

ORIGINAL ARTICLE

Relationship between Depression and Constipation: Results from a Large Cross-sectional Study in Adults

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Background/Aims: Accumulating evidence based on a few studies suggests a relationship between depression and functional constipation. This study examined whether depression is associated with a higher risk of functional constipation and whether it is gender specific.

Methods: This cross-sectional study was carried out on 3,362 adults aged 18-55 years. In this study, functional gastrointestinal symptoms were determined using an Iranian reliable and valid version of the modified Rome III questionnaire. The Iranian validated version of the hospital anxiety and depression scale was used to evaluate the psychological health. Scores of eight or more on the depression subscale in the questionnaire were considered the presence of depression. Simple and multiple binary logistic regression were used for data analysis.

Results: The mean±SD age of participants was 36.29±7.87 years, and 58.5% were female. The prevalence of depression and constipation in the study sample was 28.6% and 23.9%, respectively. In the full adjusted model, in the total sample, depressed people showed a significantly higher risk of constipation; adjusted OR (AOR), 1.69 (95% CI, 1.37-2.09). Although a significant association was observed between depression and constipation in both genders, the association was stronger in men than women (AOR, 2.28; 95% CI, 1.50, 3.63 vs. AOR, 1.55; 95% CI, 1.21, 1.99).

Conclusions: These study findings showed that depressed people are at a significantly higher risk of being affected by constipation. The current study findings justify the importance of mental health evaluations in all patients with functional gastrointestinal disorders, particularly among constipated individuals. (*Korean J Gastroenterol* 2022;80:77-84)

Key Words: Constipation; Depression; Gastrointestinal diseases; Mental health; Adult

INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are defined as a variable combination of chronic or recurrent gastrointestinal

symptoms not explained by structural or biochemical abnormalities.¹ Irritable bowel syndrome (IBS) and functional constipation (FC) are the most common functional gastrointestinal disorders. According to the Rome III criteria, these

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two disorders should be theoretically separated mainly by abdominal pain or discomfort relieved by defecation (typical of IBS). They should be mutually exclusive.² Constipation is a highly prevalent gastrointestinal motility disorder characterized by persistently difficult or infrequent (i.e., less than three times per week) defecation.³ Chronic constipation (CC) is one of the most common gastrointestinal disorders. In some populations, it is the most common digestive complaint, which leads to a large number of medical visits.⁴ In a previous cohort study in 2018, Moezi et al.⁵ evaluated the prevalence of CC and its associated factors. Among 9,000 adults in southern Iran, 752 participants (8.1%) were diagnosed with CC (9.3% and 6.7% of the female and male participants, respectively).⁵ Previous studies reported a wide range of prevalences CC (2-27% with an average of 15% in most studies).⁶ This wide range is due to different study populations and different inclusion criteria, e.g., studies that reported the prevalence based upon self-reporting showed higher prevalence than those that used the ROME criteria,⁷ or studies conducted in Southeast Asia reported lower prevalence compared to American and European studies.⁸⁻¹⁰

Several factors are associated with constipation. Based on previous studies, some risk factors for functional constipation include female sex, older age, low socioeconomic status, physical inactivity, and insufficient fluid and fiber consumption.¹⁰⁻¹² In addition, a set of psychological variables can be related to constipation. Cheng et al.¹³ investigated the prevalence of functional constipation in an Asian population and the interplay among functional constipation, anxiety/depression, perception, and coping strategies. Albani et al.¹⁴ examined anxiety and depression as potential mediators of the relationship between constipation severity and quality of life in a sample of 142 constipated patients. Fond et al.¹⁵ evaluated the associations of IBS and its subtypes with anxiety or depression. Ballou et al.¹⁶ investigated the relationship between depression and bowel habits, controlling for the clinical and demographic factors, in a representative sample of the United States population in the framework of the National Health and Nutrition Examination Survey. Mokhtar et al.¹⁷ evaluated the prevalence of depression among patients with constipation-predominant IBS (IBS-C).

Overall, accumulating evidence based on a few studies suggests a relationship between depression and functional constipation. On the other hand, more studies are needed

to provide more reliable evidence. Therefore, this study examined whether depression is associated with a higher risk of functional constipation and whether this relationship is gender specific.

