3)	112 (27)	19 (5)	81 (23)	20 (6)
	Female	280 (52.9)	9 (9)	3 (3)	135 (32)	65 (15)	80 (23)	33 (10)
Age	0–2 years	27 (5.1)	4 (4)	0 (0)	5 (1)	13 (3)	11 (3)	2 (1)
	3–5 years	82 (15.5)	3 (3)	2 (2)	22 (5)	49 (12)	30 (9)	8 (2)
	6–8 years	119 (22.5)	4 (4)	3 (3)	55 (13)	90 (21)	35 (10)	11 (3)
	9–11 years	213 (40.3)	10 (11)	1 (1)	113 (27)	160 (38)	58 (17)	22 (6)
	13–14 years	88 (16.6)	17 (18)	0 (0)	52 (12)	66 (16)	27 (8)	10 (3)
FTT	Yes	170 (32)	11 (11)	3 (3)	68 (16)	102 (24)	58 (17)	27 (8)
	No	359 (67.9)	17 (18)	3 (3)	179 (42)	276 (65)	103 (30)	26 (7)
Weight*	<5th	119 (22.5)						
	5–95th	342 (64.7)						
	>95th	25 (4.7)						
	NA	43 (8)						
Height*	<5th	105 (19.8)						
	5–50th	328 (62)						
	>95th	13 (2.5)						
	NA	83 (15.7)						
Comorbidities	Yes	140 (26.5)						
	No	389 (73.5)						

\*Weight and height in percentiles.  
FTT, failure to thrive (a child might have multiple positive histologies); *H. pylori*, *Helicobacter pylori*; NA, not applicable.

### Indications

Overall, 44.8%, 42%, 7.2%, 3.4% and 2.6% of the diagnostic EGDs were performed for chronic abdominal pain, coeliac disease, haematemesis, refractory anaemia and irritable bowel diseases, respectively (table 2).

### Endoscopic and pathological findings

In our cohort, eosinophilic esophagitis was the final diagnosis in three boys and three girls, mainly between the ages of 3 and 11 years. *H. pylori* was more prevalent in the 9–11-year-age group (27%) and was the final diagnosis

**Table 2** Indication and final diagnosis of EGDs

Indication	N	%	Final diagnosis	N	%
Abdominal pain	237	44.8	<i>H. pylori</i> gastritis	247	44
Vomiting	31	5.9	CD	68	12
Suspected coeliac disease	154	29.1	Functional abdominal pain	43	8
Anaemia	18	3.4	FMF	25	4
Esophageal varices	3	0.6	Foreign body ingestion	69	12
Haematemesis	38	7.2	Potential CD	16	3
Diarrhoea	18	3.4	Caustic ingestion	15	3
Dysphagia	16	3.0	Reflux esophagitis	12	2
IBD	14	2.6	IBD	9	2
			Others	61	11

CD, coeliac disease; EGDs, esophagogastroduodenoscopy; FMF, familial mediterranean fever; *H. pylori*, *Helicobacter pylori*; IBD, inflammatory bowel disease.

**Table 3** Correlation between indication for EGD and its appropriateness

Indication for EGD	N (529)	%	Appropriate		X <sup>2</sup>	P value	OR	95% CI	P for the OR
			Yes (488)	No (41)					
Abdominal pain	237	44.8	232	5	21.64	<0.005	8.3	2.9 to 23.7	0.0001
R/O coeliac disease	154	29.2	130	24	18.65	<0.0005	0.257	0.13 to 0.95	<0.001
Haematemesis	38	7.1	37	1	*	0.345	3.19	0.42 to 23.85	0.25
Vomiting	24	4.4	24	0	*	0.243	4.16	0.25 to 70.2	0.32
Anaemia	18	3.4	18	0	*	0.385	3.26	0.19 to 55.13	0.41
Diarrhoea	18	3.4	18	0	*	0.62	2.7	0.16 to 46.22	0.49
Dysphagia	16	2.9	16	0	*	0.62	2.7	0.16 to 46.22	0.49
R/O IBD	14	2.6	14	0	*	0.61	2.36	0.14 to 40.35	0.55
Heartburn	7	1.3	0	7	*	<0.005	0.0047	0.0003 to 0.084	0.0003
R/O varices	3	0.6	3	0	*	1	0.59	0.03 to 11.78	0.73

\*Not Available

EGD, esophagogastroduodenoscopy; IBD, inflammatory bowel disease; R/O, rule-out; Varices, esophageal varices.

in 32% of all gastric biopsies taken from female patients. Furthermore, 10% of the duodenal biopsies were from girls with coeliac disease (table 1).

