Ann Med Res 2021;28(10):1881-6

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.11.1132

Original Article

α-Galactosidase levels in irritable bowel syndrome subtypes and quality of life of patients

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Abstract

Aim: There is a requirement for a reliable serologic marker that can be used for the diagnosis of Irritable Bowel Syndrome (IBS). The aim of our study was to research whether serum levels of Alpha-galactosidase (AG) is associated with IBS and to assess quality of life (QOL) of IBS patients.

Materials and Methods: 110 adult patients who were diagnosed with IBS were evaluated. 90 patients and 25 healthy volunteers were included.

Patients were classified into subtypes: IBS-Diarrhea (IBS-D), IBS-Constipation (IBS-C), IBS-Mixed (IBS-M), and 30 patients were enrolled for each group. We administered the Short Form 36 (SF-36) to participants to evaluate QOL. Serum AG levels of participants was determined.

Results: The mean AG levels of IBS-C and control group were significantly lower than the other groups ($p<0.05$). The SF-36 questionnaire scores, except for the vitality and mental health domains, were higher significantly in the control group compared to IBS patients ($p<0.05$). The mean scores of IBS subtypes were similar. In addition, the mean physical functioning score of the control group was higher in comparison with the IBS-D group significantly ($p<0.05$).

Conclusion: Our study has shown that IBS impairs QOL in patients. In addition, we suggest that future studies needed for the role of AG deficiency in IBS patients.

Keywords: Alpha-galactosidase; irritable bowel syndrome; quality of life

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional bowel disorder defined by chronic recurrent abdominal pain or discomfort that is related with defecation problems. This disorder can be associated with reduced quality of life (QOL) and increased health care costs (1). IBS is the most common cause of admission to general practitioners (2). This functional disorder requires testing to exclude organic causes. IBS can be diagnosed by using "Rome Criteria", which is based on symptoms (3).

Although bloating, flatulence and abdominal distension present the most common complaints in gastrointestinal diseases, the mechanisms have not yet been fully understood (4). Abdominal bloating is one of the most common symptoms in patients with IBS and it may result from gas production due to colonic fermentation (5). This resulting gas is due to unabsorbed carbohydrates and indigestible oligosaccharides containing α-galactosidic linkage. In addition, α-galactosidases are hydrolytic agents, which are usually responsible for the metabolic usage of these compounds. Some studies have indicated that α-galactosidase (AG) can be used to control IBS symptoms with reduction of gas production and colonic fermentation (5).

Because of impaired QOL and health-care costs, a number of researches have been studied on diagnosis and treatment of IBS. Nevertheless, the IBS pathophysiology has not yet been understood. Some studies have attempted to identify serum biomarkers associated with IBS. A reliable serologic marker that can be used for the diagnosis of IBS has not yet been identified. This may be because of the multifactorial pathophysiology of IBS (6).

In this study, we aimed to evaluate the QOL in patients with IBS and to investigate whether serum levels of AG are associated with IBS for diagnosis and treatment.

Received: 19.11.2020 **Accepted:** 08.02.2021 **Available online:** 18.10.2021
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MATERIALS and METHODS

One hudred and ten adult patients, who were diagnosed with IBS according to Rome III criteria, in the age groups of 18-65 years, and were seen between April 2015 and April 2016 in the Gastroenterology and Internal Medicine clinics, were evaluated. This prospective observational study was conducted according to the Helsinki Declaration principles, with the approval of the Ethics Committee, dated 03.03.2015 and with the decision numbered 2015/127.

The informed consent was obtained from all participants prior to being included into the study. Patients were selected from volunteers who participated in the study with maximum variation sampling. Patients with pregnancy or lactation, malignancy, with a history of gastrointestinal system surgery, organic gastrointestinal diseases (e.g. Celiac disease, lactose intolerance), Fabry patients under treatment, and patients who have taken drugs that could affect the intestinal motility in the last 15 days were excluded. Ninety patients who did not meet the exclusion criteria and twenty five healthy volunteers were included in the statistical evaluation. Fourteen patients whose control blood samples could not be sent were excluded from study and they were not included in the statistical evaluation.

