

## Psychosocial Risk Factors in Chilean Patients with Irritable Bowel Syndrome

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### Keyword:

Irritable Bowel Syndrome; Psychosocial; Risk Factors; Chile

## 1. Abstract

### 1.1. Background and Objective:

Irritable bowel syndrome (IBS) is presented as a biopsychosocial model according to Rome criteria. In Chile there are not studies on psychosocial risk factors (PRF) in IBS. The aim was to evaluate PRF in patients with IBS and their relationship with clinical severity, phenotypes and associated pathologies.

### 1.2. Methods

A prospective cross-sectional study. Patients with IBS were included according to Rome IV criteria. PRF evaluated: sexual abuse, rape, neglect, loss or death of parents, traumatic events during childhood and adulthood, self-evaluation of happy or childhood happiness, infectious events prior to the appearance of symptoms and associated pathologies.

### 1.3. Results

114 IBS patients were evaluated, 83% women, average age  $52 \pm 15$  years, from the clinical perspective 35% severe, 48% moderate and 17% mild. 96 (84%) patients presented some PRF, highlighting 70% reporting an unhappy childhood, 61% physical or psychological abuse, 32% neglect and 24% abuse. A trend is observed that the greater the absolute number of risk factors, the greater the severity of IBS ( $p < 0.0001$ ), without differences by phenotypes. The most frequent comorbidities were depression and fibromyalgia. There is significance between the severity of IBS with fibromyalgia ( $p < 0.0001$ ) and depression ( $p = 0.012$ ), but not with anxiety disorder ( $p = 0.656$ ).

## 1.4. Conclusions

PRF are frequent in IBS patients, the higher the report the higher the clinical severity, without differences by phenotypes. Knowing the patient's PRF allows their physicians to deliver more personalized and multidisciplinary treatment.

## 2. Introduction

Irritable bowel syndrome (IBS) is defined by the Rome Criteria as a chronic recurrent disease characterized abdominal pain occurring at least once a week in the last 3 months, with a history of 6 months or more of a transit intestinal disorder (eg diarrhea or constipation), without finding a biochemical or structural alteration that explains the symptoms. Four phenotypes are recognized: (1) constipation-predominant IBS (IBS-C); (2) IBS with predominance of diarrhea (IBS-D); (3) IBS with mixed pattern (IBS-M); and (4) IBS with unclassified pattern (IBS-NC) [1]. It could affect almost a fifth of the world population, deteriorating the quality of life of patients and with a significant social and health impact. It is one of the main causes of work absenteeism and medical polyconsultations, consuming 50% more health resources than the healthy population and producing at least 26% less work output. It is more prevalent in young women, although it can be observed in 12% of older adults [2]. Its etiology and pathophysiology are still a matter of discussion, apparently having a fundamental role in the integration of mechanisms at the level of the central nervous system and in the intervention of the autonomic nervous system, known as the brain-intestine axis [3]. The central nervous system can modify sensory perception as well as motor response. Alterations have been found in concentrations of

neurotransmitters, especially serotonergic, enkephalin and substance P, among others, as well as changes in neuroimaging of the prefrontal, ventrolateral, posterior parietal and thalamic cortex [4]. Although the Rome criteria do not include psychosocial factors, in previous studies, a higher incidence of depression and anxiety disorders has been observed, with several being present prior to the onset of gastrointestinal symptoms, but it is not known if they are a risk factor or only an association. A study of more than 3,000 patients showed the presence of psychiatric comorbidity in up to 94% of patients with IBS [5]. In Chile there are few studies in relation to these variables in IBS. The objective of this research is to evaluate Psychosocial Risk Factors (PRF) in IBS patients and their relationship with clinical severity, phenotypes and associated pathologies.

### 3. Methods

A prospective cross-sectional study of patients with a diagnosis of irritable bowel syndrome (IBS) was carried out in a university center between the years 2017 and 2020. Those patients older than 18 years, in a Neurogastroenterology outpatient clinic, with a diagnosis of IBS based on Rome IV criteria were included. Organicity was ruled out with endoscopic studies, abdominal images, anti-transglutaminase levels, and general laboratory tests directed according to clinical suspicion. An interview of each study subject was conducted covering certain psychosocial risk factors (PRF): sexual abuse, rape, abandonment, loss or death of parents, traumatic events in childhood (eg bullying) and adulthood, self-evaluation of the degree of childhood happiness, events of infectious diseases prior and / or subsequent to appearance of symptoms and associated pathologies. The severity of the PRF was evaluated through a score assigning three points for each PRF (the range of all factors, therefore, being 0-27). The history of mood disorders such as depression, anxiety, was reported by each patient's psychiatrist and the diagnosis of fibromyalgia was made by a rheumatologist based on clinical symptoms and tests that ruled out organic rheumatological pathology. The study survey, consistent with the Rome IV criteria, asked about symptoms of other functional pathologies, such as symptoms of esophageal pathology (symptoms of hyperalgesia, heartburn, functional dysphagia, chest pain), functional dyspepsia and fleeting proctalgia.

