Received: 28 November 2017 | Accepted: 18 March 2018

DOI: 10.1111/ijcp.13093

REVIEW ARTICLE

WILEY THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Gastrointestinal symptoms in children: Primary care and specialist interface

Valeria Dipasquale | Domenico Corica | Simone M. C. Gramaglia | Simona Valenti | Claudio Romano

Pediatric Gastroenterology and Cystic Fibrosis Unit, Department of Human Pathology in Adulthood and Childhood "G. Barresi", University of Messina, Messina, Italy

Correspondence
Claudio Romano, Pediatric Gastroenterology and Cystic Fibrosis Unit, Department of Human Pathology in Adulthood and Childhood "G. Barresi," University of Messina, Messina, Italy.
Email: romanoc@unime.it

Summary

Aims: Gastrointestinal symptoms and diseases represent one of the major reasons for paediatricians' requests for specialist consultations and hospital admissions. One fourth of annual medical consultations for children younger than 6 years can be attributed to gastrointestinal symptoms. High-quality guidelines have been validated worldwide to provide clinical recommendations and support healthcare providers' practice. Nevertheless, overall compliance to standards of care is unsatisfactory, and children with gastrointestinal symptoms frequently undergo expensive, useless specialist consultations and laboratory evaluations. The aim of this study is to review the main epidemiological and clinical aspects, together with management strategies, of the most common gastrointestinal symptoms in children, pointing out pitfalls and practical tips in primary care management, and providing correct indications for specialist consultations.

Methods: For this review, articles published in English from 2000 to January 2018 were identified from the PubMed/Medline (http://www.ncbi.nlm.nih.gov/pubmed/) database and selected on the basis of quality, relevance to the illness and importance in illustrating current management pathways. The search used the following keywords: gastrointestinal symptoms, functional gastrointestinal symptoms, children, primary care, specialist consultations and management. Particular emphasis was placed on evidence-based guidelines and high-quality studies.

Results: Functional gastrointestinal symptoms have a high impact on the quality of life of children and families and on healthcare costs. A complete medical history and clinical examination are often sufficient to guide the primary care provider in the diagnosis, further workup or referral to a paediatric gastroenterologist.

Conclusion: Paediatric gastroenterology outpatients' clinics are among the most crowded specialists, and functional gastrointestinal symptoms and disorders are the most frequent reason for counselling. The number of specialist consultations could be reduced if guidelines were applied in primary care settings.

1 | INTRODUCTION

Paediatric gastroenterology emerged as a paediatric specialty in the 1960s. Since then, childhood coeliac disease has represented the first model of paediatric gastroenterology disease. By 1980, functional gastrointestinal disorders (FGIDs), such as functional constipation and irritable bowel syndrome (IBS), had become the most frequent reason for paediatric gastroenterology consultation.[1] Prevalence of most FGIDs in childhood has not been fully agreed on: in the US population, prevalence has recently been estimated

at about 27% among infants (0-3 years)[2] and 23.1% among children and adolescents (4-18 years),[3] based on parental report. Similar percentages have been found in the Mediterranean area of Europe, with variations in the prevalence of some FGIDs among different European countries, probably due to variability in environment, diet, microbiome and genetic background.[4] High prevalence rates of FGIDs have been recently reported in South America (16.8%) and Asia (16.5%) too.[5] Infant colic can be considered another frequent gastrointestinal diagnosis that creates anxiety in the family. Acute diarrhoea is the most prevalent diarrhoeal disorder in childhood, with an average of 0.5-2 episodes per year in children younger than 3 years in Europe.[6] Haematochezia, faltering growth, vomiting, constipation and chronic abdominal pain represent a group of conditions for which a specialist consultation is often requested. A lack of understanding of pathogenic mechanisms often leads to extensive investigations, non-effective therapies and staggering healthcare costs. Better application of guidelines, with the aim of providing a more adequate selection between children who need specialist consultations and those who should be managed in the field of primary care, is required. Herein, we point out common pitfalls and practical tips in the diagnosis and management of the most common gastrointestinal symptoms or diseases in primary care and provide correct indications for specialist consultations (Table 1).

Review criteria

This non-systematic review identified recent clinical and epidemiological studies from the PubMed/Medline (http://www.ncbi.nlm.nih.gov/pubmed/) database using the search terms gastrointestinal symptoms, gastrointestinal complaints, children, primary care, specialist consultations, management, guidelines. Case reports, editorials and other communications with low levels of evidence were excluded.

Message for the clinic

Gastrointestinal symptoms and diseases are considered the most frequent reason why primary care providers request specialist consultations for children. Infants and children of all ages with gastrointestinal symptoms frequently undergo expensive and useless specialist consultations and laboratory evaluations. The knowledge of guidelines and protocols, a complete medical history and clinical examination are often sufficient to guide the primary care provider in diagnosis and further workup.

2 | METHODS

For this review, a comprehensive search of published literature using the PubMed/Medline (http://www.ncbi.nlm.nih.gov/pubmed/) database was carried out to identify all articles published in English from 2000 to January 2018, using the keywords, or combinations of keywords: gastrointestinal symptoms, functional gastrointestinal symptoms, children, primary care, specialist consultations, management, guidelines. All of the most common gastrointestinal complaints were later included as search keywords to review literature data regarding clinical presentation, diagnosis and management strategies. Particular emphasis was placed on evidence-based guidelines and all high-quality studies illustrating current management pathways. Case reports, editorials and other communications with low levels of evidence were excluded.

