Plasma triglycerides and fasting plasma glucose may behave as sensitive acute phase reactants in irritable bowel syndrome

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ABSTRACT

Background: Irritable bowel syndrome (IBS) may be found among the most common causes of recurrent upper abdominal discomfort in the general population, nowadays.

Method: Consecutive patients with IBS and age and sex-matched control cases were studied. IBS was diagnosed according to Rome II criteria in the absence of red flag symptoms including pain, diarrhea interfering with sleep, weight loss, fever, and any pathologic physical examination finding.

Results: The study included 936 patients with IBS (592 females and 344 males) and 346 control cases. Mean age of the patients was 41.0 ± 14.7 (13-86) years. Interestingly, 63.2% of the patients were female. Prevalence of smoking was higher in the patients, significantly (35.2% versus 20.8%, p<0.001). Beside that prevalences of chronic gastritis (CG) (80.4% versus 15.0, p<0.001), antidepressants use (46.4% versus 16.1%, p<0.001), hemorrhoids (37.1% versus 7.2%, p<0.001), and urolithiasis (22.0% versus 9.5%, p<0.001) and mean values of fasting plasma glucose (FPG) (111.9 versus 105.4 mg/dL, p= 0.002) and plasma triglycerides (167.0 versus 147.3 mg/dL, p= 0.013) were all higher in the patients with IBS, significantly.

Conclusion: IBS may be a low-grade inflammatory process initiated with smoking, infections, inflammations, anxiety, depression, sleep disorders, illness fear, cancer fear, and death fear-like stresses, and eventually terminates with dysfunctions of gastrointestinal and genitourinary tracts and elevations of some metabolic parameters. There may be some significant relationships between IBS, smoking, female gender, CG, depression, hemorrhoids, urolithiasis, FPG, and plasma triglycerides. In other words, FPG and plasma triglycerides may behave as sensitive acute phase reactants in IBS.

Key words: Irritable bowel syndrome, smoking, triglycerides, fasting plasma glucose, acute phase reactants, chronic endothelial damage, atherosclerosis

Introduction

Recurrent upper abdominal discomfort may be the cause of nearly half of applications to Internal Medicine Polyclinics (1). Although gastroesophageal reflux disease, esophagitis, duodenal and/or gastric ulcers, erosive gastritis and/or duodenitis, celiac disease, chronic pancreatitis, and malignancies are found among possible causes, irritable bowel syndrome (IBS) and chronic gastritis (CG) may be two of the most commonly diagnosed disorders among all. Flatulence, periods of diarrhea and constipation, repeated toilet visits due to urgent evacuation or early filling sensation, excessive straining, feeling of incomplete evacuation, frequency, urgency, reduced feeling of well-being, and eventually disturbed social life are often reported by the patients with IBS. Although many patients relate onset of symptoms to intake of food, and often incriminate specific food items, a meaningful dietary role is doubtful in IBS. According to literature, nearly 20% of general population have IBS, and it is more common in female gender with unknown causes, yet (2). Psychological factors seem to precede onset and exacerbation of gut symptoms, and many potentially psychiatric disorders including anxiety, depression, sleep disorders, illness fear, cancer fear, or death fear usually coexist with IBS (3). For instance, thresholds for sensations of initial filling, evacuation, urgent evacuation, and utmost tolerance recorded via a rectal balloon significantly decreased by focusing the examiners' attention on gastrointestinal stimuli by reading pictures of gastrointestinal malignancies in the patients with IBS (4). In other words, although IBS is described as a physical disorder according to Rome II guidelines, psychological factors may be crucial for triggering of these physical changes in the body. IBS is actually defined as a brain-gut dysfunction according to the Rome II criteria, and it may have more complex mechanisms affecting various systems of the body via a low-grade inflammatory process (5). Eventually, IBS may even terminate with CG, urolithiasis, and hemorrhoids (6-8). Similarly, some authors studied the role of inflammation in IBS via colonic biopsies in 77 patients (9). Although 38 patients had normal histology, 31 patients demonstrated microscopic inflammation, and eight patients fulfilled criteria for lymphocytic colitis. However, immunohistology revealed increased intraepithelial lymphocytes as well as increased CD3 and CD25 positive cells in lamina propria of the group with "normal" histology. These features were more evident in the microscopic inflammation group who additionally revealed increased neutrophils, mast cells, and natural killer cells. All of these immunopathological abnormalities were the most evident in the lymphocytic colitis group who also demonstrated HLA-DR staining in the crypts and increased CD8 positive cells in the lamina propria (9). A direct link between the immunologic activation and IBS symptoms was shown by some other authors, too (10). They demonstrated not only an increased mast cell degranulation in the colon but also a direct correlation between proximity of mast cells to neuronal elements and severity of pain in IBS (10). In addition to the above findings, there is some evidences for extension of the inflammatory process behind the mucosa. Some authors addressed this issue in ten patients with severe IBS by examining full-thickness jejunal biopsies obtained via laparoscopy (11). They detected a low-grade infiltration of lymphocytes in myenteric plexus of nine patients, four of whom had an associated increase in intraepithelial lymphocytes and six demonstrated evidence of neuronal degeneration (11). Nine patients had hypertrophy of longitudinal muscles, and seven had abnormalities in number and size of interstitial cells of Cajal (11). The finding of intraepithelial lymphocytosis was consistent with some other reports in the colon (9) and duodenum, too (12). On the other hand, smoking is a well-known cause of chronic endothelial inflammation terminating with an accelerated atherosclerosis-induced end-organ insufficiencies all over the body (13). We tried to understand whether or not there are some significant relationships between IBS, smoking, and some metabolic parameters in the present study.

