



Case Control Study

High risk of temporomandibular disorder in irritable bowel syndrome: Is there a correlation with greater illness severity?

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Author contributions: Gallotta S, Bruno V, Catapano S, Mobilio N, Ciacci C and Iovino P designed the study and interpreted the data; Gallotta S, Bruno V, Ciacci C and Iovino P participated in the acquisition of the data; Gallotta S drafted the initial manuscript; Bruno V, Catapano S, Mobilio N, Ciacci C and Iovino P revised the article critically for important intellectual content.

Institutional review board statement: The study was reviewed and approved by the S. Giovanni di Dio e Ruggi D'aragona Ethical Committee of Salerno.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrolment.

Conflict-of-interest statement: There are no conflicts of interest to report.

Data sharing statement: No additional data are available.

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Manuscript source: Invited manuscript

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Received: September 21, 2016

Peer-review started: September 22, 2016

First decision: October 28, 2016

Revised: November 12, 2016

Accepted: December 8, 2016

Article in press: December 8, 2016

Published online: January 7, 2017

Abstract

AIM

To investigate the prevalence and the risk of temporomandibular disorders (TMDs) in patients with irritable bowel syndrome (IBS) (including each subtype: constipation, diarrhoea, and mixed) compared to the general population.

METHODS

Between January 2014 and December 2015 we enrolled consecutively adult patients diagnosed with IBS at the outpatient clinic of the University of Salerno and healthy controls (HC) without IBS. At enrollment, we analyzed all patients for the presence of TMDs according to the Research Diagnostic Criteria for TMD.

RESULTS

We enrolled 91 IBS patients (23 IBS-D, 30 IBS-C and 38 IBS-M) and 57 HC in the study. We found a higher risk of having TMD (OR = 3.41, 95%CI: 1.66-7.01) compared to the HC. The risk of having TMD was independent of IBS-subtype. Multiple regression analysis showed that facial pain was positively related to abdominal pain and higher level of depression.

CONCLUSION

IBS patients had a more than three times greater risk of TMD compared to HC. The risk of having TMD

was similar in different IBS subtypes. IBS patients that also fulfilled criteria for TMD seem to share along with chronic facial and abdominal pain a significant co-occurrence with psychiatric disorders and female preponderance.

Key words: Temporomandibular disorders; Irritable bowel syndrome; Chronic pain; Facial pain; Abdominal pain; Irritable bowel syndrome severity score symptoms; Irritable bowel syndrome predominant diarrhea; Irritable bowel syndrome predominant constipation; Irritable bowel syndrome mixed

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Core tip: Temporomandibular disorders (TMD) seem to occur more frequently in patients with irritable bowel syndrome (IBS). In this study we analyzed all patients for the presence of TMD according to the Research Diagnostic Criteria for Temporomandibular Disorders. Based on our results, IBS patients had a more than three times greater risk of TMD compared to healthy controls. The risk of having TMD was similar in different IBS subtypes. IBS patients that also fulfilled criteria for TMD seem to share along with chronic facial and abdominal pain a significant co-occurrence with psychiatric disorders and female preponderance.

Gallotta S, Bruno V, Catapano S, Mobilio N, Ciacci C, Iovino P. High risk of temporomandibular disorder in irritable bowel syndrome: Is there a correlation with greater illness severity? *World J Gastroenterol* 2017; 23(1): 103-109 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i1/103.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i1.103>

INTRODUCTION

Irritable bowel syndrome (IBS) is a common chronic functional disorder of the lower gastrointestinal tract characterized by chronic pain or discomfort in the abdomen associated with altered bowel habits^[1].

Patients with IBS often complain of a variety of other GI (*i.e.*, dyspepsia) and non-GI symptoms (*i.e.*, migraine headaches, fatigue, sleep problems, dizziness, depression, anxiety, irritability, lower urinary tract symptoms and many IBS patients meet diagnostic criteria for other functional disorders^[2], such as fibromyalgia (FM)^[3], interstitial cystitis/painful bladder syndrome (IC/PBS)^[4], migraine^[5], temporomandibular disorders (TMDs). However, the association between IBS and TMDs is still relatively unexplored^[6,7].

