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Abdominal pain in children: the role of possible psychosocial disorders

M. SPATUZZO[1], A. CHIARETTI[1], L. CAPOSSELA[1], M. COVINO[2], A. GATTO[3], P. FERRARA[1]

[1]Istituto di Pediatria, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy
[2]Emergency Department, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy
[3]Istituto di Pediatria, Fondazione Universitario Policlinico A. Gemelli IRCCS, Rome, Italy

Abstract. – OBJECTIVE: To evaluate the relationship between functional abdominal pain and biopsychosocial factors: the current diagnostic criteria show limits.

PATIENTS AND METHODS: This is a retrospective cohort study conducted in paediatric emergency department (ED) of a tertiary hospital in Rome. Children (0-18 years) evaluated for abdominal pain in the paediatric ED between January 2018 and December 2018 were enrolled. Patients were divided in 2 groups: organic and functional groups. The main outcome was the prevalence of different subtypes of functional disorders (according to Rome IV criteria) and the role of possible biopsychosocial disorders related to patients with functional symptoms.

RESULTS: In this study, 1130 patients were included. In the functional group, 37.6% of patients were classified as affected by functional dyspepsia, 26.7% by functional abdominal pain-non otherwise specified (FAP-nos), 20.8% by inflammatory bowel syndrome (IBS), and 15.9% by abdominal migraine. Children of our functional sample reported at least one of the items present in the inventory CSSI-24 (24-item Children's Somatic Symptoms Inventory), but more than 50% reported at least 4 of the items investigated.

CONCLUSIONS: At 6 and 12 months follow up and, new prospective studies on these disorders could improve the inclusion criteria for FGIDs, thinning the dubious rate of patients expected from the literature on the Rome IV criteria.

Key Words:
Functional abdominal pain, Children, Rome IV criteria.

Introduction

Functional gastrointestinal diseases (FGIDs) are disorders of the brain-gut interaction that represent the most common cause of chronic-recurrent abdominal pain in childhood[1]. According to the American Academy of Pediatrics and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, *chronic abdominal pain* is described as a symptom that lasts, constantly or intermittently, at least for two months and can have either a functional or an organic aetiology; it also be defined, *recurrent pain* that requires a minimum of three episodes of pain in a period of three months or more[1-3] A recent meta-analysis that collected data from about 200,000 children worldwide estimated the global aggregate prevalence for these disorders at 13.5% of the global paediatric population[3]. Based on the Rome IV criteria, 24.7% of infants and toddlers aged 0-3 years and 25% of children and adolescents aged 4-18 years fulfilled symptom-based criteria for a functional GI disorder[4].

Although FGIDs represent the most common diagnosis of chronic abdominal pain, an exact definition of their pathogenetic mechanisms is not recognized yet. In the literature, data about FGIDs are few and heterogeneous because of a vision that until the last decade looked at these disorders as a sorrow confined to the imaginary of the child, without considering their biochemical basis. However, nowadays, most of the elements supposedly implicated in the FGIDs bio-psychosocial pathogenesis are recognized: a visceral hypersensitivity, an enteric dysmotility, an alteration of the gut microbiota, the role of endoluminal factors (such as alteration of the local permeability or bile salts malabsorption), a genetic predisposition and aberrant epigenetic modifications, the influence of early life events, an inflammatory substrate triggered by gastrointestinal infections and the role of psychological factors[5-13]. A recent study showed that members of the G protein-coupled receptors located in

Corresponding Author: Antonio Gatto, MD; e-mail: antonio.gatto@policlinicogemelli.it

enteric neurons of children with FGIDs could play a role in mediating visceral hypersensitivity, becoming possible targets in pain research[14] .

Considering their complexity, functional paediatric patients need a bio-psychosocial approach that evaluates not only their being sick, *physical component*, but also their feeling sick, *psychological component*[15,16].

