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Post-COVID sindrom - aktuelni izazov u radu izabranog lekara

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Post-COVID syndrome - current challenge in the work of the general practitioner

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Sažetak

Uvod. Post-COVID sindrom se odlikuje značajnom kliničkom varijabilnošću i obuhvata sekvele oboljenja COVID-19 koje su prisutne duže od tri meseca nakon infekcije SARS-CoV-2.

Cilj istraživanja bio je utvrđivanje prisustva i trajanja post-COVID sindroma, učestalosti pojedinačnih simptoma i faktora koji mogu uticati na njihovo ispoljavanje.

Metod. Sproveli smo studiju preseka kod pacijenata koji su bili zaraženi SARS-CoV-2. Ispitanici su anketirani pomoću upitnika u drugoj polovini 2023. godine. Podaci su analizirani deskriptivnom statistikom, Kruskal-Wallis testom i Bonferonijevim testom višestrukih poređenja parova korišćenjem SPSS 26. Statistički značajnom se smatrala p vrednost <0,05.

Rezultati. Od ukupno 90 ispitanika, 15,6% nije imalo post-COVID simptome. Kod 24,4% ispitanika tegobe su trajale duže od šest meseci. Najviše je bilo zastupljeno brzo zamaranje (60%), hronični umor (53,3%) i smanjena koncentracija (45,6%). U definisanim starosnim grupama, postojala je značajna razlika za prisustvo tahikardije, znojenja i opstipacije (p<0,05). U odnosu na *body mass index*, uočena je značajna razlika za prisustvo kašlja, bola u grudima, opstipacije i poremećaja seksualne funkcije (p<0,05). U zavisnosti od pušačkog statusa, zabeležena je značajna razlika za pojavu noćnih mora, glavobolje, anksioznosti, bola u stomaku i dijareje (p<0,05). U odnosu na prisustvo komorbiditeta, postojala je značajna razlika za opadanje kose (p<0,05).

Zaključak. Za lečenje ovog stanja neophodan je holistički pristup pacijentu, pa je uloga izabranog lekara od velikog značaja.

Ključne reči: SARS-CoV-2, COVID-19, post-akutni COVID-19 sindrom

Abstract

Introduction. Post-COVID syndrome is characterized by a wide range of clinical symptoms that persist for more than three months after the initial SARS-CoV-2 infection.

Objective. Our objective was to confirm and explore the long-term effects of post-COVID syndrome, the prevalence of individual symptoms, and the factors that may influence their occurrence.

Method. In our study, we conducted a cross-sectional analysis on patients who had previously been infected with SARS-CoV-2. Participants were requested to complete the questionnaire during the latter part of 2023. The data was examined using descriptive statistics, the Kruskal-Wallis test, and the Bonferroni test for multiple pair comparisons using SPSS 26. A p-value <0.05 was considered statistically significant.

Results. Out of a total of 90 participants, 15.6% did not experience post-COVID symptoms. However, 24.4% experienced symptoms that persisted for longer than six months. The most common symptoms reported were rapid fatigue (60%), chronic fatigue (53.3%), and difficulty concentrating (45.6%). There was a significant difference in the occurrence of tachycardia, sweating, and constipation among different age groups (p<0.05). Additionally, the presence of cough, chest pain, constipation, and sexual disorders showed significant differences in relation to body mass index, (p<0.05). Furthermore, significant differences in the occurrence of nightmares, headaches, anxiety, abdominal pain, and diarrhea were noticed in relation to cigarette smoking status (p<0.05). Lastly, in relation to comorbidities, there was a statistically significant difference in the occurrence of hair loss (p<0.05).

Conclusion. A holistic approach is necessary in treating a patient with post-COVID. Therefore, the role of the general practitioner (GP) is crucial.

Keywords: SARS-CoV-2, COVID-19, post-acute COVID-19 syndrome

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Uvod

Klinički spektar oboljenja COVID-19, uzrokovanog virusom SARS-CoV-2 (engl. severe acute respiratory syndrome coronavirus 2), varira od asimptomatske infekcije do letalnog ishoda[1]. U Srbiji je do 12. aprila 2024. godine registrovano 2 615 054 obolelih i 18 057 smrtnih ishoda[2]. Virus ulazi u ćeliju preko receptora za angiotenzin konvertujući enzim 2 (ACE2), koji je prisutan u nazalnoj i oralnoj mukozi, plućima, jetri, mozgu, srcu, gastrointestinalnom traktu, bubrezima, slezini, kao i u endotelnim ćelijama arterija i vena[1]. Vezivanje virusa za ACE2 receptor, izaziva leukocitnu infiltraciju i propustljivost alveolarnog zida i krvnih sudova, ali i smanjenje surfaktanta u plućima[3]. Letalna kaskada u infekciji SARS-CoV-2 podrazumeva jaku inflamaciju sa citokinskom olujom što vodi u septički šok i multiorgansku disfunkciju[4].

Produženi COVID-19 se razvija nakon akutnog COVID-19 i podrazumeva kontinuirani simptomatski COVID-19 (4–12 nedelja) i post-COVID-19 sindrom (≥12 nedelja)[5]. Post-COVID sindrom podrazumeva trajanje simptoma najmanje dva meseca, a koji su prisutni nakon tri meseca od obolevanja od COVID-19, i ne mogu se objasniti alternativnom dijagnozom[6]. Dopunom Međunarodne klasifikacije bolesti (MKB-10), utvrđena šifra za post-COVID-19 stanje je U09.9[7]. Post-COVID uključuje oko 200 različitih simptoma koji se mogu preklapati[8]. Najprisutnije su neuropsihijatrijske, kardiovaskularne, pulmonalne, renalne, gastrointestinalne, kao i muskuloskeletne sekvele COVID-19[9]. Među tegobama, posebno se izdvajaju perzistentni umor i malaksalost, bol u grudima i mišićima, kratak dah i kognitivna disfunkcija[8].

Potencijalni patofiziološki mehanizmi post-COVID-19 sindroma podrazumevaju specifične varijacije virusa, oksidativni stres, imunološke abnormalnosti i inflamatorno oštećenje[3]. Oštećenje organa može biti uzrokovano prekomernim inflamatornim odgovorom aktiviranim virusom, perzistentnim rezervoarom SARS-CoV-2 virusa u tkivima što izaziva postinfekcijski morbiditet, kao i reaktivacijom patogena usled imunološke disregulacije[8]. Sugeriše se i da post-COVID sindrom nije samo direktan rezultat infekcije SARS-CoV-2 virusom, već može biti i posledica COVID-19 reaktivacije Epstein-Barr virusa izazvanog inflamacijom. Pokazalo se da virus SARS-CoV-2 unakrsno reaguje sa antigenima creva, bubrega, pluća, srca i mozga, i da proteini SARS-CoV-2 virusa mogu biti homologi sa epitopima proteina domaćina, što dovodi do molekularne mimikrije. U inflamaciji, mikrobiom koji značajno varira između različitih osoba, može doprineti nastanku autoantitela koja su različito reaktivna. Takođe i koagulacione abnormalnosti igraju značajnu ulogu za nastanak ovog stanja. Na ovaj način se objašnjava značajan procenat kliničkih varijacija kod pacijenata sa post-COVID sindromom[8,10–14]. Post-COVID simptomi su fluktuirajuće prirode, odnosno njihova pojava varira tokom vremena. Ne postoji definisan obrazac evolucije simptoma i pacijenti obično re-

Introduction

The clinical spectrum of COVID-19 disease, caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2), varies from asymptomatic infection to a fatal outcome[1]. Until April 12th, there were 2,615,054 cases of COVID-19 and 18,057 deaths registered in Serbia[2]. The virus enters the cell by connecting to the receptors for angiotensin-converting enzyme 2 (ACE2), which is found in nasal and oral mucosa, lungs, liver, brain, heart, gastrointestinal tract, kidneys, spleen, and endothelial cells of arteries and veins[1]. The binding of the virus with ACE2 receptor causes leukocyte infiltration and increased permeability of the alveolar wall and blood vessels but also decreases the surfactant in lungs[3]. The lethal cascade in the SARS-CoV-2 infection implies huge inflammation with a cytokine storm, leading to septic shock and multiorgan dysfunction[4].