TMDs are a heterogeneous group of diseases of the stomatognathic system that involve the temporomandibular joint (TMJ), masticatory muscles

and their related structures^[8]. The cardinal symptoms are pain in the TMJ and/or masticatory muscles, joint sounds and alterations in mandibular movement.

The prevalence of TMD is recognized to be between 5% to 12%^[9] and this data has been confirmed also in an Italian population^[10]. However, only 7% to 15% with TMDs, ask for medical help, mainly women of reproductive ages^[11].

The classification of TMDs is controversial. A diagnostic model was proposed in 1992, known as the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)^[12]. Since its publication, the RDC/TMD has been widely used in epidemiological, clinical and experimental studies^[13]. Two diagnostic axes are contemplated: axis I establishes a diagnosis based on clinical variables, while axis II allows the assessment of mandibular function, psychological status and level of TMD-related psychosocial disability.

Previous cross-sectional research has suggested an association between TMD and IBS, however these studies have methodological limitations due to a self-reported TMD diagnosis or old criteria to diagnose IBS as well as the small number of studied subjects^[14-16].

In 2013 Sanders *et al.*^[17] showed that in a group of 74 subjects with IBS symptoms the incidence of first onset of TMD was 3 times higher, compared to the group of 2632 subjects without IBS symptoms. In 2015 another study showed that the number of comorbidities, IBS included, is positively associated with TMD pain duration and intensity, whereas among all comorbidities only the presence of specific conditions, such as migraine and chronic fatigue syndrome, is associated with an increase in TMD intensity and duration^[5].

Interestingly, patients with IBS and another functional disorder, in comparison with patients with only IBS, have more severe IBS symptoms, a higher rate of psychological comorbidity such as depression, anxiety and somatization, greater impairment of quality of life, and more illness-related work absenteeism^[18,19].

To our knowledge, the association between IBS and TMD taking into account the influence of IBS subtypes and illness severity has still not been sufficiently investigated. Increased awareness of the overlap between IBS and TMD likely will result in improved diagnoses and more effective management of both diseases^[20]. Patients with IBS symptoms often are treated within a narrow gastrointestinal paradigm while clinicians ignore coexisting pain conditions, resulting in treatment failure and perpetuation of the problem.

The aims of the study were to evaluate, firstly, the risk of TMD determined on the basis of the RDC/TMD in IBS patients diagnosed by the Rome III criteria, secondly the possible association between TMD and IBS subtype or severity. Finally, we aimed to observe any association between facial pain and abdominal pain.

Table 1 Chronic pain grade classification

Grade 0	
Low disability	No TMD pain in prior 6 mo
Grade I	
Low intensity	Characteristic pain intensity < 50, and less than 3 disability points
Grade II	
High intensity	Characteristic pain intensity \geq 50, and less than 3 disability points
High disability	
Grade III	
Moderately limiting	3 to 4 disability points, regardless of characteristic pain intensity
Grade IV	
Severely limiting	5 to 6 disability points regardless of characteristic pain intensity

MATERIALS AND METHODS

IBS patients (aged 18-65 years) were consecutively recruited for this study from an outpatient clinic of the University of Salerno devoted only to functional bowel disorders and run weekly by gastroenterologists trained in the field of functional bowel disorders (FBD). All patients attending this clinic were referred from general practitioners and/or other gastrointestinal clinics. At the same time, a dentist V.B. observed all patients recruited to this study.

For the purposes of the study, we recruited also healthy controls (HC) among the patients' friends and the hospital staff, if scoring negative for IBS and with regular bowel habit similar for age and gender to IBS patients. Enrolment was done between January 2014 and December 2015. All subjects gave their written informed consent and the Ethical Committee of the University of Salerno approved the study protocol.

