

PREGLED LITERATURE – REVIEW ARTICLE

## **Irritable bowel syndrome in children - how to get diagnosed**

Sindrom nervoznih creva kod dece – kako do dijagnoze

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**Summary** Irritable bowel syndrome (IBS) is a chronic and relapsing functional gastrointestinal disorder. IBS affects 9%-23% of the population across the world. Epidemiologic studies in populations less than 18 years of age suggest higher prevalence among teenagers and children compared to adult population. The pathophysiology of IBS is not yet completely understood and seems to be multifactorial. Many pathogenetic factors, in various combinations, and not all necessarily present in each patient, can play an important role. Discomfort or abdominal pain relieved by defecation, associated with a change in stool form, is a typical clinical manifestation of IBS. Some factors, such as emotional stress and some food, may initiate and exacerbate the symptoms. A timely diagnosis of IBS is important so that treatment which will provide adequate symptomatic relief (pain and bloating, diarrhoea, constipation) can be introduced. There is no specific test for diagnosing IBS. The diagnosis is made using criteria based on clinical symptoms such as Rome criteria. Today the Rome Criteria IV is the gold-standard for the diagnoses of IBS in the adult and child populations. Treatment of patients with IBS requires a multidisciplinary approach. Some patients respond well to non-pharmacological treatment, while others require pharmacological treatment.

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**Sažetak** Sindrom iritabilnog creva (IBS) je hronični i recidivni funkcionalni gastrointestinalni poremećaj. IBS obuhvata 9% - 23% svetske populacije. Epidemiološke studije kod populacije mlađe od 18 godina ukazuju na veću prevalenciju među tinejdžerima i decom u poređenju sa odraslom populacijom. Patofiziologija IBS-a još nije u potpunosti jasna i izgleda da je multifaktorna. Mnogi patogenetski faktori, u različitim kombinacijama, i ne svi obavezno prisutni kod svakog pacijenta, mogu igrati važnu ulogu. Nelagodnost ili bol u truhu koji nestaju defekacijom, udruženi sa promenama oblika stolice, tipična je klinička manifestacija IBS-a. Mnogi faktori, kao što su emocionalni stres i neka hrana, mogu započeti i pogoršati simptome. Pravovremena dijagnoza IBS je važna da bi se primenio tretman koji će obezbediti adekvatno simptomatsko olakšanje (bol i nelagodnost, dijareja, konstipacija). Ne postoje specifični testovi za dijagnozu IBS. Dijagnoza se postavlja korišćenjem kriterijuma zasnovanih na kliničkim simptomima kao što su Roma kriterijumi. Danas su Roma IV kriterijumi zlatni standard za dijagnozu IBS-a kod adultne i dečije populacije. Lečenje bolesnika sa IBS-om zahteva multidisciplinarni pristup. Neki pacijenti dobro reaguju na ne-farmakološki tretman, dok drugi zahtevaju farmakološki tretman.

**Ključne reči:** Sindrom iritabilnog creva, deca, patogeneza, dijagnoza, Rome kriterijumi

### **Introduction**

Irritable bowel syndrome (IBS) is a chronic, relapsing, remitting and the most prevalent functional disorder of the gastrointestinal tract. This disease is characterized by abdominal pain, bloating, and changes in bowel habits that lack a known structural or anatomic explanation (1-3). Over the years, the unexplained gastrointestinal symptoms of IBS have been described in various terms, including nervous colon, mucous colitis, and irritable colon (4). The symptoms of IBS appear and disappear over time, and are often associated with other functional gastrointestinal diseases and non-gastrointestinal somatic pain disorders (5).

Patients with IBS are often referred to gastroenterology, undergo various investigations, take various medicines, have a poor quality of life. However, there is a large number of adult patients that do not report to the doctor's office or seek medical attention (6-7). Children with IBS are often absent from school and have a poor quality of life.

### **Epidemiology**

IBS is a chronic and debilitating functional gastrointestinal disorder that affects 9%-23% of the population across the

world (7). Women are two to four times more likely to develop IBS than men (8). Age-related onset of IBS symptoms occurred predominantly in patients younger than 45 years but prevalence rose again in the elderly (9).