### 4. Ethical Considerations

Patients of legal age were included who agreed and signed an informed consent to participate in this study. The data obtained were recorded in spreadsheets without including the names of the patients to protect their confidentiality. This work has the approval of the Bioethics Committee of the Hospital Clínico of Universidad de Chile.

### 5. Statistical Analysis

Categorical variables are expressed as absolute value and percentage, while quantitative variables are expressed as mean  $\pm$  standard deviation

or median (p25 - p75) as appropriate. The evaluation of the normal distribution of the data was carried out with the Shapiro-Wilk normality test. Differences were determined with the Mann-Whitney or Welch test for quantitative variables and chi-square for categorical variables ( $p < 0.05$ ). The analyzes were performed with Software Prism Version 9.0.2.

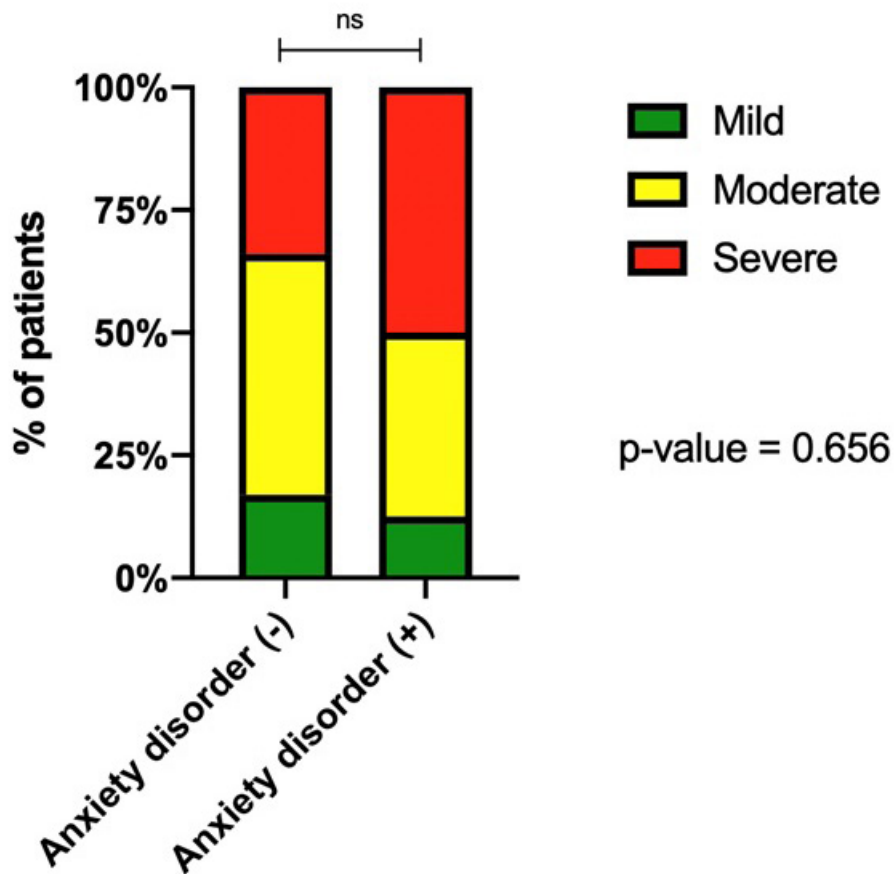
### 6. Results

One hundred fourteen patients met the inclusion criteria, of whom 95 were women (83%) and 19 were men (16.7%). The women's average age was  $52 \pm 15$  years and  $46 \pm 14$  years for the men ( $p = 0.13$ ). The mean age of the onset of symptoms in women was  $25 \pm 13$  years and  $21 \pm 11$  years in men ( $p = 0.14$ ), with an average time of diagnosis being  $18 \pm 14$  years after the onset of symptoms. Nineteen patients (16.6%) met the criteria for mild symptoms, 55 (48.2%) for moderate, and 40 (35%) for severe symptoms. The observed phenotypes according to Rome IV criteria and the characteristics of the patient group can be seen in Table No. 1. In 27 patients (24%) an infectious picture was reported prior to the onset of their symptoms. Tobacco use was self-reported in 23 patients (20%), being more frequent in men than in women (27.2% vs 18.5% respectively). The history of the use of any psychotropic drug such as serotonin reuptake inhibitor antidepressants, tricyclic antidepressants or benzodiazepines was reported by 87 patients (76.3%).

