



Analysis of systemic symptoms in COVID-19

Analiza objawów ogólnoustrojowych w przebiegu COVID-19

Adam S. Dadok¹ , Grażyna Lisowska¹ , Natalia Zięba¹ , Karolina Goroszkiewicz² ,
Grażyna Stryjewska-Makuch² , Hanna Kubik³ , Katarzyna Miśkiewicz-Orczyk¹ 

¹Katedra i Oddział Kliniczny Otorinolaryngologii i Onkologii Laryngologicznej, Wydział Nauk Medycznych w Zabrze, Śląski Uniwersytet Medyczny w Katowicach

²Oddział Laryngologii i Onkologii Laryngologicznej, Górnośląskie Centrum Medyczne im. prof. Leszka Gieca Śląskiego Uniwersytetu Medycznego w Katowicach

³Studenckie Koło Naukowe przy Katedrze i Oddziale Klinicznym Otorinolaryngologii i Onkologii Laryngologicznej, Wydział Nauk Medycznych w Zabrze, Śląski Uniwersytet Medyczny w Katowicach

ABSTRACT

INTRODUCTION: COVID-19 (coronavirus disease 2019), a disease caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection, may have a more or less severe course. The aim of this study was to analyse the symptoms which occurred in a group of people who tested positively for the presence of the genetic material of the virus.

MATERIAL AND METHODS: The analysis was based on the results of 337 questionnaires collected from Polish patients – 185 (55%) females and 152 (45%) males aged 18–86. The questionnaire included 26 questions, of which 11 were related to systemic symptoms. The frequency of their occurrence and their severity were determined according to Visual Analogue Scale (VAS).

RESULTS: The most common symptoms that occurred in over 50% of the respondents included: general weakness (91% of the respondents, severity of 6.25 on VAS), musculoskeletal pain (77%, VAS 5.67), headache (65%, VAS 5.37) and cough (56%, VAS 4.76). Runny nose, fever above 38°C and sore throat were less common and occurred in 39% of the subjects. The least frequent symptoms were diarrhoea (23%), skin lesions (7%) and vomiting (3%). When determining the correlation coefficient, it was also found that dyspnoea occurred most often with general weakness ($r = 1$), whereas general weakness was less frequently associated with musculoskeletal pain ($r = 0.8$). No statistically significant relationships were found between the frequency of the symptoms and age, gender or the presence of comorbidities in the respondents.

CONCLUSIONS: The observations showed that in the analysed group of people with SARS-CoV-2 infection, the disease had a mild-to-moderate course. General weakness, musculoskeletal pain, cough, and upper respiratory tract infection symptoms were the most common.

KEY WORDS

COVID-19, coronavirus, symptoms

Received: 25.10.2021

Revised: 12.01.2022

Accepted: 23.03.2022

Published online: 08.08.2022

Address for correspondence: lek. Adam S. Dadok, Katedra i Oddział Kliniczny Otorinolaryngologii i Onkologii Laryngologicznej, Wydział Nauk Medycznych w Zabrze, Śląski Uniwersytet Medyczny w Katowicach, ul. Marii Skłodowskiej-Curie 10, 41-800 Zabrze, tel. +48 32 373 23 95, e-mail: adamdadok.ori@gmail.com



This is an open access article made available under the terms of the Creative Commons Attribution-ShareAlike 4.0 International (CC BY-SA 4.0) license, which defines the rules for its use. It is allowed to copy, alter, distribute and present the work for any purpose, even commercially, provided that appropriate credit is given to the author and that the user indicates whether the publication has been modified, and when processing or creating based on the work, you must share your work under the same license as the original. The full terms of this license are available at <https://creativecommons.org/licenses/by-sa/4.0/legalcode>.

Publisher: Medical University of Silesia, Katowice, Poland



STRESZCZENIE

WSTĘP: COVID-19 (*coronavirus disease 2019*), choroba wywołana infekcją SARS-CoV-2 (*severe acute respiratory syndrome coronavirus 2*), może charakteryzować się mniej lub bardziej nasilonym przebiegiem. Celem niniejszego opracowania była analiza objawów, jakie wystąpiły w grupie osób z dodatnim wynikiem testu na obecność materiału genetycznego wirusa.

