Epidemiological and pathophysiological aspects of abdominal pain predominant functional gastrointestinal disorders in children and adolescents: a Sri Lankan perspective
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Chapter 1

Global prevalence and international perspective of pediatric gastrointestinal disorders

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SUMMARY
Prevalence of Functional Gastrointestinal disorders (FGIDs) has dramatically increased over the past decade and now represents a large global healthcare burden. With growing population trends and increasing predisposing factors such as obesity and psychological stress, it can be predictable that the incidence of FGIDs will increase further and become a significant healthcare problem. Although FGIDs are not life threatening, research shows that children suffering from FGIDs tend to have a lower QoL than their healthy peers and frequently miss school as a result of the disorder. In addition many FGIDs such as constipation and IBS has high healthcare expenditure and are becoming a major challenge on already-overstretched healthcare budgets, both in developing and in developed countries, competing perhaps with other prioritized diseases. These factors suggest that FGIDs need to be one of the main research focal points of the twenty-first century.
INTRODUCTION

Functional gastrointestinal disorders (FGIDs) consist of a group of chronic gastrointestinal problems characterized by recurrent symptoms that cannot be explained by structural and biochemical abnormalities. Chronic and disabling nature of symptoms and their remarkably high prevalence across the globe has identified them as a concern for pediatric public health. Initial epidemiological data and hospital-based studies from the Western world provided a notion that these disorders were possibly a result of a 'Western life-style'. However, compelling data have emerged from Asian and Latin American countries indicating that FGIDs have a global dimension in prevalence. They have come to challenge the already overstretched health budgets of both developed and developing countries and compete with other prioritized communicable and non-communicable diseases such as HIV, tuberculosis, malnutrition, obesity and malignancies. Moreover, biology and pathophysiology of FGIDs are shown to be increasingly associated with psychological stress, early adverse life events, infections and urbanization, all of which are common across the globe. In addition, certain categories of FGIDs are commonly seen among children living in deprived and disrupted societies such as those affected by war. These disorders are known to have deleterious ramifications on childhood functioning and health-related quality of life (QoL). This chapter reviews the current epidemiological trends and international perspectives of FGIDs in children.

CLASSIFICATION AND DEFINITIONS

Historical facts

Recurrent abdominal pain

In 1909, a British Pediatrician, GF Still, wrote: “I know of no symptom which can be more obscure in its causation than colicky abdominal pain in childhood”.¹ A century later, childhood abdominal pain remains a curious enigma. Recently, significant progress has been made to shed some light upon this subject.

The term ‘recurrent abdominal pain’ came into use in the 1950s, following John Apley’s use of the term.² The majority of children with recurrent abdominal pain had no recognizable organic cause for their symptoms and were thought to have abdominal pain of functional origin. However, Apley’s diagnostic entity soon proved to be too general, as it transpired that up to 68% of children with recurrent abdominal pain could be classified as having irritable bowel syndrome (IBS) using established adult diagnostic criteria.³ In addition, constipation had come to be widely acknowledged as a common organic cause for abdominal pain. Previously, constipation has been recognized as an organic disorder that could cause harm through an
accumulation of feces in the body. Traditionally, medical staff regularly prescribed laxatives to “decontaminate” the bowel, a practice that continued even up to the 1950s.4

Classification of functional gastrointestinal disorders (FGIDs)
The first internationally accepted classification system of adult FGIDs was known as the Rome I classification. This has since been iterated and updated,5 and it is currently the most widely accepted classification system for FGIDs.

The Rome II classification of FGIDs, introduced in 1999, was a historical landmark in pediatric gastroenterology.6 For the first time, FGIDs in children were formally recognized, establishing a foundation for future research and enabling researchers to link the historic ‘recurrent abdominal pain’ classification to modern FGIDs.

Rome III criteria
The currently accepted diagnostic criteria for FGIDs are known as the Rome III criteria. They were introduced in 2006 and, as discussed, developed out of the two previous criteria (Rome I and Rome II). The classification includes two separate systems, one for infants and toddlers and the other for children and adolescents.7,8 Table 1.1 gives the details of classification of FGIDs in children and adolescents. The Rome III Committee has reduced the required duration of symptoms of most FGIDs from 3 months to 2. Furthermore, a threshold of symptom frequency of at least once a week has also been introduced. *

In defecation disorders, functional fecal retention was excluded from current classification criteria as a separate diagnostic entity. However, several significant clinical characteristics of constipation have been included, such as non-retentive fecal incontinence with a frequency of occurrence of at least once a month. These modifications have made the Rome III criteria more inclusive and more useful in the diagnosis of FGIDs in children and more likely to positively diagnose the whole spectrum of FGIDs than previous Rome II criteria.9,10 However, much still needs to be done to refine them and, more importantly, to convince pediatricians to use them in day-to-day clinical practice.

