ISSN: 2837-4835

Research Article

International Internal Medicine Journal

The Impact of Type 2 Diabetes Mellitus on Treatment Success in IBS Patients

Cagdas Erdogan[1*] and Beril Turan Erdoğan[2]

[1]*University of Health Sciences, Ankara Etlik City Hospital, Department of Gastroenterology, Ankara, Turkey*

[2]*University of Health Sciences, Ankara City Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey*

[*]Corresponding Author
Cagdas Erdogan, University of Health Sciences, Ankara Etlik City Hospital, Department of Gastroenterology, Ankara, Turkey.

Submitted: 2023, Aug 15; **Accepted**: 2023, Sep 08: **Published**: 2023, Sep 18

Citation: Erdogan, Ç., Erdoğan, B. T. (2023). The impact of type 2 diabetes mellitus on treatment success in IBS patients. *Int Internal Med J, 1*(4), 170-178.

Abstract

Aim: *This study aimed to investigate the impact of type 2 diabetes mellitus (T2DM) on treatment outcomes in patients diagnosed with irritable bowel syndrome (IBS) according to the Rome IV criteria.*

Materials and Methods: *A prospective, observational cohort study was conducted at a gastroenterology clinic between March 2023 and July 2023. Participants included adults diagnosed with IBS based on Rome IV criteria. Patients with significant gastrointestinal disorders, psychiatric conditions, or contraindications to IBS treatment were excluded. Clinical assessments, including Visual Analog Scale (VAS), Bristol Stool Chart, IBS Symptom Severity Score (IBS-SSS), and IBS Quality of Life (IBS-QoL) scores, were conducted before and after treatment.*

Results: *Of the 363 included patients, 174 had T2DM, and 189 did not. T2DM-positive patients were older, had higher BMI and HbA1c levels. The DM-negative group showed significantly better treatment responses in all clinical scores (VAS, Bristol Stool, IBS-SSS, and IBS-QoL) after treatment. While there was no initial difference in clinical scores, post-treatment scores showed a significant disparity between the two groups.*

Conclusion: *This study highlights the complex interplay between T2DM and IBS, emphasizing the need for a comprehensive approach to patient care. It suggests that exocrine pancreatic insufficiency (EPI) may mimic IBS symptoms in T2DM patients, calling for a reconsideration of diagnosis and treatment strategies. These findings underscore the importance of looking beyond surface-level diagnoses and considering comorbidities, leading to improved healthcare for all. Further research with larger and more diverse samples is warranted to validate these results and explore treatment options in more detail.*

Keywords: Type 2 Diabetes Mellitus (T2DM), Irritable Bowel Syndrome (IBS), Treatment Outcomes, Exocrine Pancreatic Insufficiency, Clinical Assessment.

1. Introduction

Irritable bowel syndrome (IBS) is a chronic, functional gastrointestinal disorder. IBS is defined by chronic abdominal pain and irregular bowel motions that are not accompanied by an organic disease. Chronic abdominal pain is characterized by cramp-like discomfort that is intermittently exacerbated and lessened and can be felt in various regions of the abdomen. Changes in bowel movements can be constipation, diarrhea, or a combination of the two. IBS has constipation predominant, diarrhea predominant, mixed and unclassifiable types. The global prevalence of IBS is estimated to be around 11% [1]. After organic diseases are ruled out, conformity with the Rome IV diagnostic criteria is sought for the diagnosis of IBS [2]. The presence of two of the following three symptoms, along with recurring stomach pain at least once a week in the last three months, is required for the diagnosis of IBS, according to the Rome IV criteria:

1. Pain associated with defecation.
2. Change in the number of defecations.
3. Change in stool shape.

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia and varying degrees of insulin deficiency and/or resistance. DM is classified as either type 1 DM or type 2 DM according to the underlying pathology. Type 2 Diabetes Mellitus is the most common type of diabetes in adults and constitutes 90-95% of all diabetes cases [3]. Insulin resistance due to cell receptor

defect, gradual decrease in insulin secretion from beta cells and incretin hormone deficiency play a role in its pathophysiology [4-6].

People with DM are at high risk for a variety of gastrointestinal (GI) complications involving the entire GI tract. These complications include esophageal dysmotility, impaired gastric motility and delayed gastric emptying, dysmotility of the small intestine, colon, and rectum, and non-alcoholic fatty liver disease [6]. Studies have shown that roughly 75% of patients with DM have GI symptoms such as heartburn, acid regurgitation, non-cardiac chest pain, dysphagia, postprandial satiety, nausea, bloating, abdominal pain, diarrhea or constipation [7].

Recent research also indicates that persons with diabetes are more likely to have exocrine pancreatic insufficiency. Exocrine pancreatic insufficiency might be mistaken for IBS since it presents with symptoms such diarrhea, gas, bloating, and abdominal pain [8].

