Association between the metabolic syndrome and the irritable bowel syndrome: A cross-sectional study among a sample of Lebanese adults

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Abstract

Evidence of an association between metabolic syndrome (MetS) and irritable bowel syndrome (IBS) is emerging but is still inconclusive. The current cross-sectional study was conducted to explore the relationship between the two syndromes in a sample of Lebanese adults (n=221; mean age: 43.36 years; 62.9% females), recruited from a large urban university and its neighboring community. MetS was diagnosed based on the International Diabetes Federation criteria, and IBS was assessed using the Birmingham IBS scale. Logistic regression analyses were performed taking MetS and its components as dependent variables, and IBS and its subscales as independent variables. Covariates included sociodemographic, dietary, and lifestyle variables. MetS was positively associated with Visual Analogue Scale (VAS)-IBS (total scale (Beta=4.59, p=0.029) and VAS-Diarrhea subscale (Beta=4.96, p=0.008). Elevated blood pressure (Beta=5.02, p=0.007), elevated fasting blood sugar (Beta=4.19, p=0.033), and elevated waist circumference (Beta=5.38, p=0.010) were positively associated with VAS- Diarrhea subscale. MetS and IBS were found to be positively associated in a sample of the Lebanese adult population. We suggest that it might be of value to screen for either condition if one of the syndromes exists. Future longitudinal studies are essential to establish a causal relationship between the two syndromes to further understand the commonality related to pathogenesis and explore potential underlying mechanisms.

Keywords: Metabolic Syndrome, Irritable Bowel Syndrome, Lebanon, Adults

List of abbreviations: MetS, Metabolic Syndrome; IBS, Irritable Bowel Syndrome; Visual Analogue Scale, VAS; WHO, World Health Organization; NCEP, National Cholesterol Education Program (NCEP); TG, Triglycerides; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived Stress Scale; MEDAS, Mediterranean Diet Adherence Screener; HDL-C, High-density Lipoprotein- Cholesterol; FBS, Fasting Blood Glucose.

Introduction

Metabolic syndrome (MetS) is a disorder defined by a cluster of metabolic abnormalities encompassing hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia [(1)]. MetS is a major public health concern as a significant risk factor for cardiovascular atherosclerotic diseases and type 2 diabetes [(2)]. Several definitions of the MetS exist with obesity, insulin resistance/hyperglycemia, and dyslipidemias as common components differing in cutoff points for each component. The World Health Organization (WHO) definition was better suited as a research tool, whereas the National Cholesterol Education Program (NCEP) definition was more useful for clinical practice[(3)]. The International Diabetes Federation (IDF) produced a new set of criteria that can be used both epidemiologically and in clinical settings, compensating for differences in waist circumference and in regional adipose tissue distribution between different ethnic populations [(4,5)]. Globally, the prevalence of MetS as defined by the WHO and the NCEP varies widely among countries and ethnic groups ranging from 1- 39% [(4,5,6)]. Looking at the literature, the prevalence of MetS is higher using the IDF criteria followed by the WHO and then the NCEP. This variation is probably due to the lower cutoff of the waist circumference (WC) and the fasting glycemia established by them. Moreover, MetS is common in several rapidly developing countries in the Middle East, affecting about one in four individuals [(7,8)].

Among its neighboring countries, Lebanon, a small middle-income country in the Eastern Mediterranean Region, has a prevalence range of 31.2% to 34.6% of MetS among adults using the IDF criteria, with males presenting with a significantly higher rate than females [(9)]. Consequently, cardiovascular diseases, diabetes, and chronic disease risk factors, including obesity, have already emerged as the leading causes of morbidity and mortality in the country [(10)].

Irritable bowel syndrome (IBS) is defined as a chronic disorder of the gastrointestinal tract that is diagnosed clinically and manifested by abdominal pain and shifts in bowel habits [(11)]. Individuals suffering from IBS struggle with the adverse effects that this condition imposes on their overall quality of life [(12)]. There are three main types of IBS with either predominantly diarrhea (IBS-D), constipation (IBS-C), or both (IBS-M) [(13)]. Depending on the diagnostic criteria employed, IBS affects around 11% of the population globally, with variation by geographic region; the lowest occurring in South Asia (7.0%) and the highest in South America (21.0%) [(14)]. It is plausible that the underlying prevalence of symptoms in communities internationally is the same, but the variations reflect differences in access to health care [(15)],

acceptability of the diagnosis [16], and the significant stigma that is associated with it [17]. Studies in the Arab world are relatively scarce but show comparable results to Western countries [18]. Furthermore, looking at the Middle East and specifically Lebanon, data reveal a prevalence of 20.1% of IBS among adults and university students [19,20].

Despite the rising prevalence of MetS and IBS, the evidence on their association remains inconsistent. IBS may affect dietary patterns, food digestion, and nutrient absorption. These nutrition-related factors are closely related to MetS, implying that IBS may be a potential risk factor for MetS [21]. On the other hand, IBS is independently related to a higher prevalence of MetS and elevated triglycerides (TG) that may be linked to the pathogenesis of gastrointestinal disorders [22]. Gut dysbiosis is one of the significant factors in IBS that may influence the host's immune responses and energy homeostasis in the body, causing an upstream regulation of inflammatory cascades, insulin resistance, and impairment of the body's metabolism [23], exacerbating MetS.

Research on this association of IBS with MetS within the Middle Eastern and Arab region, specifically Lebanon, is limited. The objective of the current study is to investigate the association between MetS and IBS in a sample of Lebanese adults. Considering the unique sociodemographic and lifestyle characteristics of this population group, this study might help in highlighting some valuable insights into the relationship between these two prevalent conditions.

Materials and Methods

Design

This was a cross-sectional study.

