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Original Article

Which Alarm Symptoms Are Associated With Abnormal Gastrointestinal Endoscopy Among Thai Children?

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ABSTRACT

Purpose: Alarm symptoms (red flag signs) are crucial indications for management decisions on pediatric gastrointestinal endoscopy. We aimed to identify items in the alarm symptoms and pre-endoscopic investigations that predict abnormal endoscopy results.
Methods: A retrospective descriptive study was conducted among children aged under 18 years undergoing endoscopy. The patients were classified into normal and abnormal endoscopic groups. The incidence of alarm symptoms and pre-endoscopic investigations were compared between the groups. Univariate and multivariate logistic regression analyses were performed to determine independent risk factors for abnormal endoscopy.
Results: Of 148 participants, 66 were classified in the abnormal endoscopy group. Compared with the normal group, the abnormal group had a significantly higher prevalence of alarm symptoms. Moreover, hematemesis/hematochezia, anemia, low hemoglobin level, hypoalbuminemia, rising erythrocyte sedimentation rate, increased serum lipase, and blood urea nitrogen/creatinine ratio were significantly higher in the abnormal endoscopy group than in the normal group. Multivariate logistic regression analysis indicated that hematemesis/hematochezia and low hemoglobin level were independent risk factors for abnormal endoscopy.
Conclusion: The alarm symptoms and pre-endoscopic investigations were evaluated using predictive factors for abnormal pediatric endoscopic findings. According to multivariate logistic regression analysis, hematemesis/hematochezia and low hemoglobin levels were independent risk factors for abnormal endoscopy.

Keywords: Child; Gastrointestinal tract; Endoscopy; Risk factors

INTRODUCTION

Pediatric endoscopy, first described in the 1970s [1], is one of the most useful gastrointestinal (GI) procedures delivering high accuracy in diagnosing and managing GI conditions such as acid-peptic disease, inflammatory bowel disease (IBD), eosinophilic gastroenteritis, GI infection, intestinal tumors, and functional gastrointestinal disorders [2]. Moreover, endoscopic modalities facilitate endoscopic intervention with a low risk of complications and improved morbidity and mortality rates in pediatrics [3]. The diagnostic yield of

endoscopy is considerably dissimilar between adults and children. Among children, the overall diagnostic yield from esophagogastroduodenoscopy (EGD) and colonoscopy accounted for 14–67%, depending on the intervention and the indications of endoscopy [4-6]. Moreover, few studies have assessed the yield of pediatric endoscopy and explored the patient characteristics or indications favoring higher diagnostic yields [7-10]. Indications for endoscopy may vary in clinical settings. The presence of symptoms suggestive of an underlying organic abnormality of the GI tract is a common reason for diagnostic EGD and colonoscopy among children. Thus, alarm symptoms or red flag signs and symptoms are the most instrumental factors for decisions about endoscopy. The items in alarm symptoms include GI and extra-GI manifestations such as anorexia, weight loss, persistent diarrhea, hematochezia/hematemesis, abdominal pain away from the umbilicus, nighttime abdominal pain, dysphagia, recurrent vomiting, bowel habit change, prolonged fever, abdominal mass, extra-GI manifestations of IBD and anemia [11-14]. Despite these alarm symptoms, a low rate of complications is reported in pediatric endoscopy, and the cost-effectiveness of the procedures remains indefinite, especially among children presenting with or without alarm symptoms [7]. We aimed to identify items in the alarm symptoms and pre-endoscopic investigations to predict abnormal pediatric endoscopy results and recognize the diagnostic yield of endoscopic procedures among children. Moreover, we aimed to identify the common abnormal endoscopic appearances among children undergoing endoscopy.