Abdominal pain represents the main symptom associated with FGIDs, but it can be associated with several other symptoms. Nowadays, the analysis of these signs and symptoms is crucial, since the Rome IV criteria for functional disorders require a positive diagnosis for these diseases, not only based on the negative results of useless and even bothering laboratory or instrumental tests, but rather oriented by the reported anamnestic findings[17,18]. Nevertheless, it is important to recognize some limits to the current criteria due to the difficulties to identify a doubtful number of patients complaining of abdominal pain and in which those criteria may not be sufficient to diagnose functionality.

Patients and Methods

In this study, we analyzed retrospectively the clinical data of the paediatric patients (0-18 years) evaluated for abdominal pain in the Paediatric Emergency Department (ED) of Fondazione Policlinico Universitario A. Gemelli Hospital, Rome, between January 2018 and December 2018. We highlighted the prevalence of different subtypes of functional disorders according to Rome IV criteria. We investigated the role of possible bio-psychosocial disorders related to patients with functional symptoms analysing the symptomatic panel associated with these diseases in order to support the clinical-based diagnosis that current criteria suggest for FGIDs.

We divided the patients in 2 groups: organic (G1) and functional (G2).

The inclusion criteria for the G1 were the presence of signs and red flag symptoms for organic pathology, as indicated in the clinical report on FGIDs: involuntary weight loss, deceleration of linear growth, gastrointestinal blood loss, significant vomiting includes bilious emesis, protracted vomiting, cyclical vomiting or a pattern worrisome to the physician, chronic severe diarrhea, persistent right upper or right lower quadrant pain, unexplained fever, family history of inflammatory bowel disease, or abnormal or unexplained physical findings, alarm signs on abdominal examination include localized tenderness in the right upper or right lower quadrants, a localized fullness or mass effect, hepatomegaly, splenomegaly, costovertebral angle tenderness, tenderness over the spine, and perianal abnormalities. Other severe gastrointestinal signs can be truly considered warning signs for organic pathology[19]. Furthermore, the report to which we referred also considered signs related to other 3 districts: respiratory signs and symptoms (cough, dyspnoea, sore throat), urinary signs and symptoms (LUTS - UTI - haematuria), genital signs and symptoms (spotting or abnormal or painful menstrual bleeding - PID), skin signs (eczema, urticaria, mucosal lesions, rashes, jaundice, anaemia); laboratory tests showing ESR > 20 mm/h, CRP > 10 mg/L, white blood cells > 10,000 mm^3.

The inclusion criteria for the G2 defined by Rome IV were:

- for the diagnosis of *functional dyspepsia,* 1 or more of the following bothersome symptoms: postprandial fullness, early satiation, epigastric pain or burning not associated with defecation. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.
- for the diagnosis of *irritable bowel syndrome (IBS)*, all of the following: abdominal pain at least 4 days per month associated with one or more of the following: related to defecation, change in frequency of stool, change in form (appearance) of stool; in children with constipation, the pain does not resolve with resolution of the constipation (children in whom the pain resolves have functional constipation, not irritable bowel syndrome); after appropriate evaluation, the symptoms cannot be fully explained by another medical condition.
- for the diagnosis of *abdominal migraine,* all the following occurring at least twice: paroxysmal episodes of intense, acute periumbilical, midline or diffuse abdominal pain lasting 1 hour or more (should be the most severe and distressing symptom); episodes are separated by weeks to months; the pain is incapacitating and interferes with normal activities; stereotypical pattern and symptoms in the individual patient; the pain is associated with 2 or more of the following: anorexia, nausea, vomiting, headache, photophobia, pallor; after appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

According to the Rome IV criteria it is necessary to evaluate the recurrence or chronicization of pain in these patients. So, the enrolment of the G2 was based on the administration of a questionnaire to the parents of the patients with inclusion criteria in the first phase and to the teenagers between 12 and 18 years old. This allowed us to sub-classify G2 patients among the various classes of functional disorders:

- to assess *functional dyspepsia*, it must include one or more of the previously bothersome symptoms verified for at least 4 days per month, criteria fulfilled for at least 2 months before diagnosis;
- to assess *IBS,* all the symptoms previously reported lasted for at least two months;
- for the confirmation of abdominal migraine, all the previously reported symptoms satisfied for at least twice at least six months.