Material and methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients with upper abdominal discomfort were taken into the study. Their medical histories including smoking habit, alcohol consumption, urolithiasis, and already used medications including antidepressants at least for a period of six-month were learned. Patients with devastating illnesses including eating disorders, malignancies, acute or chronic renal failure, cirrhosis, hyper- or hypothyroidism, and heart failure were excluded. Current daily smokers at least for six-months and cases with a history of five pack-year were accepted as smokers. Patients with regular alcohol consumption (one drink a day) were accepted as drinkers. A routine check up procedure including fasting plasma glucose (FPG), total cholesterol (TC), triglycerides, high-density lipoprotein (HDL), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), albumin, creatinine, thyroid function tests, hepatic function tests, markers of hepatitis A, B, C, and human immunodeficiency viruses, urinalysis, a posterior-anterior chest x-ray graphy, an electrocardiogram, a Doppler echocardiogram in case of requirement, an abdominal ultrasonography, an abdominal x-ray graphy in supine position, rectosigmoidoscopy in patients symptomatic for hemorrhoids, and a questionnaire for IBS was performed. IBS was diagnosed according to Rome II criteria in the absence of red flag symptoms including pain, diarrhea interfering with sleep, weight loss, fever, and any pathologic physical examination finding. An upper gastrointestinal endoscopy was performed, and sample biopsies were taken in case of requirement. CG is diagnosed histologically. Although microscopic examination may also show stereotypical changes in epithelium such as degeneration, focal intestinal metaplasia, dysplasia, and glandular atrophy, infiltrations of neutrophils and monocytes into the gastric mucosa is the hallmark of CG (14). An additional intravenous pyelography was performed according to the results of the urinalysis and abdominal x-ray graphy. So urolithiasis was diagnosed either by medical history or as a result of current clinical and laboratory findings. Body mass index (BMI) of each case was calculated by measurements of Same Physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (15). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetic. An oral glucose tolerance test with 75-gram glucose was performed in cases with FPG levels between 100 and 126 mg/dL, and diagnosis of cases with 2-hour plasma glucose levels of 200 mg/dL or greater is diabetes mellitus (DM) (15). Office blood pressure (OBP) was checked after a 5-minute of rest in seated position with mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2-hours.