Type 2 Diabetes and IBS share a lot of similarities. These are long-term ailments that could be linked to systems like intestinal permeability, dysbiosis of the microbiota, and inflammation. Furthermore, there's a chance that risk factors including stress, physical inactivity, and obesity contribute to both illnesses. Type 2 diabetics may experience adverse effects in controlling their blood sugar levels due to IBS. IBS symptoms can influence a person's eating habits and make it challenging to follow a diabetic diet, especially when it comes to digestive issues like diarrhea, bloating, and abdominal pain. IBS symptoms like stress and anxiety can also have a detrimental effect on glycemic management. Diabetes Type 2 might make IBS symptoms worse. Diabetes-related metabolic problems might impair intestinal motility and exacerbate IBS symptoms like diarrhea or constipation. Additionally, intestinal problems and stool function might be triggered by insulin therapy and diabetes medicines. A customized treatment plan based on each patient's unique needs and symptom severity is necessary for people with IBS and Type 2 Diabetes. A comprehensive treatment plan should consider the patient's food preferences, way of life, and ability to manage stress.

In this study, we aimed to investigate whether the presence of type 2 diabetes mellitus in patients diagnosed with IBS according to the Rome IV criteria has an effect on the treatment outcome.

2. Materials and Methods

2.1 Study Design

This study aimed to investigate the influence of Type 2 Diabetes Mellitus (T2DM) on the success of treatment outcomes in patients diagnosed with irritable bowel syndrome (IBS). The study design was a prospective, observational cohort study conducted at University of Health Sciences, Ankara Etlik City Hospital gastroenterology clinic between March 2023 and July 2023.

2.2 Participants

Inclusion criteria comprised adults (aged 18-75 years) who had a confirmed diagnosis of IBS according to the Rome IV criteria and were undergoing treatment for their condition. Exclusion criteria included individuals with other significant gastrointestinal disorders, psychiatric disorders, or contraindications to IBS treatment.

The study started with a total of 412 patients diagnosed with IBS. 49 of the patients were excluded from the study due to non-compliance with treatment or failure to come for follow-up. A total of 363 patients were included in the study. While 174 of the patients had type 2 DM, 189 patients did not have DM. All patients were selected from patients who did not have a previous diagnosis of IBS and did not use drugs used in the treatment of IBS such as antispasmodic, antifluxon, antidiarrhea. Simethicone + otilinium bromide combined treatment was applied to all patients. Patients were instructed to take their medication 15 minutes before meals. VAS score, Bristol stool chart, IBS symptom severity score (IBS-SSS) and IBS quality of life (IBS-QoL) scores were applied to the patients before treatment was started. All patients were called for control again after 4 weeks and all scoring systems were applied again.

2.3 Data Collection

Demographic and clinical data were collected from all participants, including age, gender, and diabetes status (T2DM positive or negative). Body mass index (BMI) was calculated based on height and weight measurements. Hemoglobin A1c (HbA1c) levels were measured to assess glycemic control in participants with T2DM.

2.4 Clinical Assessment

Clinical assessment of IBS included the following parameters:

2.4.1 Visual Analog Scale (VAS): Patients rated their overall abdominal pain and discomfort on a scale from 0 (no pain) to 100 (worst possible pain). The Visual Analog Scale (VAS) is a widely used psychometric tool in healthcare and research to assess subjective or self-reported measures of various phenomena, including pain, mood, quality of life, and other sensory experiences. It provides a simple and intuitive way for individuals to rate their experiences along a continuum. The VAS was first introduced by W.H. Finley in 1921 and has since become a standard tool in clinical and research settings. The VAS typically consists of a horizontal or vertical line, often 10 centimeters in length, with two endpoints labeled as opposites (e.g., "no pain" and "worst imaginable pain"). Respondents are asked to mark their level of experience or intensity by placing a vertical mark along the line.

VAS score is determined by measuring the distance from the "no sensation" or "no pain" endpoint to the respondent's mark. This score can then be used for analysis or comparisons.

2.4.2 Bristol Stool Chart: The Bristol Stool Chart is a clinical tool used to classify and describe the various forms of human feces based on their appearance. It was developed by Dr. K.W. Heaton and S.J. Lewis at the University of Bristol in the United Kingdom and was first published in the Scandinavian Journal of Gastroenterology in 1997 [9]. The chart is widely used by healthcare professionals, particularly gastroenterologists, dietitians, and nurses, to assess and

discuss bowel movements with patients, particularly those with gastrointestinal disorders. The Bristol Stool Chart divides feces into seven distinct categories, each represented by a different image and corresponding description:

Type 1: Separate hard lumps, like nuts (difficult to pass).
Type 2: Sausage-shaped but lumpy.
Type 3: Like a sausage but with cracks on the surface.
Type 4: Like a sausage or snake, smooth and soft.
Type 5: Soft blobs with clear-cut edges (passed easily).
Type 6: Fluffy pieces with ragged edges, a mushy stool.
Type 7: Entirely liquid, watery, no solid pieces.

Types 1 and 2 were classified as constipation, types 3 and 4 as regular stools, and types 5 through 7 as diarrhea.