Subjects

Community announcements were used to invite Lebanese adults, aged 18 to 65 years, to participate in this study. Participants were asked to come to the data collection clinic fasting for at least 8 hours. Additional inclusion criteria included being aged between 18 and 65 years of Lebanese nationality, free of self-reported active infections including COVID-19, not pregnant nor lactating, and not on anti-tuberculosis drugs. The participants signed a written consent form after the study objectives and right to withdraw at any time were explained.

Data collection – questionnaires

Sociodemographic characteristics and medical history information were collected through questionnaires and included 16 questions related to age, sex, educational level, employment status, and smoking status. Questions related to personal, and family medical history of chronic diseases were also included.

Anthropometric measurements were collected and included height (cm) measured using a portable stadiometer, weight (kg) measured using a beam scale, Body Mass Index (BMI) (kg/m^2) calculated as the ratio of weight divided by the squared height in meters (m^2) and waist circumference (WC in cm) measured to the nearest 0.1 cm at the mid-point, halfway between the right iliac crest and the lower costal region using standardized measuring tape.

Birmingham IBS scale

This self-administered 11-item symptom questionnaire assesses IBS-related symptoms in the previous four weeks based on the Rome II criteria, with each question having a standard response scale. Symptoms are measured based on a 6-point Likert scale (0–5) ranging from all of the time to none and converted to 100. The scale has 3 dimensions, including pain, constipation, and diarrhea, and is designed to enable assessment of symptom burden. This scale has a high internal validity (Cronbach's α of 0.74 for pain, 0.79 for constipation, and 0.90 for diarrhea) and good external validity (r = -0.3 to -0.6) for pain and diarrhea and moderate external validity (r = -0.2 to -0.3) for constipation, with all dimensions being reproducible (ICCs 0.75 to 0.81) [(24)].

Mediterranean Diet Adherence Screener (MEDAS)

Adapted from PREvencion con DIetaMEDiterranea (PREDIMED) [(25)], this 14-item questionnaire aims to assess food intake or frequency of foods in favor of the Mediterranean diet. Responses that support the Mediterranean diet receive a score of 1, while those that do not receive a score of 0. The overall score is determined by adding up all the responses to the 14 questions. The resulting score ranges from 0 to 14, with higher scores indicating a greater adherence to the Mediterranean diet. MEDAS is a commonly used tool to assess adherence to the Mediterranean Diet that has been validated by several studies[(26,27)].

The Birmingham IBS scale and MEDAS were translated to Arabic following the best practices, i.e., forward translation to Arabic, then back translation to English by two independent

translators. The translation also ensured that participants of all levels of literacy could respond [28]. The questionnaire was pilot tested on ten adults prior to data collection; feedback from the pilot was used to produce the final version of the questionnaire. In this study, the Cronbach alpha for the Birmingham IBS scale and MEDAS were 0.794 and 0.218, respectively.

The International Physical Activity Questionnaire (IPAQ) Short Form:

The validated Arabic version of the questionnaire was used. IPAQ-Short Form includes seven questions regarding duration and frequency of light, moderate, and vigorous physical activity performed in the past week. The Metabolic Equivalent of Tasks (METs) are calculated by multiplying the total minutes expended in a certain activity by the frequency (days) by the constants of 3.3, 4.0, and 8.0 for light, moderate, and vigorous activity, respectively. The total MET values are calculated by totaling the respective MET values for all activities that were performed in periods that were more than 10 minutes in duration [29]. The IPAQ has been validated in Lebanon showing a high internal consistency (reliability) and intraclass correlation coefficient (ICC) [30].

The Pittsburgh Sleep Quality Index (PSQI)

This questionnaire consists of nine questions, four of which assess sleep duration (hours), duration needed to fall asleep, amount of time required to wake up, and time spent in bed while awake. The five other questions assess reasons for sleep troubles. A total score is computed using an algorithm adapted from the developers of the questionnaire. Higher scores (≥5) indicate poor sleep quality [31]. The PSQI was validated in Arabic showing acceptable reliability and a high convergent validity with the Insomnia Severity Index[32]. The Arabic version of PSQI that was culturally adapted by Haidar et al. (2018) [33] was used.

The 10-item Cohen Perceived Stress Scale (PSS-10):

This 10-item questionnaire assesses stress levels in the previous month by investigating feelings for which respondents find their life situation unpredictable, uncontrollable, or stressful. Answers use a 5-point scale ranging from never (0) to very often (4), with a total score ranging from 0 to 40, with higher scores indicating higher perceived stress [34,35]. The PSS shows satisfactory

validity and reliability [36]. The Arabic version of the questionnaire, validated by Chaaya et al. (2010) [37] was used.

Diagnosis of the MetS

MetS was diagnosed using the IDF criteria [38]. Participants were considered to have MetS if they had central obesity (≥ 94 cm males and ≥ 80 cm; or BMI >30kg/m^2) and two of the following factors: elevated triglycerides (≥150 mg/dL) or being treated for it; low HDL-C (<40 mg/dL in males and <50 mg/dL in females) or being treated for it; high BP (SBP≥130 or DBP≥ 85 mmHg) or being treated for hypertension; and FBG ≥100 mg/dL or were diagnosed with type 2 diabetes.

Statistical Analysis

The data were analyzed using SPSS, version 25. A descriptive analysis was done using the counts and percentages for categorical variables and mean and standard deviation for continuous measures. Normality distribution was checked using visual inspection of the histogram and verified by checking the normality line of the regression plot and the scatter plot of the residual. Independent-sample t-test was used to compare the mean of the Birmingham IBS symptom questionnaire and subscales (pain, constipation, and diarrhea) between two groups, whereas ANOVA test was used to compare three or more means. Pearson correlation test was used to evaluate the association between continuous variables and the Birmingham IBS symptom questionnaire and each of the subscales (pain, constipation, and diarrhea). Four multivariable linear regression analyses using the Enter method were performed, taking respectively the Birmingham IBS symptom questionnaire total scale and each of the subscales (pain, constipation, and diarrhea) as the dependent variable. Covariates were informed by the literature and following a purposeful bivariate analysis, whereby variables showing a *p*-value less than 0.2 were included in the regression models as independent variables. Selecting variables with a p-value < 0.2 in the bivariate analysis for entry into the regression models was adopted to ensure potentially relevant variables were not prematurely excluded during the initial stages of model building. Those variables with modest associations (p-values between 0.05 and 0.2) in bivariate

analysis might have higher associations when included in the multivariate model [39,40]. *p*-value less than 0.05 was considered significant.