Long COVID-19 develops after acute COVID-19 and involves continuous symptomatic COVID-19 (4–12 weeks) and post-COVID-19 syndrome (≥12 weeks)[5]. Post-COVID syndrome refers to symptoms that last at least two months and persist three months after the initial COVID-19 infection, without an alternative diagnosis[6]. The International Classification of Diseases (ICD-10) has assigned the code U09.9 for post-COVID-19 state[7]. Post-COVID-19 includes around 200 different symptoms, which may overlap[8]. The most common are neuropsychiatric, cardiovascular, pulmonary, renal, gastrointestinal, and musculoskeletal sequelae of COVID-19[9]. Among many symptoms, persistent fatigue and malaise, chest and muscle pain, shortness of breath, and cognitive dysfunction are the most common[8].

The potential pathophysiological mechanisms of post-COVID-19 syndrome include specific viral variations, oxidative stress, immunological abnormalities, and inflammatory damage[3]. Organ damage may be caused by an overreacting inflammatory response activated by the virus, a persistent reservoir of SARS-CoV-2 virus in the tissues causing post-infectious morbidity, as well as reactivation of the pathogen due to immunological disregulation[8]. It is suggested that post-COVID syndrome is not only a direct result of SARS-CoV-2 virus infection, but it may also be the consequence of COVID-19 reactivation of the Epstein-Barr virus, caused by inflammation. The SARS-CoV-2 virus cross-reacts with antigens of the intestines, kidneys, lungs, heart, and brain. The SARS-CoV-2 virus proteins may be similar to protein epitopes of the host, which may lead to molecular mimicry.

During inflammation, the microbiome, which varies significantly among different people, may lead to the formation of auto-antibodies that react differently. Additionally, coagulation abnormalities play an important role in the development of the disease. The significant percentage of clinical variations in patients with post-COVID syndrome can be explained in this way[8,10–14]. Post-COVID symptoms are

aguju na različite stimuluse (uglavnom fizičku ili mentalnu aktivnost i stres)[5].

U publikaciji italijanskih i američkih autora, koja se odnosi na saznanja o sekvelama COVID-19 do 2023. godine, apostrofira se činjenica da rizik u budućnosti postoji. Kada se reverzno transkribovana RNK SARS-CoV-2 integriše u genom inficiranih humanih ćelija, ona utiče na ekspresiju gena, ali može doći i do aktivne reekspresije mesecima ili godinama kasnije sa posledicama koje su još uvek potpuno nepredvidive[15]. Meta-analiza je pokazala da su kod skoro 30% ispitanika registrovani post-COVID simptomi dve godine nakon akutne infekcije SARS-CoV-2[16]. Postoje saznanja u literaturi koja impliciraju da je upotreba oralnih antivirusnih lekova povezana sa smanjenim rizikom za razvoj post-COVID sindroma. Međutim, potrebna su velika randomizovana klinička ispitivanja da potvrde navedenu činjenicu[17]. Pretpostavlja se da vakcinacija ima protektivnu ulogu i u prevenciji post-COVID sindroma, pored smanjenja rizika za nastanak teže kliničke slike COVID-19[18].

Cilj

Cilj ovog istraživanja bio je utvrđivanje prisustva i trajanja post-COVID sindroma, učestalosti pojedinačnih simptoma, kao i uticaj starosti, pušačkog statusa, prisustva komorbiditeta i vrednosti *body mass indexa* - BMI na njihovo ispoljavanje.

Metod

Dizajn istraživanja

Studija je sprovedena među pacijenatima Doma zdravlja „Novi Beograd“, kojima je dijagnostikovana COVID infekcija u periodu od 1. aprila 2020. godine do 31. decembra 2022. godine. Dijagnostikovan COVID-19 potvrđen je kod svakog ispitanika antigenskim testom ili testom reakcije lančane polimerazicaje (PCR). Ukupno je bilo 90 ispitanika koji su izabrani nasumično prilikom posete izabranom lekaru zbog drugih razloga. Starosna dob ispitanika bila je 24–76 godina. Ispitanici su anketirani pomoću upitnika u drugoj polovini 2023. godine. Svi ispitanici su potpisali informisani pristanak za učešće u istraživanju. Protokol studije odobrio je Etički odbor Doma zdravlja „Novi Beograd“.

Dizajn upitnika

Upitnik se sastojao iz tri celine. Prva celina obuhvatila je starost i pol ispitanika, vrednost BMI, pušački status, podatak o zdravstvenom stanju pre COVID infekcije i statusu hroničnih bolesti, kao i podatke vezane za COVID infekciju (datum potvrđivanja COVID infekcije, potreba za hospitalizacijom i uzrok hospitalizacije, potreba za kiseoničnom i antivirusnom

fluctuating in nature and their appearance varies over time. There is no defining pattern of the evolution of symptoms, and patients usually react to different stimuli, mainly physical or mental activity and stress[5].

The publication by Italian and American authors discusses the current understanding of the long-term effects of COVID-19 up to 2023, highlighting the potential future risks. When the RNA of the SARS-CoV-2 virus is reversly transcribed and integrates into the genome of infected human cells, it can affect gene expression and may lead to reactivation months or years later, with consequences that are still not fully understood[15].

A meta-analysis revealed that nearly 30% of participants experienced post-COVID symptoms two years after the acute phase[16]. There is literature suggesting that the use of oral antivirals reduces the risk of post-COVID syndrome. However, large, randomized clinical trials are needed to confirm this. It is presumed that vaccination plays a protective role in preventing post-COVID syndrome and reduces the risk of severe forms of COVID-19[18].

Objective

Our goal was to verify and investigate the long-term effects of post-COVID syndrome. We aimed to determine the prevalence of individual symptoms and to assess the impact of factors such as old age, smoking status, presence of other health conditions, and body mass index (BMI) on the occurrence of post-COVID syndrome.

Method

Study design

This study was conducted among patients of the Primary Healthcare Center (PHC) “Novi Beograd” who were diagnosed with COVID infection, from April 1, 2020, to December 31, 2022. COVID-19 was confirmed in each participant through a rapid antigen test or polymerase chain reaction (PCR) test. A total of 90 patients were randomly selected during their regular visit to a general practitioner for other reasons. The participants’ ages ranged from 24 to 76. They were interviewed using a questionnaire in the latter part of 2023, and all of them provided informed consent to participate in the study. The study protocol was approved by the Ethical Board of PHC “Novi Beograd.”

Questionnaire design

The questionnaire had three parts. The first part collected information on participants’ age, gender, BMI, smoking status, pre-existing health conditions, and details about their COVID infection (confirmation time, need for hospitaliza-

terapijom, vakcinalni status protiv COVID-19, kao i vrsta vakcine i podatak o obolevanju nakon vakcinacije). Druga celina obuhvatila je izjašnjavanje o prisutnosti simptoma tri meseca nakon COVID infekcije, odnosno post-COVID sindromu. Ponuđeno je 29 simptoma, a za svaki je bilo potrebno dodeliti ocenu o njihovoj prisutnosti od 1 do 5. Dodeljene ocene imaju sledeće karakteristike: 1 = nikada, 2 = ponekad /1 mesečno ili ređe/, 3 = redovno /nekoliko puta mesečno/, 4 = često /jednom nedeljno ili češće/, 5 = uvek /skoro svaki dan/. Bili su ponuđeni sledeći simptomi: brzo zamaranje, hronični umor, bol u mišićima, bol u zglobovima, gubitak u telesnoj težini, pojačano znojenje, otežano disanje/nedostatak daha, kašalj, bol u grudima, lupanje srca, mučnina, nesanica, poremećaj sna (pospanost/preterano spavanje), noćne more, glavobolja, zujanje u ušima, poremećaj osećaja čula mirisa, poremećaj osećaja čula ukusa, smanjeno raspoloženje, osećaj napetosti/teskobe/strepnje, slabije pamćenje, smanjena koncentracija, pojačano opadanje kose, pojava ospe po telu, bol u stomaku, tečne stolice, zatvor, nekontrolisano mokrenje, problemi u seksualnoj aktivnosti. Treća celina obuhvatila je dva pitanja - trajanje simptoma, kao i navođenje tegobe koja je najduže trajala.

Statistička analiza

Za analizu prikupljenih podataka korišćen je statistički paket za društvene nauke (SPSS, verzija 26.0). Kolmogorov-Smirnov test je korišćen za ispitivanje normalnosti raspodele podataka. Podaci su analizirani deskriptivnom statistikom, a kategorijalne varijable su predstavljene kao frekvencije (učestalosti) i izražene su u procentima. Za utvrđivanje razlike između varijabli od značaja korišćen je Kruskal-Wallis test. U svrhu post-hoc testiranja, primenjen je Bonferonijev test višestrukih poređenja parova. Statistički značajnom se smatrala p vrednost < 0,05. Dobijeni rezultati su prikazani tabelarno i grafički.

