



# The Association of Psychological Comorbidity with the Number of Functional Gastrointestinal Disorders

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## Quantitative Study

### Abstract

**Background:** The overlap of functional gastrointestinal disorders (FGIDs) has been reported in literature. Hence, this study aimed to examine psychological comorbidity with the number of FGIDs.

**Methods:** A total of 4763 individuals in 20 cities across Isfahan Province, Iran, were selected through cluster random sampling. The Rome III questionnaire in its complete form was used to investigate gastrointestinal symptoms. The other data collection tools consisted of the Stressful Life Events (SLE) Questionnaire, and Hospital Anxiety and Depression Scale (HADS). To analyze the data, t-test, chi-square test, and logistic regression analyses were used.

**Results:** The results of logistic regression analysis showed that the number of functional gastrointestinal disorders was the risk factor for stress level, anxiety, and depression and increased the odds ratio (OR) of these disturbances.

**Conclusion:** Increase in the number of functional gastrointestinal disorders was associated with more psychological comorbidity. Therefore, overlap of functional gastrointestinal disorders functional gastrointestinal disorders to be carefully considered and physicians should pay more attention to psychological factors when FGIDs overlap.

**Keywords:** Functional gastrointestinal disorders (FGIDs), Psychological disturbances, Rome III

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### Introduction

Functional gastrointestinal disorders (FGIDs) are common conditions (Jones, Crowell, Olden, & Creed, 2007), which are observed in

patients with both upper and lower gastrointestinal tract symptoms (Dobrek & Thor, 2009). Population-based studies in western countries consistently report prevalence rates of 10-20 percent (Drossman et al., 1993). The epidemiological data show that the frequency of occurrence of FGIDs is similar in Western and Central European

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countries and in the USA with lower incidence in the Asiatic Region. The highest ages of clinical manifestation of FGIDs are 40-50 years (Dobrek & Thor, 2009).

These disorders are characterized by the occurrence of various dyspeptic, dysmotility, and pain symptoms (Dobrek & Thor, 2009). A new classification of FGIDs based on consensus in expert committees (Rome III Diagnostic Criteria for FGIDs) is available (Van Oudenhove, Vandenberghe, Demyttenaere, & Tack, 2010). FGIDs are classified into 6 major domains of esophageal, gastroduodenal, bowel, functional abdominal pain, biliary, and anorectal disorders for adults (Drossman et al., 2006). It is common for FGIDs to coexist, and the criteria permit the coexistence of more than one FGID (Drossman et al., 2006). The overlap of pairs of FGIDs has been widely reported in the literature (Choung et al., 2011; Park et al., 2011; Suzuki & Hibi, 2011). It has been estimated that more than one-third of the general population have one or more FGIDs (Koloski, Talley, & Boyce, 2002).

Although these digestive disorders comprise a major portion of the clinical practice of both gastroenterologists and primary-care physicians, they are often regarded as challenging and frustrating. Much of this difficulty stems from the fact that the pathophysiology of FGID is not completely understood (Jones et al., 2007). However, it is accepted that these common disorders result from a complex reciprocal interaction between biological, psychological, and social factors that can be predisposing, precipitating, and/or perpetuating (Van Oudenhove et al., 2010).

Concomitant psychological disorders, notably anxiety and depressive disorders, are strongly associated with FGIDs and these psychological comorbidities correlate with severity of FGID symptoms (Wu, 2012). Anxiety and depression are frequently present in patients with different types of FGIDs, and seem to play a major part in both the perception of symptoms and the outcome of treatment (Bouchoucha et al., 2013). The

onset of the psychiatric illness often predates or coincides with the onset of bowel disorder (Walker et al., 1990). The investigation of the influence of stress has revealed that it is the factor aggravating the course of FGIDs (Dobrek & Thor, 2009). The interrelationship between digestive function and hypersensitivity with stress forms the basis of the biopsychosocial model. In this model, various stressors can transiently or permanently alter physiological stress responses (Jones et al., 2007).

Considering the correlations between psychological comorbidities and severity of FGID symptoms, it is hypothesized that these comorbidities can be likely correlated with the number of FGIDs diagnosed in a patient. Therefore, the present research studied whether the higher number of FGIDs was more associated with psychological comorbidities. Hence, the aim of the present study was to determine the association of psychological comorbidities with the number of FGIDs in a large group of community individuals with FGIDs.