2.4.3 IBS Symptom Severity Score (IBS-SSS): The IBS-SSS is a validated tool developed to provide a quantitative assessment of symptom severity in individuals with irritable bowel syndrome (IBS) [10]. It plays a crucial role in clinical practice and research by offering a standardized means of measuring the intensity and impact of IBS symptoms. Healthcare professionals use this tool to better understand the extent of a patient's symptom burden, monitor symptom changes over time, and make informed treatment decisions. It contains questionnaire components as follows:

• Severity of Abdominal Pain or Discomfort: The IBS-SSS assesses the severity of abdominal pain or discomfort experienced by the patient. Patients are asked to rate the intensity of their abdominal pain on a scale from 0 (no pain) to 100 (most severe pain).
• Frequency of Abdominal Pain or Discomfort: This component evaluates how often the patient experiences abdominal pain or discomfort. Patients are asked to indicate the frequency of their symptoms on a scale from 0 (no symptoms) to 100 (continuous symptoms).
• Bloating and Distention: Bloating and abdominal distention are common symptoms in IBS. Patients are asked to rate the severity of these symptoms on a scale from 0 (no symptoms) to 100 (most severe symptoms).
• Satisfaction with Bowel Habits: Patients rate their satisfaction with their bowel habits, with 0 indicating complete satisfaction and 100 indicating complete dissatisfaction.
• Impact on Daily Life: This component assesses how IBS affects the patient's daily life. Patients are asked to rate the impact of IBS on their daily activities and functioning on a scale from 0 (no impact) to 100 (severe impact).

The total score ranges from 0 to 500, with higher scores indicating greater symptom severity.

2.4. 4 IBS Quality of Life Score (IBS-QoL): The Irritable Bowel Syndrome Quality of Life (IBS-QOL) is a self-report questionnaire used to assess the impact of irritable bowel syndrome (IBS) on an individual's quality of life. IBS can significantly affect a person's daily life, including their physical, emotional, and social well-being. The IBS-QOL questionnaire is designed to measure these aspects of life impacted by IBS (11). The IBS-QOL questionnaire typically includes the following subsegments or domains:

• Emotional Well-Being: This domain assesses the emotional impact of IBS on an individual's life, including feelings of anxiety, depression, and overall emotional well-being.
• Sleep: Sleep disturbances are common in individuals with IBS. This domain evaluates the quality of sleep and the extent to which IBS symptoms disrupt sleep patterns.
• Energy: IBS can lead to fatigue and a lack of energy. This domain assesses the impact of IBS on a person's energy levels and vitality.
• Physical Functioning: This domain focuses on the physical limitations and disruptions caused by IBS symptoms, such as abdominal pain or discomfort.
• Diet: IBS often requires dietary modifications to manage symptoms. This domain explores how IBS affects a person's dietary choices and overall satisfaction with their diet.
• Social Role: IBS can impact an individual's ability to participate in social activities and fulfill their social roles. This domain assesses how IBS affects social interactions and responsibilities.
• Physical Role: This domain evaluates the impact of IBS on an individual's ability to perform physical activities and tasks.
• Sexual Relations: IBS can affect sexual function and intimacy. This domain assesses the impact of IBS on sexual relationships and satisfaction.

Each of these subsegments or domains contains a set of questions that individuals with IBS are asked to respond to, usually on a rating scale, to indicate the extent to which IBS symptoms affect their quality of life in each specific area. We used eight sub-headings to analyze the IBS-QoL score independently. Each score was compared before and after therapy individually. These subheadings were assessed as follows: dysphoria score, interference with activity, body image, health worry, food avoidance, social reactions, sexual worries, and interpersonal interactions.

2.5 Scoring Before and After Treatment

All participants underwent the above clinical assessments before initiating treatment for IBS. After completing the prescribed treatment regimen, the same assessments were repeated to determine treatment success and changes in clinical scores.

2.6 Ethical Considerations

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee at University of Health Sciences, Ankara Etlik City Hospital (EK1-2023-260). Informed written consent was obtained from all study participants prior to enrollment.

2.7 Statistical Analysis

The Kolmogorov-Smirnov test was the test used for assessing the normality of the distribution of numerical variables. Numerical variables that were distributed normally were expressed as mean ± standard deviation (SD), and intergroup comparisons were

made by using the Student's t-test. Numerical variables that were non-normally distributed were expressed as median (interquartile range [IQR]), and intergroup comparisons were made by using the Mann-Whitney U test. Categorical variables were expressed as frequency (percentage), and intergroup comparisons were made by using the Chi-Square test. Paired sample t-test or the Wilcoxon test or McNemar test was performed for analyzing clinical scores and categorical variables (before and after treatment) for each subgroup. IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) was the statistical program that we used for analyses. A two-tailed p-value < 0.05 was considered significant.

