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#### Defecation disorders in children: Epidemiology and risk factors

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## DEFECATION DISORDERS IN CHILDREN EPIDEMIOLOGY AND RISK FACTORS

Shaman Rajindrajith

Defecation Disorders in Children: Epidemiology and Risk Factors

Defecation Disorders In Children: Epidemiology And Risk Factors

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### Defecation disorders in children: Epidemiology and risk factors

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit van Amsterdam op gezag van de Rector Magnificus prof. dr. D.C. van den Boom ten overstaan van een door het College voor Promoties ingestelde commissie, in het openbaar te verdedigen in de Agnietenkapel op dinsdag 29 september 2015, te 12:00 uur

door

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Faculteit der Geneeskunde

## I have finally come to the conclusion that a good set of bowels is worth more to a man than any quantity of brains.

Josh Billings (1818-1885)

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#### Outline of the thesis

Healthy childhood is not the mere absence of disease but is a vibrant state of health, characterized by physical, mental and social wellbeing, which helps to achieve childhood growth, development and potential according to the genetic makeup and socio-cultural determinants (1). During the last few decades, child health has reached many important milestones including controlling of major communicable diseases through immunization, about 50% reduction in child and neonatal mortality and significant numbers of countries achieving the Millennium Development Goals (2,3). However, a new set of challenges are emerging. They mostly consist of diseases of multifactorial etiologies such as bronchial asthma, obesity, substance abuse and functional gastrointestinal disorders (FGDs). The last is being thought to be related to the result of interactions of many bio-psycho-social factors.

Functional gastrointestinal disorders in children are a set of clinical entities characterized by, recurrent vomiting, chronic recurrent abdominal pain, abdominal bloating and distension, and, disturbed defecation without identifiable structural, anatomical or biochemical anomalies. Although there are several FGDs, functional constipation (FC) is the commonest and the most studied among them. FC has a high prevalence right across many parts of the world (4). It also weighs in as a significant healthcare burden, more than many other common childhood disease such as bronchial asthma (5). Faecal incontinence has also been reported as an emerging health problem in the world. Several researchers have shown the prevalence ranges from 1.4% to 7.8% (6-8). The precise mechanisms of functional defecation disorders are ill-understood and therapeutic options are limited. These factors indicate that defecation disorders are threatening to become a major public health problem across the world in the years to come, unless, the understanding of the disorders are broadened and attention is focused on them as significant emerging problems.

Despite these evident facts, the problem has received relatively poor attention from the health authorities as they are mostly concentrating on conditions which contribute to child mortality rather than morbidity and other important non-communicable disorders such as malnutrition. In such a scenario, it is most likely that the public health impact of childhood defecation disorders is perhaps neglected.

In this thesis we tried to evaluate epidemiology, risk factors and impact of health related quality of life of children with defecation disorders in Sri Lanka.

Defecation disorders in childhood are poorly understood and not properly managed at the grass root level. This is at least partly due to poor knowledge of the clinicians in the primary healthcare services. Part one **(Chapter 1)** of the introduction provides current literature review of defecation disorders in pediatric practice.

Fecal incontinence is an enigmatic disease in children. Once the possible organic diseases are excluded, there remains a large number of children with functional fecal incontinence. Part 2 **(Chapter 2)** of the introduction of the thesis summarizes the current knowledge of functional fecal incontinence in children.

Constipation is thought to be a disease of the western world. However, in clinical practice in Sri Lankan hospitals we noted a significant proportion of children with gastroenterological problems have functional constipation. This prompt us to study the epidemiology of functional constipation in Sri Lankan children. **Chapter 3** of the thesis shows the results of the first epidemiological survey of constipation in Sri Lankan school children.

Psychological stress is a common problem in day to day life. It could be due to home related events or school related events in children. Stress is known to modulate the brain gut axis to alter the function of the intestine (9). It is possible psychological stress to play a crucial role in developing constipation in children. In **chapter 4** of the thesis we explored the possible relationship between psychological stress and constipation in children.

Civil unrest is a common problem across the world. It can range from destruction of properties in one country to full scale warfare in another. Internal displacement, hunger, poverty, lack of basic needs including toilet facilities are inevitable consequences of a full scale civil war. Moreover, sometimes children are recruited as child soldiers. Loss of parents and siblings, seeing their homes blown to pieces and forcing them into refugee camps may generate substantial psychological stresses leading to brain gut dysfunction. Sri Lanka faced 3 decades of civil war which ended in 2009. In **chapter 5** we describe the effects of civil war on childhood constipation.

Constipation in other countries leads to high healthcare burden. In a birth cohort study on young children in the US, Chitkara et al. found that the incident medical visits for constipation were indeed the highest for all gastrointestinal diseases (10). Compared to other common diseases such as childhood asthma and migraine, children with constipation demand and need more medical attention even as much as 7 times higher than asthma and 3 times higher than migraine (5). Sri Lanka has a free medical support for every citizen in the country. In this context we studied the healthcare consultation in children with constipation in Sri Lanka **(Chapter 6)**.

Health related quality of life (HRQoL) is an important concept that incorporates the patient perspectives of illness experience and functional status related to a medical condition. Assessment of HRQoL attempts to quantify multiple factors producing patient's perception of ill health. Several hospital based studies have noted children with functional constipation has poor HRQoL and sometimes it can be worse than children with organic diseases such as gastroesophageal reflux and inflammatory bowel diseases (11). In **chapter 7** we studied the effect of constipation on HRQoL in a community sample of children with constipation.

Child abuse is a major social welfare problem across the globe. Studies in adults have shown abuse as a child is a predisposing factor to develop functional gastrointestinal diseases such as irritable bowel syndrome and constipation later in life (12). In **chapter 8** we studied the effects of child maltreatment in developing constipation in children.

Fecal incontinence is a difficult clinical problem in paediatric practice. These children have a peculiar and distinctive fecal aroma around them which leads to rejection by both peers and teachers at school. This, in extreme cases, may directly or indirectly predispose to child maltreatment. At home parents and other family members believe that children may be soiling intentionally to upset others, to get attention or, because they are stressed, have emotional problems or consumed wrong food and therefore responsible for their symptoms (13). Such thinking patterns ultimately could lead to family disharmony and chaos in the family structure. The aetiology for fecal incontinence in children without organic disorders are not entirely clear. In **chapter 9** we attempt to study the different aetiologies of functional fecal incontinence in children.

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## INTRODUCTION TO DEFECATION DISORDERS

#### **Defecation Disorders in Children**

## CHAPTER

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Text Book of Pediatric Gastroenterology Hepatology and Nutrition. Editors, Guandalini S, Dhawan A, Branskri D. Expected date of publishing: 14th August 2015

#### <u>Abstract</u>

Defecation disorders denote a state of altered defecation dynamics leading to an array of clinical presentations. With the currently available epidemiological studies, it is evident that these disorders have become a set of rapidly spreading global health problems. Due to the broadening of the understanding of escalating healthcare costs and poor quality of life, these diseases demand attention of clinicians and researchers, more than at any other time in history. However, it is regrettable that only a little guidance is available for healthcare professionals to manage these disorders. Most of the therapeutic trials and investigation plans are archaic and from the viewpoint of a 21<sup>st</sup> century clinician, are not evidence based. However, new research ventures are being carried out and the horizon of the knowledge base is expanding, perhaps indicating a brighter future. In this chapter we discuss emerging concepts of definitions, epidemiology, pathophysiology, clinical evaluation and management of defecation disorders in children and adolescents.

#### Part 1: Constipation

#### **Definition**

Constipation in children has been defined in many ways. Some of these include Iowa criteria, PACCT criteria, Rome II criteria and Rome III criteria (1-4). The Rome III criteria for defecation disorders are the currently accepted definitions and are shown in **Table 1**. The thing that is common to all these successful criteria include the usage of multiple features that hang together in the clinical setting to define constipation. In Rome III definition, younger children (<4 years) should fulfil two criteria for at least one month whereas older children need to have symptoms over a period of two months.

## Table 1 – Rome III definition of functional constipation and functional nonretentive fecal incontinence

# Functional constipation Diagnostic criteria\* must include two or more of the following in a child with a developmental age of at least 4 years with insufficient criteria for diagnosis of IBS:

- Two or fewer defecations in the toilet per week
- At least one episode of fecal incontinence per week
- History of retentive posturing or excessive volitional stool retention
- History of painful or hard bowel movements
- Presence of a large fecal mass in the rectum
- History of large diameter stools which may obstruct the toilet

\* Criteria fulfilled at least once per week for at least 2months prior to diagnosis

#### Functional nonretentive fecal incontinence

Diagnostic criteria<sup>\*</sup> must include **all** of the following in a child with a developmental age at least 4 years:

- Defecation into places inappropriate to the social context at least once per month
- No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms
- No evidence of fecal retention

\* Criteria fulfilled for at least 2 months prior to diagnosis

Using a single clinical feature, such as low bowel frequency to define constipation can be misleading. It has been shown that around 0.4 to 20% of otherwise healthy children have at least one feature of Rome III criteria (5,6). Furthermore, bowel frequency is known to be variable in different regions of the world possibly depending on diet, genetics and environmental factors 5) 7). Therefore, it is imperative that the clinician's perspective is more flexible and he or she understands the changes in bowel frequency in the context of local and patient variables.

Several studies have assessed the diagnostic capability of Rome III criteria to identify functional constipation in children. A school based study including 10-16 year olds showed Rome III criteria are more inclusive in diagnosing constipation (8). Another study based on out-patients referred to a tertiary care hospital noted that 87% of children had constipation according to Rome III criteria whereas only 43% children were classified as having defecation disorders using Rome II criteria (9). Although both these studies indicate the superiority of Rome III criteria in the diagnostic process, the required duration of two months appears to be a little too long and may result in delayed treatment, especially in older children.

#### Magnitude of the problem

Constipation is a global health problem. Studies from Europe showed a prevalence range from 0.7-17.6% among children (9-14). In the United States 10% of 5-8 years olds are having constipation (6). Two studies from Brazil pointed out alarmingly higher rates of over 20% occurrence of constipation in a 1-10 year old population (14,15). More disturbing data are emerging from Asia. Prevalence of constipation in Taiwan was 32.2% in children in elementary schools and in Hong Kong 12-28%, indicating constipation is becoming a bigger problem in newly developing economies of Asia (16-18). Similarly, developing nations in Asia, like Sri Lanka also shows 15% of their school children are suffering from chronic constipation (19). These data underscore the magnitude of the disease burden and shifting its epicentre of prevalence from the West to the East. The differences in prevalence need to be interpreted with some caution as the wider variations seen may partly be due to differences in definitions used, differences in age groups included and heterogeneity of survey methods.

#### **Risk factors**

**Table 2** shows the known and identified risk factors for chronic constipation in children. In contrast to adult studies which show constipation to be more prevalent among females, several epidemiological studies among children have failed to identify gender as a risk factor to develop constipation (13, 20, 21). However, one study from Sri Lanka has shown that the prevalence is significantly higher among boys and children in low socio-economic strata (19).

Category	Risk factor
Patient related	Male sex
	Poor sleep
	Obesity
	T Cl
Dietary	Low fiber
	Consumption of junk food
	Not having regular meals with parents
	Cows milk protein allergy
Psychological	Home related stresses
	School related stresses
	Adverse life event including abuse
	Subjected to bullying
	Anxiety
	Depression
	Autistic spectrum disorders
Social	Living in war affected areas
	Living in urban areas
	Lower social class
	Hostile and aggressive family environment

#### Table 2: Risk factors for chronic constipation

Psychological stress is another risk factor that predisposes children to develop constipation. Children living in homes and studying in schools which create stress are more prone to develop chronic constipation (22). In addition, disrupted societies by civil unrest are also an important predisposing factor (23). A study from Hong Kong has shown that children not having regular meals with their parents and deprivation of sleep as independent risk factors to develop severe constipation (17). Moreover, low consumption of fiber (11, 17, 18), cow milk protein hypersensitivity (21, 24) and consumption of fast foods too often (17) are associated with constipation. Lastly, obesity has also been identified as an independent risk factor (25, 26). In a recent study, our group also noted that children who faced adverse life events such as physical, emotional and sexual abuse, have higher predilection to develop constipation. These events also predispose them to develop more somatic symptoms and lead to a poor quality of life as well (27)

#### **Quality of life**

Children with constipation have poor health related quality of life (HRQoL) scores in all domains namely, social, school, physical and emotional functioning. The scores they obtained are even lower than children suffering from organic diseases such as gastro-esophageal reflux and inflammatory bowel disease (28). Children with slow transit constipation also have been shown to have poor HRQoL (29). A school based study from Sri Lanka also confirms these findings and showed that constipation associated FI further reduces HRQoL (30).

#### Extra-intestinal symptoms and psychological problems

Children with constipation suffer from an array of somatic symptoms. In one of the studies we found that children with constipation had a multitude of somatic symptoms and high somatization scores (30). Constipation is also associated with a number of behavioral abnormalities such as autism, attention deficit hyperactivity disorder and anxiety (31-33). Abnormal personality traits were also noted in children suffering from constipation (34). In addition, children with autistic spectrum disorders are known to have very early onset disease (32).

#### Healthcare burden

Constipation is a leading cause for medical consultation in children. Documented medical visits for constipation were higher than most other gastro-intestinal diseases in children under 5 years (35). The incidence of medical presentation for children with constipation is substantially higher than other chronic episodic conditions such as asthma (7 times) and migraine headaches (3 times) (36). The mean out-patient costs and mean annual number of emergency room visits are higher in children with constipation compared to controls (36). Furthermore, employed parents of a child with constipation have a higher number of working day losses than controls. More importantly, children with constipation are noted to have higher number of days of school absenteeism (37). In addition, children with constipation show poor quality of school work (30,38). Implications of these findings on education of children are much larger than expected. Poor education invariably leads to poor earning capacity and ignorance as an adult. Therefore they become an added burden to the society at large.

#### **Pathophysiology**

Understanding of the pathophysiological mechanisms of chronic constipation in infants and children is a considerable challenge and remains in its early stages. However, available studies on physiology of the colon and rectum and studies on animal models have shed some light upon the subject.

#### Infants and young children

Stool withholding plays a major role in the development of constipation in infancy and early childhood. Passing a hard stool leading to pain, strict early toilet training, stubbornness and concentration on other activities which are more exciting than going to the toilet are possible factors for stool withholding. When the urge to pass stools comes, the withholding child tightens gluteal muscles and stands on tip toe. During this process the rectum dilates, faecal matter is accommodated and desire to pass stools disappears. A large mass of feces is formed in the rectum during this process leading to a cascade of physiological changes described below.

#### Children and adolescents

Several studies have shown that children with constipation have defective intraluminal transport involving different segments of the colon such as proximal delay, hind gut delay and recto-sigmoid hold up (39-41). Furthermore, it has been shown that children with chronic constipation have significantly delayed total colonic transit times of over 100 hours (42). Although slow transit constipation in adults is almost an exclusive disease of females (43), in children and adolescents, prevalence is more or less equal among the sexes (44).

Colonic manometry has shown several abnormalities in constipation. They include reduced frequency of high amplitude propagative contractions, and disordered patterning of spatio-temporal colonic propagative responses (45). Like slow transit constipation, all these factors may contribute to poor propulsion of fecal masses along the colonic lumen generating symptoms of constipation.

Rectal sensitivity to oncoming fecal matter and dilatation is a crucial point in normal rectal function. There is a subset of children with constipation who demonstrate poor rectal sensation (46). Furthermore, several studies in children have shown increased rectal compliance (47,48) and a megarectum (49). These factors are closely inter-related and lead to attenuation of rectal sensation and lack of desire to evacuate, leading to low bowel frequency.

In addition, contraction, rather than relaxation of the pelvic floor muscles with increasing rectal pressure (dyssynergic defecation) also prevent evacuation of stools. The balloon expulsion test has been used to measure rectal motor dysfunction in children with an array of other combined measurements. Chitkara *et al.*, demonstrated that 31% of children with functional constipation and 53% of children with functional fecal retention (using Rome II criteria) had an abnormal balloon expulsion test, and 40% to have high resting anal pressure (50).

In addition to these local factors, dysfunction of the brain-gut axis also contributes to the development and propagation of symptoms. Stress induced abnormalities in the colonic motor activity may further aggravate the motor and sensory abnormalities and worsen stool retention. Functional Magnetic Resonance Imaging studies have described a multitude of abnormalities in adults with FGD including constipation as possible mechanisms for this phenomenon (51).

#### Final pathway for both age groups

Pathophysiological mechanisms described for both age groups finally lead to retention of stools in the rectum and colon. Since colonic and rectal mucosa are designed to absorb water, stool becomes dry and hard. Molecular abnormalities in the rectal mucosa of children with constipation such as abnormalities in non-calcium mediated chloride channels lead to abnormally low chloride secretion that may further contribute to the development of hard stools (52). The mechanical dilatation of the rectum inhibits motor function of the proximal and distal hemi-colon through reflex mechanisms (53,54).

In addition, animal models have shown that accumulation of feces elongates the colon. This in turn leads to release of nitric oxide by activating mechano-sensory and myenteric descending neuronal nitric oxide synthase. Nitric oxide inhibits action potential firing in other myenteric sensory neurons driving peristaltic nerve circuits, inhibiting colonic contractile activity (occult reflex), thereby seriously hampering evacuation (55,56). It has been shown that children with increased rectal wall compliance have prolonged colonic transit time which further strengthens the possibility of occult reflex (47). Interactions of these inextricably linked mechanisms in a complex manner, rather than in isolation, lead to generation and propagation of symptoms in children with constipation.

#### **Clinical features**

#### Infants and young children

The most common reason for constipation in infants and toddlers is an acquired behavior component after experiencing painful bowel movements (57). When the desire to pass a stool occurs, they tend to cry and withhold stools by tightening their gluteal muscles and pelvic floor. This is evident in infants as they tighten the legs and in young children as they stand on tip toe and tighten their muscles till the desire for passing a stool goes off. These children also have low stool frequency, passing large diameter, rock hard and sometimes bloody stools infrequently and occasional leaking of semisolid to liquid stools into underwear. In addition poor appetite and abdominal distension are also notable features.

#### Older children and adolescents

This group tends to present with classic symptoms of constipation. The presenting complaint very often is reduced stool frequency. The other features include, passing hard stools, pain while passing stools, frequent episodes of fecal incontinence and infrequent passage of a large diameter stool which may obstruct the toilet. Some older children also show withholding postures although these are not seen as commonly as in younger children. Abdominal bloating is another important feature in children and seen especially in adolescents (58). Abdominal pain, anorexia and behavioural abnormalities are also important features in this age group.

#### Clinical evaluation of children with defecation disorders

Clinical evaluation is the most important tool in diagnosing defecation disorders in children and adolescents. It includes a thorough history, tenacious physical examination and careful interpretation of findings in a logical manner. This process helps to actively identify functional defecation disorders, exclude possible organic diseases that can mimics functional defecation disorders, and recognize complications.

#### Clinical history

Although the presenting features are obvious in the majority, clinical features may be subtle in some children. Therefore a high degree of suspicion is essential during history taking. Onset and duration of symptoms need to be clarified first. Very early onset disease in infancy suggests the possibility of organic diseases such as Hirschsprung disease, ano-rectal malformations and metabolic diseases. Details of bowel habits are the cornerstone in diagnosing constipation **(Box 1)**.

#### Box 1: Bowel habit questions for defecation disorders

Stool frequency
Consistency
Nature of the stools
Incontinence
Withholding behaviour
Pain during defecation
Blood in stools

Use of validated stool scales for infants (59) (Amsterdam stool scale) and children (modified Bristol stool scale) (60) helps to obtain more accurate description of stools. Apart from that, it is also important to question on other gastrointestinal symptoms from children. Abdominal pain is noted in 10-70% of children with constipation. Poor appetite, nausea, vomiting and abdominal bloating are other important features that need to be inquired during history taking. Children with chronic constipation also tend to suffer from a myriad of somatic symptoms and identifying these features would help in clinical management (19). Urinary symptoms and incontinence are also seen in some children (61-64) and refractory vulvo-vaginitis is a known feature, especially in pre pubertal girls (65).

Past medical history, specially concentrating on drugs that may cause constipation is also an important part in the evaluation. Surgical issues such as corrected anorectal malformations, and Hirschsprung disease are well known to present with constipation (66, 67). Dietary history particularly concentrating on fiber content is an integral part as underconsumption of fiber might lead to constipation (17, 18). Introduction of cow's milk to infant's diet is a risk factor to develop constipation among them [68, 69]. Psychological abnormalities need also to be looked into as some children develop personality problems, anxiety and depression with constipation (22, 70).Finally details of social and family history should not be overlooked. Constipation is notably prevalent in children from the lower socio-economic strata, living in disrupted deprived areas and urban areas (19, 23). In addition, adverse life events such as physical, sexual and emotional maltreatment should also need to be evaluated carefully in children with constipation as these factors are known to predispose children to develop constipation (27) Some children with constipation also have first degree relatives with similar problems (11, 19).

#### Physical examination

The physical examination should start with assessment of growth. Growth faltering and short stature are features of organic causes (endocrine, metabolic etc) for constipation. On the other hand, obesity is also a known predisposing factor for defecation disorders such as constipation and fecal incontinence (26). Dysmorphic features are present in children with syndromes who are having constipation (71). All children with defecation disorders need a detail developmental assessment. Those with long term neurological dysfunctions such as cerebral palsy tend to have both constipation and fecal incontinence. Furthermore, this would also help to identify children with autistic spectrum disorders who have a tendency to develop constipation (31).

Abdominal examination may reveal the presence of abdominal distension and past surgical scars of abdominal surgery. Palpable fecal masses in the lower abdomen indicate fecal loading and is a feature present in about 50% of children with constipation (72). However, gaseous distension is more in favor of constipation predominant irritable bowel syndrome.

Perianal examination may reveal abnormal position of anus (73) Smear of feces and perianal excoriation of skin indicates fecal incontinence. Fissures and tags can also be noted in children with chronic constipation who passes hard stools or may indicate sexual abuse. Patulous anus is associated with lower motor neuronal damage which can be associated with fecal incontinence. Digital examination of the rectum is an essential part in evaluating children with defection disorders. During the process one should assess resting tone, the squeeze pressure of the sphincter complex, nature of fecal loading, size of the faecal mass and the size of the rectum.

Neurological examination should concentrate specially on features of spinal bifida, motor and sensory deficits in the lower limbs and perianal sensory testing. One should look for perianal sensory loss and absence of anal wink.

#### **Investigations**

Constipation is a clinical diagnosis. Using currently accepted clinical criteria, the majority of the children who present to a medical facility can be diagnosed and managed successfully. Specialized investigations are therefore only needed when the diagnosis is uncertain or when they do not respond to standard management strategies. Investigations are also warranted in children who are suspected to have organic reasons for defecation disorders during history taking and physical examination.

#### Radiological tests

Colonic transit time is usually assessed by using radiological methods. It generally gives an idea of propulsive function of the colon and helps to identify segments with abnormal motility. It is usually measured using radio-opaque markers or scintigraphic methods. In marker studies, the markers are ingested as a meal or swallow as a capsule and abdominal X-rays are obtained to count the number of markers in different segments of the colon. In scintigraphy, the patient is given a meal containing radioisotope and multiple images are taken using a gamma camera to assess the radioisotope count in each region. Several studies have shown abnormalities in total and segmental transit times in children with functional constipation using radio-opaque markers (39, 40) A Dutch study noted children with functional constipation having colonic transit time over 62 hours. This cut-off value has a sensitivity of 52% and specificity of 91% (42). Colonic transit time also has an inverse relationship with the number of defecations per week (39). Using colonic scintigraphy, Sutcliffe et al. found delay in transit in patients with constipation (41).

Ultrasonography has also been used to assess the degree of fecal retention in the rectum. Using a transabdominal approach, several studies have measured the rectal diameter to determine fecal loading in the rectum using different methods and have shown that children with chronic constipation do have a larger rectal diameter, when compared to controls. Bijos et al. using recto-pelvic ratio (dividing the transverse

diameter of the rectal ampulla by the transverse diameter of the pelvis) illustrated that in children with functional constipation the mean recto-pelvic ratio was  $0.22 \pm 0.05$ compared to healthy controls  $0.15 \pm 0.04$  (74). Another study measured the impression of the rectum behind the urinary bladder seen as a crescent. The median rectal crescent in children with constipation was 3.4 cm (range 2.10 to 7.0; IQR 35.3) as compared with 2.4 cm (range 1.3 to 4.2; IQR 0.72) in healthy controls (75). Klijn et al also found a significant difference in mean rectal diameter between the constipated group (4.9 cm) and the control group (2.1 cm). The cut-off value was 3.3 cm, where >3.3 cm indicated constipation (76). The results are promising and wider availability and non-invasive nature of the test makes it an ideal investigation. However, methods need to be standardized and more studies are needed before recommending routine use of ultrasonography in assessing children with constipation.

Furthermore using endosonography techniques, Keshtgar et al. have shown that children with chronic constipation have a thickened external anal sphincter complex. However, they were unable to demonstrate a significant relationship between thickened anal sphincter, ano-rectal manometry and amplitude of sphincter contractions (77). The clinical utility value of this finding is yet to be determined.

Plain abdominal X-ray is used to demonstrate fecal loading in the colon and rectum. Several scoring systems are used to assess the degree of impaction. However, sensitivity and specificity of these tests are variable and also the inter and intra observer reliability are poor (78) Therefore, it is difficult to recommend the use of plain x-ray films of the abdomen as an investigation.

The other radiological investigations such as defecography and contrast enemas have no place in clinical evaluation of children with constipation. Magnetic resonance imaging of the spinal cord is an important investigation in children with refractory defecation disorders as some children have been shown to have significant abnormalities such as spina bifida occulta and terminal filum lipoma. Importantly, gluteal cleft deviation was found in 3 of 4 patients with these abnormalities (79, 80).

#### Physiological tests

Ano-rectal manometry combined with balloon expulsion test is an important investigation to understand the function of the ano-rectal unit and pelvic floor muscles. It provides information about anal sphincter function, mechanisms of continence and defecation, rectal sensation, rectal compliance and ano-rectal reflexes (81). Several studies have demonstrated several abnormalities of ano-rectal function in children with constipation. They include increased rectal sensory threshold, reduced rectal contractility, high resting anal pressure and failure of relaxation of the external anal sphincter with rising rectal pressure (46-49). Furthermore, a subset of children was found to have an abnormal balloon expulsion test (50). Feinberg and co-workers have shown there is a correlation between the number of fecal incontinence episodes and the volume of first urge, and high volume required to elicit recto-anal inhibitory reflex. They also found a significant correlation between presence of withholding behaviour and the maximum volume tolerated (82).

Colonic manometry allows the measurement of pressure/force from multiple regions within the colon in real time (83) and helps to discriminate between normal colonic physiology and colonic myopathies and neuropathies. A number of colonic motor patterns have been identified such as antegrade high amplitude propagating contractions, low amplitude propagating sequences, nonpropagating contractions and retrograde propagating pressure waves (84). In contrast to conventional manometry which used a limited number of sensors, arrival of high resolution manometry allows researchers and clinicians to study three dimensional pressure plots to study gastrointestinal pathophysiology more closely. An elegant study using this technique has clearly shown children with slow transit constipation having definitive abnormal motor patterns (post-bisacody induced high amplitude propagatory contractions) which can serve to diagnose colonic neuropathy (85).

#### Other investigations

Association between cow milk protein (CMP) allergy and constipation is still a debatable subject. Two research reports from Italy have found association between constipation and cow milk protein sensitivity (68, 69). A more recent study from Irastorza and colleagues found 51% patients with constipation responding to a CMP elimination diet, but no significant differences were noted between the group of responders and non-responders regarding atopic/allergic history and laboratory results (86). Therefore, testing for CMP allergy is not recommended. Importance of hypothyroidism as an etiological factor for constipation in children is overstated. Bennett and Heuckeroth studied 56 children with hypothyroidism, and noted that only one child had constipation as the presenting complaint (87). Other serological tests such as screening for celiac disease and hypercalcemia are also not recommended as they rarely uncover diseases without supportive evidence from the history and physical examination.

#### **Management**

Effective management of constipation requires a multifaceted approach. A stepwise management protocol is shown in **Figure 1**. The main steps include, life style modification, toilet training, use of laxatives and enemas, biofeedback therapy, nerve stimulation and surgical interventions. However, it is important to realise that the data in the paediatric literature to support evidence based use of treatment strategies are limited, especially regarding old laxatives such as lactulose and bisacodyl. Therefore, the management mostly depends on individual experiences and limited number of trials of new drugs.