Overlapping functional pathology was found in most of the patients. Of these, 69 patients referred symptoms of esophageal pathology, 84 dyspeptic symptoms and 25 patients fleeting proctalgia. Only 16 of the patients did not report associated or overlapping symptoms. No differences were observed in the presence of PRFs in patients with exclusive IBS and those with symptoms of other overlapping functional pathologies. Of the comorbidities, the most frequent was depressive disorder, followed by fibromyalgia and mixed anxiety disorder as presented in Table 2. When evaluating the relationship between comorbidities and severity of symptoms, a statistically significant difference for fibromyalgia and depression ( $p < 0.0001$  and  $0.012$  respectively) but not for anxiety disorder or others, as is shown in Figure 1. Of the risk factors consulted, 96 patients (84%) presented some PRF, and of them 80 (70.1%) reported having had an "unhappy childhood", represented by incidents of mistreatment, abuse, abandonment, loss of parents or a close relative, as can be seen in detail in Table 3.

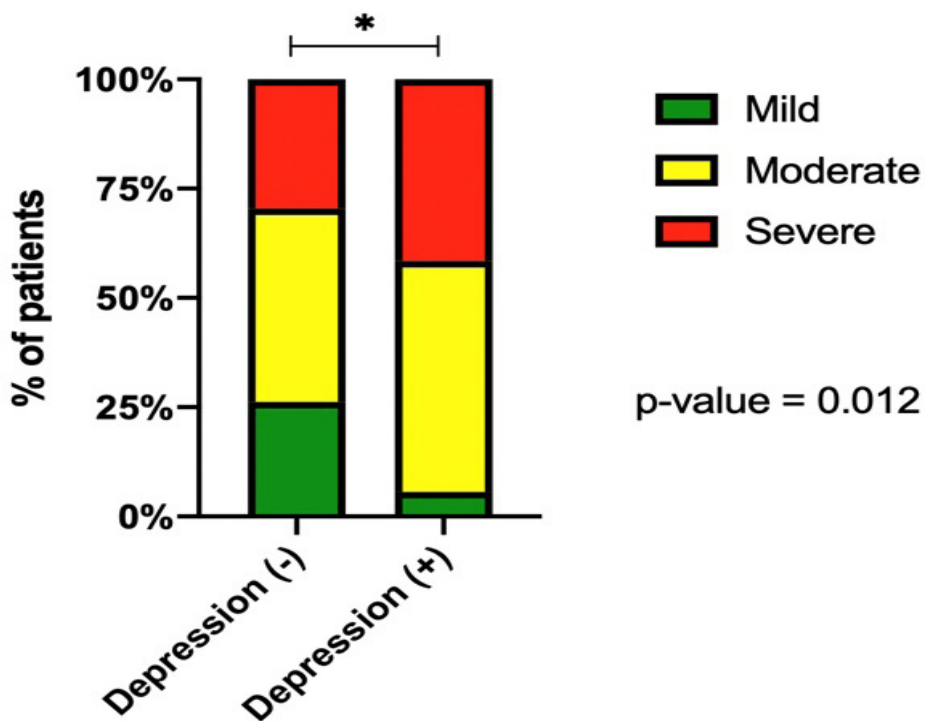
To determine the PRF severity score, 3 points were assigned to the presence of each of the following events: abuse, rape, parental abandonment, loss or death of parents, loss or death of a close relative, abuse in childhood and abuse in adulthood. The PRF severity score in our group was  $13 \pm 4$  points,  $8.5 \pm 0.7$  points and  $6.4 \pm 3.9$  points in patients with severe, moderate and mild clinical symptoms respectively ( $p < 0.0001$ ), without significant differences by IBS phenotypes (Figure 2).