*H. pylori* gastritis was the most common final diagnosis in 247 (44%) children. EGDs were performed for foreign body removal in 69 patients and for assessing postcaustic ingestion in 15 cases, which accounted for 16% of the total endoscopies performed during the study period. A final diagnosis of functional abdominal pain and FMF was reached in 8% and 4% of the children following normal EGD, respectively (table 2)

#### Appropriateness and diagnostic yield of the EGDs

Four hundred and eighty-eight (92%) EGDs were deemed appropriate. Conversely, 41 (7.7%) EGDs were considered to be inappropriate. The highest chances of having an appropriate procedure were when the indication was

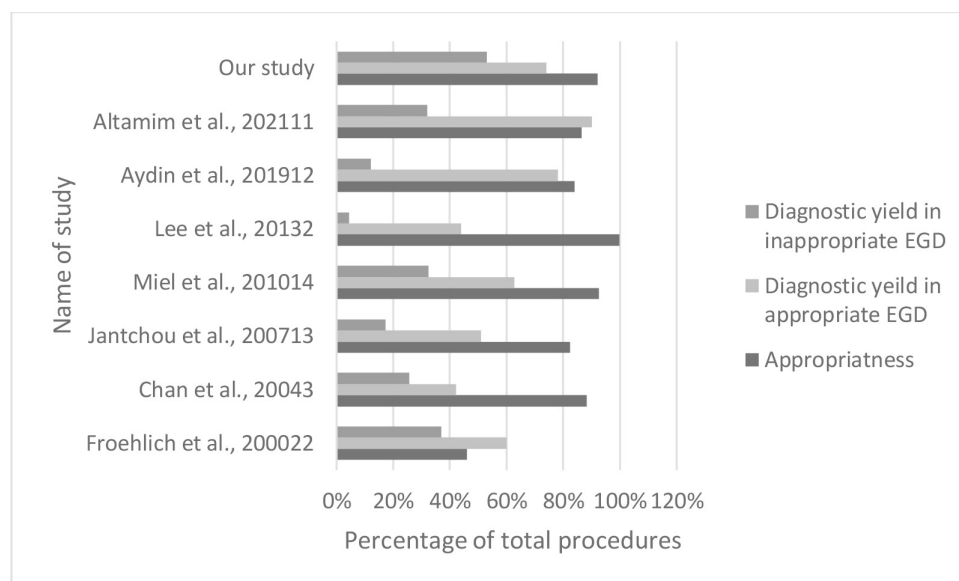
abdominal pain ( $p < 0.0005$ , OR: 8.3, 95% CI: 2.9 to 23.7). Conversely, the highest chances of having an inappropriate procedure were when the indication was heartburn ( $p < 0.0005$ , OR: 0.0047, 95% CI: 0.0003 to 0.084) (table 3).

In the 529 EGDs performed, 871 biopsies were taken from the oesophagus, stomach, duodenum or a combination of two or three sites. Positive findings were noted in 645 (74.0%) of these biopsies (figure 1).

The highest positive yield was in biopsies taken from the oesophagus (66%), while the lowest positive yield was in biopsies taken from the stomach (42%).

#### Correlation between the appropriateness and final diagnosis

After reaching final diagnoses, 448 EGDs were performed appropriately, and 32 EGDs were performed inappropriately. The odds of having an appropriate procedure were lower for functional abdominal pain than for other final

**Figure 1** Appropriateness and diagnostic yield. EGD, esophagogastroduodenoscopy.

**Table 4** Correlation between appropriateness and final diagnosis

Final diagnosis	Appropriate		X <sup>2</sup>	P value	OR	95% CI	P for the OR
	Yes (488)	No (32)					
<i>H. pylori</i> gastritis	228	19	0.046	0.83	1.1	0.53 to 2.19	0.83
Coeliac disease	67	1	3.99	0.05	6.1	0.81 to 45.1	0.079
Functional abdominal pain	35	8	10.47	0.001	0.27	0.12 to 0.63	0.002
FMF	23	2	*	0.7	0.9	0.2 to 3.98	0.88
Potential coeliac	15	1	*	1	1.35	0.17 to 10.45	0.78
Reflux esophagitis	11	1	*	0.6	0.86	0.11 to 6.82	0.89
R/O IBD	9	0	*	1	0.72	0.04 to 13.7	0.83