Rezultati

Ukupno 90 ispitanika anketirano je za ovo istraživanje. Karakteristike ispitanika (godine života, pol, BMI, pušenje, komorbiditeti) prikazani su u tabeli 1. Ispitanici su bili starosti od 24 do 76 godina, od kojih je 51 (56,7%) bilo ženskog pola, a 39 (43,3%) muškog pola. Zastupljenost normalno uhranjenih i sa prekomernom telesnom težinom bila je slična (38,9% i 40%, redom), dok je jedna petina ispitanika bila gojazna. Nikada nije pušilo cigarete 45,6% ispitanika, dok su 18,9% bili aktivni pušači. Bez komorbiditeta bilo je 53,3% ispitanika, dok je hipertenzija bila zastupljena kod 22,2% ispitanika, astma/HOBP kod 5,6%, diabetes mellitus kod 2,2%, a istovremeno prisustvo dve ili tri navedene bolesti (hipertenzija, astma/HOBP, diabetes mellitus) registrovano je kod 8,9% ispitanika. Druge hronične bolesti su registrovane kod 7,8% ispitanika.

tion and reason, oxygen and antiviral therapy requirement, COVID-19 vaccination status, type of vaccine received, and any subsequent COVID infections after vaccination). The second part gathered data on symptoms experienced three months after the initial COVID infection, specifically related to post-COVID syndrome. We provided a list of 29 symptoms, and for each one, it was necessary to rate its presence on a scale from 1 to 5. The ratings were as follows: 1 = never, 2 = sometimes/once a month or less, 3 = regularly/several times a month, 4 = often/once a week or more, 5 = always/almost every day. The symptoms included rapid fatigue, chronic fatigue, muscle pain, joint pain, weight loss, excessive sweating, difficulty breathing/breathlessness, cough, chest pain, heart palpitations, nausea, insomnia, sleep disorders (sleepiness/excessive sleeping), nightmares, headache, tinnitus, taste and smell disorder, low mood, the feeling of anxiety/distress/dread, poor memory, low concentration, increased hair loss, the appearance of body rash, abdominal pain, liquid stools, constipation, uncontrolled urination, and sexual activity dysfunction. The third part included two questions – symptom duration and stating the symptom that lasted the longest.

Statistical analysis

We used the Statistical Package for the Social Sciences (SPSS, version 26.0) for data analysis. The Kolmogorov-Smirnov test was used to examine the normality of data distribution. Data were analyzed using descriptive statistics, and categorical variables were presented as frequencies and percentages. We utilized the Kruskal-Wallis test to establish differences between the variables of importance. For post-hoc testing, we applied the Bonferroni test for multiple pair comparisons. A p-value of < 0.05 was considered statistically significant. The results were presented in tables and figures.

Results

In this research, a total of 90 participants were surveyed. The participants' characteristics including age, gender, BMI, smoking, and comorbidities are presented in Table 1. The age of the participants ranged from 24 to 76 years. Among the participants, 51 (56.7%) were females and 39 (43.3%) were males. The incidence of normal body weight and overweight participants was similar (38.9% and 40% respectively), while one-fifth of the participants were obese. Among the participants, 45.6% had never smoked, while 18.9% were active smokers. Additionally, 53.3% of the participants did not have any comorbidities, 22.2% had hypertension, 5.6% had asthma/COPD, 2.2% had diabetes mellitus, and 8.9% had a simultaneous presence of two or three of the mentioned diseases. Other chronic diseases were reported in 7.8% of the participants.

Tabela 1. Karakteristike ispitanika
Table 1. Participants' characteristics

Karakteristike ispitanika / Participants' characteristics	**N (%)**
Godine života / Age	
24–35	16 (17,8)
36–45	15 (16,7)
46–55	15 (21,1)
56–65	17 (18,9)
66–76	23 (25,6)
Pol / Gender	
ženski / female	51 (56,7)
muški / male	39 (43,3)
BMI (kg/m2)	
<18,5	1 (1,1)
18,5–24,9	35 (38,9)
25,0–29,9	36 (40,0)
≥30,0	18 (20,0)
Pušenje / Smoking	
ne / no	41 (45,6)
ne, u poslednjih 5 godina / not in the last 5 years	19 (21,1)
povremeno / sometimes	8 (8,9)
svakodnevno / daily	17 (18,9)
elektronske cigarete / electronic cigarettes	5 (5,6)
Komorbiditeti / Comorbidities	
bez / without	48 (53,3)
hipertenzija / hypertension	20 (22,2)
astma; HOBP / asthma; COPD	5 (5,6)
dijabetes melitus / diabetes mellitus	2 (2,2)
2 ili više iznad navedenih / 2 or more of the above-mentioned	8 (8,9)
drugi / others	7 (7,8)

Podaci vezani za vakcinaciju protiv SARS-CoV-2, kao i hospitalizaciju i terapiju tokom COVID infekcije prikazani su u tabeli 2. Vakcinisanih protiv virusa bilo je 66 ispitanika (73,3%), dok je pre zaražavanja virusom bilo vakcinisano njih 47 (52,2%). Tokom infekcije virusom osam ispitanika (8,9%) je bilo hospitalizovano, dok je na kiseoničnoj terapiji bilo četiri ispitanika (4,4%). Antivirusnu terapiju dobijalo je 34 ispitanika (37,8%).

The data regarding vaccination against SARS-CoV-2, hospitalization, and therapy during COVID infection are presented in table 2. Out of the total participants, 66 (73.3%) were vaccinated against SARS-CoV-2, while before contracting the virus, 47 (52.2%) were vaccinated. During COVID infection, eight participants (8.9%) required hospitalization, and four (4.4%) needed oxygen therapy. Antiviral therapy was used by 34 participants (37.8%).

Tabela 2. Podaci vezani za SARS-CoV-2
Table 2. Data related to SARS-CoV-2

	N(%)
Vakcinacija protiv SARS-CoV-2 / Vaccination against SARS-CoV-2	
Ne / No	24 (26,7)
Da / Yes	66 (73,3)
Vakcinacija pre infekcije SARS-CoV-2 / Vaccination before SARS-CoV2	
Ne / No	43 (47,8)
Da / Yes	47 (52,2)
Hospitalizacija tokom infekcije SARS-CoV-2 / Hospitalization during SARS-CoV-2 infection	
Ne / No	82 (91,1)
Da / Yes	8 (8,9)
Kiseonična terapija tokom infekcije SARS-CoV-2 / Oxygen therapy during SARS-CoV-2 infection	
Ne / No	86 (95,6)
Da / Yes	4 (4,4)
Antivirusna terapija tokom infekcije SARS-CoV-2 / Antiviral therapy during SARS-CoV-2 infection	
Ne / No	56 (62,2)
Da / Yes	34 (37,8)

Prisustvo i trajanje post-COVID simptoma prikazano je u tabeli 3 (odnosi se na period nakon isteka tri meseca od utvrđivanja COVID infekcije). Ukupno 14 ispitanika (15,6%) nije imalo post-COVID simptome, pri čemu sedam muškaraca i sedam žena. Svi ostali ispitanici, njih 84,4% imali su dva ili više simptoma. Kod 28,9% ispitanika tegobe su trajale kraće od dva meseca, kod 31,1% trajale su duže od dva, a kraće od šest meseci, a kod 24,4% duže od šest meseci.

The table 3 shows the presence and duration of post-COVID symptoms three months after the confirmation of COVID infection. Out of the total participants, 14 (15.6%) reported having no post-COVID symptoms, with seven being males and seven females. The remaining 84.4% reported experiencing two or more symptoms. Specifically, 28.9% of participants experienced symptoms for less than two months, 31.1% for longer than two months but less than six months, and 24.4% for longer than six months.

