

# **RESEARCH ARTICLE**

Open Access

# Changes in stress intensity associated with gastrointestinal health in students population during the COVID-19 lockdown

Lejla Usanovic<sup>1</sup>, Nikolina Tomic<sup>1</sup>, Nerma Custovic<sup>2</sup>, Beate Niesler<sup>3,4</sup>, Lejla Pojskic<sup>1</sup>

<sup>1</sup>Institute for Genetic Engineering and Biotechnology-University of Sarajevo, Sarajevo, Bosnia and Herzegovina, <sup>2</sup>Department of Gastroenterology, Clinical Center of Sarajevo University, Sarajevo, Bosnia and Herzegovina, <sup>3</sup>Institute of Human Genetics, Heidelberg University Hospital, Heidelberg, Germany, <sup>4</sup>Interdisciplinary Center for Gut Health, Heidelberg University, Heidelberg, Germany

# ABSTRACT

**Introduction:** The COVID-19 pandemic and the restrictions from routine life habits had a tremendous impact on psychological and physical health of youth. It is known that stress, anxiety and depression can be associated with the development of gastrointestinal (GI) symptoms and known to exacerbate present GI symptoms. The pandemic has forced many changes in the behavior of student population such as the studying in an asocial environment. The aim of this study was to examine and quantify the influence of stress onto the quality of life and GI symptoms in the student population in Bosnia and Herzegovina (B&H), before and during the pandemic lockdown.

**Methods:** A total of 279 students from B&H were assessed for their GI and emotional status in pre-COVID period and during the COVID period using validated instruments: GI symptom rating scale (GSRS), Visceral Sensitivity Index, and the Patient Health Questionnaire 15-item Somatic Symptom Severity Scale.

**Results:** The results showed that moderate and severe GI symptoms were more frequently present among student population at the time of the pandemic than in period before pandemic. The most pronounced symptoms were bloating syndrome and abdominal pain syndrome according to the GSRS.

**Conclusions:** We concluded that concern for one's health and changed way of life are directly related to a worsening of the symptoms of GI disorders in the student population. Further research should go in the direction of early prevention of GI disorders that take root in early youth and later develop into chronic forms.

Keywords: COVID-19; gastrointestinal symptoms; social lockdown; students

### INTRODUCTION

The student population represents the healthiest segment of the society, but in recent years, there has been a constant increase in the morbidity and mortality among students as well as of chronic diseases and disorders, deformities, growth and development disorders, injuries, and mental health problems (1). So called" academic stress" can leave serious and long-term consequences including diverse gastrointestinal (GI) disorders that are increasingly associated with populations exposed to stress (2,3). Students are exposed to stress almost every day and especially during the examination periods (2-5).

Many people suffering from different GI problems state that the worsening of symptoms is associated with their exposure to psychological distress. At present, it is

Submitted: 25 October 2022/Accepted: 09 February 2023

DOI: https://doi.org/10.17532/jhsci.2023.1997



confirmed that psychological factors such as stress, anxiety, or depression are genuinely important in the development of disorders of GI physiological functioning (3). These psychological factors may be considered rather as cofounding risk factors, than causative. They can, together with social conditions and early life events, make GI disorders worse and define the onset and severity of GI illness as well as its clinical outcome (4). The interaction of environmental factors and genetics, also known as G × E interaction, may influence on occurrence and outcomes of depression (5). Thus, it is very important to discover the effects of genes in so-called environmental pathogens such as traumatic and stressful life experiences (5). Caspi et al. confirmed, in their study, that  $G \times E$  interaction they analyzed, extends to the natural development of depression, posing 5-HTT gene as a good candidate gene for investigating in stressful conditions mentioned above (5).

The COVID-19 pandemic has changed global everyday life and the life of students. During this time, lectures and examinations were conducted mostly online. The interaction with teachers and peers is much different now and as such leads to discomfort and causes overall uncertainty.