3 | INFANT COLIC

3.1 | General overview

Infant colic is a behavioural phenomenon in infants aged 1-4 months and involves long periods of inconsolable and hard-to-calm crying. In 1954, Wessel et al[7] described colicky infants as "healthy and well-fed, had paroxysms of irritability, fussing or crying lasting for a total of 3 hours a day, occurring on more than 3 days in any 1 week for a period of 3 weeks" (Wessel et al's "rule of threes" criteria). A worldwide survey promoted in 2015 by both the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and North American Society for Pediatric Gastroenterology Hepatology and Nutrition (NASPGHAN)[8] found prevalence rates ranging from 2% to 73%, with a median of 17.7%. Prevalence of infant colic varies widely, since it is influenced by caregivers' perceptions of the intensity and duration of crying bouts and the method by which data on crying are collected. A systematic review of 15 community-based surveys of the occurrence of infantile colic found prevalence rates ranging from 3% to 28% in prospective studies and from 8% to 40% in retrospective studies.[9] The aetiology of infant colic is not fully understood. Different hypotheses have been proposed, including overproduction of intestinal gas,[10] disturbance of pathways in the central nervous system,[11] psychosocial causes (such as negative or inadequate maternal-infant bonding, parental overstimulation or insecure parental attachment),[12] gastrointestinal-related causes, such as hypersensitivity to cow's milk protein, gastroesophageal reflux (GER) or motility disorders of the gastrointestinal tract.[13] Only in 5% of infants presenting excessive crying can an organic cause be demonstrated, including central nervous system diseases (such as subdural haematoma), dyschezia, GER, acute otitis, bone fractures (perhaps from physical abuse), or a foreign body in the eye.[14] Savino et al[15] demonstrated an increased presence of hydrogen gas produced by anaerobic gram-negative bacteria, and lower counts and specific colonisation patterns of intestinal lactobacilli in colicky infants. A very recent (2018) meta-analysis including 4 double-blind, placebo-controlled randomised trials involving 345 infants with colic (174 probiotic and 171 placebo)[10] found that *Lactobacillus reuteri* DSM 17938 is effective in improving infant colic symptoms (crying and fussing), and can be recommended for breastfed infants with colic. Data for formula-fed infants with colic are still not conclusive.

TABLE 1 Primary care of main paediatric gastrointestinal symptoms

	Pitfalls	Tips[a]	Referral to paediatric gastroenterologist
Infant colic	• Elimination diet • Acid suppression	• Reassure family • Encourage breastfeeding	• Associated with other GI and/or systemic symptoms, such as vomiting, diarrhoea and FG
Acute diarrhoea	• Delayed re-feeding • Antibiotic therapy • Diet modification	• Oral and/or intravenous rehydration • Continue feeding • Prevention/early recognition of dehydration	• Chronic diarrhoea and other associated GI and/or systemic symptoms, such as vomiting, diarrhoea and FG
Vomiting	• Delayed oral rehydration • Inappropriate management of antiemetic drugs	• Oral and/or intravenous rehydration • Consider ondansetron use	• Persistent, recurrent or cyclic vomiting • Associated alarm symptoms[b]
Chronic abdominal pain	• Scarce relevance to patient's history and clinics • Useless diagnostic tests and therapies	• Consider functional cause • Start long follow-up	• Associated FG, fever, bleeding or haematochezia, vomiting, etc.
Faltering growth	• Delayed diagnosis • Identification of NOFG	• Growth history • Auxological assessment • Feeding pattern evaluation • Food diary	• Predicted weight for length < 70% • First-line management failure • Abuse or neglect • Signs of traumatic injury • Severe impairment of the caregiver
Constipation	• Underestimate • Delayed laxative therapy • Delayed toilet training	•Alert for alarm signs of organic constipation[b]	• First-line treatment failure • Alarm signs for organic constipation[b]
Haematochezia	• Differential diagnosis between minor and major GIB • Frequent access to paediatric emergency room • Useless endoscopic evaluation	• Perform rectal and anal exploration • Careful evaluation of both entity and timing of blood loss • Rule out intestinal obstruction or surgical causes • Risk factors and associated signs evaluation	• Persistence > 2 weeks • Associated symptoms (fever, abdominal pain or persistence >2 weeks

FG, faltering growth; NOFG, non-organic failure to thrive; GI, gastrointestinal; LGIB, lower gastrointestinal bleeding.
[a]Careful history and complete physical examination have to be considered as the first practical steps in the management of all paediatric gastrointestinal symptoms.
[b]See text.

3.2 | When to refer

Infant colic, like other FGIDs, is diagnosed according to the symptom-based Rome criteria, which have been developed by working committees of the Rome Foundation through literature review and a consensus process. Diagnoses are based on medical history and physical examination. The 2016 revised Rome IV criteria for infant colic have abandoned Wessel's criteria as a requirement for diagnosis and focused on factors that have been shown to cause distress in parents.[16] One of the most common pitfalls in primary care of infant colic is to start an elimination diet, also in the mother, if the infant is breastfed, and/or therapy with drugs that inhibit acid gastric secretion in suspected GER.[16,17] Practical tips in the management could include helping caregivers cope with the infant's symptoms and providing support for the infant-family relationship.[16] It is necessary to reassure parents that the disorder disappears spontaneously within a few months. Simethicone, a bland, over-the-counter drug, with antimeteoric activities, is the most prescribed and/or self-prescribed product. Recently, it has been suggested that *Chamomilla* L., *Melissa officinalis* L, tyndallised *L. acidophilus* (H122) and *Lactobacillus reuteri* DSM 17938 are significantly more effective than simethicone in improving colic symptoms.[18] Breastfeeding should be encouraged because there are no differences in the frequency of infant colic between breastfed and bottle-fed infants.[16] No testing is necessary, unless specific abnormalities are detected by history and examination. Specialist consultation is not requested in the absence of other gastrointestinal symptoms, such as vomiting, weight loss and diarrhoea.