Tabela 3. Prisustvo i trajanje post-COVID simptoma (podrazumeva se period nakon isteka tri meseca od utvrđivanja COVID infekcije)
Table 3. Presence and duration of post-COVID symptoms (pertains to the period three months following the confirmation of COVID infection)

Prisustvo i trajanje post-covid simptoma / Presence and duration of post-covid symtoms	**N (%)**
Nisu bili prisutni post-covid simptomi / Not present post-covid symptoms	14 (15,6)
Bili su prisutni i trajali su kraće od 2 meseca / They were present and lasted less than 2 months	26 (28,9)
Bili su prisutni i trajali su od 2 do 6 meseci / They were present and lasted 2 to 6 months	28 (31,1)
Bili su prisutni i trajali su duže od 6 meseci / They were present and lasted more than 6 months	22 (24,4)

Učestalost pojedinačnih post-COVID simptoma kod ispitanika u našem istraživanju prikazani su u tabeli 4. Tegobe koje su bile najviše zastupljene su brzo zamaranje (60%), hronični umor (53,3%), smanjena koncentracija (45,6 %), mijalgija (41,1%), slabije pamćenje (40%), tahikardija (38,8%), nesanica (38,8%), znojenje (35,6%), dispneja (34,4%), kašalj (34,4%), artralgije (33,3%), smanjeno raspoloženje (32,2%), anksioznost (32,2%), pospanost (30%).

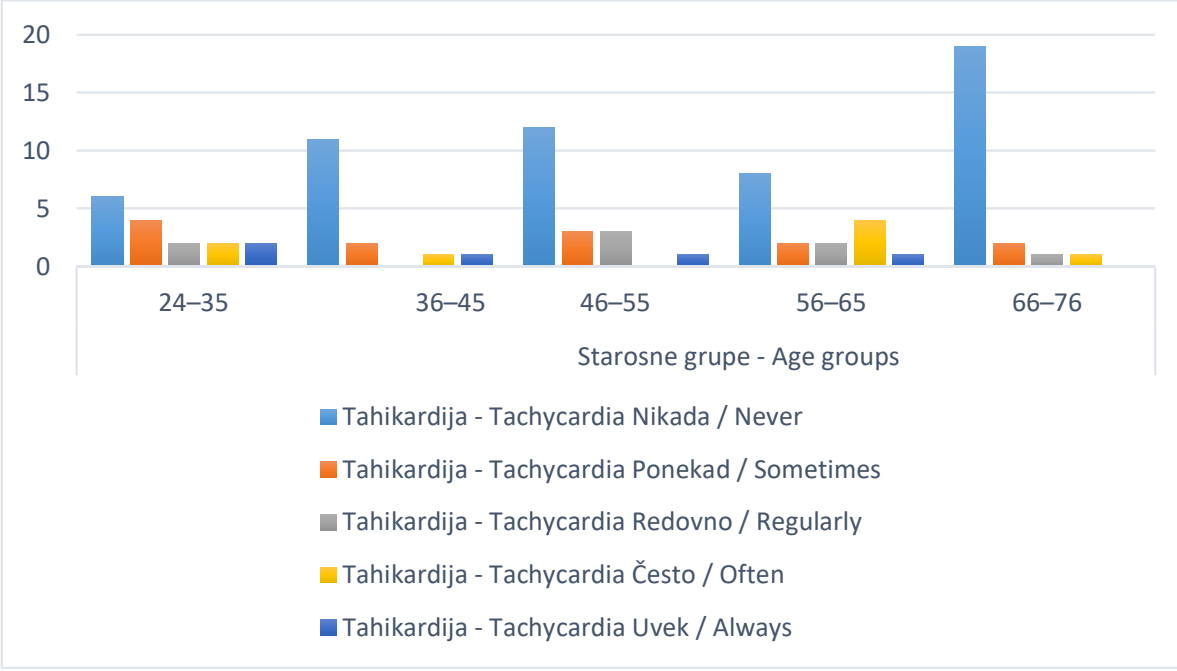
The table 4 presents the occurrence of individual post-COVID symptoms in our participants. The most frequent symptoms reported were rapid fatigue (60%), chronic fatigue (53.3%), decreased concentration (45.6%), muscle pain (41.1%), impaired memory (40%), rapid heartbeat (38.8%), insomnia (38.8%), sweating (35.6%), shortness of breath (34.4%), cough (34.4%), joint pain (33.3%), low mood (32.2%), anxiety (32.2%), and drowsiness (30%).

Tabela 4. Učestalost post-COVID simptoma
Table 4. Incidence of post-COVID symptoms

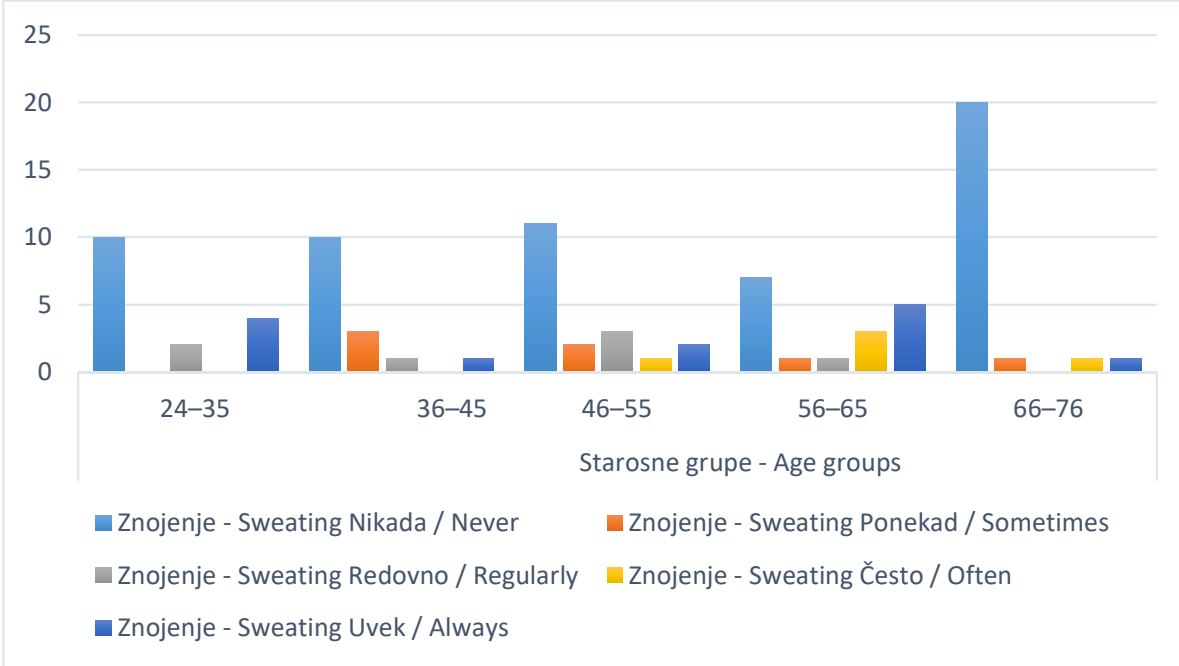
Post-covid simptomi / Post-covid symptoms	**N (%)**				
	Nikada / Never	**Ponekad / Sometimes**	**Redovno / Regularly**	**Često / Often**	**Uvek / Always**
brzo zamaranje / rapid fatigue	36 (40,0)	15 (16,7)	9 (10,0)	8 (8,9)	22 (24,4)
hronični umor / chronic fatigue	42 (46,7)	16 (17,8)	10 (11,1)	7 (7,8)	15 (16,7)
mijalgija / myalgia	53 (58,9)	8 (8,9)	14 (15,6)	6 (6,7)	9 (10,0)
artralgije / arthralgia	60 (66,7)	10 (11,1)	8 (8,9)	5 (5,6)	7 (7,8)
gubitak telesne težine / weight loss	76 (84,4)	7 (7,8)	3 (3,3)	2 (2,2)	2 (2,2)
znojenje / sweating	58 (64,4)	7 (7,8)	7 (7,8)	5 (5,6)	13 (14,4)
dispneja / dyspnea	59 (65,6)	12 (13,3)	4 (4,4)	6 (6,7)	9 (10)
kašalj / cough	59 (65,6)	12 (13,3)	4 (4,4)	6 (6,7)	9 (10)
bol u grudima / chest pain	67 (74,4)	12 (13,3)	7 (7,8)	2 (2,2)	2 (2,2)
tahikardija / tachycardia	56 (62,2)	13 (14,4)	8 (8,9)	8 (8,9)	5 (5,6)
mučnina / nausea	74 (82,2)	7 (7,8)	6 (6,7)	1 (1,1)	2 (2,2)
nesanica / insomnia	56 (62,2)	7 (7,8)	12 (13,3)	8 (8,9)	7 (7,8)
pospanost / drowsiness	63 (70,0)	10 (11,1)	7 (7,8)	4 (4,4)	6 (6,7)
noćne more / nightmares	76 (84,4)	8 (8,9)	1 (1,1)	2 (2,2)	3 (3,3)
glavobolja / headache	58 (64,4)	14 (15,6)	9 (10,0)	4 (4,4)	5 (5,6)
tinitus / tinnitus	70 (77,8)	6 (6,7)	7 (7,8)	1 (1,1)	6 (6,7)
poremećaj čula mirisa / sense of smell disorder	70 (77,8)	8 (8,9)	4 (4,4)	2 (2,2)	6 (6,7)
poremećaj čula ukusa / sense of taste disorder	73 (81,1)	7 (7,8)	4 (4,4)	2 (2,2)	4 (4,4)
smanjeno raspoloženje / poor mood	61 (67,8)	12 (13,3)	5 (5,6)	5 (5,6)	7 (7,8)
anksioznost / anxiety	61 (67,8)	11 (12,2)	5 (5,6)	6 (6,7)	7 (7,8)
slabije pamćenje / bad memory	54 (60,0)	21 (23,3)	6 (6,7)	3 (3,3)	6 (6,7)
smanjena koncentracija / low concentrtion	49 (54,4)	19 (21,1)	13 (14,4)	3 (3,3)	6 (6,7)
pojačano opadanje kose / increased hair loss	69 (76,7)	6 (6,7)	2 (2,2)	2 (2,2)	11 (12,2)
ospa / rash	85 (94,4)	2 (2,2)	1 (1,1)	1 (1,1)	1 (1,1)
abdominalna bol / abdominal pain	78 (86,7)	9 (10,0)	3 (3,3)	0 (0,0)	0 (0,0)
dijareja / diarrhea	77 (85,6)	7 (7,8)	4 (4,4)	1 (1,1)	1 (1,1)
opstipacija / opstipation	81 (90,0)	6 (6,7)	3 (3,3)	0 (0,0)	0 (0,0)
nekontrolisano mokrenje / uncontrolled urination	82 (91,1)	5 (5,6)	1 (1,1)	0 (0,0)	2 (2,2)
poremećaj seksualne funkcije / sexual function disorder	81 (90,0)	4 (4,4)	2 (2,2)	2 (2,2)	1 (1,1)