MATERIALS AND METHODS

A retrospective descriptive study was conducted among children aged 0–18 years undergoing a GI endoscopy at the Pediatric Department, Phramongkutklao Hospital, between February 2015 and December 2022. The endoscopic procedures were performed by experienced pediatric gastroenterologists, and the indication for the conducted procedures was as per the European Society of Gastrointestinal Endoscopy and the European Society for Paediatric Gastroenterology Hepatology and Nutrition Pediatric gastrointestinal endoscopy guidelines, announced in 2016 [13]. Endoscopic procedures were performed routinely under appropriate anesthesia [3]. Histopathologic assessments were performed by general and gastrointestinal pathologists in the Histopathology Department of Phramongkutklao Hospital. We excluded children receiving endoscopic surveillance, routine endoscopic therapy, and therapeutic endoscopies, such as foreign body retrieval, caustic agent ingestion, endoscopic dilation, and portal hypertension treatment. Patients with incomplete or insufficient medical records were excluded from the study.

Data collection

Electronic medical records were reviewed for relevant data. Demographic data, clinical manifestations, alarm symptoms (hematemesis/hematochezia, abdominal pain away from the umbilicus, bowel habit change (>2 weeks), dysphagia/recurrent vomiting, persistent diarrhea (>2 weeks), anemia, weight loss/failure to thrive, night pain, anorexia, prolonged fever (>2 weeks), and extra-GI manifestation of IBD), comorbidities, endoscopic indications, pre-endoscopic investigations, endoscopic procedures, endoscopic findings and postendoscopic diagnoses were all included in the data gathering. Recurrent abdominal pain was diagnosed if it persisted longer than 2 months. Pre-endoscopic laboratory findings were defined as abnormal. Low hemoglobin levels by age, increased C-reactive protein (CRP) levels (CRP >3 mg/L), rising erythrocyte sedimentation rate (ESR) (ESR >20 mm/hr), and hypoalbuminemia (serum albumin <3.5 g/dL) were defined as the abnormal cut-off

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[15-17]. Significant endoscopic findings such as ulcers, erosion, stenosis, and hemorrhage were used to classify abnormal endoscopy groups. These findings should be compatible with the symptoms as well as the abnormal histologic findings. Instead, the normal endoscopic group was defined by the absence of significant abnormalities or only a minor endoscopic or histologic abnormality incompatible with the children's illness [3]. An endoscopic appearance, including a histologic finding resulting in a definite diagnosis or a specific treatment, was referred to as a positive diagnostic yield. We classified children into the abnormal and normal endoscopy groups. Demographic data, the incidence of alarm symptoms, and pre-endoscopic investigations were compared between the groups. Univariate and multivariate logistic regression analyses were used to identify the independent risk factors for abnormal endoscopy findings.

Statistical analysis

Continuous data were analyzed using the student's *t*-test, and categorized data were compared using chi-square or Fisher's exact test. A *p*-value<0.05 was considered significant. Univariate logistic regression analysis was performed to identify significant items of alarm symptoms, and those with *p*-value<0.2 were subsequently subjected to multivariate logistic regression analysis to identify independent items. The association of a particular variable was expressed as an odds ratio (OR) with a 95% confidence interval (CI). Data were collected and analyzed using using IBM SPSS Statistics for Windows, Version 22.0 (IBM Co.). This study was conducted according to the principles of the Helsinki Declaration and was approved by the ethics committee of Phramongkutklao Hospital and College of Medicine with IRB number S025h/65 since April 2022. The ethics board decided to omit formal consent.

RESULTS

Overall, 148 children were enrolled in this study, of which 48.6% were male, and the mean age of this cohort was 136.93±62.7 months, with a mean body mass index (BMI) of 18.52±5.28 kg/m^2. The number of procedures totaled 181, including 131 EGDs and 50 colonoscopies. The most common indication for endoscopy was chronic abdominal pain (37.2%). The endoscopic indications comprised GI bleeding (31.0%), recurrent vomiting (9.5%), chronic diarrhea (8.1%), and dysphagia (7.4%). Regarding alarm symptoms, 141 (95.3%) of 148 children revealed at least one item of alarm symptoms. Hematemesis/hematochezia was the most typical alarm symptom (33.8%), followed by abdominal pain away from the umbilicus (29.7%), a change in bowel habit (25.7%), and dysphagia/recurrent vomiting (25.0%). Comorbidities were revealed in 38% of children. Common comorbidities in this cohort comprised children with immunosuppressive therapy (9.5%), developmental-psychological disorders (9.5%), epilepsy (5.4%), and end-stage renal disease (2.7%). The demographic data of children in this cohort are presented in **Table 1**.