Ethical approval of research

This research received ethical approval from the Institutional Review Board (IRB) at the Lebanese International University (Ethical approval no: LIUIRB-220201-SH-111). The study's objectives, protocol, and the right to withdraw at any time were communicated to the participants prior to data collection. Subjects provided written consent, and only those consenting were included in the study.

Sample size calculation

Sample size calculation was performed using G*Power 3.1.9.7 software to detect a mean difference of IBS total score between those having or not having a MetS. Based on a medium effect size (Cohen's d = 0.5), an alpha level of 0.05, and a power of 0.80, a minimum sample needed was 128 participants [41,42].

Result

Sample description

The sociodemographic and other characteristics of the participants are displayed in Table 1. A total of 230 participants were enrolled in the study. The majority of participants were female (62.9%), and more than half of them were married (55.7%), having a low socio-economic status (50.5%), do not have any profession (53.0%), and 46.2% have a university degree. The majority of the participants do not smoke cigarettes (71.5%) and 58.4% of them do not smoke the waterpipe. The presence of MetS was found in 44.3% of the participants, and only 18.1% have diabetes, 28.5% have disorders of Lipid Metabolism (DLM), and 20.8% have hypertension. More than half of the participants have a family history of diabetes (54.5%) and hypertension (57.3%). The participants' average age was 43.36 ± 16.05 years.

Description of the Visual Analogue Scale (VAS) for irritable bowel syndrome (IBS)

Table 2 describes the median, mean, SD, and range of the scales used in this study. The

mean VAS-IBS total scale was 16.98 ± 15.16 with a median of 14.54 and a range from 0 to 100.

Correlates of the IBS total scale and subscales

The bivariate analysis taking the IBS total scale and subscales as the dependent variables is displayed in Appendix 1. Linear regression models taking the IBS total scale and subscales as the dependent variables. The analysis presented in Table 3 was adjusted over the following variables: sex, marital status, education level, profession, family history of dyslipidemia, physical activity, smoking, sleep quality, stress, and adherence to the Mediterranean diet.

In the first model, considering MetS as the independent variable, MetS was positively associated with the VAS-IBS total scale (Beta=4.59, p=0.029) and the VAS-Diarrhea subscale (Beta=4.96, p=0.008). Being a male was negatively associated with the VAS-IBS total scale and subscales. Being a smoker was positively associated with the VAS-IBS total scale (Beta=4.80, p=0.043); however, higher adherence to the Mediterranean diet was negatively associated with the VAS-IBS total scale (Beta = -1.02, p = 0.023). A significantly higher stress scale was positively associated with the VAS- Abdominal pain subscale (Beta=0.36, p=0.006). Also, a high level of physical activity was positively associated with the VAS- Diarrhea subscale (Beta = 4.41, p = 0.043) (Table 3, Model 1).

For model 2, considering TG levels as an independent variable, male sex was negatively associated with the VAS- IBS total scale, the VAS- Abdominal pain, and the VAS- Constipation subscales. In addition, the adherence to the Mediterranean diet was negatively associated with the VAS- IBS total scale and the VAS- Abdominal pain subscale (Table 3, Model 2).

In the third model, when considering HDL levels as the independent variable, male sex was negatively associated with the VAS- IBS total scale, the VAS- Abdominal pain, and the VAS- Constipation subscales. Being a smoker (Beta=4.97, p=0.041) and having a lower sleep quality (Beta=0.60, p=0.047) were positively associated with the VAS-IBS total scale. Finally, higher adherence to the Mediterranean diet was negatively associated with the VAS- IBS total scale and the VAS- Abdominal pain subscale (Table 3, model 3).

In the fourth model, taking blood pressure as the independent variable, elevated blood pressure was positively associated with the VAS- IBS Diarrhea subscale (Beta = 5.02, p = 0.007). Being a smoker (Beta=4.87, p=0.042) was positively associated with the VAS-IBS total scale, and high physical activity (Beta = 4.30, p = 0.047) was positively associated with the VAS-

Diarrhea subscale. In addition, higher adherence to the Mediterranean diet was negatively associated with the VAS- IBS total scale and the VAS- Abdominal pain subscale (Table 3, Model 4).

In the fifth model, considering FBS as the independent variable, elevated FBS (Beta = 4.19, p = 0.033) was positively associated with the VAS- Diarrhea subscale. Male sex was positively associated with the VAS- IBS total scale, the VAS- Abdominal pain subscale, and the VAS- Constipation subscale. Being a smoker (Beta = 4.84, p = 0.044) was positively associated with the VAS-IBS total scale; in contrast, higher adherence to the Mediterranean diet was negatively associated with the VAS- IBS total scale and the VAS- Abdominal pain subscale (Table 3, Model 5).

Finally, in the sixth model, taking WC as the independent variable, elevated WC (Beta = 5.38, p = 0.010) was positively associated with the VAS- Diarrhea subscale. Male sex was positively associated with the VAS- IBS total scale and subscales. On the other hand, higher adherence to the Mediterranean diet (Beta = -1.81, p = 0.013) was negatively associated with lower VAS-Abdominal pain subscale (Table 4, Model 6).

Discussion

Through this cross-sectional study, we explored the association between the MetS and IBS in a sample of the Lebanese adult population. Overall, we found a high prevalence of MetS (44.3%), and after adjustment for potential confounding factors, we identified a significant positive association between MetS and IBS total score and with the IBS diarrhea subscale, and between elevated blood pressure, elevated fasting blood sugar, and elevated WC and the IBS diarrhea subscale.

