

A Study of Psychological Factors Associated with Functional Gastrointestinal Disorders and Use of Health Care

Sang-Yeol Lee¹, Han-Seung Ryu², Suck-Chei Choi², Seung-Ho Jang¹

Departments of ¹Psychiatry and ²Internal Medicine, Wonkwang University School of Medicine, Iksan, Korea

Objective: The purpose of this study was to analyze the symptoms of depression, anxiety, and childhood trauma in functional gastrointestinal disorder (FGID) patients who visited the brain-gut axis clinic.

Methods: The study participants included 99 individuals who were diagnosed with FGID by gastroenterologists, 88 individuals who had no FGID but showed symptoms of FGID based on the Rome criteria, and 79 individuals who did not show any symptoms or were diagnosed with FGID. Symptoms of depression, anxiety, and childhood trauma were evaluated by the Korean version of Beck-depression inventory-II (K-BDI-II), Korean version of Beck anxiety inventory (K-BAI), and Korean version of childhood trauma questionnaire (K-CTQ), respectively.

Results: The BDI score, BAI score, and CTQ score were significantly different between the groups. The group also had higher odds for developing anxiety as compared to the control group (odds ratio [OR] = 10.215, 95% confidence intervals [CI]: 2.49–41.76). Additionally, the FGID group had higher odds for developing symptoms of depression (OR = 5.554, 95% CI: 2.06–14.97) and experiencing physical violence (OR = 3.128, 95% CI: 1.53–6.38) than the non-FGID group.

Conclusion: This study showed that FGID patients were more likely to have symptoms of depression, severe anxiety, and childhood trauma, which were the risk factors of FGID.

KEY WORDS: Gastrointestinal diseases; Depression; Anxiety; Childhood trauma; Brain gut axis.

INTRODUCTION

Many symptoms of the functional gastrointestinal disorder (FGID), such as abdominal pain, nausea, indigestion, diarrhea, and constipation originate in the digestive system. However, both diagnosis and effective treatment regime are scant since the underlying structural and biochemical causes remain elusive [1].

Because of the difficulties faced in the diagnosis of FGID in practical examinations, the Rome criteria have been used to diagnose FGID. The advantage of the Rome criteria lies in the grouping of similar symptoms that appear on different anatomical locations such as the esophagus, stomach, duodenum, intestine, biliary tract, anus,

and rectum [2]. Since 2016, the Rome IV criteria include a spectrum of disorders such as functional heartburn (FH), functional dyspepsia (FD), irritable bowel syndrome (IBS) and functional constipation [3].

With recent studies revealing significant brain-gut interactions, the Rome IV criteria have evolved to factor in variations resulting from immune abnormalities, food choices, environmental factors, childhood trauma, infection, behavior of parents, cultural characteristics, genetic factors, personality traits, and cognition [4].

A person's cognition and mood are influenced by environmental stress factors such as fear and anger, which affects the gastrointestinal motility through the autonomic nervous system by regulating the release of corticotrophin hormone [5]. Along with changes in the gastrointestinal motility, mucosal microinflammation is one of the mechanisms that can lead to various gastrointestinal symptoms. Recent studies have proposed a microbiome-gut-brain axis, where changes in the gut microbiome can modulate brain functions, and vice-versa [6].

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Address for correspondence: Seung-Ho Jang
Department of Psychiatry, Wonkwang University School of Medicine, 895 Muwang-ro, Iksan 54538, Korea
E-mail: sh-jang82@hanmail.net
ORCID: <https://orcid.org/0000-0002-3479-0552>

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Previous studies have analyzed the association between FGID and psychological symptoms [7]. In a study of outpatients diagnosed with dysthymic disorders, 25% met the criteria of IBS, while 39% of those diagnosed with mood disorders were also diagnosed with IBS, which became worse with progressive symptoms of depression [8]. Anxiety is also one of the factors affecting gastrointestinal symptoms. The patients are more likely to utilize health care when the symptoms of depression and anxiety increase in FD patients [9]. In patients with major depressive or anxiety disorders, the severity of the gastrointestinal symptoms could be based on the psychological status and could result in incorrect illness behavior [10]. An experience of psychosocial trauma is known to affect physical and mental health, and a significant number of FGID patients report psychosocial trauma and abuse [11]. In a study of a local community, the symptoms of IBS were significantly correlated with sexual, emotional, or verbal abuse that occurred throughout the childhood and adolescence, and symptoms of FD and FH were also associated with such abuse [12].