Ten-day twice daily measurements of blood pressure at home (HBP) were obtained in all cases, even in normotensives in the office due to the risk of masked hypertension after an education about proper blood pressure (BP) measurement techniques (16). The education included recommendation of upper arm devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest for a period of 5-minute in seated position before measurements. An additional 24-hour ambulatory blood pressure monitoring was not required due to the equal efficacy of the method with HBP measurements to diagnose hypertension (HT) (17). HT is defined as a mean BP of 140/90 mmHg or greater on HBP measurements, and white coat hypertension (WCH) is defined as an OBP of 140/90 mmHg or greater, but a mean HBP value of lower than 140/90 mmHg (16). Eventually, all patients with IBS were collected into the first and age and sex-matched control cases were collected into the second groups. Mean values of BMI, FPG, TC, triglycerides, HDL, and low-density lipoprotein (LDL) and prevalences of smoking, CG, antidepressants use, hemorrhoids, urolithiasis, WCH, HT, and DM were detected in each group and compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 936 patients with the IBS (592 females and 344 males) and 346 control cases. Mean age of the patients was 41.0 ± 14.7 (13-86) years. Interestingly, 63.2% of the patients were female. Prevalence of smoking was higher in the patients with IBS, significantly (35.2% versus 20.8%, p<0.001). Beside that prevalences of CG (80.4% versus 15.0, p<0.001), antidepressants use (46.4% versus 16.1%, p<0.001), hemorrhoids (37.1% versus 7.2%, p<0.001), and urolithiasis (22.0% versus 9.5%, p<0.001) and mean values of FPG (111.9 versus 105.4 mg/dL, p= 0.002) and plasma triglycerides (167.0 versus 147.3 mg/dL, p= 0.013) were all higher in the patients with IBS (Table 1). Due to the limited number of cases with alcoholism among the study cases, regular alcohol consumption was not included in comparison.

Table 1: Comparison of patients with irritable bowel syndrome and control cases

Variables	Patients with IBS*	*p*-value	Control cases
Number	936		346
Mean age (year)	*41.0 ± 14.7 (13-86)*	Ns†	41.4 ±14.4 (15-82)
Female ratio	*63.2%*	Ns	63.0%
Smoking	*35.2%*	*<0.001*	*20.8%*
Chronic gastritis	*80.4%*	*<0.001*	*15.0%*
Antidepressants use	*46.4%*	*<0.001*	*16.1%*
Hemorrhoids	*37.1%*	*<0.001*	*7.2%*
Urolithiasis	*22.0%*	*<0.001*	*9.5%*
Mean BMI‡ (kg/m2)	27.2 ±5.6 (15.0-51.1)	Ns	27.7 ±5.9 (16.5-49.0)
WCH§	27.7%	Ns	31.4%
HT‖	12.8%	Ns	14.7%
*Mean FPG** (mg/dL)*	*111.9 ± 42.8 (66-392)*	*0.002*	*105.4 ± 32.9 (70-323)*
DM***	8.3%	Ns	10.0%
Mean TC**** (mg/dL)	199.8 ±43.9 (105-352)	Ns	196.5 ±43.6 (110-296)
Mean triglycerides (mg/dL)	*167.0 ± 106.5 (20-622)*	*0.013*	*147.3 ± 102.9 (27-857)*
Mean LDL***** (mg/dL)	125.4 ±35.8 (10-282)	Ns	124.0 ±32.5 (54-231)
Mean HDL****** (mg/dL)	46.6 ±13.5 (24-124)	Ns	45.0 ±10.3 (26-72)

*Irritable bowel syndrome †Nonsignificant (p>0.05) ‡Body mass index §White coat hypertension ‖Hypertension
**Fasting plasma glucose ***Diabetes mellitus ****Total cholesterol *****Low-density lipoprotein
******High-density lipoprotein