#### Life style modifications

Constipation is known to be associated with psychological stress related to home, school and society (22, 23). These factors need to be addressed during the consultation. Children with psychological stress need to be identified and coping mechanisms need to be taught as part of the day-to-day lifestyle. Home and school related punishment is another factor that is known to predispose children to develop constipation which can easily be avoided (27). Although widely believed, a high fiber diet does not relieve constipation. Several trials including different types of fibers failed to show any clinically meaningful therapeutic benefit in children (88-90). Two systematic reviews

also illustrate limited clinical value of fiber in the management (91,92) In addition, increasing dietary fiber intake with extensive behavioral interventions does not reduce the requirement of laxatives (93). Similarly, increase in consumption of water has also shown not to increase stool frequency or soften stools (94).

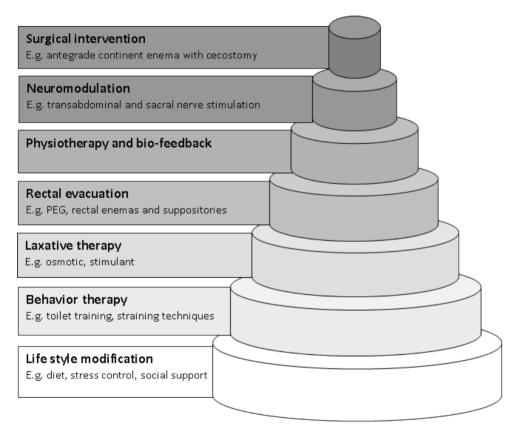


Figure 1: Stepwise management of constipation

#### Toilet training and behavioral therapy

Stool withholding plays a crucial role in developing constipation in young children. Aiming to prevent this phenomenon, children with constipation need to re-learn to properly pass stools in the toilet. As the first step, negative attitude regarding stools need to be eliminated. This facilitates and prepares the child mentally to pass stools in the toilet or potty. The child is encouraged to use the toilet regularly usually after each meal as the gastro-colic reflex facilitates generation of high amplitude propagatory contractions which help to evacuate stools. The proper seating method (up right posture) to bring the ano-rectum to the correct angle to facilitate the passage of stools also needs to be taught. Proper positioning of legs and relaxing them with the pelvic floor and anal sphincters also can be learned. Once the child masters these techniques, it is necessary to teach him/her proper straining methods to facilitate the passage of stools. This process needs to be a regular practice and could be encouraged with a reward system. (95). A Cochrane review has shown positive evidence indicating that adding behavioral therapy to conventional laxatives has benefits in treating children with constipation(96).It is obvious that behavioral therapy alone cannot cure constipation. However, given the importance of the part played by stool withholding behavior in childhood constipation (especially in infants and younger children), toilet training and behavioral modifications are inseparable parts in day to day clinical management.

#### Fecal disimpaction from rectum

It had been shown that 40-100% of children with constipation have a large rock hard fecal mass in the rectum (97). After evacuation of the fecal mass children are more likely to respond to maintenance therapy (98). Several studies have proved that oral administration of polyethylene glycol (PEG) is both successful and cost-effective in the majority of children with fecal impaction (99-101) Therefore, oral route is recommended as the initial step in rectal evacuation.

Rectal enemas or suppositories are recommended for children who do not respond to oral drugs. A study by Bekkali et al failed to show a significant difference between PEG and rectal enemas on evacuation of rectum loaded with feces (101). However, it is imperative to realize the invasive nature of rectal therapy specially when the child has pain, discomfort and may suffer from morbid fear of manipulations around the perianal region by medical professionals. In a minority of cases even sedation is recommended before rectal administration especially when the child is not co-operative. Rectal medications that can be used are phosphate, docusate sodium, mineral oil enemas and bisacodyl suppositories.

#### Maintenance Treatment

Once disimpaction is achieved, it is imperative that the clinician should concentrate on maintenance therapy. This facilitates passage of stools and prevents re-impaction. **Table 3** shows the details of the drugs that is currently used in the management of childhood constipation.

#### Lubricant laxatives

Although there are no placebo-controlled trials involving lubricant laxatives, two trials comparing mineral oil with lactulose have noted statistically significant better response rates with mineral oil. When comparing mineral oil with PEG the response rates were almost similar (102). Contrary to this Tolia et al found PEG is superior to mineral oil in relieving symptoms (103). However, due to the risk of life threatening lipoid pneumonia, mineral oil is not recommended for young infants and children with swallowing difficulties, especially those who are neurologically handicapped.

#### Osmotic laxatives

Osmotic laxatives are the group of choice used in the maintenance phase. As a group they exert an osmotic effect which helps to increase the water content in the colon and hence softening stools with minimal adverse effects. Lactulose and PEG are the two most commonly used drugs in this group.

Although widely used, lactulose has never been compared with a placebo in a controlled trial. Perkin et al compared lactulose with senna using a small number of children. They noted a greater clinical response to senna (improving defecation frequency) when compared to lactulose (104). A recent randomized controlled trial using lactulose and a mixture of fibers showed that both therapeutic modalities are comparable without major side effects (90).

Drug Class	Drug	Dosages
Osmotic laxatives	Lactulose	1-2 g/kg, once or twice/day
	PEG 3350	maintenance : 0.2-0.8 g/kg/day
	PEG 4000	
		fecal disimpaction: 1-1.5 g/kg /day(with a maximum of 6 consecutive days)
	Milk of magnesia (magnesium	2-5 y: 0.4-1.2 g/day,once or divided
	hydroxide)	6-11 y:1.2 -2.4 g/day,once or divided
		12-18 y: 2.4-4.8 g/day,once or divided
Fecal softeners	Mineral oil	1-18 y:1-3ml/kg/day, once or divided, max. 9
		ml/day
Stimulant laxatives	Bisacodyl	3-10 y: 5 mg /day
	Senna	> 10 y: 5-10 mg /day
	Sodium picosulfate	2-6 y: 2.5-5 mg once or twice/day
	6-12 y: 7.5-10 mg /day	6-12 y: 7.5-10 mg /day
		> 12 y: 15-20 mg /day
		1 month-4 y: 2.5-10 mg once/day
		4-18 y: 2.5-20 mg once/day
Rectal laxatives/enemas	Bisacodyl	2-10 y:5 mg once /day
		>10 y: 5-10 mg once /day cusate < 6 y: 60 ml
	Sodium docusate	
		> 6 y: 120 ml
	Sodium phosphate	1-18 y: 2.5 ml/kg, max. 133 ml/dose
	NaCl neonate < 1 kg: 5ml, > 1kg: 1	neonate < 1 kg: 5ml, > 1kg: 10 ml
		> 1 y: 6 ml/kg once or twice/day
	Mineral oil	2-11 y: 30-60 ml once/day
		> 11 y: 60-150 ml once/day

### Table 3: Dosages of most frequently used oral and rectal laxatives

A Cochrane reviews has concluded the superiority of PEG over both placebo and lactulose (105). However, it is important to realize that comparison of these studies is extremely difficult as the study designs, age groups and PEG preparations are different. PEG also shows an excellent safety profile. Therefore, in clinical practice, it is recommended to use both drugs as first line drugs in the maintenance phase.

#### Stimulant laxatives

Bisacodyl and senna stimulate peristaltic movements and enhance fecal evacuation. However, there are no good quality trials to evaluate stimulant laxatives in childhood constipation. Studies comparing senna with lactulose and mineral oil demonstrated that children using senna had a poorer response (104). Another study comparing the effect of adding senna, placebo or no medication for children with fecal incontinence receiving behavioral therapy found no significant difference in outcome (106). Despite the lack of well-designed trials these drugs are commonly used in day-to-day clinical practice, often in combination with osmotic laxatives. The National Institute for Clinical Excellence (NICE) guidelines of the United Kingdom recommend the addition of add stimulant laxatives to PEG when the response is noted to be suboptimal (107).

#### <u>New drugs</u>

#### Prucalopride

Prucalopride belongs to the class of dihydro-benzofuran-carboxamide derivatives. The drug has a clear gastroprokinetic activity and selective and high affinity for 5-HT4 receptor agonists that stimulate lower gastrointestinal motility. The efficacy of the drug was tested in an open label 8 weeks trial involving 37 children. According to the results the average number of spontaneous bowel movements normalized to a mean of 6.8 per week whereas the average number of faecal incontinence episodes decreased from 5.6 in the first week to 3.4 in week 8. Most of the children were using other laxatives as well during the trial (108). Although the results of this open label trial looks promising and safe, further studies are needed before recommending the use of prucalopride for constipation in children.

#### Lubiprostone

Lubiprostone is a locally acting CIC-2 chloride channel activator specific to the gastrointestinal tract. It promotes intestinal secretion of chloride ions and fluid and gastrointestinal motility. It has a good track record in treating adults with constipation. In an open label trial lubiprostone was shown to be safe and effective in improving spontaneous bowel movements, reducing episodes of faecal incontinence, and reducing many other symptoms of constipation in children and adolescents less than 17 years (109).

#### **Biofeedback and physiotherapy**

Ano-rectal function can be modified with the use of biofeedback. The purpose of biofeedback is to improve ano-rectal function and sensation (110). Several studies have shown efficacy of biofeedback in correcting defecation dynamics, but a well conducted large randomized controlled trial failed to find additional clinical benefits of biofeedback in children with constipation. (1, 48, 111, 112) However, despite this finding it is vital to assess this therapeutic modality in combination with pelvic floor physiotherapy and muscle training as pelvic floor dys-synergia is a recognized physiological abnormality, especially in older children.

#### **Neuromodulation**

Neuromodulation has been identified as a successful therapeutic modality for elimination disorders (113) although the working mechanism is far from clear. Two trials have shown that sacral neuromodulation is effective in treating adults and children with slow transit or normal transit constipation (114, 115). The adverse events (mainly pain) were minimal. A well-designed sham controlled trial with a larger patient sample and a long-term follow up is needed to confirm these encouraging data. Transabdominal electrical stimulation has also been studied as an option for treatment of resistant slow transit constipation. Using this technique, Clarke et al illustrated children with slow transit constipation generating significantly higher frequency of high amplitude and total propagatory sequences (116). In addition, the same research group studying 39 children with slow transit constipation has shown that transcutaneous electrical stimulation (TES) delivered by a physiotherapist (3 twenty minutes sessions a week) increases defecation frequency in 30%, reduced fecal incontinence in 75%,

abdominal pain in 59% and reduces the need for appendicostomy washouts in 43% (117). Yet again further studies are needed to confirm these findings and use of this in clinical practice.

#### Surgical interventions

Injection of botulinum toxin (single or multiple) to the internal anal sphincter is effective in some children with dyssynergic defecation. Adverse effects frequently encountered include transient anal and abdominal pain and occurrence of fecal incontinence yet again resolves spontaneously (118). Antegrade continent enema with appendicostomy or laparoscopic assisted percutaneous cecostomy has been used in treatment resistant constipation. The success rates are high and functional outcomes are excellent. It had been shown that the procedure improves bowel frequency and quality of life and reduces number of episodes of incontinence (119). PEG solution, and normal saline are effective, including a stimulant laxative, as cleansing agents. Commonly seen complications include granulation tissues around stoma, leakage, and minor infections. Major complications such as fistulae, peritonitis, and stenosis of the stoma are only seen in a minority (120). Other surgical procedures such as sigmoid resection, colorectal resection, subtotal colectomy, and proctocolectomy with ileo-anal anastomosis are only reserved for children with intractable constipation who failed to respond to all other therapeutic modalities (121).

#### Part 2: Functional fecal incontinence

#### Introduction and epidemiology

Fecal incontinence is defined as passing stools in inappropriate places including one's underwear by a child whose development age is over 4 years (122). Once organic causes are excluded, functional fecal incontinence is mainly due to two possible reasons. These are constipation associated fecal incontinence and functional non-retentive fecal incontinence. Since the former has already been discussed in detail in the first part of the chapter in this section, we will now concentrate on functional non-retentive fecal incontinence (FNRFI).

Like constipation, fecal incontinence (FI) is also a widespread problem. Epidemiological studies have shown the rates to range from 0.8 to 4.1% in the West and 2 to 7.8% in

Asia (122). We conducted an epidemiological survey and found that the majority of children (80%) with FI had constipation associated (retentive) FI and only 20% truly had FNRFI (123). FI is commoner among males and children from low socio-economic strata (123, 124) In addition, bullying, psychological stress, behavioral and upbringing problems, and poor social and school performances are commonly seen in children with FI (123, 125).

#### **Functional Non-retentive FI**

Rome III criteria to define FNRFI are given in Box 1. These children pass normal stools in the toilet with a normal defecation pattern. They do not show features of constipation such as posturing, pain or difficulty in passing stools either. However, they pass entire bowel motion into their underwear at least once a month. The patho-physiological mechanism for this disease is still an enigma to pediatric gastroenterologists. Several studies have clearly demonstrated the normal colonic transit times (both segmental and total) in children with FNRFI (126, 127). Similarly ano-rectal manometry and barostat studies found that all parameters (rectal compliance, sensory thresholds) are within the normal range (128). Although several psychological and behavioral abnormalities have been described in association with FNRFI, it is not clear whether these are causative factors or long term effects of fecal incontinence (129, 130). Clinical evaluation of children with defecation disorders have been previously discussed in this chapter.

Investigations should be directed to exclude constipation associated FI from FNRFI when the two entities are not apparent on clinical history and physical examination. When colonic transit times were compared, children with constipation associated FI were found to have significantly delayed total colonic transit, as against children with FNRFI (126).

Ano-rectal manometry is helpful in differentiating these clinical entities. Children with constipation associated FI show higher threshold for rectal sensation than FNRFI and there is no difference in maximum anal resting tone and abnormal defecation dynamics between the two groups (127). Children with retentive FI have significant thickening of the internal anal sphincter on anal endosonography and the thickness is well correlated to symptom score, fecal incontinence score, megarectum score and size of the megarectum on manometry (77). Such abnormalities have not been noted in FNRFI. In

addition to these studies MRI of the spine is also useful in some children to rule out organic causes of FI when there are subtle features of spinal bifida occulta on physical examination.

Management of children with FNRFI is challenging and often a long road, fraught with successes and failures. Education and strict toilet training following an individualized behavioral routine and positive reinforcement are the four main cornerstones in management (123). Conventional treatment modalities such as oral or rectal laxatives and biofeedback are not helpful in the management. Loperamide was found to be effective in a child with FNRFI in a case report and further studies are needed to assess its efficacy (131). They usually run a relapsing and remitting course and a long term follow up study has shown that at the age of 18 years 85% of them are symptom free and having normal bowel habits (132).

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Review Article: Fecal incontinence in children: Epidemiology, pathophysiology, clinical evaluation and management

# CHAPTER

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#### Summary

**Background** Fecal incontinence (FI) in children is a significant gastrointestinal problem, with great personal and social impacts. It is characterized by recurrent loss of fecal matter into the underwear. Both functional and organic causes contribute to its etiology with the former predominating.

**Aims** To review epidemiology, pathophysiology, clinical evaluation, and management of functional fecal incontinence in children.

**Method** A Pubmed search was conducted using search terms f(a)ecal incontinence, and encopresis. Articles on epidemiology, pathophysiology, clinical evaluation, investigation and management of functional FI in children were retrieved and assessed.

**Results** Community prevalence of this distressing problem ranges from 0.8% to 7.8% globally. Male: female ratio varies from 3:1 to 6:1. The diagnosis of FI is often based on established clinical criteria. The majority (82%) have constipation associated functional FI. Biopsychosocial factors play a crucial role in the pathogenesis. Limited physiological testing of anorectal function is recommended in the diagnostic procedures, particularly in children with atypical symptoms and possible organic disorders. Management of FI needs a multidisciplinary approach which includes establishment of an effective doctor-patient partnership, understanding the underlying mechanisms, pharmacotherapy, and behavioral treatment. Approximately 15% of children with functional nonretentive fecal incontinence (FNRFI) had the same symptoms at the age of 18 years.

**Conclusions** Although significant therapeutic advances have been made for retentive FI, treatment options for FNRFI are still limited. There are many unanswered questions about the management. Limited long term outcome data show that the majority outgrow FI. However, a substantial proportion of children progress to adulthood with FI.

#### **Introduction**

Fecal incontinence (FI) is a pediatric gastroenterological problem with profound personal and family impacts (1). The affected children present with a history of voluntary and/or involuntary passage of stools into the underwear (2). The characteristic aroma of faeces in these children predisposes them to stigmatization, rejection and bullying at school, which subsequently result in school avoidance and social withdrawal (3).

Fecal incontinence was originally described in children who were neurologically handicapped. Subsequently, it had been observed in a significant percentage of otherwise healthy children (4). Irrespective of the differences in underlying pathology (organic or functional), these children have significantly lower quality of life and most of the time suffer silently (5,6). Therefore, it is not surprising that they develop behavioral, emotional and upbringing problems, learning difficulties, depression, and also frequently subjected to maltreatment (7). This review appraises the definitions, epidemiology, pathophysiology, diagnostic evaluation, therapeutic advances and clinical care of children with functional FI.

#### <u>Methods</u>

The goal of this article is to review the current literature on functional faecal incontinence. A comprehensive search of the published literature was conducted in PubMed using the key words f(a)ecal incontinence and encopresis. They were combined with MeSH terms, epidemiology, pathophysiology, and management. The search was limited to articles in English as full manuscripts form on preschoolers, children, and adolescents. Children with organic fecal incontinence (postsurgical and neurological) were excluded. References within studies that were relevant to the topic were manually searched. Abstracts of articles identified were reviewed, and the full-text of articles related to functional constipation associated FI and functional nonretentive FI were retrieved and reviewed in depth. Relevant articles from adult literature were also included when there was a dearth of evidence from pediatric studies.

#### **Definitions**

FI denotes passage of stools into underwear in a child over the age of 4 years. This term replaces the previously used terms encopresis and faecal soiling. FI could be of functional or organic in origin. The common reasons for FI are listed in **Table 1**. The scope of this article is to understand functional FI and hence the organic causes for FI will not be discussed further.

#### Table 1 - Causes of fecal incontinence in children

#### Functional causes

Functional constipation associated fecal incontinence Functional nonretentive fecal incontinence

#### Organic causes

Repaired anorectal malformations Post surgical Hirschsprung disease Spinal dysraphysm Spinal cord trauma Spinal cord tumors Cerebral palsy Myopathies affecting the pelvic floor and external anal sphincter

Depending on underlying pathophysiological mechanisms, functional FI is broadly classified into retentive and nonretentive FI (NRFI), using the latest Rome III classification of pediatric functional gastrointestinal diseases (8). Children with retentive FI fulfil the criteria for constipation, and have a rectum loaded with faeces leading to overflow incontinence. In contrast, those with FNRFI have no evidence of fecal retention (8). The Rome III definition for functional constipation and functional nonretentive fecal incontinence are summarized in **Table 2.** These criteria appear to be useful in both clinical and research fields to diagnose functional FI in children.

## Table 2 – Rome III definition of functional constipation and functional nonretentive fecal incontinence

#### Functional constipation

Diagnostic criteria\* must include two or more of the following in a child with a developmental age of at least 4 years with insufficient criteria for diagnosis of IBS:

- Two or fewer defecations in the toilet per week
- At least one episode of fecal incontinence per week
- History of retentive posturing or excessive volitional stool retention
- History of painful or hard bowel movements
- Presence of a large fecal mass in the rectum
- History of large diameter stools which may obstruct the toilet

\* Criteria fulfilled at least once per week for at least 2months prior to diagnosis

#### Functional nonretentive fecal incontinence

Diagnostic criteria\* must include **all** of the following in a child with a developmental age at least 4 years:

- Defecation into places inappropriate to the social context at least once per month
- No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms
- No evidence of fecal retention
- \* Criteria fulfilled for at least 2 months prior to diagnosis

Adopted from reference (8)

#### **Epidemiology**

FI is estimated to affect 0.8% to 4.1% children in Western societies (7, 3). Recent studies from Asia have shown FI to be a significant problem in Iran, South Korea, and Sri Lanka, ranging from 2 to 7.8% (9-11). Recently a Sri Lankan study including children of 10-16 years, has reported a higher prevalence of FI in younger children at the age of 10 years (5.4%), while in children aged 16 years a much lower prevalence was reported (<1%) (11). A study from The Netherlands also noted that children of 5-6 years have higher odds of developing FI than children of 11-12 years, (7) indicating possible

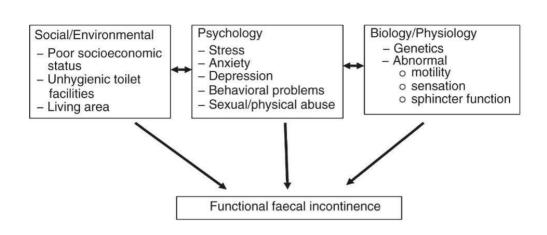
maturity of bodily functions. Several studies have noted that the majority of children with functional FI present for medical attention between 7 and 8 years of age (12-14).

Functional FI is either due to retentive (constipation associated) or functional nonretentive FI. Epidemiological studies in the past have not attempted to differentiate these two entities. It is important to differentiate between retentive and nonretentive FI as these two conditions differ in etiology and management. In a previous epidemiological survey we have shown that retentive FI (constipation associated FI) is 4.5 times commoner than FNRFI, underscoring the significance of constipation in the etiology of FI (11).

Hospital based studies have reported functional FI in 3%-4.4% of children attending general pediatric clinics (12,13) and 21% attending tertiary care pediatric gastroenterology units (14). Until recently, FI and constipation were regarded as psychiatric disorders and some of these children were managed at psychiatry clinics. In fact, 5.7% of the children attending a psychiatric unit were found to have FI (15). In many previous studies (both community and hospital based), prevalence of FI is significantly higher in boys, with a male to female ratio varying from 3:1 to 6:1 (7,11,13,14,16-18).

#### **Risk factors for functional FI**

Biopsychosocial factors play a pivotal role in the onset and continuation of symptoms in children with FI **(Figure 1)**. Two studies have identified low socioeconomic background as a risk factor for functional FI in children (7, 11). Inadequate toilet facilities and unclean or unhygienic toilets may be discouraging these children from using toilets, leading to stool withholding and retentive FI. Delay in seeking health care for defecation disorders such as constipation would also be a probable contributory factor for FI in such socioeconomic backgrounds. Other risk factors possibly contributing to retentive FI are living in urban areas (19) and war affected zones (20).



#### Figure 1Biopsychosocial model of Fecal incontinence in children

Hospitalization of the child for another illness and bullying at school have also been suggested as risk factors for FI (3, 11). Psychological and behavioral abnormalities like aggressive behavior, social withdrawal, anxiety, depression, disruptive behavior, and poor school and social performances were commonly noted in children with functional FI (21,22). Learning difficulties, upbringing problems and oppositional behavior, were also noted to be higher in these children (3,7). Analysis of child behavior checklist had shown that approximately one third of children with FNRFI had psychological disturbances and behavioral problems (23,24).

Psychological stress is known to alter the output of the brain-gut axis in functional gastrointestinal diseases such as irritable bowel syndrome (25,26). Similarly, altered functions of brain-gut axis, triggered by psychological abnormalities, probably result in changes of anorectal functions in these children leading to functional FI.

#### **Pathophysiology**

Chapter

#### Constipation associated (Retentive) fecal incontinence

FI is a significant problem associated with functional constipation. Both epidemiological and hospital studies have shown FI in 75-90% of children with constipation (14,27). A recent epidemiological survey has shown that 80% of children with FI are suffering from constipation (11). Incontinence of feces can occur both during the day and at night.

Nocturnal incontinence is considered to be an indicator of severe accumulation of feces in the rectum.

The primary reason for FI in constipation is fecal retention. Fecal retention is common in children with stool withholding behavior and painful defecation. When a child feels the urge to pass stools, knowing that this process would lead to pain, he or she hides, stands on tip toe and contracts external anal sphincter, pelvic floor muscles and gluteal muscles to suppress defecation. Fecal retention in the rectum leads to a cascade of physiological and pathological consequences. Voluntary suppression of desire to pass stools leads to prolongation of total and segmental colonic transit times, aggravating fecal retention and leads to stool accumulation in the entire colon (megacolon) (28). Furthermore, mechanical rectal distension is known to inhibit motor activities of right and left hemicolon and sigmoid colon by a reflex mechanism (29,30,31). These intestinal reflexes further suppress defecation. Water is absorbed from the retained stools through rectal mucosa leading to hard stools. In addition, abnormally low chloride secretion due to abnormalities in non-calcium mediated chloride channels in the rectal mucosa may further contribute to development of dry and hard fecal masses (32).

This process creates a vicious cycle of progressive accumulation of feces and hardening of the fecal mass. Rectum and sigmoid colon gradually dilate causing megarectum and megacolon which lead in diminished propulsive contractile forces of the rectal musculature (33,34). In addition, rectal sensitivity is blunted due to intrinsic rectal hyposensitivity (35) or due to constant accumulation of feces (36). Finally, semi-liquid feces seeps between the fecal mass and rectal wall, and escapes through the anal canal when the sphincter muscles are relaxed. The volume of stools that leaks out is small and most of the time just stains the underwear.

#### Functional nonretentive fecal incontinence (FNRFI)

Children with FNRFI pass stools into inappropriate places without evidence of stool retention. The majority of them have complete evacuation of bowel, not just staining of the underwear as in retentive incontinence. The pathophysiology of FNRFI is still far from clear.

In patients with FNRFI, total and segmental colonic transit times are within normal limits (24,37,38). Abnormalities in defecation dynamics shown upon anorectal manometry, include inability to relax the external anal sphincter during defecation. It is likely to be an acquired control mechanism in which after the loss of the first stool in the underwear, the child contracts the external anal sphincter to retain the rest of the stool (23,37). In contrast to retentive FI, the rectal compliance and sensitivity thresholds as measured by rectal barostat were normal in these children. In addition barostat studies have also not revealed abnormalities in anorectal function in children with FNRFI (39). It is unlikely that the altered physiological functions of the large bowel such as colonic transit, rectal compliance or sensitivity are responsible for FNRFI. Psychosocial factors and deranged defecation dynamics may also play a role in the pathogenesis. Further studies are needed to evaluate other possible pathophysiological mechanisms of FNRFI.

#### Evaluation of a child with FI

#### **Clinical History**

In the majority of patients, a thorough history and complete physical examination are sufficient to establish the diagnosis of FI and the underlying pathology (40). The initial consultation for FI may be embarrassing to the child as well as to the parents. Therefore, the pediatrician should listen attentively and put them at ease during consultation. It is very important to ask relevant questions, since child and family are unlikely to come up with details of symptoms. The physician should assure the child and the family that their complaints are being taken seriously. A good rapport with the family is helpful to extract all important information needed to ensure optimum care for the child.

Elaborate history on bowel habits is the key element in the history. Typically children with FNRFI pass complete bowel motion into the underwear. Passing small amounts of

stools which denotes overflow incontinence is usually present in severe constipation (8,13). The diurnal variation of incontinence is also important to asses as nocturnal fecal leakage is associated with severe constipation. In contrast, children with FNRFI have accidents during day time, usually in the afternoon (27). Reduced frequency of bowel motions, bulky stools, withholding posture, hard stools and pain or difficulty in passing stools are features suggestive of functional constipation (41). In contrast to this, if the child does pass stools regularly in the toilet and passes one bowel motion in the underwear at least once a week without pain or difficulty, is more in favor of FNRFI (42). Children with functional FI are often noted to have associated urinary symptoms. Daytime wetting has been reported in 29% and 34%children with FI. Furthermore, urinary tract infection is seen in 11% of these children (43).

It is important to identify problems such as social isolation, excessive dependency, behavioral and emotional upbringing problems, learning difficulties, anxiety, depression and possible child maltreatment which are often associated with FI (7,13,22,23). These often contribute to poor quality of life. Addressing these co-morbidities is important in successful management.

By definition FNRFI is only diagnosed in children whose developmental age over 4 years (8). Furthermore, FI is often seen in children with developmental abnormalities. Therefore, a detailed developmental assessment is crucial in the evaluation of a child with FI. This part is often neglected in the assessment of a child with FI and need to be specially emphasized. In addition previous medical and surgical history including corrective surgeries of the anorectum would be helpful to rule out possible organic causes of FI.

#### Physical examination

A thorough physical examination, including general, abdominal and neurological evaluation together with a digital rectal examination, is mandatory in assessing children with FI. Smell of feces and general demeanor of the child are also important to note. Interaction between parents and the child will give clues to a strained relationship between them. General examination should concentrate on growth parameters and subtle dysmorphic features (which may be associated with constipation) (44).