© 2023 Lejla Usanovic, et al.; licensee University of Sarajevo - Faculty of Health Studies. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/ by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

<sup>\*</sup>Corresponding author: Lejla Pojskić, Institute for Genetic Engineering and Biotechnology-University of Sarajevo, Sarajevo, Bosnia and Herzegovina, Zmaja od Bosne 8, 71000 Sarajevo, Bosnia and Herzegovina. E-mail: lejla.pojskic@ingeb.unsa.ba

These changes in the way of studying are very stressful, as something new to what students were used to. In general, there are observations suggest that during this pandemic time, many people exhibited various stress-or anxiety-related responses (6). Recently, Kamp et al. (2021) reported correlation of COVID-19 pandemic with increased self-reported psychological distress and GI symptoms among individuals with irritable bowel syndrome (IBS) and comorbid anxiety and/or depression (7). The study of Alzahrani et al. (2020) showed that pandemic stress exacerbated symptoms of patients with IBS and impacted their activities of daily life (8). Moreover, Abenavoli et al. (2021) detected an increase of GI symptoms during the lockdown period in a population of medical students that may, as they suggested, be correlated to changed dietary habits and anxiety state due to a concern for one's health (9). Furthermore, there are results of some studies that have shown that various factors which are results of prevention and control measures had negative effects on students' mental health and health in general in the COVID-19 pandemic (10,11).

In this study, we analyzed self-reported stress-induced GI symptoms in the student population of Bosnia and Herzegovina (B&H) in the examination periods, before and during COVID-19 pandemic to find out whether it makes sense to investigate more deeply the effect of stress as a non-genetic factor on neurogastric disorders, and to determine the genetic predisposition for GI disorders triggered by stress.

# METHODS

A total of 279 students from the University of Sarajevo, B&H, volunteered to participate in the study. This sample is nationally representative, as students were randomly recruited and come from different parts of B&H. All students participated in the study after providing written informed consent. The study was conducted in the academic years 2015/2016, 2016/2017 (before COVID), and 2020/2021 (COVID). The first group included students surveyed in the 2016 winter examination period and the 2017 summer examination period, and the second group included students in the 2021 winter examination period during the COVID-19 pandemic, when lectures and examinations were conducted online. There is no overlap between groups 1 and 2. Ethical approval for this study was granted by the Ethics Committee of University of Sarajevo-Institute of Genetic Engineering and Biotechnology.

All subjects completed basic personal information as well as self-assessment standardized tools for stress-induced GI symptoms including the GI symptom rating scale (GSRS), visceral sensitivity index (VSI), and the Patient Health Questionnaire 15-item (PHQ-15) Somatic Symptom Severity Scale (PHQ-15). All questionnaires were previously translated and back-translated for English and Bosnian language (12).

The GSRS, as a 13 point Likert scale, combines five symptom clusters: Reflux, abdominal pain, indigestion, diarrhea, and constipation. The GSRS is well-documented as reliable and valid, and norm values for a general population are available. The original interview-based questionnaire was modified to become a self-administrated questionnaire (13). According to Chahal-Kummen et al. (2018), a total score more or equal than 3 was used as a cut-off value for determination of symptom (14).

The VSI, a 15-item scale, demonstrates excellent reliability as well as good content, convergent, divergent, and predictive validity (15). Total scores ranged from 0 (no GI-specific anxiety) to 75 (severe GI-specific anxiety). According to Labus et al. 2007, we used 38 as the cut-off value, because patients with diagnosed IBS from that study had 38 and more as a VSI result score (16).

The PHQ-15, a 15 point Likert scale, is a valid and moderately reliable questionnaire for the detection of patients in a primary care setting at risk for somatization disorders. The total PHQ-15 score ranges from 0 to 30 and scores of  $\geq 5$ ,  $\geq 10$ ,  $\geq 15$  represent mild, moderate, and severe levels of somatization (17-19). For prevalence determination, 10 as a cutoff value was used in this questionnaire because the range of 10 up to 30 was noted as the medium and high somatic symptom severity by Kroenke et al. (2002) (17).

Descriptive statistics was performed in Excel and it was presented as means±standard deviations (SD), along with 95% confidence intervals. For the quantitative statistics, we performed Mann–Whitney in the Past 4.3 (20).

### RESULTS

In this study, the total number of subjects included before the COVID pandemic (Group 1) and during COVID pandemic (Group 2) who participated was 279, including 71% of female and 29% of male, aged from 18 to 44 (22.96  $\pm$ 4.21). The demographic data for the present study participants are summarized in Table 1. Of the total number of study participants, 3.94% had previously been diagnosed with a GI disorder, including Morbus Crohn disease, gastroesophageal reflux disease, inflammation of the small intestine (enteritis), and gastritis. They were excluded from further analyses. All analyzed subjects filled all three questionnaires completely (Table 2).