SUBJECTS AND METHODS

1. Study design and subjects

The present study was a cross-sectional study in the framework of the SEPAHAN project. The SEPAHAN study examined the epidemiological aspects of functional gastrointestinal disorders and their relationship with lifestyle and psychiatric factors on 10,500 non-academic staff apart from the treatment department of Isfahan University of Medical Sciences and Health Services in April 2010. The sample consisted of non-academic staff working in 50 centers across Isfahan province, Iran. The staff were directly involved in health services, working in hospitals, university campuses, and health centers. In the SEPAHAN study, the questionnaires were distributed in two stages with a short time interval (3 to 4 weeks) to increase the rate of response and participation of individuals and the accuracy of the collected data. In the first stage, a demographic information questionnaire, nutritional performance, health search behaviors, and food intake, and in the second set of questionnaires. The participants were asked about information about gastrointestinal and mental and physical illnesses, personality traits, perceived stresses, and coping styles. The response rate in the first stage was 86.1% and in the second stage was 64.64%. After merging the data in these two stages, complete information was obtained from 4,763 people. In the current secondary study, 3,362 with complete data on all variables were included. More complete information on the SEPAHAN project can be found in other published articles.¹⁸

2. Depression assessment

The hospital anxiety and depression scale (HADS) was used to evaluate depression. The HADS contains 14 items and consists of two subscales of anxiety and depression. Each item is rated on a four-point scale, with the anxiety and depression subscales separately obtaining a maximum score of 21. Scores of eight or more on either subscale are considered a significant case of psychological morbidity, and 0-7 were normal.¹⁹ The validated Persian version of HADS with Cronbach alpha of

0.86 for depression subscale was used.²⁰

3. Constipation assessment

Functional gastrointestinal symptoms were determined using an Iranian reliable and valid modified version of Rome III questionnaire,²¹ which diagnoses functional gastrointestinal disorders and consists of six major domains, with functional oesophageal disorders and functional gastrointestinal disorders being two domains in the questionnaire for adults. Each domain contains several questions to aid in diagnosing these disorders based on Rome III criteria. According to the Rome III criteria, constipation was defined as the presence of at least one or two of the following symptoms, for at least 3 months, with the onset at least 6 months preceding this study.

- 1) Straining during in at least 25% of defecations (at least often).
- 2) Lumpy or hard stools in at least 25% of defecations (at least often).
- 3) Sensation of incomplete evacuation in at least 25% of defecations (at least sometimes).
- 4) Sensation of anorectal obstruction/blockage in at least 25% of defecations (at least sometimes).
- 5) Manual maneuvers facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor) (at least sometimes).
- 6) Fewer than three defecations per week.

4. Other variables

Self-administered questionnaires were used to collect information regarding age (years), sex (male, female), marital status (married, single), education level (under diploma, diploma (12-years formal education), collegiate), and anthropometric measures, including weight, height, and body mass index ($BMI = \text{weight [kg]} / \text{height square [m}^2\text{]}$). Smoking and physical activity based on self-reported questions were also evaluated. The participants were divided into three categories “nonsmoker”, “ex-smoker”, or “current smoker”. The general practice physical activity questionnaire was used to evaluate physical activity levels.²² The level of physical activity in the current study was considered to be less than 1 hour/week/more than 1 hour/week. Usual dietary intakes during the preceding 12 months were assessed using a validated 106-item self-administered semi-quantitative dish-based food frequency questionnaire (FFQ) designed especially for adults living in Isfahan

province.²³ The semi-quantitative FFQ included 36 questions to assess the intake of most commonly consumed fruits and vegetables (raw or cooked as mixed dishes). Those fruits and vegetables that are consumed raw include cucumbers, tomatoes, dates, raisins, herbs, dried berries, salad, citrus, apples or pears, cherries, apricot, plum, raw onions, kiwi, strawberries, grapes, pomegranate, mulberry, banana, figs, and all kinds of fruit juice. Daily intakes of nutrients (g/day), including individual dietary fiber, were calculated for each participant using the US department of agriculture's nutrient databank.²⁴ Fluid intake was evaluated through questions on the consumption of water, soft drinks, yogurt drink (“dough”), and other beverages, before, after, or during meals, which the participants could answer as never, sometimes, often, or always.²⁵ Data on the current use of psychotropic medications (including nortriptyline, amitriptyline or imipramine, fluoxetine, citalopram, fluvoxamine, and sertraline) as (yes/no) were gathered using a self-reported questionnaire and a history of any predisposing chronic diseases (non-disease/disease), including diabetes mellitus and cardiovascular diseases, was also collected from the participants.