## Anxiety disorder and IBS severity

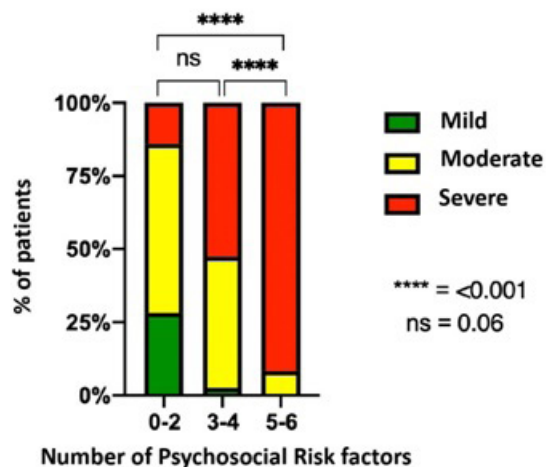


**Figure 1:** Relationship between comorbidities and IBS severity. There is significance between the severity of IBS with (A) fibromyalgia ( $p < 0.0001$ ) and (B) depression ( $p = 0.012$ ), but not with (C) anxiety disorder ( $p = 0.656$ ).

## Depression and IBS severity



## Psychosocial risk and IBS Severity



**Figure 2:** Relationship between number of psychosocial risk factors and severity of Irritable Bowel Syndrome. There is a statistically significant difference between those with less than 2 risk factors and more than 5, and between less than 4 and more than 5. A trend is observed that the greater the absolute number of risk factors, the greater the severity of IBS.

**Table 1:** Patient's demographic and clinical characteristics by gender.

	Men n = 19 (%)	Women n = 95 (%)	Total n = 114 (%)
Age onset of symptoms (years) (mean;SD)	21 ( $\pm$ 11)	25 ( $\pm$ 13)	24 ( $\pm$ 12)
Age at IBS diagnosis (years) (mean;SD)	38 ( $\pm$ 14)	41 ( $\pm$ 14)	41 ( $\pm$ 14)
Duration of symptoms prior to diagnosis (years) (mean;SD)	18 ( $\pm$ 15)	17 ( $\pm$ 14)	18 ( $\pm$ 14)
IBS phenotype			
Diarrhea	9 (47.4)	41 (43.2)	50 (43.9)
Mixed	3 (15.8)	24 (25.2)	27 (23.7)
Constipation	1 (5.2)	22 (23.2)	23 (20.2)
Indeterminate	6 (31.6)	8 (8.4)	14 (12.3)
Symptom severity:			
Mild	4 (21)	15 (15.8)	19 (16.7)
Moderate	12(63.2)	43 (45.3)	55 (48.2)
Severe	3(15.8)	37 (38.9)	40 (35)
Overlap:			
Esophageal disorders	9 (47.4)	60 (63,2)	69 (60.5)
Dyspepsia	13 (68.4)	71 (74.7)	84 (73.7)
Proctalgia	9 (47.4)	16 (16.8)	25 (2.9)
Benzodiazepine use	5 (26.3)	50 (52.6)	55 (48.4)
Antidepressants SSRI	6 (31.5)	43 (45.3)	49 (43)
Antidepressants Tricyclics	4 (21)	17 (17.8)	21 (18.4)
Other drugs	6 (31.5)	34 (35.8)	40 (35.1)

**Table 2:** Comorbidities in IBD patients by gender.

	Men n = 19(%)	Women n = 95(%)	Total n = 114(%)
Depression	9 (47.4)	44 (46.3)	53 (46.5)
Fibromyalgia	1 (5.2)	31 (32.7)	32 (28.1)
Anxiety disorder	1 (5.2)	7 (7.4)	8 (7)
Panic disorder	2 (10.5)	7 (7.4)	9 (7.9)
Bipolar disorder	0	6 (6.3)	6 (5.4)

**Table 3:** Psychosocial Risk Factors referred by patients with IBS.

	Men n =19 (%)	Women n = 95 (%)	Total n = 114 (%)
Unhappy childhood	13 (68.4)	67 (70.5)	80 (70.1)
Bullying	4 (21)	5 (5.2)	9 (7.9)
Child maltreatment	10 (52.6)	39 (41.0)	38 (33)
Abandonment in childhood	6 (31.5)	30 (31.6)	36 (31.6)
Loosing a parent	8(42.1)	13 (13.7)	21 (18.4)
Loosing a close relative	1 (5.2)	16 (16.8)	17 (14.9)
Abuse (physical or psychological) in childhood	1 (5.2)	26 (27.4)	27 (23.7)
Rape	0	14 (14.7)	14 (12.3)
Abuse (physical or psychological) in adulthood	9 (47.4)	61 (64.2)	70 (61.4)