* The Rome III revised duration and symptom thresholds do not apply to abdominal migraine and cyclical vomiting syndrome.
Table 1.1 Classification of childhood functional gastrointestinal disorders (FGIDs) in Rome III criteria

1. Vomiting and aerophagia
   1a. Adolescent rumination syndrome
   1b. Cyclic vomiting syndrome
   1c. Aerophagia

2. Abdominal pain-related FGIDs
   2a. Functional dyspepsia
   2b. Irritable bowel syndrome
   2c. Abdominal migraine
   2d. Childhood functional abdominal pain

3. Constipation and incontinence
   3a. Functional constipation
   3b. Nonretentive fecal incontinence

Box 1.1 - Limitations of the Rome II classification system

Several studies have shown a significant percentage of children with non-organic recurrent abdominal pain to have FGIDs. Walker et al.\textsuperscript{11} showed that 73\% of children with ‘full terminology of recurrent abdominal pain’ can be classified into FGIDs such as IBS and functional abdominal pain by using the Rome II criteria. A school-based study from Asia has shown that 73\% of children with recurrent abdominal pain have FGIDs.\textsuperscript{12} However, Rome II criteria had limitations. A prospective study in school children demonstrated that at least 8\% of children with chronic abdominal pain for a 3-month duration could not be assigned to a particular functional gastrointestinal disorder group using Rome II criteria.\textsuperscript{13} Another study found only a fair agreement between physicians and parents using Rome II criteria.\textsuperscript{14} Furthermore, two additional studies on defecation disorders illustrated that Rome II criteria for defecation disorders were too restrictive and would exclude a significant proportion of children when applied to clinical settings.\textsuperscript{15,16} These findings paved the way to modify the Rome II criteria.
EPIDEMIOLOGY OF FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS)

Vomiting and aerophagia

Aerophagia

Aerophagia is a functional gastrointestinal disorder characterized by repetitive swallowing of air that leads to abdominal distension, excessive belching and/or flatus. Clinically, children with aerophagia present with non-distended abdomen in the morning and gradual distension of the abdomen throughout the day. Excessive belching is noted during the day. In addition, frequency of passing flatus increases, especially during the night. On physical examination, the abdomen shows gross distension and the percussion note is tympanic all over the abdomen. Although it seems benign, in severe cases aerophagia leads to serious complications such as pneumoperitonium, volvulus and intestinal perforation.17,18,19

Until recently, there were no studies assessing the epidemiology of aerophagia. Initially, aerophagia was believed to be more prevalent in children with chronic neurological conditions such as Rett’s syndrome and autism.20,21 However, subsequent studies have found aerophagia in a significant percentage of otherwise healthy children. In a prospective study among 243 black American schoolchildren, attending a community primary care clinic, Uc and co-workers22 reported aerophagia in 2.4%. Only a few studies have assessed the community prevalence of aerophagia. Two recent school-based studies in 10- to 16-year-olds have reported this condition in 6.3% and 7.5%, respectively.23,24 In these studies there was no significant gender difference in prevalence.23,24 Higher prevalence of aerophagia was observed in older children but there was no clear correlation with age. The identified risk factors were lower socio-economic status, large family size, having a working mother, living in an urban area and exposure to stressful life events. Furthermore, children with aerophagia had difficulty in sleeping and missed school because of their symptoms.

Cyclic vomiting syndrome

Cyclic vomiting syndrome (CVS) is a clinical entity associated with recurrent episodes of severe nausea and vomiting that may last for hours to days with well-demarcated symptom-free intervals. The disorder is typically associated with negative laboratory, endoscopic and radiological test results. There is a stereotypical pattern of symptoms in most of the individuals with regard to time of day, duration and onset of symptoms. Vomiting begins late night or early morning with intense nausea, often triggered by psychological distress. Associated symptoms include pallor, listlessness, retching, abdominal pain, headache and photophobia.7,25
Data on the epidemiology of CVS in children is limited. A population-based survey from Aberdeen, Scotland, involving children aged 5-15 years, has shown the prevalence of cyclical vomiting to be 1.9% in the United Kingdom.\(^\text{26}\) Reported prevalence of CVS is 2.3% in Australia,\(^\text{27}\) 0.5% in Sri Lanka\(^\text{10}\) and 1.9% in Turkey.\(^\text{28}\) Although overall sex ratio for the whole population was 1:1, cyclic vomiting was commoner among boys in the younger age group of less than 7 years. The sex ratio reversed in children older than 7 years. Travel, stress, tiredness and lack of sleep were the recognized precipitating factors. In a prospective surveillance study in Ireland, the incidence of CVS was found to be 3.5/100,000 children per annum. In this study, the median age of diagnosis was 7.42 years and the median age of onset was 4 years. The majority of children missed school because of their symptoms, indicating the disabling nature of the disease.\(^\text{29}\) Current research is inconclusive, as there seems to be considerable heterogeneity and variability of the prevalence rates in different studies conducted in different geographical locations.