The diagnosis of IBS was made based on the Rome III criteria, together with the exclusion of any organic disease, with complete physical examination, blood tests, flexible sigmoidoscopy and additional tests when indicated. Four different patterns of IBS resulted from the predominant bowel symptom: (1) diarrhoea predominant (IBS-D); (2) constipation predominant (IBS-C); (3) mixed IBS (IBS-M); and (4) unsubtyped IBS^[21]. The IBS severity score was obtained using the severity index (IBS-SSS)^[22]. This is a validated scoring system using easily obtained variables: current abdominal pain by visual analog scale (VAS) of 0-100 and frequency of abdominal pain; current abdominal distension by VAS of 0-100; the degree of satisfaction of evacuative behavior by VAS 0-100; the degree of IBS interference with normal work and social activities by VAS 0-100. IBS patients were then divided into three severity groups: mild (75 to 175), moderate (175-300), and severe (> 300).

According to the Italian version of the RDC/TMD criteria (Available from: <http://www.rdc-tmdinternational.org>. Accessed (1 December 2013) all subjects from the two groups were investigated

for TMD. The following elements were considered in the assessment of TMD: each patient's responses to the validated subjective-symptoms questionnaire, an interview that included the patient's detailed medical history, and the results of a physical examination. The history questionnaire included questions about prior trauma to the head and neck, awareness of bruxism, various diurnal and nocturnal parafunctional habits, muscle fatigue, locking, clicking, or crepitation in the temporomandibular joint during mandibular function, impaired mandibular movement, pain during mandibular function or while at rest, and prior treatment for TMD.

The clinical examination of RDC/TMD axis I consisted of the evaluation of masticatory muscles (temporal, masseter, medial, and lateral pterygoid), the temporomandibular joint, the range of mandibular movement in opening, lateral, and protrusive excursions, and temporomandibular joint sounds. Manual palpation has been reported as the technique most commonly used to assess muscle pain; thus the examination of masticatory muscles was performed via bilateral manual palpation.

Instead, the RDC/TMD axis II has permitted the severity of chronic pain to be rated by means of the Graded Chronic Pain Scale (GCPS). The GCPS comprises the assessment of seven items assessed: 3 items assessing the intensity of pain on a 10 point scale, including the current pain; 3 items assessing the impact of pain on a 10 point scale; and one item regarding the number of days of inability due to facial pain. The scoring criteria are simple to use and allow the categorization of pain into five levels of pain-related impairment (Table 1).

Furthermore, the RDC/TMD axis II has dealt with the assessment of depression and somatization levels by means of the depression and somatization scales of the Symptom Checklist 90R (SCL-90R)^[23]. A total of 31 items were included in the axis II, belonging either to the Depression and Vegetative Symptom Scale or to the Somatization Scale^[24]. The mean scale score is calculated by simply adding the scores of the single item together. This allows patients to be rated as having normal, moderate or severe levels of impairment regarding depression and nonspecific physical symptoms (Table 2).

Statistical analysis

Data are presented as mean \pm SE, unless otherwise indicated. $P < 0.05$ was considered statistically significant. χ^2 test and analysis of variance (ANOVA) were used to compare categorical and continuous data, respectively. The risk in IBS patients of having TMD compared to HC was analysed using a binary logistic regression. We then performed a subgroup analysis to test the risk of having TMD according to each IBS subgroup (IBS-D, IBS-C and IBS-M) using univariate logistic models. Two multivariate linear regression

Table 2 Depression and somatization classification

Classification	Normal	Moderate	Severe
Depression	< 0.535	≥ 0.535, ≤ 1.105	> 1.105
Nonspecific physical symptoms (including the painful symptoms)	< 0.500	≥ 0.500, ≤ 1.000	> 1.000
Nonspecific physical symptoms (excluding the painful symptoms)	< 0.428	≥ 0.428, ≤ 0.857	> 0.857

analyses were performed to analyze the relationships between illness severity of TMD and IBS taking into account age, sex, IBS severity, IBS subtypes and depression. The SPSS for Windows version 12.0 statistical package (SPSS, Chicago, Ill., United States) was used for the data analysis.

RESULTS

IBS Patients

None of the eligible patients refused to participate in the study. We enrolled 91 consecutive IBS patients (71 females, mean age 36.6 ± 1.4 years) and 57 healthy controls (HC) (37 females, mean age 34.2 ± 1.7 years) in the study. Gender and age distribution were not significantly different among groups (χ^2 test, $P = 0.08$ and Student t test, $P = 0.3$).