Discussion

Smoking-induced vasculitis may be the second common vasculitis just after obesity in the world. It is a major risk factor for the development of atherosclerotic end-organ insufficiencies including coronary heart disease (CHD), peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), and stroke (13, 18). Its atherosclerotic effect is the most obvious in Buerger's disease. Buerger's disease is an obliterative vasculitis characterized by inflammatory changes in small and medium-sized arteries and veins, and it has never been documented in the absence of smoking in the literature. Although the well-known strong atherosclerotic effects of smoking, some studies reported that smoking in human being and nicotine administration in animals are associated with lower BMI values (19). Some evidences revealed an increased energy expenditure during smoking both on rest and light physical activity (20), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (21). According to an animal study, nicotine may lengthen intermeal time and simultaneously decreases amount of meal eaten (22). Additionally, BMI seems to be the highest in the former, the lowest in the current and medium in never smokers (23). Smoking may be associated with postcessation weight gain but evidences suggest that risk of weight gaining is the highest during the first year after quitting and decreases with the following years (24). Similarly, although CHD was detected with similar prevalence in both genders, prevalence of smoking and COPD were higher in males with the CHD against the higher values of BMI, LDL, and triglycerides and higher prevalences of WCH, HT, and DM in females (25). This result may indicate both the strong atherosclerotic and weight decreasing roles of smoking (26). Similarly, the incidence of a myocardial infarction is increased six-fold in women and three-fold in men who smoked at least 20 cigarettes per day (27). In other words, smoking may be more harmful for women regarding the atherosclerotic end-points probably due to the greater BMI and its consequences in the females. Similarly, smoking is consistently higher in men in the literature (18). So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite. On the other hand, smoking-induced weight loss may be related with the chronic vascular endothelial inflammation all over the body, since loss of appetite is one of the chief symptoms of disseminated inflammation in the body. Clinicians can even understand healing of patients by means of normalizing appetite. Several toxic substances found in cigarette smoke get into the circulation via the respiratory tract, and cause a vascular endothelial inflammation until the clearence from the circulation. But due to the repeated smoking habit of the individuals, the clearence process never terminates. So the patients become ill with loss of appetite, permanently. In another definition, smoking-induced weight loss is an indicator of being ill instead of being healthy (21-23). After smoking cessation, appetite normalizes with a prominent weight gain but the returned weight is their normal and physiological weight, actually. On the other hand, there may be several underlying mechanisms terminating with the IBS in smokers. First of all, smoking-induced chronic vascular endothelial inflammation may disturb epithelial functions for absorption and excretion in the gastrointestinal and genitourinary tracts. These functional problems may terminate with the symptoms and components of IBS including loose stool, diarrhea, constipation, and urolithiasis. Secondly, diarrheal losses-induced urinary changes may even cause urolithiasis (6, 7). Thirdly, smoking-induced sympathetic nervous system activation may cause motility disorders in the gastrointestinal and genitourinary tracts. Fourthly, smoking-induced loss of appetite may terminate with obstipation. Finally, immunosuppression secondary to smoking-induced chronic vascular endothelial inflammation may even terminate with gastrointestinal and genitourinary tract infections causing loose stool, diarrhea, and urolithiasis since some types of bacteria can provoke urinary supersaturation and modify the environment to form crystal deposits in the urine. In fact, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infection with bacteria that possess the enzyme, urease. Similarly, prevalence of urolithiasis was higher in the patients with IBS in the present study, significantly (22.0% versus 9.5%, $p<0.001$).

Chronic endothelial damage may be the major underlying cause of aging and death by causing end-organ insufficiencies in human being (28). Much higher BP of the afferent vasculature may be the major accelerating factor by causing recurrent injuries on vascular endothelial cells. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Therefore the term of venosclerosis is not as famous as atherosclerosis in the literature. Due to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood supply to the terminal organs, and increase systolic and decrease diastolic BP further. Some of the well-known accelerating factors of the inflammatory process are physical inactivity, sedentary lifestyle, excess weight, animal-rich diet, smoking, alcohol, chronic inflammations, prolonged infections, and cancers for the development of terminal consequences including obesity, HT, DM, cirrhosis, PAD, COPD, CHD, CRD, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, early aging, and premature death (29). Although early withdrawal of the accelerating factors can delay terminal consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, and aging, endothelial changes can not be reversed completely due to their fibrotic natures. The accelerating factors and terminal consequences are researched under the titles of metabolic syndrome, aging syndrome, or accelerated endothelial damage syndrome in the literature, extensively (30, 31).