**Rumination syndrome**

Rumination syndrome is defined as effortless, repetitive, painless regurgitation of partially digested food into the mouth soon after the meal, which is subsequently re-chewed and re-swallowed, or in the alternative, expelled.\(^\text{7}\) Rumination syndrome is thought to be common in children who are neurologically handicapped with developmental abnormalities and learning difficulties.\(^\text{30,31}\) In clinical settings, rumination syndrome is frequently misdiagnosed as gastro-esophageal reflux, gastroparesis and recurrent vomiting. These misconceptions and misdiagnoses and poor awareness among clinicians have led to underdiagnosis of this important and sometimes disabling disease in children. However, recent data show its increasing prevalence among otherwise healthy people with normal cognitive function.\(^\text{32-34}\)

Data for this disorder have been derived from case series from tertiary care referral centers and therefore include a bias towards severe cases. A recent small-scale epidemiological survey in Sri Lanka noted a prevalence of 4% among 12-to 16-year-old children in a semi-urban school.\(^\text{10}\)

**Abdominal pain predominant functional gastrointestinal disorders**

**Functional dyspepsia**

Functional dyspepsia is a disorder characterized by the presence of persistent or recurrent pain or discomfort that does not subside with defecation and which is localized to the central region of the abdomen above the umbilicus.\(^\text{7}\) Epidemiology of functional dyspepsia has not been adequately studied across the world. A school-based study in Italy of children aged 6-19 years using Rome II criteria have noted ulcer-like dyspepsia in 3.4% of children and dysmotility-like
dyspepsia in 3.7%. A prospective survey from the same country and that included children of a much more diverse age range showed a prevalence of 0.3%. A study from Asia has evaluated prevalence of AP-FGIDs in children and shown a prevalence of functional dyspepsia of 2.5%. The prevalence was higher among girls than boys. A detailed symptom analysis showed that the majority of children have pain several times a week and the pain is short-lasting (less than 1 hour). Furthermore, children with functional dyspepsia also suffer from a range of intestinal-related symptoms such as bloating, loss of appetite, nausea, burping and flatulence, as well as extra-intestinal symptoms such as headaches, limb pains, sleeping difficulties and light-headedness.

**Irritable bowel syndrome (IBS)**

IBS denotes the presence of abdominal pain that is relieved by defecation and/or associated with change in bowel frequency and/or consistency of the stool with the onset of pain. Even though, epidemiology of IBS has been studied in details in adults, research assessing this important disease condition in children is sparse and limited. Early studies from the Western world led to the belief that IBS is a disease of affluent societies. Emerging data from Asia, both in children and adults, have suggested otherwise. Studies on prevalence of IBS in Europe and the USA are old and many having conducted nearly a decade ago. According to these studies prevalence of IBS among school children in the United Kingdom and the United States are 1.29% and 10.05%, respectively. In addition, a higher prevalence (20%) was observed in children in Russia (Western Siberia) according to the Rome II criteria. In contrast to this, a prospective study from Italy using the same criteria reported a much lower prevalence (0.21%). Wide variation in the age of the recruited in different studies may have contributed to these differences in reported prevalence of IBS. Two of the studies found that IBS is much more common among girls and prevalence increases as they grow older. To date, no study has used the sub-classification criteria of IBS.

In the last decade, however, the epidemiology of IBS has been well studied. Most of these studies have been fairly large and have included over 400 children, and used Rome II or Rome III criteria to establish the diagnosis. The prevalence of IBS in Asian countries varies between 2.8%, in Sri Lankan children aged 10-16 years, to 25.7%, in Korean girls. Furthermore, studies from other developed nations in Asia such as Japan have also shown high prevalence of IBS (14.6 -19%). Prevalence in China varies between 13.25% - 20.72%, and a study from Sri Lanka has shown a prevalence of 6.2%. Figure 1.1 and Table 1.2 show the distribution and prevalence of epidemiological studies of IBS around the world.
Figure 1.1 - Global distribution of irritable bowel syndrome in children