IBS patients were classified as follow: 23 (25.3%) as IBS-D, 30 (33.0%) as IBS-C and 38 (41.8%) as IBS-M. On the basis of IBS-SSS, in our IBS population we had 11(12.1%) mild IBS, 41 (45.1%) moderate and 39 (42.9%) severe IBS. The severity score was 120.0 ± 7.0 in mild IBS patients, 247.9 ± 6.8 in moderate IBS patients, and 361.3 ± 6.9 in severe IBS patients.

Risk of TMD in IBS compared to HC

According to the RDC/TMD classification criteria, the IBS group had a greater than three times risk of having TMD (OR = 3.41, 95%CI: 1.66-7.01), compared to HC. In fact, TMD was diagnosed in 50 (54.9%) IBS patients and 15 (26.3%) HC (χ^2 test, $P = 0.001$).

IBS patients compared to HC had significantly more facial pain (37.4% vs 19.3%, $P = 0.02$), TMJ locking (13.2 vs 3.5, $P = 0.05$) and TMJ clicking (41.8 vs 17.5, $P = 0.002$). TMJ crepitation was higher although it does not reach statistical significance (20.9 vs 10.5, $P = 0.10$).

From the RDC/TMD axis II the severity of chronic pain rated by means of the GCPS in IBS was grade I low intensity in 22.0%, grade II in 12.1% and grade III in 2.2%. IBS patients compared to HC had a significantly higher score of depression (0.95 ± 0.6 vs 0.62 ± 0.7 , $P = 0.001$), of nonspecific physical symptoms (including the painful symptoms) (1.28 ± 0.1 vs 0.6 ± 0.06 , $P < 0.001$) and of nonspecific physical symptoms (excluding the painful symptoms) (1.1 ± 0.08 vs 0.5 ± 0.07 , $P < 0.001$).

Relationship between TMD and the type and severity of IBS

The risk of having TMD was similar in all three IBS subtypes, around three times higher than HC [IBS-D vs HC OR = 3.05 (95%CI: 1.11-8.37), IBS-C vs HC = 3.66 (1.44-9.30), IBS-M vs HC 3.46 (1.44-8.25)]. The respective prevalence was IBS-D 52.2% - IBS-C 56.7% - IBS-M 55.3%.

Looking at the severity of IBS, there was not a significant higher IBS-SSS score in IBS patients with or without TMD (281.2 ± 12.5 vs 261.7 ± 17.1 , $P = 0.35$).

There was a significant positive correlation between the severity of chronic pain rated by means of the GCPS and the IBS-SSS ($R = 0.17$, $P = 0.04$). When multiple linear regression analysis was performed the GCPS was significantly related only to gender independent of age, IBS subtypes and IBS-SSS and depression (Table 3).

Multiple linear regression analysis showed that the current facial pain scoring from 0 to 10 was significantly related to the current abdominal pain (0-10 VAS) and to higher level of depression independent of gender, age, IBS subtypes and IBS-SSS (Table 4).

DISCUSSION

Our results showed that IBS patients had a TMD risk more than three times greater than HC. This increased risk is independent of any specific IBS subtype. Facial pain was positively related to abdominal pain and higher level of depression.

Studies on the association between TMD and IBS are scarce. In 1998 Korszun *et al*^[14] reported the presence of IBS in 46% of 39 patients who self-reported TMD diagnosis. In 2000 Aaron *et al*^[15] showed that IBS was present in 64% of 25 TMD patients, however diagnosis of IBS was made using the Manning criteria. In 2001, Jones *et al*^[16] presented at DDW an abstract in which the presence of self-reported TMD diagnosis was 16% in 270 patients with IBS. Recently, in 2013 Sanders *et al*^[17] in the multi-site OPPERA project performed a continuing prospective cohort study purposefully designed to investigate the etiology of first-onset TMD and variation in its genetic, biological and psychosocial determinants. Applying a rigorous methodology together with the large size of the study they demonstrated that incidence of first onset TMD was 3 times higher in people with IBS on enrolment as in people without IBS. IBS predicted first-onset TMD after adjustment for demographic characteristics and pain disorders; however their effects were rendered statistically non significant in the presence of other overlapping conditions. In this study the assessment of irritable bowel syndrome (IBS) symptoms was based on Rome III criteria using two questions (52 and 53) that asked about bowel movements and the experience of discomfort or pain