A total of 148 GI endoscopy cases were diagnosed, and 82 (55.4%) of those were classified in the normal endoscopy group, whereas the abnormal endoscopic group consisted of 66 cases (44.6%). Children with normal and abnormal endoscopies were compared and revealed no significant differences in sex (46.3 vs. 51.5% of males; *p*-value=0.531) and co-morbidities (34.1 vs. 43.9; *p*-value=0.224) between the groups. The age (146.61±59.69 vs. 124.89±64.69 months) and BMI (19.55±6.01 vs. 17.22±3.84 kg/m^2) of children undergoing abnormal endoscopy were significantly lower than that of children undergoing normal endoscopy with *p*-values 0.044 and 0.013, respectively.

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Table 1. Demographic data, indication of endoscopy, and alarm symptoms of patients in this study

Demographic profiles of children	Results
Total number of children	148
Male	72 (48.6)
Age (mo)	136.93±62.70/152.5 (92.5–190.0)
BMI (kg/m^2)	18.52±5.28/17.47 (14.61–20.58)
Indications of endoscopy	
Chronic abdominal pain	55 (37.2)
Upper GI bleeding (hematemesis)	27 (18.2)
Lower GI bleeding (hematochezia)	19 (12.8)
Recurrent vomiting	14 (9.5)
Chronic diarrhea	12 (8.1)
Dysphagia	11 (7.4)
Others	
Acute abdominal pain (6), weight loss (2), anemia (1), abdominal mass (1)	10 (6.8)
Duration of admission (d)	28.69±146.40/3.04 (1.37–9.64)
Duration of symptoms (mo)	152.6±255.95/50.50 (9.0–181.0)
Procedure	
EGD	131
Colonoscopy	50
Presence of alarm symptoms	141 (95.3)
Hematemesis/hematochezia	50 (33.8)
Abdominal pain away from the umbilicus	44 (29.7)
Bowel habit change	38 (25.7)
Dysphagia/recurrent vomiting	37 (25.0)
Persistent diarrhea	33 (22.3)
Anemia	28 (18.9)
Weight loss/failure to thrive	24 (16.2)
Night pain	18 (12.2)
Anorexia	14 (9.5)
Prolonged fever	3 (2.0)
Extra-GI manifestation of IBD	3 (2.0)
Co-morbidities	
Immunosuppressive therapy	14 (9.5)
Behavior/developmental/psychiatric disorders	14 (9.5)
Epilepsy	8 (5.4)
End-stage renal disease	4 (2.7)
Others	
Delayed development (3 cases), hematologic malignancy (3), congenital/cyanotic heart disease (3), primary immune deficiency (2), thyroiditis/hyperthyroidism (2), cow's milk protein allergy (1), chronic liver disease (1), dysautonomia (1) and previous GI surgery (1)	17 (11.5)

Values are presented as number only, number (%), mean±standard deviation, or median (interquartile range).
BMI: body mass index, GI: gastrointestinal, EGD: esophagogastroduodenoscopy, IBD: inflammatory bowel disease.

At least one alarm symptom was identified among all 66 children (100.0%) in the abnormal group; however, these items were identified among 75 of 82 children (91.4%) in the normal group and reached a statistical significance between groups (p=0.0171). On comparing the alarm symptoms between the two groups, hematemesis/hematochezia (12.2 vs. 60.6%) and anemia (4.9 vs. 36.4%) were found to be significantly higher among patients with an abnormal endoscopy than those among patients with normal endoscopy with p-values of <0.001 and <0.001, respectively.

However, the remaining items, such as changing bowel habits (29.3 vs. 21.2%), dysphagia/recurrent vomiting (23.2 vs. 27.3%), persistent diarrhea (22.0 vs. 22.7%), failure to thrive (12.2 vs. 21.2%), and anorexia (7.3 vs. 12.1%) were not significantly different between the groups. Children with normal endoscopy had a significantly higher prevalence of chronic

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abdominal pain symptoms (72.0 vs. 37.9%, $p<0.001$) than those with normal endoscopy. Nevertheless, the site of the pain away from the periumbilical area (47.5 vs. 64.0%) and nighttime symptoms (23.7 vs. 16.0%) did not significantly differ.