Individual interviews were conducted in order to collect data. All participants were questioned by the research physician in terms of IBS symptoms (eg, change in bowel habits, abdominal pain, pain relieved by defecation). Their body mass index (BMI) was calculated according to the equation (weight/height squared=kg/m²). Patients were subclassified as in accordance with the Bristol stool form scale based on Rome III classification and 30 patients were enrolled to the study from each group. The Short Form 36 (SF-36) which is available documentation from the Rand Corporation was used to assess quality of life during individual interviews.

Enzyme activity in dry blood spot samples was determined by dried blood spot (DBS) method using filter paper containing DBS as a DNA source. Two milliliters of blood was taken from patients and dropped on to the DBS paper, allowed to dry, and kept at room temperature. Subsequently, the DBS papers were sent to the relevant laboratory (Archimed Laboratories, Vienna, Austria) to measure the AG levels. The enzyme activities were calculated in µmol/L/h by tandem mass spectrometry in the laboratory. Enzyme levels were calculated for a second time from 9 patients whose AG levels were below the cut-off value of 1.2 µmol/l/h determined by the laboratory. 9 patients with control enzyme levels above 1.2 were included in the study. 14 patients with enzyme levels below 1.2 were excluded from study because control blood samples could not be sent. There were no subjects with the cut-off value which was below 1.2 µmol/l/h in the blood samples of control group.

Descriptive values of the obtained data were calculated as standard deviation (SD), mean, standard error (SE), number and % frequencies. One-Way ANOVA was used for the comparison of the groups in terms of age and BMI, and Pearson chi-square analysis was used in the comparison of the groups in terms of gender distribution. Significant difference existed between groups in terms of age and BMI but the difference in gender distribution was not significant. For this reason, the analysis of covariance model was used to correct for age and BMI values when the differences between the groups were analyzed for AG and eight subscales of SF-36. In addition, the relationships between the subscales of SF-36 and AG were examined separately by Pearson correlation analysis in each group. In the calculations, the SPSS program (version 18) was used and P <0.05 was accepted statistically significant.

RESULTS

No significant difference was observed between IBS patients and the control group in gender distribution in terms of demographic characteristics (p>0.05). The BMI and mean age of the control group was lower than the other three groups significantly (p<0.05). Descriptive values of age and BMI measurements are presented in Table 1.

When we analyzed all groups together, the mean AG levels of the IBS-C and the control group were lower than the other groups significantly (p<0.05). Otherwise, no significant difference existed between the mean AG levels of the IBS-D and the IBS-M group. When we evaluated each group separately, the AG levels of the IBS-C group were lower when compared with the control group. The mean and standard errors in Table 2 are the adjusted values calculated after the effect of age and BMI difference was removed. In addition, the mean levels of AG in each group are represented in Figure 1.

Table 1. Comparison of mean age and BMI of IBS patients and control groups

	İBS-D			İBS-C			İBS-M			Control			P value
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Age (years)	30	36.20	12.965	30	42.07	14.391	30	35.40	13.093	25	**24.60**[1]	2.598	**<0.0001**
BMI (kg/m²)	30	25.827	5.0279	30	27.493	5.9176	30	26.603	6.0172	25	**22.856**[1]	3.2819	**0.011**

[1]Significantly lower than other groups according to P-value; N: number of person; SD: Standart Deviation