Table 3 Multiple regression analysis; the chronic pain grade scale by age, gender, depression, irritable bowel syndrome-symptom severity scale and irritable bowel syndrome subtypes

	Unstandardized coefficients		Standardized coefficients β	t	Significance	95%CI	
	β	SE				Lower	Upper
Constant	-0.220	0.530		-0.414	0.680	-1.274	0.834
Age	-0.007	0.007	-0.121	-1.124	0.264	-0.020	0.006
Gender	0.436	0.204	0.229	2.132	0.036	0.029	0.842
Depression	0.352	0.184	0.201	1.911	0.059	-0.014	0.718
IBS-SSS	-0.034	0.124	-0.290	-0.274	0.785	-0.280	0.213
IBS subtypes	0.032	0.109	0.031	0.292	0.771	-0.185	0.249

Dependent variable: Chronic pain grade scale. IBS: Irritable bowel syndrome.

Table 4 Multiple regression analysis; facial pain by age, gender, abdominal pain, depression, irritable bowel syndrome-symptom severity scale and irritable bowel syndrome subtypes

	Unstandardized coefficients		Standardized coefficients β	t	Significance	95%CI	
	β	SE				Lower	Upper
Costant	-0.891	0.720		-1.239	0.217	-2.314	0.531
Age	-0.001	0.012	-0.008	-0.104	0.917	-0.024	0.022
gender	0.292	0.338	0.071	0.866	0.388	-0.375	0.960
Abdominal pain VAS	0.220	0.083	0.396	2.644	0.009	0.056	0.384
IBS-SSS	-0.485	0.274	-0.329	-1.770	0.079	-1.026	0.057
Depression classification	0.473	0.189	0.205	2.501	0.014	0.099	0.848
Subtypes di IBS e HC	0.204	0.200	0.130	1.019	0.310	-0.191	0.598

Dependent variable: facial pain VAS (0-10). VAS: Visual analog scale; IBS: Irritable bowel syndrome; HC: Healthy controls.

in the abdomen that lasted at least one day a week during the previous three weeks^[17].

Compared to the previous literature, our study has taken into account several factors. Firstly, our population was enrolled in a tertiary outpatients clinic devoted only to functional bowel disorders and run weekly by gastroenterologists trained in the field of functional bowel disorders (FBD) together with a dentist. The presence of TMD in this population of patients with IBS and HC was evaluated according to the RDC/TMD criteria that are worldwide-accepted criteria for the diagnosis of these disorders. Therefore, our study results could be more generalizable for IBS patients seeking treatment. Secondly, to give strength to our study, the diagnosis of IBS and its different subtypes was based on a standardized questionnaire according to Rome III criteria and not on the patients' subjective evaluation of their bowel habits. Moreover, we took into account the severity of IBS demonstrating a weak but significant correlation between the chronic grade of TMD pain and IBS severity according to Francis *et al.*^[22]; however, in the regression analysis this correlation was lost taking into account other factors. In fact, women resulted significantly related to the chronic grade of TMD confirmed that gender is a risk factor in TMD^[11]. Finally, facial pain that is common in patients with TMD is strongly and positively related to abdominal pain and higher level of depression. We inquired about current facial and abdominal pain

to avoid a recall bias. Chronic abdominal pain is the predominant feature in IBS. In fact the newest Rome IV criteria published last May eliminated the term discomfort from the diagnostic criteria and focused only on recurrent abdominal pain^[25].

Furthermore, psychological status has been assessed and controlled for all subjects using RDC/TMD axis II by means of the 31 items belonging either to the Depression and Vegetative Symptom Scale or to the Somatization Scale^[24].