We compared pre-endoscopic investigations and found that compared with children undergoing normal endoscopy, those undergoing abnormal endoscopy had a significantly higher prevalence of low hemoglobin levels by age (36.5 vs. 60.6%, $p=0.005$) as well as hypoalbuminemia (9.7 vs. 25.0%, $p=0.018$). Moreover, the prevalence of rising ESR, serum lipase levels, and BUN/creatinine (Cr) ratio were also significantly higher among children with abnormal endoscopy. **Table 2** presents the specific details regarding alarm symptoms and pre-endoscopic examinations between groups.

Table 2. Comparison of alarm symptoms and pre-endoscopic investigations between children with abnormal and normal endoscopy

Profiles and parameters of children	Normal endoscopy (82 cases)	Abnormal endoscopy (66 cases)	*p*-value
Male	38 (46.3)	34 (51.5)	0.531
Age (mo)	146.61±59.69/158 (117.0–191.0)	124.89±64.69/138 (64.8–180.8)	0.044*
BMI (kg/m^2)	19.55±6.01/18.36 (14.9–21.2)	17.22±3.84/16.77 (14.4–18.8)	0.013*
Duration of admission (d)	25.78±139.94/2.09 (1.1–5.8)	32.29±155.06/5.37 (2.0–16.0)	0.004*
Duration of symptoms (d)	182.44±254.67/76.5 (28.0–257.3)	115.53±254.58/29 (4.3–113.0)	0.003*
Co-morbidities	28 (34.1)	29 (43.9)	0.224
Alarm symptoms			
Presence of alarm symptoms	75 (91.4)	66 (100.0)	0.017*
Hematemesis/hematochezia	10 (12.2)	40 (60.6)	<0.001*
Bowel habit change	24 (29.3)	14 (21.2)	0.265
Dysphagia/recurrent vomiting	19 (23.2)	18 (27.3)	0.567
Persistent diarrhea	18 (22.0)	15 (22.7)	0.910
Anemia	4 (4.9)	24 (36.4)	<0.001*
Weight loss/failure to thrive	10 (12.2)	14 (21.2)	0.139
Anorexia	6 (7.3)	8 (12.1)	0.321
Prolonged fever	1 (1.2)	2 (3.0)	NA
Extra-GI manifestation of IBD	0 (0.0)	3 (4.5)	NA
Chronic abdominal pain	59 (72.0)	25 (37.9)	<0.001*
Abdominal pain away from the umbilicus	28 (47.5)	16 (64.0)	0.165
Nighttime abdominal pain	14 (23.7)	4 (16.0)	0.429
Pre-endoscopic Investigations			
Hemoglobin (g/dL)	12.24±2.17/12.8 (11.0–13.5)	11.06±2.72/11.35 (9.3–12.9)	0.005*
Low hemoglobin level	30 (36.5)	40 (60.6)	0.005*
WBC (cell/cu.mm)	9,001.5±4,434.61/8,000 (6,275–9,900)	9,894.7±4,110.25/8,900 (6,600–12,550)	0.087
PMN (%)	57.23±16.75/57.5 (47.0–66.1)	62.85±18.49/64.6 (48.0–75.8)	0.052
Eosinophils (%)	2.61±2.94/2 (1.0–3.4)	1.76±2.28/1 (0.0–2.0)	0.027*
Absolute eosinophil count (cell/cu.mm)	228.96±283.12/126.6 (46.3–276.8)	183.16±350.91/98.85 (0.0–198.0)	0.119
Platelet count (cell/cu.mm)	338,612.5±137,073.25/315,000 (260,250–374,250)	325,075.76±180,139.29/293,500 (221,750–409,250)	0.294
ESR (mm/hr)	20.00±18.56/12 (9.0–24.0)	27.80±17.54/26 (16.8–38.0)	0.097
Rising ESR (>20 mm/hr)	7 from 21 (33.3)	13 from 20 (65.0)	0.043*
CRP (mg/L)	6.16±10.16/1.17 (0.8–4.8)	24.85±25.41/22.98 (2.9–44.2)	0.099
Rising CRP (>3 mg/L)	4 from 14 (28.6)	4 from 6 (66.7)	0.111
Albumin (g/dL)	4.34±0.57/4.5 (4.2–4.7)	3.85±0.87/4 (3.4–4.6)	<0.001*
Hypoalbuminemia (<3.5 g/dL)	7 from 82 (9.7)	16 from 64 (25.0)	0.018*
Amylase (U/L)	25.21±14.99/22 (20.0–27.8)	40.96±52.02/25 (23.0–34.0)	0.052
Lipase (U/L)	26.80±16.13/21.55 (17.0–31.3)	65.44±119.55/41 (20.9–50.0)	0.010*
BUN/Cr ratio	21.24±24.82/17.53 (11.6–21.0)	36.28±31.93/25.67 (17.5–40.5)	<0.001*