FMF, familial mediterranean fever; *H. pylori*, *Helicobacter pylori*; IBD, inflammatory bowel disease; R/O, rule out.

diagnoses (OR=0.27; 95% CI: 0.12 to 0.63, p=0.002), and there was a statistically significant association between functional abdominal pain as a final diagnosis and the appropriateness of the procedure (X<sup>2</sup>=10.47, p=0.001). An association was also noted between the definitive diagnosis of coeliac disease and the appropriateness of the procedure (X<sup>2</sup>=3.99, p=0.05; OR: 6.1, 95% CI: 0.81 to 45.1, p=0.079) (table 4).

Nine patients did not have a final diagnosis documented in their files. Furthermore, inappropriate EGDs were performed in 32 patients with a definitive diagnosis confirmed in their files. Ten of these patients had normal histological findings: eight and two were diagnosed with functional abdominal pain and FMF, respectively. In 19 patients (59.4%), an incidental positive histological finding of *H. pylori* gastritis was noted (table 4).

## DISCUSSION

The science of paediatric gastroenterology evolved rapidly in the last two decades, mandating the evolution of guidelines to control the diagnostic and therapeutic procedures in this field (such as upper and lower endoscopy) to minimise inappropriate procedures leading to unnecessary personnel exhaustion and health costs. Most paediatric gastroenterology guidelines were established using research mostly done in European countries and North America.<sup>9</sup>

Until performing this study, there were no Middle Eastern or local guidelines established in paediatric gastroenterology, which would have considered the sociocultural and economic factors of the patients who might govern several management decisions. The lack of local or national guidelines led physicians in Jordan to abide by the NASPGHAN, ESGE or ESPGHAN guidelines when managing paediatric gastroenterological pathologies.<sup>1 2 10 11</sup>

Appropriate care is defined as when the expected health benefit to the patient for any management or procedure exceeds the predicted health risks of that management.<sup>9</sup> At the same time, differentiating paediatric patients with serious GI pathologies from those with functional GI

pathologies can be very challenging for paediatric gastroenterologists, and this might govern the appropriateness of the procedure performed.<sup>12</sup>

In our study, 92.2% of all diagnostic EGDs were performed appropriately, while 7.8% were performed inappropriately (table 3). Jantchou *et al*<sup>13</sup> reported that inappropriate EGDs comprised approximately 18% of the total procedures; they contributed this significantly high percentage to referrals from office doctors outside the hospital.<sup>13</sup> In another cohort, Miele *et al*<sup>14</sup> found that inappropriate procedures reduced significantly after the publication of the Rome II criteria for functional GI disorders. Nevertheless, 26% of all procedures were still considered inappropriate.<sup>14</sup> On the other hand, Lee *et al*<sup>2</sup> reported an overall inappropriateness for EGDs of 0.3%, and an overwhelming 99.7% of the cases were considered appropriate (figure 1). They stated that the low percentage of inappropriate EGDs conducted in their service was attributed to the fact that all referrals for GI endoscopy from office-based paediatricians were initially screened by one of the practicing gastroenterologists before being subjected to endoscopy.<sup>2</sup>

Many studies reported different diagnostic yield percentages ranging from 44% to 90% (figure 1); simultaneously, the percentage of diagnostic yield improved in the most recent years, reflecting advancements in guidelines and stronger adherence to them. Our study showed a diagnostic yield of 74%, which is close to that reported in a similar study done performed by Altamimi *et al* in Jordan.<sup>11</sup>

We attribute this relatively high percentage of inappropriate procedures to the Open Access system in our hospital. For example, general paediatricians in primary and secondary centres with no paediatric gastroenterology services can require an upper or lower GI endoscopy; these referred patients will undergo the procedure without being screened by our gastroenterologists and continue their care with their primary physicians.<sup>3</sup>

The electronic files did not document whether the patients were referred by general paediatricians. However, as we in our service abide by the NASPGHAN, ESGE and



ESPGHAN guidelines,<sup>1 4</sup> we anticipated that the Open Access system would explain the higher percentage of inappropriate procedures.