Presence of palpable fecal masses in the lower abdomen in a child with FI indicates long standing stool retention (45). Examination of spine and perianal area is important when assessing a child with FI. Perianal fissures are a feature of chronic constipation. Perianal examination could also reveal surgical scars which would be suggestive of an organic pathology such as repaired anorectal malformations.

Digital examination of the rectum is one of the crucial steps in evaluating a child with FI. Clinicians should explain the importance of rectal examination to both parents and the child before performing it, to alleviate any fears and anxieties. In addition, this examination should be performed by a clinician who is experienced enough to detect and interpret the physical findings (46). First, the examiner should assess the resting tone of the sphincter. Then a voluntary squeeze will provide information on neuromuscular integrity of perineal muscles and external anal sphincter (47). Large fecal masses are found in the rectum of over 90% of the children with constipation associated FI (48). Children with FNRFI show no retention of stools (49). The differences in clinical characteristics between retentive and nonretentive FI are summarized in **Table 3**.

#### Investigations

FI is a clinical diagnosis which is mainly based on history and examination. There are a few investigations which are useful in some patients in whom the underlying pathology for FI is not quite clear, as well as for those not responding to standard treatment. For these patients with FI, physiological testing can be very useful both for confirming the diagnosis and for assessing objective improvement after the intervention (50).

#### Abdominal X-ray

A plain abdominal radiograph has been a routine investigation to assess fecal loading and to identify megarectum and megacolon in children with constipation associated FI. Several scoring systems have been published to assess fecal loading (51,52,53). All these methods have wide inter- and intra-observer variability (27,54). Furthermore, there is no scientific evidence to suggest that abdominal X-ray enhances the diagnosis or changes the management in a meaningful way (55).

Clinical feature	Nontetentive fecal	Retentive fecal
	incontinence	incontinence
Abdominal pain	30-46%	41-66%
Large diameter stools	0-20%	61-80%
Posturing	10%	78%
Painful motions	20-30%	50-75%
Blood in stools	10%	56%
Night time fecal incontinence	12%	30%
Enuresis	40-45%	25-29%
Palpable abdominal mass	0%	35%
Palpable rectal mass	0%	31%

Table 3 - Clinical characteristics of retentive and nonretentive fecal incontinence

Adopted from references (11,37,92).

Berger and colleagues in a systematic review on the value of radiological tests in diagnosing constipation. It showed that abdominal radiograph has a wide range of sensitivity (60-80%) and specificity (43-99%) (56). Another study using spinal X-rays has reported occult spinal defects in significant percentages of children with constipation (47.7%) and FNRFI (77.8%) (57). However clinical significance of these findings is yet to be established. Based on these observations, plain abdominal radiograph cannot be recommended in evaluation of children with fecal incontinence, either to assess fecal loading or occult spinal defects.

#### Colonic transit studies

Radio-opaque markers are commonly used for assessment of colonic transit time (58,59). This simple non-invasive method provides information on colonic motor function and helps to localize the anatomical segments which contribute to delay in transit. In a Dutch study, 50% of children with constipation were found to have delayed total colonic transit of which 2/3 had a significant delay in the rectosigmoid (38) sit. Furthermore, colonic transit negatively correlated with severity of symptoms such as lower defecation frequency and frequency of FI. Follow up data on these children have shown that children with delayed transit responded poorly to standard clinical

management strategies (38). Delayed total or segmental colonic transit times have been observed in children with constipation associated FI in two other studies (60,61).

Other transit studies using radio nuclear markers have reported similar results. For example, Cook et al., studying 101 children with chronic constipation, reported retention of radioactivity in the proximal colon at 48 hours in 50%, indicating delayed transit. Further analysis of images has shown that most of these children have delayed transit in ascending and transverse colon (62).

Benninga and colleagues have compared colonic transit times of children with constipation associated FI and solitary encopresis (FNRFI). In this study 50% of children with constipation associated FI had significantly delayed total colonic transit time. In contrast, 88% of children with FNRFI had normal colonic transit times (37). It was also noted that all mean segmental transit times (right colon, left colon and rectosigmoid) were significantly delayed in children with retentive FI compared to FNRFI. (24,63).

A recent prospective study comparing children with constipation associated FI, FNRFI and recurrent abdominal pain observed longer total and segmental transit times in the former group (24). These findings provide a rationale for recommending measurement of colonic transit time to differentiate constipation associated FI from FNRFI, when the clinical assessment is inconclusive.

#### Anorectal manometry

Ano-rectal manometry with rectal sensory testing is the preferred method to diagnose functional weakness of external or internal anal sphincters. In addition it also able to detect abnormalities in rectal sensation and rectal compliance (29,47). Distension of a balloon in the rectum in a stepwise manner helps to determine the rectal sensory threshold, rectal compliance, and also to assess the level at which the child feels the urge and pain (maximum tolerable volume).

Manometric studies are useful to differentiate between constipation associated FI and FNRFI. It has been shown that children with constipation associated FI have higher

threshold for rectal sensation [25 ml (5-360)] (largest volume of balloon to provoke rectal sensation) than those with FNRFI [15 ml (20-90)] (FNRFI). There was no difference in maximum anal resting tone between two groups and the proportion of children with abnormal defecation dynamics was nearly comparable (41% vs. 54%, constipation associated FI vs. FNRFI) (37). Another study involving a small number of children with constipation associated FI and FNRFI confirmed this finding (64).

Using a rectal barostat, a significantly higher mean rectal compliance in children with constipation (22mm) was found than in FNRFI (12mm). Because of this higher compliance, children with constipation associated FI require a larger volume of stools to reach the intrarectal pressure that trigger the urge to defecate. (39). In addition, another comparative study between these two groups has shown that children with fecal incontinence (without constipation) had complete relaxation of internal sphincter before sensation of stools in the rectum (65). When children with both constipation and faecal incontinence were compared with children with constipation only, the duration of relaxation of the internal anal sphincter, time to maximum relaxation and time to recover adequate resting tone are significantly higher within the former group (63). This may probably contribute to the pathophysiology of incontinence which has not been described in children with FNRFI.

#### Anal endosonography

Ultrasonography provides reliable information on the structural integrity of anal sphincters and the presence of feces in the rectum. Endosonographic appearance of the normal anal canal has been well documented in children (66,67). Endosonography in children with functional constipation and associated FI has revealed significant thickening of the internal anal sphincter (68). Thickness of the internal anal sphincter notably correlates with the symptom score, soiling score, megarectum score on abdominal palpation and size of the megarectum on manometry (68). No such abnormalities have been described in children with FNRFI. This investigation is painless and minimally invasive, but gives critical information regarding anal sphincters and their function to differentiate both entities.

#### Other investigations

Other investigations including imaging of the spinal cord, contrast studies and colonic manometry have a limited value in evaluation of a child with functional fecal incontinence.

MRI of the spinal cord is only indicated in children with suspected organic diseases of the spinal cord on clinical history and physical examination (37). Bekkali and coworkers noted that almost all patients with defecation disorders who have had spinal abnormalities upon MRI had abnormalities such as deviation of the gluteal cleft detectable on physical examination (69).

Contrast studies such as contrast enemas; defecography and functional investigation such as saline infusion test have not been evaluated to differentiate constipation associated FI from FNRFI. Contrast studies are more valuable when FI is due to postsurgical causes such as corrected Hirschsprung disease and corrected anorectal malformation (70). These films are helpful to precisely locate the position of the vagina and rectum which is essential for decision making during the surgical repair.

Colonic manometry enables direct measurement of colonic motor activity. This test may suggest the presence of an underlying neuropathy or myopathy in children with intractable constipation (71). Van den Berg et al. showed children with severe constipation had generalized colonic hypomotility and absence of colonic response to bisacodyl (72). Colonic manometry data on FNRFI are not available.

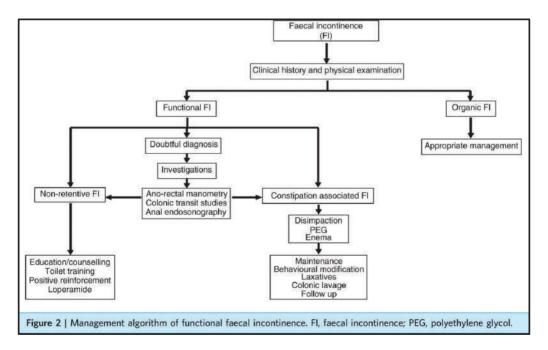
In summary, the two functional tests namely, colonic transit studies, anorectal manometry and endosonographic imaging of the anorectal sphincter complex are helpful in differentiating FNRFI from constipation associated FI and should be judicially used in situations where clinical distinction is not apparent. Other studies usually used in children with FI are only helpful to diagnose organic disorders and therefore only need to be considered when there is clinical evidence of organic diseases.

#### **Management**

#### Education and demystification

It is important that both parents and the child have a basic understanding of the pathophysiology of FI for effective management. The pediatrician should explain the underlying causes for FI using simple language and drawings if necessary. During consultation, adequate time and opportunity should be given to the parents and the child to express their views and concerns and to clear any doubts. This process alleviates anxiety, eliminates false beliefs, and helps to build a good therapeutic alliance between the physician and the family. This is very important to augment the compliance of future management steps (73-75).

There is very little research data on this important aspect in management of FI. A previous study conducted in children with functional defecation disorders (both retentive FI and FNRFI) has shown that 15% of affected children improve with a nonaccusatory approach to management including education, demystification and toilet training. This underscores the importance of nonaccusatory education and demystification in the management of functional FI (76). **Figure 2** summarizes the management of FI in children,



#### General measures

FI leads to constant or episodic leaking of stools. Liquid stools in particular contain digestive enzymes that irritate and erode the skin, compromise integrity of the skin and affect the role of the skin as a protective barrier. In addition, vigorous scrubbing, in attempts to remove soiling, strips away the protective horny layer of the epidermis. This impairs both its integrity and efficiency to function as a barrier. Epidermis of children is replaced fairly quickly (every 26 days) than that of adults (48 days). Nonetheless, recurrent exposure to faecal matter can produce a vicious cycle of skin damage and inflammation, together with, loss of skin integrity (77).

Prompt and gentle cleaning of the perianal area using moist wipes, rather than dry toilet paper after each episode of incontinence, is much more effective in preventing skin damage (73). A barrier cream such as zinc oxide is useful to prevent skin excoriation. Perianal fungal infections associated with FI are treated with topical antifungal agents (47,78).

#### **Dietary** interventions

The therapeutic value of increase of dietary fiber intake has shown variable success in children with FI. Fiber supplements increase stool bulk and reduce watery stools, and hence are expected to reduce frequency of FI. However, there are no published data to support this approach (47). So far, dietary fiber supplements have not shown a significant therapeutic efficacy in management of constipation associated FI (79-81). There are no clinical trials on altering dietary fiber in children with FNRFI. Therefore, modifying dietary fiber intake is still not recommended for children with functional FI.

#### <u>Pharmacotherapy</u>

Pharmacotherapy for FI includes antidiarrheal drugs that reduce fecal output and laxatives that control constipation. There is a scarcity of well-designed randomized controlled trials on treatment of functional FI in children and there is little evidence to guide its management.

Loperamide is an opiate receptor agonist. It reduces diarrhoea by multiple mechanisms related to transport of water and electrolytes and inhibiting peristaltic movements (by

inhibiting the release of acetylcholine and prostaglandin during bowel distension) (82,83). Loperamide also increases the internal anal sphincter tone (84). It has an excellent safety profile. Although it had been used in adults with FI (84), experience in childhood fecal incontinence is limited. One case report has shown a significant clinical improvement of an adolescent with FNRFI following loperamide therapy (85).

The main aim of pharmacotherapy for constipation associated FI is to empty the loaded rectum and to maintain soft stools during follow up. Polyethylene glycol is shown to be effective in both disimpaction and preventing re-accumulation of stools. Children treated with polyethylene glycol had less episodes of FI, (86--88) lower frequency of re-impaction (89) and incurred significantly lower healthcare costs (87). A systematic review has shown that polyethylene glycol is more effective in the treatment of constipation than other osmotic laxatives (90).

However, other drugs such as senna and lactulose are also frequently used during the maintenance phase (91). It is difficult to recommend one drug over another in management of constipation and associated FI, due to the lack of evidence on effectiveness of laxatives. However, judicious use of osmotic and stimulant laxatives, along or in combination is needed to prevent accumulation of feces in the lower gut that predispose children to constipation associated FI.

Unlike retentive FI, non-retentive FI responds poorly to laxatives. In a prospective study, children treated with biofeedback with added oral laxatives had higher frequency of FI than the children with biofeedback alone (92). The softened stools in children with FNRFI may have aggravated the symptoms.

#### Biofeedback therapy

Biofeedback training involves habit training based on reinforcement and uses instrument-assisted exercises designed to improve physiological control of sphincters. It enhances rectal sensations, strengthens the external anal sphincter, increases muscle coordination during contraction and relaxation, and ultimately helps to achieve effective defecation as well as continence (93). Biofeedback therapy improves defecation dynamics in children with constipation associated FI (94), but has failed to achieve a significant improvement in the clinical outcome (95). Similarly, children with FNRFI trained in biofeedback have not shown a better outcome than those on conventional therapy in the long term follow up, even after improvement of defecation dynamics (23). Therefore, on the currently available data, biofeedback has doubtful therapeutic value in the treatment of children withfunctional FI.

#### Behavioral therapy

Behavioral therapy (toilet training in combination with reward system and diminishing toilet phobia) in combination with cognitive therapy (psychotherapy, and family therapy or educational support) aims to lower the distress, restore normal bowel habits by positive reinforcement, and re-establish self-respect. The process also encourages of both the child and the parents to continue treatment (42). Behavioral therapy has shown to be effective in reducing episodes of FI, when combined with intense medical management (96). In a systematic review which analyze 18 trials conducted in children with functional retentive (constipation associated) FI), the combined treatment of behavioral interventions and laxatives improve FI more than laxatives alone (97).

Behavioral therapy is the corner stone in the management of FNRFI since there is no convincing evidence on effectiveness of medical therapies. Structured toilet routine, maintaining a bowel diary and strict adherence to individualized behavioral program are the only management options that have been found to be successful in FNRFI, so far (18).

Behavioral therapy is a noninvasive treatment modality and it also provides a valuable insight to parents and children regarding the disease. Therefore, adding behavioral therapy to other conventional management seems a rational approach for the management of functional FI in children.

#### Surgical interventions

So far, surgical interventions are only reserved for intractable constipation associated FI. Antegrade continent enema (ACE) has shown to be useful in constipation associated FI in children. A study assessing 32 patients who had ACE treatment for intractable slow transit constipation has shown reduction in number of episodes of FI and abdominal

pain and improvement in mood. Disadvantages of this procedure is that some patients experience complications related to stoma such as stenosis, mucus leak, fecal leak, and catheter related pain (98). Improvement in the surgical techniques such as laparoscopic placement of the tube has made the procedure more simple and acceptable to patients.

#### **Prognosis**

Prognosis of childhood functional FI is generally variable. One study showed that approximately 50% of affected children develop at least one relapse with in the first five years after initial remission (99). In this study the authors also found that children with retentive FI had less recovery rates. Furthermore, at the age of 16 years, one third of children were still symptomatic, indicating the possibility of progression to adulthood (99). However, a recent systematic review found that the majority of children with retentive FI recover within 6-12 months of treatment and the recovery has no relationship to the age of onset, family history and severity of the disease (100).

Only one study has described long term follow up in children with FNRFI. In this study 106 children with FNRFI were followed up for 10 years. The clinical success was defined as having less than one episode of FI in 2 weeks. The authors noted that after 2 years of medical and behavioral therapy in a tertiary care center, only 29% of children had been successfully treated. When treatment success was analyzed according to biological age, at the age of 12 years 49% of children were still suffering from FI. At the age of 18 years, 85% of patients with FNRFI were free of symptoms. This study clearly shows that at 18 years 15% of adolescents with FNRFI progress into adulthood with FI (18). Therefore, contrary to the common belief that children with functional FI grow out of their symptoms, a significant subset of them suffer from FI as adults irrespective of the etiology of functional FI.

#### **Conclusions and future research**

Functional FI remains a chronic devastating gastroenterological problem in children, with a worldwide prevalence varying from 0.8 to 7.8%. The majority of them are suffering from chronic retentive FI while the other subset has NRFI. Although pathophysiological mechanisms of retentive FI are fairly elucidated, mechanisms of FNRFI need further study. The diagnosis is usually based on established clinical criteria

and judicial use of physiological testing is only indicated in children unresponsive to standard management. Although significant therapeutic advances have been made for retentive FI, further studies especially clinical trials using novel therapeutic agents are urgently needed. Treatment options for NRFI are still limited and there are many unanswered questions about the management. Limited long term outcome data show that the majority outgrow FI with advancing age. However a substantial proportion of children progress to adulthood with FI.

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## Constipation

Constipation in children: an epidemiological study in Sri Lanka using Rome III criteria

## CHAPTER

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3

#### <u>Abstract</u>

Constipation is a common paediatric problem, but little is known of its prevalence in Asia. A cross sectional survey was conducted in randomly selected children, aged 10-16 years, in 5 randomly selected schools, in 3 different provinces in Sri Lanka. Two schools were from Eastern province affected by the separatist war. A previously validated, selfadministered questionnaire was filled under the guidance of research assistants. Constipation was defined using Rome III criteria.

Out of 2694 children included in the analysis, 416 (15.4%) had constipation. Symptoms independently associated with constipation were straining (71.6% vs. 28.4%), bleeding per rectum (14.2% vs. 2.2%) and abdominal pain (55% vs. 35.2%). Prevalence of constipation was higher in those with a family history of constipation (49% vs. 14.8%), living in a war affected area (18.1% vs. 13.7%), and studying in an urban school (16.7% vs. 13.3%).

In conclusion, chronic constipation is a significant problem affecting 15% of Sri Lankan school children and adolescents. It is more common in children from urban schools and living in war affected areas.



#### **Introduction**

Childhood constipation is a frequently overlooked global health problem, growing up to a proportion of a public health issue in many parts of the world. Its impact on quality of life of affected children and their parents is often underappreciated (1). Constipation was found to be the commonest cause for abdominal pain in children presenting to acute care clinics and emergency department (2). Up to 30% of affected children continued to have symptoms beyond puberty (3). The prevalence of childhood constipation varies from 0.7% to 29.6% (4).

Prevalence of constipation is likely to vary depending on dietary and genetic factors. Most of the epidemiological studies on constipation are from western world. Unlike most western countries, the majority of Asian countries have rice based staple diet with relatively high fiber content. Up to date there is a significant lack of epidemiological data on constipation from this region.

The present research assessed the epidemiology of constipation in Sri Lankan children and adolescents aged 10-16 years. To our knowledge this is the first epidemiological survey on constipation using Rome III criteria.

#### Methods

An island-wide cross-sectional survey was conducted in 5 randomly selected state schools (three urban and two rural) in three provinces of Sri Lanka (two schools were from the Eastern province affected by the separatist war). Details regarding the bowel habits and defecation behaviors were obtained with demographic and family characteristics and other symptoms using a self-administered questionnaire, developed from the Questionnaire on Pediatric Gastrointestinal Symptoms (5).

Data was collected from January 2007 to June 2007, after obtaining consent from school administration and parents. Questionnaire was distributed in an examination setting, to ensure confidentiality and privacy. The questions were in native language (Sinhalese) and were simple and easy to understand. Research assistants were present while filling the questionnaire and explanations were given.

Constipation was defined using Rome III criteria. (6) Since this is an epidemiological study, we did not use the diagnostic criterion of palpable fecal mass in rectum.

Data were analyzed using EpiInfo [EpiInfo 6, version 6.04 (1996)]. *P*< 0.05 was taken as significant. Multiple logistic regression analysis was performed on variables that were found to have significant association.

This study protocol was approved by the Ethical Review Committee of the Sri Lanka College of Pediatricians.

#### <u>Results</u>

A total of 2770 questionnaires were distributed and 2694 (97.3%) were included in the analysis [males 1368 (50.8%), mean age 13.2years, SD 1.7years]. In 76 questionnaires excluded from the study, information given was not sufficient either to diagnose or exclude constipation.

According to Rome III criteria, 416 (15.4%) had constipation [230 (55.3%) males]. Multiple-logistic regression analysis failed to show an independent association between male sex and constipation [adjusted OR 1.2, 95% CI 0.9-1.5, p=0.15].

There was a significant negative correlation between prevalence of constipation and age (r= -0.86, 95% CI -0.87 to -0.85, p<0.0001) (males r= -0.79, 95% CI -0.82 to -0.77, p<0.0001, females r= -0.85, 95% CI -0.87 to -0.83, p<0.0001) (Figure 1).

**Table 1** demonstrates the association between demographic and family factors and constipation. Following multiple logistic regression analysis, living in a war affected area (adjusted OR 1.5, 95% CI 1.1-1.9, p=0.009), studying in an urban school (adjusted OR 1.4, 95% CI 1.1-1.9, p<0.02) and having a family history of constipation (adjusted OR 6.0, 95% CI 3.4-10.8, p<0.0001) remained independently associated with constipation.



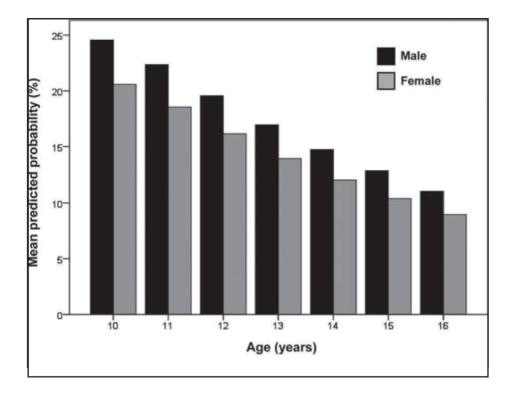


Figure 1 Mean predicted probability of constipation according to age and sex.

## Table 1 Distribution of subjects according to sociodemographic characteristics and prevalence of constipation in each category

Variable		Controls	Children with	Prevalence of
		(N=2278)	constipation	constipation in
		n (%)	(N=416)	each category
			n (%)	(%)
Family size	Only child	183 (8)	31 (7.5)	14.5
	2-3 children	1660 (72.9)	295 (70.9)	15.1
	≥children	435 (19.1)	90 (21.6)	17.1
Birth order*	Eldest	867 (41.4)	151 (39.2)	14.8
	Youngest	655 (31.3)	100 (26)	13.2
	Other	573 (27.3)	134 (34.8)	19
Mother	Employed	676 (29.7)	100 (24)	12.9
	Housewife	1602 (70.3)	316 (76)	16.5
Maternal	Leading profession (eg:	31 (1.4)	9 (2.2)	22.5
employment	doctor)			
	Lesser profession (eg:	148 (6.5)	23 (5.5)	13.4
	teacher)			
	Skilled non-manual (eg: Clerk)	76 (3.3)	12 (2.9)	13.6
	Skilled manual	80 (3.5)	20 (4.8)	20
	Unskilled/unemployed	1943 (85.3)	352 (84.6)	15.3
Father's	Leading profession	296 (13)	51 (12)	14.7
employment				
	Lesser profession	179 (7.9)	23 (5.5)	11.4
	Skilled non-manual	289 (12.7)	56 (13.5)	16.2
	Skilled manual	821 (36)	143 (34.4)	14.8
	Unskilled/unemployed	693 (30.4)	143 (34.4)	17.1
Location of the	Urban	1414 (62.1)	283 (68)†	16.7
school				
	Rural	864 (37.9)	133 (32)	13.3
Home province	Eastern province (war	883 (38.8)	195 (46.9)‡	18.1
	affected)			
	Western province	715 (31.4)	123 (29.5)	14.7
	Southern province	680 (29.8)	98 (23.6)	12.6
Family history of	Positive	25 (1.1)	24 (5.8)§	49
constipation				
	Negative	2253 (98.9)	392 (94.2)	14.8

\*Families with more than one child

†OR 1.3 (95% CI 1.03 to 1.63), p= 0.023

‡OR 1.39 (95% CI 1.12 to 1.73) p= 0.0022 versus the other provinces

§ OR 5.52 (95% CI 3.01 to 10.11) p< 0.00001



Bowel habits and symptoms associated with constipation are presented in **Table 2 and Table 3**. Following multiple logistic regression analysis, straining during defecation (adjusted OR 5.7, 95% CI 4.4-7.9, p<0.0001), blood in stools (adjusted OR 3.98 95% CI 2.4-6.6, p<0.0001) and abdominal pain (adjusted OR 1.8, 95% CI 1.4-0.2.3, p<0.0001) were independently associated with constipation.

		No	Percentage
Defecation frequency	<3 per week	212	(51%)
	3-6 per week	53	(12.7%)
	Once daily	104	(25%)
	>one per day	47	(11.3%)
Stool consistency	Hard	111	(26.7%)
	Normal	227	(54.6%)
	Soft	21	(5%)
	Changing consistency	57	(13.7%)
Large diameter stools	Yes	277	(66.6%)
	No	139	(33.4%)
With-holding posture	Yes	213	(51.2%)
	No	203	(48.8%)
Painful bowel motions	Yes	299	(71.9%)
	No	117	(28.1%)
Fecal incontinence	None	343	(84.1%)
	< once per week	33	(8.1%)
	≥ one per week	32	(7.8%)
	No response	8	-

#### Table 2 – Bowel habits of children with constipation

#### Table 3 – Symptoms associated with constipation

	Constipation	controls	Constipation vs. controls	
	No (%)	No (%)	OR (95% CI)	p value*
Abdominal pain	229 (55%)	802 (35.2%)	2.25 (1.81-2.8)	<0.0001
Nausea	44 (10.6%)	120 (5.3%)	2.13 (1.46-3.1)	<0.0001
Vomiting	44 (10.6%)	86 (3.8%)	3.01 (2.03-4.48)	<0.0001
Weight loss	67 (16.1%)	213 (9.4%)	1.86 (1.37-2.53)	<0.0001
Loss of appetite	81 (19.5%)	264 (11.6%)	1.84 (1.39-2.45)	0.0001
Straining	298 (71.6%)	646 (28.4%)	6.38 (5.03-8.1)	<0.0001
Blood in stools	59 (14.2%)	50 (2.2%)	7.36 (4.88-11.11)	<0.0001

\* X<sup>2</sup>test

#### **Discussion**

We have found constipation in 15.4% of Sri Lankan school children and adolescents. To the best of our knowledge, this is the first epidemiological study to use Rome III criteria to assess its prevalence in a developing country.

Previous studies have reported wide variation in prevalence of constipation around the world (7-12). This was mainly due to geographical factors, differences in definitions used and age distribution of study populations. This study included school children of 10-16 years and epidemiology of constipation in this age group has not been studied in depth previously. Most of the previous epidemiological studies on constipation included younger children and had used diverse definitions and therefore, it was difficult to make comparisons.

In our study, the highest prevalence of constipation (24.0%) was reported in children aged of 10 years and the lowest (5.0%) at the age of 16 years. We found a significant negative correlation between age and the prevalence of constipation which has not been reported previously. After multivariate analysis, there was no significant gender difference in prevalence of constipation, in agreement with several other studies (7,12,13). When considering the age specific prevalence, in children less than 12 years,



constipation was higher in females and after 12 years this reversed (Figure 1). This is in agreement with previous studies from Asia which have shown high prevalence of constipation in girls of 3-12 years (9,14).

Furthermore, constipation was significantly higher in those with a history of constipation among the first degree relatives. Likewise, Roma *et al.* also found a positive family history in 62.5% children with constipation (15). The family size, birth order, maternal employment, and social class had no such association with constipation.

Percentage of our subjects with stool frequency less than 3 per week (51%) was similar to that reported by van den Berg *et al.* (57.0%) (16), while painful defecation and withholding behavior were seen more frequently than in previously studies (10).Contrarily to this, hard stool was present in a lower percentage of children than reported earlier(10). Straining during defecation and presence of blood in stools were similar to previously reported (8). Similar to our study, faecal incontinence was reported in 19.0% of Brazilian school children with constipation (8).

The symptoms independently associated with constipation were straining, presence of blood in stools and abdominal pain. Most of these symptoms are non-specific. However, it is important that clinicians should not overlook these symptoms. Loening-Baucke *et al.* recently reported constipation as the commonest cause for abdominal pain in children cared at emergency department and acute clinics (2).Furthermore, using Rome III criteria, a recent Sri Lankan study reported constipation in 12.7% of patients with recurrent abdominal pain (17).