Table 2. AG results in groups

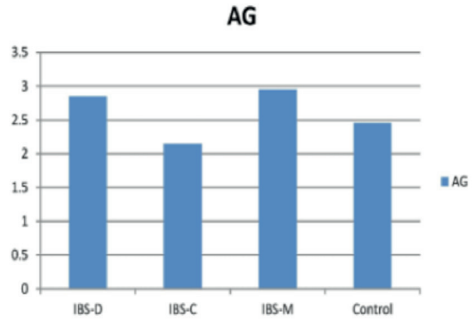
	Groups	Mean	SE	P value
AG (µmol/L/h)	İBS-D (n=30)	2.847	.177	0.007
	İBS-C (n=30)	**2.149**[1]	.185	
	İBS-M (n=30)	2.956	.178	
	Control (n=25)	**2.455**[1]	.210	

[1]Significantly lower than other groups according to P value
SE: Standard error

Table 3. Comparison of results of SF-36 subscales between groups

SF-36 subscale	Groups	Mean	SE	P-value
General health	İBS-D (n=30)	44.878	3.298	<0.0001
	İBS-C (n=30)	56.496	3.443	
	İBS-M (n=30)	49.314	3.303	
	Control (n=25)	74.254[1]	3.907	
Physical functioning	İBS-D (n=30)	69.132	3.456	0.014
	İBS-C (n=30)	73.396	3.608	
	İBS-M (n=30)	73.338	3.462	
	Control (n=25)	86.761[2]	4.095	
Role, physical	İBS-D (n=30)	37.919	6.931	<0.0001
	İBS-C (n=30)	55.528	7.236	
	İBS-M (n=30)	44.097	6.942	
	Control (n=25)	86.948[1]	8.212	
Role, emotional	İBS-D (n=30)	32.996	7.025	<0.0001
	İBS-C (n=30)	45.892	7.334	
	İBS-M (n=30)	32.102	7.036	
	Control (n=25)	80.067[1]	8.323	
Social functioning	İBS-D (n=30)	53.889	4.336	<0.0001
	İBS-C (n=30)	56.914	4.526	
	İBS-M (n=30)	59.338	4.342	
	Control (n=25)	82.330[1]	5.137	
Bodily pain	İBS-D (n=30)	51.891	3.640	<0.0001
	İBS-C (n=30)	49.644	3.800	
	İBS-M (n=30)	55.307	3.645	
	Control (n=25)	76.989[1]	4.312	
Mental health	İBS-D (n=30)	59.202	3.027	0.238
	İBS-C (n=30)	59.554	3.160	
	İBS-M (n=30)	57.843	3.031	
	Control (n=25)	67.121	3.586	
Vitality	İBS-D (n=30)	41.440	3.636	0.080
	İBS-C (n=30)	43.317	3.796	
	İBS-M (n=30)	41.690	3.642	
	Control (n=25)	54.863	4.308	

[1]Significantly higher than other groups according to P-value
[2] Significantly higher than IBS-D. SE: Standard Error; n: number of person



AG: Alpha-galactosidase; IBS-C: Irritable Bowel Syndrome- constipation-predominant IBS-D: Irritable Bowel Syndrome-diarrhea-predominant; IBS-M:Irritable Bowe Syndrome-mixed type

Figure 1. AG results in groups

Table 4. Relationship between AG and SF-36 subscales

SF-36 subscale		AG			
		İBS-D	İBS-C	İBS-M	Control
General health	r	.206	.109	.152	-.072
	P	.276	.568	.422	.732
	N	30	30	30	25
Physically functioning	r	-.261	.032	-.299	-.049
	P	.164	.866	.108	.816
	N	30	30	30	25
Role, physical	r	.213	.100	-.153	.107
	P	.258	.598	.421	.611
	N	30	30	30	25
Role, emotional	r	.011	.054	.249	.129
	P	.955	.776	.184	.538
	N	30	30	30	25
Social functioning	r	.073	.295	.091	-.107
	P	.700	.114	.632	.612
	N	30	30	30	25
Bodily pain	r	.094	.095	.211	.108
	P	.622	.619	.263	.609
	N	30	30	30	25
Mental health	r	.046	.084	.102	.147
	P	.808	.658	.591	.483
	N	30	30	30	25
Vitality	r	-.004	.023	-.134	-.168
	P	.984	.906	.480	.423
	N	30	30	30	25