Table 1.2 - Prevalence of IBS in the world

<table>
<thead>
<tr>
<th>Country</th>
<th>Year of publication</th>
<th>Age group (years)</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sri Lanka</td>
<td>2012</td>
<td>10-16</td>
<td>6.2</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>2011</td>
<td>10-16</td>
<td>4.9</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>2010</td>
<td>12-16</td>
<td>7.0</td>
</tr>
<tr>
<td>Japan</td>
<td>2011</td>
<td>15</td>
<td>14.6</td>
</tr>
<tr>
<td>China</td>
<td>2011</td>
<td>12-18</td>
<td>19.9</td>
</tr>
<tr>
<td>China</td>
<td>2010</td>
<td>10-18</td>
<td>20.72</td>
</tr>
<tr>
<td>China</td>
<td>2005</td>
<td>6-18</td>
<td>13.25</td>
</tr>
<tr>
<td>Iran</td>
<td>2009</td>
<td>14-19</td>
<td>4.1</td>
</tr>
<tr>
<td>Korea</td>
<td>2007</td>
<td>15-17 (girls only)</td>
<td>25.7</td>
</tr>
<tr>
<td>Italy</td>
<td>2004</td>
<td>0-12</td>
<td>0.21</td>
</tr>
<tr>
<td>Russia</td>
<td>2001</td>
<td>14-17</td>
<td>20.0</td>
</tr>
<tr>
<td>USA</td>
<td>1996</td>
<td>12-16</td>
<td>10.0</td>
</tr>
<tr>
<td>UK</td>
<td>1996</td>
<td>11-17</td>
<td>1.29</td>
</tr>
<tr>
<td>Italy</td>
<td>2004</td>
<td>0-12</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Several researchers have studied subtypes of IBS in children using Rome criteria described for adults. Classification of IBS according to the bowel habits of the individual is extensively used in adult studies and clinical trials. The following subtypes have been identified in this classification: diarrhea-predominant IBS, constipation-predominant IBS, mixed IBS (alternating diarrhea and constipation) and unsubtyped IBS (not falling into any of the aforementioned categories depending on predominant bowel habits). Using this sub-classification, in two studies Zhou et al. have shown that unsubtypable IBS predominates among Chinese children. Other countries such as Korea, Iran and Sri Lanka have shown wide variations in distribution of subtypes of IBS.

Table 1.3 – Distribution of IBS subtypes around the world

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>Sri Lanka</td>
<td>Sri Lanka</td>
<td>China</td>
<td>China</td>
<td>Iran</td>
<td>Korea</td>
</tr>
<tr>
<td>Sample size</td>
<td>1717</td>
<td>417</td>
<td>3671</td>
<td>2013</td>
<td>1436</td>
<td>1517</td>
</tr>
<tr>
<td>Diagnostic criteria</td>
<td>Rome III (child)</td>
<td>Rome III (child)</td>
<td>Rome III (adults)</td>
<td>Rome III (adults)</td>
<td>Rome II (adults)</td>
<td>Rome II (adults)</td>
</tr>
<tr>
<td>IBS-C (%)</td>
<td>27.1</td>
<td>26.7</td>
<td>20.14</td>
<td>20.14</td>
<td>52.5</td>
<td>34.6</td>
</tr>
<tr>
<td>IBS-D (%)</td>
<td>28.0</td>
<td>26.7</td>
<td>17.76</td>
<td>18.47</td>
<td>11.8</td>
<td>26.9</td>
</tr>
<tr>
<td>IBS-M/IBS-A (%)</td>
<td>27.1</td>
<td>33.3</td>
<td>10.27</td>
<td>10.31</td>
<td>18.6</td>
<td>38.5</td>
</tr>
<tr>
<td>IBS-U (%)</td>
<td>17.8</td>
<td>13.3</td>
<td>51.1</td>
<td>51.08</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Functional abdominal pain

Functional abdominal pain according to the Rome III criteria is a different clinical entity compared to the recurrent abdominal pain described by Apley. The definition includes persistent or recurrent pain episodes, at least once a week for 2 months, without the presence of organic diseases. Epidemiology of this disorder is not well studied in children. A study carried out in Sri Lanka has shown a prevalence of 4.4%. Another study in Sri Lanka has also
shown that functional abdominal pain has the highest prevalence rates among all of the FGIDs in children.48