4 | ACUTE DIARRHOEA

4.1 | General overview

Acute diarrhoea is defined as an episode of diarrhoea with acute onset, typically lasting 5-7 days and self-limiting. In the vast majority of cases, it is due to an acute gastrointestinal infection

and may be associated with vomiting or fever.[6] Rotavirus is the most severe and frequently reported enteric pathogen of childhood diarrhoea.[6,19] Worldwide, acute gastroenteritis affects 3-5 billion children each year and accounts for 1.5-2.5 million deaths per year, or 12% of all deaths among children less than 5 years of age.[20] In developed countries, such as Europe, acute gastroenteritis seldom causes deaths, but puts a heavy burden on the healthcare system.[19] Acute gastroenteritis causes 6%-11% of all hospital admissions of children under the age of 5 years each year in Europe.[19] This percentage rises to 13% in the United States.[21] In general, developing countries have a higher rate of hospital admissions compared with developed countries, probably due to the fact that children in developed countries have a better nutritional status and better primary care. Recently, an increase in both emergency admissions to hospital and hospitalisation rates has been observed worldwide, although implementation of guidelines has reduced intravenous rehydration.[6] In 2014, ESPGHAN and the European Society for Paediatric Infectious Diseases (ESPID) developed evidence-based guidelines for the management of acute gastroenteritis in children.[6] In low-risk countries, paediatric populations, acute diarrhoea does not generally require a specific diagnostic workup and is best managed using a few simple, well-defined medical interventions.[6] Home treatment under medical supervision is usually sufficient to prevent or treat mild dehydration; hospitalisation and intravenous rehydration could be necessary in the case of moderate-severe dehydration.[6] According to ESPGHAN/ESPID guidelines, the administration of specific probiotic strains for which efficacy is established, such as *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*,[22] or of racecadotril or diosmectite, can be considered in addition to oral rehydration.[6] Antibiotic therapy is not needed routinely but only for specific pathogens (such as Shigella) or in high-risk settings (including developing countries) and/or children.[6] The most important host-related risk factors for severe acute diarrhoea are young age (infants younger than 3 months), feeding practice (predominant breastfeeding may reduce the risk) and underlying immune deficiencies and/or chronic disease.[6]

4.2 | When to refer

The common pitfalls in primary care of diarrhoea are initiation of empirical antibiotic therapy, delay in re-feeding, giving directions for prolonged dietary restrictions, and referral to a specialist also in cases of acute episodes. Stool cultures are often requested, but are not helpful in most cases.[6] In acute diarrhoea, only 1.5%-5.6% of stool specimens submitted are positive for enteric pathogens.[23] C-reactive protein (CRP) and procalcitonin measurements, as well as faecal markers (calprotectin, lactoferrin) are not routinely recommended.[6] Practical tips in the management of acute diarrhoea are to promptly offer hypo-osmolar oral rehydration solutions (ORS) to prevent dehydration, to continue feeding (or increase breastfeeding during, and increase all feeding after, the period of diarrhoea), and to recognise signs of dehydration. The best 3 individual examination signs for assessment of dehydration are prolonged capillary refill time, abnormal skin turgor and abnormal respiratory pattern.[6] In the case of an episode of diarrhoea that lasts more than 4 weeks (persistent or chronic diarrhoea), Rome IV criteria can guide a positive, symptom-based diagnosis of functional postinfectious disease.[16,24] Specialist consultation should be requested only in the case of persistent or chronic diarrhoea and associated symptoms, such as fever, blood in the stool and weight loss.

5 | VOMITING

5.1 | General overview

Vomiting in children represents a common occurrence related to several conditions, such as acute gastroenteritis or GER. It can be classified as acute, chronic and cyclic. Most causes are acute, benign and self-resolving, such as acute gastroenteritis with rotavirus infection, which is the main cause of acute vomiting in children under the age of 3 years.[6,21] Assessment of a child with vomiting should start with a complete history and physical examination. Description of the vomit content allows to distinguish non-bilious from bilious vomiting. The management of acute vomiting is primarily oriented to the control and correction of vomiting complications, such as fluid depletion, electrolyte imbalance and metabolic acidosis. Symptomatic pharmacological treatment for acute vomiting in childhood is still a matter of debate and is not systematically included in current practice recommendations.[6] In any child with recurrent, stereotypical episodes of intense nausea and vomiting, with inter-episodes of wellness periods, cyclic vomiting syndrome (CVS) should be suspected, according to the 2008 NASPGHAN consensus statement.[25] Identification of the possible cause and initiation of a diagnostic and therapeutic programme is mandatory in chronic or cyclic vomiting.