Values are presented as number (%), mean±standard deviation, or median (interquartile range).
BMI: body mass index, GI: gastrointestinal, IBD: inflammatory bowel disease, WBC: white blood cell, PMN: polymorphonuclear cells, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, BUN: blood urea nitrogen, Cr: creatinine, NA: not available.
*Significance at $p<0.05$.

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Esophageal ulcer/erosion was the most frequent abnormal finding of the esophagus (14.0%). Gastric ulcer/erosion/inflammation (36.8%) and antral nodularity (10.5%) were the most prevalent abnormalities of the stomach. The most common abnormal finding in the colon and rectum was ulcer/erosion/inflammation, comprising 12 (46.2%) and 13 cases (50.0%), respectively. In this cohort, peptic ulcer disease (21.2%) was the most frequently identified postendoscopic diagnosis, followed by colitis/proctitis (15.2%), *Helicobacter pylori* (HP)-induced gastritis (13.6%), esophageal ulcer (9.1%), and gastritis/duodenitis (9.1%). The list of abnormal endoscopic findings and postendoscopic diagnoses (66 cases) are shown in **Table 3**.

The details of abnormal endoscopic findings according to the alarm symptoms were listed. Abnormal endoscopy was revealed in 40 of 50 children (80.0%) who had hematemesis/hematochezia. Common findings were 13 cases of gastric erosion or ulcer and 12 cases of colonic erosion or ulcer. For children with abdominal pain away from the umbilicus, abnormal findings were detected in 16 of 44 (36.4%), and gastric erosion or ulcers were

Table 3. Endoscopic findings and post-endoscopic diagnoses among children with abnormal endoscopy

Endoscopic region and Post-endoscopic diagnosis	Case (%)
Esophagus	
Ulcer/erosion	8 (14.0)
Stenosis of the lower esophagus	2 (3.5)
Varices	2 (3.5)
Others	
Inflammation (1), stricture (1), vascular malformation (1)	3 (5.3)
Stomach	
Ulcer/erosion/inflammation	21 (36.8)
Antral nodularity	6 (10.5)
Varices	1 (1.8)
Duodenum	
Ulcer/erosion	8 (14.0)
Stenosis	2 (3.5)
Ileum	
Inflammation	3 (11.5)
Polyps	1 (3.8)
Colon	
Ulcer/erosion/inflammation	12 (46.2)
Polyps	2 (7.7)
Others	
Stenosis (1), lymphoid hyperplasia (1), vascular malformation (1)	3 (11.5)
Rectum	
Ulcer/erosion/inflammation	13 (50.0)
Polyps	5 (19.2)
Post-endoscopic diagnosis	
Duodenal/gastric ulcer	14 (21.2)
Colitis/proctitis	10 (15.2)
HP gastritis	9 (13.6)
Gastritis/duodenitis	6 (9.1)
Esophageal ulcer/erosion	6 (9.1)
Polyps (colon/pectum)	5 (7.6)
IBD	4 (6.1)
Others	
Vascular malformation (2 cases), rectal ulcer (2), duodenal stenosis (2), achalasia (2), esophageal stricture (1), prolapse gastropathy (1), sigmoid volvulus (1), esophageal varices (1)	12 (18.1)

Values are presented as number (%).
EGD: esophagogastroduodenoscopy, HP: *Helicobacter pylori*, IBD: inflammatory bowel disease.
Total number of children with abnormal endoscopy 66 cases (57 cases of EGD and 26 cases of colonoscopy).