Our findings are in line with previous research showing a significant positive association between MetS and its components and IBS [21,43,44]. Specifically, through a cohort study involving 5104 subjects and spanning 5 years, Wang et al. (2022) [45] reported more than twice the odds of developing IBS in patients with MetS. Furthermore, in line with our results, Wang et al. (2022) [45] reported higher odds of IBS with elevated WC levels, and Kumar et al. (2022) [46] reported higher FBS and higher WC in patients with IBS. Finally, through a case-control study, Lee et al. (2015) [47] showed an independent positive association between elevated WC and higher visceral adiposity, and IBS, especially, IBS diarrhea.

Human studies stress the impact of hyperglycemia, hyperinsulinemia, and metabolic syndrome on painful neuropathy, whereas improved metabolic control in humans has led to improvement of neuropathy. Moreover, there is a close relation between luminal and intracellular glucose concentrations, expression of glucose transporters, and the release of gut hormones[48]. High levels of C-peptide, insulin, gastric inhibitory peptide, and leptin increase the excitability of the hypersensitive nervous system often found in IBS and thereby lead to increased symptoms[49,50].

Furthermore, looking at the mechanism behind the association between high obesity levels. specifically visceral obesity and high risk of diarrhea, studies indicate accelerated small intestinal transit and distal colonic transit times in obese patients, leading to bile acid malabsorption and thus diarrhea[51,52]. Visceral fat has also been found to increase the release of pro-inflammatory cytokines, which in turn alters intestinal permeability, leading to loose stools and increased stool frequency[47].

Finally, one potential mechanism for the relationship of hypertension with IBS may be that higher blood pressure could alter the tight junction proteins and gut permeability in the intestine, release proinflammatory cytokines and thereby, increase the risk of IBS [53,54].

Although evidence hints at a prevailing positive trend between IBS and MetS, studies are still inconclusive. Javadeka et al. (2021) [55] did not find an association between IBS and MetS among young adults. One explanation for this may be due to the exclusion of the patients with already known components of the MetS to nullify the confounding effects of change in lifestyle, diet, and drugs on gut function.

While the exact mechanisms driving the positive correlation between IBS and MetS remain elusive, microbiota alterations emerge as a plausible explanation for this association [56,57]. Specifically, shifts in microbial composition and quantity, gut microbiota-mediated immune dysregulation, and intestinal barrier dysfunction emerge as core pathophysiologies of gastrointestinal dysmotility and metabolic disease [56]. On one hand, microbial dysbiosis could lead to metabolic dysregulation. Suggested mechanisms include but are not limited to changes to gut barrier function and metabolic inflammation and effects on body weight regulation and insulin sensitivity [35,47]. On the other hand, metabolic abnormalities can drive gastrointestinal disturbances. For example, hyperglycemia is associated with intestinal barrier dysfunction and increases the risk for enteric infection. In addition, visceral adiposity, for which WC is a proxy,

increases the release of pro-inflammatory cytokines and this in turn may alter intestinal permeability, leading to chronic diarrhea [44]. To date, it remains unclear whether gastrointestinal dysfunction or metabolic disorder comes first.

To better understand the pathophysiological interaction between the two diseases, the link at the molecular level should be further investigated. The pathology of these diseases shares common features, including adipose tissue dysregulation, inadequate immune response, and inflammation [58]. As a central metabolic organ for integration and control of whole-body energy homeostasis, the adipose tissue has emerged as an important endocrine regulator that secretes cytokines and hormones, referred to as adipokines, which have pro- or anti-inflammatory activities. Moreover, changes in enteroendocrine functions have also been implicated in the pathogenesis of both diseases [0]. Glucagon-like peptide-1 (GLP-1) has gained attention as a key player in the pathogenesis of metabolic and inflammatory diseases due to its function in modulating stress and promoting anti-inflammatory signaling. The insulinotropic and glucose-lowering effects of GLP-1 have long been shown to be impaired in obesity and type 2 diabetes.

Furthermore, the reason why sleep disorders are associated with IBS remains unclear. The gut–brain axis plays an important role in the pathogenesis of IBS. The central nervous system (CNS), autonomic nervous system (ANS), enteric nervous system (ENS), and hypothalamic pituitary adrenal (HPA) axis are thought to be involved[60]. Sleep deprivation led to modification of the ANS activity, autonomic dysregulation[61]. The HPA axis has been reported to be inhibited by sleep and increased secretion of ACTH and cortisol [61,62]. Moreover, chronic sleep disruption can also cause reversible changes in gut microbiota associated with IBS symptoms[63]. Finally, elevated levels of dipeptidyl peptidase 4 (DPP-4) seen in sleep deprivation can be an early indicator of metabolic disorders and were associated with increased inflammation in gastrointestinal disorders[64].

Concerning sex variances, as found elsewhere [21,65], females in our study exhibited a higher likelihood of having IBS in comparison with males [66,67,68]. This could be attributed to the impact of female sex hormones on gut motility. Noteworthy, we found that participants with higher adherence to the Mediterranean diet were less likely to report IBS symptoms; this is possibly due to the diet's beneficial influence on gut microbiota and gut barrier [44]. The Mediterranean diet boasts various attributes that can enhance gut health, including its rich phenol content that exhibits anti-inflammatory properties, leading to reduced expression of inflammatory molecules,

and the higher presence of microbiota that produce short-chain fatty acids, aiding in the maintenance of intestinal epithelium function [68].

To the best of our knowledge, this study is the first to evaluate the relationship between IBS and MetS in a sample of Lebanese adults, using validated questionnaires and objective measurement of both biochemical and anthropometric indices. Furthermore, this study was sufficiently powered. Nevertheless, our results are limited by their cross-sectional design, which cannot be used to infer causality. Additionally, the sample was collected after community announcement, which leads us to accept a possibility of self-selection bias; also, being free from infections was a self-reported inclusion criterion. Lastly, the percentage of female participants was much higher than that of males this limitation is common in such types of studies.