All patients who satisfied the inclusion criteria in the first phase but didn't maintain compliance with these criteria in the second one have been classified as children with functional abdominal pain-not otherwise specified (FAP-nos) if all of the following requirements were satisfied at least 4 times per month for at least two months: episodic or continuous abdominal pain that does not occur solely during physiologic events (e.g. eating, menses); insufficient criteria for irritable bowel syndrome, functional dyspepsia, or abdominal migraine. After an appropriate evaluation, the abdominal pain cannot be fully explained by another medical condition.

Patients not satisfying these criteria were excluded from the G2, due to the failure to adhere to the Rome IV Committee criteria.

To investigate psychosocial disorders, we used the HEADSSS 3.0 questionnaire, actually used to investigate psychosocial factors in children and adolescents[20]. We also added: items for the diagnosis of major depressive disorder and generalized anxiety disorder, in agreement with the DSM-V; items for assessing exposure to stressful environments in at least three contexts between school, family and health; we evaluated alterations of the coping (tendency to catastrophism or avoidant profile) in these children; the possible diagnosis of alexithymia in accordance with the TAS-20 scale; we investigate cases of family conflict, maltreatment and abuse in these children.

Moreover, we evaluated the presence of enteric and extraintestinal symptoms, relying on the CSSI-24 inventory for somatization disorders[21].

Results

In this study, we collected the data of 1130 paediatric patients (0-18 years) evaluated for abdominal pain. One hundred and seventy-six patients met the criteria for the G2, 75 of them were lost at the 3-month follow-up and 101 patients were finally enrolled; 493 patients were included in G1 and 461 were labeled as "doubts".

In G1, 243 patients (49.3%) were females and 250 patients (50.7%) were males. In G2, 57 patients (56.4%) were females and 44 patients (43.6%) were males.

We stratified by age the patients in 3 groups: 0-6 years; 7-12 years; 13-18 years. In G1 there were 154 patients (31.2%) between 0-6 years; 170 patients (34.5%) between 7-12 years; 169 patients (34.3%) 13-18 years. In G2 there were 17 patients (16.8%) between 0-6 years; 43 patients (42.6%) between 7-12 years; 41 patients (40.6%) 13-18 years.

We found that G1 is fairly leveled between male, female and the three age groups analysed, while G2 presents a clear disproportion towards the female and the higher age groups.

In G1, as red flags for organic disease, we found extra-district signs in 38% of patients, fever in 32.6%, the persistence of pain in the right quadrants 16%, impaired abdominal objectivity 8.3%, nocturnal symptoms 7.7%, severe diarrhea or chronic 6.2%, persistent or bilious vomiting 5.9%, blood loss in vomiting and stool in 3.8%, familiarity 3.4%, dysphagia or odinophagy 2.6%, perirectal pathologies 2.2%.

In G2, at 3-month follow-up, 37.6% of patients were classified as affected by functional dyspepsia, 26.7% by FAP-nos, 20.8% by IBS and 14.9% by abdominal migraine.

Between the patients with IBS, 52.4% were classified as IBS-C (constipation), 33.3% IBS-D (diarrhea) e 14.3% IBS-M (mixed).