5.2 | When to refer

The most common pitfall in primary care is the inappropriate prescription of antiemetic drugs, such as domperidone. Several antiemetic agents are available and are often used off-label to prevent or reduce vomiting in children with acute gastroenteritis.[26] In many European countries, the dopamine receptor antagonist domperidone is the antiemetic drug of choice.[27] Domperidone is licensed in Europe for the "treatment of nausea and vomiting," also in the paediatric population, despite lack of evidence on efficacy. Recently, authorisation for the use of domperidone has been subjected to restrictions due to the possible risk of severe arrhythmias.[28] A systematic evaluation of all Cochrane reviews evaluating commonly used interventions in children with vomiting due to acute gastroenteritis by Freedman et al[29] showed significant reduction in hospital admission and intravenous rehydration rates with oral ondansetron use. This is a selective serotonin receptor blocker that inhibits initiation of the vomiting reflex in the periphery. Recently, it has been demonstrated that ondansetron reduces the risk of intravenous rehydration

by over 50%, both with placebo and domperidone.[30] However, a clearance on safety in children is needed before a final recommendation is made, because of a warning regarding possible cardiac effects (such as prolongation of the QT interval).[31] Practical tips in the management are to carry out a careful history that includes information regarding alert symptoms, such as prolonged duration of vomiting, nocturnal episodes of vomiting, presence of blood, abdominal pain, or fever, and a thorough physical examination. According to ESPGHAN/ESPID guidelines,[6] vomiting due to acute gastroenteritis can be managed effectively with the administration of ORS alone. In children who continue to vomit or refuse ORS, a single oral dose of ondansetron (0.15-0.30 mg/kg for intravenous therapy, or 2-8 mg orally) may reduce the need for intravenous rehydration.[6] Specialist consultation is requested in the case of chronic or cyclic vomiting, and in the presence of red flags, such as unstable vital signs, abdominal signs (bilious vomiting, tenderness), acidotic breathing, abnormal neurological examination and papilledema. Primary care providers can perform basic diagnostic tests (abdominal ultrasound, blood cell count, inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate, serum electrolytes, amylase, lipase, urinalysis, haemogasanalysis, blood glucose, blood ammonia and transglutaminase antibodies) before referring the patient to a paediatric gastroenterologist.

6 | CHRONIC ABDOMINAL PAIN

6.1 | General overview

Functional abdominal pain (FAP) and functional dyspepsia (FD) can be considered the most frequent causes of chronic abdominal pain in children and adolescents. The guide symptom is abdominal pain with different localisations, and there is often an overlap between these 2 conditions. Rome IV criteria should be applied to recognise the functional nature of chronic abdominal pain in children and adolescents.[24] The last working committee introduced the term "functional abdominal pain-not otherwise specified (FAP-NOS)" to be used when there are not criteria for the diagnosis of other functional abdominal pain disorders, such as IBS, FD or abdominal migraine.[24] For clinical purposes, FAP can still be used. A mean of 25%-54% of elementary school children report abdominal pain, weekly.[32] Childhood chronic abdominal pain is accompanied by notable functional impairments, reduced quality of life and school absenteeism. The Rome IV criteria require that symptoms cannot be attributed to another medical condition "after appropriate medical evaluation," substituting the Rome III criteria requirement of "no evidence" for organic disease, which may have prompted a focus on testing.[24] This change permits selective or no testing to support a positive diagnosis.[24] IBS is the most variable cause of chronic abdominal pain in children with associated stool modifications. Paediatric IBS can be divided into subtypes reflecting the predominant stool pattern (IBS with constipation, IBS with diarrhoea, IBS with constipation and diarrhoea, and unspecified IBS).[24] IBS patients often receive a diagnosis of functional constipation.[24] FD has a high prevalence in children, varying from 3% to 27%,[33] and is described as a chronic or intermittent disorder characterised by postprandial fullness, early satiety, and/or epigastric pain or burning not associated with defecation.[24] Most patients with FD have meal-related symptoms.[34] Physiologic, genetic, environmental and psychological factors are involved; some subtle structural abnormalities have been linked to FD, such as gastric abnormalities (impaired accommodation, delayed emptying and hypersensitivity), *Helicobacter pylori* gastritis, erosive prepyloric changes, duodenal inflammation and increased eosinophil counts.[35]

6.2 | When to refer

According to the last working committee of the Rome Foundation,[24] in a child presenting with FAP, the conservative approach is generally appropriate. A detailed history may evaluate the onset, duration, frequency and character of the abdominal pain; the presence of triggering or relieving factors; a change in stool frequency and/or consistency; different features to establish symptom concordance with FAP subtypes. In addition, the presence of previous abdominal surgery or recent gastrointestinal infections should also be considered. A family history of IBS, chronic pain or anxiety, personal, familiar or social factors that may cause emotional upset, such as parental separation, bullying and/or concerns regarding school performance, can be considered.[36] Red flags or alarm symptoms include family history of inflammatory bowel disease (IBD), coeliac disease or peptic ulcer disease; persistent right upper or right lower quadrant pain; dysphagia; odynophagia; persistent vomiting; gastrointestinal blood loss; nocturnal diarrhoea; arthritis; perirectal disease; involuntary weight loss; deceleration of linear growth; delayed puberty; and unexplained fever.[24] Some limited tests such as blood count and differential C-reactive protein levels, coeliac disease serology, determination of faecal calprotectin and screening for Giardia lamblia can be requested. Determination of faecal calprotectin is increasingly being utilised as a non-invasive screening for intestinal mucosal inflammation and appears to be superior to standard testing, such as C-reactive protein.[24] In the case of possible IBS with diarrhoea, infection, coeliac disease, carbohydrate malabsorption, and, less commonly, IBD, all warrant particular focus. The usefulness of pharmacological treatment in children with FAP is very low.[24] An elimination diet reducing intake of fermentable oligosaccharides, disaccharides, monosaccharides and polyols for all subtypes of IBS seems to show promising efficacy in the adult population but has not been confirmed in children.[36] In FD, an empirical therapeutic approach including acid-suppression therapy may be attempted.[37] The common pitfall in primary care for chronic abdominal pain is the inability to clinically recognise the functional pattern and to make a positive diagnosis, rather than using exhaustive investigations to exclude an underlying organic cause. Practical tips include explaining the diagnosis and mechanisms of chronic abdominal pain to patient and family, to start a clinical follow-up, and to aim for the resumption of a normal lifestyle with regular school attendance and normal sleep pattern. Chronic abdominal pain is the gastrointestinal symptom for which an overuse of empirical therapy and/or useless and

immediate referring for paediatric gastroenterology consultation is most frequently reported.[37] Specialist consultation may be requested in the presence of alarm signals for organic disease, or also in selected cases of chronic abdominal pain to reinforce the abovementioned concepts.