In the present study, MetS and IBS were positively associated in a sample of the general Lebanese adult population. We suggest that it might be of value to screen for either condition if one of the syndromes exists to facilitate early detection and intervention. Future longitudinal studies are essential to establish a causal relationship between MetS and IBS, further understand the common pathogenesis, and explore potential underlying mechanisms.

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Declaration of Interests

The authors declare no conflict of interest.

Authorship

R.R. and M.A. contributed to the conceptualization; M.A., S.H., N.M., D.P., and R.R. developed the methodology; T.M. and R.R. performed the formal analysis; S.H. and N.M. conducted the investigation; data curation was handled by S.H. and N.M.; the original draft was prepared by M.A., S.H., N.M., D.P., and R.R.; T.M. reviewed and edited the manuscript; T.M. also handled visualization; D.P. and R.R. provided supervision; project administration was managed by S.H. and N.M.; funding was acquired by M.A., S.H., N.M., and R.R.

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Table 1. Sociodemographic and other characteristics of the participants (N=221).

Variable	N (%*)
Sex	
Male	82 (37.1%)
Female	139 (62.9%)
Marital Status	
Single/Widowed/Divorced	98 (44.3%)
Married	123 (55.7%)
Education Level	
University degree	102 (46.2%)
High school	41 (18.6%)
Middle education	37 (16.7%)
Primary education	30 (13.6%)
Illiterate	11 (5.0%)
Socioeconomic Status	
Low	111 (50.5%)
Medium	102 (46.4%)
High	7 (3.2%)
Profession	
Yes	103 (47.0%)
No	116 (53.0%)
Cigarette Smoking	
Never	158 (71.5%)
Previous smoker	16 (7.2%)
Smoker	47 (21.3%)
Waterpipe Smoking	
Never	129 (58.4%)
Previous smoker	22 (10.0%)
Smoker	70 (31.6%)
Presence of Metabolic Syndrome	
Yes	98 (44.3%)

No	123 (55.7%)
Having Type 1 or Type 2 Diabetes	
No	181 (81.9%)
Yes	40 (18.1%)
Family History of Type 1 Or Type 2 Diabetes	
No	100 (45.5%)
Yes	120 (54.5%)
Having Dyslipidemia	
Yes	63 (28.5%)
No	158 (71.5%)
Family History of Dyslipidemia	
Yes	85 (38.6%)
No	135 (61.4%)
Having Hypertension	
Yes	46 (20.8%)
No	175 (79.2%)
Family history of Hypertension	
Yes	126 (57.3%)
No	94 (42.7%)
	Mean (SD)
Age	43.36 (16.05)

*Valid percentages are presented

Table 2. Description of the Visual Analogue Scale for Irritable Bowel Syndrome (N=221).

	Mean (SD)	Median	Minimum	Maximum
VAS-IBS abdominal pain	20.75 (23.63)	13.33	0	100
VAS-IBS constipation	25.06 (29.99)	13.33	0	100
VAS-IBS diarrhea	9.88 (13.37)	4.00	0	100
VAS-IBS total	16.98 (15.16)	14.54	0	100

Abbreviation: VAS, Visual Analogue Scale**;** IBS, Irritable Bowel Syndrome**;** SD, Standard Deviation.

Table 3. Linear regression analysis taking the irritable bowel syndrome as the dependent variables.

	VAS-IBS total		**VAS-IBS abdominal pain**		**VAS-IBS constipation**		**VAS-IBS diarrhea**	
	UB (95% CI)	p-value	UB (95% CI)	p-value	UB (95% CI)	p-value	UB (95% CI)	p-value
Model 1: Taking the Metabolic Syndrome as independent variable								
Metabolic Syndrome (Yes vs. No*)	**4.59 (0.48; 8.71)**	**0.029**	5.32 (-1.25; 11.90)	.112	0.01 (-8.13; 8.15)	.999	**4.96 (1.29; 8.63)**	**.008**
Sex (Male vs. Female*)	**-8.37 (-12.76; -3.98)**	**<0.001**	**-9.73 (-16.53; -2.93)**	**.005**	**-12.58 (-21.68; -3.47)**	**.007**	**-4.08 (-7.91; -0.24)**	**.037**
Marital status (Married vs. Single*)	-1.56 (-5.65; 2.53)	0.453						
Education Level (University vs. None*)	3.36 (-0.82; 7.56)	0.115	2.40 (-4.09; 8.90)	.066				
Smoking (Yes vs. No*)	**4.80 (0.15; 9.45)**	**0.043**	6.96 (-0.47; 14.40)	.350			3.37 (-0.85; 7.59)	.117
Sleep Quality (PSQI)	.50 (-0.09;	0.097	.44 (-0.49;	.122	0.77 (-0.44;	.214	0.32 (-0.18;	.209

	1.09)		1.39)		1.99)		0.82)	
Stress (PSS)	.23 (-0.05; 0.51)	0.110	**.36 (-0.09; 0.81)**	**.006**	0.52 (-0.06; 1.10)	.082		
Adherence to Mediterranean Diet (MEDAS)	**-1.02 (-1.91; -0.14)**	**0.023**	-2.01 (-3.43; -0.59)	.066				
Profession (Employed vs. Unemployed)					0.19 (-8.11; 8.50)	0.963		
Family History of Dyslipidemia (Yes vs. No*)							3.18 (-0.34; 6.70)	.077
Physical Activity (Moderate vs. Low*)							-0.46 (-4.55; 3.63)	.825
Physical Activity (High vs. Low*)							**4.41 (0.15; 8.67)**	**.043**
Model 2: Taking Triglycerides levels as independent variable								
Triglyceride (Elevated vs.	2.54 (-1.55;	0.223	3.38 (-3.10;	.305	-1.95 (-10.00;	.633	2.94 (-0.72;	.115