U odnosu na prisustvo pojedinačnih post-COVID tegoba u definisanim starosnim grupama, postojala je statistički značajna razlika za sledeće tegobe: za tahikardiju (između starosnih grupa 24–35 godina i 66–76 godina (p=0,044)), za znojenje (između starosnih grupa 56–65 godina i 66–76 godina (p=0,016)), za opstipaciju (između starosne grupe 56–65 godina u poređenju sa starosnim grupama 66–76, 36–45 i 24–35 godina (p=0,002, p=0,008, p=0,046, redom)) (Grafikoni 1–3).

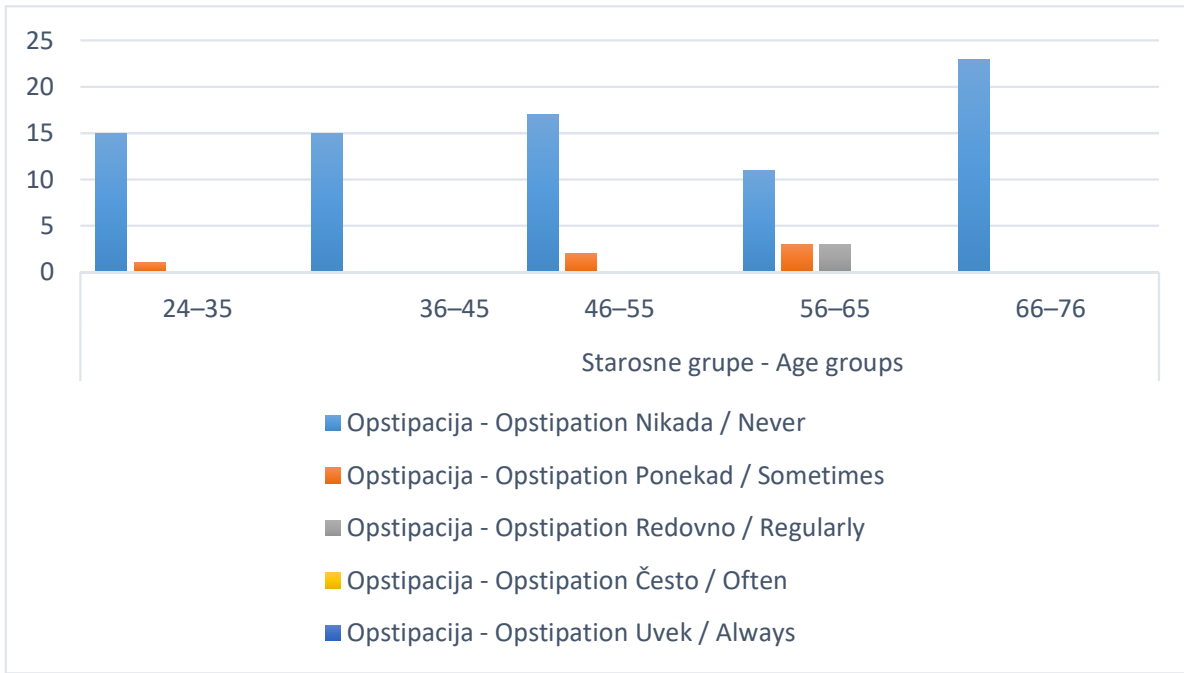
There were statistically significant differences in the presence of certain post-COVID symptoms among different age groups. These include tachycardia (p=0.044) between the age groups 24–35 and 66–76, sweating (p=0.016) between the age groups 56–65 and 66–76, and constipation (p=0.002, p=0.008, p=0.046) between the age groups 56–65 and 66–76, 36–45, and 24–35, respectively (Figures 1–3).



Grafikon 1. Pojava tahikardije u definisanim starosnim grupama
Figure 1. Tachycardia occurrence across age groups



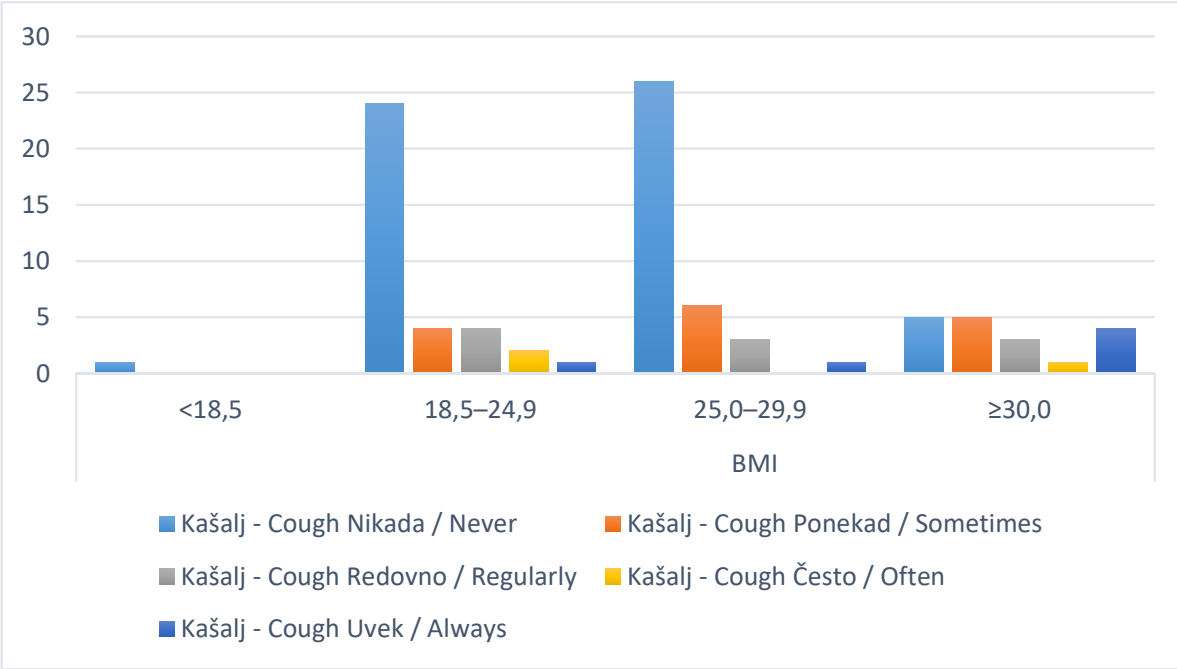
Grafikon 2. Pojava znojenja u definisanim starosnim grupama
Figure 2: Sweating frequency across age groups