*Abdominal migraine*

Abdominal migraine is a well-known cause for abdominal pain in children. In the current Rome III criteria, it is recognized as paroxysmal episodes of intense periumbilical pain lasting for more than 1 hour with associated symptoms such as nausea, anorexia, vomiting, headache, photophobia and pallor. Affected children are otherwise well between attacks and the period between episodes may last for weeks to months.7 Abdominal migraine has been recognized as a common cause of recurrent abdominal pain in children in several hospital-based studies using Rome II or Rome III criteria.10,11,49 In a study using International Classification of Headache Disorders, 4.4% children evaluated for abdominal pain had abdominal migraine.50 An epidemiological survey conducted in the United Kingdom, using International Headache Society criteria, noted 4.1% of children as having abdominal migraine.51 In this study, the prevalence of abdominal migraine was higher among girls and attacks were associated with exposure to stressful events, travel, tiredness and consumption of certain food items. In a Sri Lankan school-based survey involving children aged 10-16 years, It was found that only 1% of children suffered from abdominal migraine according to the accepted criteria.10 It was also noted that this disorder is associated with family- and school-related psychological stress. Other painful conditions such as headache and limb pains, photophobia, light-headedness and sleeping difficulties were commonly associated with abdominal migraine. In addition other functional abdominal symptoms such as bloating, loss of appetite, flatulence, burping, nausea and vomiting were also commonly seen in children with this disorder.23

*Functional defecation disorders*

*Functional constipation*

Functional constipation is a cosmopolitan problem with prevalence rates varying by geographical location and environmental consideration. Rates are high enough to be considered a public health issue. Epidemiology of functional constipation has been well studied in both the Western world and Asia using well-established criteria. Studies from Western countries during the first decade of the new millennium have shown a prevalence ranging from 0.7% in Italy to 16% in the United States.22,36 A significant number of studies have been conducted in both developed and developing nations across Asia.47,52-57 In these studies, particularly among developed countries in the Asian region, prevalence of functional constipation is more or less close to the prevalence in the Western world.52,54-56 Similarly, studies from South America, particularly in Brazil, have shown higher prevalence rates of functional constipation (20%-

20
28%), similar to the developed nations in Asia. In addition, studies from Sri Lanka have revealed that functional constipation as an emergent issue, with a prevalence rates ranging between 4.2% and 15.4%. Data from Asian countries constantly challenge the common paradigm that constipation is a disease of the Western countries. Rapidly changing dietary habits, lifestyles and stressful events in the developing Asian economies such as Korea, China and Sri Lanka may have contributed to closing the gap in prevalence of constipation between different nations and regions of the world.

Table 1.4 - Prevalence of constipation in the world

<table>
<thead>
<tr>
<th>Country</th>
<th>Year of publication</th>
<th>Age group (years)</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hong Kong/China</td>
<td>2005</td>
<td>3-5</td>
<td>29.6</td>
</tr>
<tr>
<td>Hong Kong/China</td>
<td>2008</td>
<td>3-5</td>
<td>28.8</td>
</tr>
<tr>
<td>Korea</td>
<td>2010</td>
<td>5-13</td>
<td>6.7</td>
</tr>
<tr>
<td>Iran</td>
<td>2010</td>
<td>14-19</td>
<td>2.5</td>
</tr>
<tr>
<td>Taiwan</td>
<td>2011</td>
<td>7-12</td>
<td>32.2</td>
</tr>
<tr>
<td>Taiwan</td>
<td>2012</td>
<td>6-15</td>
<td>12.2</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>2012</td>
<td>10-16</td>
<td>15.4</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>2010</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>USA</td>
<td>2009</td>
<td>5-8</td>
<td>10</td>
</tr>
<tr>
<td>Turkey</td>
<td>2007</td>
<td>7-12</td>
<td>7.2</td>
</tr>
<tr>
<td>Turkey</td>
<td>2003</td>
<td>2003</td>
<td>12.4</td>
</tr>
<tr>
<td>Sweden</td>
<td>2006</td>
<td>2.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Italy</td>
<td>2005</td>
<td>0-0.5</td>
<td>17.6</td>
</tr>
<tr>
<td>Italy</td>
<td>2004</td>
<td>0-12</td>
<td>0.7</td>
</tr>
<tr>
<td>Italy</td>
<td>2005</td>
<td>0-12</td>
<td>2.6</td>
</tr>
<tr>
<td>Brazil</td>
<td>1999</td>
<td>8-10</td>
<td>20</td>
</tr>
<tr>
<td>Brazil</td>
<td>2002</td>
<td>1-10</td>
<td>26.8</td>
</tr>
<tr>
<td>Greece</td>
<td>1999</td>
<td>2-14</td>
<td>15</td>
</tr>
<tr>
<td>Greece</td>
<td>1999</td>
<td>2-14</td>
<td>6</td>
</tr>
<tr>
<td>Finland</td>
<td>2004</td>
<td>10-11</td>
<td>1.5</td>
</tr>
</tbody>
</table>
Fecal incontinence is defined as passing stools in inappropriate places irrespective of the amount. It is a common problem in the pediatric age range and has significant social repercussions on affected children. Prevalence of functional fecal incontinence ranges from 0.8% to 4.1% in Western countries. Recent studies from Asia noted much higher prevalence ranging from 2% in Sri Lanka to 7.8% in Korea. Epidemiological studies on fecal incontinence have not attempted to differentiate between various types of functional fecal incontinence up until recently although these subtypes have different pathophysiological mechanisms. A school-based survey conducted in Sri Lanka has shown that the majority of children suffering from functional fecal incontinence are having constipation-associated fecal incontinence. Only 0.4% of them had functional non-retentive fecal incontinence. This study has also highlighted that the bowel habits of these children are quite different from children with constipation-associated fecal incontinence.
GLOBAL PERSPECTIVE OF FUNCTIONAL GASTROINTESTINAL DISORDERS