## Methods

### Study design and participants

The current study was part of the "Study on the Epidemiology of Psychological, Alimentary Health and Nutrition" (SEPAHAN) (Adibi et al., 2012). In the SEPAHAN study, data were collected in two separate phases to increase accuracy as well as response rate. In the first phase, all participants were asked to complete a self-administered questionnaire on demographic and lifestyle factors including nutritional habits and dietary intakes. In the second phase, further information on GI functions and different aspects of psychological variables were collected using a number of other self-administered questionnaires (response rate: 86.16%). In the current analysis, we used data on 4,763 adults who had completed the questionnaires on demographic data, symptoms of FGIDs, life events, and psychological disturbances such

as depression and anxiety. The protocol of the study was approved by the Ethics Committee of Isfahan University of Medical Sciences (Isfahan, Iran) and was clarified for all the participants, and a written informed consent was obtained from all participants.

### Measures

**Demographic factors:** In the current study, demographic information included age, sex, marital status consisting of married and unmarried (single, divorced, or widowed) and educational level consisting of graduate and undergraduate.

**FGID Symptom Checklist:** To assess the presence or absence of different symptoms of FGIDs including dyspepsia, irritable bowel syndrome (IBS), abdominal pain, functional constipation, and functional diarrhea, Rome III questionnaire was used. The diagnosis of FGIDs was based on this self-administered questionnaire (Attanasio, Andrasik, Blanchard, & Arena, 1984).

**Stressful Life Events Questionnaire:** The Stressful Life Events (SLE) questionnaire measures the frequency and the perceived intensity of different stressors of daily life. In addition, the values of stressors on individuals' health that determine risk of stress-related illness are assessed by this questionnaire. It is comprised of 46 items in 11 domains, including home life, financial problems, social relations, personal conflict, occupational conflict, educational concerns, occupational security, loss and separation, sexual life, daily life, and health concerns. In order to assess the effect of stressors and whether or not stress contributes to illness, participants were asked to determine whether they had experienced any of a series of 46 life events in the last year. Each stressful life event had a different "weight" for the participants who experienced them.

The more events the individuals had experienced, the higher the score they obtained. With increase in total score and the weight of each event, the likelihood of individuals becoming ill also increased. A cut-off point of 100 was considered as risk of stress-

related illness (high stress) (Roohafza et al., 2011; Sali et al., 2013).

**Hospital Anxiety and Depression Scale (HADS):** The Hospital Anxiety and Depression Scale (HADS) consists of 14 items that can be divided into two scales; anxiety ( $\alpha = 0.82$ ) and depression ( $\alpha = 0.84$ ). Each scale consists of 7 items, with a total score ranging from 0 to 21. Higher scores reflect more anxiety and more depression. Threshold points for clinical levels of anxiety and depression were set at a score  $\geq 11$  (Snaith, 2003).

### Statistical analysis

Data were analyzed using SPSS software (version 15.0, SPSS Inc., Chicago, IL, USA). All P-values  $< 0.05$  were considered significant. Continuous variables were expressed as mean  $\pm$  SD and differences between groups were analyzed using t-test. Qualitative variables were expressed as frequency and chi-squared test was used to compare frequencies between groups.

Binary logistic regression analyses were used to find the associations between the number of FGIDs and psychological disturbances (stress level, anxiety, and depression). The dependent variables were levels of stress (low/high), and presence of anxiety (yes/no) and depression (yes/no), and the independent variables were the number of FGIDs. Odds ratios (OR) were reported with the corresponding 95% confidence intervals.

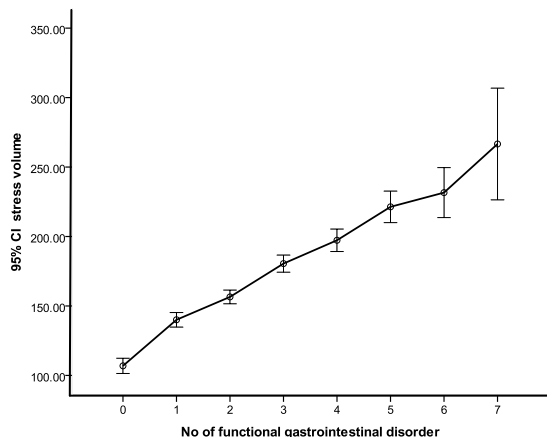
## Results

A total of 4763 respondents with mean  $\pm$  SD age of  $36.58 \pm 8.09$  years (men:  $38.59 \pm 8.61$ ; women:  $35.16 \pm 7.38$ ) were included in the study. The study population consisted of 2657 (55.8%) women, 3776 (79.3%) married individuals, and 2650 (55.6%) graduates. The scores of demographic and psychological characteristics (scores of stress, depression, and anxiety) according to the number of FGIDs are presented in table 1. The occurrence of 0-7 FGIDs was observed in 847 (17.5%), 1019 (21.4%), 1056 (22.2%), 844 (17.7%), 540 (11.3%), 306 (6.4%), 119 (2.5%), and 32 (0.7%) participants, respectively.