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detected in 14 children. Overall, mucosal erosion and ulcers were the common findings in children with alarm symptoms. The features of these findings are shown in **Table 4**.

Multivariate logistic regression analysis indicated the items hematemesis/hematochezia (OR, 5.352; 95% CI, 1.127–25.428; p=0.035) and low hemoglobin level (OR, 4.198; 95% CI, 1.063–16.958; p=0.041) to be independent risk factors for abnormal endoscopy. However, weight loss, hypoalbuminemia, age, BMI, polymorphonuclear cells count, eosinophil count, and BUN/Cr ratio were not significant factors in detecting an abnormality for pediatric endoscopy. The details of the analysis are summarized in **Table 5**.

The overall endoscopic diagnostic yield in this cohort was demonstrated at 44.6%. The most commonly detected abnormality among children was hematemesis/hematochezia in 84.8% of children, followed by persistent diarrhea (41.7%), dysphagia (36.4%), and recurrent vomiting (28.6%). Chronic abdominal pain was the most frequent indication for endoscopy

Table 4. Details of abnormal endoscopic findings according to alarm symptoms

Alarm symptoms	Abnormal/total cases of endoscopy	Findings
Hematemesis/hematochezia	40/50 (80.0)	Gastric erosion or ulcer 13, colonic erosion or ulcer 12, duodenal ulcer 8, esophageal ulcer or erosion 6, colonic/rectal polyps 6, esophageal varices 2, vascular malformation (colon) 1, gastric varices 1
Abdominal pain away from the umbilicus	16/44 (36.4)	Gastric erosion or ulcer 14, esophageal ulcer 1, esophageal stricture (achalasia) 1, duodenal ulcer 1
Bowel habit change	14/38 (36.8)	Colonic erosion or ulcer 13, colonic polyps 3
Dysphagia/recurrent vomiting	18/37 (48.6)	Esophageal ulcer or erosion 8, gastric erosion or ulcer 5, esophageal stricture 3 (achalasia), duodenal stenosis 2
Persistent diarrhea	15/33 (45.5)	Colonic erosion or ulcer 13, colonic polyps 3
Anemia	24/28 (85.7)	Gastric erosion or ulcer 10, colonic erosion or ulcer 8, duodenal ulcer 6, esophageal ulcer or erosion 3, esophageal varices 2, colonic or rectal polyps 2, gastric varices 1, vascular malformation (stomach) 1, vascular alformation (colon) 1
Weight loss/failure to thrive	14/28 (50.0)	Colonic erosion or ulcer 11, gastric erosion or ulcer 3, esophageal ulcer or erosion 2, esophageal stricture 2, duodenal ulcer 2
Night pain	4/18 (22.2)	Gastric erosion or ulcer 3, rectal ulcer 1
Anorexia	8/14 (57.1)	Colonic erosion or ulcer 6, gastric erosion or ulcer 4, esophageal erosion or ulcer 1
Prolonged fever	2/3 (66.7)	Gastrtic erosion or ulcer 1, duodenal ulcer 1
Extra-GI manifestation of inflammatory bowel disease	3/3 (100.0)	Colonic erosion or ulcer 3, gastric erosion or ulcer 1

Values are presented as number (%). GI: gastrointestinal.