Analyzing the somatization disorders associated with the abdominal pains, we verified that all of the children of our functional sample reported at least one of the items of the inventory CSSI-24, but above all more than 50% reported at least 4 of the items investigated. Subsequently, we investigated which symptoms were the most transversally present identifying abdomi-

nal swelling, chronic fatigue, pallor and correlation of pain with meals. We also analyzed the symptoms prevalent in detail in each group of functional disorders: in children suffering from functional dyspepsia, the main symptoms were excessive belching (31.6%), globus pharyngeus (15.8%) and heartburn (23.7%); in the group with IBS the main associations were with headache, confusion or amnesia (28.6%); patients suffering from abdominal migraine reported headache (100%), photophobia (100%), nausea (73%), vomiting (66%), dizziness, heartburn, amnesia (20%); finally, an association between FAP-nos and nausea (29.6%), vomiting (14.8%) or heartburn, amnesia, muscular pain (11%) were found. (Table I).

A very interesting result comes from the impact of the psychosocial factors analyzed. The presence of almost all the items investigated was referred by over half of the children in the sample: family conflicts (53.4%), confusion about their feelings (68.3%), inability to express their emotions (64.3%), the negative outcome of school and extra tests (68.3%), low self-esteem (62.3%), exposure to abuse episodes (29.7%), reported recurrent stress episodes (77.2%), constant anxiety and concerns (83.1%), difficulty concentrating (67.3%), sleep disorders (44.6%), food disorders (29.7%), loss of interest in the activities (86.1%) and frequent irritability and crying (89.1%).

These data allowed us to diagnose psychosocial disorders associated with FGIDs, satisfying in particular, the diagnosis for anxiety disorder or depression 44.6% of patients, alexithymia 66%, coping alterations 79%. Recurrent exposure to stressful episodes were reported in 77% of patients, cases of hardship and family conflicts in 53%. Almost 30% of these children referred types of abuse, with a higher prevalence of neglect or bullying. It must be considered that who is exposed to abuse in many cases do not report it, so the number of cases could be a small part of the real data. (Table II).

Discussion

In accordance with literature (8.2%) we estimate the aggregate prevalence of functional disorders at 8.9%[22]. These results confirm that the use of the most recent evidence available could avoid a misdiagnosis of functional disorders in a significant slice of patients. As far as the functional group is concerned, we noticed how the prevalence percentage of each functional disorder

Table I. Percentage of symptoms of functional disorder.

	Functional dyspepsia (38 pts)	IBS* (21 pts)	Abdominal migrain (15 pts)	**FAP-nos (27 pts)	Total (101 pts)
Nausea	5.3%	4.8%	73%	29.6%	21.8%
Vomit	2.6%	19%	66.6%	14.8%	17.9%
Abdominal swelling	71%	85.7%	80%	88.8%	80.1%
Excessive belching	31.6%	14.2%	0%	0%	14.9%
Headache	0%	28.6%	100%	0%	20.8%
Blurry vision	0%	0%	0%	0%	0%
Photophobia	0%	0%	100%	0%	14.9%
Chronic fatigue	47.4%	71.4%	80%	55%	59.4%
Dizziness	0%	0%	20%	0%	14.9%
Shaking	0%	0%	0%	3.7%	0.9%
Hot/Cold	0%	0%	20%	0%	2.9%
Globus pharyngeus	15.8%	0%	0%	0%	5.9%
Chest pain	0%	0%	0%	0%	0%
Heartburn	23.7%	9.5%	20%	11%	16.9%
Dyspnea	0%	0%	0%	0%	0%
Fainting	0%	0%	6.6%	3.7%	1.9%
Confusion or amnesia	7.9%	28.6%	20%	11.1%	14.9%
hearing loss	0%	0%	0%	0%	0%
Paling	71%	57.1%	100%	77.7%	74.3%
Muscular pain	0%	0%	0%	11.1%	2.9%
Hoarse voice or voice loss	0%	0%	0%	0%	0%
Pain related to meals	55.3%	57.1%	60%	88.8%	65.3%

*IBS: irritable bowel syndrome, **FAP-nos: functional abdominal pain-not otherwise specified.

Table II. FGIDs-related psychosocial disorders.