MATERIAŁ I METODY: Analizę przeprowadzono na podstawie wyników ankiety przeprowadzonej wśród 337 polskich pacjentów – 185 (55%) kobiet oraz 152 (45%) mężczyzn w wieku 18–86 lat. Kwestionariusz zawierał 26 pytań, z czego 11 dotyczyło objawów ogólnoustrojowych. Określono częstość ich występowania oraz nasilenie w skali VAS (Visual Analogue Scale).

WYNIKI: Do najczęstszych objawów, występujących u ponad 50% ankietowanych, należą: ogólne osłabienie (91% ankietowanych, nasilenie 6,25 w skali VAS), bóle układu mięśniowo-szkieletowego (77%, VAS 5,67), bóle głowy (65%, VAS 5,37) oraz kaszel (56%, VAS 4,76). Chorobie rzadziej towarzyszyły katar, gorączka powyżej 38°C oraz bóle gardła, które wystąpiły u 39% pacjentów. Najrzadziej występowały biegunka (23%), zmiany skórne (7%) oraz wymioty (3%). Określając współczynnik korelacji, stwierdzono również, iż duszności występowały najczęściej z ogólnym osłabieniem ($r = 1$), natomiast rzadziej ogólnemu osłabieniu towarzyszyły bóle mięśniowo-szkieletowe ($r = 0,8$). Nie stwierdzono statystycznie istotnych zależności między częstością występowania danych objawów a wiekiem, płcią czy chorobami współistniejącymi u ankietowanych.

WNIOSKI: Obserwacje wykazały, iż w analizowanej grupie zakażonych SARS-CoV-2 choroba miała przebieg łagodny lub umiarkowany. Najczęstszymi objawami były: ogólne zmęczenie, bóle mięśniowo-szkieletowe, kaszel oraz objawy niezłyty górnych dróg oddechowych.

SŁOWA KLUCZOWE

COVID-19, koronawirus, objawy

INTRODUCTION

In November 2019, an infection caused by a new type of RNA virus from the coronavirus group, later named SARS-CoV-2 (*severe acute respiratory syndrome coronavirus 2*), was described for the first time in the city of Wuhan (Hubei province, central China) by the International Committee on Taxonomy of Viruses (ICTV) [1,2].

The World Health Organization (WHO) named the disease caused by SARS-CoV-2 COVID-19 (*coronavirus disease 2019*). The first cases of infection were detected in people associated with the local fish market, Huanan Wholesale Seafood Market, in Wuhan [3]. The number of infections grew dynamically. After 30 days, the epidemic spread throughout China. The first cases of COVID-19 in Europe were detected at the beginning of January, whereas in Poland the first case was diagnosed on March 4, 2020 [4,5]. WHO declared COVID-19 a pandemic on March 11, 2020 [6]. By June 20, 2021, there had been over 179.15 million of cases of SARS-CoV-2 infection in 192 countries and territories. Currently, this number includes nearly 11.57 million active cases, 163.71 million recoveries and nearly 3.88 million deaths [7]. The pandemic has covered all continents, including Antarctica [8].

SARS-CoV-2 spreads in two main ways: directly, through droplets ejected by an infected person during coughing, sneezing, speaking or even singing, and indirectly, through contact with contaminated objects or by inhaling the aerosol generated during aerosol-generating procedures, including medical ones [9].

Preventive measures are of paramount importance in reducing the risk of infection and the rate at which the virus spreads. The basic methods include: frequent hand washing, avoiding large groups of people, maintaining social distance, using personal protective equipment such as masks, surface disinfection, and airing the premises. Early detection, isolation and prompt initiation of treatment of COVID-19 patients are also important [9,10]. The gold standard in COVID-19 diagnostics is the reverse-transcription polymerase chain reaction (RT-PCR) molecular test, in which the material for testing is most often taken from the nasopharynx. The sensitivity of this method is approx. 70%, whereas its specificity is approx. 95%. These figures result from many factors such as the quality of collection and storage of the material for testing, the onset and severity of symptoms, and the viraemia level of the sample [11]. Other methods of testing for COVID-19 include serological and antigen tests. Diagnostics is often extended to laboratory blood tests in which lymphocytopenia, thrombocytopenia, leukopenia, slight thrombocytopenia and elevated levels of alanine aminotransferase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH) and parameters of inflammatory markers are noteworthy. Computed tomography of the lungs has a high diagnostic value, followed by chest USG and X-ray, whose diagnostic value is slightly lower [12,13,14]. SARS-CoV-2 infection can manifest itself in various forms and produce a wide range of clinical symptoms typical of viral infections. In some patients (approx. 45%), COVID-19 infection is asymptomatic, whereas in 80% of symptomatic patients, it is mild [15]. In