As described above, various psychosocial factors are known to affect FGID, but research on these factors is very limited. Furthermore, difficulties in communication between the gastroenterologists and the psychiatrists restrict an integrated approach to FGID prognosis and diagnosis. Therefore, in this study, we examined how symptoms of depression, anxiety, and childhood trauma varies between the FGID, non-FGID, and control groups. Our findings will provide insights into how these factors influence FGID-related health care utilization.

METHODS

Participants

This study was conducted from September 2017 to December 2018. A total of 99 individuals (FGID group), diagnosed with FGID at the Brain-Gut Stress Clinic of the Wonkwang University Hospital, were enrolled in this study. Additionally, 88 individuals who had no FGID but showed symptoms of FGID based on the Rome criteria (non-FGID group), and 79 individuals who did not show any symptoms or diagnosis of FGID (control group). The Wonkwang University Institutional Review Board (IRB) approved this study (no. WKUH 2018-04-010-009), and informed consent was obtained from all patients enrolled in this study.

Korean Version of Beck Depression Inventory-II

Symptoms of depression were assessed using the Korean Version of the Beck Depression Inventory Second Edition (K-BDI-II). K-BDI-II is a 21-questionnaire document that helps in cognitive, somatic and affective evaluation of symptoms related to depression. Each question consists of the 4-points Likert scales ranging from 0 to 3 (9 or less: normal, 10–15: mild, 16–23: moderate, and 24–63: severe). The validity and reliability of K-BDI-II were evaluated and translated to the Korean language by Sung *et al.* [13]. In this study, the high-risk group had a score of 16 points or above.

Korean Version of Beck Anxiety Inventory

A Korean version of the Beck Anxiety Inventory (K-BAI) was used to measure anxiety. K-BAI consists of 21 questions including those related to the subjective, somatic, neuropathic, muscular, and respiratory symptoms of anxiety. It measures how much anxiety a patient has experienced over the past week, and each item is graded on a 4-point scale ranging from 0 to 3. Yook and Kim [14] evaluated the reliability of the K-BAI. The scores were classified as mild (22–26 points), moderate (27–31 points), and severe (> 32 points). In this study, the group with a score of 27 and above was classified as the high-risk group.

Korean version of Childhood Trauma Questionnaire

Childhood trauma was assessed with the Korean version of the Childhood Trauma Questionnaire (K-CTQ). The K-CTQ is a self-report instrument covering 28 items, which were divided into 5 sub-categories of emotional negligence (basic emotional needs are not provided), physical negligence (basic physical needs such as food and safety are not provided), emotional abuse (threatened with words or actions), physical abuse (physical injury), and sexual abuse (sexually contacted by force) and rated on a scale of 1–5 points. The validity of the K-CTQ was conducted by Kim *et al.* [15]. In this study, the high-risk group score for each sub-category is mentioned below: sexual abuse ≥ 8 , physical abuse ≥ 8 , emotional abuse ≥ 10 , physical negligence ≥ 8 , and emotional negligence ≥ 15 [16].

Statistics

Demographic and psychosocial characteristics were compared in each group by calculating the mean and

standard deviation of continuous variables and the frequency and percentage of categorical variables. Statistical differences between groups were analyzed using the one-way ANOVA test. We assessed the risk factors of FGID in all sub-categories of depression, anxiety and CTQ by conducting a logistic regression analysis after adjusting for sex, age, and educational differences. Statistical analyses were performed using the SPSS 21.0 software (IBM, Armonk, NY, USA).