## 7. Discussion

In our study, PRFs were present in most of the patients, being of greater relevance in patients with more severe IBS. Psychosocial factors have an influence on each component of the biopsychosocial model and can be an agent from early stages of life. Population studies showed greater risk of developing IBS, even in those suffering trauma during fetal life. Population studies showed greater risk even in those with trauma during fetal life, in those born with low weight or maternal stress [6]. This might lead to a dysfunction of the brain-gut axis, triggering IBS. PRFs as stressful events can influence digestive functions, perception of symptoms, behavior in the face of illness and quality of life. On the other hand, visceral pain can affect central pain perception, mood, and behavior [7]. This could be valid both for IBS and for other functional disorders, given the high prevalence that we observed of overlap with esophageal disorders, dyspepsia and functional proctalgia in the study's patients. In our group, more than two-thirds reported having an unhappy childhood. This concept, being somewhat broad, can be interpreted very differently by different people, so we tried to find objective illustrative incidents when asking about details of their childhood. We heard reports of abuse by parents in a third of the cases, abandonment in a third, and the loss of a parent and / or loved one and a history of abuse during childhood as well. This correlation of PRF with IBS was also observed in an Australian study in more than 300 patients with IBS, where 31% had lost one of their parents, 19% had an alcoholic father and two thirds reported an unhappy childhood or unsatisfactory relationship with their parents [8]. Regarding the question of happy or

unhappy childhood, we independently evaluated 57 subjects without IBS and only 3% considered themselves to have had an unhappy childhood. Another interesting relationship that has been observed in other studies shows that children of mothers with IBS have more difficulty in school, greater absenteeism, more medical visits for abdominal pain and a higher diagnosis of IBS in adulthood than children of mothers without IBS [9]. We did not evaluate the influence of a parent's IBS as a factor. With regard to abuse, especially during childhood, there is no clarity as to its relationship with IBS. This is because a clear relationship between abuse and IBS has not been found with respect to the general population. It has been suggested that abuse can trigger psychological stress, somatization and other psychiatric disorders that are associated with an increased risk of IBS [10]. The prevalence of a history of abuse in patients with gastrointestinal symptoms varies according to the population studied. Cultural differences and educational and socio-economic level that can alter self-report rates must be considered. Another factor to consider is the types of abuse, which can be physical, verbal or sexual, and the latter ranging from exhibitionism to rape. Of the data published in patients with IBS, sexual abuse has been reported in 17 to 50% of IBS patients [11]. In our local experience, a quarter reported having had been abused and 12% having had been raped, raising a concern about a much higher impact on women over men, and that this PRF is being under-diagnosed in our culture. The most frequent psychiatric diagnoses found in the population with IBS are mood disorders such as depression and dysthymia, followed by anxiety disorders and somatoform disorders [12]. Patients with depression have more IBS

than healthy control group. In some studies, a frequency of depression of 31.4% in patients with IBS, 21.4% in IBD and 17.5% in the healthy population has been found [13]. Nevertheless, the incidence of self-reported depressive symptoms does not differ significantly from those who consult for other gastrointestinal symptoms [14]. In our group, the frequency of depression as a comorbidity was 46%, similar in men and women, which is twice the incidence of depression in Chile, reported as 15.8% in the latest national Health survey [15]. A higher frequency of anxiety has also been observed in patients with IBS, being present from 16.5% to 47% of patients [16]. In our group, we observed approximately 15% of patients with generalized anxiety disorder or panic attacks but we did not see a relationship with the severity of IBS. Patients with IBS tend to have more than one psychiatric comorbidity, and in turn, psychiatric patients have more IBS than the general population [17]. It should be noted that it is a special group of patients, with chronic pain, with multiple medical consultations, with most of the studies carried out in tertiary health centers, similar to that observed in other studies [18]. In addition, there are different scales that measure anxiety, a fact that can alter the frequency of reported cases. A definitive diagnosis must be made by a trained psychologist or psychiatrist using structured interviews for the data to be comparable. Among the limitations of the study is the nature of the symptoms and psychosocial factors that can be difficult to quantify objectively. Instead, because the study population was drawn from patients of a tertiary care center dedicated to neurogastroenterology, the sample could be biased by including more patients with moderate and severe symptoms (85% of patients in our series) than the population of IBS patients as a whole. We must consider that sociodemographic, educational, and socioeconomic factors, not reported, could also influence the results. The contribution of this work lies in being the first to describe a population of Chilean adults with IBS and psychosocial risk factors. The results can suggest avenues of further research.

## 8. Conclusion

In conclusion, psychosocial risk factors are present in a large percentage of IBS patients, with those reporting more risk factors having more severe IBS symptoms, however, there are no significant differences in the correlation of the number of PRFs to the severity of symptoms among the various IBS phenotypes. Knowing the psychosocial risk factors in these patients could help deliver more personalized and multidisciplinary treatment.

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