In this study, we researched the diagnostic yield of the EGDs performed; 74.1% of all biopsies were positive for a specific pathology. Thus, our study numbers were higher than those of some other studies conducted in the same field by Noble *et al*,<sup>15</sup> who reported a positive diagnostic yield of 55% in all EGDs performed. However, they excluded patients with coeliac disease, who comprised a significant portion of the study population in our research.

EGDs performed for coeliac disease have a high positive yield as the positive predictive value of this indication closely parallels the reported positive predictive value of the most commonly used antibodies (tissue transglutaminase IgA) for screening for coeliac disease.<sup>16</sup> This leads to questions regarding the necessity of small-bowel biopsy to establish the diagnosis of coeliac disease, as has been the established practice recommended in the guidelines set by the ESPGHAN.<sup>17 18</sup>

Lee *et al*<sup>9</sup> had a similar percentage of positive yield in their study; the probability of detecting a positive endoscopic finding in EGD was 79%; this might be attributed to the same study settings as ours, that is, a university tertiary hospital<sup>2</sup> (figure 1).

Even normal EGDs performed appropriately will positively impact the management of paediatric patients. In our population, patients with FMF comprised a high percentage of patients with chronic abdominal pain that may have presented atypically;<sup>19 20</sup> thus, we performed EGD to rule out other causes of chronic abdominal pain. Thomson *et al*<sup>21</sup> reported that 45% of the patients had a contributive yield due to EGD findings. Moreover, they considered that negative test results equally contributed to patient care. They believe that the impact of normal findings on patient management was more difficult to quantify than positive findings.<sup>21 22</sup> On the other hand, Bonilla and Saps<sup>23</sup> argued against encouraging normal endoscopy as a positive yield in directing diagnosis or reassuring functional pathologies in paediatrics; they urged the use of the Rome III criteria supported by negative laboratory tests to prevent conducting EGDs for ruling out functional GI pathologies.<sup>14 23</sup>

Moreover, several studies have shown that it may be challenging to rule out clinically significant diseases in children based on the endoscopic appearance of the upper GI tract, thereby rendering biopsies during paediatric EGD necessary even in the absence of gross endoscopic findings.<sup>24 25</sup>

In correlating the appropriateness and yield of these procedures, we had a significant percentage of patients with incidental asymptomatic *H. pylori* gastritis. The incidental finding of *H. pylori*-associated gastritis without duodenal or gastric mucosal lesions rarely gives rise to symptoms or progresses to more severe disease complications during childhood. Hence, ESPGHAN and NASPGHAN jointly recommend against management,<sup>26 27</sup>

rendering this finding a negative contributory yield in EGDs.

The main shortcoming of the present study was its retrospective nature; accordingly, we had some incomplete charts. Another drawback was that this study was conducted at one centre only; although it was a referral centre, the inclusion of more than one paediatric gastroenterology service would have been more representative.

## CONCLUSION

In conclusion, the present study showed that the appropriateness and diagnostic yield of procedures performed at our centre are similar to those performed internationally, suggesting that the ESPGHAN, ESGE, modified NASPGHAN and ASGE guidelines are applicable universally, even to a middle eastern country such as Jordan. Following these guidelines provided acceptable predictability of a positive yield in our cohort, which can be improved by encouraging general paediatricians to follow these guidelines when managing or referring patients. In the Middle East, where other causes of chronic abdominal pain are prevalent (FMF), a prudent approach to EGD should be adopted, and international guidelines should be applied vigorously to minimise inappropriate procedures.

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**Contributors** Authors' contributions: SB: The guarantor; conceived and designed the study and wrote the paper. MO: contributed data or analysis tools and performed the analysis EA: extensive review of the paper and data analysis. SA-D: collected the data, and contributed data or analysis tools by developing a phone application for data collection. KEW, MA, MB and MA-K: collected the data, and contributed data or analysis tools by developing a phone application for data collection.

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**Data availability statement** Data are available upon reasonable request.

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