**Table 1.** Demographic and psychological characteristics according to the number of functional gastrointestinal disorders

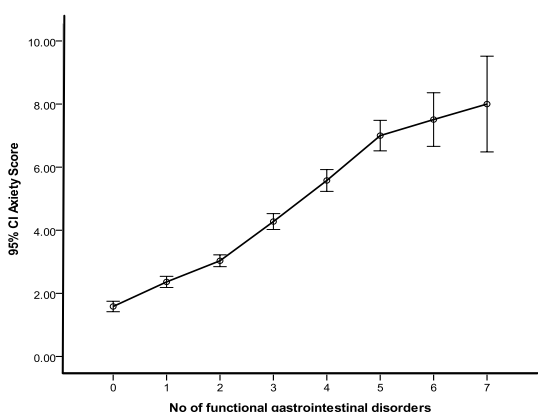
Variables	Number of functional gastrointestinal disorders								P-value	
	0	1	2	3	4	5	6	7		
<b>Demographic characteristics</b>										
Age (Mean ± SD)	36.98 ± 8.67	36.65 ± 8.23	36.09 ± 7.65	36.99 ± 8.04	36.12 ± 7.90	36.42 ± 7.87	35.84 ± 6.93	40.96 ± 11.05	0.020	
Sex										
Number (%)	Male	416 (49.1)	511 (50.1)	468 (44.3)	356 (42.2)	212 (39.3)	92 (30.1)	33 (27.7)	18 (56.3)	< 0.001
Number (%)	Female	431 (50.9)	508 (49.9)	588 (55.7)	488 (57.8)	328 (60.7)	214 (69.9)	86 (72.3)	14 (43.8)	
Educational level										
Number (%)	Undergraduate	370 (44.9)	410 (41.5)	388 (37.7)	360 (43.8)	228 (42.8)	145 (49.0)	64 (56.6)	21 (70.0)	< 0.001
Number (%)	Graduate	454 (55.1)	579 (58.5)	642 (62.3)	461 (56.2)	305 (57.2)	151 (51.0)	49 (43.4)	9 (30.0)	
Marital Status										
Number (%)	Married	652 (79.2)	792 (79.7)	839 (81.3)	681 (82.4)	448 (84.8)	239 (79.7)	99 (85.3)	26 (83.9)	0.139
Number (%)	Unmarried	171 (20.8)	202 (20.3)	193 (18.7)	145 (17.6)	80 (15.2)	61 (20.3)	17 (14.7)	5 (16.1)	
<b>Psychological characteristics</b>										
Depression score (Mean ± SD)	4.65 ± 2.90	5.24 ± 2.92	5.87 ± 2.96	6.62 ± 3.32	7.55 ± 3.39	8.71 ± 3.68	9.30 ± 3.60	9.46 ± 3.67	< 0.001	
Anxiety score (Mean ± SD)	1.58 ± 2.42	2.36 ± 2.84	3.03 ± 3.06	4.27 ± 3.67	5.57 ± 4.05	7.00 ± 4.29	7.50 ± 4.61	8.00 ± 4.21	< 0.001	
Stress score (Mean ± SD)	106.89 ± 81.32	140.05 ± 84.81	156.51 ± 82.03	180.50 ± 91.41	197.29 ± 95.91	221.35 ± 101.11	231.60 ± 99.09	266.59 ± 111.61	< 0.001	

Psychological variables scores according to the number of FGIDs are shown in figures 1-3. As is seen, with increase in the number of FGIDs, the scores of these variables also increase.