Constipation was significantly high in war affected areas. Terrorist activities (e.g. bomb blast, abductions) and the war to liberate Eastern province were going on during the time of the study. Constipation is reported to be associated with physical or emotional trauma (18). The constant anxiety, stress and feeling of insecurity related to war and terrorism, probably have affected the bowel habits of children in war torn areas. The stress related modulation of brain-gut axis is known to affect gut motility and bowel habits (19) and probably play a role in the etiology of constipation. Furthermore, similar to previous studies (20), prevalence of constipation was higher in children living in urban areas. High consumption of junk foods with low fiber content (15) and living more sedentary life (21) might have contributed to this.

In conclusion, constipation is seen in 15.0% of Sri Lankan school children and adolescents aged 10-16 years. The prevalence rate is higher in children living in urban areas and war affected regions of the country. This study proves that constipation is not anymore a disease confined to western countries and has taken a turn to become more of a global health problem.



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Association between Constipation and Stressful Life Events in a Cohort of Sri Lankan Children and Adolescents

# CHAPTER

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#### Summary

Emotional stress is associated with some functional gastrointestinal diseases, but its role in etiology of functional constipation is unclear. This island-wide, questionnairebased, cross-sectional survey was conducted to assess the association between constipation and emotional stress, in 10 - 16-year-olds. Constipation was defined using Rome III criteria. Out of 2699 children included in the analysis, 416 (15.4%) had constipation. Constipation was higher in those exposed to stressful events (odds ratio 2.52, p<0.0001). Separation from the best friend, failure in an examination, severe illness of a family member, loss of job by a parent, frequent punishment by parents and living in an area affected by separatist war remained independently associated with constipation (p<0.05). In conclusion, constipation was significantly higher in children exposed to stressful life events. Modulation of gut motility through brain-gut axis probably alters colonic transit and ano-rectal functions, causing constipation.

#### **Introduction**

Childhood constipation is a common cosmopolitan problem which accounts for 3% of visits to general pediatric clinics (1) and 25% visits to gastroenterology clinics in the USA (2). Its prevalence varies from 0.7% in Italy to 29.6% in Hong Kong (3). The exact etiology of this common problem is obscured and the majority suffer from functional constipation. The definite cause of constipation is unclear in those with functional constipation and psychological abnormalities are considered as contributory factors. Previous studies reported significant physical or psychological trauma and history of personal health problems in children with constipation (4), while others have demonstrated clinical range of scores in the Child Behavior Check List in one-third of children with functional constipation (5). However, other studies failed to demonstrate such association (6).

Psychological stress affects gastrointestinal function through the brain–gut axis. It is known to be associated with other functional gastrointestinal diseases such as functional abdominal pain and irritable bowel syndrome in children (7) and adults (8). Up to now there are no systematic studies to assess the association between day-to-day stresses and childhood constipation. This study assessed the impact of common family-and school-related stressful events and war on constipation.

#### Materials and Methods

This was a cross-sectional survey conducted in Sri Lanka. Three provinces of the country were randomly selected to represent the island. Two rural and three urban schools were also randomly selected from these provinces and two of these schools were from government controlled areas in the Eastern province affected by the separatist war. The school administration and the parents were informed before distribution of questionnaires and their consent was obtained.

A previously validated, self-administered, structured questionnaire was administered to children. We used the setting of a typical examination in the school to make certain that children would not see questionnaires of the others. The questionnaire was in the native language (Sinhalese) and questions were simple and easy to understand. Research assistants were present with students throughout while they filled the questionnaire and explanations were given if and when necessary. The data collection started in January 2007 and was completed within 6 months.

Details regarding the demographic characteristics, bowel habits and associated symptoms were obtained with details of exposure to stressful life events during the previous 3 months. Stool consistency was determined using the Bristol stool chart (9). Constipation was defined using Rome III criteria [10]. Since this is an epidemiological study, we did not use the diagnostic criterion of palpable fecal mass in rectum or abdomen to diagnose constipation in our patients.

Rome III criteria used for diagnosing constipation in this study

Two or more of the following criteria fulfilled in a child of at least 4 years, once per week for at least 2 months:

- 1. Two or fewer defecations per week.
- 2. At least one episode of fecal incontinence per week.
- 3. Retentive posturing or excessive volitional stool retention.
- 4. History of large diameter stools that may obstruct the toilet.
- 5. Painful or hard bowel motions.

Data were analyzed using Chi-square and Fisher's exact test using EpiInfo (EpiInfo 6, version 6.04 (1996) Centers of Disease Control and Prevention, Atlanta, Georgia, USA and World Health Organization, Geneva, Switzerland). A p-value<0.05 was taken as significant. Multiple logistic regression analysis was performed on variables that were found to have significant associations. This study protocol was approved by the Ethical Review Committee of the Sri Lanka College of Pediatricians.

#### Results

A total of 2770 questionnaires were distributed and 2699 (97.4%) were included in the analysis [1368 (50.6%) males, mean age (SD) 13.17 (1.72) years]. According to Rome III criteria, 416 (15.4%) had constipation and they were compared with 2283 children without constipation (controls). **Table 1** compares the demographic data of children with constipation and controls.

Table 1: Demographic and family characteristics of children with constipation compared with controls

Variable	Constipation (n=416)	Controls	
		(n=2283)	
Age distribution			
Mean age	12.74 years	13.2 years	
SD	1.72 years	1.7 years	
Sex distribution			
Male	230 (55.3%)	1138 (49.8%)	
Female	186 (44.7%)	1145 (50.2%)	
Family size			
Only child	31 (7.5%)	183 (8 % )	
2–3 children	295 (70.9%)	1665 (72.9%)	
4 children	90 (21.6%)	435 (19.1%)	
Birth order <sup>a</sup>			
Eldest	151 (39.2%)	867 (41.3%)	
Youngest	100 (26%)	655 (31.2%)	
Other	134 (34.8%)	578 (27.5%)	
Father's social class			
Leading profession	51 (12.2%)	297 (12.7%)	
Lesser Profession	23 (5.5%)	160 (7.8%)	
Skilled non manual	56 (13.5%)	290 (12.7%)	
Skilled manual	143 (34.4%)	822 (36%)	
Unskilled	143 (34.4%)	694 (30.4%)	

\*Families with more than one child.

#### Stressful life events and constipation

Patients with constipation have been exposed to significantly more stressful life events (mean 2.44, SD 2.28) than controls (mean 1.42, SD 1.69) (p<0.0001, unpaired t-test). **Table 2** demonstrates the association between different stressful life events and constipation. After multiple logistic regression analysis, separation from the best friend [adjusted odds ratio (OR) 1.35, p=0.017], failure in an examination (adjusted OR 1.43, p=0.03), severe illness in a family member (adjusted OR 1.64, p=0.001), loss of job by a parent (adjusted OR 1.84, p=0.016) frequent punishment by parents (adjusted OR 1.77, p=0.003) and living in a war affected area (adjusted OR 1.48, p=0.001) remained independently associated with constipation.

**Figure 1** shows the relationship between defecation frequency and stressful life events. Mean bowel frequency has a negative correlation with the number of stressful life events exposed both in constipated children (r=0.713, CI=0.92 to 0.198, p=0.014) and controls (r=0.932, CI= 0.752 to 0.227, p=0.008).

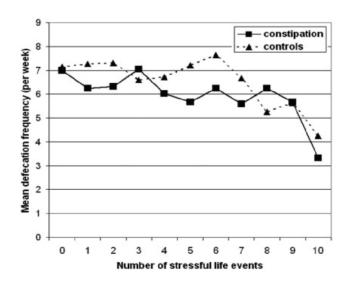


FIG. 1. Correlation between defecation frequency and number of stressful life events.

Association between exposure to stressful life events and bowel habits in patients with constipation is demonstrated in **Table 3**. None of them significantly differ in patients exposed to emotional stress (p>0.05).

(m/416)         (m/416)         (m/416)           cent stressful life events         342 (82.2)         1           stressful events         342 (82.2)         1           ool         59 (14.2)         74 (17.8)           on         59 (14.2)         7           on         53 (12.7)         1           on         53 (12.7)         1           on         53 (12.7)         1           on school         133 (32)         1           on school         133 (32)         1           on school         133 (32)         1           m best friend         133 (32)         1           entities         133 (32)         1         1           in a close family member         5 (19.7)         1         1           in a close family member         5 (19.7)         1         1           a parent         30 (7.2)         3         1         1	•	Constipation	Controls		
N (%)     N (%)       342 (82.2)     1478 (64.7)       74 (17.8)     805 (35.3)       59 (14.2)     219 (9.5)       4 (1)     7 (0.3)       53 (12.7)     118 (5.2)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       133 (32)     519 (22.7)       159 (38.2)     783 (34.3)       82 (19.7)     244 (10.7)       54 (13)     128 (5.6)       30 (7.2)     62 (12.3)       30 (7.2)     62 (2.7)       8 (1.9)     117 (0.5)       57 (13.7)     162 (7.1)       20 (4.8)     51 (2.2)       65 (15.6)     140 (6.1)       31 (7.5)     84 (3.7)       195 (46.8)     883 (38.7)	Stresstul event	(n1/4416)	(n%2283)	OR	a
342 (82.2)       1478 (64.7)         74 (17.8)       805 (35.3)         59 (14.2)       219 (9.5)         4 (1)       7 (0.3)         53 (12.7)       118 (5.2)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         82 (19.7)       244 (10.7)         54 (13)       128 (5.6)         30 (7.2)       58 (13.9)         30 (7.2)       62 (2.7)         8 (1.9)       21 (0.9)         8 (1.9)       1179 (7.8)         30 (7.2)       62 (2.7)         8 (1.9)       21 (0.9)         8 (1.9)       1140 (6.1)         31 (7.5)       84 (3.7)         ess       74 (17.8)       203 (8.9)         195 (46.8)       883 (38.7)		N (%)	N (%)	(95% CI)	
342 (82.2)       1478 (64.7)         74 (17.8)       805 (35.3)         59 (14.2)       219 (9.5)         4 (1)       7 (0.3)         53 (12.7)       118 (5.2)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         159 (38.2)       783 (34.3)         82 (19.7)       244 (10.7)         54 (13)       128 (5.6)         30 (7.2)       581 (12.3)         58 (13.9)       179 (7.8)         30 (7.2)       62 (2.7)         8 (1.9)       117 (0.5)         57 (13.7)       128 (5.6)         110 (6.1)       21 (0.9)         8 (1.9)       21 (0.9)         8 (1.9)       1140 (6.1)         31 (7.5)       84 (3.7)         195 (46.8)       883 (38.7)	Exposure to recent stressful life events				
74 (17.8)       805 (35.3)         59 (14.2)       219 (9.5)         4 (1)       7 (0.3)         4 (1)       7 (0.3)         53 (12.7)       118 (5.2)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         159 (38.2)       783 (34.3)         82 (19.7)       244 (10.7)         54 (13)       128 (5.6)         rmember       106 (25.5)       281 (12.3)         sr       58 (13.9)       179 (7.8)         sr       8 (1.9)       21 (0.9)         sr       8 (1.9)       21 (0.9)         sr       8 (1.9)       111 (0.5)         sr       51 (2.2)       31 (7.5)         arents       65 (15.6)       140 (6.1)         31 (7.5)       84 (3.7)       0ther illness         74 (17.8)       203 (8.9)       883 (38.7)	Yes	342 (82.2)	1478 (64.7)	2.52 (1.92–3.31)	<0.00001
59 (14.2)       219 (9.5)         4 (1)       7 (0.3)         53 (12.7)       118 (5.2)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       519 (22.7)         133 (32)       53 (12.7)         159 (38.2)       783 (34.3)         82 (19.7)       54 (10.7)         54 (13)       128 (5.6)         rmember       106 (25.5)       281 (12.3)         r       58 (13.9)       179 (7.8)         sr       30 (7.2)       62 (2.7)         15       8 (1.9)       21 (0.9)         8 (1.9)       117 (0.5)         57 (13.7)       162 (7.1)         20 (4.8)       51 (2.2)         arents       65 (15.6)       140 (6.1)         31 (7.5)       84 (3.7)         other illness       74 (17.8)       203 (8.9)	No	74 (17.8)	805 (35.3)		
59 (14.2)59 (14.2)219 (9.5)ol $4(1)$ $7(0.3)$ n school $53(12.7)$ $118(5.2)$ niend $133(32)$ $519(22.7)$ exam $159(38.2)$ $53(4.3)$ exam $159(38.2)$ $783(34.3)$ exam $159(38.2)$ $783(4.3)$ exam $159(38.2)$ $783(4.3)$ eramily $159(38.2)$ $783(4.3)$ family- $54(13)$ $128(5.6)$ rember $82(19.7)$ $244(10.7)$ rember $58(13.9)$ $179(7.8)$ rember $58(13.9)$ $179(7.8)$ rember $8(1.9)$ $21(0.9)$ t $8(1.9)$ $21(0.9)$ t $8(1.9)$ $21(0.9)$ t $8(1.9)$ $21(0.9)$ t $8(1.9)$ $51(2.2)$ of parents $65(15.6)$ $140(6.1)$ of the parents $65(15.6)$ $140(6.1)$ hild for other illness $74(17.8)$ $203(8.9)$ tarea $195(46.8)$ $883(38.7)$	School-related stressful events				
ol         4 (1)         7 (0.3)           n school         53 (12.7)         118 (5.2)           niend         133 (32)         519 (22.7)           nend         133 (32)         519 (22.7)           exam         159 (38.2)         783 (34.3)           exam         159 (38.2)         54 (10.7)           exam         32 (19.7)         244 (10.7)           eramiy         82 (13.9)         128 (5.6)           nember         54 (13)         128 (5.6)           rmember         106 (25.5)         281 (12.3)           rmember         58 (13.9)         179 (7.8)           rmember         58 (13.9)         179 (7.8)           t         30 (7.2)         62 (2.7)           t         8 (1.9)         110 (5.5)           t         8 (1.9)         179 (7.8)           t         8 (1.9)         170 (7.8)           t         8 (1.9)         110 (0.5)	Change in school	59 (14.2)	219 (9.5)	1.56 (1.13–2.14)	0.0006
n school         53 (12.7)         118 (5.2)           riend         133 (32)         519 (22.7)           exam         159 (38.2)         783 (34.3)           exam         159 (38.2)         783 (34.3)           exam         159 (38.2)         783 (34.3)           eram         159 (38.2)         783 (34.3)           ion         82 (19.7)         244 (10.7)           Family         54 (13)         128 (5.6)           rember         56 (13.9)         128 (5.6)           in member         106 (25.5)         281 (12.3)           in member         58 (13.9)         179 (7.8)           in member         58 (13.9)         179 (7.8)           it         30 (7.2)         62 (2.7)           of parents         8 (1.9)         110 (0.5)           it         8 (1.9)         110 (0.5)           it         8 (1.9)         110 (0.5)           it         8 (1.9)         51 (2.2)           of the parents         65 (15.6)         140 (6.1)           of the parents         65 (15.6)         140 (6.1)           her         31 (7.5)         84 (3.7)           her         195 (46.8)         83 (38.7)	Suspension from school	4 (1)	7 (0.3)	3.16 (0.78-12.03)	0.13
riend133 (32)519 (22.7)exam159 (38.2)783 (34.3)exam159 (38.2)783 (34.3)ion82 (19.7)244 (10.7)Family-54 (13)128 (5.6)Family member106 (25.5)281 (12.3)in member58 (13.9)179 (7.8)in member58 (13.9)179 (7.8)in member58 (13.9)179 (7.8)in member58 (13.9)179 (7.1)if parents8 (1.9)11 (0.5)if parents8 (1.9)11 (0.5)if parents5 (15.6)140 (6.1)ov the parents65 (15.6)84 (3.7)her31 (7.5)84 (3.7)hild for other illness74 (17.8)83 (38.7)if area195 (46.8)883 (38.7)	Frequent punishment in school	53 (12.7)	118 (5.2)	2.68 (1.87–3.82)	<0.00001
exam         159 (38.2)         783 (34.3)           ion         82 (19.7)         244 (10.7)           Family-         54 (13)         248 (10.7)           Family-         54 (13)         128 (5.6)           re family member         106 (25.5)         281 (12.3)           re mber         58 (13.9)         179 (7.8)           rember         58 (13.9)         179 (7.8)           rember         58 (13.9)         179 (7.3)           rember         58 (13.9)         179 (7.3)           rember         58 (13.9)         179 (7.3)           rember         58 (1.9)         179 (7.3)           rember         8 (1.9)         21 (0.9)           rt         8 (1.9)         11 (0.5)           rt         8 (1.9) <t< td=""><td>Separation from best friend</td><td>133 (32)</td><td>519 (22.7)</td><td>1.6 (1.26–2.02)</td><td>0.00006</td></t<>	Separation from best friend	133 (32)	519 (22.7)	1.6 (1.26–2.02)	0.00006
on         82 (19.7)         244 (10.7)           Family-         54 (13)         244 (10.7)           re family member         54 (13)         128 (5.6)           re family member         106 (25.5)         281 (12.3)           re family member         58 (13.9)         179 (7.8)           r member         58 (13.9)         179 (7.8)           r member         58 (1.9)         179 (7.3)           r member         58 (1.9)         179 (7.3)           r member         58 (1.9)         179 (7.3)           of parents         8 (1.9)         170 (7.1)           ft         8 (1.9)         11 (0.5)           t         8 (1.9)         140 (6.1)           her         31 (7.5)         84 (3.7)           hild for other illness         74 (17.8)         883 (38.7)	Sitting for government exam	159 (38.2)	783 (34.3)	1.19 (0.95–1.48)	0.136
Family-       54 (13)       128 (5.6)         te family member       106 (25.5)       281 (12.3)         member       58 (13.9)       179 (7.8)         member       58 (13.9)       179 (7.8)         of parents       58 (13.9)       179 (7.8)         of parents       8 (1.9)       179 (7.8)         of parents       8 (1.9)       21 (0.9)         t       8 (1.9)       11 (0.5)         ts       20 (4.8)       51 (2.2)         oy the parents       65 (15.6)       140 (6.1)         her       31 (7.5)       84 (3.7)         hild for other illness       74 (17.8)       83 (38.7)	Failure in an examination	82 (19.7)	244 (10.7)	2.05 (1.54–2.43)	<0.00001
Ily member       106 (25.5)       281 (12.3)         ber       58 (13.9)       179 (7.8)         ber       58 (1.9)       179 (7.8)         ants       8 (1.9)       62 (2.7)         ents       8 (1.9)       21 (0.9)         sold       7.2)       62 (2.7)         parents       8 (1.9)       11 (0.5)         parents       65 (13.7)       162 (7.1)         parents       65 (15.6)       140 (6.1)         parents       65 (15.6)       84 (3.7)         r other illness       74 (17.8)       203 (8.9)         195 (46.8)       883 (38.7)	Being bullied at school Family- related stressful events	54 (13)	128 (5.6)	2.51 (1.77–3.56)	<0.00001
ber         58 (13.9)         179 (7.8)           30 (7.2)         62 (2.7)           ants         8 (1.9)         21 (0.9)           ants         8 (1.9)         21 (0.5)           57 (13.7)         162 (7.1)           57 (13.7)         162 (7.1)           parents         65 (15.6)         140 (6.1)           parents         65 (15.6)         84 (3.7)           r other illness         74 (17.8)         203 (8.9)           195 (46.8)         883 (38.7)	Severe illness in a close family member	106 (25.5)	281 (12.3)	2.44 (1.88–3.16)	<0.00001
ants 30 (7.2) 62 (2.7) ants 8 (1.9) 21 (0.9) 8 (1.9) 11 (0.5) 57 (13.7) 162 (7.1) 20 (4.8) 51 (2.2) parents 65 (15.6) 140 (6.1) 31 (7.5) 84 (3.7) r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Death of a close family member	58 (13.9)	179 (7.8)	1.9 (1.37–2.64)	0.00007
nts 8 (1.9) 21 (0.9) 8 (1.9) 11 (0.5) 57 (13.7) 162 (7.1) 20 (4.8) 51 (2.2) parents 65 (15.6) 140 (6.1) 31 (7.5) 84 (3.7) r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Loss of job by a parent	30 (7.2)	62 (2.7)	2.78 (1.73–4.46)	<0.00001
8 (1.9)       11 (0.5)         57 (13.7)       162 (7.1)         57 (13.7)       162 (7.1)         20 (4.8)       51 (2.2)         parents       65 (15.6)       140 (6.1)         31 (7.5)       84 (3.7)         r other illness       74 (17.8)       203 (8.9)         195 (46.8)       883 (38.7)	Divorce or separation of parents	8 (1.9)	21 (0.9)	2.11 (0.85-5.06)	0.11
57 (13.7) 162 (7.1) 20 (4.8) 51 (2.2) parents 65 (15.6) 140 (6.1) 31 (7.5) 84 (3.7) r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Remarriage of a parent	8 (1.9)	11 (0.5)	4.05 (1.48–10.9)	0.003
20 (4.8) 51 (2.2) parents 65 (15.6) 140 (6.1) 31 (7.5) 84 (3.7) r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Birth of a sibling	57 (13.7)	162 (7.1)	2.08 (1.49–2.45)	<0.00001
parents 65 (15.6) 140 (6.1) 31 (7.5) 84 (3.7) r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Frequent domestic fights	20 (4.8)	51 (2.2)	2.21 (1.26–3.85)	0.0043
31 (7.5) 84 (3.7) r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Frequent punishment by the parents	65 (15.6)	140 (6.1)	2.83 (2.04–3.95)	<0.00001
r other illness 74 (17.8) 203 (8.9) 195 (46.8) 883 (38.7)	Father's alcoholism Other	31 (7.5)	84 (3.7)	2.11 (1.35–3.29)	0.0007
195 (46.8) 883 (38.7)	Hospitalization of the child for other illness	74 (17.8)	203 (8.9)	2.22 (1.64–2.99)	<0.00001
	Living in a war affected area	195 (46.8)	883 (38.7)	1.4 (1.13–1.74)	0.002

Table 2: Bowel habits and stressful life events

		Churren ( )
	Stracchil avanta na sitiwa	Stressful events
	Stressful events positive	negative
	(n=342) N (%)	(n=74) N (94)
Stool consistency	14 (70)	N (%)
Hard	91 (26.6)	23 (31.1)
Normal	187 (54.7)	23 (51.1) 38 (51.3)
Mushy	20 (5.8)	1 (1.4)
-		
Changing consistency Large diameter stools	44 (12.9)	12 (16.2)
No	116 (33.9)	27 (36.5)
<pre>No <once month<="" pre=""></once></pre>	78 (22.8)	27 (30.3)
1–3 times/month	32 (9.4)	5 (6.8)
≥once/week	116 (33.9)	32 (43.2)
Retentive posturing	110 (00.7)	52 (43.2)
No	162 (47.4)	40 (54)
<once month<="" td=""><td>53 (15.5)</td><td>12 (16.2)</td></once>	53 (15.5)	12 (16.2)
1–3 times/month	27 (7.9)	5 (6.8)
≥once/week	100 (29.2)	17 (23)
Painful bowel motions	100 (27.2)	1, (23)
No	101 (29.5)	19 (25.7)
<once month<="" td=""><td>146 (42.7)</td><td>36 (48.6)</td></once>	146 (42.7)	36 (48.6)
1–3 times/month	66 (19.3)	17 (23.6)
≥once/week	29 (8.5)	2 (2.7)
Straining	()	_ ()
No	98 (28.7)	23 (31.1)
<once month<="" td=""><td>154 (45)</td><td>36 (48.6)</td></once>	154 (45)	36 (48.6)
1–3 times/month	68 (19.9)	13 (17.6)
≥once/week	22 (6.4)	3 (4)
Fecal incontinence		
No	287 (83.9)	65 (87.8)
<once month<="" td=""><td>14 (4.1)</td><td>5 (6.8)</td></once>	14 (4.1)	5 (6.8)
1–3 times/month	11(3.2)	2 (2.7)
≥once/week	30 (8.8)	2 (2.7)

Table 3: Association between exposure to stressful life events and bowel habits of children with constipation



#### Symptoms and exposure to stress

Associated symptoms and exposure to stress **Table 4** describes the relationship between associated symptoms and exposure to stressful life events in patients with constipation. In multiple logistic regression analysis abdominal pain (adjusted OR 1.85, p=0.026) and loss of weight (adjusted OR 13.23, p=0.012) were significantly common in those exposed to stress.

	Stressful events	Stressful events		
	positive (n=342)	negative (n=74)		
	N (%)	N (%)	OR (95% CI)	P*
Abdominal pain	196 (57.3)	32 (43.2)	1.72 (1-2.97)	0.048
Nausea	42 (12.3)	1 (1.4)	10.11 (1.44–204.37)	0.01
Vomiting	43 (12.6)	1 (1.4)	10.35 (1.48–209.13)	0.0089
Weight loss	66 (19.3)	1 (1.4)	17.22 (2.49–345.32)	0.0003
Loss of appetite	71 (20.8)	10 (13.5)	1.65 (0.77-3.64)	0.22

### Table 4: Relationship between exposure to stressful life events and associated symptomsin patients with constipation

\*Chi-square test.

#### **Discussion**

In this study, constipation was significantly higher in those exposed to family- and school-related stressful life events. The stressful events significantly associated with constipation included separation from the best friend, failure in an examination, severe illness in a family member, loss of job by a parent, frequent punishment by parents and living in a war-affected area.

Even though, previous studies have demonstrated a strong association between functional constipation and psychological symptoms such as anxiety and depression in adults (11,12), the exact relationship between emotional stress and childhood functional constipation has not been assessed sufficiently. The few studies performed in relation to this, have assessed this effect indirectly. In 7 –12-year-old children in Turkey, Inan et al. (14) demonstrated an association between constipation and major physical or psychological trauma, history of personal health problems and abnormal oral habits.

However, this study did not assess the impact of common family and school related stressful events. They considered abnormal oral habits as an indirect measurement of stress and suggested stress as an associated factor for constipation. This probably underestimates the actual relationship between constipation and stress, since only severe emotional stress would cause such abnormal oral habits (4).

According to Lisboa et al. (13) aggressiveness in the family, in the form of punishments is associated with chronic constipation in children. Similarly, we also found a higher prevalence of constipation in those who undergo frequent parental punishment. Furthermore, similar to our study both Inan et al. and Lisboa et al. did not find any association between constipation and divorce or separation of parents (4,13). Lisboa et al. reported an association between constipation and difficulties in the school (13). Similarly, we found an association between constipation and examination failure. Other stressful events independently associated with constipation in our study were separation from the best friend, loss of job by a parent and severe illness in a family member.

The separatist war in the eastern province of the country has been going on for nearly 30 years. When we administered the questionnaire in this province, full-scale security operations to liberate this area from the separatists. We found a significantly higher prevalence of constipation in children living in war affected areas compared with rest of the country. Even though the association between war and childhood constipation has not been studied, previous studies have reported effects of war on functional gastrointestinal diseases such as irritable bowel syndrome in adults. In Nicaragua, a population-based door-to-door interviews showed that incidence of irritable bowel syndrome was three times higher in adults who experienced war trauma during the Sandinista rebellion period. Furthermore, the odds for irritable bowel syndrome were quite high depending on whether the individual witnessed an execution, had a family member killed or injured, suffered from physical or psychological abuse or had multiple trauma (14). Another study, on Gulf war veterans, reported higher prevalence of irritable bowel syndrome and bloating during and after deployment (15). Therefore, these data confirm the important role of war-related psychological stresses in developing functional gastrointestinal diseases.

We found a significant negative correlation between mean bowel frequency and number of stressful life events faced by them, which has not been reported previously. This highlights the effect of emotional stress on lower bowel functions in children. It is possible that failure to cope with stressful situations results in stress internalization and in turn leads to anxiety and psychological distress.

Slow colonic transit, an important pathophysiological factor in functional constipation, is associated with psychological symptoms such as anxiety and depression (16,17). In addition, anxiety and psychological stress may contribute to the development of pelvic floor dyssynergia by increasing pelvic floor muscle tension (18). Abnormal psychological states have also been shown to correlate with rectal mucosal blood flow suggesting that psychological factors are likely to influence gut function via autonomic efferent neural pathways (19). These distresses may act via the enteric nervous system to inhibit colonic motility and thus prolonged colonic transit as reported by Chan et al. (11). These suggest a link between the central brain activity, enteric nervous systems and ano-rectal dysfunction. Further studies are required to assess the exact relationship between them.