5. Statistical analysis

The continuous and categorical basic characteristics of the study subjects are presented as the mean (SD) and frequency of chronic diseases (percentage), and compared between study groups using independent samples *t*-test and chi-squared test, respectively. Binary logistic regression analysis was used to find the association between depression and constipation. The ORs were reported with the corresponding 95% CIs. Multiple binary logistic regression was used to estimate the adjusted ORs (95% CI) in association analyses between depression and constipation.

Separate models were used to fit the association between constipation and depression. In simple binary logistic regression analysis, this study only evaluated the crude association between depression and constipation. Multivariable analyses were performed in the first model, adjusting for age, sex, marital status, and education level. Further adjustment was made for smoking habits, physical activity, fluid consumption, fruits, vegetables, and total dietary fiber intakes. In the final model, further adjustment was made for chronic disease and psychotropic medication use. All statistical analyses were conducted using Statistical Package for Social

Sciences (SPSS, Inc., Chicago IL, United States; version 16). $p < 0.05$ was considered significant in all statistical analyses.

RESULTS

The mean \pm standard deviation age of the 3,674 study subjects was 36.29 ± 7.87 years, and 58.5% were female. Table 1 lists the general characteristics of the study population

stratified according to the status of functional constipation. The prevalence of FC in this study was 23.9% (15% in men and 30.2% in women). The prevalence of functional constipation was higher in women ($p < 0.001$) and less physically active people ($p < 0.05$). The weight and fluid consumption were significantly lower in constipated people ($p < 0.001$ for both). In contrast, those who consumed psychotropic medicines ($p < 0.001$) and depressed people were affected more

Table 1. General Characteristics of Participants Based on Categories of Functional Constipation

Variable	Functional constipation		p-value
	No (n=2,560)	Yes (n=802)	
Age (years)	36.25 ± 7.94	36.42 ± 7.63	0.623 ^a
Sex			<0.001 ^b
Male	1,193 (85)	210 (15)	
Female	1,367 (69.8)	592 (30.2)	
Education level			0.583 ^b
Under diploma	982 (76.7)	299 (23.3)	
Collegiate	1,578 (75.8)	503 (24.2)	
Marital Status			0.418 ^b
Married	2,042 (75.9)	648 (24.1)	
Single	430 (78.5)	118 (21.5)	
Divorced or widowed	41 (74.5)	14 (25.5)	
Smoking habits			0.424 ^b
Non smoker	2,209 (76.2)	689 (23.8)	
Current smoker	75 (79.8)	19 (20.2)	
Physical activity			0.016 ^b
Less than 1 hour/week	1,547 (74.6)	526 (25.4)	
More than 1 hour /week	823 (78.5)	225 (21.5)	
Weight (kg)	69.24 ± 13.55	66.76 ± 11.75	<0.001 ^a
BMI (kg/m^2)	24.89 ± 3.83	24.96 ± 3.81	0.632 ^a
Total dietary fiber (g/day)	22.67 ± 9.69	21.99 ± 9.36	0.082 ^a
Fruits (g/day)	319.43 ± 245.24	304.76 ± 234.21	0.135 ^a
Vegetables (g/day)	238.34 ± 131.22	235.70 ± 130.93	0.619 ^a
Fluid consumption (L/day)	1.35 ± 0.58	1.26 ± 0.51	<0.001 ^a
Psychotropic medicines			<0.001 ^b
No	2,441 (76.9)	734 (23.1)	
Yes	119 (63.6)	68 (36.4)	
Chronic diseases			0.592 ^b
Non disease	2,444 (76.2)	762 (23.8)	
Disease	116 (74.4)	40 (25.6)	
Depression			<0.001 ^b
No	1,878 (79.8)	476 (20.2)	
Yes	629 (66.7)	314 (33.3)	

Values are presented as number (%) or mean \pm standard deviation. $p < 0.05$ is considered as significant.

BMI, body mass index.

^at-test; ^bChi-squared test.

significantly by constipation ($p < 0.001$) (Table 1).