Many cases develop in early childhood (10). Epidemiologic studies in populations less than 18 years of age suggest higher prevalence among teenagers and children compared to adult population (11). In a Sri Lankan study of 1717 school children aged 10-16 years randomly selected from 4 provinces; 107 children were diagnosed with IBS symptoms as per Rome III criteria. The overall prevalence of IBS was found to be 6.23% with a higher prevalence amongst girls (12). The influence of gender on IBS has been reported in several studies and most authors report a higher prevalence in the females than males (12-14). This finding has been attributed to possible hormonal changes and it has been noted that the symptoms of IBS appear to be worse with menstrual cycles (15).

### **Etiopathogenesis**

The pathophysiology of IBS is not yet completely understood and seems to be multifactorial (4,6,12). Many pathogenetic factors in various combinations, and not all necessarily present in each patient, can play an important role. It is unclear which among these factors is the trigger or how these conditions converge to initiate IBS (16).

Possible risk factors of IBS in children included young age, food allergies, gastroenteritis during childhood, preference for fried food, anxiety, psychological insults during childhood, and parental constipation (15). Factors potentially involved in the pathogenesis of irritable bowel syndrome are: genetic predisposition, altered intestinal motility, intestinal hypersensitivity, enteric infection/inflammation, altered intestinal immunity, altered gut microbiota and food intolerance (7,13-18).

The influence of genetic predisposition in the development of IBS has been well researched. Having a parent with IBS is a greater predictive factor for IBS than having a twin with IBS, which indicates that environmental factors may play a greater role than genetic ones (17). Traditionally, IBS has been conceptualized as a condition of altered intestinal motility (leading to diarrhea or constipation), intestinal hypersensitivity (leading to abdominal discomfort or pain), and psychopathology (7,15). In patients with IBS, environmental stress or strong emotion via the brain-gut axis can lead to dysmotility throughout the small and large intestine. Patients with IBS have an even greater motility response to stressors when compared with normal subjects (19-21). Intestinal hypersensitivity occurs as a result of stimulation of various receptors of visceral afferent nerve fibres in the gut wall, triggered by bowel distention or bloating, and is a possible explanation for IBS symptoms (22). The brain-gut axis plays an important role in pain perception related to the gut. In young children, it is difficult

to assess pain and validated measures of infant crying and chronic pain assessment are currently not available (23).

There is a clear increased prevalence of current psychological distress among patients who seek medical care for IBS. Symptoms of anxiety, depression, paranoia and global psychological symptoms are commonly encountered in these patients (7).

Enteric inflammation has been noted in some patients with IBS after prolonged infectious enteritis (postinfectious IBS) (18). Furthermore, the microbiota is altered in IBS and such alterations may contribute to the pathogenesis of the disorder (24). A better understanding of the gut microbiota in healthy children is of critical importance in order to improve our understanding of the role of the gut microbiota in pediatric IBS. Patients with IBS tend to report that their symptoms are often exacerbated by certain foods. The classical IgE-mediated food allergy does not seem to play an important role in IBS (25). In recent years, it has been observed that the ingestion of gluten causes abdominal discomfort and IBS-like symptoms in subjects without a diagnosis of celiac disease (the so-called gluten sensitivity). Most likely, the gluten, as other well-known factors, alters the intestinal permeability, activating the enteric and autonomous nervous systems and producing the typical symptoms of IBS (26).

### **Clinical symptoms and signs**

Discomfort or abdominal pain relieved by defecation, associated with a change in stool form, is a typical clinical manifestation of IBS (4). Recurrent abdominal pain of childhood is an important feature of IBS. Apley et al was first described first recurrent abdominal pain (13). Some factors, such as emotional stress and some foods, may exacerbate the clinical manifestation of IBS. Patients with IBS complain of an altered bowel habit, ranging from diarrhoea, constipation, or alternating diarrhoea and constipation. Up to a third of patients will move from one group to another. Patients with IBS and constipation may experience a sensation of incomplete evacuation and periods of constipation can last from days to months alternating with diarrhoea or normal bowel function (27).

Bloating or feeling of abdominal distension are very frequent complaints in IBS and may be included in the diagnostic criteria for IBS in the future. Bloating is an important symptom of IBS and must be part both of the symptom complex and of the outcome measures of drug trials (4, 27). Most adults with the condition experience episodes of symptom exacerbation, followed by periods of remission. Comorbidity with other functional gastrointestinal disorders is high and can be caused by shared visceral hypersensitivity pathophysiological mechanisms (4,5). There are comorbidity with some nongastrointestinal disorders, including psychiatric disorders (depression, anxiety and somatoform disorders) (4,7).