r: Correlation Coefficient; P: P-value; N: number of person

The mean bodily pain, role physical, social functioning, role emotional, and general health scores of the control group were higher in comparison with the other three groups significantly ($p<0.05$). Any other significant differences were not observed with the SF-36 scores of other three groups. The mean physical functioning score

of the control group was higher in comparison with the IBS-D group significantly. No significant difference was detected in mental health and vitality scores between the groups (p>0.05). The descriptive values of the 8 subscales of the SF-36 scale and comparison of the results of IBS subtypes are shown in Table 3.

The relationship between AG and SF-36 subscales in each group separately is presented in the table below. There was no significant relationship between AG and SF-36 subscales in all 4 groups as shown in Table 4.

In this study, we aimed to evaluate the QOL of patients with IBS and to investigate whether serum levels of AG are associated with IBS; AG deficiency was not detected in IBS subtypes. The mean AG level was 2.84 µmol/L/h in the IBS-D group, 2.95 µmol/L/h in the IBS-M group, 2.14 µmol/L/h in the IBS-C group, and 2.45 µmol/L/h in the control group. The mean AG levels of the IBS-C and the control group were lower than the other groups significantly. When the SF-36 results were evaluated, the mean score of the control group was higher in all subscales significantly, except for vitality and mental health, in comparison with the mean scores of IBS patients. No significant difference was observed between the mean scores of the IBS subtypes. In addition, the mean physical functioning score of the control group was higher significantly in comparison with the IBS-D group.

DISCUSSION

In our study, we analyzed levels of AG in patients with IBS and healthy controls. The AG levels of the IBS-C and the control group were lower than the other groups significantly when we analyzed all groups together. In addition, the AG levels of the IBS-C group were lower in comparison with the control group when we evaluated each group seperately.

IBS is a common functional gastrointestinal disorder in the general population. IBS is not life threatening but it does impair QOL (1,2,7). Although an IBS diagnosis is based on symptoms, endoscopy, computed tomography or ultrasound imaging, fecal tests, blood tests or other investigations are used to exclude organic disorders (8). These tests are associated with high health care costs. For this reason, a number of studies have recently been conducted on biomarkers to diagnose IBS and to differentiate IBS from organic diseases such as inflammatory bowel disease and functional gastrointestinal disorders (9,10). However, the obtained data is insufficient. It is thought that IBS has multifactorial pathophysiology and heterogeneity.

Several studies have investigated the use of certain pro-inflammatory cytokines as markers in IBS diagnosis, considering that they play a role in IBS pathophysiology (6,11,12). Mujagic et al. have recently reported that single non-invasive biomarkers for IBS have only led to modest results. For this reason, recent researches have mostly examined biomarker panels (12). There are also studies that have identified biologic markers in the diagnosis of IBS, such as proteins, volatile organic metabolites, and genes (12).

Abdominal bloating is one of the most annoying symptom in IBS and, is reported by >80% of patients (13). Different mechanisms may cause abdominal bloating in IBS (14). Since the pathophysiology of this symptom has not yet been well defined, researchs on this subject is continuing. A study has shown that patients complaining of bloating because of increased production of gas (5), suggesting that from the pathophysiologic point of view this mechanism may have a role. More than 60% of patients with IBS describe worsening of symptoms after meals. Reducing the consumption of carbohydrates alleviates IBS symptoms (15). In a double-blind randomized study, with the aim of reducing gas production and colonic fermentation to control IBS symptoms; AG has been shown to decrease flatulence in healthy volunteers after a carbohydrate enriched meal (5).