For decades, gastrointestinal infections in the developing world and inflammatory bowel disease in the West were considered to be the main causes of gastrointestinal-related morbidity and mortality. However, with the availability of oral rehydration therapy, vaccination against gastrointestinal infections and therapeutic advances such as immunosuppressants and monoclonal antibodies, the disease burden of gastrointestinal infections has been reduced and the natural history of inflammatory bowel disease has been modified. Against this backdrop, FGIDs in children are emerging as one of the most prevalent types of disorders and they are receiving greater attention in the twenty-first century.

Type and geographical distribution

In summary, the geographical burden of FGIDs is shifting from the West to the East, where the prevalence of most subtypes is increasing. The fast-growing population will probably identify Asia as the epicenter of FGIDs in the future. Follow-up data with regard to the course of life and long-term prognosis of childhood FGIDs are limited. The available data suggest that a significant percentage (25%-30%) of children with functional constipation and fecal incontinence grow up to be adults with persistent symptoms. In addition, in a small retrospective study by Kahn et al., childhood constipation appeared to be a predictor of IBS in adulthood.

Age distribution

Relationship between age and FGIDs has been evaluated to reveal a wide variation and heterogeneity in symptoms for all subtypes. The main reason for this is that different studies have recruited children in different age groups, varying from birth to 19 years. Therefore, a precise age distribution in epidemiology cannot be described with certainty. However, several trends have been highlighted. For example, a study among school children in Sri Lanka has illustrated a negative correlation between prevalence of AP-FGIDs. A more descriptive analysis of IBS patients by the same group of researchers has found linear reduction of probability in developing IBS with age. On the other hand, three other epidemiological studies from the United States and China have noted a trend of increasing prevalence of IBS with age.

Similarly, the majority of previous studies have shown a reduction of prevalence of defecation disorders with age. Two epidemiological studies from Sri Lanka have demonstrated that both constipation and fecal incontinence show the highest prevalence at the age of 10 years and a decline with advancing age. A study from the Netherlands also noted a similar reduction in
prevalence of fecal incontinence with age. It is likely that maturation provides better control over bodily functions, including bowel habits.

In contrast to this, the few available studies on aerophagia and rumination syndrome have not shown a significant relationship between their prevalence and age. The mean age of developing cyclical vomiting is between 4.6 and 6.9 years. These contrasting findings need further epidemiological evaluation.

Figure 1.3 - Age related prevalence of abdominal pain predominant FGIDs in children

Gender distribution
Sex difference studies among adults have clearly shown that several FGIDs, such as IBS and constipation, are found with higher frequency among females. In contrast, gender differences of most FGIDs are not clearly visible in children. Some previous studies have shown a clear female preponderance in development of AP-FGIDs in children. These studies have shown a higher prevalence of functional dyspepsia and IBS in girls than in boys, which is comparable with previous adult studies conducted in IBS and functional dyspepsia around the world. Newly developed Asian economies, the Middle East and developing nations such as Sri Lanka also show a similar female preponderance in prevalence of IBS. A convincing biological reason for this phenomenon has never been articulated. Effects of female sex
hormones on gastrointestinal tract and brain-gut interactions have been suggested as a possible reason. However, since most of the children included in previous studies are of young age and have not achieved menarche to acquire a fully mature hormonal profile of a female, the gender difference seen in the AP-FGIDs cannot be fully attributed to the effects of female sex hormones. It is also possible that factors other than gender specific hormonal difference, such as true biological differences between males and females, may play an important role in the natural history of the AP-FGIDs that predisposing girls to develop them. Sex-related biological differences in the integration, processing and modulation of pain may also be key mechanisms responsible for the greater female prevalence of many chronic pain disorders such as FGIDs. Psychosocial factors, including how boys and girls are socialized to express emotions differently, are also likely to play an important part in sex differences in prevalence. These considerations lie outside the scope of the present chapter.