Table 5. Multivariate regression analysis of children with a difference in alarm symptoms and investigations

Items	p-value	Adjusted odds ratio	95% CI
Weight loss	0.729	1.356	0.242–7.584
Hematemesis/hematochezia	0.035*	5.352	1.127–25.428
Low hemoglobin level	0.041*	4.198	1.063–16.958
Hypoalbuminemia	0.208	3.025	0.540–16.958
Age	0.120	0.991	0.98–1.002
BMI	0.826	0.986	0.872–1.115
PMN	0.568	1.014	0.967–1.062
Eosinophil	0.187	0.784	0.564–1.125
BUN/Cr ratio	0.711	0.995	0.972–1.020

CI: confidence interval, BMI: body mass index, PMN: polymorphonuclear cells, BUN: blood urea nitrogen, Cr: creatinine.
*Significance at p<0.05.

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Table 6. Diagnostic yield of endoscopy for different endoscopic indications

Indications	Total number (cases)	Positive diagnostic yield (cases)	Diagnostic yield (%)
Chronic abdominal pain	55	11	20.0
Hematemesis/hematochezia	46	39	84.8
Recurrent vomiting	14	4	28.6
Persistent diarrhea	12	5	41.7
Dysphagia	11	4	36.4
Acute abdominal pain	6	2	33.3
Weight loss	2	1	50.0
Anemia	1	0	0.0
Abdominal mass	1	0	0.0
Total	148	66	44.6

in this population, and the diagnostic yield for this indication was 20%. The details of diagnostic yield classified by endoscopic indications are demonstrated in **Table 6**.

DISCUSSION

Alarm symptoms are one of the most important indications for organic diseases. In our study, the prevalence of alarm symptoms was significantly higher among children in the abnormal endoscopic group than in the normal endoscopic group. This finding was compatible with the outcome described by Akbulut et al. [8] in 2018, evaluating a diagnostic yield of EGD among children with abdominal pain. Children with alarm symptoms exhibited a significantly higher prevalence of positive diagnostic yield of endoscopy compared with those without alarm symptoms (63.6 vs. 43.5%, p=0.015) [8]. However, the alarm symptoms are inconsistently considered to determine investigations, as Reedy et al. [18] in 2019 reported a study of EGD among 287 children with abdominal pain without alarm symptoms. The data revealed that 7% of children had to change clinical management after undergoing endoscopy, and the abnormal endoscopic findings consisted of eosinophilic esophagitis, *Candida* esophagitis, celiac disease, nonspecific helminth infection, and HP infection [18]. Moreover, Tolone et al. [19] in 2017 revealed that 57% of children with recurrent abdominal pain with no alarm symptoms were diagnosed with organic diseases after undergoing nonendoscopic investigations. The data revealed that 22% of these conditions were lactose intolerance, 20% celiac disease, 2.4% cow milk allergy, 10% ureteral calculi, and 1% teniasis. These findings suggest and create awareness that children exhibiting persistent GI symptoms should be referred to pediatric gastroenterologists, and further investigations should be considered even in the absence of alarm signs [19].

Our study revealed a significantly higher incidence of abnormal endoscopic findings when children presented with clinical GI hemorrhage and anemia. This finding was compared with that of a related study among children with chronic abdominal pain, identifying that children with anemia, weight loss, and pain after waking from sleep were significant factors for abnormal endoscopy [8]. Furthermore, a recent study by Altamimi et al. [9] reported the result of multivariate analysis among children younger than 60 months, suggesting that abdominal pain, dysphagia/odynophagia, and heartburn were predictive of abnormal upper GI endoscopy. Wang et al. [20] reported dysphagia, GI bleeding, and recurrent vomiting as the most predictive factors for abnormal EGD on multivariate analysis. For pediatric colonoscopy, Wu et al. [10] revealed that pediatric colonoscopy was most effective among children presenting with lower GI hemorrhage and persistent diarrhea.

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In our cohort, we revealed that younger age is a major factor associated with an abnormal endoscopy. However, this finding contrasted with that of the study by Helin et al. [21] about EGD among children under 7 years presenting nonspecific GI or respiratory symptoms. The information from this study showed low diagnostic yield (<20%) unless presenting alarm symptoms [21]. The difference in results may have been caused by procedural differences, the number of children, and the endoscopic indications from our cohort.