Abdominal pain and weight loss were more common in patients who were exposed to stressful life events. Previous studies have reported an association between emotional stress and gastrointestinal symptoms such as abdominal pain in children (7). These findings show that effects of stress on gastrointestinal function are wider in children with constipation and affect other parts of the gastrointestinal tract leading to multiple symptoms. The effects of profound stress in the biologically predisposed individual may lead to a reduced ability of the central nervous system to filter visceral and somatic sensations, possibly at the cingulated cortex and related regions associated with the interface of emotion and pain. This may not only lead to lower sensation thresholds (visceral hypersensitivity), but also the reporting of multiple symptoms (20).

We conclude that constipation in children and adolescents is associated with exposure to stressful life events. Modulation of gut motility through brain gut axis probably impairs colonic transit and anorectal functions causing constipation in them. Therefore it is important to consider stress as an important precipitant of constipation and consider its impact during the treatment of affected children.

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# Constipation During and After the Civil War in Sri Lanka: a Pediatric Study

# CHAPTER

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### Summary

Constipation is a common childhood disease. It is associated with exposure to stressful events. Sri Lanka was involved in three decades of civil war causing significant emotional stress. This study assessed the prevalence of childhood constipation during and after war. Data were collected from 10- to 16-year olds in five randomly selected schools, in three provinces (two schools from Eastern province), using a validated, self-administered questionnaire. Constipation was diagnosed using Rome III criteria. Phase I was conducted during the war to liberate Eastern province from separatist groups. Phase II was conducted 2 years after the war in same schools. During Phase I, prevalence of constipation was significantly higher in Eastern province (18.1%) compared with Western (14.2%) and Southern (12.6%) provinces (p=0.009). Constipation was significantly lower in Eastern province in Phase II (10%) compared with Phase I (p<0.0001). This study highlights the possible link between devastating emotional effects of civil war and childhood constipation.

# Introduction

Constipation is a worldwide problem among children. Its prevalence in children ranges from 0.7% to 29.3% (1). In over 90% of them, the aetiology is obscured and thought to be of functional in origin (2).

Psychological factors, such as emotional stress, affect gastrointestinal motility and sensation including lower bowel functions. Several studies have reported an association between emotional stress and constipation in children (3,4), but its association with war has not been studied previously. According to an adult study, irritable bowel syndrome (IBS) was commoner in those exposed to civil war in Nicaragua (5). Another study found a higher prevalence of IBS in adults who were exposed to the Second World War as early as 6–18 months of age (6). Emotional stress associated with the war may lead to dysregulation of the function of the brain gut-axis and would have contributed to these observations (7).

Sri Lanka was involved in three decades of civil war with disruption of human life and social infrastructure. Northern and Eastern provinces were the main areas affected by the war. Suicidal attacks, bombing and other acts of violence were common in these areas. Furthermore, deliberate attacks on the border villages and public transport were also reported in these provinces. These would have resulted in a significant emotional stress for the school children living in these areas. Therefore, we hypothesized that abnormal bowel habits and constipation were more common in children living in war-affected Eastern province.

Eastern province was liberated from terrorist groups in July 2007. Restoration of public facilities, resettlement of internally displaced people and normalization of the civil life after the end of war are likely to reduce the emotional stress in the school children living in this area. Therefore, in this study, we also investigated the hypothesis that reduction in exteroceptive stress after the end of civil war normalizes the bowel habits and hence reduces the prevalence of constipation of the children.

# <u>Methods</u>

This study was conducted in two phases.

#### <u>Phase I</u>

This phase was conducted from January to June 2007. Children aged 10–16 years, in five randomly selected schools, in three randomly selected provinces of Sri Lanka were recruited. Two schools were from Eastern province affected by war. Terrorist activities (e.g. bomb blast, abductions) and the war to liberate Eastern province from terrorists were going on during this phase of this study.

Information regarding socio-demographic factors and bowel habits was collected using a validated, self-administered questionnaire. It was developed based on the Questionnaire on Pediatric Gastrointestinal Symptoms (8). Questionnaire was in native language and questions were simple and easy to understand. It was administered in an examination setting, to ensure confidentiality and privacy. Research assistants were present during administration of the questionnaire to verify doubts and to help children in answering questions. School administration and parents were informed prior to administration of the questionnaire and consent was obtained. Constipation was diagnosed using Rome III criteria (9). This phase of the study has been published previously (4,10).

#### <u>Phase II</u>

Phase II was conducted 2 years after (March to July 2009) the end of the war and liberation of the Eastern province from separatist groups. By then, internally displaced personals were resettled and most of the public facilities (e.g. roads, schools, hospitals, etc) were restored. The same questionnaire was distributed in a similar setting, to children aged 10–16 years in the same five schools included in Phase I and in two additional schools randomly selected from Uva province. Uva province was included in Phase II because this province consists of multi-ethnic population as in Eastern province.



Data were analyzed using X<sup>2</sup>-test using EpiInfo [EpiInfo 6, version 6.04 (1996) Centers of Disease Control and Prevention, Atlanta, GA, USA and World Health Organization, Geneva, Switzerland]. p<0.05 was taken as significant. Multiple logistic regression analysis was performed on variables that were found to have significant association with constipation in univariable analysis.

This study protocol was approved by the Ethical Review Committee of the Sri Lanka College of Pediatricians.

#### **Results**

During Phase I of this study, a total of 2770 school children were recruited. Of them, 1368 (50.8%) were males. Age ranged from 10 to 16 years with a mean age of 13.2 years, SD of 1.7 years. During Phase II of this study, 2164 children were recruited and 1173 (55%) were males. During this phase, the age range was same as in Phase I (mean age 13.5 years, SD 1.7 years). Properly filled, 97.3 and 98.7% questionnaire were included in the analysis from Phase I and Phase II of this study, respectively.

**Table 1** shows prevalence of constipation during and after the civil war in all provinces. After multiple logistic regression analysis, constipation was significantly higher among those living in war-affected areas during Phase I [adjusted odds ratio (OR) 1.5, 95% confidence interval (CI) 1.1–1.9, p=0.009]. During Phase II, prevalence of constipation has decreased in all three provinces (Eastern, Southern and Western) compared with Phase I of this study. However, there was a statistically significant reduction in prevalence of constipation in previously waraffected Eastern province compared with Phase I (p<0.0001).

# Table 1:Prevalence of constipation during and after war

	Prevalence of constipation		
	During war	After war	
	n(%)	n(%)	
Eastern province <sup>a</sup>	195(18.1) <sup>b</sup>	71(10) <sup>c</sup>	
Southern province	98(12.6)	51(11)	
Western province	123(14.2)	67(12.1)	
Uva province	_	45(11)	

<sup>a</sup>War-affected area

<sup>b</sup>p=0.009,Eastern province vs other two provinces

<sup>c</sup> <0.0001,Eastern province, during war vs after war

**Figures 1 and 2** show the mean predicted probabilities for constipation according to age groups. During the war (Phase I), mean predicted probabilities were significantly higher in all age groups in waraffected Eastern province compared with other two provinces. Two years after the war (Phase II), mean predicted probabilities for constipation were slightly lower in the Eastern province and did not show a significant difference from other two provinces (Fig. 2).

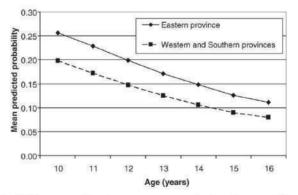


FIG. 1. Mean predicted probabilities according to age groups-during the war (Phase I).

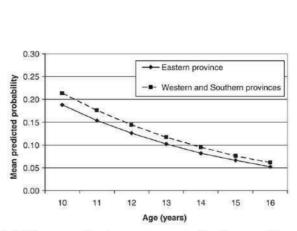


FIG. 2. Mean predicted probabilities according to age groups-after the war (Phase II).

Chapter

Other factors independently associated with constipation during both phases were having a history of constipation in first-degree relatives (adjusted OR 6.0, 95% CI 3.4–10.8, p<0.0001 in Phase I and adjusted OR 4.65, 95% CI 2.59–8.34, p<0.0001 in Phase II) and exposure to family and school-related stressful events other than war (adjusted OR 2.28, 95% CI 1.74–3.0, p<0.0001 in Phase I and adjusted OR 1.93, 95% CI 1.4–2.66, p<0.0001 in Phase II). Constipation was significantly higher in children studying in urban schools during Phase I (adjusted OR 1.4, 95% CI 1.1–1.9, p=0.02), but not during Phase II (adjusted OR 1.46, 95% CI 0.88–1.53, p=0.302).

**Table 2** illustrates bowel habits of the study sample during and after the civil war. During the war, painful defecation and stool withholding were significantly more common in war-affected area. When bowel habits during Phases I and II were compared, hard stools, painful defecation, large volume stools and stool withholding posture showed significant reduction after the war in the war affected Eastern province. In the other two areas, there was a significant reduction in painful defecation and stool withholding after the war and rise in low defecation frequency.

	War-affected East	tern Province	Southern and Western provinces		
	During war,n(%)	After war,n(%)	During war,n	(%After war n(%)	
Defecation					
frequency<3/week	59 (5.5)	50 (7.1)	203 (12.6) <sup>b</sup>	178 (17.6)	
Hard stools	87 (8.1) <sup>a</sup>	39 (5.5)	114 (7.1)	62 (6.1)	
Painful defecation	244 (22.6) <sup>a,b</sup>	60 (8.5)	299 (18.5) <sup>a</sup>	68 (6.7)	
Large volume stools	191 (17.7) <sup>a</sup>	91 (12.8)	246 (15.2)	129 (12.7)	
withholding posture	148 (13.7) <sup>a,b</sup>	55 (7.8)	175 (10.8) <sup>a</sup>	82 (8.1)	
Fecal incontinence	14 (1.3)	9 (1.3)	41 (2.5)	23 (2.3)	

Table 2: Bowel habits of the study sample during and after war

<sup>a</sup>p<0.05, during war vs. after war

<sup>b</sup>p<0.05, Eastern province vs. Southern and western provinces

#### **Discussion**

To the best of our knowledge, this is the first study to assess the prevalence of constipation in school-aged children during and after a civil war. In this study, during the period of war, prevalence of constipation was significantly higher in war-affected Eastern province compared with other areas of the country. There was a significant reduction in prevalence of constipation and related symptoms in this province 2 years after the end of war.

Physical or psychological trauma has been identified as an important risk factor for constipation in children (3). Furthermore, family and school-related stressful life events are also known to precipitate functional gastrointestinal diseases including constipation (4,11). Phase I of this study was conducted during the civil war to liberate Eastern province from separatist group in Sri Lanka. During this period, there were events such as random checking of houses, bomb blasts and abduction and recruitment of children by separatist group as child soldiers and for other war-related activities. Many schools were closed from time-to-time and children were forced to leave schools because of bomb threats. There were some civilian casualties also. Public transport system in the war-affected Eastern province was constantly under the threat of landmines and claymore mines. Furthermore, there were deliberate, preplanned attacks against civilians living in the border villages of the Eastern province. The psychological trauma and stress generated by these events probably



have resulted in high prevalence of constipation observed in children living in waraffected area during this period. Catani et al. (12) have shown a linear relationship between the numbers of war related stressful events and prevalence of posttraumatic stress disorders in Sri Lankan children. Psychological stress is a key factor, which causes significant alterations in functions of the brain-gut axis (7). In genetically and psychologically vulnerable individuals, this results in alterations of physiological functions of the lower gut, predisposing children to develop constipation.

We have observed a significant reduction in prevalence of constipation 2 years after the end of war and liberation of this province from terrorist groups. Restoration of the dayto-day life after the end of the war would have reduced war-related stressors in these children which would have contributed to the significant reduction observed in prevalence of constipation. Most of the other factors associated with constipation have remained constant during both phases. We have also demonstrated a higher predicted probability of constipation in war-affected areas during Phase I and a significant reduction in it after the war. So far, no other study has demonstrated a reduction in the prevalence of constipation after removal of stressful life events.

In this study, we observed a higher prevalence of abnormal bowel habits (painful defecation and stool withholding) in children living in war-affected area during Phase I, compared with other provinces of the country. Furthermore, clinical features related to stool withholding such as retentive posturing, large diameter stools and pain while passing stools were significantly decreased in the war-affected area after the end of war. The relationship between psychological factors and individual bowel habits has not been reported previously. Some studies have demonstrated abnormalities such as delayed colonic transit among patients with anxiety and depression. Furthermore, emotional distress leads to pelvic floor tension (13), alteration in rectal mucosal blood flow (14) and altered rectal sensitivity (15). Previous animal studies have reported sustained bowel dysfunction (decreases number of stools and decreased stool weight) and visceral hypersensitivity in rats exposed to prolonged and variable stress (16). We have previously shown high prevalence of painful defecation, large diameter stools and

stool withholding in children exposed to family and school-related stressful life events (4).

In conclusion, this study underscores the significant association between civil war and childhood constipation. The stress and anxiety related to war probably affect brain-gut axis, and alter lower gut functions, leading to constipation. This highlights the possible link between devastating emotional effects of the civil war, gastrointestinal regulatory mechanisms and etiology of functional constipation.

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Children and Adolescents with Chronic Constipation: How Many Seek Healthcare and What Determines it?

# CHAPTER

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### Summary

This island-wide cross-sectional survey was conducted to assess the healthcare consultations in Sri Lankan children with constipation. Children aged 10-16 years were randomly selected from five randomly selected schools in three randomly selected provinces of Sri Lanka. Data were collected using a pre-tested questionnaire based on Rome III criteria. Of the 2770 questionnaires distributed, 2694 (97.3%) properly filled questionnaires were included in the analysis. From 416 (15.4%) children with chronic constipation, only 16 (3.8%) had sought medical advice during the previous 12 months. Younger children and those with a similar family history were more likely to seek healthcare. The majority of children with symptoms indicating severe constipation such as painful defection, large volume stool, fecal incontinence and blood stained stools had not sought medical help for their symptoms. Parents should pay more attention to bowel habits of their children to identify and treat constipation early to prevent complications.

#### Introduction

Chronic constipation in children is characterized by low defecation frequency, fecal incontinence, retentive posturing, painful or hard stools and frequent passage of large diameter stools. According to previous epidemiological studies, constipation is a significant health issue in both developing and developed countries (1,2). Relapsing and remitting nature of symptoms often create significant demands on limited and already stretched pediatric and gastroenterology services. In a birth cohort study, Chitkara et al. (3) have found that constipation has the highest number of medical visits for all gastrointestinal diseases. In 2011, Choung et al. (4), studying the same birth cohort showed that children with constipation also have higher rates of medical consultation for other minor illnesses than that of healthy children. According to Everhart and Ruh, chronic constipation is one of the leading causes for ambulatory healthcare visits of children in USA (5). In addition, children with constipation have visited medical clinics more frequently than those with other chronic medical conditions such as bronchial asthma and migraine (4). According to a previous study, the additional costs attributable to children with constipation, relative to the general pediatric population is ~\$3.9 billion (6).

A previous study involving a community sample of adults has shown that female gender, higher educational level, abdominal pain and prolonged defection are associated with healthcare consultation (7). Furthermore, Pare *et al.* (8) noted that healthcare seeking for constipation is higher in females. Identifying healthcare seeking patterns in children with constipation would be important in planning and allocation of pediatric healthcare resources and expenditure.

Most of the studies on childhood constipation are from the Western world. Little is known of the situation in developing countries, particularly in Asia. In a previous epidemiological study, we have shown that constipation is a common problem in Sri Lankan school children, affecting 15.4% (2) and also documented its association with stressful life events [9]. In this article, we have assessed the healthcare seeking behaviour in a sample of school children with chronic constipation.

#### **Materials and Methods**

Sri Lanka consists of nine provinces. We conducted a school-based survey in three randomly selected provinces. From these provinces, five schools were randomly selected (three urban and two rural). From each school, 12 classes were randomly selected from academic years (grades) 6-11 (two from each academic year). All children aged 10-16 years in the selected classes, who were present on the day of the survey, were included in the study.

#### Data collection

A self-administered, structured questionnaire was administered to children. This questionnaire has been previously validated and used in Sri Lankan school children aged 10-16 years (10). It contained four parts. The first part included demographic data about the child and the family. The second contained questions to explore whether the child had faced family and school-related stressful life events. The third had questions to evaluate the bowel habits (developed from Rome III self-administered questionnaire for children (11). In the fourth part, we inquired about other medical conditions, associated symptoms and healthcare seeking for constipation. The questionnaire was in the native language (Sinhala) and questions were simple and easy to understand. School administration and parents were informed about the survey and consent was obtained before conduction the study. Consent was also obtained from each child who participated in the study. Since the questionnaire was collected on the same day there were no non-responders. We used the setting of a typical examination in the school to make certain that children do not see questionnaires of the others. Research assistants were present during the whole time with students while they were filling the questionnaire and explanations were given as and when the need arose. The data collection was started in January 2007 and completed within 6 months.

#### **Definitions**

We used Rome III criteria to diagnose functional constipation (12). Since this is an epidemiological study, we did not use the diagnostic criterion of palpable faecal mass in rectum or abdomen to diagnose constipation in our patients. A child who has sought medical advice for symptoms of constipation during the previous 12 months was defined as a healthcare seeker (13).

# <u>Data analysis</u>

Data were analyzed using  $x^2$  and Fisher exact test using EpiInfo [EpiInfor 6 version 6.04 (1996) Centers for Disease Control and Prevention, Atlanta, Georgia, USA and World Health Organization, Geneva, Switzerland]. The P< 0.05 was considered to be statistically significant. Multiple logistic regression analysis was performed on variables that were found to have significant association with healthcare consultation.

# Ethical approval

This study protocol was approved by the Ethical Review Committee of the Sri Lanka College of Pediatricians.

### <u>Results</u>

# Prevalence of healthcare consultation among children with constipation

In this epidemiological survey, 2770 questionnaires were distributed and 97.3% (2694) were included in the analysis. Incompletely filled 76 questionnaires were excluded from the study According to Rome III criteria 416 (15.4%) had constipation. Out of them, only 16 (3.8%) had consulted a doctor during the previous 12 months for symptoms of constipation.

### Socio-demographic variables associated with healthcare consultation

**Table I** illustrates socio-demographic variables of consulters and non-consulters. Age < 12 years was a significant factor associated with healthcare seeking. Children with family history of constipation also sought healthcare more frequently than children without family history. Mothers of all children who have sought healthcare were not employed.

Variable	Health-care Consulters,	Non- Consulter n(%)	
	n(%)		
Sex			
Boys	10(4.4)	220(95.5)	
Girls	6(3.2)	180(96.8)	
Age(years)			
10-12	15(6.6)*	212(93.4)	
13-16	1(0.5)	188(99.5)	
Family size			
Only child	2(6.5)	29(93.5)	
2-3 children	9(3.1)	286(96.9)	
>4 children	5(5.6)	85(94.4)	
Maternal employment			
Leading profession	0	9(100)	
(eg:doctor,engineer)			
Lesser profession	0	23(100)	
(eg:nurse,teacher)			
Skilled non-manual	0	12(100)	
(eg:clerk)			
Skilled manual	0	20(100)	
Unskilled manual	16(4.5)	336(95.5)	
Father's social class			
Leading profession	3(5.9)	48(94.1)	
Lesser profession	1(4.2)	23(95.8)	
Skilled non-manual	2(3.6)	54(96.4)	
Skilled manual	5(3.5)	137(96.5)	
Unskilled unemployed	5(3.5)	138(96.5)	
Family history of constipation			
Positive	5(20.8)†	19(79.2)	
Negative	11(2.8)	381(97.2)	

Table 1: Prevalence of healthcare consultation in children with constipation according to socio-demographic and family characteristics.

\*Odds ratio(OR)=13.3(95% CI 1.83-21.5),p=0.03.

Chi-square test

<sup>†</sup>OR=9.11(95% CI 2.47-32.47),p=0.0001.chi-square test

**Table 2** shows the bowel habits and defecation behavior associated with healthcare consultation. During univariable analysis, defecation frequency < 3 per week, large volume stools, withholding posture, painful defecation, fecal incontinence and blood stained stools were significantly higher in children seeking healthcare. However, following multiple logistic regression analysis, none of them had an independent association (P.0.05).

	Healthcare	Non		
Symptoms	Consultation	consultation	OR(95% CI)	p-value*
	(n=16),n(%)	(n=400)(%)		
Defecation frequency <3/week	8(50)	99(24.8)	3.04(1.01-9.19)	0.048
Hard stools	3(18.8)	109(27.3)	0.62(0.14-2.37)	0.64
Large volume stool	5(31.3)	38(9.5)	4.33(1.23-14.47)	0.02
Withholding posture	11(68.8)	132(33)	4.47(1.4-15.1)	0.007
Painful defecation	5(31.3)	71(17.8)	2.11(0.62-6.83)	0.29
Straining	4(25)	98(24.5)	1.03(0.27-3.53)	0.80
Fecal incontinence	5(31.3)	40(10)	4.09(1.17-13.62)	0.02
Blood stained stools	6(37.5)	36(9)	6.76(2.0-22.3)	0.0005

### Table 2:Association between bowel habits and health-care consultation

\*Chi-square test

# Associated symptoms and healthcare consultation

**Table 3** shows healthcare consultation according to other symptoms association with constipation. Except vomiting, which was more common among healthcare consulters, we did not find any other significant difference between the two groups.

	Healthcare	Non-	OR	P-value*
Symptoms	consulters	consulters	(95% CI)	
	n (%)	n(%)		
Abdominal pain	9 (56.3)	215 (53.8)	1.12 (0.37-3.37)	0.95
Nausea	3 (18.8)	39 (9.8)	2.14 (0.46-8.53)	0.45
Vomiting	5 (31.3)	38 (9.5)	4.33 (1.23-14.47)	0.017
Loss of appetite	6 (37.5)	74 (18.5)	2.64 (0.82-8.22)	0.12
Loss of weight	5 (31.3)	61 (15.3)	2.6 (0.76-7.8.48)	0.15

Table 3: Health-care consultation according to associated symptoms

\*Chi-square test.

# Stressful life events and healthcare consultation

When we compared the healthcare consultation between children who were exposed to family and school-related stressful life events [14 (4.1%)] and who were not [2 (2.7%)], we did not find a statistically significant difference between these two groups (odds ratio 1.54, 95% confidence interval 0.82-10.01, P=0.82,  $X^2$  test).

### **Discussion**

We observed a very low rate of healthcare consultation (3.8%) among Sri Lankan children suffering from chronic constipation. Healthcare consultation was higher in children below 12 years and those with family history of constipation. The majority of children with symptoms indicating significant constipation had not seen a doctor for their symptoms.

Although we found 416 children with chronic constipation in this survey, only 3.8% had sought healthcare for their symptoms during the previous 12 months. Sri Lanka is a country in which healthcare is provided completely free of charge. The average distance from a dwelling house to a healthcare facility is 1.4km (14). Therefore, we expected higher healthcare seeking in the sample of children with constipation. When taking these factors into consideration, it was surprising to see that the vast majority of children with chronic constipation had not sought medical advice for their symptoms.

There are no previous community or school-based studies assessing healthcare consultation patterns in children with constipation to compare our findings. However, in comparison, a very high percentage (70%) of Sri Lankan children with recurrent abdominal pain had seen a doctor for their symptoms as documented in a previous study (13). Pain and discomfort are important factors for children to see a doctor. In this study, more than 50% of constipated children complained of abdominal pain but only 4% of had consulted a doctor for their symptoms. Unlike the results from the current study, an adult study from Canada had noted that 43% of self-reported cases of constipation had sought health care for their symptoms (8). Another study among Spanish adults in the community had found that 16% of the subjects with constipation had sought medical advice (7). Generally, it is a parent who takes a child to a health care facility. It is possible that older children and teenagers had not discussed their bowel habits with parents and therefore parents were unaware that these children were suffering from constipation. In addition, the relatively lower doctor-patient ratio in Sri Lanka (1:1815) (15), compared to Canada (1:470) and Spain (1:300) (16) with consequent long waiting lists may have discouraged our patients from seeking healthcare.

Predictors of healthcare seeking for children with chronic constipation remain poorly understood. Demographic variables favouring healthcare seeking in our study were age<12 years and a family history of constipation. Parents may be more aware of bowel habits of younger children and possibly recognize symptoms of constipation more frequently than in older children. Familial predisposition is a known fact in childhood constipation. Previous studies had shown positive family history as an important risk factor of developing constipation (2,17). Parents with constipation are likely to identify symptoms of constipation in their children more easily than parents who do not have constipation. We did not find a gender difference in healthcare seeking in our sample. In contrast, adult studies have shown that females seek more healthcare than males (7,8). Higher prevalence of constipation demonstrated among females in adult studies (18) would have contributed to this difference. Since economic status is a significant determinant of healthcare seeking, we expected to find a low prevalence of healthcare consultation in children from lower social class.However, in contrast to our hypothesis, lower social class was not a significant factor. Similarly, another study using a birth cohort follow-up, failed to show social class as a determinant of healthcare seeking for constipation in children (3). Furthermore, mothers of all children who sought healthcare in our sample were unemployed.

Symptom severity is one of the key determinants of healthcare consultation for any disease. In previous studies Boey et al. (19) have shown that severity of abdominal pain is a leading factor for healthcare seeking for recurrent abdominal pain in children. Furthermore, Talley et al. (20) have also shown that severity of pain is a wellestablished factor for healthcare seeking in adults with irritable bowel syndrome. Therefore, we expected that children with symptoms of severe constipation would seek healthcare more frequently. Moreover, symptoms such as fecal incontinence causes social embarrassment and associated developmental, behavioral and upbringing problems (21). In addition, parents often think that the child is responsible for the incontinence and are frustrated as they may have to compromise other family activities (22). However in contrast to our assumptions, 40 out of 45 children with fecal incontinence (89.9%) had not sought medical care. Similarly, presence of blood in the stool is an alarming symptom which we expected to lead to higher healthcare consultation in order to exclude sinister diseases. However, 85.7% of children with blood stained stools had not consulted a doctor for their symptoms. Furthermore, the multiple logistic regression analysis between bowel habits and healthcare consultation failed to show an independent association. In this study, presence of vomiting was significantly associated with healthcare consultation. However, unlike previous adult studies (7), we failed to find an association between abdominal pain and healthcare seeking.

Psychological factors such as stressful life events are known to be associated with constipation and fecal incontinence (9,23). Previous studies have demonstrated a significant association between psychological disturbances and healthcare consultation in functional gastrointestinal diseases (24). Therefore, we expected that exposure to stressful life events would be a predisposing factor for healthcare seeking. Contrary to our suppositions, we did not find a significant association between exposure to stressful events and healthcare consultation. We did not analyze the association between

individual stressful life events and healthcare consultation because of the relatively smaller numbers of healthcare consulters in our study.

The pertinent question which arose when interpreting this data was why the vast majority of children had not sought healthcare consultation, despite having pain and symptoms of significant constipation. It is possible that the 10-16 year-olds included in this study were too embarrassed to discuss their bowel habits with parents and therefore, suffered from this condition silently. Furthermore, symptoms may not have been continuous and may even have resolved spontaneously. The majority of children with constipation show spontaneous resolution of symptoms in 6-12 months (25). However, it is imperative to understand that at least 30% of affected children do not outgrow constipation and progress into adulthood with ongoing symptoms [26]. This may eventually lead to pathological problems such as dilated rectum and abnormal defection dynamics. Social isolation and getting bullied at school are identified consequences of persistent fecal incontinence (27). Furthermore, persistent constipation can significantly reduce the quality of life of affected children (28). Early diagnosis and treatment will prevent these complications. Therefore, it is the responsibility of the healthcare professionals to educate children and the general public regarding symptoms of constipation, enabling them to identify the disease and to seek medical care early.

There are several strengths of this study. This was a population-based study involving a large number of school children. Study sample represents Sri Lankan children of 10-16 years, and hence the results of the study could perhaps be generalized. Furthermore, data has been collected using a validated and pre-tested questionnaire and currently accepted Rome III criteria were used to diagnose constipation. Research assistants were present while children were filling the questionnaires to provide assistance and to verify doubts. This process would also eliminate the possibility of answering questions without understanding. However, as in any questionnaire based survey we have to rely upon children reporting their symptoms and healthcare seeking. Another drawback in the study was the relatively small number of children who reported seeking healthcare, decreasing the power of the study when determining predictors of healthcare consultation.

In conclusion, healthcare consultation for chronic constipation in Sri Lankan school children and adolescents is quite low despite the majority of them having features suggestive of significant constipation. Socio-demographic factors such as younger age and family history of constipation were significantly associated with healthcare seeking it is essential to educate general public regarding features of chronic constipation and bring affected children to medical attention early to avoid complications.