Sex-specific prevalence of constipation is more complex and is currently unclear. A few large studies have shown a predilection of girls to develop constipation but the ratios are not statistically significant. Several other studies have noted almost equal prevalence between girls and boys. A study from Sri Lanka noted higher prevalence of constipation in boys. This is in contrast to the data from adult studies, which show a clear, statistically significant female preponderance. Progesterone is known to increase transit time of the large and small bowel in women and childbirth-associated physiological disruption of pelvic floor muscles may have contributed to the higher prevalence of functional constipation in the older population. Lack of these physiological phenomena in children would have contributed to lack of gender difference in prevalence of constipation in children and adolescents. Several studies from both developed and developing countries have convincingly demonstrated that functional fecal incontinence is clearly more common among boys.

The only available epidemiological study on aerophagia does not show a difference of prevalence between girls and boys. Some recent studies on CVS have found no gender difference in prevalence while others have found that CVS has a higher prevalence rate among girls. Finally, hospital-based data have illustrated a higher prevalence of rumination syndrome among females.

**Sociodemographic factors**

Sociocultural influences on the development and persistence of a wide variety of FGIDs are not evidently seen in the pediatric literature. Although studies on most of the FGIDs do not show a significant influence by sociocultural factors, defecation disorders such as functional
constipation and functional fecal incontinence are clearly more common among children from low socio-economic strata. Poor toilet facilities and large number of family members sharing the same toilet may lead to fecal withholding, which predispose children to develop both constipation and functional fecal incontinence. In addition, delayed seeking of medical care for constipation may also contribute to the development of defecation disorders in children from disadvantaged socioeconomic backgrounds. Furthermore, children living in socially disrupted environments, such as areas affected by war, have higher chances of developing functional defecation disorders.

**Growth**

Pediatric obesity and overweight are rising global health problems. Apart from associations with many chronic diseases, including hypertension, hypercholesterolemia and non-alcoholic steatohepatitis, obesity in children seems to predispose them to develop AP-FGIDs, although the mechanisms are not clear. Several other investigators have noted that functional defecation disorders, both constipation and fecal incontinence, are significantly more common in children with obesity. Obese children are known to have poor gastric accommodation. In addition, 10% of morbidly obese children have delayed colonic transit time. These mechanisms may at least partly explain the increase in FGIDs seen in obese children.

**Psychological factors and child abuse**

Psychological factors are well recognized and principal contributory factors to the development of FGIDs in children. Psychological stress is known to alter receptor functions of the central corticotrophin-releasing factor signaling system, inducing acute and chronic stress-induced visceral hyperalgesia. This is thought to be a major pathophysiological mechanism for the development of FGIDs. Stressful life events have become a common problem in the day-to-day lives of children. A series of epidemiological investigations from Sri Lanka has shown that several FGIDs are associated with school- and home-related stress. In addition, other studies from Asian populations have also shown that frequency of IBS is increased in children exposed to stress.

Child maltreatment is a major social welfare problem. Every year about 4%-16% of children are physically abused and one in ten is neglected or psychologically abused. Exposure to multiple types and repeated episodes of maltreatment increases the risk of severe psychological harm. The association between being abused during childhood and the development of FGIDs as an adult is well known. Emerging data show such associations also exists in children. A preliminary study, from Sri Lanka, has indicated that child abuse is associated with AP-FGIDs.
**Infections**

Gastrointestinal infections are a common health problem in children. It is estimated that each year 1 billion children in the world under the age of 5 years suffer from gastroenteritis. Although the majority recovers without consequences, a small percentage progress to develop FGIDs such as IBS - known as post-infectious IBS (PI-IBS). PI-IBS is much more common after infection with *Campylobacter* species. Two studies have clearly demonstrated an association between bacterial gastroenteritis and IBS in children. Saps *et al.* have reported a significant incidence of post-infectious (bacterial) AP-FGIDs. Preliminary investigations suggest that 36% of children exposed to bacterial enteritis subsequently developed FGIDs, with 31% diagnosed with PI-IBS. Pediatric data from Walkerton Health Study demonstrated a higher incidence of IBS after exposure to a bacterial gastroenteritis outbreak with *Escherichia coli* and *Campylobacter* species.

These studies have demonstrated that children are at risk of developing IBS after gastrointestinal infections. Gastrointestinal infections are a common occurrence in the developing world. It has been noted that a poorly nourished child living in socially impoverished and cramped conditions without access to proper sewerage disposal and running water will have eight or more gastrointestinal infections a year when compared to a child living with better sanitary facilities. These contentions imply that children living in the developing world have a higher predilection to develop PI-IBS than children in the developed world and that this will become a significant burden for these low-income countries with comparatively small health budgets.

