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An Association between Telomere Length and Irritable Bowel Syndrome in Korean Populations

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Telomere shortening has been suggested as an indicator of aging and psychiatric disorders. However, few studies have explored the relationship between telomere length (TL) and irritable bowel syndrome (IBS). We investigated the association between TL and IBS in 43 IBS patients using quantitative polymerase chain reaction. The clinical characteristics and severity of IBS, assessed by the visual analogue scale, were also analyzed. The average TL was 4.40 ± 3.87, with TL shortening tending to be associated with female sex and smoking. However, these associations did not reach statistical significance. Correlation analysis showed a negative correlation between IBS severity and TL (r = -0.285, p = 0.083), although this was not statistically significant. No other clinical characteristics were significantly associated with TL. This is the first study to examine the relationship between TL and IBS. Our findings suggest that TL may have potential as a predictor for IBS diagnosis.

Keywords: Irritable bowel syndrome, Telomere, Visual analogue scale

Introduction

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder characterized by chronic abdominal pain, diarrhea, constipation, and fluctuating bowel movement patterns between constipation and diarrhea. Some patients may also experience bloating, a feeling of incomplete bowel evacuation, and general discomfort [1]. Approximately 11% of the global population is affected by IBS, with female representing 55% of those impacted [2,3]. Its prevalence ranges from 10% to 25% in the United States, 17% to 21% in South America, 7% to 9% in South Asia, and 5.6% in the Middle East and Africa [2-4]. Notably, the prevalence of IBS is higher among college students in their 20s compared to other age groups [5]. Recent studies suggest that IBS poses social, economic, and psychological challenges, significantly affecting quality of life. Additionally, diagnosing and treating IBS can be difficult due to its influence on the visceral-brain axis, which is linked to mental health issues such as anxiety and depression [6].

Telomeres are specialized structures located at the ends of chromosomes that, along with their associated protein complexes, protect DNA and maintain genomic stability [7]. Each cell division results in the loss of telomeric repeats due to the incomplete replication of the chromosome's 3' end, leading to critically short telomeres that can trigger cellular senescence or crisis [8]. Telomere length (TL) progressively decreases with age; however, this decline is accelerated by oxidative stress and inflammation. TL is established at birth in individu-

als and reflects the cumulative effects of inflammation and oxidative stress throughout life [9,10]. Telomeres may be linked to various diseases, particularly those related to aging and neurodegeneration [11-13]. However, there was only one study about telomere change and its clinical characteristics in IBS patients [14]. This study showed that patients with IBS presented shorter TL when compared to healthy controls. For better understand this relationship, we aimed to determine clinical characteristics of patients with IBS and telomere in this study. As telomere may vary depending on age and genetic status, this study was performed in college students without hereditary disorder.

Methods

Participants

Participants who met the inclusion criteria were recruited through advertisements on bulletin boards in Daegu, South Korea. The inclusion criteria were as follows: (1) college students aged 18 years or older; (2) those who fulfilled the Rome III Diagnostic Criteria for IBS [1]; (3) no prior history of surgeries or diagnosed gastrointestinal disorders, such as obstructive bowel disorders, inflammatory bowel diseases, or lactose malabsorption; and (4) no previous history of psychiatric illnesses. A total of 43 participants with IBS were contacted. The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Keimyung University (40525-201809-BR-84-02).

The severity of IBS symptoms was assessed by previous criteria [15]. These criteria include seven items, and after excluding the categorical questions regarding the presence of abdominal pain or bloating, the remaining five questions were rated on a visual analogue scale (VAS), each worth 100 points. The questions are as follows: Q1 = abdominal pain, Q2 = bloating and flatulence, Q3 = bowel habits (diarrhea and constipation), Q4 = perception of psychological well-being, and Q5 = daily life-related gastrointestinal problem. The severity was determined by the total score of these five items, classified as follows: 75-174 = mild, 175-299 = moderate, and 300-500 = severe. Our previous study indicated that the reproducibility of this scale at the time of development was stable at 85%, with a Cronbach's α value of 0.72 reflecting its reliability.

DNA extraction

Blood samples were collected from 43 participants to obtain serum. Informed consent was verbally obtained from all participants and/or their legal guardians. The Institutional Review Board of Keimyung University Dongsan Medical Center approved the research protocols. Genomic DNA was extracted from the serum using a DNA extraction kit (Qiagen Inc.). The quantity and quality of the extracted DNA were assessed using a NanoDrop 1000 (Thermo Fisher Scientific).

Telomere length analysis

The TL of each chromosome was analyzed by quantitative polymerase chain reaction (qPCR). To analyze quantitative TL relative to nuclear DNA (S), primers for assessing the TL were selected using specific amplification (T) and ß-globin primers were used for nuclear DNA, according to a previous study [16]. qPCR was performed using the LightCycler 480 II system (Roche Diagnostics). TL was presented as T/S values and calculated as follows: $T/S = 2 - \Delta Ct$ where ΔCt = average Ct telomere - average Ct ß-globin.