**Figure 1.** Stress score according to the number of functional gastrointestinal disorders

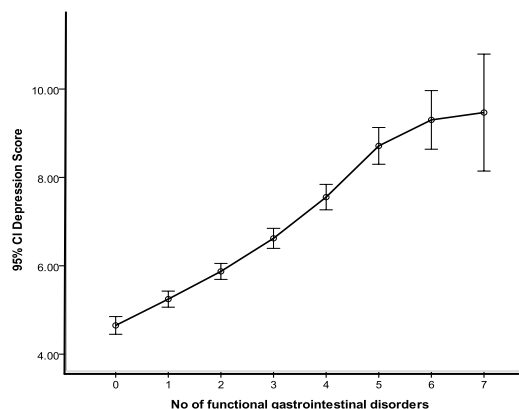
As shown in figure 2, for comparison of the number of FGIDs according to psychological status, the percentage of stress, anxiety, and depression levels are recorded in two categories. About 3338 (70.1%) respondents had high level of stress. Moreover, about 1338 (28.1%) and 654 (13.7%) of the individuals had depression and anxiety symptoms, respectively. These percentages increased with increase in the number of FGIDs, as individuals with 7 FGIDs had higher stress (at risk of disease), depression, and especially anxiety.



**Figure 2.** Anxiety score according to the number of functional gastrointestinal disorders

Furthermore, the frequency of psychological variables according to the

number of FGIDs is depicted in figure 4. The frequency of these variables increased with increase in the number of FGIDs. Individuals with higher number of FGIDs had higher stress, depression, and especially anxiety.



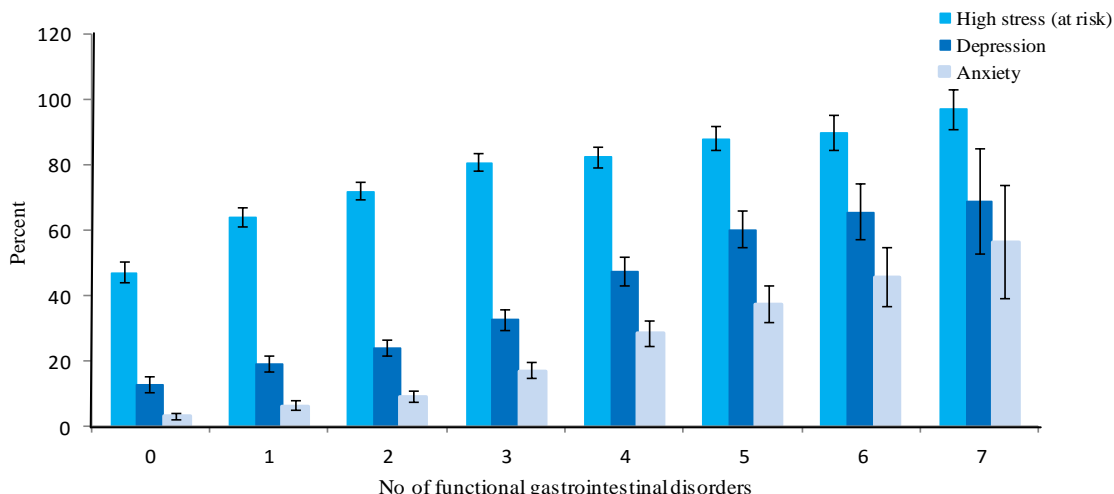
**Figure 3.** Depression score according to the number of functional gastrointestinal disorders

To examine the associations between number of FGIDs and psychological status, binary logistic regression analyses were conducted. The results are provided in table 2. The overlap of FGIDs was the risk factor for stress level, anxiety, and depression. However, the overlap of FGIDs was more important in the occurrence of anxiety.

**Discussion**

In accordance with the main aim of the study, the results showed that higher number of FGIDs was associated with increased stress, depression, and anxiety levels. In other words, increased number of FGIDs increases the OR to psychological disturbances. This is consistent with findings of a limited number of previous studies, most of which have studied the information on relationships between the assessed variables (Bouchoucha et al., 2013; Bennett et al., 1998; Park et al., 2013; Lee et al., 2010).

In fact, our results support the association of the overlap of FGIDs with high levels of psychological comorbidity. Bennett et al. reported significant relationships between the number of FGIDs and severity of emotional distress (state anxiety, depression, anger, and goal frustration).