Normal*)	6.65)		9.88)		6.10)		6.61)	
Sex (Male vs. Female*)	**-7.06 (-11.31; -2.81)**	**0.001**	**-8.25 (-14.76; -1.74)**	**.013**	**-12.40 (-21.16; -3.63)**	**.006**	-2.79 (-6.52; 0.93)	.140
Marital status (Married vs. Single*)	-1.58 (-5.73; 2.57)	0.453						
Education level (University vs. None*)	2.81 (-1.39; 7.01)	0.189	1.88 (-4.63; 8.40)	.569				
Smoking (Yes vs. No*)	4.66 (-0.02; 9.36)	0.051	6.78 (-0.69; 14.25)	.075			3.30 (-0.98; 7.58)	.130
Sleep Quality (PSQI)	0.54 (-0.05; 1.14)	0.072	.49 (-0.45; 1.43)	.309	0.81 (-0.40; 2.03)	.187	0.37 (-0.12; 0.87)	.143
Stress (PSS)	0.24 (-0.04; 0.53)	0.099	.37 (-0.08; 0.83)	.111	0.51 (-0.07; 1.10)	.085		
Adherence to Mediterranean Diet (MEDAS)	**-0.91 (-1.80; -0.02)**	**0.043**	**-1.88 (-3.29; -0.46)**	**.009**				
Profession (Yes					-0.05	.990		

vs. No*)					(-8.41; 8.30)			
Family History of Dyslipidemia (Yes vs. No*)							2.97 (-0.61; 6.56)	.104
Physical Activity (Moderate vs. Low*)							-0.76 (-4.89; 3.36)	.715
Physical Activity (High vs. Low*)							3.93 (-0.36; 8.22)	.073
Model 3: Taking High-density Lipoprotein- Cholesterol levels as independent variable								
HDL-C Level (Low vs. Normal*)	-0.89 (-5.69; 3.90)	0.714	-1.84 (-9.39; 5.70)	.631	-5.81 (-14.74; 3.11)	.201	1.39 (-2.70; 5.48)	.503
Sex (Male vs. Female*)	**-6.84 (-11.21; -2.46)**	**0.002**	**-7.59 (-14.36; -0.82)**	**.028**	**-11.29 (-20.21; -2.36)**	**.013**	-2.96 (-6.81; 0.89)	.131
Marital Status (Married vs. single*)	-1.09 (-5.27; 3.09)	0.608						
Education Level (University vs.	1.97 (-2.32; 6.28)	0.366	.39 (-6.30; 7.08)	.909				

None*)								
Smoking (Yes vs. No*)	**4.97 (0.21; 9.73)**	**0.041**	7.23 (-0.32; 14.79)	.061			3.32 (-1.02; 7.67)	.133
Sleep Quality (PSQI)	**0.60 (0.009; 1.19)**	**0.047**	.57 (-0.36; 1.51)	.226	0.85 (-0.35; 2.06)	.164	0.43 (-0.06; 0.93)	.088
Stress (PSS scale)	0.22 (-0.06; 0.51)	0.127	.34 (-0.11; 0.80)	.141	0.49 (-0.09; 1.07)	.100		
Adherence to Mediterranean Diet (MEDAS)	**-0.91 (-1.80; -0.02)**	**0.044**	**-1.89 (-3.31; -0.47)**	**.009**				
Profession (Yes vs. No*)					0.40 (-7.87; 8.67)	.924		
Family History of Dyslipidemia (Yes vs. No*)							3.33 (-0.24; 6.91)	.067
Physical Activity (Moderate vs. Low*)							-0.79 (-4.95; 3.36)	.706
Physical							3.55	.104

Activity (High vs. Low*)							(-0.74; 784)	
Model 4: Taking blood pressure as independent variable								
Blood pressure (Elevated vs. Normal*)	1.15 (-2.84; 5.16)	0.569	-1.05 (-7.44; 5.33)	.746	-4.76 (-12.82; 3.28)	.245	**5.02 (1.41; 8.63)**	**.007**
Sex (Male vs. Female*)	**-7.23 (-11.56; -2.90)**	**0.001**	**-7.84 (-14.47; -1.20)**	**.021**	**-11.52 (-20.41; -2.64)**	**.011**	-3.50 (-7.23; 0.22)	.066
Marital status (Married vs. Single*)	-1.26 (-5.39; 2.86)	0.546						
Education level (University vs. None*)	2.38 (-1.76; 6.53)	0.259	.79 (-5.56; 7.15)	.807				
Smoking (Yes vs. No*)	**4.87 (0.16; 9.57)**	**0.042**	6.93 (-0.54; 14.42)	.069			3.59 (-0.62; 7.81)	.094
Sleep Quality (PSQI)	0.57 (-0.01; 1.17)	0.057	.58 (-0.35; 1.53)	.221	0.84 (-0.35; 2.05)	.167	.33 (-0.16; 0.83)	.186
Stress (PSS)	0.22 (-0.06; 0.51)	0.121	.36 (-0.10; 0.81)	.124	0.54 (-0.04; 1.12)	.071		

Adherence to Mediterranean Diet (MEDAS)	**-0.94 (-1.84; -0.04)**	**0.040**	**-1.83 (-3.27; -0.40)**	**.012**				
Profession (Yes vs. No*)					-0.33 (-8.65; 7.98)	.937		
Family History of Dyslipidemia (Yes vs. No*)							3.48 (-0.04; 7.00)	.053
Physical Activity (Moderate vs. Low*)							-0.36 (-4.45; 3.73)	.862
Physical Activity (High vs. Low*)							**4.30 (0.06; 8.54)**	**.047**
Model 5: Taking Fasting Blood Sugar levels as independent variable								
FBS (Elevated vs. Normal*)	0.07 (-4.18; 4.32)	0.974	-3.56 (-10.30; 3.18)	.299	-5.22 (-13.69; 3.24)	.225	**4.19 (0.34; 8.04)**	**.033**
Sex (Male vs. Female*)	**-7.03 (-11.33; -2.72)**	**0.001**	**-7.49 (-14.07; -0.91)**	**.026**	**-11.85 (-20.64; -3.06)**	**.008**	-3.23 (-6.97; 0.51)	.090