7 | FALTERING GROWTH

7.1 | General overview

Faltering growth (FG) refers to children whose weight or weight gain is significantly lower compared with children of the same age, gender and ethnicity, and is recognised as reflecting relative undernutrition.[38] FG can occur at every age during childhood, but is most frequent during the first 2 years.[38] The time of the first hospital visit is usually from 8 to 18.7 months.[39] Prevalence of FG seems to be higher in families with lower socioeconomic status and, generally, in developing countries. In the United States, FG is reported with a prevalence of 5-10% in primary care settings and accounts for 1%-5% of paediatric hospital admissions for children younger than 2 years of age.[40] Similar percentages have been reported in Europe, as in the United Kingdom, where the prevalence of FG among healthy children ranges from 5% to 9%.[41] There is no consensus on the diagnostic criteria that should be used to define FG; the following are frequently reported in literature: (1) weight below the 3rd or 5th percentile for age, depending on the growth chart used, either World Health Organization (WHO) growth charts (http://www.who.int/childgrowth) or Centers for Disease Control and Prevention (CDC) charts (http://www.cdc.gov/growthcharts); (2) weight below 80% of the ideal weight for age; (3) weight decrease that crosses 2 major percentile lines on growth chart.[42] Others include height-for-weight less than the 3rd percentile, or weight-for-height less than the 10th percentile, or weight-for-age less than 2 standard deviations below the mean for age.[42] The National Institute for Health and Care Excellence (NICE) defines FG in infants and children as a sustained drop in 1, 2 or 3 weight centile spaces, if birthweight was below the 9th, between the 9th and 91st and above the 91st centiles on the WHO growth charts, respectively.[43] Hosseini et al[44] proposed the Waterlow and Gomez classification (on the WHO Growth Charts) to categorise the degree of FG severity and to facilitate recognition of FG by primary care providers.

Faltering growth usually has a multifactorial aetiology. However, it can be divided into organic and non-organic FG (NOFG). NOFG (also called "psychosocial FG") may be determined by poverty, neglect, abnormal parental feeding practice (including nocturnal feeding, force feeding, persecutory feeding, mechanistic feeding, prolonged feeding, conditional distraction), and child's improper behaviours at mealtimes.[38] NOFG is the most serious complication of non-organic feeding disorders (NOFEDs), occurring in up to 40%-50% of cases,[45] and described as a stunted growth secondary to poor caloric intake in the absence of organic disease or swallowing impairment. Population-based studies found underlying organic disease in only 5%-10% of children with FG.[46] Organic causes of FG may be further divided into inadequate caloric intake, inadequate absorption, excessive caloric expenditure and defective utilisation of calories. Neurological and gastrointestinal disorders combined are responsible for 60-80% of all organic causes. Before suspecting an NOFG, the most frequent causes of organic FG should be excluded. Medical history should rule out symptoms such as dysphagia, odynophagia, choking or recurrent pneumonia, feeding interrupted by crying suggestive of pain, vomiting or diarrhoea. Family growth history and pattern are crucial. A physical examination should look for the presence of any pathological signs that would hint at the presence of organic disease, such as dysmorphic features, skin rashes, neurological or cardiological findings, organomegaly, lymphadenopathy and abnormal genitalia.[45] The association of baseline tests, such as complete blood examination, full biochemistry panel, thyroid function tests, coeliac serology, urinalysis and urine culture, may be of support.[45]

7.2 | When to refer

The common pitfall in primary care of FG is the inability (or difficulty) to detect causes of NOFG, such as improperly prepared formula (eg, over-diluting formula) or an inadequate supply of breast milk, breastfeeding difficulties (physician should see a complete breastfeed), and child's improper behaviour at mealtimes.[45] Practical tips in the management of FG include carrying out a simple set of clinical history, physical examination and feeding pattern evaluations (including the amount and frequency of meals, as well as the type of food and liquids consumed, child's behaviour at mealtimes, suspected symptoms such as anorexia, extreme hunger and frequent meals not accompanied by weight gain). Specialist consultation is requested when nutritional status is <70% of the predicted weight for length, a child fails to improve during primary care management, suspicion of abuse or neglect exists, signs of traumatic injury are recognised, or severe impairment of the caregiver is evident.