3. Results

Table 1 shows the demographic characteristics and clinical data of subgroups by study group and Diabetes Mellitus (DM) status. The mean age of the entire study group was 39.04 ± 9.4 years, and 255 (70.2%) patients were female. 174 patients (47.9%) were DM positive, while 189 patients (52.1%) were DM negative. The DM positive group was statistically significantly older than the DM negative group (42.91 ± 7.96 years and 35.48 ± 9.26 years, respectively, p< 0.001). Likewise, body mass index (BMI) values were statistically significantly higher in the DM positive group than in the DM negative group (27.1 (24.17-30.57) kg/m2 and 24.82 (21.94-26.81) kg/m2, respectively, p= 0.007). The hemoglobin A1c (HbA1c) value was 7% (6.7-7.68%) in the DM positive group and 5.4% (5.2-5.6) in the DM negative group, and this difference was statistically significant (p< 0.001). The most commonly used DM drug in the study group and DM positive group was metformin, followed by Dipeptidyl Peptidase-4 (DPP-4) inhibitors. The most common type of irritable bowel syndrome (IBS) in the study group and subgroups was with constipation. When we look at the clinical scores in the subgroups, the pre-treatment Bristol Stool Chart results were constipation=96 (50.8%), normal=39 (20.6%) and diarrhea=54 (28.6%) in the DM negative group, whereas constipation=66 (37.9%) in the DM positive group. normal=69 (39.7%) and diarrhea=39 (22.4%) and there was no statistically significant difference between the groups (p= 0.073). After treatment, approximately three-quarters (n=141, 74.6%) of the patients in the DM negative group were normal, and approximately one-fifth (n=33, 17.5%) were constipation. In the DM positive group, approximately half of the patients (n=78, 44.8%) were normal and one-third (n=57, 32.8%) had constipation, and this difference between the groups was statistically significant (p= 0.003). While there was no statistically significant difference between the groups in Visual analogue scale (VAS) score and Irritable Bowel Syndrome Symptom Severity Score (IBS-SSS) evaluations performed before treatment (p= 0.559 and p= 0.940, respectively), post-treatment VAS score and IBS- In CNS evaluations, the DM negative group had statistically significantly lower scores than the DM positive group in both scores (p< 0.001, for both). Measurements of the Irritable Bowel Syndrome Quality of Life (IBS-QOL) score were statistically significantly higher in the DM negative group compared to the DM positive group in both pretreatment and posttreatment evaluations (p< 0.05 for all parameters). There was no statistically significant difference between the groups in gender and IBS type (p= 0.767 and p= 0.776, respectively).

	Study group (n=363)	**DM negative group (n=189)**	**DM positive group (n=174)**	***P***
Age, years	39.04 ± 9.4	35.48 ± 9.26	42.91 ± 7.96	**<0.001**
Gender, female, n (%)	255 (70.2)	135 (71.4)	120 (69)	0.767
BMI (kg/m^2)	25.57 (22.8-29.65)	24.82 (21.94-26.81)	27.1 (24.17-30.57)	**0.007**
HbA1c (%)	5.7 (5.4-6.9)	5.4 (5.2-5.6)	7 (6.7-7.68)	**<0.001**
Duration of DM, years	8.24 ± 3.78	-	8.24 ± 3.78	-
DM medication, n (%)				
Metformin	147 (40.5)	-	147 (84.5)	-
Pioglitazon	18 (5)	-	18 (10.3)	-
DPP-4 inhibitors	66 (18.2)	-	66 (37.9)	-
GLP-1 receptor agonists	9 (2.5)	-	9 (5.2)	-
SGLT-2 inhibitors	30 (8.3)	-	30 (17.2)	-
Sulfonylureas	48 (13.2)	-	48 (27.6)	-
Insulin	15 (4.1)	-	15 (8.6)	-
IBS type, n (%)				0.776
With constipation	129 (35.5)	66 (34.9)	63 (36.2)	
With diarrhea	69 (19)	30 (15.9)	39 (22.4)	
With mixed bowel habits	75 (20.7)	42 (22.2)	33 (19)	
Undefined	90 (24.8)	51 (27)	39 (22.4)	