Marital status (Married vs. single*)	-1.22 (-5.37; 2.92)	0.561						
Education level (University vs. None*)	2.22 (-1.92; 6.37)	0.292	.36 (-6.00; 6.72)	.911				
Smoking (Yes vs. No*)	**4.84 (0.12; 9.56)**	**0.044**	6.62 (-0.87; 14.11)	.083			3.86 (-0.39; 8.11)	.075
Sleep Quality (PSQI)	0.59 (-0.001; 1.19)	0.050	.64 (-0.30; 1.59)	.182	0.88 (-0.32; 2.10)	.152	0.34 (-0.15; 0.84)	.177
Stress (PSS)	0.23 (-0.05; 0.52)	0.117	.35 (-0.10; 0.81)	.125	0.52 (-0.06; 1.11)	.078		
Adherence to Mediterranean Diet (MEDAS)	**-0.90 (-1.79; -0.01)**	**0.047**	**-1.82 (-3.23; -0.40)**	**.012**				
Profession (Yes vs. No*)					0.11 (-8.15; 8.38)	.978		
Family History of Dyslipidemia (Yes vs. No*)							3.21 (-0.33; 6.75)	.076
Physical							-0.92	.656

Activity (Moderate vs. Low*)							(-5.02; 3.17)	
Physical activity (High vs. Low*)							3.97 (-0.28; 8.22)	.067
Model 6: Taking Waist circumference as independent variable								
Waist Circumference (Elevated vs. Normal*)	3.16 (-1.46; 7.79)	0.179	2.71 (-4.61; 10.03)	.466	-2.28 (-11.48; 6.92)	.626	**5.38 (1.27; 9.48)**	**.010**
Sex (Male vs. Female*)	**-8.33 (-12.99; -3.67)**	**0.001**	**-9.28 (-16.58; -1.97)**	**.013**	**-11.50 (-21.25; -1.76)**	**.021**	**-5.06 (-9.19; -0.94)**	**.016**
Marital status (Married vs. Single*)	-1.63 (-5.78; 2.52)	0.440						
Education level (University vs. None*)	2.52 (-1.59; 6.63)	0.229	1.31 (-5.03; 7.66)	.683				
Smoking (Yes vs. No*)	4.64 (-0.05; 9.33)	0.052	6.83 (-0.65; 14.31)	.073			3.19 (-1.04; 7.42)	.139
Sleep Quality (PSQI)	0.54 (-0.05; 1.14)	0.072	.51 (-0.43; 1.46)	.284	0.82 (-0.40; 2.03)	.187	0.32 (-0.17; 0.82)	.204

Stress (PSS)	0.23 (-0.05; 0.51)	0.116	.35 (-0.10; 0.81)	.126	0.52 (-0.06; 1.10)	.081		
Adherence to Mediterranean Diet (MEDAS)	-0.83 (-1.72; 0.05)	0.065	**-1.81 (-3.23; -0.39)**	**.013**				
Profession (Yes vs. No*)					0.06 (-8.25; 8.37)	.989		
Family History of Dyslipidemia (Yes vs. No*)							3.52 (-0.01; 7.04)	.051
Physical Activity (Moderate vs. Low*)							-0.78 (-4.87; 3.29)	.704
Physical activity (High vs. Low*)							3.52 (-0.67; 7.72)	.099

Abbreviations: VAS, Visual Analogue Scale**;** IBS, Irritable Bowel Syndrome**;** PSQI, Pittsburgh Sleep Quality Index**;** PSS, Perceived Stress Scale**;** MEDAS, Mediterranean Diet Adherence Screener**;** HDL-C, High-density Lipoprotein- Cholesterol; FBS, Fasting Blood Glucose

*Reference category.

Numbers in Bold indicate statistical significance.

Supplementary Material

Supplementary 1. Bivariate analysis taking the irritable bowel syndrome as the dependent variable (N=221).

	VAS-IBS total	VAS-IBS abdominal pain	VAS-IBS constipation	VAS-IBS diarrhea
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Presence of Metabolic Syndrome				
Yes	18.18 (16.76)	22.44 (25.67)	24.14(31.58)	12.04(16.44)
No	16.03 (13.75)	19.40(21.87)	25.79(28.76)	8.16(10.05)
p-value	0.298	0.342	0.686	0.042
Components of Metabolic Syndrome				
HDL-C Level				
Abnormal	16.22(15.12)	20.16(22.98)	22.55(28.85)	10.06(14.09)
Normal	18.94(15.21)	22.25(25.34)	31.50(32.07)	9.41(11.43)
p-value	0.232	0.556	0.046	0.749
Waist Circumference				
Normal	17.08(14.37)	20.45(22.53)	29.49(31.03)	7.61(9.21)
Abnormal	16.94(15.58)	20.90(24.22)	22.88(29.32)	11.00(14.91)
p-value	0.947	0.896	0.123	0.040
Fasting Blood Sugar				
Normal	17.19(16.00)	21.91(24.74)	26.53(30.46)	8.75(12.64)
Abnormal	16.52(13.16)	18.13(20.85)	21.76(28.83)	12.41(14.67)
p-value	0.762	0.273	0.276	0.061
Triglycerides Level				
Normal	15.91(14.41)	18.94(21.39)	25.26(29.49)	8.48(10.56)
Abnormal	18.61(16.18)	23.48(26.55)	24.77(30.89)	12.00(16.60)
p-value	0.195	0.182	0.906	0.080