From the results of three questionnaires, it is evident that moderate and severe symptoms are more pronounced in the group of students examined during the COVID-19

**TABLE 1.** Distribution of subjects' number, sex, and age into two subjected groups

Groups	Subjects (n)	Sex		Age	
		F (%)	M (%)	Min	Max
Total	279	71	29	18	44
Group 1	193	64.3	35.7	18	44
Group 2	86	87	13	18	38

N: Number, F: Female, M: Male, Min: Minimum, Max: Maximum

**TABLE 2.** Description of questionnaires filled by all participants and according to subgroups (Data are expressed as: Mean±SD [95% confidence interval])

-			
Groups	GSRS	VSI	PHQ-15
Total	1.93±0.96	72.00±16.08	7.50±4.71
Group 1	1.75±0.77	72.40±16.69	6.99±4.56
Group 2	2.36±1.21	71.24±14.60	8.62±4.83

GSRS: Gastrointestinal symptom rating scale, VSI: Visceral sensitivity index, PHQ-15: Patient health questionnaire 15-item somatic symptom severity scale

pandemic (Table 2 and Figure 1). The scores were significantly higher for the Group 2 than for the Group 1 on the GSRS (z = 4.8801, p < 0.001) and the PHQ-15 (z = 2.003, p = 0.045172). However, there was no significant difference in the total VSI (z = 0.80704, p = 0.41964) score. Within the GSRS questionnaire, bloating syndrome (average value = 2.91) and abdominal pain syndrome (average value 2.69) are the most pronounced in the Group 2.

Our results point out the effect of stress as a non-genetic factor on neuro-GI disorders and that could be the basis for further determining genetic contribution or predisposition for stress or even their interaction in predisposing to GI disorders. Determination of non-genetic and genetic factors both together could facilitate early prevention of neuro-GI disorders in the youth.

## DISCUSSION

COVID-19 pandemic has a huge impact on the way and the quality of human life. Lockdown period and various measures such as the social distancing, isolation, and quarantine during the pandemic have limited social and physical activities of the population leading to increased prevalence of different mental disorders (21). Association of psychological distress with the consequences of the COVID-19 pandemic and suppression measures was also proven (22). Many studies confirmed that psychological distress and certain stressful life events can deeply influence GI disorders symptoms and the onset of associated anxiety (23).

Reports from the literature highlight how the prevalence of GI symptoms is significantly higher during the COVID-19 pandemic than in the previous year under normal circumstances (24). In addition, an increase of GI symptoms during the lockdown period in a population of medical students was detected (9). Similarly, results of our study showed that moderate and severe self-reported stress-induced GI symptoms are more pronounced in the group of students examined during the COVID-19 pandemic (Group 2) than in the group examined before (Group 1). In particular, scores were significantly higher for the Group 2 than for the Group 1 on the two questionnaires, the GSRS and the PHQ-15, respectively. These results suggest that the medium

and high somatic symptom severity is more present among the second group subjects, raising also a bloating syndrome and abdominal pain syndrome as the most pronounced in the second group within the GSRS questionnaire (Table 3). No significant difference was observed in the total VSI score which is actually a measure of GI symptom-specific anxiety (GSA) which stems from fear of GI symptoms (25).

Stress is a well-known factor in the alterations of the braingut axis leading to various GI symptoms (3) what has been proven to be common in the student population during the stressful periods (2). Furthermore, our results and the results of other studies confirmed that younger people are more likely to experience anxiety, depression, and psychological abnormalities (26,27) as well as increase of different GI symptoms (9) under the COVID-19 pandemic compared to normal conditions. Precisely, higher anxiety and depression scores were measured during pandemic (26) and Impact of Event Scale indicated that majority of queried people felt horrified and apprehensive due to the pandemic (27). Furthermore, results of web-based survey related to GI symptoms and anxiety state during pandemic showed that in a population of medical students, GI symptoms increased due to concern for one's health (9). The data presented emphasize the role of stress related to the pandemic. It can be concluded that concern for one's health and changed way of life are directly related to a worsening of the symptoms of GI disorders in the student population.

Our research showed significantly higher scores of the VSI questionnaire related to everyday thinking about the possible occurrence of GI problems and consequent anxiety and disruption of daily activities compared to GSRS and PHQ-15 questionnaires related to the frequency of objective GI symptoms. Our results are in accordance with other studies showing that people are more fearful for their health during the COVID pandemic compared to pre-COVID period (26,28). Despite psychological factors may influence the occurrence and exacerbation of GI symptoms, part of the results of our study (VSI compared to GSRS and PHQ-15) indicate also that genetic factors could play a key role in the occurrence of GI problems within a population exposed to an equal amount of psychological pressure.