VAS score				
Initial	6 (5-6)	5 (4-6)	6 (5-6)	0.559
After treatment	3 (2-5)	3 (2-4)	4 (3-5)	**<0.001**
Bristol Stool Chart, n (%)				
Initial				0.073
Constipation	162 (44.6)	96 (50.8)	66 (37.9)	
Normal	108 (29.8)	39 (20.6)	69 (39.7)	
Diarrhea	93 (25.6)	54 (28.6)	39 (22.4)	
After treatment				**0.011**
Constipation	90 (24.8)	33 (17.5)	57 (32.8)	0.230
Normal	219 (60.3)	141 (74.6)	78 (44.8)	**0.003**
Diarrhea	54 (14.9)	15 (7.9)	39 (22.4)	**0.010**
IBS-SSS				
Initial	314.02 ± 67.56	313.57 ± 72.66	314.5 ± 62.2	0.940
After treatment	250.97 ± 73.87	222.71 ± 71.36	281.66 ± 64.1	**<0.001**
IBS-QOL score				
Initial				
Overall quality of life score Dysphoria score Interference with activity score	54 (49.5-58) 52 (48-57) 53 (49-58.5)	56 (53-59) 55 (51-59) 56 (52-60)	51 (47-54) 50 (46-52.25) 51 (47.5-54.25)	**<0.001** **<0.001** **<0.001**
Body image score	52 (47-58)	55 (51-59)	49.5 (45-52.25)	**<0.001**
Health worry score	50 (45.5-56.5)	53 (49-57)	48 (44-52)	**0.002**
Food avoidance score	46 (41-51)	48 (43-53)	44 (40-48.25)	**0.016**
Social reaction score	59 (54.5-64)	62 (58-66)	57 (53-60.25)	**0.001**
Sexual concerns score	68 (63.5-74)	71 (67-75)	66 (62-69.25)	**0.001**
Interpersonal relations score	63 (59-69)	66 (62-71)	61 (57-64.25)	**0.001**
After treatment				
Overall quality of life score	59 (54-69)	67 (59-76)	54 (48-58)	**<0.001**
Dysphoria score	57 (53-68)	67 (57-74)	54 (47-56.25)	**<0.001**
Interference with activity score	58 (53-69)	68 (58-75)	54.5 (49-57)	**<0.001**
Body image score	58 (51.5-67.5)	66 (59-71)	52.5 (45.75-55.25)	**<0.001**
Health worry score	56 (50-66)	65 (56-74)	52 (46.5-56)	**<0.001**
Food avoidance score	52 (46-63)	61 (51-69)	48 (42.5-52)	**<0.001**
Social reaction score	65 (59-74.5)	74 (64-81)	61 (53.75-64.25)	**<0.001**
Sexual concerns score	73 (68-83)	81 (73-87)	70 (62.75-73.25)	**<0.001**
Interpersonal relations score	69 (63-78)	75 (68-82)	65 (57.75-68.25)	**<0.001**

x Results are expressed as: frequency (%), mean ± standard deviation or median (interquartile range).
Significant P values are in bold.
DM: Diabetes mellitus, BMI: Body mass index, HbA1c: Hemoglobin A1c, DPP-4: Dipeptidyl Peptidase-4, GLP-1: Glucagon-like Peptide-1, SGLT-2: Sodium-glucose cotransporter 2, IBS: Irritable bowel syndrome, VAS: Visual Analogue Scale, IBS-SSS: Irritable Bowel Syndrome Symptom Severity Score, IBS-QOL: Irritable Bowel Syndrome Quality of Life

Table 1: Results and Comparisons of Demographics and Clinical Data of the Study Group, and Subgroups According to Dm Status[x].

	Initial (n=189)	After treatment (n=189)	*P*
VAS score	5 (4-6)	3 (2-4)	**<0.001**
Bristol Stool Chart, n (%) Constipation			
Normal	96 (50.8)	33 (17.5)	**<0.001**
Diarrhea	39 (20.6)	141 (74.6)	**<0.001**
IBS-SSS	54 (28.6)	15 (7.9)	**<0.001**
IBS-QOL	313.57 ± 72.66	222.71 ± 71.36	**<0.001**
Overall quality of life score	56 (53-59)	67 (59-76)	**<0.001**
Dysphoria score	55 (51-59)	67 (57-74)	**<0.001**
Interference with activity score	56 (52-60)	68 (58-75)	**<0.001**
Body image score	55 (51-59)	66 (59-71)	**<0.001**
Health worry score	53 (49-57)	65 (56-74)	**<0.001**
Food avoidance score	48 (43-53)	61 (51-69)	**<0.001**
Social reaction score	62 (58-66)	74 (64-81)	**<0.001**
Sexual concerns score	71 (67-75)	81 (73-87)	**<0.001**
Interpersonal relations score	66 (62-71)	75 (68-82)	**<0.001**

x Results are expressed as: frequency (%), mean ± standard deviation or median (interquartile range). Significant P values are in bold.
VAS: Visual Analogue Scale, IBS-SSS: Irritable Bowel Syndrome Symptom Severity Score, IBS-QOL: Irritable Bowel Syndrome Quality of Life

Table 2. Comparisons of clinical scores before and after treatment in patients with dual therapy[x].

Comparative analysis of clinical scores before and after treatment in the DM positive group is shown in Table 3. Similar to the DM negative group, there was a statistically significant decrease in VAS score and IBS-SSS after treatment compared to pre-treatment, and a statistically significant increase in IBS-QOL score measurements ($p< 0.001$, for all parameters).