RESULTS

Demographic Characteristics of Participants

There was no statistically significant difference in the demographic variables: sex ($\chi^2 = 3.593, p = 0.166$), age ($t = 2.596, p = 0.076$), marital status ($\chi^2 = 14.989, p = 0.132$), education ($\chi^2 = 7.708, p = 0.103$), income ($\chi^2 = 3.502, p = 0.744$), smoking ($\chi^2 = 0.245, p = 0.885$), and alcohol ($\chi^2 = 4.905, p = 0.086$) (Table 1).

Table 1. Demographic and clinical characteristics of participants

Variable		Control group (n = 79)	Non-FGID group (n = 88)	FGID-group (n = 99)	t/ χ^2	p value
Sex	Male	22 (27.8)	17 (19.3)	31 (31.3)	3.593	0.166
	Female	57 (72.7)	71 (80.7)	68 (68.7)		
Age (yr)		41.96 ± 9.04	41.40 ± 9.41	44.59 ± 11.63	2.596	0.076
Marital status	Unmarried	18 (22.8)	27 (30.6)	17 (17.2)	14.989	0.132
	Married	59 (74.7)	56 (63.6)	69 (69.7)		
	Divorced	0 (0.0)	1 (1.1)	2 (2.0)		
	Separation	1 (1.3)	3 (3.4)	4 (4.0)		
	Bereaved	1 (1.3)	1 (1.1)	7 (7.1)		
Education (yr)	Low (< 10)	15 (19.0)	14 (15.9)	15 (15.2)	7.708	0.103
	Middle (10–13)	27 (34.2)	35 (39.8)	52 (52.5)		
	High (> 13)	37 (46.8)	39 (44.3)	32 (32.3)		
Income	Low	28 (35.4)	28 (31.8)	38 (38.4)	3.502	0.744
	Middle	39 (49.4)	45 (51.5)	43 (43.4)		
	High	12 (15.2)	15 (17.0)	18 (18.2)		
Smoking	Yes	7 (8.9)	9 (10.2)	11 (11.1)	0.245	0.885
	No	72 (91.1)	79 (89.8)	88 (88.9)		
Alcohol	Yes	32 (40.5)	47 (53.4)	56 (56.6)	4.905	0.086
	No	47 (59.5)	41 (46.6)	43 (43.4)		

Values are presented as number (%) or mean ± standard deviation. Low: < 2,000 USD/mo, Middle: 2,000–5,000 USD/mo, High: > 5,000 USD/mo.

FGID, functional gastrointestinal disorder; USD, United States dollar.

Table 2. Comparison of depressive symptom and anxiety among the FGID, non-FGID and control group

Variable		Control group (n = 79)	Non-FGID group (n = 88)	FGID group (n = 99)	F	Post-hoc
K-BDI-II	Sum of K-BDI-II	7.15 ± 6.09	10.27 ± 6.99	16.83 ± 10.31	33.256***	1 < 2 < 3
	Affective	2.72 ± 2.90	3.93 ± 3.06	6.49 ± 4.61	24.839***	1 < 2, 1 < 3
	Cognitive	1.57 ± 1.92	2.20 ± 2.45	4.04 ± 4.01	16.560***	1 < 2, 1 < 3
	Somatic	2.86 ± 2.22	4.14 ± 2.37	6.29 ± 3.14	38.587***	1 < 2 < 3
K-BAI	Sum of K-BAI	6.58 ± 8.29	15.93 ± 12.23	19.49 ± 15.27	24.237***	1 < 2, 1 < 3
	Subjective	1.68 ± 1.95	3.77 ± 2.93	6.62 ± 5.23	38.661***	1 < 2 < 3
	Somatic	1.38 ± 2.19	2.91 ± 2.66	4.08 ± 3.13	21.629***	1 < 2 < 3
	Neuropathy	1.14 ± 1.70	2.72 ± 2.55	3.36 ± 3.33	15.696***	1 < 2, 1 < 3
	Muscular	1.10 ± 1.45	3.08 ± 2.31	4.20 ± 3.25	33.733***	1 < 2 < 3
	Respiratory	1.28 ± 1.92	3.45 ± 2.95	1.23 ± 1.97	26.271***	1 < 2, 3 < 2

Values are presented as mean ± standard deviation. 1: control group, 2: non-FGID group, 3: FGID group.