some patients, SARS-CoV-2 causes severe lung inflammation, which may be fatal. The most common symptoms described in the literature are fever, cough, tiredness, and dyspnoea, but during the pandemic, different frequencies and severities of systemic symptoms in COVID-19 patients have been reported [16].

A thorough analysis of the most common COVID-19 symptoms increases the chance of faster diagnosis and treatment, which significantly slows down the pandemic.

MATERIAL AND METHODS

We performed a retrospective analysis of questionnaire studies of 337 Polish patients, which had been approved by the Ethics Committee (approval number: PCN/CBN/0022/KB/143/21). The questionnaires and data for our analysis were collected from January to June 2021. All the subjects had SARS-CoV-2 infection, which was confirmed by a positive PCR test.

185 (55%) females and 152 (45%) males participated in the study. All the respondents were of legal age, the youngest patient was 18 years old, and the oldest was 86. The mean age of all the respondents was 44 years. The questionnaire contained 26 questions, 11 of which concerned systemic symptoms such as: fever above 38°C, cough, dyspnoea, runny nose, musculoskeletal pain, general weakness, headache, sore throat, diarrhoea, skin lesions, and vomiting. The frequency of individual symptoms and their severity were determined using a 10-point Visual Analogue Scale (VAS). Additionally, demographic and statistical analysis of the patients was performed, including blood group type, body mass index, smoking and the presence of comorbidities such as type II diabetes, respiratory, cardiovascular, autoimmune and oncological diseases.

Statistical analysis

In this study, percentages and means with standard deviations are reported. All the correlations are tetrachoric – appropriate for calculating the relationship between binary variables (here: the presence or absence of a given symptom). The analyses were performed using Stata MP 17.0 software.

RESULTS

In the present study, among the 337 patients, the most common systemic symptom was general weakness. It occurred in the vast majority of the respondents, i.e. 91%. The patients rated the symptom severity as 6.25 (± 2.37) on VAS. The second most common complaint was musculoskeletal pain. It was reported by 77% of

the respondents who rated the mean severity in accordance with VAS as 5.67 (± 2.49). Cough occurred in 56% of the COVID-19 patients. The mean severity of this symptom was determined by the respondents as 4.76 (± 2.56). Another symptom typical of the respiratory system was dyspnoea. It was reported by 32% of the patients, and its severity was 4.83 (± 2.59) on VAS. Headache and sore throat were reported by 65% and 39% of the respondents, respectively, and their severity according to VAS was 5.37 (± 2.41) and 4.28 (± 2.16). Common symptoms reported in our study were runny nose and fever $> 38^\circ\text{C}$, occurring in 38% and 39% of the patients, respectively. The mean duration of the fever was 4.78 days (± 3.86). The severity of runny nose was estimated by the patients at 4.35 (± 2.28) on VAS. Gastrointestinal complaints such as diarrhoea and vomiting were reported by 23% and 3% of the patients, respectively. The severity of diarrhoea was assessed as per VAS by the respondents at an average of 4.24 (± 4.24). Skin lesions occurred relatively rarely, only in 7% of the patients. The frequency of individual symptoms is summarized in the Figure 1.

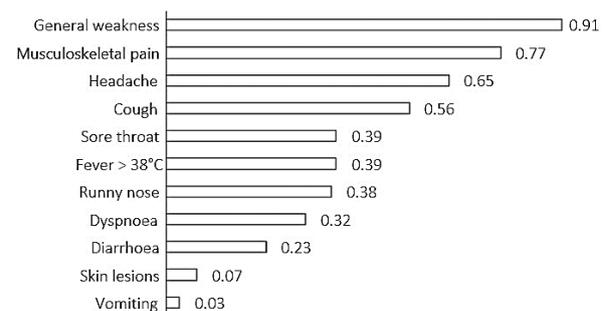


Fig. 1. Distribution of number of individuals declaring occurrence of systemic symptoms.