## Diagnosis

A timely diagnosis of IBS is important so that therapy which will provide adequate symptomatic relieve can be introduced. Though, when making a diagnosis, consideration should be given to the fact that the symptoms of IBS are similar to those of organic disorders and can co-exist with organic diseases. The first attempt at establishing a diagnostic criteria that would define IBS dates back to 1970 by Manning and Associates (28). Following this, more attention was paid to this functional digestive problem, such that in Rome a Rome Foundation was formed which played a pivotal role in creating a diagnostic criteria and operationalizing the dissemination of new knowledge in the field of all functional gastrointestinal disorders. An international group of pediatric gastroenterologists gathered together in Rome in 1995 to define the diagnostic criteria for IBS in childhood and this was published in 1999 as part of the larger Rome II criteria. Later, these criteria were modified by the entire Roma IV criteria (29,30). (Table 1)

**Table 1.** Rome IV Criteria for Diagnosing IBS

Abdominal pain at least 4 days per month associated with one or more of the following:

- Related to defecation
- A change in frequency of stool
- A change in form (appearance) of stool

Similar to the adult Rome criteria, IBS can now be divided into subtypes reflecting the predominant stool pattern (IBS-C, with constipation, IBS-D, with diarrhoea, IBS-M, with constipation and diarrhoea, and unspecified IBS-U, the symptoms cannot be categorized into one of the above three subtypes) (30,31).

If a child suffers from constipation and abdominal pain related to defecation or a change in frequency/form of stools, the child should first be treated for constipation and, if despite successful treatment, the abdominal pain persists, the child should be considered to suffer from IBS with constipation.

It is important to ask the patient to clarify the timing, severity, and location of their pain or discomfort, and whether this is generalised abdominal pain. Great care should be taken to rule out any organomegaly, tenderness and/or abdominal mass in the right iliac fossa.

In children that meet the diagnostic criteria for IBS, other digestive diseases should be excluded, and the following investigations be undertaken: blood count, biochemical and inflammatory markers, serological screening for celiac disease, and Lactosa intolerance test. The decision to undertake further investigations (e.g. rectosigmoidoscopy or colonoscopy) is dependent on the presence of alarming symptoms: recurrent unexplained fever, rectal bleeding, night time pain or diarrhea, weight loss, family history of inflammatory bowel disease, persistence of severe vomiting or diarrhea, pallor, stools that may be difficult to flush away, raised inflammatory markers and delay in progression of puberty (13,16).

In patients with IBS-D, a differential diagnostic that includes the following should be considered: microscopic colitis, ulcerative colitis, Crohn's disease, celiac disease, Giardiasis, lactose malabsorption, bacterial small bowel contamination, malabsorption of bile salts and colorectal cancer.

## Treatment and prognosis

Before commencing with treatment, the patient should be educated and made aware of the nature of IBS. Amongst other things, patients should be informed about the normal frequency of intestinal emptying, which ranges from three times per day to three times a week. The most important step in managing children with IBS is to explain the diagnosis to parents and the child if age appropriate. Treatment of patients with IBS requires a multidisciplinary approach. Treatment is on an individual basis and dependent on the dominant symptoms. Not all patients respond to the same treatment. Particular attention should be paid to aggravating factors in IBS such as nutrition, stress, and psychological factors. Some patients respond well to non-pharmacological treatment, while others require pharmacological treatment. Despite numerous studies that have considered numerous therapeutic options, an ideal IBS therapy algorithm cannot yet be formed (1,2,7,9,17).

In most adult patients and children with IBS symptoms persists but they do not worsen, while the rest may experience worsening or complete resolution. Factors that may contribute to a poor prognosis include: uncertainty or doubt with regards to the effect of medicinal therapy, damage to the bowel as a result of existing symptoms, long standing IBS, chronic stress exposure and comorbidity of psychiatric illnesses.

## Conclusion

IBS is a common disorder in children and adolescents. Since IBS is the result of interaction between biological, social and psychological factors it is necessary to influence all of these factors in order to prevent this syndrome. Early diagnosis will avoid unnecessary testing of children and improve the quality of life. The major goal in managing IBS in this population is to control the symptoms and eliminate factors that can exacerbate the condition.

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