FGID, functional gastrointestinal disorder; K-BDI-II, Korean version of Beck Depression Inventory-II; K-BAI, Korean version of Beck Anxiety Inventory.

*** $p < 0.001$.

Comparison of Symptoms of Depression and Anxiety among the FGID, Non-FGID, and Control Group

The control group showed the lowest K-BDI-II scores: total K-BDI-II score ($F = 33.256, p < 0.001$) and the scores for affective ($F = 24.839, p < 0.001$), cognitive ($F = 16.560, p < 0.001$), and somatic ($F = 38.587, p < 0.001$) symptoms. The control group also showed the lowest K-BAI scores: total K-BAI score ($F = 24.237, p < 0.001$) and the scores for subjective ($F = 38.661, p < 0.001$), somatic ($F = 21.629, p < 0.001$), neuropathy ($F = 15.696, p < 0.001$), muscular ($F = 33.733, p < 0.001$), and respiratory ($F = 26.271, p < 0.001$) symptoms. In addition, significant differences in the total K-BDI-II and somatic symptom scores were found between the FGID and non-FGID groups. The FGID and non-FGID groups showed significant differences in subjective, somatic, and muscular symptoms (Table 2).

Comparison of Childhood Trauma among the FGID, Non-FGID and Control Group

There were significant differences in the total K-CTQ score ($F = 12.248, p < 0.001$) and the scores for emotional ($F = 11.607, p < 0.001$) and physical neglect ($F = 9.768, p < 0.001$), and the control group had the lowest K-CTQ score (Table 3).

The Adjusted Odds Ratio of FGID based on Symptoms of Depression, Anxiety, and Childhood Trauma between the Non-FGID and Control Group

A multivariate logistic regression analysis was performed to identify factors affecting FGID symptoms. The analysis revealed that only anxiety (odds ratio [OR] = 10.215, 95% confidence interval [CI]: 2.49–41.76) was a significant factor (Table 4).

Table 3. Comparison of childhood trauma among the FGID, non-FGID and control group

Variable	Control group (n = 79)	Non-FGID group (n = 88)	FGID group (n = 99)	F	Post-hoc
K-CTQ					
Sum of K-CTQ	46.62 ± 11.79	46.55 ± 11.01	54.33 ± 13.82	12.248***	1 < 2, 1 < 3
Emotional neglect	20.61 ± 8.03	20.14 ± 6.10	24.86 ± 7.88	11.607***	1 < 2, 1 < 3
Physical abuse	5.90 ± 1.65	6.01 ± 1.81	6.53 ± 2.99	1.971	n.s.
Sexual abuse	5.24 ± 0.87	5.60 ± 1.49	5.90 ± 2.55	2.820	n.s.
Emotional abuse	6.13 ± 1.68	6.34 ± 2.21	6.58 ± 3.32	0.681	n.s.
Physical neglect	8.75 ± 3.41	8.45 ± 3.18	10.47 ± 3.54	9.768***	1 < 2, 1 < 3

Values are presented as mean ± standard deviation. 1: control group, 2: non-FGID group, 3: FGID group. FGID, functional gastrointestinal disorder; K-CTQ, Korean version of Childhood Trauma Questionnaire; n.s., non-specific. *** $p < 0.001$.

Table 4. Adjusted odds ratio of FGID according to depressive symptom, anxiety, and childhood trauma between non-FGID and control group

Variable	β	OR	95% CI	p value
Depressive symptom				
Low	1.0			
High	-0.234	0.791	0.12–5.26	0.809
Anxiety				
Low	1.0			
High	2.324	10.215	2.49–41.76	< 0.001
Emotional neglect				
Low	1.0			
High	0.871	2.389	0.98–5.79	0.054
Physical abuse				
Low	1.0			
High	0.194	1.214	0.31–4.72	0.779
Sexual abuse				
Low	1.0			
High	-0.445	0.641	0.14–2.79	0.553
Emotional abuse				
Low	1.0			
High	0.722	2.058	0.37–11.21	0.404
Physical neglect				
Low	1.0			
High	-0.725	0.485	0.23–1.02	0.055

FGID, functional gastrointestinal disorder; OR, odds ratio; CI, confidence interval.