Table 2 lists the general characteristics of the study pop-

ulation stratified according to the status of depression. The prevalence of depression in this study was 28.6% (20.8% in

Table 2. General Characteristics of Participants Based on the Categories of Depression

Variable	Depression		p-value
	No	Yes	
Age (years)	36.13±7.94	36.32±7.61	0.562 ^a
Sex			<0.001 ^b
Male	10.82 (79.2)	285 (20.8)	
Female	1,272 (65.9)	658 (34.1)	
Education level			<0.001 ^b
Under graduate and diploma	837 (66.9)	414 (33.1)	
University graduate	1,517 (74.1)	529 (25.9)	
Marital Status			0.001 ^b
Married	1,901 (72.2)	733 (27.8)	
Single	380 (70.0)	163 (30.0)	
Divorced or widowed	26 (49.1)	27 (50.9)	
Smoking habits			0.063 ^b
Non smoker	2,064 (72.6)	779 (27.4)	
Current smoker	58 (63.7)	33 (36.3)	
Physical activity			<0.001 ^b
Less than 1 hour/week	1,394 (63.6)	2,034 (66.4)	
More than 1 hour/week	797 (36.4)	1,027 (33.6)	
Weight (kg)	69.12±13.19	67.16±12.99	<0.001 ^a
BMI (kg/m ²)	24.91±3.70	24.85±4.10	0.712 ^a
Total dietary fiber (g/day)	22.83±9.60	21.65±9.64	0.001 ^a
Fruits (g/day)	330.54±247.86	276.67±218.09	<0.001 ^a
Vegetables (g/day)	241.78±129.20	227.71±137.19	0.006 ^a
Fluid consumption (L/day)	1.32±0.56	1.34±0.58	0.548 ^a
Psychotropic medicines			<0.001 ^b
No	2,278 (72.2)	837 (27.8)	
Yes	76 (41.8)	106 (58.2)	
Chronic diseases			<0.001 ^b
Non disease	2,272 (96.5)	3,146 (95.4)	
Disease	52 (3.5)	151 (45.7)	
Constipation			<0.001 ^b
No	1,878 (74.9)	2,507 (25.1)	
Yes	476 (61.3)	790 (39.7)	

Values are presented as number (%) or mean±standard deviation. $p < 0.05$ is considered as significant.

BMI, body mass index.

^at-test; ^bChi-squared test.

Table 3. Relationship between Depression and Constipation by the Logistic Regression Model

	Total (OR [95% CI])	Men (OR [95% CI])	Women (OR [95% CI])
Crude	1.97 (1.66, 2.33)	2.64 (1.91, 3.64)	1.52 (1.24, 1.86)
Model 1 ^a	1.83 (1.52, 2.21)	2.78 (1.94, 3.99)	1.59 (1.28, 1.97)
Model 2 ^b	1.76 (1.43, 2.17)	2.31 (1.54, 3.46)	1.62 (1.27, 2.07)
Model 3 ^c	1.69 (1.37, 2.09)	2.28 (1.50, 3.63)	1.55 (1.21, 1.99)

OR, odds ratio; CI, confidence interval.

^aAdjusted for age, sex, marital status and education level only in the whole population; ^bFurther adjustment was made for smoking habits, physical activity, fluid consumption, fruits, vegetables, and total dietary fiber; ^cFurther adjustment was made for chronic disease, psychotropic medicines.

men and 34.1% in women). The prevalence of depression was significantly higher in women ($p<0.001$), less educated ($p<0.001$), current smokers (marginally, $p=0.063$), constipated people ($p<0.001$), less activated ($p<0.001$), and people with chronic diseases ($p<0.001$). The mean weight ($p<0.001$) and mean intake of dietary fiber ($p=0.001$), fruits ($p=0.006$), and vegetables ($p<0.001$), were significantly lower in depressed people than in non-depressed people (Table 2).

The crude and multivariable-adjusted OR (95% CI) of constipation across the categories of depression are illustrated in Table 3. In the crude model, in the total sample, depressed people showed a higher significant risk of constipation OR, 1.97 (95% CI, 1.66-2.33). The risk of constipation in depressed people was 1.97 times that of non-depressed people. Although observed a significant association was observed between depression and constipation in both genders, the association was stronger in men than women (OR, 2.64; 95% CI, 1.91, 3.64 vs. OR, 1.52; 95% CI, 1.24, 1.86). In men, the risk of constipation in depressed people was 2.64 times that of non-depressed people, and in women, the risk of constipation in depressed people was 1.52 times that of non-depressed people.