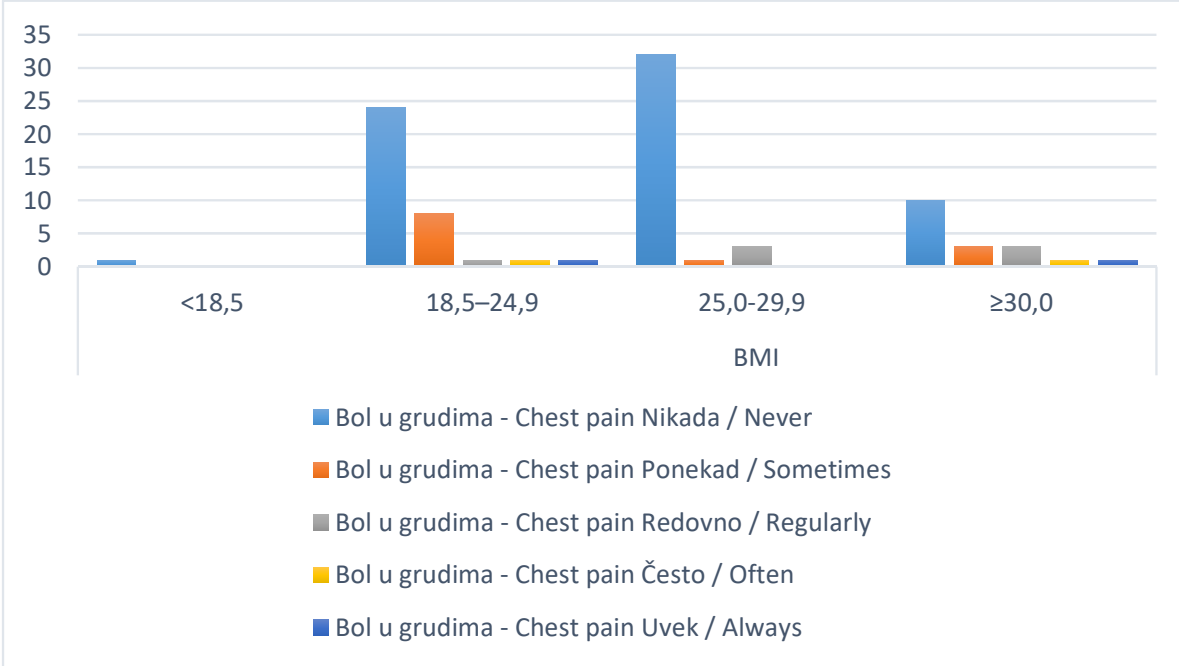
Grafikon 3. Pojava opstipacije u definisanim starosnim grupama
Figure 3: Constipation prevalence across age groups

Kod ispitanika koji su gojazni (BMI ≥ 30) u odnosu na BMI 18,5–24,9 i 25,0–29,9, pronađena je statistički značajna razlika za prisustvo kašlja (p=0,017, p=0,004, redom). Takođe, za prisustvo bola u grudima i opstipacije postojala je statistički značajna razlika između ispitanika sa BMI ≥ 30 i ispitanika sa BMI 25,0–29,9 (p=0,04, p=0,027, redom), kao i za poremećaj seksualne funkcije između ispitanika sa BMI ≥ 30 i ispitanika sa BMI 18,5–24,9 (p=0,009) (Grafikoni 4–7).

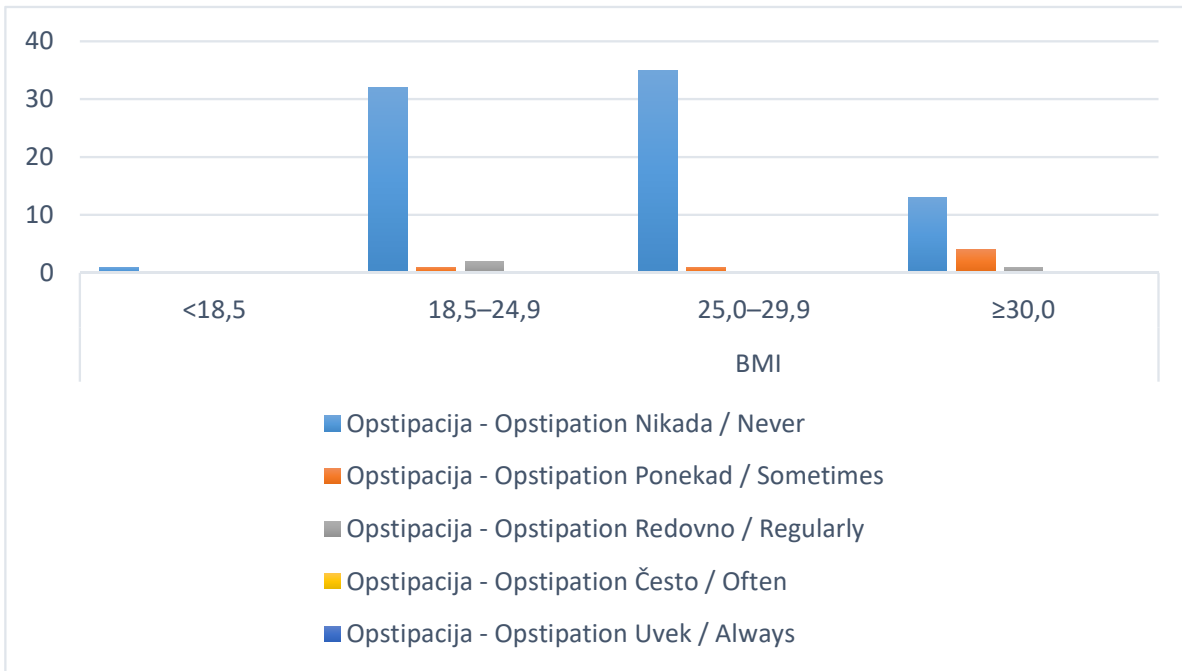
In the study, we observed statistically significant differences in symptoms between obese participants (BMI ≥ 30) and those with lower BMIs. Specifically, we found that cough showed significant differences compared to BMIs of 18.5–24.9 (p=0.017) and 25.0–29.9 (p=0.004). Additionally, there were significant differences in chest pain and constipation between participants with BMI ≥ 30 and those with a BMI of 25.0–29.9 (p=0.04, p=0.027, respectively). Moreover, sexual function disorders differed significantly when comparing participants with BMI ≥ 30 and those with a BMI of 18.5–24.9 (p=0.009) (Figures 4–7).



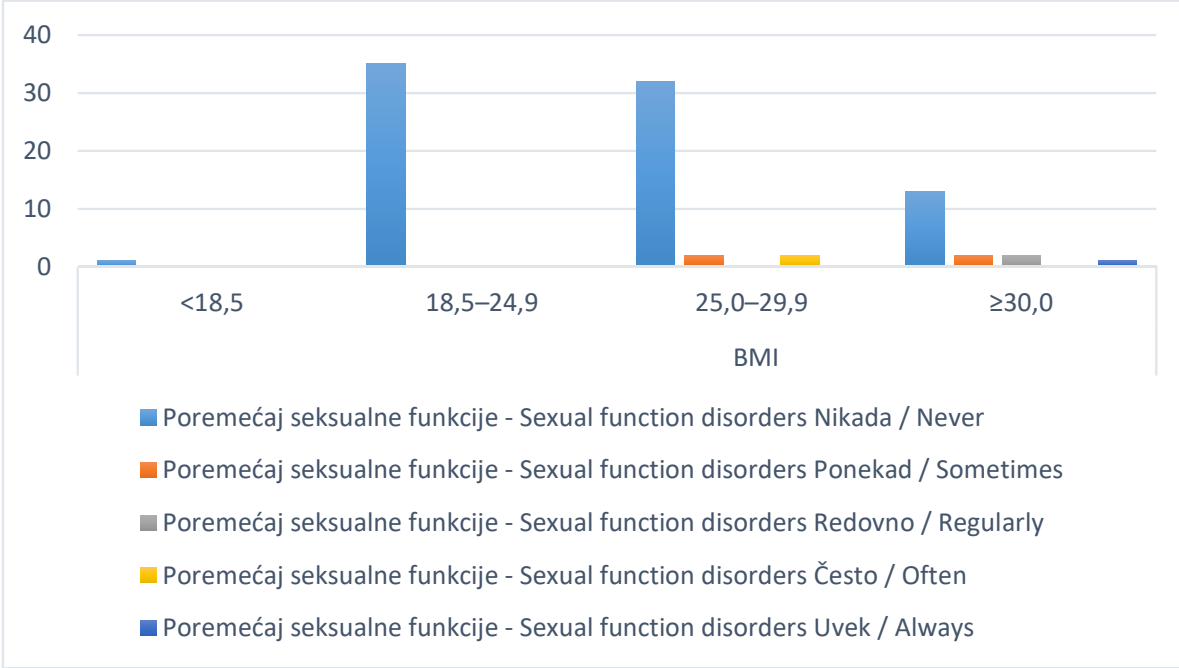
Grafikon 4. Pojava kašlja u zavisnosti od vrednosti BMI
Figure 4: Cough occurrence based on BMI