Each measurement was performed in triplicate and five serially diluted control samples were included in each experiment.

Statistical analysis

All statistical analyses were conducted using the SPSS statistical software, version 25.0, for Windows (IBM Corp.). The chi-square test was employed to examine the associations between the variables. A two-tailed p-value of less than 0.05 was regarded as indicating statistical significance.

Results

In the present study, TL was successfully measured in all 38 participants. The average TL was 4.40 ± 3.87, and participants were categorized into high and low TL groups based on the median value. The clinical characteristics of individuals with IBS and their TL were examined, with the findings summarized in Table 1. IBS was classified into three subtypes: diarrhea-predominant, constipation-predominant, and mixed types, none of which showed a significant association with TL. Female and smoking habits showed a tendency towards shorter TL, although these associations were not statistically significant ($p = 0.192$ and $p = 0.157$, respectively). Other clinical characteristics did not demonstrate any relationship with TL.

The average severity score of IBS symptoms in this study was 319.42 ± 64.84. Correlation analysis indicated a trend towards a negative association between IBS severity and TL ($r = -0.285$, $p = 0.083$; Fig. 1), although this relationship was

Table 1. Clinical significance of TL in irritable bowel syndrome

Variable	TL		*p*-value
	Shorter	Longer	
Subtype			0.372
Diarrhea-predominant	2 (66.7)	1 (33.3)	
Constipation-predominant	0 (0)	1 (100)	
Mixed	23 (67.6)	11 (32.4)	
Sex			0.192
Male	2 (40.0)	3 (60.0)	
Female	23 (69.7)	10 (30.3)	
Smoking			0.157
No	22 (71.0)	9 (29.0)	
Yes	3 (42.9)	4 (57.1)	
Drinking			0.715
No	15 (68.2)	7 (31.8)	
Yes	10 (62.5)	6 (37.5)	
Sleep partner			0.653
No	19 (67.9)	9 (32.1)	
Yes	6 (60.0)	4 (40.0)	
Night duty			0.510
No	18 (69.2)	8 (30.8)	
Yes	7 (58.3)	5 (41.7)	
Cardiovascular disease			0.160
No	25 (67.6)	12 (32.4)	
Yes	0 (0)	1 (100)	
Inflammatory bowel disease			0.351
No	19 (70.4)	8 (29.6)	
Yes	6 (54.5)	5 (45.5)	
Anxietas tibiarum			0.653
No	19 (67.9)	9 (32.1)	
Yes	6 (60.0)	4 (40.0)	
Visual analogue scale			0.353
Mild	0 (0)	1 (100)	
Moderate	7 (63.6)	4 (34.1)	
Severe	18 (69.2)	8 (30.8)	

Values are presented as number (%).
TL, telomere length.

not statistically significant. The correlation between VAS scores and TL was also examined, with the results shown in Table 2. TL was found to be negatively correlated with bloating (Q2) (r = -0.283, p = 0.086), though this correlation did not reach statistical significance. Most of VAS scores correlated to each other.

Discussion

Telomeres, the protective caps at the ends of chromosomes, have been implicated in the pathogenesis of various diseases. In numerous chronic conditions, such as cardiovascular diseases, diabetes, and neurodegenerative disorders, telomere shortening has been associated with cellular aging and tissue dysfunction [9-11]. TL serves as a biomarker of cellular health, as its reduction reflects diminished replicative capacity of cells, leading to increased susceptibility to disease. In cancer, while short telomeres can contribute to genomic instability and tumorigenesis, some cancers exhibit abnormally long telomeres that enable uncontrolled cell division [16,17]. As such, understanding the role of telomeres in disease mechanisms could offer new insights into disease prevention, prognosis, and potential therapeutic strategies.

A previous study demonstrated that patients with IBS had significantly shorter telomeres compared to healthy controls [14].

Moreover, TL was shorter in IBS patients attributed to mental or psychological factors than in those affected by other factors. Interestingly, TL was longer in IBS patients who had taken antidepressants. In this study, we also confirmed the relationship between TL and the clinical features of IBS. To control for variables related to age and TL, the study was conducted exclusively with patient groups from specific age ranges. Unexpectedly, TL was found not to be associated with any clinical characteristics of IBS.