8 | CONSTIPATION

8.1 | General overview

Constipation may be defined as delayed or difficult passage of stools that persists for more than 2 weeks.[47] Constipation represents one of the major reasons for consultations with general paediatricians and accounts for 25% of referrals to paediatric gastroenterologists, worldwide.[48] The peak incidence of childhood constipation occurs between 2 and 4 years of age, when toilet training starts.[47] The most common type of childhood constipation is functional, accounting for 90%-95% of all cases.[47] Rome IV criteria are recommended for the diagnosis of functional constipation for all age groups, based on history and physical examination.[24] Abdomen plain radiographs are not routinely recommended, but they may be necessary when faecal impaction is suspected but physical examination is unreliable or not possible (eg, in children who refuse rectal examination, and in obese children).[47] Organic causes of constipation can be found,

such as anatomic obstructions, Hirschsprung's disease, spinal problems, and other metabolic and neuroenteric abnormalities,[24,47] in a low percentage of children (5%). In these cases, an appropriate laboratory investigation and imaging study is warranted.[47] In children >12 months of age, constipation treatment consists of 3 phases.[47] The first-phase lasts about 2 days and is the clean-out phase, to identify and clear out hard, chronically accumulated stool (disimpaction) with oral use of osmotic agents and laxatives. The second phase lasts between 2 and 6 months and aims to restore muscle tone to the sphincter by the use of stool softeners, hyperosmotic laxatives, non-absorbable salts or combinations; a stool diary, dietary instructions for constipation—a balanced diet including grains, fruits and vegetables is recommended[47]—and instructions for toilet training (eg, a constipated child should have a routine scheduled toilet sitting for 3–10 minutes, according to age, once or twice a day) are useful too. The third phase lasts between 4 and 6 months and aims to restore regular bowel movements and avoid relapses by cutting down laxative use and by increasing daily fibre and fluid intake.[47] Normal physical activity is recommended.[47] The prognosis for full recovery has been reported as 50% and 80% at 5- and 10-year follow-up, respectively, with the vast majority of patients no longer taking laxatives.

8.2 | When to refer

The common pitfalls in primary care of constipation are to underestimate the problem, to delay therapy with osmotic laxatives and adequate toilet training. A delay in initial medical treatment for >3 months from symptom onset correlates with longer duration of symptoms. The practical tips are to avoid progressive accumulation of faeces in the rectum causing overflow incontinence and non-voluntary expulsion of faeces or encopresis. Specialist consultation is required when treatment fails or alarm signs for organic constipation (red flags) are present. Red flags are represented by the onset, before 12 months of age, of delayed passage of meconium, lack of faecal retention and faecal leakage (soiling), malnutrition, empty rectal ampulla, pigmentary abnormalities, extra-intestinal manifestations (vomiting, fever, ill-appearance), gallbladder diseases and resistance to standard treatment.[47]

9 | HAEMATOCHEZIA

9.1 | General overview

Haematochezia describes bright red blood per rectum, which often arises from the distal colon or rectum.[49] Lower gastrointestinal bleeding (LGIB) refers to any form of gastrointestinal bleeding originating distal to the ligament of Treitz, at the duodenojejunal junction.[49] In childhood, LGIB is a more common complaint than upper gastrointestinal bleeding (UGIB) and is mostly self-limiting.[50,51] A recent nationwide emergency department (ED) database analysis from 2006 to 2011 reported about 450 000 paediatric ED visits (ages birth to 19 years) for gastrointestinal bleeding, of which UGIB accounted for 20% and LGIB for 30%.[51] In childhood, patient age is one of the most important factors in narrowing the aetiology of haematochezia at presentation.[49] The most common causes are allergic colitis and anorectal fissures in infants, with colorectal polyps, infectious enterocolitis and anorectal fissures in older children.[50]

No standards of care are currently available for managing haematochezia and, in general, gastrointestinal bleeding in children. The 2017 Italian Society of Paediatric Gastroenterology, Hepatology and Nutrition (SIGENP) position paper,[50] based on systematic literature search and experts' opinion, aimed to provide recommendations based on current evidence for best practice in the management of paediatric UGIB and LGIB. The diagnostic approach for haematochezia includes extensive history taking and physical examination. Visual inspection of the perianal area and digital rectal examination should always be considered in the case of haematochezia, to detect the possibility of anal fissure (frequent sign of constipation), streptococcal cryptitis or rectal polyp.[50] Endoscopy is the method of choice for the localisation of GIB in paediatric patients.[50,52] Haematochezia requires colonoscopy if it lasts more than 1 week or recurs (twice a week for 4 weeks or 3 times per month for 3 months).[50,52]

9.2 | When to refer

The common pitfall in primary care is not performing a complete physical examination, including observation of the perianal region and a digital rectal exploration, as well as not being able to distinguish between minor bleeding and major bleeding, with consequent frequent access to the emergency room. Practical tips include ruling out intestinal obstruction or surgical causes (which represent the main priority for the physician in evaluating a patient with haematochezia), identifying the entity of blood loss, checking for recurrent bleeding and the presence of possible risk factors, including coagulopathy, sepsis and trauma. Baseline tests (such as blood count, liver and kidney function, blood coagulation) and a pre-anaesthesia examination may be useful and considered case by case. Testing for *Clostridium difficile* infection and stool cultures for pathogenic bacteria may be useful, especially in the setting of fever or diarrhoea. Specialist consultation is requested generally in chronic minor gastrointestinal bleeding, such as rectal bleeding, to exclude IBD, polyps and allergic colitis.

10 | CONCLUSION

Gastrointestinal symptoms are common in infants and children of all ages. They represent a frequent reason for emergency admission to hospital and/or specialist consultations. Over the last few years, there has been an increase in the diagnosis of organic diseases in paediatric populations, such as inflammatory bowel diseases, peptic disease by Helicobacter pylori and coeliac disease. In most cases, however, gastrointestinal symptoms in children are secondary to a functional aetiology and are not associated with organic diseases. The increase in high-quality guidelines and consensus publications (Rome Criteria, acute diarrhoea, constipation, etc.) has not been

followed by an improvement in primary care management, due to failure to implement them. All this has led to excessive access to secondary care with a significant increase in costs. A better application of guidelines is warranted, and this manuscript can offer a first-step support to primary care management.