Grafikon 5. Pojava bola u grudima u zavisnosti od vrednosti BMI
Figure 5: Chest pain occurrence based on BMI



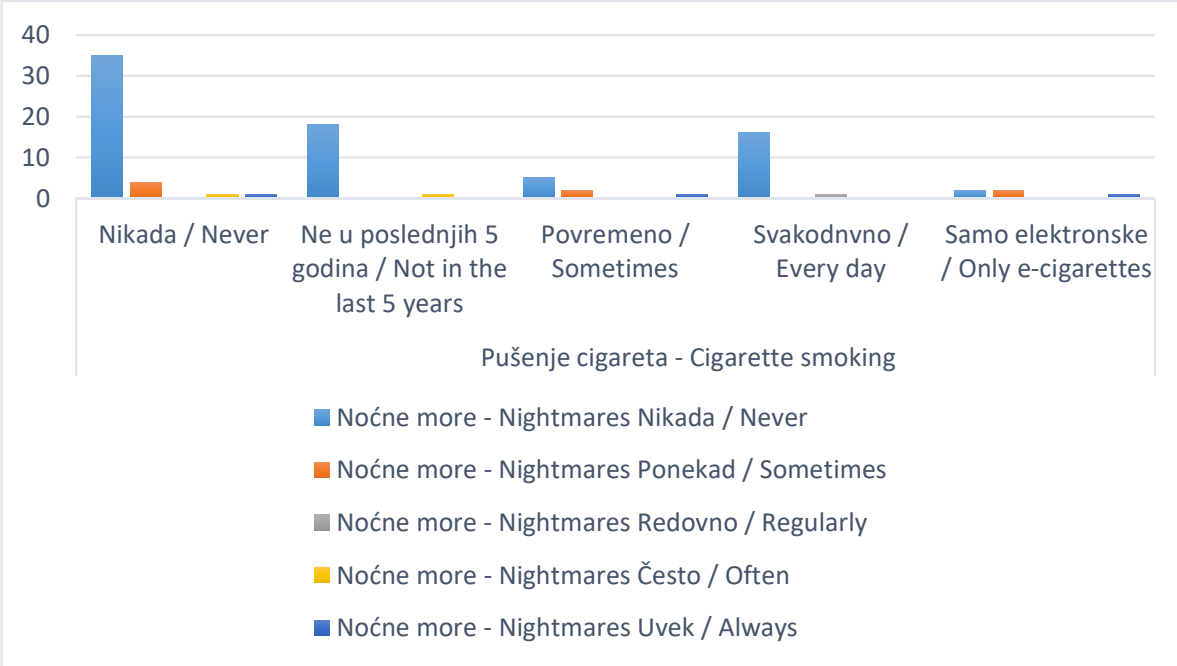
Grafikon 6. Pojava opstipacije u zavisnosti od vrednosti BMI
Figure 6: Constipation occurrence based on BMI



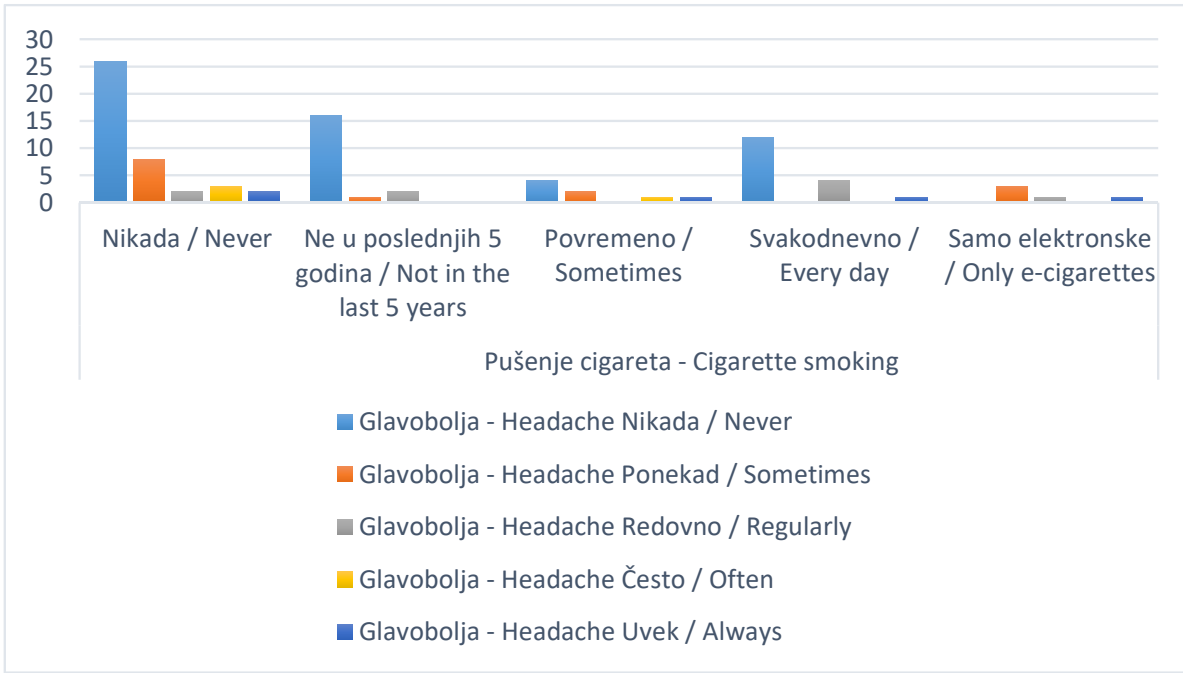
Grafikon 7. Poremećaj seksualne aktivnosti u zavisnosti od vrednosti BMI
Figure 7: Sexual dysfunction based on BMI

U zavisnosti od pušačkog statusa, zabeležena je statistički značajna razlika za pojavu noćnih mora kod ispitanika koji puše samo elektronske cigarete u odnosu na ispitanike koji ne puše u poslednjih pet godina i u odnosu na ispitanike koji puše svakodnevno (p=0,032, p=0,039, redom). Za pojavu glavobolje je postojala statistički značajna razlika za ispitanike koji ne puše u poslednjih pet godina i kod onih koji puše samo elektronske cigarete (p=0,013). Za pojavu anksioznosti postojala je statistički značajna razlika za ispitanike koji puše samo elektronske cigarete u odnosu na nepušače (p=0,002), u odnosu na nepušače u poslednjih pet godina (p=0,007) i u odnosu na one koji puše svakodnevno (p=0,050). Za bol u stomaku postojala je statistički značajna razlika za ispitanike koji puše elektronske cigarete u odnosu na nepušače (p=0,018), kao i u odnosu na nepušače u poslednjih pet godina (p=0,021). Za pojavu dijareje je postojala statistički značajna razlika između između nepušača i pušača (p=0,035) (Grafikoni 8–12).