Fabry disease, caused by an AG-A enzyme deficiency, is a lysosomal storage X-linked disease. Gastrointestinal symptoms of Fabry disease usually mimic IBS symptoms (16). A study, which was conducted, by Hoffman et al. showed that 52% of adult Fabry patients had GI complaints and the most common complaint is abdominal pain, affected up to one third of the patients. After enzyme (AG) replacement therapy, a significant (p<0.05) 14% reduction was observed in abdominal complaints (16). In our study, conducted with the available data, the mean AG level measured was 2.84 µmol/L/h in the IBS-D group, 2.95 µmol/L/h in the IBS-M group, 2.14 µmol/L/h in the IBS-C group, and 2.45 µmol/L/h in the control group. The mean AG levels of the IBS-C and control group were lower than the other groups significantly. This finding points to a probable relationship between the AG deficiency and IBS or constipation. The cut-off value determined by the laboratory, where it was measured, was 1.2 µmol/L/h. All of the results from our study were above the cut-off value. Different mean values for AG levels have been reported in different studies. According to the literature, the mean AG level in healthy men was determined to be 2.93±1.7 µmol/L/h (17).

IBS is more common in patients under the age of 60. Symptoms typically begin between the ages of 30 and 50 (18). Our study agrees and had mean ages of patients between 35 and 45. No significant difference was detected in age distribution between the IBS subtypes.

Some studies indicate that IBS symptoms may be related to high BMI (19). In our study, there was no difference between the mean BMI of the groups but patients were overweight when classified according to BMIs. In agreement with our study, Kibune-Nagasako et al. showed that a large proportion of IBS patients were overweight or obese and that there were no differences between the mean BMI of the subtypes (20).

As in all chronic diseases, QOL is affected in IBS patients. This is especially true in relation to patient's symptoms and the fact that satisfaction from their lives is diminished.

Social and physical functions are also negatively affected. Although considered as an important outcome marker for chronic diseases, QOL cannot completely evaluate the impact of disease or its treatment in routine clinical practice (21).

The measurement of QOL is of specific importance in terms of diseases for which there are currently no biological markers, like IBS. Clinically, assessment of QOL of IBS patients may lead professionals to check outcomes after treatment simplify contact with patients and offer optimal care (22). Therefore, the American College of Gastroenterology has recommended regular evaluation of QOL in patients with IBS (23).

There exist various general-health related QOL questionnaires such as the WHO-QOL, and the SF-36 to measure QOL (24).Some studies; using these forms, which were investigating the relation between the QOL and IBS subtype, have not shown any difference. These general questionnaires do not include the particular items related to IBS and could have reduced the effect of gastrointestinal symptoms on QOL. Therefore, instruments specific for diseases have been developed and validated, like the IBS-QOL questionnaire (24).

Different studies conducted in several countries by using the SF-36 have shown poorer QOL in IBS patients than the general population (25). In our study, the SF-36 quality of life scale was used to assess differences between the IBS patients and the control group, and in the IBS subtypes. No significant difference was observed between the IBS subtypes. Comparing the groups, the mean bodily pain, role physical, social functioning, role emotional, and general health scores of the control group were higher significantly in comparison with the other 3 groups ($p<0.05$). The mean physical functioning score of the control group was higher in comparison with the IBS-D group significantly and except this, there was no significant difference. Singh et al. reported that patients with IBS-D and IBS-M significantly have a worse QOL than the IBS-C subtype. In addition, IBS-D patients have more prevention with their activities of daily living and refrain food more often in comparison with the IBS-C patients (24).

CONCLUSION

IBS is a common high prevalence gastrointestinal disorder, which has unclear mechanism and impairs health-related quality of life. This causes economic losses. The data obtained for the diagnosis is insufficient. We analyzed AG levels in IBS patients in order to contribute future diagnosis and treatment. The AG levels in IBS-C patients were lower than other groups and this finding provides an opportunity to reveal the link between low AG levels and IBS. Future studies comparing the obtained data will give a clearer result.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical Approval: This prospective observational study was conducted according to the Helsinki Declaration principles, with the approval of the Ethics Committee of Duzce University, dated 03.03.2015 and with the decision numbered 2015/127.

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