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Quality of life and somatic symptoms in children with constipation: a school based study

# CHAPTER

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#### Abstract

**Objective:** Chronic constipation is a common problem among Sri Lankan school children. We assessed the Health Related Quality of Life (HRQoL) and somatization in school children with constipation.

**Methods:** This cross sectional survey was conducted in children aged 13-18 years, in 4 schools in Gampaha district of Sri Lanka. Data were collected using a pretested, self administered questionnaire with questions on bowel habits, somatisation and HRQoL. Constipation was diagnosed using Rome III criteria.

**Results:** A total of 1792 children were included in the analysis [males 975 (54.4%), mean age 14.4 and SD 1.3 years]. Hundred and thirty eight(7.7%) fulfilled Rome criteria for constipation. Children with constipation had lower HRQoL scores for physical (83.6 vs. 91.4 in controls, p<0.0001), social (85.0 vs. 92.7, p=0.0001), emotional (73.6 vs. 82.7, p=0.0001), school functioning (75.0 vs. 82.5 p<0.0001), and lower overall scores (79.6 vs. 88.0, p=0.0001). HRQoL scores were lower in those with fecal incontinence (70.0 vs. 81.1,p=0.004). Patient perceived severity of abdominal pain (r=-0.22, p=0.01) and severity of bowel symptoms (r=-0.22, p=0.01) showed significant negative correlation with total HRQoL scores. Total somatization score also found to be negatively correlated (r=- 0.47 p<0.0001) with HRQoL.

**Conclusions:** Children with constipation have lower HRQoL scores than controls in physical, social, emotional and school functioning. They also have a wide range of somatic symptoms. These issues need to be addressed during clinical evaluation of children with constipation to understand the impact of the disease on the life of affected children and to provide optimal care.



# **Introduction**

Health related quality of life (HRQoL) is a broad concept that incorporates the patient's perceptions, illness experience and functional status related to a medical condition (1). Assessment of HRQoL quantifies multiple factors producing patient's perception of ill-health, and is very valuable in diseases which do not have an objective biological marker to compute the impact of the disease on the affected individuals.

Functional constipation is a chronic, troublesome disease with relapsing and remitting nature. It shows an alarmingly high prevalence in many parts of the world (2,3) and seems to have a cosmopolitan distribution (4). Even though, constipation is not a life threatening condition, many of its associated symptoms such as abdominal pain, fecal incontinence and pain during motions affect the physical, social, and emotional wellbeing.

Previous hospital based studies from tertiary care centers have shown that children with constipation have poor quality of life. Clarke and co -workers have compared quality of life of children with slow transit constipation and healthy controls. In that study, total HRQoL scores in children with slow transit constipation were significantly lower than in controls (5). Another study from Brazil also found poor HRQoL in children with constipation, especially in physical and psychological domains (6). Youssef et al. (7) have shown that children with chronic constipation had lower HRQoL than children with inflammatory bowel disease and gastro-esophageal reflux indicating that constipation continues into adulthood, it influences negatively on social contact and intimacy, in up to 20% of adults (8). Despite these observations, there are no studies that formally address the physical, social and emotional impact of chronic constipation in children in the community.

Studies among adults have shown that patients with functional gastrointestinal diseases have more somatic symptoms than healthy individuals (9). Furthermore, patients with more somatic symptoms were known to seek medical advices for their gastrointestinal symptoms than controls (9). Although somatization is a known phenomenon in children, its association between constipation and HRQoL is unknown. The main aims of this project were to a) study HRQoL in children/adolescents suffering from chronic constipation, b) study the somatic symptoms of children with chronic constipation and c) assess the effects of somatization on HRQoL.

#### <u>Methods</u>

#### Study population

This study was conducted in Gampaha district of Sri Lanka. The district has 501mixedschools. Of them 166 schools have children with an age range of 13-18 years. We randomly selected 4 schools out of them. From each school all classes from (academic years) 9 to 12 were selected. All children in these classes who were within the age range of 13-18 years were invited to take part in the study.

#### Instruments of data collection

We used a self-administered questionnaire to collect data from the sample. It consisted of 4 main parts.

#### Part 1 - Questionnaire on childhood functional gastrointestinal diseases

This questionnaire was based on Rome III diagnostic questionnaire for paediatric functional gastrointestinal diseases (10). This questionnaire has been previously translated to native language and undergone validation.

#### Part 2 - Quality of life assessment questionnaire

PedsQL is a tool used to assess health related quality of life in children. We used Quality of Life Inventory of teenagers of 13-18 years. It is a self-reported questionnaire and has been validated for the relevant age group. We obtained the translated and validated version of the Sinhala questionnaire (native language of Sri Lanka) from the MAPI institute with permission to use it for this particular research. The inventory has 23 items and encompasses physical (8 items), emotional (5 items), social (5 items), and school functioning (5 items). A 5-point response scale is used (0 = never a problem; 4 = almost always a problem). Items were reverse scored and linearly transformed to a zero to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0) with higher scores indicating better health-related quality of life. Final HRQoL scores were computed out of 100.



# Part 3 - Child Somatization index (CSI)

CSI is designed to assess somatic symptoms and their severity that do not necessarily require organic aetiology. There were 24 somatic symptoms on the scale. Each item was scaled from 0 (not at all) to 4 (a whole lot) (11). The number of somatic symptoms and the total score (calculated by summing up scores given by each study participant for all 24 symptoms) were taken into account when the final score was calculated. Total somatization score was computed out of 96. Permission was obtained to use this questionnaire. It was translated to the native language (Sinhala) using standard forward and back translation technique and pretested for Sri Lankan children of the same age group.

# Part 4 - Symptom severity assessment

Symptom severity of abdominal pain and severity of bowel symptoms were assessed using a visual analogue scale (100mm) rating between 0% to 100% where 0% is not having symptoms at all and 100% is having very severe symptoms.

# Methods of data collection

We visited the selected 4 schools before the planned day of data collection. All questionnaires were shown to the principal of the school and class teachers and permission was obtained to conduct the study. We sent the consent forms to the parents of each child selected for the study and consent was obtained. Assent was also obtained from children before distributing the questionnaire.

Questionnaires were distributed under an examination setting. Children were encouraged to fill all the questionnaires independently. Trained research assistants were present in the classroom to supervise children and impartial explanation were provided whenever the need arose.

# **Definitions**

Constipation was diagnosed using Rome III criteria defined by Rasquin *et al* in 2006(12). Children fulfilling 2 out of the following criteria at least once per week for at least 2 months were defined as having constipation.

- a. Two or fewer defecations in the toilet per week
- b. At least one episode of fecal incontinence per week
- c. History of retentive posturing
- d. History of painful or hard bowel movements
- e. History of large diameter stools that may obstruct the toilet

# Ethical approval

Ethical approval for the study was obtained from the Ethical Review Committee of the Sri Lanka College of Paediatricians.

# Statistical analysis

The data were analyzed using EpiInfo (EpiInfo 6, version 6.04 (1996), Centers for Disease Control and Prevention, Atlanta, Georgia, USA and World Health Organization, Geneva, Switzerland). Demographic factors between patients and controls were analyzed using  $X^2$  test. Total HRQoL scores and somatisation scores were compared using unpaired t-test. Multiple logistic regression analysis was used to evaluate independent association between factors identified as significant in the univariate analysis. p< 0.05 was considered as significant.

#### **Results**

# **Demographic Characteristics**

Thousand eight hundred and fifty five questionnaires were distributed and 1792 (96.7%) properly filled questionnaires were included in the analysis. There were 975 (54.4%) males [mean age 14.4years, SD 1.3]. A total of 138 (7.7%) of children had constipation. Constipation was significantly more prevalent in males (9.7% in boys vs.5.2% in girls, p<0.0001). Those who did not satisfy the criteria for a diagnosis of constipation were used as controls.



# Health related Quality of Life in children with constipation

**Table 1** shows the mean HRQoL scores in children with constipation and controls. Children with constipation had lower HRQoL scores than controls in all 4 domains (physical, emotional, social and school functioning). The mean overall HRQoL scores of children with constipation and control are illustrated in **Figure 1**.Mean HRQoL of boys with constipation (76.5) does not significantly differ from that of girls with constipation (81.1) (p=0.11).

Quality of life domains	Constipation ( <i>n</i> =138)		Controls ( <i>n</i> =1654)		<i>p</i> value*
	Mean	SD	Mean	SD	_
Physical functioning	83.6	15.6	91.4	10.9	< 0.0001
Emotional functioning	73.6	23.1	82.7	17.2	< 0.0001
Social functioning	85.0	18.3	92.7	11.3	< 0.0001
School functioning	75.0	20.6	82.5	16.6	< 0.0001
Overall quality of life score	79.6	15.4	88.0	10.5	< 0.0001

# Table 1 – Health related quality of life scores for children with constipation and controls

\* Unpaired t-test

**Figure 2**compares the mean HRQoL scores of children suffering from constipation who had fecal incontinence with those who do not have fecal incontinence. The data clearly indicate that children with constipation and fecal incontinence have lower HRQoL than children with constipation alone (p=0.02).

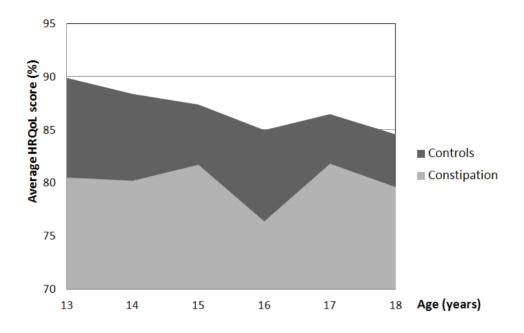
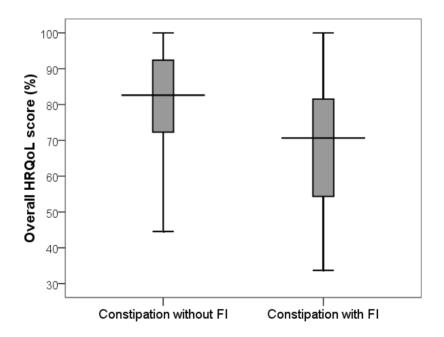
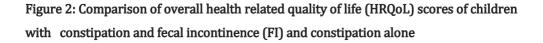


Figure 1: Comparison of average health related quality of life (HRQoL) scores in children with constipation and controls according to age







**Table 2** shows the factors related to HRQoL in children with constipation. Patient perceived severity of abdominal pain and severity of bowel symptoms showed significant negative correlation with total HRQoL scores. In addition, total somatization score was also found to be negatively correlated with HRQoL.

	Correlation	<i>p</i> value	
	coefficient*		
Age	-0.12	0.15	
Severity of abdominal pain/discomfort	-0.22	0.01	
Frequency of abdominal pain/discomfort	-0.05	0.55	
Severity of bowel symptoms	-0.22	0.01	
Frequency of defecation	0.08	0.61	
Total somatization score	-0.47	< 0.0001	

\* Pearson correlation coefficient

# Somatization scores in children with constipation

**Table 3** compares all 24 items of the child somatization inventory between children with constipation and controls. Except vomiting, scores obtained for all other somatic symptoms were higher in children with constipation. The mean somatization score of males with constipation (15.9) is not significantly different from that of females with constipation (15.6) (p=0.9).

Items	Constij	pation	Cont	rols	p value*
	( <i>n</i> =138)		( <i>n</i> =1654)		-
	Mean	SD	Mean	SD	
Headache	1.5	1.1	1.3	1.0	0.007
Faintness or dizziness	0.5	0.8	0.4	0.7	0.01
Pain – heart of chest	0.7	1.0	0.5	0.8	0.002
Low energy, slowed down	1.0	1.2	0.5	0.9	< 0.0001
Pain –lower back	0.9	1.3	0.5	0.9	< 0.0001
Sore muscles	0.8	1.1	0.4	0.8	< 0.0001
Trouble getting breath	0.7	1.2	0.3	0.7	< 0.0001
Hot or cold spells	0.8	1.0	0.4	0.8	< 0.0001
Numbness or tingling	0.9	1.1	0.5	0.8	< 0.0001
Weakness	0.8	1.0	0.5	0.9	< 0.0001
Heavy feeing in arms, legs	0.5	1.0	0.2	0.6	< 0.0001
Nausea, upset stomach	0.8	1.0	0.3	0.7	< 0.0001
Constipation	0.7	1.0	0.2	0.5	< 0.0001
Loose bowel movements, diarrhea	0.4	0.8	0.2	0.5	< 0.0001
Pain – stomach	1.1	1.1	0.7	0.9	< 0.0001
Heart beating too fast	0.7	1.0	0.3	0.7	< 0.0001
Difficulty in swallowing	0.3	0.8	0.2	0.5	0.001
Losing voice	0.4	0.9	0.2	0.6	0.001
Blurred vision	0.6	1.0	0.3	0.7	< 0.0001
Vomiting, throwing up	0.4	0.8	0.2	0.5	< 0.0001
Feeling bloated, gassy	0.4	0.8	0.2	0.6	< 0.0001
Food makes you sick	0.2	0.5	0.1	0.4	0.09
Pain – Knees, elbows, joints	0.5	1.0	0.3	0.7	< 0.0001
Pain – arms, legs	0.9	1.2	0.6	0.9	< 0.0001
Total somatization score	16.0	12.1	8.3	8.6	< 0.0001

# Table 3- Somatization scores for children with constipation and controls

\* Unpaired t-test



# **Discussion**

Studies assessing HRQoL and somatization in children with chronic constipation are sparse. The main findings of the current study are, a) a significantly lower HRQoL in children with chronic constipation in all four main domains (physical, social, emotional and school functioning); b) significantly higher somatization scores in affected children and c) significant negative correlation between HRQoL and scores obtained for somatization and severity of symptoms.

There were no published community based data on HRQoL in children with constipation for us to make a direct comparison of our results. However, two previous studies have assessed the quality of life in children with chronic constipation using PedsQL questionnaire in tertiary care centres and reported similar results. Youssef and co -workers (7) have assessed HRQoL in 80 children with chronic constipation and compared them with other chronic gastroenterological problems such as inflammatory bowel disease, gastroesophageal reflux and healthy controls. According to their results, the impact of constipation on quality of life of affected children is similar to that of inflammatory bowel disease. Inflammatory bowel disease is recognized as an entity with severe intestinal inflammation, and a myriad of intestinal and extra-intestinal symptoms. These comparative results indicate severe ramifications of constipation on HRQoL in children. In another study, children with slow transit constipation were found to have lower total quality of life scores than healthy children (5). The quality of life scores reported in children with constipation in two previous studies mentioned above were lower than that reported in the current study. Both of these studies were conducted in tertiary care centers. Children included in these studies are more likely to have severe symptoms and more complication, and therefore, lower HRQoL scores than in the present school based study.

Lower HRQoL is also reported in other functional gastrointestinal disorders. A recent school based study from Japan has reported significantly lower quality of school work in children with irritable bowel syndrome, aerophagia and cyclic vomiting. They failed to find such difference in children suffering from constipation (13). The low prevalence of constipation (0.3%) in the cohort included in this study may partly contribute to the results.

Fecal incontinence or episodic leaking of feces into the underwear is a troublesome symptom frequently associated with chronic constipation. This certainly causes social embarrassment, rejection by peers, and emotional problems in children (14). It has also been shown that children with fecal incontinence are vulnerable for bullying (15,16). Therefore, it is not surprising that the results of the current study show significantly lower HRQoL in children with constipation and fecal incontinence compared to constipation alone. In contrast to our results Youssef and co-workers (7)did not find a significant decrement in mean HRQoL scores in children with fecal incontinence. Using a different questionnaire (Defecation Disorder List) to measure HRQoL, a Dutch study has shown lower HRQoL scores in social and emotional domains for children with constipation associated fecal incontinence. However, the validity of the instrument used in that study was not proven beyond doubts and hence the reliability of the results is questionable (16).

To our knowledge, this is the first study that has assessed the somatization in children with constipation. We found significantly higher mean somatization score in our children with constipation than in controls. Mean somatization scores, obtained for each individual somatic symptom assessed, were significantly higher in children with constipation than that of controls, expect for vomiting (Table 3). In previous studies we have reported presence of somatic symptoms in children with abdominal pain predominant functional gastrointestinal diseases and aerophagia (17-19).

Presence of other somatic symptoms and their severity significantly contribute to the suffering of the affected children and hence to the poorer quality of life. In our study, a significant negative correlation between HRQoL and scores obtained for somatization index, severity of abdominal pain and bowel symptoms were shown up. Somatic symptoms such as aches, pains and altered bodily function have a significant impact on daily activities hence on HRQoL. In addition, abdominal pain and bowel symptoms can really be bothersome and contribute to escalation of suffering in children with constipation. None of the previous studies have assessed the factors related to lower HRQoL in children with constipation for us to make a comparison.



In this study we have included a large number of children and adolescents with constipation to give an adequate power to draw conclusions. The questionnaires on HRQoL, gastrointestinal symptoms and somatization are internationally accepted tools. They have been pretested and validated in Sri Lankan settings before using in this study. The main limitation in this epidemiological survey is that we did not conduct a physical examination of study participants and although we used Rome III criteria to diagnose constipation we did not use the criterion on presence of fecal masses in the rectum. Furthermore, we did not attempt to exclude possible organic diseases leading to constipation. However, organic causes presenting as constipation are rare and only seen in a minority of affected children (20). In this study, we used a generic questionnaire to assess HRQoL that is not specific for constipation. Generic questionnaires like PedQL has a great ability to detect the global impact of a disease on psychological, social, physical and school related aspects of a child. Some have argued that generic quality of life lacks precision and sensitivity to identify important effects of distinctive symptoms of functional constipation such as faecal incontinence (16). A precise instrument to assess HRQoL in children with defecation disorders is yet to be developed.

In conclusion, we found that children with chronic constipation had a lower HRQoL and higher degree of somatization than controls. Somatization, severity of abdominal pain, and severity of bowel symptoms were significantly associated with decrement of HRQoL. Our findings indicate deleterious ramifications of chronic constipation on quality of life of affected children. These issues need to be addressed during clinical evaluation of children with constipation to understand the impact of the disease on the life of the affected children and to provide optimal care for them.

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Association between child maltreatment and constipation: a school based survey using Rome III criteria

# CHAPTER

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# Abstract

#### Background

Child abuse leads to multiple physical and psychosomatic sequel. Aim of this study was to evaluate the association between child abuse and constipation among school children.

#### Methods

Children aged 13-18 years were selected from four semi-urban schools in Gampaha district, Sri Lanka. A self-administered, questionnaire was used for data collection. Information regarding socio-demographic factors and gastrointestinal symptoms, child abuse and somatisation were collected. Constipation was diagnosed using Rome III criteria.

#### Results

A total of1792 children were included in the analysis [males 749 (5 4.9%), mean age 14.4 years, SD 1.3 years]. Hundred and thirty eight(7.7%) fulfilled Rome III criteria for constipation. The number of children exposed to physical, emotional and sexual abuse, were respectively 438 (24.4%), 396 (22.1%) and 51 (2.8%). Prevalence of constipation was significantly higher in those exposed to sexual (5.8% vs 2.6% p=0.03), emotional (40.9% vs 20.8%, p<0.0001) abuse, and physical abuse (41.6% vs. 23.2%, p<0.0001). Mean somatisation score was higher in the total group of abused children with constipation (mean 18.6, SD 12.5) compared to those without (mean 13.9, SD 12.3) (p=0.027). Children with a history of abuse did not seek healthcare more often than children without this history. Patient perceived severity of bowel symptoms were higher in children with physical (23.7 vs 19.7 p= 0.001) and emotional (25.4 vs 19.3 p<0.0001) abuse.

# Conclusions

Childhood constipation shows a significant association with physical, sexual and emotional abuse. Children with constipation complain of more somatic symptoms and bowel symptoms when they are exposed to abuse.

# **Background**

Child maltreatment is a major public health and social-welfare problem with a global dimension (1). It has a deleterious effect on physical and mental health of victims throughout their lives. Maltreatment is defined as all forms of physical, sexual and emotional ill treatments and neglect that result in actual or potential harm to the child's health, development or dignity (2).Prevalence of child abuse is significantly high in both developed and developing countries. In the developed world 4-16% of children are physically abuse, and 5-10% children are exposed to penetrative sexual abuse and 10% are neglected or psychologically abused (1). In the developing world the rates of psychological and physical abuse are 83% and 64% respectively (3).Although psychological and physical consequences of child maltreatment are studied in detail, association between abuse and gastrointestinal illnesses have been under-recognized in pediatric research.

Studies have clearly shown that abuse as a child increases the vulnerability of developing functional gastrointestinal diseases (FGIDs) including functional dyspepsia and irritable bowel syndrome (IBS) in adults (4,5). These patients have more intense symptoms, poor status of health and higher healthcare utilization (6). In addition, detailed physiological studies have shown that adults suffering from IBS with a history of abuse have abnormalities in fMRI and hypothalamo-pituitary –adrenal axis (HPA axis) (7,8).These findings indicate long term repercussions of abuse on physiology of bodily function in individuals. However, all these studies in adults inquire about child abuse as a retrospective event. Although there is converging evidence showing a significant association between abuse and chronic pain in adults (9), others have questioned the relationship between two entities (1).

Nonetheless, there is a clear lack of evidence evaluating the association between child maltreatment and development of FGIDs in children. Van Tilburg et al. have shown that abused children had developed unexplained abdominal pain during childhood (10). Furthermore, two hospital based surveys in psychiatric clinics have also illustrated that fecal incontinence is commonly associated with sexual abuse in children (11,12).

Constipation is common in children and adolescents across the world (13). Previous studies have suggested low socio-economic status, living in war zones, consumption of junk food and diet low in fiber are potential contributory factors for constipation (14-17). We have previously shown that constipation and fecal incontinence are associated with stressful life events (18). There is a large body of evidence that child maltreatment leads to post traumatic stress disorders (19). Therefore, it is possible that these events can contribute to development of constipation.

Somatization is a common clinical issue in FGID patients. Studies among adults have also clearly shown that abuse history was associated with more somatic symptoms (7).Association between these factors has not been studied in children.

In this study we specifically aimed to assess a) an association between history of child maltreatment and constipation in children and adolescents b) the impact of child maltreatment on somatization in children with constipation and c) the relationship between abuse and healthcare consultation in children with constipation.

# <u>Methods</u>

#### Study Type and subjects

This was a cross-sectional survey conducted in Gampaha district of Sri Lanka. Four schools of the district were randomly selected from 427 of schools. From each school, all classes from grade 9 to 12 were selected. All children in these classes were invited to take part in the study.

#### Conduction of data collection

Researchers visited all selected schools, the questionnaire was discussed with school authorities and permission was obtained to conduct the study. All children in the selected classes and their parents/guardians received an invitation to participate the study. Consent and ascent were obtained from parents and children respectively. Participants were asked to fill all parts of the survey independently. Four research assistants were available in the classroom to supervise children.



# Questionnaires

We used previously validated questionnaires for data collection. They were in native language (Sinhalese).

# 1. Rome III questionnaire for functional gastrointestinal disease

This questionnaire was developed based on Rome III diagnostic questionnaire for pediatric FGIDs (20). We used parts A and B (section on abdominal pain related FGD) and part C (section on bowel habits) of the questionnaire.

# 2. Questionnaire on child maltreatment

The questionnaire on child maltreatment included questions to identify all 3 main domains of child abuse (physical, sexual and psychological domains). The prevalence of abuse of any form was considered positive if a participant answered affirmatively to the type of abuse.

# 3. Childhood somatization inventory (CSI)

CSI is designed to assess somatic symptoms and their severity that do not necessarily require organic etiology. There were 24 somatic symptoms on the scale ranging from 0 (not at all) to 4 (a whole lot). The number of somatic symptoms and the total score (calculated by summing up scores given by study participant for all 24 symptoms) were taken into account when the final score was calculated (21).

# 4. Symptom severity assessment

Symptom severity of abdominal pain and severity of bowel symptoms were assessed using a visual analogue scale (100mm) rating between 0% to 100% where 0% is not having symptoms at all and 100% is having very severe symptoms.

# 5. Healthcare consultation

In this section, children were inquired about their visit to a doctor during the past 2 months specifically due to constipation.

# **Diagnosis of constipation**

Constipation was diagnosed using Rome III criteria (22). Children fulfilling 2 out of following criteria at least once per week for at least 2 months were diagnosed as having constipation.

- a. Two or fewer defecations in the toilet per week
- b. At least one episode of fecal incontinence per week
- c. Retentive posturing
- d. Painful or hard bowel movements
- e. Large diameter stools that may obstruct the toilet

# Definition of child abuse

Child abuse (physical, sexual and emotional) were defined using standard definitions (23).

# Ethical approval

Ethical approval for this study was obtained from the Ethical review committee of the College of Pediatricians of Sri Lanka.

# Statistical analysis

The data were analyzed using EpiInfo (EpiInfo 6, version 6.04 (1996), Centers of Disease Control and Prevention, Atlanta, Georgia, USA and World Health Organization, Geneva, Switzerland). p< 0.05 was considered as significant. Logistic regression analysis controlling for other demographic variables was conducted to determine the association between types of abuse and constipation Fisher exact test was used to analyze the association between categorical variables and constipation.

# <u>Results</u>

# Sample characteristics and Prevalence of constipation

We received 1855 questionnaires of which 1792 (96.7%) were properly filled and were included in the analysis. Of them, 975 (54.4%) were males [mean age 14.4 years, range 13-18 years, SD 1.3]. According to the Rome III criteria, 138 (7.7%) children had constipation. Constipation was more prevalent among boys (68.8% vs. 31.2% in girls,

p<0.0001). Children not meeting the Rome III criteria for constipation (1654) served as control group.

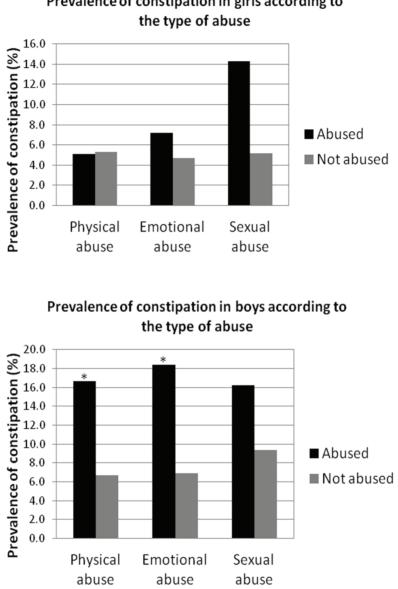
# Prevalence of abuse in constipation and control subjects

In this sample 438 (24.4%) children were physically abused, 396 (22.1%) were emotionally abused and 51 (2.8%) were sexually abused. Physical (65.3% vs. 34.7%,p<0.0001) and sexual abuses (56.6% vs. 43.4% p=0.008) were more common among boys (Figure 1). Compared with controls, children with constipation had a significantly higher prevalence of physical, sexual and emotional abuse (Table 1). Physical and emotional abuse were the strongest predictors of developing constipation (p<0.0001).

Children with	Controls	
constipation		<i>p</i> value*
<i>n</i> (%)	<i>n</i> (%)	
57 (41.6%)	381 (23.2%)	< 0.0001
56 (40.9%)	340 (20.8%)	< 0.0001
8 (5.8%)	43 (2.6%)	0.03
	<b>constipation</b> <b>n (%)</b> 57 (41.6%) 56 (40.9%)	n (%)         n (%)           57 (41.6%)         381 (23.2%)           56 (40.9%)         340 (20.8%)

Table 1: Constipation and child abuse

\*Chi-square test



# Prevalence of constipation in girls according to

\*P<0.05 *X*<sup>2</sup> test



# Symptom severity of constipation and abuse

The association between patient perceived severity of bowel symptoms and abuse are included in **Table 2.** Children with a history of physical and emotional abuse have more severe symptoms than children who had not exposed to abuse.

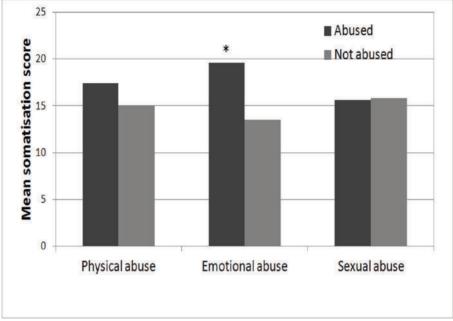
Type of abuse	Abused	Not abused	p value*
	Mean (SD)	Mean (SD)	
Physical abuse	23.7 (23.0)	19.7 (21.0)	0.001
Emotional abuse	25.4(22.6)	19.3 (21.1)	< 0.0001
Sexual abuse	26.4 (21.6)	20.6 (21.5)	0.05

Table 2: Patient perceived severity of bowel symptoms according to child abuse

\*Unpaired t-test

# Somatization in children with abuse and constipation

**Figure 2** shows mean somatization scores of children who faced the main 3 types of abuse. Among children with constipation, the somatization index was higher in those who experienced emotional abuse (19.8 vs. 13.5 p=0.004). Somatization index was higher in the total group of abused children with constipation (mean score 18.6, SD 12.5) compared to those without (mean score 13.9, SD 12.3) (p=0.027).