Ryc. 1. Rozkład liczby osób, które deklarowały wystąpienie objawów ogólnoustrojowych.

In our study, we also analysed the correlation coefficient (r) of systemic symptoms in COVID-19 at the level of significance of $p < 0.1$. There was a full positive correlation between dyspnoea and general weakness ($r = 1$). There was an average correlation between general weakness and musculoskeletal pain ($r = 0.8$), whereas the correlations between cough and general weakness ($r = 0.48$), cough and dyspnoea ($r = 0.45$), dyspnoea and pain musculoskeletal ($r = 0.38$), dyspnoea and fever ($r = 0.35$) were rather low. Additionally, a statistical analysis was performed of the frequency of the individual symptoms depending on age, sex and comorbidities. In all the studied groups, the difference was statistically insignificant. In the case of comorbidities, no relationship with the risk of a given systemic COVID-19 symptom was observed.



DISCUSSION

Since the outbreak in China in November 2019 until today, COVID-19 has been a major challenge for the global healthcare system. The course of COVID-19 can vary widely. It can take the form of asymptomatic infection, but also severe respiratory failure requiring mechanical ventilation and often leading to death. The analysis and knowledge of the most common systemic symptoms and testing for the presence of SARS-CoV-2 are extremely important for rapid diagnosis of the disease, isolation and treatment of COVID-19 patients. The most common symptoms recognized by WHO are fever, a dry cough and tiredness [17]. The above symptoms are most often included in epidemiological screening questionnaires.

The study by Wan et al. [18] analysed systemic symptoms in 135 patients hospitalized at Chongqing University Three Gorges Hospital due to COVID-19 infection. The most common symptom was fever, occurring in 88.9% of patients, followed by cough (76.5%) and tiredness/muscle pain (32.5%). Dyspnoea was only present in severe cases (18% of all). The mean age of the patients was 47 years. The study included 46.7% of females and 53.3% of males.

A study by Chen et al. [19], which included the most common symptoms in 99 patients hospitalized at Wuhan Junyintan Hospital, provided similar results. Fever occurred in 83% of patients, cough in 82%, and muscle pain in 11%. The mean age of the patients was 55.5 years old, there were 32% women and 68% men.

In a meta-analysis, Grant et al. [20] summarized 148 papers from 9 countries analysing the symptoms in a total of 24,410 patients with a positive PCR test for SARS-CoV-2. The most common complaints were: fever (78% of patients), cough (57%), tiredness (31%), and dyspnoea (23%). The study included mostly the results of patients from Asia, i.e. from China (17,011), and from Australia (4237). The types of the most common symptoms reported in these studies are similar to those present in our study. However, it is noteworthy that there was a smaller incidence of fever and cough in our study, and more frequent reports of tiredness and musculoskeletal pain. The differences between the results of the studies from Asia and ours may be due to several reasons. The first one is that the Asian studies took into account the symptoms of patients hospitalized in the course of COVID-19, i.e. patients in a moderate to severe condition, characterized by a greater incidence of high fever, persistent cough and dyspnoea. In our study, only 5% of the patients required hospitalization, of which 4% required passive oxygen therapy, and 1% stayed in the Intensive Care Unit.

Lechien et al. [21] analysed the medical history of 1420 European patients with mild to moderate COVID-19. The most common systemic symptom in this study was

headache (72.3%). Cough and muscle pain occurred in 56% and 62.5% of patients, respectively. The much lower incidence of fever was noteworthy (45.4%) as well as the higher frequency of rhinitis symptoms: runny nose (60.1%) and nasal congestion (67.2%). The above results are similar to ours, which indicates that most patients had mild to moderate COVID-19.

Another reason for the differences in the severity and type of systemic symptoms are potential mutations in the virus, which may differ in terms of the frequency of triggered symptoms. It can also be assumed that various symptoms are presented by different groups of patients in different regions of the world [22].