In the full adjusted model in the total sample, depressed people showed a significantly higher risk of constipation (AOR, 1.69; 95% CI, 1.37-2.09). The risk of constipation in depressed people was 1.69 times that of non-depressed people. Although a significant association was observed between depression and constipation in both genders, the association was stronger in men than women (AOR, 2.28; 95% CI, 1.50, 3.63 vs. AOR, 1.55; 95% CI, 1.21, 1.99). In men, the risk of constipation in depressed people was 2.28 times that of non-depressed people, while in women, the risk of constipation in depressed people was 1.55 times that of non-depressed people.

DISCUSSION

In the current secondary analysis of a large cross-sectional study of general adults, depression was significantly associated with an increased risk of constipation. This is the first study to evaluate the relationship between depression and constipation in a large representative adult sample in Iran.

The prevalence of FC in this study was 23.9% (15% in men and 30.2% in women), which was higher than the reported

prevalence in a recently published systematic review and meta-analysis. The estimated global prevalence of FC based on ROME III was 10.4% (6.5-14.9).²⁶ On the other hand, in previous studies in western countries, the estimated FC prevalence was less than that reported in the present study. According to a systematic review in North America, the prevalence ranged from 1.9% to 27%, with an average of 15% in most studies.⁶ According to another meta-analysis, the pooled prevalence in South America was 18%, and 16% in northern and southern Europe, while they were 14% and 11% in the middle eastern and southeast Asian studies, respectively.¹⁰ In a study conducted in Tehran province, 2.4% of the general population were diagnosed with FC based on the Rome III criteria.²⁷ Another study conducted in Isfahan showed that 9.6% of the participants had constipation, according to self-reports.²⁸ Another study conducted in Kerman, showed a prevalence of 9.4%.²⁹

The estimated FC prevalence in the present study, unlike other studies conducted in Iran, was higher than in western countries. This was attributed to different lifestyles in the Iranian population.^{27,30} Currently, the intake of fibers (vegetables and fruit) has decreased in the Iranian diet, while the consumption of bread and rice has increased.³¹ The second reason for this higher prevalence may be the style of the Iranian toilet. On normal defecation, relaxation of the puborectalis and external anal sphincter with increased intra-abdominal pressure straightens the anorectal angle and leads to defecation. Because of less hip flexion in an Iranian toilet, the anorectal angle is narrower than in a European toilet. This wide-angle helps complete evacuation.³²

In this study, 33.3% and 20.2% of depressed and non-depressed people, respectively, had constipation. These findings are consistent with previous studies that found depression to be associated with constipation. For example, Moezi et al.⁵ revealed a significant association between depression and constipation. Ballou et al.¹⁶ reported a significant association between depression and constipation.

In previous studies, the relationship between mood and gastrointestinal disorders is unique from other chronic illnesses because of the significant interplay between the central nervous system and the gastrointestinal tract, also known as the brain-gut axis. For example, studies of neuronal stress pathways found that the corticotropin-releasing factor (CRF) in the brain plays a significant role in mediating the relation-

ship between emotional distress and changes in the upper and lower gastrointestinal (GI) motor function.^{33,34} In functional GI disorders, such as IBS, functional dyspepsia, and CC or diarrhea, dysfunction of the autonomic nervous system, which acts directly on CRF, may play a role in changing the bowel habits and gastric emptying.³⁵ Similarly, depression is associated with hyperactivity of the CRF neuronal pathways,³⁶ and CRF receptors have been suggested as a possible treatment target for depression and GI disorders^{37,38} consistent activation of the stress pathways mentioned above may lead to dysfunction in the brain-gut axis, making depressed patients more susceptible to symptoms, such as chronic diarrhea or chronic constipation.¹⁶

In particular, psychiatric disorders, such as depression, may be associated with constipation due to the effect of the disease itself or to other associated factors. Patients with depression and other psychiatric disorders generally have unhealthy lifestyles, such as poor diet, poor fluid intake,³⁹ and inactivity, as observed in the present study population. This may contribute to the occurrence of constipation.⁴⁰

These findings on the depression among constipation patients are an excellent start to alerting medical practitioners in this country regarding the importance of having to refer patients to the appropriate physicians. Nevertheless, this study has several limitations. The most important among them is that no causal inferences can be drawn because of the cross-sectional design. The other limitation of this study was that information was unavailable regarding previous medical utilization by patients. While everyone in this study received an initial medical consultation to determine the constipation severity, there is no information regarding which previous medical treatment is most suitable. Depressed people are at a significantly higher risk of constipation. These study findings justify mental health evaluations in all patients with functional gastrointestinal disorders, particularly among constipated individuals.

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