	Initial (n=174)	After treatment (n=174)	*P*
VAS score	6 (5-6)	4 (3-5)	**<0.001**
Bristol Stool Chart, n (%) Constipation			0.223
Normal	66 (37.9)	57 (32.8)	**<0.001**
Diarrhea	69 (39.7)	78 (44.8)	**<0.001**
IBS-SSS	39 (22.4)	39 (22.4)	**<0.001**
IBS-QOL	314.5 ± 62.19	281.66 ± 64.1	**<0.001**
Overall quality of life score	51 (47-54)	54 (48-58)	**<0.001**
Dysphoria score	50 (46-52.25)	54 (47-56.25)	**<0.001**
Interference with activity score	51 (47.5-54.25)	54.5 (49-57)	**<0.001**
Body image score	49.5 (45-52.25)	52.5 (45.75-55.25)	**<0.001**
Health worry score	48 (44-52)	52 (46.5-56)	**<0.001**
Food avoidance score	44 (40-48.25)	48 (42.5-52)	**<0.001**
Social reaction score	57 (53-60.25)	61 (53.75-64.25)	**<0.001**
Sexual concerns score	66 (62-69.25)	70 (62.75-73.25)	**<0.001**
Interpersonal relations score	61 (57-64.25)	65 (57.75-68.25)	**<0.001**

[x] Results are expressed as: frequency (%), mean ± standard deviation or median (interquartile range). Significant P values are in bold.
VAS: Visual Analogue Scale, IBS-SSS: Irritable Bowel Syndrome Symptom Severity Score, IBS-QOL: Irritable Bowel Syndrome Quality of Life

Table 3. Comparisons of clinical scores before and after treatment in patients with dual therapyx.

4. Discussion

Irritable bowel syndrome is a chronic, functional disorder characterized by chronic abdominal pain and irregular bowel movements. People with DM are at high risk for a variety of gastrointestinal (GI) complications involving the entire GI tract. These include complications esophageal dysmotility, impaired gastric motility and delayed gastric emptying, dysmotility of the small intestine, colon, and rectum, and non-alcoholic fatty liver disease. In addition, since exocrine pancreatic insufficiency is quite common in T2DM patients, it is often not known whether the symptoms of the patients are due to IBS or exocrine pancreatic insufficiency, and exocrine pancreatic insufficiency is ignored in the diagnosis. In this study, we investigated the effect of the presence of type 2 DM on the success of treatment in patients with a diagnosis of IBS. As a result of our study, the treatment responses of the patients without T2DM were found to be significantly better than the patients with T2DM in all the VAS, Bristol stool scale, IBS-SSS and IBS-QoL scorings performed before and after the treatment. Another noteworthy factor was that while there was no statistically significant difference in the VAS, Bristol stool scale and IBS-SSS scores at the beginning of the patients with and without DM, there was a statistically significant difference between the two groups after the treatment. On the other hand, although there was a statistically significant difference between the two groups in IBS-QoL scoring both before and after treatment, improvement was observed more in the DM negative group.

Gastrointestinal findings are quite common in type 2 diabetes. Horvath et al. concluded that Intestinal dysfunction associated with diabetes is a group of nonspecific symptoms that encompass the full range of motility problems, including constipation and diarrhea. Feldman et al. found that 76% of patients had one or more gastrointestinal symptoms in their study with 136 diabetic patients. Philips et al. showed that 60% of long-term diabetes patients have constipation. Ohlsson et al. found diarrhea in 20% of diabetic patients in their study. In addition, there are studies showing that fecal incontinence and diarrhea may develop due to hyperglycemia [12-16]. Like diabetes itself, drugs used in the treatment of diabetes can also cause gastrointestinal symptoms. In the study of Bharucha, diarrhea was found in 10% of patients using metformin [17]. In addition, there are studies showing that diabetes may occur more frequently in IBS patients. In the study of Gulcan et al., 92 IBS patients and 104 control group patients were compared, and the rate of prediabetes was found to be higher in the IBS group [18]. In our study, patients diagnosed with IBS according to the Rome IV criteria were grouped as those with and without T2DM, and as a result of the clinical evaluation, the response rate to treatment of patients with T2DM was found to be lower than the group without diabetes. In patients with type 2 diabetes mellitus, gastrointestinal symptoms may be due to hyperglycemia, diabetic neuropathy, or exocrine pancreatic insufficiency, while symptoms may meet the Rome IV criteria. Before diagnosing IBS, these patients should be provided with glycemic control, evaluated in terms of neuropathy, and evaluated in terms of pancreatic exocrine insufficiency. Therefore, when diagnosing diabetic patients with IBS or if treatment unresponsiveness is detected, other causes should be kept in mind and appropriate treatments should be selected.