Obesity may be found among one of the terminal consequences of the metabolic syndrome because after development of obesity, nonpharmaceutical approaches provide limited benefit either to heal obesity or to prevent its complications. Excess weight may cause a chronic low-grade inflammation on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess weight in all age groups (32). The low-grade chronic inflammatory process may even cause genetic changes on the epithelial cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system. The effects of excess weight on BP were shown in the literature, extensively (33). For example, incidence of sustained normotension (NT) was higher in the underweight (80.3%) than the normal weight (64.0%, $p<0.05$) and overweight groups (31.5%, $p<0.05$),

(31.5%, $p<0.05$), significantly, and 52.8% of cases with HT had obesity against 14.5% of cases with the NT ($p<0.001$) (34). So the dominant triggering cause of the metabolic syndrome appears as weight gain, which is probably the main cause of insulin resistance, hyperlipoproteinemias, impaired fasting glucose, impaired glucose tolerance, and WCH via the chronic low-grade inflammation on vascular endothelium all over the body (35). Prevention of the weight gain with physical activity, even in the absence of a prominent weight loss, will probably result with resolution of many parameters of the syndrome (36-39). But according to our experiences, excess weight may actually be a consequence of physical inactivity instead of an excessive eating habit, thus prevention of weight gain can not be achieved by diet, alone (40). Additionally, limitation of excess weight as an excessive fat tissue around abdomen under the heading of abdominal obesity is meaningless, instead it should be defined as overweight or obesity via the BMI since adipocytes function as an endocrine organ, and they produce a variety of cytokines and hormones all over the body (35). The eventual hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with chronic endothelial inflammation, insulin resistance, and elevated BP values. Similarly, the Adult Treatment Panel (ATP) III reported that although some people classified as overweight with larger muscular masses, most of them also have excessive fat tissue predisposing to HT, DM, CHD, and stroke-like terminal end-points of the metabolic syndrome, actually (15).

Although ATP II determined the normal triglycerides values as lower than 200 mg/dL (41), WHO in 1999 (42) and ATP III in 2001 (14) reduced the normal limits as lower than 150 mg/dL. Although these values are usually used to define borders of the metabolic syndrome, whether or not much more lower limits can provide additional benefits for human health is unclear. In a previous study (43), patients with the triglycerides values lower than 60 mg/dL were collected into the first, lower than 100 mg/dL into the second, lower than 150 mg/dL into the third, lower than 200 mg/dL into the fourth, and 200 mg/dL and higher were collected into the fifth groups, respectively. Prevalence of smoking was the highest in the fifth group which may also indicate a close relationship between smoking and hypertriglyceridemia in the metabolic syndrome (43). The body weight also increased progressively from the first towards the fifth groups, parallel to the increased values of plasma triglycerides (43). Interestingly, prevalences of HT, DM, and CHD showed their most significant increases after the triglycerides value of 100 mg/dL (43). As an opinion of us, significantly increased triglycerides values by aging may be secondary to aging-induced decreased physical and mental activities those eventually terminate with obesity and its consequences. Interestingly, the mean age increased from the lowest triglycerides containing group up to the group with triglycerides values of lower than 200 mg/dL, gradually, then decreased. The similar trend was also observed with LDL, BMI, and WCH. These trends may be due to the fact that although the borderline high triglycerides values (150-199 mg/dL) is seen together with physical inactivity, overweight, obesity, DM, CRD, smoking, and alcohol-like acquired causes, the high triglycerides (200-499 mg/dL) and very high triglycerides values (500 mg/dL or higher) may actually be secondary to both acquired and genetic causes (15). But although the underlying causes of the high and very high triglycerides values may be a little bit different, probably risks of the terminal end-points of the metabolic syndrome do not change in these groups. For example, prevalence of HT and DM were the highest in the highest triglycerides containing group in the above study (43). Eventually, although some authors reported that lipid assessment in cardiovascular diseases can be simplified by the measurements of TC and HDL without the need of triglycerides (44), the present study and most of the others indicated causal associations between triglycerides-mediated pathways and the metabolic syndrome (45, 46). Similarly, another study indicated a significant relationship between higher triglycerides values and CHD in Western populations, too (47).