\*P<0.05 unpaired t-test

# Figure 2: Mean somatization score according to the type of abuse in children with constipation

# Healthcare Consultation for constipation in children with abuse

**Table 3** assess the association between child abuse and healthcare consultation in children with constipation. Prevalence of healthcare consultation was higher in children exposed to physical and emotional abuse and lower in those exposed to sexual abuse, than children not abused, but this was not statistically significant (p>0.05).

Type of abuse	Abused	Not abused	<i>p</i> value*	
	<i>n</i> (%)	n (%)		
Physical abuse	21 (36.8%)	21 (26.3%)	0.26	
Emotional abuse	22 (39.3%)	20 (24.7%)	0.35	
Sexual abuse	2 (25.0%)	37 (29.4%)	1.00	

\*Chi-square test

# **Discussion**

To the best of our knowledge, this is the first study assessing the association between constipation and child maltreatment. We found that children with a history of abuse have a higher tendency to develop constipation during childhood. In addition, children with constipation develop more somatic symptoms and severe bowel symptoms when they exposed to abuse.

Child abuse is a problem across the globe. In developed countries, every year about 4-16% of children are physically abused, one in ten is psychologically abused and 5-10% are exposed to penetrative sexual abuse (1). Exposure to abuse as a child has far reaching consequences such as psychological maladjustments, drug and alcohol misuse, risky sexual behavior, obesity and criminal behavior (1). However, gastrointestinal consequences of child abuse have never been a research priority in pediatric literature. In this study, we found that child maltreatment is significantly associated with constipation in children. In accordance with an earlier study, in the current study also, constipation was more prevalent among boys (14). We also noted high prevalence of physical and sexual abuse in boys. Therefore, the higher prevalence of abuse might have contributed to higher prevalence of constipation among them.

We also found that constipated children, exposed to abuse, have much severe bowel symptoms than children not exposed to such events. This association was much more significant in children faced to physical and emotional abuse. Small number of sexually abused children among the constipated group would have contributed to the lack of significant difference in that group. This finding indicates the deleterious effects of abuse on not only develop constipation but also its significant contribution to severity of bowel symptoms.

Community based studies to assess the association between child abuse and defecation disorders in children are non-existing. However, one clinic based study assessed the predictive value of fecal soiling as an indicator of child sexual abuse. It compared healthy controls, children attending to a psychiatry unit and children experienced sexual abuse. The soiling rate in the abused group differed significantly from healthy controls but not from the psychiatric group. Similar rates of soiling were reported among abused children with and without penetration and the psychiatric sample (12). Another study noted that 36% of 23 children with a history of sexual abuse had faecal soiling (11). However, lack of a control group in this study makes it difficult to interpret the results. In addition, several studies among adults have shown a possible association between abuse as a child and development of IBS later in life (24,25).

Underlying neurobiological mechanisms for this phenomenon has also not received much attention from pediatric researchers. Exposure to abuse generates significant psychological stress both acutely and in long term. Stress has a significant impact on the gastrointestinal tract. We have previously shown that exposure to home and school related stress is a significant risk factor in developing constipation in children (18). Animal studies have shown exposure to stress predispose them to develop stress-induced visceral hypersensitivity (26), altered defecation (27), intestinal mucosal dysfunction (28) and alterations in HPA axis (29). The HPA axis has been implicated in the pathophysiology of post-traumatic stress disorders in children (30,31). In general, traumatized children show significantly elevated cortisol levels compared with control groups. A study of children with post-traumatic disorders living in stable situations showed increased levels of 24-hour urinary cortisol in comparison to healthy controls (32).

In addition, studies in adults with IBS also revealed stress induced alterations in gastrointestinal motility, visceral sensitivity, autonomic dysfunction and hypothalamopituitary-adrenal dysfunction (33). Several fMRI studies have also shown that abuse leads to activation of anterior midcingulate and posterior cingulate cortex with deactivation in the anterior cingulated cortex supragenual region an area associated with down-regulation of pain signals in adults with FGIDs including constipation (7).These evidence suggests that abuse leads to alteration of both hypothalamopituitary-adrenal axis and brain-gut axis that predispose individuals to develop FGIDs. Although these studies are from adults, there is no reason to believe that the mechanisms will differ when applied to children. Therefore, it is likely that in children exposed to stress induced by abuse, these pathophysiological mechanisms may play an important role in initiating and perpetuating symptoms of constipation. Somatic symptoms are an integral part of FGIDs in children and adults. We have previously shown that children with abdominal pain predominant functional gastrointestinal diseases (34) and aerophagia (35) had number of somatic symptoms. Creed and co-workers found higher level of somatization in adults with IBS when there was a history of sexual abuse in the past (36).We found higher mean somatization scores among children with constipation when there was a history of abuse than children without a history of abuse. These findings suggest development of adverse health effects of child abuse in children is diverse and not only psychological.

In this study children with constipation who experienced abuse did not seek medical care for their symptoms more frequently when compared with those who did not have a history of abuse. Contrary to this, studies among adults have noted history of abuse is associated with more healthcare seeking for FGIDs such as IBS (37). In Sri Lanka, parents take children to medical consultation. Our study sample mainly consists of adolescents who are independent and may be not discussing their bowel habits with parents. Therefore, parents may not be aware that their children are suffering from constipation. Previous studies have shown that most of the time perpetrator of abuse is a close family member (38). It may also be possible that strained relationship due to repeated abuse by parents prevent children discussing their intimate problems such as bowel symptoms with them delaying seeking healthcare.

Potential limitations of this study include possibility of recall bias. Nevertheless, it may be low as we only questioned about recent events up to 2 months in the questionnaire. Under-reporting of both abuse and bowel symptoms due to shame may also be a potential limitation. However, the questionnaire was anonymous and this was explained to the participants. Lack of physical examination on study subjects is another limitation which we could not overcome in this large epidemiological survey.

# **Conclusions**

In conclusion, we found that physical, sexual and emotional abuses are more prevalent in children suffering from constipation. In addition, somatization scores are higher in children with constipation who have concomitant history of abuse. In this light, it is recommendable that history of abuse needs to be inquired in children and adolescents with a history of severe constipation. Furthermore, addressing these issues by therapeutic interventions such as counselling and targeted cognitive-behavioral therapy will improve the overall management of chronic constipation and psycho-social wellbeing of children.

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# Fecal Incontinence

Constipation-associated and Nonretentive Fecal Incontinence in Children and Adolescents: An Epidemiological Survey in SriLanka

# CHAPTER

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# <u>Abstract</u>

#### **Objectives:**

Fecal incontinence (FI) has a great effect on quality of life of children with the condition. Epidemiological data related to FI from developing countries are sparse. Studies differentiating functional nonretentive and retentive (constipation-associated) FI are not available.

# Patients and Methods:

This was an island-wide, cross-sectional study. Information was collected from children (ages 10–16 years) from 5 randomly selected schools in 3 geographically and socioeconomically different provinces in Sri Lanka, using a validated, self-administered questionnaire. FI was defined as defecation into places inappropriate to the social context, at least once per month, for a minimum period of 2 months. Constipation was diagnosed using Rome III criteria.

# Results:

A total of 2770 questionnaires were distributed and 2686 (97.0%) were included in the analysis. Of them, 55 (2.0%) had FI (mean age 11.96 years, SD 1.59 years, 43 [78.2%] boys). Forty-five (81.8%) had constipationassociated FI and 10 (18.2%) had nonretentive FI. The highest prevalence of FI was seen in children aged 10 years (5.4%). A significant negative correlation was observed between age and the prevalence of FI (r¼0.893, P¼0.007). FI was significantly higher in boys (boys 3.2 %, girls 0.9%), those exposed to recent school- and family-related stressful life events, and those from lower social classes (P<0.05).

# Conclusions:

FI is not uncommon among children and adolescents of 10 to 16 years of age in Sri Lanka with a male predilection. Some predisposing factors, such as exposure to stressful life events and being bullied at school, which are similar to those described in the literature for FI, could be clearly recognized.

# **Introduction**

Fecal incontinence (FI) is defined as involuntary loss of formed or liquid stools into the child's underwear after developmental age 4 years (1). Prevalence of FI varies from less than 1% to more than 4% in children around the world (2–6). It is more common among boys (7), younger children, and those from lower socioeconomic background (4).

Even though FI is uncommon, it is worrisome to the affected children, their families, and physicians who manage them. Children with FI leak stools into their underwear, smell bad, and have social isolation and excessive dependency. They commonly have behavioural, emotional, and upbringing problems (4,5,8). Moreover, they often have learning difficulties and frequently face child abuse (4). In addition, anxiety and depression are more common among these children (9). Parents are also frustrated because they may have to compromise family activities (10). Furthermore, approximately 15% of affected children continue to have symptoms as adults (11).

All of the previous epidemiological data on FI are from the developed countries, and its prevalence in developing countries and Asia is lacking. This study assessed the prevalence of FI in Sri Lankan schoolchildren and adolescents and the factors associated with it.

#### <u>Methods</u>

This was a school-based, island-wide, cross-sectional survey in Sri Lanka. Three provinces were randomly selected out of 9 provinces in the country, and from them, 5 schools were randomly selected from the list of schools. In every selected school, 12 classes were randomly selected from academic years 6 to 11 (2 from each academic year), and all of the children in selected classes (ages 10 – 16 years) were included in the study. Two schools were from the Eastern Province affected by the separatist war.

Details regarding bowel habits during the preceding 2 months (developed from the Questionnaire on Pediatric Gastrointestinal Symptoms) (12) were collected with demographic information, exposure to stressful life events during the previous 3 months, and presence of other symptoms using a validated, self-administered questionnaire (see the online-only questionnaire at http://links.lww.com/MPG/A18). The questionnaire was in the native language (Singhalese). School administration and parents were informed before the study and consent was obtained. The questionnaire was administered in examination setting to ensure confidentiality and privacy and was filled out under the guidance of research assistants.

FI was defined as defecation into places inappropriate to the social context, at least once per month, for a minimum period of 2 months (13). Nonretentive fecal incontinence (NRFI) and constipation were defined using Rome III criteria (13). Because this study was a questionnaire-based epidemiological study, we did not perform rectal examinations in children.

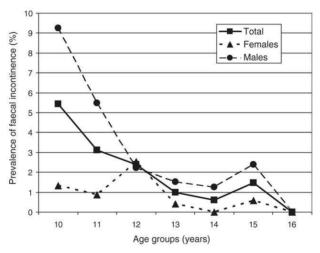
Data were analyzed using x<sup>2</sup> and Fisher exact test using EpiInfo (EpiInfo 6, version 6.04 [1996] Centers for Disease Control and Prevention, Atlanta, GA, and World Health Organization, Geneva, Switzerland). P<0.05 was taken as significant. Multiple logistic regression analysis was performed on variables that were found to have significant association. This study protocol was approved by the Ethical Review Committee of the Sri Lanka College of Pediatricians.

# Results

A total of 2770 questionnaires were distributed, of which 2686 (97.0%) were included (mean age 13.2 years, SD 1.7 years, 1362 [50.7%] boys). A total of 84 (3%) incompletely filled-out questionnaires were excluded from the analysis.

# Prevalence of FI

Fifty-five (2.0%) subjects had FI (mean age 12.0 years, SD 1.6 years, 43 [78.2%] boys). Forty-five (81.8%, prevalence of 1.7%) had constipation-associated FI and 10 (18.2%, prevalence 0.4%) had NRFI. The highest prevalence was seen in children aged 10 years (5.43%) **(Fig. 1)**. A significant negative correlation was observed between age and the prevalence of FI (r=0.89 P=0.007). According to logistic regression analysis, FI was significantly higher in boys (adjusted odds ratio [OR] 3.88, 95% confidence interval [CI] 1.90–7.94, P<0.0001). The boy-to-girl ratio of FI was 3.6:1. Children fulfilling the criteria for FI were compared with 2631 children without FI (controls).



 $\ensuremath{\textit{FIGURE 1}}$  . Prevalence of fecal incontinence according to age and sex.

# Sociodemographic Variables and FI

**Table 1** shows the association between FI and demographic characteristics. Multiple logistic regression analysis shows that FI was significantly higher in children with unskilled and unemployed fathers (adjusted OR 1.22, 95% CI 1.08–1.39, P=0.001), whereas it was not so in children living in the war-affected area (adjusted OR 0.55, 95% CI 0.29–1.07, P=0. 077).

Variable	Fecal incontinence	Controls	
	(n=55) no.(%)	(n=2631) no (%)	
Sex			
Male	43(78.2)*	1319(50.1)	
Female	12(21.8)	1312(49.9)	
amily size			
Only child	5(9.1)	211(8)	
2-3 children	37(67.3)	1910(72.6)	
>=4 children	13(23.6)	510(19.4)	
Birth order <sup>†</sup>			
Eldest	22(44)	990(40.9)	
Youngest	14(28)	799(33)	
Other	14(28)	631(26.1)	
Father's social class			
Leading profession(eg: doctor,engineer)	5(9.1)	431(16.5)	
Lesser profession(eg: nurse,teacher)	5(9.1)	285(10.9)	
Skilled nonmanual(eg: clerk)	7(12.8	427(16.4)	
Skilled manual(eg: electrician,mason)	19(34.5)‡	1007(38.6)	
Unskilled unemployed	19(34.5)	461(17.6)	
Not living	-	20	
laternal employmen			
Leading profession	2(3.6)	78(3)	
Lesser profession	3(5.5)	211(8)	
Skilled non- manual	3(5.5)	171(6.5)	
Skilled manual	0	97(3.7)	
Unskilled unemployed	47(85.4)	2071(78.8)	
Mother not living	-	3	
ocation of school			
Urban	30(54.5)	1688(64.2)	
Rural	25(45.5)	943(78.8)	
iving area			
War-affected area	14(25.5)	1068(40.6)	
Other	41(74.5)§	1563(59.4)	

Table 1: Demographic and family characteristics of children with fecal incontinence compared with controls

\*Odds ratio(OR)3.56(95% CI 1.8-7.2). P=0.00007

<sup>†</sup>Families with more than 1 child

<sup>‡</sup>OR 2.46(95% CI 1.35-4.47).P=0.0023.

§OR 2(95% CI 1.05-3.87).P=0.033.

# Association between FI and Exposure to Stressful Events

**Table 2** shows the association between FI and exposure to stressful life events. After multiple logistic regression analysis, exposure to stressful life events (adjusted OR 4.94, 95% CI 1.76– 13.88, P=0.002), being bullied at school (adjusted OR 2.57, 95% CI 1.19– 5.52, P¼0.016), and hospitalization of the child for another illness (adjusted OR 2.74, 95% CI 1.32–5.69, P=0.007) remained significant.

Stressful event	Fecal incontinence	Controls
	(n=55) no.(%)	(n=2631) no.(%)
Exposure to recent stressful Life events		
Yes	50(90.9)***	1757(66.8)
No	5(9.1)	874(33.2)
School-related stressful events		
Change in school	13(23.6)**	263(10)
Suspension from school	2(3.6)**	8(0.3)
Frequent punishment in school	14(25.5)†	156(5.9)
Separation from best friend	18(32.7)	630(23.9)
Sitting for Examination	26(47.3)	909(34.5)
Failure in an examination	15(27.3)***	307(11.7)
Being bullied at school	18(32.7)†	162(6.2)
Family related stressful events		
Sever illness in a family member	20(36.3)†	363(13.8)
Death of a family member	8(14.5)	226(8.6)
Loss of job by parent	5(9.1)*	83(3.2)
Birth of a sibling	13(23.6)+	205(7.8)
Frequent domestic fights	7(12.7)†	61(2.3)
Frequent punishment by parents	14(25.5)†	191(7.3)
Father's alcoholism	7(12.7)**	107(4.1)
Divorce or separation of parents	3(5.5)*	25(1)
Other		
Hospitalization of the child other illnes	ss 21(38.1)†	252(9.6)

#### Table 2: Distribution of responders according to exposure to stressful life events

\*P<0.05, \*\*P<0.01, \*\*\*P<0.001, \*P<0.0001

#### Bowel Habits in Children with FI

**Table 3** compares the bowel habits in children with NRFI and constipation-associated FI. Following multiple logistic regression analysis, bulky stools were significantly less common in those with NRFI (adjusted OR 0.59, 95% CI 0.004–0.79, P=0.032). The bowel habits of all 55 children with FI and controls are also presented in **Table 3**. After multiple logistic regression analysis, painful defecation (adjusted OR 2.53, 95% CI 1.10–5.83, P=0.029), bulky stools (adjusted OR 5.25, 95% CI 2.39–11.53,P<0.0001), retentive posturing (adjusted OR 4.07, 95% CI 1.98 – 8.34, P<0.0001), and blood-stained stools (adjusted OR 9.17, 95 % CI 2.39–11.53, P<0.0001) were significantly more common in those with FI.

	Patients with nonretentive fecal		Patients with fecal incontinence		
	incontinence vs constipation		vs controls		
	associated fecal incontinence				
	Nonretentive	Constipation	Fecal	Controls	
	Fecal	associated fecal	incontinence	(n3631) n	
	incontinence	incontinence	(n=55) n (%)	(%)	
	(n=10)	(n=45)n (%)			
	n (%)				
Defecation frequency					
<3 /week	3 (30)	9 (20)	12 (21.8)**	246 (9.3)	
3-6/week	2 (20)	14 (31.1)	16 (29.1)	300 (11.4)	
Once daily	5 (50)	15 (33.3)	20 (36.4)	1888 (71.8)	
>once a day	0 (0)	7 (15.6)	7 (12.7)	197 (7.5)	
Stool consistency					
Hard	0	6 (13.3)	6 (10.9)	190 (7.2)	
Normal	9 (90)	20 (44.4)	29 (57.2)	2116 (80.4)	
Soft	1 (10)	9 (20)	10 (18.2)	39 (1.5)	
Changing consistency	0	10 (22.2)	10 (18.2)	286 (10.9)	
Large diameter stools	2†(20)	36 (80)**	38 (69.1)***	393 (14.9)	
Retentive posturing	1†(10)	35 (77.8)**	36 (65.5)***	283 (10.8)	
Painful motions	2†(20)	34 (75.6)**	36 (65.5)***	497 (18.9)	
Straining	5 (50)	34 (75.6)	39 (70.9)***	891 (33.9)	
Blood in stools	1†(10	25 (55.6)*	26 (47.3)***	80 (3)	

#### Table 3: Bowel habits of children with fecal incontinence and controls

\*P=0.01,\*\* p<0.001, \*\*\*p<0.00001; X<sup>2</sup> test

<sup>†</sup>symptoms seen occasionally (less than once a month)

#### Other Symptoms Seen in Children With FI

Other gastrointestinal symptoms seen in these patients included abdominal pain, nausea, and vomiting **(Table 4**). Abdominal pain was reported in 30 (66.7%) children with constipationassociated FI and 3 (30%) patients with NRFI. After performing multiple logistic regression analysis, abdominal pain was independently associated with FI (adjusted OR 2.52, 95% CI 1.29–4.91, P=0.007).

		Fecal incontinence vs controls					
	Fecal	incontinence	Controls (n=2631) n (%)		OR (95% CI)	P*	
(n=55) n (%)							
Abdominal pair	1 3	33 (60)	999 (37.9)	2	2.45 (1.38-4.38)	0.001	
Nausea	7	7 (12.7)	156 (5.9)		2.31 (0.94-5.34)	0.04	
Vomiting	1	1 (14.5)	121 (4,6)		5.19 (2.46-10.71)	< 0.0001	
Weight loss	8	8 (14.5)	272 (10.3)		1.48 (0.64-3.29)	0.43	
Loss of appetite		9 (16.3)	333 (12.7)		1.35 (0.61-2.89)	0.54	

Table 4 :Symptoms associated with Fecal incontinence

CI- Confidence intervals OR- Odds ration

\*p X<sup>2</sup> test

#### **Discussion**

In this epidemiological study, we found FI in 2% of children and adolescents. Previous studies from Western countries showed prevalence of FI ranging from 0.8% among 10 to 12 years old to 4.1% in 5 to 6 years old (2,4). In contrast, hospital-based studies have reported higher prevalence of FI (3%–5.7%) (14,15). Much higher prevalence (15%) was reported in obese children (16).

It is of paramount importance to distinguish between retentive FI and NRFI because their management strategies are entirely different (17). The major drawback of all previous studies is that no attempt was made to discriminate between these 2 entities. Constipation-associated FI was 4.5 times more common than NRFI. This indicates the probable significance of constipation in the pathogenesis of FI.

In this study, prevalence of FI was highest at the age of 10 years and showed a significant negative correlation with the age. van der Wal et al (4) have shown a relatively lower prevalence in older children, but failed to report an exact correlation. It is possible that older children may have a better control over their bodily functions including bowel motions. Furthermore, as in previous studies, FI was more common among boys (1,4,14). Prevalence of FI was higher in those from lower socioeconomic background, which is in agreement with a study done among

Dutch children (4). Poor toilet facilities leading to stool withholding and delay in seeking health care are likely contributory factors.

In our study, children exposed to stressful life events were more likely to develop FI. The stressful life events that associated with FI were being bullied at school and hospitalization of the child for other illnesses. According to Joinson et al (5), bullying (both bully and victim) was significantly higher in children who had frequent FI. Bullying is a common problem in schools and occurs in toilets, which could prevent children from using school toilets (18). Similarly, the condition of toilets in Sri Lankan hospitals is unsatisfactory and children admitted to hospitals are likely to withhold stools. In addition, fecal retention associated with bed rest probably contributes to FI in hospitalized children. Emotional stress is known to be associated with other functional gastrointestinal diseases (19,20). It seems likely that stress modulates colonic motility through brain gut axis, leading to pathogenesis of both retentive and NRFI in our study sample.

A previous study has shown a high incidence of FI among children evacuated from London during World War II (21). In contrast to this, we did not find a higher prevalence of FI among children living in war-affected areas. Compared with the previous study, our children were not evacuated from their homes, not living in refugee camps, and experienced no severe disruption to their lifestyle. This has probably reduced the influence of war on their bowel habits.

Bowel habits significantly associated with FI were pain during defecation, bulky stools, and retentive posturing. Unlike in a previous study, we fail to find a significant association betweenFI and stool frequency of fewer than 3 per week (4). In the present study, large-caliber stools and abdominal pain were significantly associated with FI, which is similar to the findings by Levine (14). Another clinical feature associated with FI was blood in the stool, which is most likely to be due to anal fissures caused by chronic constipation. We compared bowel habits of children with retentive FI and NRFI, which has not been reported previously. Largediameter stools, which indicate stool retention, were significantly less common in those with NRFI. We did not find a significant difference in defecation frequency and consistency between these 2 groups.

In this school-based epidemiological study, which involved a large number of schoolchildren, it was not possible to perform rectal examination. Therefore, we were restricted to use only symptombased criteria for the diagnosis of constipation-associated FI. Similar to this study, most of the previous epidemiological surveys had used only symptom-based criteria to diagnose constipation (22) and FI (4,5). Even though physical examination is recommended in diagnosis of defecation disorders, previous studies have reported low rates of rectal examination in children with FI (23). The value of rectal examination in pediatric defecation disorders has not been reported previously, but in elderly patients, digital rectal examination was reported to be unreliable as an indicator of constipation (24).

The main problem we encountered when diagnosing constipation using Rome III criteria was the requirement of weekly symptoms. Three children with defecation frequency of less than 3 per week also had FI once per month, which satisfy criteria for FI, but not sufficient to diagnose constipation-associated FI. None of them had any other symptom related to fecal retention including large-diameter stools, painful defecation, and stool-withholding behavior. In previous studies, the presence of large-diameter stools had been considered the best indicator of fecal retention (25) and this symptom was not present in any of these 3 children. Furthermore, all 3 of them had complete bowel evacuation to their underwear, not just staining or leaking small amount of stools, which indicate stool retention. Therefore, they were diagnosed as having NRFI.

#### **Conclusions**

Two percent of schoolchildren and adolescents, aged 10 to 16 years, are experiencing FI. The majority of them have constipation-associated (retentive) FI. NRFI is relatively uncommon in children. FI is more common in boys, those from low socioeconomic background, and those who are exposed to stressful life events.

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# Summary and future perspectives

#### Summary and future perspectives

Childhood defecation disorders specially constipation is a widely prevalent disease in children and is threatening to become a global public health problem. In certain part of Asia almost one third of school children are suffering from chronic constipation. Although the pathophysiology of constipation is not known to the precision, there seems to be associations with significant number or socio-cultural factors. Several studies in the past have shown association between constipation and stress, adverse life events including abuse, urbanization and living in societies that are torn apart by civil wars and riddled by poverty. Some of the other functional gastrointestinal diseases such as irritable bowel syndrome are of no exception to this phenomenon. Epidemiological drivers of this group of diseases are largely unknown and thus limits the possible preventive strategies. Furthermore, the healthcare consultation patterns of children with constipation and effects of constipation on children living in the community are also ill understood. Therefore, this thesis is dedicated to study epidemiological factors, healthcare consultation, and quality of life of children with constipation.

In the first part of the introduction, (Chapter 1) we reviewed the current knowledge on epidemiology, risk factors, clinical evaluation, investigations and management of defecation disorders (constipation and functional nonretentive fecal incontinence) in children. We found that constipation is prevalent in many continents. Novel data emerging from both developed countries, emerging economies and developing countries from Asia have proved that constipation is not any more a disease of the western civilization or diseases of affluence. The chapter also identified the possible predisposing factors and co-morbidities of constipation. In addition we also reviewed the healthcare expenditure of some of constipation to show the economic impact they can pose on healthcare budgets of both developing and developed countries alike. We also reviewed in detail the clinical assessment of children with both constipation and functional nonretentive fecal incontinence stressing the value of clinical evaluation (history and physical examination including rectal examination) in the diagnosis of functional defecation disorders. We also reviewed the current state of art investigations and management strategies of defecation disorders in children pointing the value of simultaneous use of both pharmacological and non pharmacological management strategies.

Fecal incontinence (FI) is defined as passing stools into the underwear after the development age of 4 years, and basically could be due to functional or organic in origin. Although a lot of research has been done on this area there are hardly and review of this knowledge in the recent literature. **In the second part of the introduction (Chapter 2)**, we reviewed the current data on definition, epidemiology, risk factors, pathophysiology, clinical evaluation, investigation, management and prognosis of children with functional FI. FI is prevalent in both western and eastern societies equally and the majority of children with FI have constipation associated FI and functional nonretentive FI is only found in a minority. Psychosocial factors identified as a major contributory factor to develop FI in children. We also developed a new biopsychosocial model and a new management algorithm for children with FI using published literature.

Constipation is a common disease in children and the estimated prevalence vary between 0.7% in Italy to 29.6% in Hong Kong. Although a significant number of studies were carried out in the west, the epidemiology of constipation in children living in developing countries is largely unknown. Furthermore, most of the studies up to now has studied children of younger age and data on prevalence of constipation among adolescents is sparse. The chapter 3 of the thesis studied the epidemiology and risk factors of constipation in Sri Lankan children. In this study using Rome III criteria, we found 15.3% of children and adolescents in Sri Lanka are suffering from chronic constipation. Several predisposing factors such as living in war affected area, attending to an urban schools and family history of constipation were identified. In addition, we also demonstrated the prevalence of constipation had an inverse relationship with the age. Straining during defecation, blood in stools, and abdominal pain were demonstrated as associated factors of constipation. Therefore, this study demonstrated that constipation is not any more confined to developed world with westernized life style and Sri Lankan children with constipation had number of risk factors and associations which are unique to them.

Stressful live events are a common occurrence in day to day lives of a human being. Children are not exempted from stress. They also face to stressful situations both at home and school. In **chapter 4** we studied the effect of home and school related stresses on developing constipation in children. We found both home and school related stressful life events are associated with constipation in children. It implies that control of these predisposing factors could open up a window to control constipation.