**Figure 4.** Frequency of psychological variables according to the number of functional gastrointestinal disorders

Psychosocial disturbance was strongly related to the overall severity and extent of functional gut disturbance (the number of coexistent FGID subgroups). The study by Bouchoucha et al. (2013) showed that levels of depression and state and trait anxiety are higher in patients with several sites of complaint. In addition, Park et al. (2013) found that the load of symptoms consistent with FGID in each patient (i.e., the number of FGID symptom clusters per patient) correlated with psychological comorbidity (higher rates of depression and anxiety). As previously mentioned, functional dyspepsia (FD) and IBS are the most common FGIDs and most studies are conducted on them. For example, Lee et al. (2010) reported that depressive mood was significantly related to FD and FD-IBS overlap, but not to IBS alone. Patients with FD-IBS overlap had a lower quality of life (QOL) than patients with FD alone or IBS alone (Wang et

al., 2008). Overlaps between FD and IBS significantly worsen health-related QOL (HRQOL) in most domains (Kaji et al., 2010).

Our results were inconsistent with the findings of Mikocka-Walus, Turnbull, Andrews, Moulding, and Holtmann (2008). In their study, participants with no FGID had a significantly better physical QOL than those with more than two FGIDs. However, there was no relationship between the number of FGIDs, mental QOL, anxiety, or depression (Mikocka-Walus, Turnbull, Andrews, Moulding, & Holtmann, 2008). This is probably due to the fact that their study was performed in IBD patients. In contrast to IBS, psychological disorders in IBD patients are more a reaction to the disease itself than a cause for it and associate with poorer QOL (Mikocka-Walus et al., 2008). Furthermore, the lack of association may be because of their study's smaller sample size (n = 61).

**Table 2.** Crude and adjusted odds ratios of number of functional gastrointestinal disorders and psychological variables (adjusted based on age and sex)

Number of functional gastrointestinal disorders	Stress level	Anxiety	Depression
	Reference	Reference	Reference
1	1.54 (1.13, 2.11)	1.90 (1.15, 3.15)	1.55 (1.17, 2.05)
2	1.96 (1.45, 2.65)	2.67 (1.66, 4.31)	2.05 (1.56, 2.69)
3	3.53 (2.63, 4.76)	5.81 (3.67, 9.20)	3.04 (2.32, 3.99)
4	5.08 (3.72, 6.94)	10.91 (6.87, 17.31)	5.76 (4.33, 7.66)
5	7.67 (5.42, 10.87)	15.81 (9.72, 25.72)	8.99 (6.45, 12.52)
6	10.47 (6.52, 16.82)	22.49 (12.58, 40.20)	11.64 (7.21, 18.78)
7	19.03 (7.82, 46.30)	37.48 (15.04, 93.40)	13.21 (5.44, 32.07)

One reason for this finding may be that development in a number of FGIDs can be in the sense of involving more parts of the GI tract, and consequently, growth of numbers of FGIDs and intensification of severity of symptoms. Another reason may be that the brain-gut axis is conceptualized as the bidirectional connection system between the GI tract and the brain (Van Oudenhove et al., 2010). As the brain affects the gut, similarly, activity in the gut can affect mood and behavior in the brain (Dalton, 2016). Thus, it follows that a rise in the number of FGIDs can influence the emotional system more and cause more severe psychological comorbidities. In this regard, investigators have showed that among individuals who did not have high levels of anxiety and depression at baseline, those with a FGID at baseline had significantly higher levels of anxiety and depression at follow-up (Koloski et al., 2012). Moreover, Suzuki and Hibi (2011) indicated that overlap of FGIDs is associated with more severe symptoms than any FGIDs alone. Furthermore, psychiatric comorbidity is strongly correlated with the severity of digestive symptoms and degree of impairment (Haug, Mykletun, & Dahl, 2002; Van Oudenhove et al., 2008).

The strength of this study was utilizing a large sample to reliably assess the effect of the number of FGIDs on psychological disturbances. The limitations of this study were reliance on self-report data which may be biased regarding the occurrence of symptoms, and also existence a problem regarding whether GI symptoms were functional or organic; nevertheless, using a validated questionnaire for the Rome III criteria. In addition, FGIDs were not separated.

In summary, overlap of FGIDs occurs in the general population and there are relationships between the overlap of FGIDs and psychological disturbances, namely increase in the number of disorders was associated with more psychological comorbidity. Overlap of FGIDs strengthens the importance of a complete assessment of

other FGIDs when a patient is diagnosed with a functional disorder. Thus, it needs to be carefully considered and physicians should pay more attention to psychological factors when FGIDs overlap.

### Conflict of Interests

Authors have no conflict of interests.

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