FIGURE 1. Frequency of symptom's levels set by cutoff values (three for GSRS, 38 for VSI, and 10 for PHQ-15) within the study groups, Group 1 (pre-COVID time) and Group 2 (COVID time).

|--|

Groups	Abdominal pain syndrome	Bloating syndrome	Constipation syndrome	Diarrhea syndrome	Satiety syndrome
Group 1	1.97	2.12	1.66	1.51	1.58
Group 2	2.69	2.91	2.10	1.92	2.36

GSRS: Gastrointestinal symptom rating scale

# CONCLUSIONS

This paper is a pilot study in which we found that it makes sense to investigate more deeply the effect of stress as a non-genetic factor on neurogastric disorders, and to determine the genetic predisposition to stress causing GI disorders. Further research should go in the direction of early prevention of GI disorders that take place in early youth and later develop into chronic forms. Herein, close monitoring of psychological and physical health status as well as various behavioral modification could be very helpful.

### **CONFLICTS OF INTEREST**

The authors declare that they have no competing interests.

### REFERENCES

- Ilić Živojinović JB. Analysis of the Correlation between Socio-Environmental Factors and Academic Stress and Mental Health of Students, PhD [Dissertation]. Serbia: University of Belgrade; 2014. (In Serbian).
- Balmus IM, Robea M, Ciobica A, Timofte D. Perceived stress and gastrointestinal habits in college students. Acta Endocrinol (Buchar) 2019;15(2):274-5. https://doi.org/10.4183/aeb.2019.274
- Konturek PC, Brzozowski T, Konturek SJ. Stress and the gut: Pathophysiology, clinical consequences, diagnostic approach and treatment options. J Physiol Pharmacol 2011;62(6):591-9.
- Drossman DA. The functional gastrointestinal disorders and the Rome III process. Gastroenterology 2006;130(5):1377-90.

https://doi.org/10.1053/j.gastro.2006.03.008

 Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington H, et al. Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT Gene. Science 2003;301(5631):386.

https://doi.org/10.1126/science.1083968

 Taylor S, Landry CA, Paluszek MM, Fergus TA, McKay D, Asmundson GJ. Development and initial validation of the COVID stress scales. J Anxiety Disord 2020;72:102232.

https://doi.org/10.1016/j.janxdis.2020.102232

 Kamp KJ, Levy RL, Munson SA, Heitkemper MM. Impact of COVID-19 on individuals with irritable bowel syndrome and comorbid anxiety and/or depression. J Clin Gastroenterol 2022;56(2):e149-52.

https://doi.org/10.1097/MCG.000000000001515

- Alzahrani MA, Alshamrani AS, Ahmasani IM, Alahmari FS, Asiri AH, Alshehri AM, et al. Coronavirus disease 2019 pandemic stress and its effects on irritable bowel syndrome patients in Saudi Arabia. Medicine (Baltimore) 2020;99(51):e23711. https://doi.org/10.1097/MD.00000000023711
- Abenavoli L, Cinaglia P, Lombardo G, Boffoli E, Scida M, Procopio AC, et al. Anxiety and gastrointestinal symptoms related to COVID-19 during Italian lockdown. J Clin Med 2021;10(6):1221.

https://doi.org/10.3390/jcm10061221

 Son C, Hegde S, Smith A, Wang X, Sasangohar F. Effects of COVID-19 on college students' mental health in the United States: Interview survey study. J Med Internet Res 2020;22(9):e21279. https://doi.org/10.2196/21279

https://doi.org/10.2196/21279

 Yang C, Chen A, Chen Y. College students' stress and health in the COVID-19 pandemic: The role of academic workload, separation from school, and fears of contagion. PLoS One 2021;16(2):e0246676. https://doi.org/10.1371/journal.pone.0246676

110ps.//doi.org/10.1371/jou11ai.pone.0240070

12. Boeckxstaens GE, Drug V, Dumitrascu D, Farmer AD, Hammer J, Hausken T,

et al. Phenotyping of subjects for large scale studies on patients with IBS. Neurogastroenterol Motil 2016;28(8):1134-47.