There are some limitations in this study. First, the small number of IBS patients could have affected our results especially in the analyses of the IBS-SSS association with TMD. However, facial pain is significantly correlated to higher abdominal pain and depression. In 2011 the Rome foundation working team stated that the physiological factors contributing to severity have both visceral and central nervous system contributions. As severity increases, the central nervous system provides a greater contribution and this is manifest by its co-association with psychosocial distress and comorbidities that increased symptom reporting and maladaptive coping^[26].

Moreover, based on the current design, we were unable to investigate on the pathophysiological link between IBS and TMD. For instance, patients with both IBS and TMD are not only more pain sensitive^[27] but also demonstrate reduced pain inhibition, possibly because of dysfunction of endogenous pain inhibition

systems in accordance with the theory of a generalized upregulation of pain processing in chronic pain conditions^[28].

This may predispose to the development of other chronic pain syndromes (*i.e.*, IBS leading to TMD) or may lead to the transition from a localized pain disorder to a widespread pain disorder^[29].

In addition, psychological symptoms were shown to contribute to these sensory dysfunctions and may be involved in pain modulation processes that are related to chronic pain.

These findings could be clinically relevant, suggesting that in order to improve IBS symptoms other existing comorbidities need to be assessed, probably in interdisciplinary clinics hosting multiple health professions.

In addition, studies about the treatment of these co-morbid conditions have shown that a simultaneous therapeutic approach to multiple diseases is more effective than the separate treatment of each^[20]. Thus a multidisciplinary therapy should be encouraged. Likewise, future research elucidating neurobehavioral processes underlining chronic pain is welcomed.

COMMENTS

Background

Irritable bowel syndrome (IBS) is a functional intestinal disorder characterized by chronic pain or discomfort in the abdomen associated with altered bowel habits. IBS commonly overlap with other comorbid pain conditions. The association between IBS and temporomandibular disorders (TMDs) remains largely unexplored.

Research frontiers

It has been recently highlighted by Rome IV criteria that a variety of other GI (*i.e.*, dyspepsia) and non-GI symptoms (*i.e.*, migraine headaches, fibromyalgia, interstitial cystitis, dyspareunia) are frequently present in IBS patients; the presence of these concomitant symptoms lends further support to the diagnosis and should be considered for a better management of these patients.

Innovations and breakthroughs

These results showed that IBS patients had a higher risk of having TMD compared to Healthy Controls and demonstrated that IBS patients that fulfilled criteria for TMD share along with chronic facial and abdominal pain a significant co-occurrence with psychiatric disorders and female preponderance. Compared to similar studies in previous literature, this study evaluated the presence of TMD according to the RDC/TMD criteria that are worldwide-accepted criteria for the diagnosis of these disorders together with a diagnosis of IBS and its different subtypes based on a standardized questionnaire according to Rome III criteria and not on the patients' subjective evaluation of their bowel habits. Moreover, the authors inquired about current facial and abdominal pain to avoid a recall bias. Chronic abdominal pain is the predominant feature in IBS. In fact, the newest Rome IV criteria published last May eliminated the term discomfort from the diagnostic criteria focused only on recurrent abdominal pain.

Applications

IBS patients could be better treated through patient-centered management that takes into account other coexisting comorbidities. A simultaneous therapeutic approach to multiple diseases is more effective than the separate treatment of each. Thus a multidisciplinary therapy should be encouraged.

Terminology

TMDs are a heterogeneous group of diseases of the stomatognathic system

that involve the temporomandibular joint (TMJ), masticatory muscles and their related structures. The cardinal symptoms are pain in the TMJ and/or masticatory muscles, joint sounds and alterations in mandibular movement.

Peer-review

Serena Gallota and co-workers aimed to investigate the prevalence and the risk of TMDs in patients with IBS, included in a prospective study. They showed that IBS patients had a higher risk of having TMD compared to healthy controls and demonstrated that in this study group IBS patients that fulfilled also criteria for TMD share along with chronic facial and abdominal pain a significant co-occurrence with psychiatric disorders and female preponderance.

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P- Reviewer: Carroccio A, Lakatos PL **S- Editor:** Qi Y
L- Editor: A **E- Editor:** Wang CH





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