Another important hypothesis is the different expression of genes between populations. The influence of the ACE2 gene encoding angiotensin-converting enzyme 2 – which is, according to recent reports, a likely receptor for SARS-CoV-2 – is taken into account [23]. The study by Cao et al. [24] determined the differences in ACE2 expression in human cells between different populations, which may have a significant impact on the risk of infection and the severity of systemic symptoms.

In the course of COVID-19, symptoms involving systems other than the respiratory one are also noteworthy. Infections manifested by the involvement of other organs, such as the kidneys, heart, central nervous system, liver, skin, and the endocrine or digestive system, are described [4]. In our study, a relatively large number, i.e. 23% of the respondents, reported diarrhoea in the course of COVID-19. In Megyeri's et al. [25] study, based on various reports, the incidence of diarrhoea ranged from 2% to 49.5%. The pathogenesis of this symptom is related to the fact that in the course of COVID-19 the intestinal wall is attacked by SARS-CoV-2, which may lead to increased permeability and a reduction in the protective barrier of the intestinal wall. The causes are also sought in the aforementioned ACE2 receptor, whose expression is greater in the intestinal walls than in the lungs [26].

CONCLUSIONS

1. Most of the patients participating in the study had mild to moderate COVID-19, which is reflected in the frequency and type of reported systemic symptoms.
2. In the course of mild-to-moderate COVID-19, general weakness, musculoskeletal pain, cough and upper respiratory tract infection symptoms were the most common.
3. There were no significant correlations between the occurrence of the reported systemic symptoms and age, gender or the presence of comorbidities in the patients.



Author's contribution

Study design – A.S. Dadok, G. Lisowska, N. Zięba

Data collection – A.S. Dadok, N. Zięba, K. Goroszkiewicz, G. Stryjewska-Makuch

Data interpretation – A.S. Dadok, G. Lisowska, G. Stryjewska-Makuch, K. Miśkiewicz-Orczyk

Statistical analysis – A.S. Dadok, N. Zięba, H. Kubik

Manuscript preparation – A.S. Dadok, G. Lisowska, N. Zięba, H. Kubik

Literature research – A.S. Dadok, N. Zięba, K. Goroszkiewicz, K. Miśkiewicz-Orczyk