Blood Pressure				
Normal	16.92(15.54)	21.56(24.80)	26.91(31.15)	8.15(12.43)
Abnormal	17.07(14.66)	19.55(21.85)	22.32(28.12)	12.44(14.35)
p-value	0.943	0.535	0.265	0.023
Sex				
Male	11.57(14.09)	14.71(19.67)	15.36(23.90)	7.41(13.21)
Female	20.18(14.90)	24.31(25.07)	30.79(31.77)	11.33(13.30)
p-value	<0.001	0.002	<0.001	0.035
Marital Status				
Single/Widowed/Divorced	18.51(16.47)	22.99(26.21)	26.93(29.56)	10.77(14.05)
Married	15.77(13.97)	18.97(21.28)	23.57(30.36)	9.17(12.83)
p-value	0.182	0.220	0.409	0.377
Education Level				
Illiterate	27.60(14.96)	41.21(26.30)	38.18(35.16)	13.09(13.51)
Primary Education	13.15(11.40)	14.88(15.91)	20.66(31.38)	7.60(9.87)
Elementary Education	16.65(13.04)	21.26(27.43)	24.86(28.57)	8.97(11.44)
Secondary Education	17.78(13.43)	23.57(26.03)	27.47(30.33)	8.48(9.96)
University Degree	16.77(17.09)	18.95(21.81)	24.05(29.50)	11.09(15.88)
p-value	0.112	**0.022**	0.539	0.567
Socioeconomic Status				
Low	18.24(16.20)	22.58(23.20)	25.40(30.96)	11.35(15.72)
Medium	15.47(14.14)	19.21(24.63)	23.46(28.38)	8.43(10.48)
High	15.06(6.61)	13.33(14.90)	32.38(28.13)	5.71(7.25)
p-value	0.388	0.413	0.703	0.201
Employment Status				
Yes	15.88(16.39)	20.45(23.47)	22.13(29.30)	9.39(15.51)
No	17.96(14.11)	21.03(24.00)	27.75(30.60)	10.24(11.16)
p-value	0.315	0.857	0.168	0.642
Cigarette Smoking				
Yes	21.04(18.55)	26.66(27.38)	28.93(31.58)	12.93(17.35)
No	15.89(13.97)	19.15(22.33)	24.02(29.55)	9.05(12.01)

p-value	0.039	0.088	0.320	0.078
Having Type 1 or Type 2 Diabetes				
Yes	16.72(13.46)	16.16(19.73)	21.00(30.40)	14.50(16.52)
No	17.04(15.54)	21.76(24.33)	25.96(29.90)	8.86(12.40)
p-value	0.904	0.175	0.344	0.047
Family History of Type 1 or Type 2 Diabetes				
Yes	16.42(13.33)	18.94(22.75)	24.16(30.31)	10.26(12.74)
No	17.61(17.21)	22.60(24.50)	26.20(29.86)	9.48(14.20)
p-value	0.563	0.253	0.618	0.666
Having Dyslipidemia				
Yes	18.81(14.02)	21.26(26.25)	29.31(32.97)	11.04(11.21)
No	16.57(15.84)	20.72(22.65)	25.11(29.79)	8.96(13.01)
p-value	0.341	0.882	0.378	0.277
Family History of Dyslipidemia				
Yes	18.73(15.07)	21.80(25.78)	26.74(30.10)	12.09(14.32)
No	15.79(15.18)	20.19(22.30)	23.75(29.93)	8.38(12.58)
p-value	0.162	0.625	0.472	0.045
Having Hypertension				
Yes	15.88(14.63)	16.81(19.41)	20.14(27.84)	12.78(15.35)
No	17.43(15.50)	21.66(24.86)	26.82(30.59)	9.26(12.95)
p-value	0.545	0.223	0.183	0.120
Having Family History of Hypertension				
Yes	16.69(14.00)	19.04(23.05)	25.39(29.75)	10.06(12.72)
No	17.37(16.65)	23.01(24.30)	24.63(30.45)	9.64(14.26)
p-value	0.741	0.217	0.852	0.817
Sleep quality (PSQI scale)				
Normal	12.70(13.34)	15.68(20.54)	18.90(27.42)	7.20(12.17)

Sleep disturbance	19.66(15.65)	23.92(24.92)	28.92(30.96)	11.55(13.86)
p-value	0.001	0.011	0.013	0.018
Physical activity				
Low	15.64(14.13)	18.68(21.06)	23.37(31.38)	9.18(11.30)
Moderate	16.93(13.08)	20.69(21.80)	28.15(28.89)	7.94(9.81)
High	18.56(18.18)	23.65(28.76)	23.01(27.86)	12.83(18.36)
p-value	0.503	0.445	0.525	0.096

	Correlation coefficient	**Correlation coefficient**	**Correlation coefficient**	**Correlation coefficient**
Age	-0.003	-0.086	0.021	0.054
p-value	0.961	0.205	0.754	0.425
Sleep quality (PSQI scale)	0.253	0.191	0.197	0.163
p-value	**<0.001**	**0.004**	**0.003**	**0.015**
Stress (PSS scale)	0.213	0.181	0.213	0.052
p-value	**0.001**	**0.007**	**0.001**	0.438
Physical activity (IPAQ scale)	0.089	0.108	0.014	0.086
p-value	0.224	0.138	0.845	0.242
MEDAS	-0.101	-0.159	-0.050	-0.016
p-value	0.135	0.018	0.463	0.809

Abbreviations: VAS, Visual Analogue Scale**;** IBS, Irritable Bowel Syndrome**;** PSQI, Pittsburgh Sleep Quality Index**;** PSS, Perceived Stress Scale**;** IPAQ, International Physical Activity Questionnaire; MEDAS, Mediterranean Diet Adherence Screener**;** HDL-C, High-density Lipoprotein- Cholesterol

Numbers in Bold indicate statistical significance.

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