In this study, we observed a potential correlation between TL and the severity of IBS, although this correlation did not reach statistical significance. Our findings suggest that more severe IBS symptoms are associated with shorter TL, which is consistent with previous research indicating shorter TL in individuals with IBS compared to healthy controls [14]. Additionally, telomere shortening was linked to symptoms such as bloating and flatulence. Several studies have shown that mental and psychological factors in IBS are associated with shorter telomeres [18,19]. The stress induced by the severity of IBS may contribute to cellular senescence, leading to telomere shortening. Several hypotheses have been proposed to explain this mechanism. For example, changes in the intestinal microbiome in IBS may alter physiological and metabolic processes, potentially triggering cellular senescence [20,21]. Other research suggests that elevated glucocorticoid levels in IBS could accelerate stress-related aging of the epigenome, promoting telomere shortening [22,23]. However, the precise mechanisms underlying telomere regulation in IBS remain unclear, and further studies are needed to explore the detailed molecular pathways involved.

This is the first study to explore the relationship between IBS severity and TL; however, it has some limitations. The

Table 2. Correlation between visual analogue scale and TL

Variable	TL	Age	Q1	Q2	Q3	Q4	Q5	Sum
TL								
r	1	0.092	−0.157	−0.283	−0.081	−0.205	−0.074	−0.285
p-value		0.581	0.346	0.086	0.627	0.217	0.660	0.083
Age								
r		1	−0.329*	−0.132	0.086	0.114	0.270	0.015
p-value			0.031	0.398	0.583	0.466	0.080	0.924
Q1								
r			1	0.506**	−0.070	−0.067	−0.023	0.380*
p-value				0.001	0.657	0.671	0.883	0.012
Q2								
r				1	−0.061	−0.008	0.063	0.521**
p-value					0.699	0.961	0.686	0.000
Q3								
r					1	0.655**	0.407**	0.709**
p-value						0.000	0.007	0.000
Q4								
r						1	0.286	0.716**
p-value							0.063	0.000
Q5								
r							1	0.535**
p-value								0.000

TL, telomere length; Q1, abdominal pain; Q2, bloating and flatulence; Q3, bowel habits (diarrhea and constipation); Q4, perception of psychological well-being; Q5, daily life-related GI problem.
*$p < 0.05$, ** $p < 0.01$.

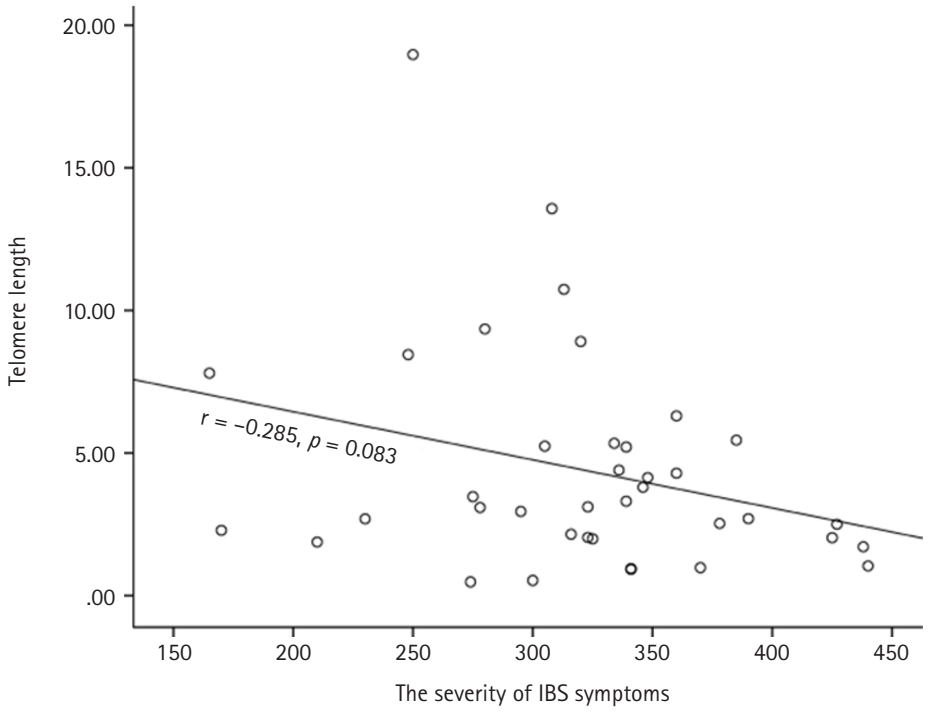

Fig. 1. Negative correlation between IBS severity and telomere length. IBS, irritable bowel syndrome.

sample size was small, and there is a lack of data on the progression of IBS. Additionally, the VAS is subjective, as it assesses disease severity based on a questionnaire. Therefore, further long-term follow-up studies using objective experimental models are needed. IBS is not classified as a major disease, but, ongoing research is essential to improve the quality of life for patients.

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Ethics approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Keimyung University (40525-201809-BR-84-02).

Conflict of interest

The authors have nothing to disclose.

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