Somatization Disorders	100.0%
Alterations in Coping	79.0%
Stress	77.0%
Alexithymia	66.0%
Difficult Familiar situations	53.0%
Anxiety and Depression Disorders	44.6%
Abuse	29.7%

FGIDs: Functional gastrointestinal diseases.

agreed with literature, except for the abdominal migraine: 3.2% *vs*. 3% of patients classified as functional dyspepsia; 2.4% *vs*. 2.4% as FAP-nos; 1.8% *vs*. 2.3% as irritable bowel syndrome. More than half of these patients belonged to the IBS-C group, one-third of the IBS-D group and less than 15% had a IBS-M, a value that was globally agreeing with previous findings in the literature. More significant is the evidence on abdominal migraine from our survey turns out to be 1.5% *vs*. 0.5%.

In addition to the functional cases, between the 1130 patients investigated, 43.6% were classified in G1. Among the organic criteria investigated, the most significant signs were fever and extra-district signs of pathology that cannot be classified as possible somatization disorders, according to the CSSI-24 inventory. Data on the abnormal abdominal evaluation, on the persistence of pain in the right abdominal quadrant, on the persistence of the nocturnal symptoms, such as to awaken the patient, and data on severe diarrhea and vomiting are also significant. Less important are the results for familiar organic gastrointestinal pathology, for perirectal pathologies, blood losses in vomiting or in feces and difficulty in swallowing.

Results on sex and age of patients classified in the 2 groups are the same of the literature; in G2 the frequency of the disorders is higher in the female, as opposed to G1 in which we found the same value. Likewise, a more equitable percentage distribution of patients of G1 in the 3 age groups considered (0-6 years, 7-12 years, 13-18 years) contrasts with the result of G2 which is unbalanced towards school age groups. This result could therefore further prove the weight of the psychosocial factor in the context of functional disorders.

Finally, we analyzed data about patients that did not match the criteria for G1 and G2 at the first evaluation to the emergency room for acute abdominal pain.

The literature on acute abdominal pain reports a number of patients between 35 and 40% without red flags and symptoms at the onset. With regard to this group of patients, as demonstrated by this study, a possible discriminating element could be represented by a more correct approach and a more adequate management, aimed not only to seek inclusion and/or exclusion criteria for the two organic and functional groups but also to investigate the presence of signs and symptoms that could be possible expressions of discomfort, going beyond the simple anamnestic feedback on the school progress to which the physiological anamnesis of the child is often limited.

Among the psychosocial factors, we found that the presence of almost all the items investigated was reported by over half of the children in the sample. This allowed us to diagnose psychosocial disorders associated with FGIDs. In particular, up to 50% of these children satisfy the diagnosis for anxiety disorder or depression, alexithymia, coping alterations, recurrent exposure to stressful episodes, where cases of hardship and family conflicts were reported. Finally, more than 50% of these children reported at least 4 of the investigated symptoms and somatization disorders.

Conclusions

This retrospective study evaluates the relation between functional abdominal pain and biopsychosocial factors. These data were useful because, in a context where recent evidence requires a clinical diagnosis, a 6 and 12 month follow up and new prospective studies on the enrolled population could allow to widen the inclusion criteria: supporting Rome criteria and thinning the dubious slice of patients.

Above all, data in this study show two limitations: the questionnaires were mainly administered only to adults and children aged between 12 and 18 years, and, in addition, those exposed to mistreatment and abuse are often reluctant to report it[23-25].

We think that new observational studies are necessary to investigate the impact of these and other psychosocial factors in the pathogenesis and outcomes of these functional disorders. We believe essential an holistic and multidisciplinary approach to the paediatric patient evaluated for an apparent recurring abdominal pain because they may conceal a wider discomfort in the background of this symptom.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Authors' Contribution

P. Ferrara, M. Spatuzzo and A. Chiaretti were responsible for the study's conception/design, investigation and data analysis as well as the drafting of the manuscript. M. Covino, A. Gatto and L. Capossela performed data analysis and interpretation. The authors read and approved the final manuscript.

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