- https://doi.org/10.1111/nmo.12886
- AstraZeneca C. 2022. Available from: https://www.astrazeneca.com/patient-reported-outcomes/gastrointestinal.html [Last accessed on 2021 Apr 04].
- Chahal-Kummen M, Blom-Høgestøl I, Eribe I, Kristinsson J, Mala T. Abdominal pain before and after Roux-en-Y gastric bypass. Surg Obes Relat Dis 2018;14(11):S127-8. https://doi.org/10.1016/j.soard.2018.09.282
- Labus JS, Bolus R, Chang L, Wiklund I, Naesdal J, Mayer EA, et al. The Visceral Sensitivity Index: Development and validation of a gastrointestinal symptom-specific anxiety scale. Aliment Pharmacol Ther 2004;20(1):89-97. https://doi.org/10.1111/j.1365-2036.2004.02007.x
- Labus JS, Mayer EA, Chang L, Bolus R, Naliboff BD. The central role of gastrointestinal-specific anxiety in irritable bowel syndrome: Further validation of the visceral sensitivity index. Psychosom Med 2007;69(1):89-98. https://doi.org/10.1097/PSY.0b013e31802e2f24
- Kroenke K, Spitzer RL, Williams JB. The PHQ-15: Validity of a new measure for evaluating the severity of somatic symptoms. Psychosom Med 2002;64(2):258-66. https://doi.org/10.1097/00006842-200203000-00008
- Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: A systematic review. Gen Hosp Psychiatry 2010;32(4):345-59.

https://doi.org/10.1016/j.genhosppsych.2010.03.006

 De Vroege L, Hoedeman R, Nuyen J, Sijtsma K, van der Feltz-Cornelis CM. Validation of the PHQ-15 for somatoform disorder in the occupational health care setting. J Occup Rehabil 2011;22(1):51-8.

https://doi.org/10.1007/s10926-011-9320-6

- Hammer Ø, Harper DAT, Ryan PD. Past: Paleontological statistics software package for education and data analysis. Palaeontol Electronica 2001;4(1):4-9.
- Hu S, Tucker L, Wu C, Yang L. Beneficial effects of exercise on depression and anxiety during the Covid-19 pandemic: A narrative review. Front Psychiatry 2020;11:587557. https://doi.org/10.3389/fpsyt.2020.587557
- Lorant V, Smith P, Van den Broeck K, Nicaise P. Psychological distress associated with the COVID-19 pandemic and suppression measures during the first wave in Belgium. BMC Psychiatry 2021;21(1):112. https://doi.org/10.1186/s12888-021-03109-1
- Oshima T, Siah KT, Yoshimoto T, Miura K, Tomita T, Fukui H, et al. Impacts of the COVID-19 pandemic on functional dyspepsia and irritable bowel syndrome: A population-based survey. J Gastroenterol Hepatol 2021;36(7):1820-7. https://doi.org/10.1111/jgh.15346
- Nakov R, Dimitrova-Yurukova D, Snegarova V, Nakov V, Fox M, Heinrich H. Increased prevalence of gastrointestinal symptoms and disorders of gut-brain interaction during the COVID-19 pandemic: An internet-based survey. Neurogastroenterol Motil 2022;34(2):e14197.

https://doi.org/10.1111/nmo.14197

- Trieschmann K, Chang L, Park S, Naliboff B, Joshi S, Labus JS, et al. The visceral sensitivity index: A novel tool for measuring GI-symptom-specific anxiety in inflammatory bowel disease. Neurogastroenterol Motil 2022;34(9):e14384. https://doi.org/10.1111/nmo.14384
- Liu X, Luo WT, Li Y, Li CN, Hong ZS, Chen HL, et al. Psychological status and behavior changes of the public during the COVID-19 epidemic in China. Infect Dis Poverty 2020;9(1):58.

https://doi.org/10.1186/s40249-020-00678-3

 Zhang Y, Ma ZF. Impact of the COVID-19 pandemic on mental health and quality of life among local residents in Liaoning Province, China: A cross-sectional study. Int J Environ Res Public Health 2020;17(7):2381.

https://doi.org/10.3390/ijerph17072381

 Shi L, Lu ZA, Que JY, Huang XL, Liu L, Ran MS, et al. Prevalence of and risk factors associated with mental health symptoms among the general population in China during the coronavirus disease 2019 pandemic. JAMA Netw Open 2020;3(7):e2014053. https://doi.org/10.1001/iamanetworkopen.2020.14053