REFERENCES

1. Coronavirusidae Study Group of the International Committee on Taxonomy of Viruses. The species *Severe acute respiratory syndrome-related coronavirus*: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat. Microbiol.* 2020; 5(4): 536–544, doi: 10.1038/s41564-020-0695-z.
2. Li Q., Guan X., Wu P., Wang X., Zhou L., Tong Y. et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* 2020; 382(13): 1199–1207, doi: 10.1056/NEJMoa2001316.
3. Zhu N., Zhang D., Wang W., Li X., Yang B., Song J. et al. A novel coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.* 2020; 382(8): 727–733, doi: 10.1056/NEJMoa2001017.
4. World Health Organization. Origin of SARS-CoV-2, 26 March 2020. Available at: <https://apps.who.int/iris/handle/10665/332197> [accessed on 20 June 2020].
5. Pierwszy przypadek koronawirusa w Polsce. Portal gov.pl [online], 04.03.2020. Available at: <https://www.gov.pl/web/zdrowie/pierwszy-przypadek-koronawirusa-w-polsce> [accessed on 20 June 2020].
6. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. World Health Organization [online], 11 March 2020. Available at: <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19--11-march-2020> [accessed on 20 June 2020].
7. Coronavirus disease (COVID-2019) situation reports. World Health Organization [online]. Available at: <https://covid19.who.int/> [accessed on 20 June 2020].
8. Frame B., Hemmings A.D. Coronavirus at the end of the world: Antarctica matters. *Soc. Sci. Humanit. Open* 2020; 2(1): 100054, doi: 10.1016/j.ssoho.2020.100054.
9. Lotfi M., Hamblin M.R., Rezaei N. COVID-19: Transmission, prevention, and potential therapeutic opportunities. *Clin. Chim. Acta* 2020; 508: 254–266, doi: 10.1016/j.cca.2020.05.044.
10. Bi Q., Wu Y., Mei S., Ye C., Zou X., Zhang Z. et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study [published correction appears in *Lancet Infect. Dis.* 2020; 20(7): e148]. *Lancet Infect. Dis.* 2020; 20(8): 911–919, doi: 10.1016/S1473-3099(20)30287-5.
11. Güner R., Hasanoğlu I., Aktaş F. COVID-19: Prevention and control measures in community. *Turk. J. Med. Sci.* 2020; 50(3): 571–577, doi: 10.3906/sag-2004-146.
12. Pascarella G., Strumia A., Pilięgo C., Bruno F., Del Buono R., Costa F. et al. COVID-19 diagnosis and management: a comprehensive review. *J. Intern. Med.* 2020; 288(2): 192–206, doi: 10.1111/joim.13091.
13. Goudouris E.S. Laboratory diagnosis of COVID-19. *J. Pediatr.* 2021; 97(1): 7–12, doi: 10.1016/j.jpeds.2020.08.001.
14. Abbasi-Oshaghi E., Mirzaei F., Farahani F., Khodadadi I., Tayebinia H. Diagnosis and treatment of coronavirus disease 2019 (COVID-19): Laboratory, PCR, and chest CT imaging findings. *Int. J. Surg.* 2020; 79: 143–153, doi: 10.1016/j.ijssu.2020.05.018.
15. Oran D.P., Topol E.J. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. *Ann. Intern. Med.* 2020; 173(5): 362–367, doi: 10.7326/M20-3012.
16. Alimohamadi Y., Sepandi M., Taghdir M., Hosamirudisari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. *J. Prev. Med. Hyg.* 2020; 61(3): E304–E312, doi: 10.15167/2421-4248/jpmh2020.61.3.1530.
17. Coronavirus disease (COVID-19). World Health Organization [online]. Available at: https://www.who.int/health-topics/coronavirus#tab=tab_3 [accessed on 20 June 2020].
18. Wan S., Xiang Y., Fang W., Zheng Y., Li B., Hu Y. et al. Clinical features and treatment of COVID-19 patients in northeast Chongqing. *J. Med. Virol.* 2020; 92(7): 797–806, doi: 10.1002/jmv.25783.
19. Chen N., Zhou M., Dong X., Qu J., Gong F., Han Y. et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395(10223): 507–513, doi: 10.1016/S0140-6736(20)30211-7.
20. Grant M.C., Geoghegan L., Arbyn M., Mohammed Z., McGuinness L., Clarke E.L. et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. *PLoS One* 2020; 15(6): e0234765, doi: 10.1371/journal.pone.0234765.
21. Lechien J.R., Chiesa-Estomba C.M., Place S., Van Laethem Y., Cabaraux P., Mat Q. et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. *J. Intern. Med.* 2020; 288(3): 335–344, doi: 10.1111/joim.13089.
22. Jungreis I., Sealfon R., Kellis M. SARS-CoV-2 gene content and COVID-19 mutation impact by comparing 44 *Sarbecovirus* genomes. *Nat. Commun.* 2021; 12(1): 2642, doi: 10.1038/s41467-021-22905-7.
23. Baj J., Karakuła-Juchnowicz H., Teresiński G., Buszewicz G., Ciesielka M., Sitarz R. et al. COVID-19: Specific and non-specific clinical manifestations and symptoms: The current state of knowledge. *J. Clin. Med.* 2020; 9(6): 1753, doi: 10.3390/jcm9061753.
24. Cao Y., Li L., Feng Z., Wan S., Huang P., Sun X. et al. Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations. *Cell Discov.* 2020; 6: 11, doi: 10.1038/s41421-020-0147-1.
25. Megyeri K., Dernovics Á., Al-Luhaibi Z.I.I., Rosztóczy A. COVID-19-associated diarrhea. *World J. Gastroenterol.* 2021; 27(23): 3208–3222, doi: 10.3748/wjg.v27.i23.3208.
26. de Oliveira A.P., Lopes A.L.F., Pacheco G., de Sá Guimarães Nolêto I.R., Nicolau L.A.D., Medeiros J.V.R. Premises among SARS-CoV-2, dysbiosis and diarrhea: Walking through the ACE2/mTOR/autophagy route. *Med. Hypotheses* 2020; 144: 110243, doi: 10.1016/j.mehy.2020.110243.