This study's results showed that children undergoing endoscopy with chronic abdominal pain had a markedly higher percentage of normal endoscopic findings, even with the presence of alarm symptoms. This finding differed from the data from another researcher, showing a significantly higher diagnostic value of endoscopy among children with recurrent abdominal pain in a high-suspicion setting compared with patients in a low-suspicion setting (34 vs. 6%, p<0.001). The risk factors of the high suspicion group comprised nocturnal diarrhea, bloody stool, weight loss, history of food impaction, extra-intestinal features or family history of IBD, hypoalbuminemia, iron deficiency anemia, elevated ESR, positive stool occult blood testing, high fecal calprotectin, and positive serum tissue transglutaminase IgA levels. Thus, these factors could be used to determine the need for further investigations [22].

We discovered that low hemoglobin levels, increased ESR, hypoalbuminemia, rising serum lipase levels, and higher BUN/Cr ratios were prognostic factors for obtaining abnormal endoscopic findings for pre-endoscopic investigations. These findings confirmed that these parameters are vital surrogate markers to determine the organic diseases of the GI tract, such as persistent intestinal infection, intestinal inflammation, celiac disease, and IBD [15,23]. Levels of serum pancreatic enzymes, namely, amylase and lipase, were likely to be increased in non-pancreatic disorders or conditions such as intestinal inflammation, gut obstruction, duodenal ulceration, coeliac disease, peritonitis, acute cholecystitis, renal insufficiency, head injury, burns, shock, diabetic ketoacidosis, and a critical illness [24,25], which could be possible causes for increased pancreatic enzyme levels. Our study reported a significant rise in serum lipase levels among children with abnormal endoscopy due to various possible co-incidences.

In this study, the overall endoscopy diagnostic yield was 44.6%. Compared with the diagnostic yield of pediatric endoscopy involving different procedures, the yield for EGD was 39–63% [9,20,26-28], and the yield for colonoscopy was 33–75% [10,28-30] from related reports. If we categorized the diagnostic yield by endoscopic indication, the diagnostic yield varied from 20% among children with chronic abdominal pain to 85% among children with clinical GI bleeding.

According to a prior study, children with rectal bleeding undergoing colonoscopies had an overall yield of 64–77% for GI hemorrhage. Furthermore, the common findings were colitis (22–36%) and polyps (26–27%) [10,31]. Another report from Kawada et al. [29] demonstrated that abnormal colonoscopy in 56 of 197 cases (28.4%) with lower GI bleeding revealed juvenile polyps (20%) to be the most common finding. However, the prevalence of abnormal EGD among children with upper GI bleeding was reported at 57–75% [32,33]. For chronic abdominal pain, we observed a prevalence of abnormal endoscopy (20%). A previous systematic review among children reported a diagnostic yield of 3.6% and revealed that endoscopy in this situation presented an unclear effect on the change in treatment, quality of life, and cost-effectiveness [34]. Furthermore, a negative endoscopy did not decrease the severity or improve the functional score among children with functional abdominal pain

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disorders [35]. Proper patient selection can increase the diagnostic yield and reduce the likelihood of low-value interventions in such situations.

This study had limitations. We retrospectively reviewed electronic medical records that were incomplete. Furthermore, this study represented data from a single tertiary medical center. Thus, the findings of this study may not be entirely applicable in other settings. Some investigations were unavailable and excluded from this study, such as fecal calprotectin, hydrogen breath test, and a screening test for celiac disease. We did not include pre- and postendoscopic therapy to compare between groups owing to concerns about the exactness of the data. Children's age ranges were wide in the present study, and young children may not have the same indicationsfor endoscopy as adolescents. Most endoscopic procedures were performed by a single endoscopist; however, the histopathologic results were not reported by the same or designated pathologists.

In conclusion, the alarm symptoms and pre-endoscopic investigations were evaluated using predictive factors for abnormal pediatric endoscopic findings. Of these factors, hematemesis/hematochezia, anemia, low hemoglobin level, hypoalbuminemia, high ESR levels, rising lipase levels, and high BUN/Cr ratio were significantly associated with an abnormal endoscopy. Furthermore, according to multivariate logistic regression analysis, hematemesis/hematochezia and low hemoglobin levels were found to be independent risk factors for abnormal endoscopy.

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