Table 5. Adjusted odds ratio of FGID according to depressive symptom, anxiety, and childhood trauma between FGID and non-FGID group

Variable	β	OR	95% CI	p value
Depressive symptom				
Low	1.0			
High	1.715	5.554	2.06–14.97	< 0.001
Anxiety				
Low	1.0			
High	-0.502	0.606	0.28–1.31	0.199
Emotional neglect				
Low	1.0			
High	-0.209	0.812	0.29–2.21	0.682
Physical abuse				
Low	1.0			
High	0.647	1.909	0.58–6.23	0.284
Sexual abuse				
Low	1.0			
High	0.738	2.092	0.65–6.78	0.219
Emotional abuse				
Low	1.0			
High	-0.720	0.487	0.12–1.92	0.304
Physical neglect				
Low	1.0			
High	1.140	3.128	1.53–6.38	0.002

FGID, functional gastrointestinal disorder; OR, odds ratio; CI, confidence interval.

The Adjusted Odds Ratio of FGID based on Symptoms of Depression, Anxiety, and Childhood Trauma between the FGID and Non-FGID Group

A multivariate logistic regression analysis was performed to determine factors affecting FGID-related health care utilization. The analysis revealed that symptoms of depression (OR = 5.554, 95% CI: 2.06–14.97) and physical negligence (OR = 3.128, 95% CI: 1.53–6.38) were statistically significant factors (Table 5).

DISCUSSION

In this study, we examined how symptoms of depression, anxiety, and childhood trauma varies between the FGID, non-FGID and control groups.

The FGID group was more likely to experience symptoms of depression and anxiety, as compared to the non-FGID and control groups. In previous studies, Lee *et al.* [17] reported that emotional stress and symptoms of depression are independent risk factors for FD and IBS, and Pinto-Sanchez *et al.* [18] found that patients with FGID or various gastrointestinal symptoms were more likely to experience symptoms of depression and anxiety. In this study, there was a statistically significant difference between the FGID and non-FGID groups in somatic symptoms as measured by the K-BDI-II and subjective, somatic, and muscular symptoms as measured by BAI. Therefore, along with the symptoms of depression, the anxiety experienced by FGID patients is a crucial factor in determining FGID-related health care utilization.

Concerning childhood trauma, there was a statistically significant difference in emotional negligence and physical negligence. Experiences of psychological trauma, such as physical and sexual abuse in childhood, are known to affect physical and mental health even in adulthood [19]. Such experiences can not only lead to vomiting, sexual dysfunction, severe gastrointestinal disorders, somatization disorders, and depressive and anxiety disorders but also to disruptive doctor-patient relationships, which could lead to incorrect illness behavior [20]. To date, childhood trauma has been mostly known to result from a reduction in the secretion of brain-derived neurotropic factor, loss of the brain volume, and deregulation of epigenetic factors [21]. In particular, excessive secretion of cortisol or corticotrophin-releasing factor due to hyperthalamo-pituitary-adrenal axis hyperactivity in people with

childhood trauma has been suggested to be a major cause of FGID [22]. Research on psychological factors related to FGID has indicated that childhood abuse, mental disorders, psychological distress, tendency to report a large number of physical symptoms, inadequate coping with stress and lack of social support or relationships can lead to lower threshold level of the nervous system, increase gastrointestinal motility, and cause hyperactivity of the nervous system [23]. This study showed that differences between FGID, non-FGID and control groups were statistically significant only in the emotional negligence and physical negligence sub-categories of K-CTQ. Drossman *et al.* [24] found that only 17% childhood trauma patients reported their problems to therapists or medical professionals. In Asian cultures, sexual abuse has been under-reported due to cultural dynamics [25]. Sexual abuse has also been reported in Asian migrant populations overseas [26]. Therefore, in this study, there was a high possibility of under-reporting of childhood trauma and sexual abuses, and some recall bias cannot be eliminated. Most of the subjects were likely to have a lack of awareness regarding childhood trauma because they grew up in a period of rapid industrialization, where the society did not support and protect the vulnerable populations from different social issues.