Sri Lanka underwent a 3 distressing decades of civil war. The whole country was in a turmoil with bomb blasting, recruiting children as child solders by the terrorist groups, destruction of properties and killing innocent people in border villages. The public transport system was under constant attacks with claymore mines. These events lead to significant stressful situation in children living in war zones as well as other parts of the county. In **chapter 5** we studied the effects of civil war on constipation in children. The first part of the study was conducted during the civil war and the second part was carried out 2 years after the end of the war. We clearly demonstrated reduction of the prevalence of constipation 2 years after the civil war.

Chronic relapsing and remitting nature of symptoms of constipation demands higher healthcare needs. It is known that children with constipation seek more healthcare than children with other chronic diseases such as asthma and headache and they incur much higher health care expenditure than children with other chronic diseases. However, healthcare consultation patterns among children with constipation in the community are not known. In **Chapter 6** we studied healthcare consultation patterns and their determinants in children and adolescents with chronic constipation. In this study only 3% of children with constipation sought medical help for their symptoms. After analyzing sociodemographic factors, bowel habits, associated symptoms and psychological stress, family history of constipation was the only identifiable significant factor associated with healthcare consultation. Although we expected children with severe symptoms such as FI, and children with more psychological stress would seek more healthcare than the controls there were no significant difference between groups with regards to healthcare consultation. It was possible that our inclusion of older children and adolescents who may be reluctant to discuss their bowel habits with parents led to our observations.

Health related quality of life (HRQoL) is an important concept to study patient's perspective of a disease specially when the disease does not have an objective biological marker. Studies among children with constipation have shown that they have poorer HRQoL than children with organic diseases such as inflammatory bowel disease, Furthermore, children with FGDs such as irritable bowel syndrome, rumination syndrome and aerophagia are known to have array of somatic symptoms in addition to their bowel symptoms. In **chapter 7** we studied the HRQoL and somatic symptoms of children with chronic constipation. In this study children with chronic constipation had significantly poorer HRQoL in all 4 areas of quality of life, namely school, social, physical, and emotional functioning. The HROoL of children with constipation associated FI is much lower than children with constipation alone indicating the repercussion of constant leaking of stools without their bodily control. Children with chronic constipation had a large number of somatic symptoms indicating they also suffer from extraintestinal symptoms like other children with FGDs. More importantly, abdominal pain severity, patient perceived severity of bowel symptoms, low bowel frequency and higher total somatization score were negatively correlated with HRQoL score. These findings indicate deleterious ramifications of constipation on HRQoL of children and necessity of addressing them during clinical evaluation of children with chronic constipation in view to provide optimal care for them.

Child abuse is a major socio-welfare problem. It is well known that child abuse leads to many unwanted health related problems. Studies among adults have recognized the association between adverse life events including abuse as a child and developing irritable bowel syndrome as an adult. Detailed physiological studies have also demonstrated these patients had abnormal functional MRI scan studies demonstrating changes in the amigdaloid nucleus and prefrontal cortex. Although great deal of studies have investigated many aspects of child abuse up to now hardly any published literature discussed its effects on developing functional constipation as a child. **Chapter 8** of the thesis studied the effects of abuse on constipation. We studied a sample of school children using questionnaires on child abuse, somatization, and questionnaire of functional gastrointestinal diseases. Our findings showed that children with constipation had exposure to all 3 forms of child abuse than controls indicating abuse as a possible predisposing factor to develop constipation in children. In addition, patient

preserved severity of bowel symptom score was higher in children with constipation who were abused physically or emotionally compared to children with constipation alone. Finally we also found higher somatization index in the total group of abused children with constipation compared to those without. These novel findings suggest a possible association between child abuse and chronic constipation exposing another deleterious effect of abuse whatever the form it takes. Based on the findings we suggest considering child abuse in children with chronic constipation and inquiring about abuse during the clinical evaluation.

Fecal incontinence is a defecation disorder denotes by frequent leaking of fecal matter into the underwear. Characteristic aroma around children with FI due to constant leaking of faeces, often leads to rejection by peers, and frequent punishments by parents. Children with FI are often the centre piece of family disputes. Therefore, these children have serious repercussions such as anxiety, depression and up bringing problems. Both organic and functional diseases lead to FI. The 2 main reasons for functional FI are constipation associated FI and functional nonretentive FI. Although epidemiology of FI in children was studied by many researchers none of the published literature characterized these 2 entities. Chapter 9 of the thesis studied the epidemiology of FI among school children of Sri Lanka. In this epidemiological survey we included 2586 school children. Prevalence of FI was 2%. The majority (81%) had constipation associated FI and FNRFI was less common among children. When compare bowel habits of these 2 entities, we noted that children with constipation associated FI tend to have more tendency to retain stools compare to children with FNRFI. In addition, demographic factors such as younger age, male gender and poor socioeconomic conditions were identified as predisposing factors to develop FI. Furthermore, we identified psychological stress posed by house hold and school predisposes children to develop FI.

Based on the findings of this thesis we would like to conclude that constipation and fecal incontinence are common problems in Sri Lanka. Many sociodemographic factors predispose children and adolescents to develop defecation disorders. Our finding of inverse relationship between constipation and fecal incontinence with the age indicates younger children have higher predilection to develop defecation disorders. Clinicians who attend to children with constipation also need to aware of associated symptoms such as abdominal pain and bleeding per rectum. In addition, a detail social history would undoubtedly help to identify predisposing factors for defecation disorders in children.

Stressful life events whatever the form it takes predispose children to develop constipation. In addition, stress related to much larger scale problems such as civil war also seems to be associated with constipation. Home related events such as alcoholism, and frequent punishments and school related events such as failure of exam are preventable events. Therefore, the family, school and the society including politicians and decision makers at large, should work towards building a environment safer to growing children and adolescents to prevent them developing constipation.

Low healthcare consultation behavior of children with constipation, even with severe symptoms is worrisome finding specially in a country where healthcare delivery is free of charge. Further studies are needed to unravel more details about this finding. Till such time we strongly recommend to develop an awareness program to educate both school children and their parents to early identification of constipation and bring these children to medical attention as it is well known that delayed presentations would adversely affect the prognosis.

It is important to note that children with constipation in the community have low HRQoL. Long standing symptoms, recurrent nature of constipation and fecal incontinence and associated psychological consequences are likely to influence poor HRQoL in children with constipation. Reduction of physical, mental, and social functioning ultimately affects school performances creating a vicious cycle of psychological stress, aggravating symptoms and spiraling down of HRQoL. Interference with school performances commonly associated with poor education which invariably leads to poor earning capacity as an adult creating a burden to the society at large. Therefore, it is imperative to early identification of these children and treats them according to the standard guidelines to minimize long term repercussions.

The noted association between child abuse and constipation is although novel, a disturbing finding. It indicates deleterious effects of child abuse on the gastrointestinal tract and the brain gut axis. With ever increasing other predisposing factors, child abuse will also contribute to developing constipation in children. We strongly suggest it is high time that paediatric gastroenterologists to join hands with their colleagues such as general pediatricians, psychiatrists and legal medical officers to combat against child abuse to minimize the rising tide of constipation.

#### Samenvatting en toekomstperspectief

Defecatiestoornissen, en met name obstipatie (verstopping) komen veel voor op de kinderleeftijd en dreigen een wereldwijd probleem voor de volksgezondheid te worden. In bepaalde delen van Azië heeft bijna een derde van de schoolgaande kinderen chronische constipatie. De pathofysiologie van obstipatie is nog altijd niet goed opgehelderd, maar er zijn aanwijzingen dat er associaties zijn met een aantal socioculturele factoren. In het verleden hebben verschillende studies namelijk een relatie aangetoond tussen obstipatie en stress. Enkele voorbeelden hiervan zijn seksueel misbruik, verstedelijking en leven in samenlevingen die uit elkaar worden verscheurd door burgeroorlogen en doorzeefd zijn door armoede. Stress speelt ook een belangrijke rol in de pathofysiologie van andere functionele gastro-intestinale aandoeningen, zoals het prikkelbaredarmsyndroom. Aangezien de oorzaken van deze ziektebeelden grotendeels onbekend zijn, is preventie moeilijk. Het is tevens onbekend hoe vaak kinderen met obstipatie gebruik maken van de gezondheidszorg. Dit proefschrift heeft als doel het bestuderen van socio-culturele factoren die mogelijk met obstipatie geassocieerd zijn. Daarnaast wordt getracht om het gebruik van de gezondheidszorg en kwaliteit van leven van kinderen met obstipatie in kaart te brengen.

Het eerste deel van de inleiding (Hoofdstuk 1) beschrijft de huidige kennis omtrent de epidemiologie, risicofactoren, klinische kenmerken, diagnostiek en de behandeling van defecatiestoornissen (obstipatie en functionele non-retentieve feces incontinentie) bij kinderen. Studies laten zien dat obstipatie een wereldwijd probleem is geworden. Niet alleen in Westerse landen komt obstipatie veel voor maar ook in opkomende economieën en ontwikkelingslanden in Azië. Ook worden de zorguitgaven beschreven die het gevolg zijn van obstipatie en wat voor enorme economische impact dit heeft op de begrotingen van zowel ontwikkelingslanden als ontwikkelde landen. Ook wordt in dit hoofdstuk nog eens het belang onderstreept van een uitvoerige anamnese en uitgebreid lichamelijk onderzoek, inclusief het rectaal toucher bij kinderen met obstipatie en functionele non-retentieve feces incontinentie. Tenslotte wordt uitgebreid stil gestaan bij de huidige diagnostiek en het belang daarvan en worden zowel de farmacologische- als de nonfarmacologische behandelingen van kinderen met defecatiestoornissen besproken. Feces incontinentie (FI) wordt bij kinderen vanaf een ontwikkelingsleeftijd van 4 jaar gedefinieerd als ongewild en ongecontroleerd verlies van ontlasting in het ondergoed en kan van functionele of organische aard zijn. Hoewel er reeds veel onderzoek is verricht op dit gebied, ontbreekt het aan systematisch literatuuronderzoek. **In het tweede deel van de introductie (Hoofdstuk 2)**, hebben we de huidig beschikbare literatuur doorzocht naar data over de definitie, epidemiologie, risicofactoren, pathofysiologie, klinische evaluatie, het diagnostisch onderzoek, de behandeling en prognose van kinderen met functionele FI. FI komt in gelijke mate voor in westerse en oosterse landen. Bij de meeste kinderen met FI is sprake van obstipatie-gerelateerde FI, terwijl slechts bij een minderheid sprake is van functionele non-retentieve FI (*functional nonretentive FI, FNRFI*). Psychosociale factoren blijken een grote rol te spelen in de ontwikkeling van FI bij kinderen. We hebben een biopsychosociaal model en behandelingsalgoritme ontwikkeld voor kinderen met FI, gebaseerd op de huidig beschikbare literatuur.

Obstipatie is een veelvoorkomend ziektebeeld bij kinderen en heeft een geschatte prevalentie variërend tussen 0.7% in Italië en 29.6% in Hong Kong. Hoewel een significant aantal studies zijn uitgevoerd in de westerse wereld, is er weinig bekend over de epidemiologie van obstipatie bij kinderen in ontwikkelingslanden. Daarnaast focussen de meeste gepubliceerde studies zich op jonge kinderen en is er weinig informatie beschikbaar over de prevalentie van obstipatie bij jongvolwassenen. Hoofdstuk 3 van dit proefschrift beschrijft de epidemiologie van en risicofactoren voor obstipatie bij kinderen in Sri Lanka. Op basis van de Rome III criteria, was er sprake van chronische obstipatie onder 15.3% van de kinderen en jongvolwassenen. Gevonden predisponerende factoren voor de ontwikkeling van obstipatie waren onder andere het leven in een oorlogsgebied, het gaan naar een school in een stedelijke omgeving en een familieanamnese belast met obstipatie. Daarnaast vonden we een omgekeerde relatie tussen leeftijd en de prevalentie van obstipatie. Persen tijdens de stoelgang, bloed in de ontlasting en buikpijn werden gevonden als factoren geassocieerd met obstipatie. Deze studie toont aan dat obstipatie zich niet beperkt tot de westerse wereld en levensstijl. Daarnaast vonden we een aantal specifieke risicofactoren voor en kenmerken van obstipatie uniek voor de Sri Lankaanse populatie.

Stressvolle *life events* komen regelmatig voor in het dagelijks leven. Kinderen worden hiervan niet ontzien. Zij worden zowel thuis als op school blootgesteld aan stressvolle situaties. In **hoofdstuk 4** hebben we onderzocht wat het effect is van stress, zowel in de thuissituatie als op school, op de ontwikkeling van obstipatie bij kinderen. Wij vonden dat zowel stressvolle *life events* thuis als op school geassocieerd zijn met obstipatie bij kinderen. Dit impliceert dat het onder controle krijgen van deze predisponerende factoren mogelijkheden biedt voor de behandeling van obstipatie.

Sri Lanka is drie decennia lang blootgesteld aan een schrijnende burgeroorlog. Het hele land was in beroering door bombardementen, kinderen die als kindsoldaten werden gerekruteerd door terroristische groeperingen, vernietigingen van eigendomen en het vermoorden van onschuldige mensen in grensgebieden. Het openbaar vervoer werd verwoest door mijnen. Door deze gebeurtenissen werden kinderen die in oorlogsgebieden woonden, maar ook die in andere delen van het land woonden, blootgesteld aan zeer stressvolle situaties.

In **hoofdstuk 5** hebben wij onderzocht wat het effect van de burgeroorlog is op obstipatie bij kinderen. Het eerste deel van de studie werd uitgevoerd tijdens de burgeroorlog, het tweede gedeelte werd twee jaar na afloop van de burgeroorlog uitgevoerd. Er werd een duidelijke daling van de prevalentie van obstipatie aangetoond twee jaar na de burgeroorlog.

De chronische en terugkerende aard van de symptomen van obstipatie eisen grotere behoeften aan gezondheidszorg. Het is bekend dat kinderen met obstipatie meer gebruik maken van de gezondheidszorg en zorgen voor hogere gezondheidszorgkosten, dan kinderen met andere chronische ziekten, zoals astma en hoofdpijn. Echter, de patronen van het zorggebruik van kinderen met obstipatie zijn niet bekend. In **hoofdstuk 6** onderzochten wij de patronen van zorggebruik en de voorspellende factoren hiervan bij kinderen en adolescenten met chronische obstipatie. In deze studie zocht slechts 3% van de kinderen met obstipatie medische hulp voor hun symptomen. Na het analyseren van de sociaal demografische factoren, stoelgang, geassocieerde symptomen en psychologische stress, was obstipatie in de medische familiegeschiedenis de enige significant geassocieerde factor in het zorggebruik. Hoewel we hadden verwacht dat kinderen met ernstige symptomen zoals FI en kinderen met psychologische stress, meer gebruik van gezondheidszorg zouden maken dan kinderen in de controlegroep, waren er geen significante verschillen tussen deze groepen met betrekking tot zorggebruik. Het is mogelijk dat de inclusie van oudere kinderen en adolescenten, die terughoudend zijn in het bespreken van hun stoelgang met ouders, heeft geleid tot onze waarnemingen.

Gezondheid gerelateerde kwaliteit van leven (Health Related Quality of Life, HRQoL) is een belangrijk concept voor het bestuderen van het perspectief van de patiënt op een ziekte, in het bijzonder wanneer de ziekte geen objectieve biologische marker heeft. Onderzoek bij kinderen met obstipatie heeft aangetoond dat deze kinderen een slechtere HRQoL hebben dan kinderen met een organische aantoonbare ziekte, zoals inflammatoire darmziekte. Bovendien rapporteren kinderen met functionele gastrointestinale klachten zoals prikkelbaredarmsyndroom, ruminatiesyndroom en aerofagie naast hun darmklachten vaak een scala aan andere somatische symptomen. In **hoofdstuk 7** onderzochten wij de HRQoL en somatische symptomen van kinderen met chronische obstipatie. In dit onderzoek lieten kinderen met chronische obstipatie een significant slechtere HRQoL zien op alle vier domeinen binnen kwaliteit van leven, namelijk school. sociaal. fysiek en emotioneel functioneren. De HRQoL van kinderen die met obstipatie geassocieerde FI hebben, is veel lager dan bij kinderen zonder bijkomende FI. Dit geeft de weerslag van het constant lekken van feces, zonder lichamelijke controle, aan.

Kinderen met chronische obstipatie hadden een groot aantal somatische klachten, wat er op wijst dat ze, net als kinderen met andere functionele gastro-intestinale stoornissen, ook lijden aan extra-intestinale symptomen. Belangrijker nog, de ernst van de buikpijn, de door de patiënt waargenomen ernst van de buikklachten, een lage defecatiefrequentie en een hogere totale somatisatiescore waren negatief gecorreleerd met de HRQoL score. Deze bevindingen benadrukken de schadelijke gevolgen van obstipatie op de HRQoL van kinderen. Om de zorg te optimaliseren, is het noodzakelijk om hier aandacht aan te besteden tijdens de klinische evaluatie van kinderen met chronische obstipatie. Kindermishandeling is een grote sociaal-maatschappelijk probleem. Het is bekend dat kindermisbruik leidt tot veel ongewenste gezondheidsproblemen. Studies bij volwassenen hebben het verband tussen ingrijpende levensgebeurtenissen op de kinderleeftijd, met inbegrip van kindermishandeling, en de ontwikkeling van prikkelbaredarmsyndroom bij volwassenen aangetoond. Functionele MRI onderzoeken bij deze patiënten hebben aangetoond dat er sprake is van abnormale processen in het brein, met name door veranderingen in de amygdala en de prefrontale cortex. Hoewel een groot aantal studies veel verschillende aspecten van kindermishandeling heeft onderzocht, is er tot nu toe nauwelijks literatuur gepubliceerd die de effecten op de ontwikkeling van functionele obstipatie bij kinderen heeft beschreven. Hoofdstuk 8 van dit proefschrift beschrijft een studie naar de effecten van kindermishandeling op obstipatie. We bestudeerden schoolkinderen met behulp van vragenlijsten over kindermishandeling, somatisatie en functionele gastro-intestinale stoornissen. Onze resultaten toonden aan dat kinderen met obstipatie vaker waren blootgesteld aan alle drie de vormen van kindermishandeling dan kinderen in de controlegroep, wat impliceert dat kindermishandeling mogelijk een predisponerende factor is voor het ontwikkelen van obstipatie op de kinderleeftijd. Daarnaast was de door de patiënt waargenomen ernst van de buikklachten hoger bij kinderen met obstipatie die fysiek of emotioneel waren misbruikt in vergelijking met kinderen waarbij dit niet het geval was. Tot slot vonden we in de groep kinderen die het slachtoffer waren geweest van kindermishandeling ook een hogere somatisatie index bij kinderen met obstipatie, vergeleken met kinderen zonder obstipatie. Deze nieuwe bevindingen suggereren een mogelijk verband tussen kindermishandeling en chronische obstipatie en tonen het schadelijke effect van kindermishandeling aan, ongeacht de vorm van mishandeling. Op basis van deze bevindingen suggereren we dat kindermishandeling moet worden overwogen bij kinderen met chronische obstipatie en dat hier actief naar moet worden gevraagd tijdens de klinische evaluatie.

FI is een defecatiestoornis die zich gekenmerkt door frequent verlies van ontlasting in het ondergoed. De karakteristieke geur die deze kinderen omringt leidt vaak tot afwijzing van leeftijdsgenoten, en bestraffing door ouders. Ook zijn kinderen met FI vaak het middelpunt van geschillen binnen het gezin. Hetgeen resulteert in het voorkomen van angststoornissen en depressies bij deze kinderen.

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Fl kan veroorzaakt worden door zowel organische als functionele ziekten. De 2 belangrijkste redenen voor Fl zijn obstipatie-geassocieerde FI en FNFRI. Hoewel veel onderzoekers de epidemiologie van FI in kinderen bestudeerd hebben, worden deze 2 klinische entiteiten in geen enkel onderzoek gekarakteriseerd. In **Hoofdstuk 9** wordt de epidemiologie van FI bij schoolgaande kinderen in Sri Lanka beschreven. Hiervoor werden 2586 schoolgaande kinderen geïncludeerd. De prevalentie van FI was 2%. De meerderheid (81%) had obstipatie geassocieerde FI, terwijl FNFRI veel minder vaak werd gezien bij deze kinderen. Wanneer gekeken werd naar het ontlastingspatroon van deze 2 aandoeningen, werd opgemerkt dat kinderen met obstipatie geassocieerde FI eerder de neiging hebben om de ontlasting actief op te houden in vergelijking met kinderen met solitaire feces incontinentie. Ook bleken demografische factoren zoals een lagere leeftijd, mannelijk geslacht en lage socio-economische condities predisponerende factoren te zijn voor FI. Daarnaast, maakt psychologische stress binnen het gezin of op school kinderen meer vatbaar voor het ontwikkelen van FI.

Gebaseerd op de bevindingen van dit proefschrift concluderen wij dat obstipatie en feces incontinentie veel voorkomende problemen zijn in Sri Lanka. Veel sociodemografische factoren maken kinderen en adolescenten vatbaarder voor het ontwikkelen van defecatiestoornissen. De omgekeerde relatie die wij vonden tussen obstipatie en FI en leeftijd, geeft aan dat jongere kinderen een grotere kans hebben om defecatiestoornissen te ontwikkelen. Artsen die kinderen met obstipatie behandelen, moeten daarom alert zijn op symptomen die vaak samengaan met de obstipatie zoals buikpijn en rectaal bloedverlies. Daarnaast zou het afnemen van een gedetailleerde sociale anamnese ongetwijfeld helpen bij het identificeren van predisponerende factoren voor het ontwikkelen van defecatie stoornissen bij kinderen.

Life-events die gepaard gaan met stress, maken kinderen vatbaar voor het ontwikkelen van obstipatie, ongeacht het soort life-event dat kinderen doormaken. Daarnaast lijkt stress die gerelateerd is aan problemen van grotere omvang, zoals een burgeroorlog, ook geassocieerd met obstipatie. Gebeurtenissen in de huiselijke omgeving, zoals alcoholisme en veelvuldig straffen, en gebeurtenissen op school, zoals faalangst, zijn gebeurtenissen die voorkomen kunnen worden. Daarom is het van belang dat het gezin, de school en de gemeenschap werken aan een veiligere omgeving waarin kinderen en adolescenten kunnen opgroeien, om te voorkomen dat zij obstipatie ontwikkelen.

Vooral in een land waar de gezondheidszorg gratis is, is laag gezondheidszorggebruik van kinderen met obstipatie, zelfs als ze ernstige klachten hebben, zorgelijk. Toekomstige studies moeten deze bevinding verder ontrafelen. Tot die tijd wordt het aanbevolen een bewustwordingsprogramma te ontwikkelen, om zowel schoolkinderen als hun ouders, voorlichting te geven over vroege opsporing van obstipatie en deze kinderen medische hulp te bieden, omdat het bekend is dat een late presentatie aan een zorgverlener de prognose negatief kan beïnvloeden.

Het is belangrijk om op te merken dat kinderen met obstipatie in de algemene bevolking een lage HRQoL hebben. Dit is waarschijnlijk gerelateerd aan de langdurige, recidiverende aard van obstipatie en fecesincontinentie en de psychologische gevolgen ervan. Een verminderd fysiek, mentaal en sociaal functioneren zal uiteindelijk schoolprestaties beïnvloeden, leidend tot een vicieuze cirkel van psychologische stress, een verergering van klachten en een neerwaartse spiraal van HRQoL. De negatieve invloed op de schoolprestaties is geassocieerd met een laag opleidingsniveau, leidend tot een matig verdienvermogen op de volwassen leeftijd, hetgeen maatschappelijk belastend is. Het is belangrijk om deze kinderen vroegtijdig op te sporen en ze te behandelen volgens de huidige richtlijnen, om langetermijngevolgen tot een minimum te beperken.

De associatie tussen kindermishandeling en obstipatie is hoewel nieuw, een verontrustende bevinding. Het geeft aan dat kindermishandeling schadelijke is voor het maagdarmkanaal en de *hersen-darm-as.* Naast andere steeds toenemende predisponerende factoren, zal kindermishandeling bijdragen aan het ontwikkelen van obstipatie bij kinderen. Wij adviseren met klem dat het de hoogste tijd is dat kindermaag-darm-leverartsen de handen ineen slaan met collega's als algemeen kinderartsen, psychiaters en medisch-juridische medewerkers om kindermisbruik tegen te gaan, en zodoende de toename van obstipatie te beperken.

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- **28.** Constipation in children: diagnosis and management. Rajindrajith S, Devanarayana NM. *Sri Lanka Journal of Child Health*, 2009; 38: 127-135.
- **29. Helicobacter pylori infection in children. Rajindrajith S**, Devanrayana NM, de Silva HJ. *The Saudi Journal of Gastroenterology* 2009; 15: 86-94.
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- 31. Constipation and functional faecal retention in a group of school children in a district in Sri Lanka. Rajindrajith S, Devanarayana NM, Mettananda S, Perera P, Jasmin S, Karunarathna U, Adhihetty D, GoonewardenaR. Sri Lanka Journal of Child Health 2009; 38: 60-64.
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#### **Invited Book Chapters**

- Chapter 6 Clinical evaluation of children with constipation: History and physical examination. Invited book chapter. Rajindrajith S, Devanarayana NM. In: Constipation in children. Editor Ramon NN. Nova Publishers. 2013.
- Chapter 1 Prevalence and international perspectives of functional gastrointestinal disease in children. Invited book chapter. Rajindrajith S, Devanarayana NM, Benninga MA. In: Psychosocial aspects of children with gastroenterological conditions. Editor Martin C. Oxford University Press, Oxford. Invited book chapter
- Chapter- Defecation disorders in children: Invited book chapter. Rajindrajith S, Devanarayana NM, Benninga MA. In Pediatric Gastroenterology Hepatology, and Nutrition. Editors, Guwandalini S, Barr P, Dhawan A. Submitted.
- Chapter Constipation in Children: Invited book chapter. Rajindrajith S, Devanarayana Paediatric Text Book for General Practitioners. Editors, Mudiyanse R, Dissanayake P. Submitted 2015.
- Chapter : Abdominal pain in Children Invited book chapter. Devanarayana NM, Rajindrajith S. Paediatric Text Book for General Practitioners. Editors, Mudiyanse R, Dissanayake P. Submitted 2015.

#### **INVITED LECTURES**

#### 1. Functional dyspepsia in children

In 4<sup>th</sup> Biennial Congress of Asian Neurogastroenterology and Motility Association, 2015, New Delhi, India.

# 2. Abdominal pain in children

The Joint Scientific Sessions of Awissawella Clinical Society Meeting with Sri Lanka Medical Association. 8<sup>th</sup> November 2014 Awissawella, Sri Lanka.

#### 3. Abdominal pain in children

The 7<sup>th</sup> Scientific Sessions of Galoya Nimna Clinical Society Meeting.

25 – 27 September 2014 Ampare, Sri Lanka.

#### 4. Constipation in children

The First Federation of Neurogastroenterology and Motility Associations Meeting.

5 – 7 September 2014 in Guangzhou, China.

#### 5.Irritable bowel syndrome in children

In Annual Scientific Sessions of the Sri Lanka College of Paediatricians, 26-29 2014, Colombo, Sri Lanka.

# 6. Irritable bowel syndrome in children

In Annual Scientific Sessions of the Pakistan Society of Gastroenterology and Pakistan Society of Hepatology, 17-20 April 2014, Bhurban, Pakistan.

# 7. Constipation in children: Epidemiology and risk factors.

In Annual Scientific Sessions of the Pakistan Society of Gastroenterology and Pakistan Society of Hepatology, 17-20 April 2014, Bhurban, Pakistan.

# 8. Abdominal pain in children: missing piece of the jigsaw puzzle

In 26<sup>th</sup> scientific sessions of the Kandy Society of Medicine February 7-8 2014 Kandy, Sri Lanka.

# 9. Constipation in adolescents

In 4<sup>th</sup> Asian Pacific Single Topic Conference on Functional GI Disorders. . Jan 10-12 2014. Tagaytay City, Philippine.

# 10. Epidemiology and risk factors of constipation in children

In 13<sup>th</sup> Scientific Sessions of the Commonwealth Association of Paediatric Gastroenterology and Nutrition 2013 Colombo, Sri Lanka.

# 11. Management of chronic constipation in children

In 3<sup>rd</sup> Biennial Congress of Asian Neurogastroenterology and Motility Association, 2013, Peanang, Malaysia.

# 12. Rotavirus diarrhoea

In 6<sup>th</sup> Asian Congress of Pediatric Infectious Disease 2012, Colombo, Sri Lanka.

# 13. Abdominal pain in children: is it in the stomach or intestine

In The International Digestive Disease Forum 2012, Hong Kong.