**Diet and food allergies**

Dietary habits have been studied as possible mechanisms for FGIDs in children. According to a recent retrospective study, 19% of children with cow’s milk protein allergy during infancy have developed AP-FGIDs later on in life. IBS was reported to be the most common FGID within this group of allergy sufferers. Similarly, constipation has also been associated with cow’s milk protein allergy in children. Furthermore, several studies have reported improvement of symptoms of constipation with an elimination diet. However, most of these retrospective studies are limited by a lack of appropriate independent allergy corroborations or diagnosis and significant recall bias. These limitations have reduced the applicability of the results in general terms and careful clinical appraisal and laboratory confirmation are needed before recommending a bovine milk-elimination diet for FGIDs in children.
Fibre is an important component in the human diet. It is recommended that a child should take a reasonable amount of fibre-containing foods in his or her diet (age+ 5 g per day). Fibre is known to improve stool frequency, stool volume and colonic transit time. Several studies have shown low-fibre diet as a risk factor for developing constipation in children. Two studies from Asia noted low mean intake of dietary fibre in young children with functional constipation, especially in terms of fruits and vegetables. In addition, another study has also shown an association between constipation and consumption of fast food, which is known to be low in fibre. Therefore, a diet low in fibre is a risk factor for developing functional constipation in children.

Quality of life

Even though FGIDs are not life threatening, they are known to lead to a lower quality of life (QoL) for the children who have them. Significantly lower QoL scores have been reported in all four domains (i.e. physical, emotional, social and school functioning domains) in affected children. Youssuf et al. studied QoL in a group of children with functional abdominal pain and compared the results against those of children suffering from inflammatory bowel disease, children suffering from gastro-esophageal reflux and healthy children. Children with functional abdominal pain had lower physical and emotional scores than healthy children. Furthermore, QoL scores of children with functional abdominal pain were comparable with children suffering from inflammatory bowel disease and gastro-esophageal reflux. These two studies clearly indicate clearly the low QoL in children with abdominal pain-predominant FGIDs. Moreover, the scores are similar to severe organic disorders such as inflammatory bowel disease, indicating a significant component of suffering in these children.

Several studies have shown poor QoL in children with functional constipation. According to one study from the United States, the mean quality of life score of children with functional constipation was lower than that of children with organic disorders such as reflux oesophagitis. Another study, performed in Australia, also noted similar findings in children with slow transit constipation. In addition, both studies have clearly shown that QoL ratings on parent reports were significantly lower than that of child reports.

Co-morbid factors

A large number of co-morbid factors are known to be associated with FGIDs in children. Some studies from Sri Lanka found extra-intestinal symptoms such as headache, limb pain, photophobia and sleeping difficulties more frequently in children with AP-FGIDs than in controls. Similarly, Dong, et al. noted an association between functional headache and
irritable bowel syndrome in Chinese children. Children with aerophagia were also noted to have an array of extra-intestinal symptoms. These symptoms can significantly contribute to the suffering and poor QoL of children who are already having pain and discomfort. In this light, extra-intestinal symptoms need to be addressed in the management of children with FGIDs.

**Healthcare seeking**

Although FGIDs are a considerable problem in the community, healthcare-seeking patterns for this group of disorders in children are not well understood. Evaluating ambulatory healthcare data, one study reported that chronic constipation is a common cause for an ambulatory healthcare visit for children in the United States. Two other studies have assessed the healthcare use of children with constipation in a single-birth cohort at different time points. The first study noted that children suffering from constipation have the highest number of medical appointments in comparison with all other gastrointestinal complaints. The second study illustrated that children with constipation seek medical care more often than children with other illnesses such as bronchial asthma and migraine. In contrast, another study from Sri Lanka has shown that despite high prevalence rates, healthcare-seeking for chronic constipation remains very low (3.8%). Younger age, family history of constipation and associated vomiting were significant predictive factors for visits to a doctor. Healthcare-seeking for other FGIDs in children have not been studied in depth in different parts of the world with different healthcare systems; therefore, further research into this important area would aid in the planning and allocation of healthcare resources for FGIDs in a global level.

**SUMMARY**

Prevalence of FGIDs has dramatically increased over the past decade and now represents a large global healthcare burden. With growing population trends and increasing predisposing factors such as obesity and psychological stress, it can be predictable that the incidence of FGIDs will increase further and become a significant healthcare problem. Although FGIDs are not life threatening, research shows that children suffering from FGIDs tend to have a lower QoL than their healthy peers and frequently miss school as a result of the disorders. In addition, many FGIDs such as constipation and IBS has high healthcare expenditure and are becoming a major challenge on already-overstretched healthcare budgets, both in developing and in developed countries, competing perhaps with other prioritized diseases. These factors suggest that functional gastrointestinal diseases need to be one of the main research focal points of the twenty-first century.
REFERENCES


72. Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. Am J Gastroenterol 2011;106:1582-91.