The group with a high risk of anxiety had the odds ratio of 10.215 as compared to the control group and the non-FGID group. The symptoms of depression and physical negligence in the high-risk groups had the odd ratios of 5.554 and 3.128, respectively as compared to the non-FGID and FGID groups. Anxiety refers to a mental state that is often associated with mood swings or loss of affection, and depression is a feeling resulting from sadness, frustration, lethargy, or disappointment. Recently, the tripartite model has been getting a lot of attention since this model used depression and anxiety as different factors [27]. The main concepts of the tripartite model are positive affect (PA), negative affect, and physiological hyperarousal (PH). High PA indicates happiness, joy, and motivation, while low PA indicates lethargy and lack of pleasure or motivation. Depressive disorders are mainly associated with low PA and anxiety disorders are associated with high PH [28]. The comparative results between the FGID, non-FGID and control groups showed that anxiety is a significant factor in the manifestation of FGID. This suggests that subjective anxiety due to physio-

logical hyperarousal is important in FGID development.

Additionally, symptoms of depression were distinguishing factors between the FGID and non-FGID groups, indicating that the majority of patients who visit the clinic with symptoms of FGID experience severe psychosocial distress, such as uncontrolled lethargy and loss of motivation, and this may lead to FGID-related health care utilization. However, the causal relationship between depression and a hospital visit is difficult to analyze since many patients visit hospitals or clinic due to gastrointestinal symptoms that are independent of symptoms of depression. However, gastrointestinal symptoms may be severe enough to require hospital visits for treatment and this can result in depression. Regardless of this causal relationship, proper treatment of comorbid depression is strongly recommended. Irritable bowel syndrome studies have reported that the treatment of accompanying depression improves both mental and gastrointestinal symptoms [29]. Therefore, the patients who visited the clinic with FGID should be provided with not only internal medical treatment but also professional evaluation of psychological symptoms and active psychosocial interventions such as the use of appropriate psychiatric medications, cognitive behavioral therapy, psychotherapy, and internal meditations. There is also a need for education on different aspects of mental health, along with physical and emotional protection in childhood and adolescence to prevent an adulthood onset of FGID.

This study has some limitations. First, the scale for identifying psychological characteristics is based on self-report questionnaires, which could be compromised due to recall bias and/or under-reporting. Second, there is a limit to derivative reasoning based on cross-sectional data. Third, subjects in the control and non-FGID groups did not undergo evaluation by gastroenterologists. Fourth, there was a limitation in generalizing the study results because the patients visited tertiary care specialty centers. Last but not least, due to the insufficient number of subjects, a comparative analysis was not performed for the FGID sub-type variables.

Nonetheless, this study is highly reliable because psychiatrists evaluated psychopathology and psychosocial characteristics in patients who were diagnosed with FGID by gastroenterologists. Moreover, the sub-factors of symptoms of depression and anxiety were evaluated, and a comparative evaluation between the FGID, non-FGID

and control groups was performed. In summary, various therapeutic interventions to minimize the impacts of psychosocial risk factors are required for the clinical management of FGID patients.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization and article design: Seung-Ho Jang, Sang-Yeol Lee, Han-Seung Ryu, and Suck-Chei Choi. Data acquisition and analysis: Seung-Ho Jang and Sang-Yeol Lee. Writing—original draft: Han-Seung Ryu and Suck-Chei Choi. All authors approved the final manuscript and agreement with submission.

■ ORCID

Sang-Yeol Lee	https://orcid.org/0000-0003-1828-9992
Han-Seung Ryu	https://orcid.org/0000-0002-9359-0075
Suck-Chei Choi	https://orcid.org/0000-0003-1338-3306
Seung-Ho Jang	https://orcid.org/0000-0002-3479-0552

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