ACKNOWLEDGEMENTS

None.

AUTHOR CONTRIBUTIONS

All authors participated in the interpretation of collected literature and in the drafting, critical revision and approval of the final version of the manuscript.

DISCLOSURES

The authors have nothing to disclose.

ORCID

Claudio Romano http://orcid.org/0000-0001-8827-2091

REFERENCES

1. Koppen IJ, Nurko S, Saps M, Di Lorenzo C, Benninga MA. The pediatric Rome IV criteria: what's new? *Expert Rev Gastroenterol Hepatol*. 2017;11:193-201.
2. van Tilburg MA, Hyman PE, Walker L, et al. Prevalence of functional gastrointestinal disorders in infants and toddlers. *J Pediatr*. 2015;166:684-689.
3. Lewis ML, Palsson OS, Whitehead WE, et al. Prevalence of functional gastrointestinal disorders in children and adolescents. *J Pediatr*. 2016;177:39-43.
4. Scarpato E, Kolacek S, Jojkic-Pavkov D, et al.; MEAP Group. Prevalence of functional gastrointestinal disorders in children and adolescents in the Mediterranean region of Europe. *Clin Gastroenterol Hepatol*. 2017 Nov 9. pii: S1542-3565(17)31316-2.
5. Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. *PLoS ONE*. 2015;10:e0126982.
6. Guarino A, Ashkenazi S, Gendrel D, Lo Vecchio A, Shamir R, Szajewska H. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014. *J Pediatr Gastroenterol Nutr*. 2014;59:132-152.
7. Wessel A, Cobb JC, Jackson EB, Harris GS Jr, Detwiler AC. Paroxysmal fussing in infancy, sometimes called colic. *Pediatrics*. 1954;14:421-435.
8. Vandenplas Y, Abkari A, Bellaiche M, et al. Prevalence and health outcomes of functional gastrointestinal symptoms in infants from birth to 12 months of age. *J Pediatr Gastroenterol Nutr*. 2015;61:531-537.
9. Lucassen PL, Assendelft WJ. Systematic review of the occurrence of infantile colic in the community. *Arch Dis Child*. 2001;84:398-403.
10. Sung V, D'Amico F, Cabana MD, et al. *Lactobacillus reuteri* to treat infant colic: a meta-analysis. *Pediatrics*. 2018;141(1):pii: e20171811.
11. Milidou I, Søndergaard C, Jensen MS, Olsen J, Henriksen TB. Gestational age, small for gestational age, and infantile colic. *Paediatr Perinat Epidemiol*. 2014;28:138-145.
12. Van den Berg MP, van derEnde J, Crijnen AA, et al. Paternal depressive symptoms during pregnancy are related to excessive infant crying. *Pediatrics*. 2009;124:e96-e103.
13. Indrio F, Riezzo G, Raimondi F, Di Mauro A, Francavilla R. Gut motility alterations in neonates and young infants. *J Pediatr Gastroenterol Nutr*. 2013;57:S9-S11.
14. Freedman SB, Al-Harthy N, Thull-Freedman J. The crying infant: diagnostic testing and frequency of serious underlying disease. *Pediatrics*. 2009;123:841-848.
15. Savino F, Bailo E, Oggero R, et al. Bacterial counts of intestinal *Lactobacillus* species in infants with colic. *Pediatr Allergy Immunol*. 2005;16:72-75.
16. Benninga MA, Nurko S, Faure C, St James Roberts I, Schechter NL, Nurko S. Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterology*. 2016;150:1443-1455.
17. Gieruszczak-Białek D, Konarska Z, Skórka A, Vandenplas Y, Szajewska H. No effect of proton pump inhibitors on crying and irritability in infants: systematic review of randomized controlled trials. *J Pediatr*. 2015;166:767-770; e3.
18. Ummarino D, Martinelli M, Giugliano FP, et al. PP-12 efficacy of a standardized extract of matricariae *Chamomilla* L., *Melissa officinalis* L. and tyndallized *Lactobacillus acidophilus* (H122) compared with Lactobacillus Reuteri (DSM 17938) and with simethicone for the treatment of infantile colic. *J Pediatr Gastroenterol Nutr*. 2015;61:525.
19. The Pediatric ROTavirus European CommitTee (PROTECT). The paediatric burden of rotavirus disease in Europe. *Epidemiol Infect*. 2006;134:908-916.
20. King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR Recomm Rep*. 2003;52(RR-16):1-16.
21. Malek MA, Curns AT, Holman RC, et al. Diarrhea- and rotavirus-associated hospitalizations among children less than 5 years of age: United States, 1997 and 2000. *Pediatrics*. 2006;117:1887-1892.
22. Guarino A, Guandalini S, Lo Vecchio A. Probiotic for prevention and treatment of diarrhea. *J Clin Gastroenterol*. 2015;49(Suppl 1):S37-S45.
23. Guerrant RL, Van Gilder T, Steiner TS, et al.; Infectious Diseases Society of America. Practice guidelines for the management of infectious diarrhea. *Clin Infect Dis*. 2001;32(3):331.
24. Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, van Tilburg M. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology*. 2016;150:1456-1468.
25. Li BU, Lefevre F, Chelimsky GG, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition consensus statement on the diagnosis and management of cyclic vomiting syndrome. *J Pediatr Gastroenterol Nutr*. 2008;47:379-393.
26. Zanon D, Gallelli L, Rovere F, et al. Off-label prescribing patterns of antiemetics in children: a multicenter study in Italy. *Eur J Pediatr*. 2013;172:361-367.
27. Pfeil N, Uhlig U, Kostev K, et al. Antiemetic medications in children with presumed infectious gastroenteritis-pharmacoepidemiology in Europe and Northern America. *J Pediatr*. 2008;153:659-662.
28. EMA. CMDh confirms recommendations on restricting use of domperidone-containing medicines. EMA/236452/2014, 25 April 2014. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Domperidone_31/Position_provided_by_CMDh/WC500165647.pdf. Accessed September 13, 2016.
29. Freedman SB, Ali S, Oleszczuk M, Gouin S, Hartling L. Treatment of acute gastroenteritis in children: an overview of systematic reviews of interventions commonly used in developed countries. *Evid Based Child Health*. 2013;8:1123-1137.