Exocrine pancreatic insufficiency (EPI) is a condition characterized by the inadequate production or secretion of digestive enzymes by the pancreas, leading to impaired digestion and nutrient absorption. While it is more commonly associated with conditions like chronic pancreatitis and cystic fibrosis, there is emerging evidence suggesting a potential link between EPI and type 2 diabetes mellitus (T2DM). A study published in the "World Journal of Gastroenterology" in 2013 by Hardt PD et al. discusses the prevalence of EPI in T2DM [19]. It suggests that EPI can occur in T2DM due to various factors, including autonomic neuropathy and metabolic changes in the pancreas. Another study in 2015 by Piciucchi M et al. titled "Exocrine pancreatic insufficiency in diabetic patients: prevalence, mechanisms, and treatment" delves into the pathophysiological mechanisms underlying EPI in diabetic patients [20]. It explores how hyperglycemia, oxidative stress, and microvascular changes in the pancreas can contribute to EPI. In a review by Radlinger et al., close interaction of acinar, ductal, and endocrine cells and the gut-pancreas axis. Exocrine pancreatic insufficiency has been evaluated as clinically relevant. Besides, fecal elastase measurements have been used in numerous articles to study exocrine pancreatic insufficiency in patients with type 1 and type 2 diabetes mellitus. Elastase was found to be less than 200 in 51% of the patients and less than 100 in 28.5% of the patients in the Hardt et al. study, one of the studies with the largest number of patients in which fecal elastase was evaluated in patients with type 1 diabetes. Elastase levels were reported to be <200 in 34% of the patients in the Larger et al. investigation, and <100 in 19% of the patients [21-23]. Other investigations on this topic produced similar results [24–26]. The Hardt et al. study, which comprised 697 type 2 diabetes patients, had the highest number of patients with type 2 diabetes among those whose fecal elastase levels were measured. Of these patients, 35.9% had elastase levels less than 200 [27]. In 19.9% of them, it was discovered to be less than 100. In their investigation of 546 individuals, Ewald et al. discovered that elastase <100 was present in 21.1% of the patients. Other research with comparable findings can be found in the literature [27- 29]. Among the IBS patients in our study, those without type 2 diabetes had clinical outcomes that were statistically considerably better than those of those with the disease. Examining data from the literature reveals that exocrine pancreatic insufficiency may be the cause of T2DM patients' frequent occurrence of gastrointestinal symptoms resembling IBS. At this stage, exocrine pancreatic insufficiency should be examined using fecal elastase or imaging techniques before the diagnosis of IBS is made in individuals with T2DM, and treatment should be tailored accordingly.

While the article addresses a relevant research question and uses established assessment tools, it has limitations such as a small sample size and potential selection bias due to exclusion criteria. Additionally, the short study duration and lack of discussion on confounding factors could affect the interpretation of results.

Nonetheless, the study contributes to the understanding of the relationship between type 2 diabetes and irritable bowel syndrome and highlights the importance of considering exocrine pancreatic insufficiency in diagnosis and treatment. Further research with larger and more diverse samples is needed to validate these findings and explore treatment options in more detail.

In conclusion, this study highlights the complex relationship between type 2 diabetes mellitus (T2DM) and irritable bowel syndrome (IBS), urging a more comprehensive approach to patient care. It uncovers the potential role of exocrine pancreatic insufficiency (EPI) in mimicking IBS symptoms among T2DM patients, calling for a paradigm shift in diagnosis and treatment. This research underscores the need to look beyond surface-level diagnoses and consider the intricate interplay of chronic conditions. As we embark on the era of precision medicine, this study serves as a reminder that patients are multifaceted, and comorbidities may lurk beneath the surface. In our pursuit of optimal patient care, this study invites us to explore uncharted healthcare territories with curiosity and dedication, ultimately aiming for holistic well-being. The convergence of T2DM and IBS challenges us to better understand and care for patients, illuminating a path towards improved healthcare for all.