The acute phase response is a facet of the innate immune system that occurs in response to infections, infarctions, foreign bodies, autoimmune disorders, allergies, neoplasms, traumas, or burns-like various stresses of the body. Certain mediators known as acute phase reactants (APR) are increased or decreased during the acute phase response (48, 49). These markers are commonly measured in clinical practice as indicators of acute illnesses. The terms of acute phase proteins and APR are usually used synonymously, although some APR are polypeptides rather than proteins. An acute phase reaction classically presents with fever, tachycardia, and leukocytosis. Positive APR are those whose concentrations increase with inflammations. Negative APR are those whose concentrations decrease during an acute phase response. The acute phase response is predominantly mediated by the pro-inflammatory cytokines including TNF, IL-1, and IL-6 secreted by immune cells. In case of inflammations, infections, and tissue damages, neutrophils and macrophages release such cytokines into the circulation. The liver and some other organs respond by producing many positive APR to them. Some of the well-known positive APR are CRP, ESR, fibrinogen, ferritin, procalcitonin, hepcidin, haptoglobin, ceruloplasmin, complement proteins, and serum amyloid A. CRP is involved in innate immunity, and responsible for activating the complement pathway. Serum CRP rises rapidly, with a maximal concentration reached within two days, and falls quickly once the inflammation has resolved. Measurement of CRP is a useful indicator of inflammations in clinic. It correlates with ESR, but not always directly. This is due to the ESR being largely dependent on elevation of fibrinogen with a half-life of approximately one week. Therefore ESR remains higher for a longer period of time despite the removal of the inflammatory stimulus. Whereas CRP rises with a half-life of 6-8 hours, rapidly and then returns to normal in case of a successful treatment, quickly. On the other hand, productions of some other APR are suppressed at the same time which are called as negative APR. Some of the well-known negative APR are albumin, transferrin, retinol-binding protein, antithrombin, transcortin, and alpha-fetoprotein. The suppression of such proteins is also used as an indicator of inflammations. The physiological role of suppressed synthesis of such proteins may be protection of amino acids for the production of positive APR, sufficiently. Due to the same underlying cause, productions of HDL and LDL may also be suppressed in the liver. For example, although the similar age, gender distribution, smoking, and BMI in both groups, triglycerides, DM, and CHD were higher whereas LDL were lower in patients with plasma HDL values of lower than 40 mg/dL, significantly (50). So HDL and LDL may actually behave

as some negative APR in the human body. Similarly, although the lower mean age, BMI, FPG, and LDL, the highest CHD of the group with HDL values of lower than 40 mg/dL can also be explained by the same hypothesis (51). Beside that although the mean triglycerides, fibrinogen, CRP, and glucose values were higher in cases with ischemic stroke, the oxidized LDL values did not correlate with the mean age, stroke severity, and outcome in another study (52). Additionally, significant alterations occurred in the lipid metabolism and lipoproteins compositions during infections, and plasma triglycerides increased whereas HDL and LDL decreased in another study (53). Furthermore, a 10 mg/dL increase of plasma LDL values was associated with a 3% lower risk of hemorrhagic stroke in another study (54). Similarly, the highest prevalences of HT and DM parallel to the increased values of LDL and HDL, and the highest prevalences of COPD, CHD, and CRD in contrast to the lowest values of LDL and HDL may show initially positive but eventually negative APR natures of LDL and HDL in the plasma (55). So the most desired values were between 80 and 100 mg/dL for LDL, between 40 and 46 mg/dL for HDL, and lower than 60 mg/dL for triglycerides in the plasma (47, 51).

As a conclusion, IBS may be a low-grade inflammatory process initiated with smoking, infections, inflammations, anxiety, depression, sleep disorders, cancer fear, and death fear-like stresses, and eventually terminates with dysfunctions of gastrointestinal and genitourinary tracts and elevations of some metabolic parameters. There may be some significant relationships between IBS, smoking, female gender, CG, depression, hemorrhoids, urolithiasis, FPG, and plasma triglycerides. In other words, FPG and plasma triglycerides may behave as sensitive APR in IBS.

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