30. Marchetti F, Bonati M, Maestro A, et al.; SONDO (Study ONdansetron vs DOmperidone) Investigators. Oral ondansetron versus domperidone for acute gastroenteritis in pediatric emergency departments: multicenter double blind randomized controlled trial. *PLoS ONE*. 2016;11:e0165441.
31. Ondansetron: new dose restrictions. *Prescriber Update*. 33(3):21. September 2012. http://www.medsafe.govt.nz/profs/PUArticles/OndansetronSept2012.htm. Accessed 23 March 2017.
32. Saps M, Seshadri R, Sztainberg M, Schaffer G, Marshall BM, Di Lorenzo C. A prospective school-based study of abdominal pain and other common somatic complaints in children. *J Pediatr*. 2009;154:322-326.
33. Ganesh M, Nurko S. Functional dyspepsia in children. *Pediatr Ann*. 2014;43:e101-e105.
34. Quigley EM, Lacy BE. Overlap of functional dyspepsia and GERD diagnostic and treatment implications. *Nat Rev Gastroenterol Hepatol*. 2013;10:175-186.
35. Rosen JM, Cocjin JT, Schurman JV, Colombo JM, Friesen CA. Visceral hypersensitivity and electromechanical dysfunction as therapeutic targets in pediatric functional dyspepsia. *World J Gastrointest Pharmacol Ther*. 2014;5:122-138.
36. Chumpitazi BP, Hollister EB, Oezguen N, et al. Gut microbiota influences low fermentable substrate diet efficacy in children with irritable bowel syndrome. *Gut Microbes*. 2014;5:165-175.
37. Romano C, Valenti S, Cardile S, Benninga MA. Functional dyspepsia: an enigma in a conundrum. *J Pediatr Gastroenterol Nutr*. 2016;63:579-584.
38. Yoo SD, Hwang EH, Lee YJ, Park JH. Clinical characteristics of failure to thrive in infant and toddler: organic vs nonorganic. *Pediatr Gastroenterol Hepatol Nutr*. 2013;16:261-268.
39. Daniel M, Kleis L, Cemeroglu AP. Etiology of failure to thrive in infants and toddlers referred to a pediatric endocrinology outpatient clinic. *Clin Pediatr (Phila)*. 2008;47:762-765.
40. Cole SZ, Lanham JS. Failure to thrive: an update. *Am Fam Physician*. 2011;83:829-834.
41. Grimberg A, Ramos M, Grundmeier R, et al. Sex-based prevalence of growth faltering in an urban pediatric population. *J Pediatr*. 2009;154:567-572. e2.
42. Olsen EM, Petersen J, Skovgaard AM, Weile B, Jørgensen T, Wright CM. Failure to thrive: the prevalence and concurrence of anthropometric criteria in a general infant population. *Arch Dis Child*. 2007;92:109-114.
43. National Guideline Alliance (UK). *Faltering Growth – recognition and management*. London: National Institute for Health and Care Excellence (UK); 2017.
44. Hosseini F, Borzouei B, Vahabian M. Failure to thrive severity determination by new design curves in standard growth charts. *Acta Med Iran*. 2011;49:795-800.
45. Romano C, Hartman C, Privitera C, Cardile S, Shamir R. Current topics in the diagnosis and management of the pediatric nonorganic feeding disorders (NOFEDs). *Clin Nutr*. 2015;34:195-200.
46. Wright C, Birks E. Risk factors for failure to thrive: a population-based survey. *Child Care Health Dev*. 2000;26:5-16.
47. Tabbers MM, Di Lorenzo C, Berger MY, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN. *J Pediatr Gastroenterol Nutr*. 2014;58:258-274.
48. Xinias I, Mavroudi A. Constipation in Childhood. An update on evaluation and management. *Hippokratia*. 2015;19:11-19.
49. Sahn B, Bitton S. Lower gastrointestinal bleeding in children. *Gastrointest Endoscopy Clin N Am*. 2016;26:75-98.
50. Romano C, Oliva S, Martellossi S, et al. Pediatric gastrointestinal bleeding: perspectives from the Italian Society of Pediatric Gastroenterology. *World J Gastroenterol*. 2017;23:1328-1337.
51. Pant C, Olyaee M, Sferra TJ, Gilroy R, Almadhoun O, Deshpande A. Emergency department visits for gastrointestinal bleeding in children: results from the Nationwide Emergency Department Sample 2006–2011. *Current Med Res Opin*. 2015;31:347-351.
52. Franke M, Geiß A, Greiner P, et al. The role of endoscopy in pediatric gastrointestinal bleeding. *Endosc Int Open*. 2016;4:E1011-E1016.

How to cite this article: Dipasquale V, Corica D, Gramaglia SMC, Valenti S, Romano C. Gastrointestinal symptoms in children: Primary care and specialist interface. *Int J Clin Pract*. 2018;e13093. https://doi.org/10.1111/ijcp.13093