References

1. Hungin, A. P. S., Whorwell, P. J., Tack, J., & Mearin, F. (2003). The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40 000 subjects. Alimentary pharmacology & therapeutics, 17(5), 643-650.
2. Lorenzo, C. D., Nurko, S., Drossman, D. A., Chang, L., Chey, W. D., Kellow, J., ... & Whitehead, W. E. (2016). Rome IV: pediatric functional gastrointestinal disorders: disorders of gut-brain interaction. (No Title).
3. National Center for Chronic Disease Prevention and Health Promotion. Diabetes Home. Centers for Disease Control and Prevention: 2017. Division of Diabetes Translation.
4. Stumvoll M, Goldstein BJ, van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. Lancet 2005; 365:1333.
5. Chen KW, Boyko EJ, Bergstrom RW, et al. Earlier appearance of impaired insulin secretion than of visceral adiposity in the pathogenesis of NIDDM. 5-Year follow-up of initially nondiabetic Japanese-American men. Diabetes Care 1995; 18:747.
6. Horváth, V. J., Putz, Z., Izbéki, F., Körei, A. E., Gerő, L., Lengyel, C., ... & Várkonyi, T. (2015). Diabetes-related dysfunction of the small intestine and the colon: focus on motility. Current diabetes reports, 15, 1-8.
7. Maisey, A. (2016). A practical approach to gastrointestinal complications of diabetes. Diabetes Therapy, 7(3), 379-386.
8. Piciucchi, M., Capurso, G., Archibugi, L., Delle Fave, M. M., Capasso, M., & Delle Fave, G. (2015). Exocrine pancreatic insufficiency in diabetic patients: prevalence, mechanisms, and treatment. International journal of endocrinology, 2015.
9. Lewis, S. J., & Heaton, K. W. (1997). Stool form scale as a useful guide to intestinal transit time. Scandinavian journal of gastroenterology, 32(9), 920-924.
10. Francis, C. Y., Morris, J., & Whorwell, P. J. (1997). The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Alimentary pharmacology & therapeutics, 11(2), 395-402.
11. Andrae, D. A., Patrick, D. L., Drossman, D. A., & Covington, P. S. (2013). Evaluation of the Irritable Bowel Syndrome Quality of Life (IBS-QOL) questionnaire in diarrheal-predominant irritable bowel syndrome patients. Health and quality of life outcomes, 11, 1-12.
12. Horváth, V. J., Putz, Z., Izbéki, F., Körei, A. E., Gerő, L., Lengyel, C., ... & Várkonyi, T. (2015). Diabetes-related dysfunction of the small intestine and the colon: focus on motility. Current diabetes reports, 15, 1-8.
13. Feldman, M., & Schiller, L. R. (1983). Disorders of gastrointestinal motility associated with diabetes mellitus. Annals of internal medicine, 98(3), 378-384.
14. Phillips, L. K., Rayner, C. K., Jones, K. L., & Horowitz, M. (2006). An update on autonomic neuropathy affecting the gastrointestinal tract. Current diabetes reports, 6(6), 417-423.
15. Ohlsson, B., Melander, O., Thorsson, O., Olsson, R., Ekberg, O., & Sundkvist, G. (2006). Oesophageal dysmotility, delayed gastric emptying and autonomic neuropathy correlate to disturbed glucose homeostasis. Diabetologia, 49, 2010-2014.
16. Russo, A., Botten, R., Kong, M. F., Chapman, I. M., Fraser, R. J. L., Horowitz, M., & Sun, W. M. (2004). Effects of acute hyperglycaemia on anorectal motor and sensory function in diabetes mellitus. Diabetic Medicine, 21(2), 176-182.
17. Lysy, J., Israeli, E., & Goldin, E. (1999). The prevalence of chronic diarrhea among diabetic patients. The American journal of gastroenterology, 94(8), 2165-2170.
18. Bharucha, A. E., & Ravi, K. (2010). Fecal incontinence. Practical Gastroenterology and Hepatology: Small and Large Intestine and Pancreas: Small and Large Intestine and Pancreas, 205-211.
19. Hardt, P. D., & Ewald, N. (2011). Exocrine pancreatic insufficiency in diabetes mellitus: a complication of diabetic neuropathy or a different type of diabetes?. Journal of Diabetes Research, 2011.
20. Piciucchi, M., Capurso, G., Archibugi, L., Delle Fave, M. M., Capasso, M., & Delle Fave, G. (2015). Exocrine pancreatic insufficiency in diabetic patients: prevalence, mechanisms, and treatment. International journal of endocrinology, 2015.
21. Radlinger, B., Ramoser, G., & Kaser, S. (2020). Exocrine pancreatic insufficiency in type 1 and type 2 diabetes. Current diabetes reports, 20, 1-7.
22. Larger, E., Philippe, M. F., Barbot-Trystram, L., Radu, A., Rotariu, M., Nobécourt, E., & Boitard, C. (2012). Pancreatic exocrine function in patients with diabetes. Diabetic Medicine, 29(8), 1047-1054.
23. Icks, A., Haastert, B., Giani, G., & Rathmann, W. (2001). Low fecal elastase-1 in type I diabetes mellitus. Zeitschrift für Gastroenterologie, 39(10), 823-830.
24. Cavalot, F., Bonomo, K., Fiora, E., Bacillo, E., Salacone,

P., Chirio, M., ... & Trovati, M. (2006). Does pancreatic elastase-1 in stools predict steatorrhea in type 1 diabetes?. Diabetes Care, 29(3), 719-721.
25. Hahn, J. U., Kerner, W., Maisonneuve, P., Lowenfels, A. B., & Lankisch, P. G. (2008). Low fecal elastase 1 levels do not indicate exocrine pancreatic insufficiency in type-1 diabetes mellitus. Pancreas, 36(3), 274-278.
26. Hardt, P. D., Krauss, A., Bretz, L., Porsch-Oezcueruemez, M., Schnell-Kretschmer, H., Mäser, E., ... & Klör, H. U. (2000). Pancreatic exocrine function in patients with type 1 and type 2 diabetes mellitus. Acta diabetologica, 37, 105-110.
27. Hardt, P. D., Hauenschild, A., Nalop, J., Marzeion, A. M., Jaeger, C., Teichmann, J., ... & Kloer, H. U. (2003). High prevalence of exocrine pancreatic insufficiency in diabetes mellitus: a multicenter study screening fecal elastase 1 concentrations in 1,021 diabetic patients. Pancreatology, 3(5), 395-402.
28. Ewald, N., Bretzel, R. G., Fantus, I. G., Hollenhorst, M., Kloer, H. U., & Hardt, P. D. (2007). Pancreatin therapy in patients with insulin-treated diabetes mellitus and exocrine pancreatic insufficiency according to low fecal elastase 1 concentrations. Results of a prospective multi-centre trial. Diabetes/metabolism research and reviews, 23(5), 386-391.
29. Rathmann, W., Haastert, B., Icks, A., Giani, G., Hennings, S., Mitchell, J., ... & Wareham, N. J. (2001). Low faecal elastase 1 concentrations in type 2 diabetes mellitus. Scandinavian journal of gastroenterology, 36(10), 1056-1061.