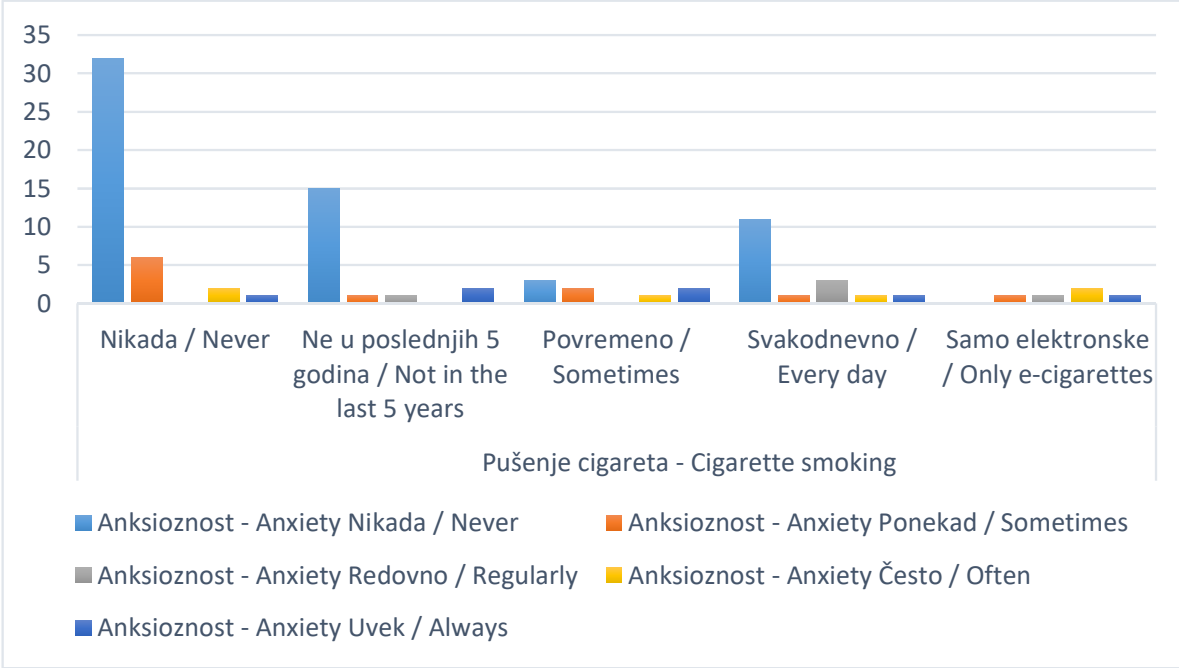
In our study, we observed significant differences in the occurrence of nightmares, headaches, anxiety, abdominal pain, and diarrhea based on smoking status. Specifically, we found that participants who only smoke e-cigarettes had a higher occurrence of nightmares compared to those who haven't smoked in the last five years and those who smoke every day (p=0.032, p=0.039, respectively). Additionally, we observed a statistically significant difference in the occurrence of headaches between those who haven't smoked in the last five years and those who only smoke e-cigarettes (p=0.013). Furthermore, we found that anxiety occurrence was significantly different between those who smoke only e-cigarettes and non-smokers (p=0.002), non-smokers in the last five years (p=0.007), and everyday smokers (p=0.050). In the case of abdominal pain, we observed a statistically significant difference between e-cigarette smokers and non-smokers (p=0.018), as well as between e-cigarette smokers and non-smokers in the last five years (p=0.021). Finally, we found a significant difference in the occurrence of diarrhea when comparing non-smokers and smokers (p=0.035) (Figures 8–12).



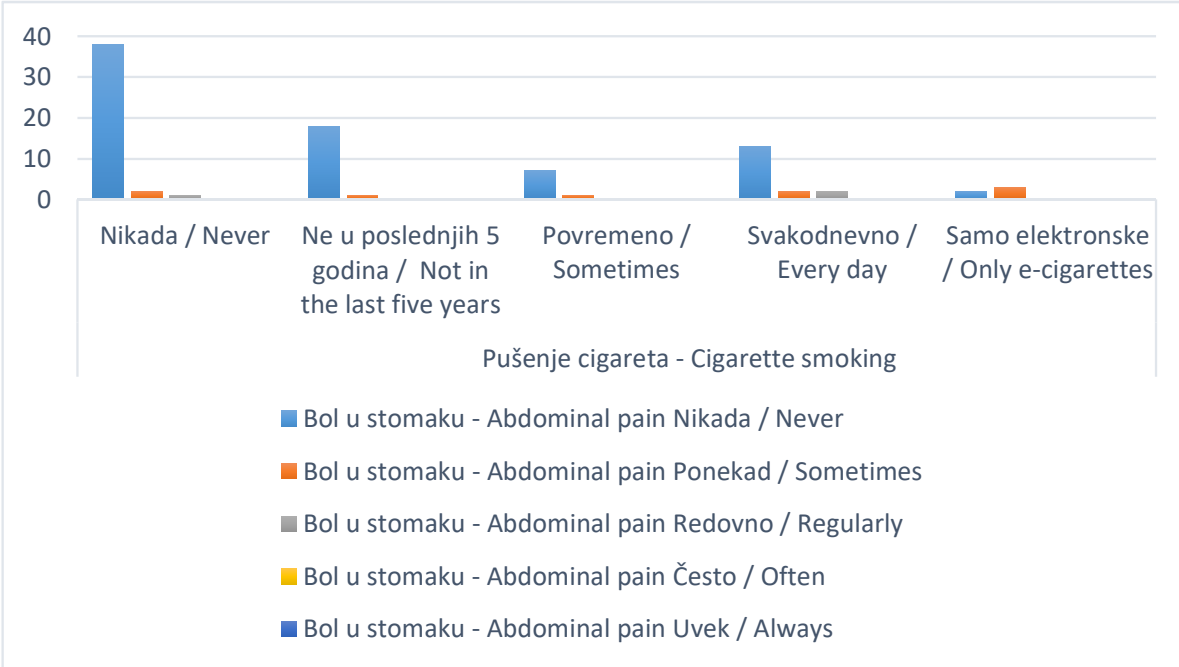
Grafikon 8. Pojava noćnih mora u zavisnosti od pušačkog statusa
Figure 8. The occurrence of nightmares depending on smoking status



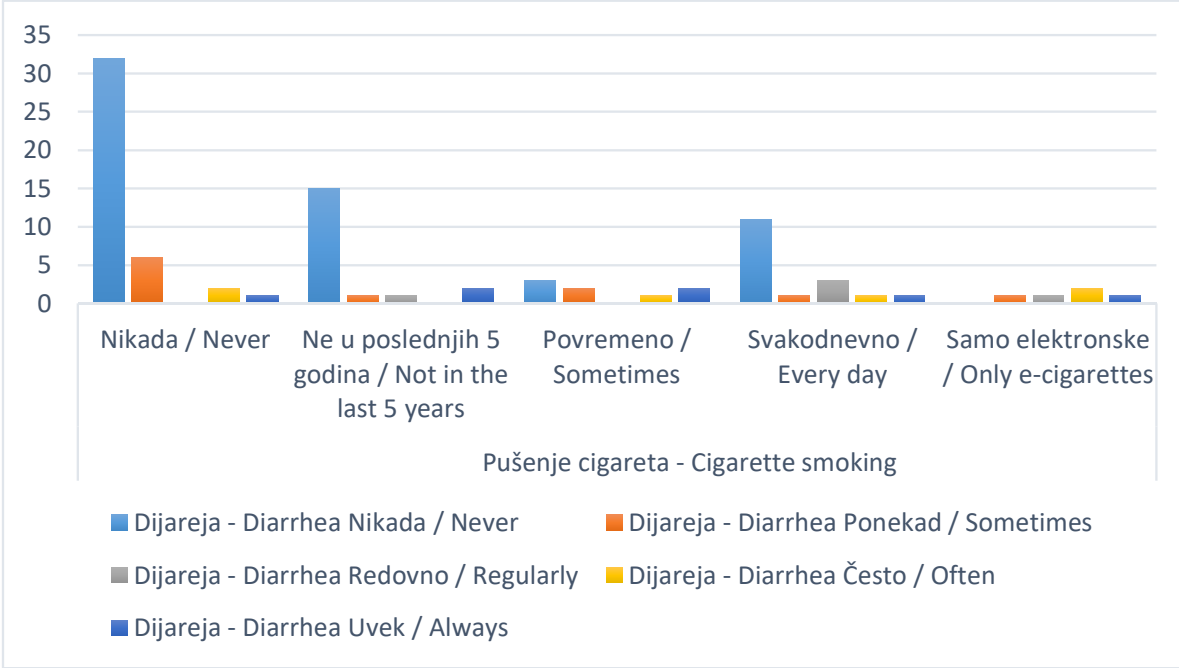
Grafikon 9. Pojava glavobolje u zavisnosti od pušačkog statusa
Figure 9. The occurrence of headache depending on smoking status



Grafikon 10. Pojava anksioznosti u zavisnosti od pušačkog statusa
Figure 10. The occurrence of anxiety depending on smoking status



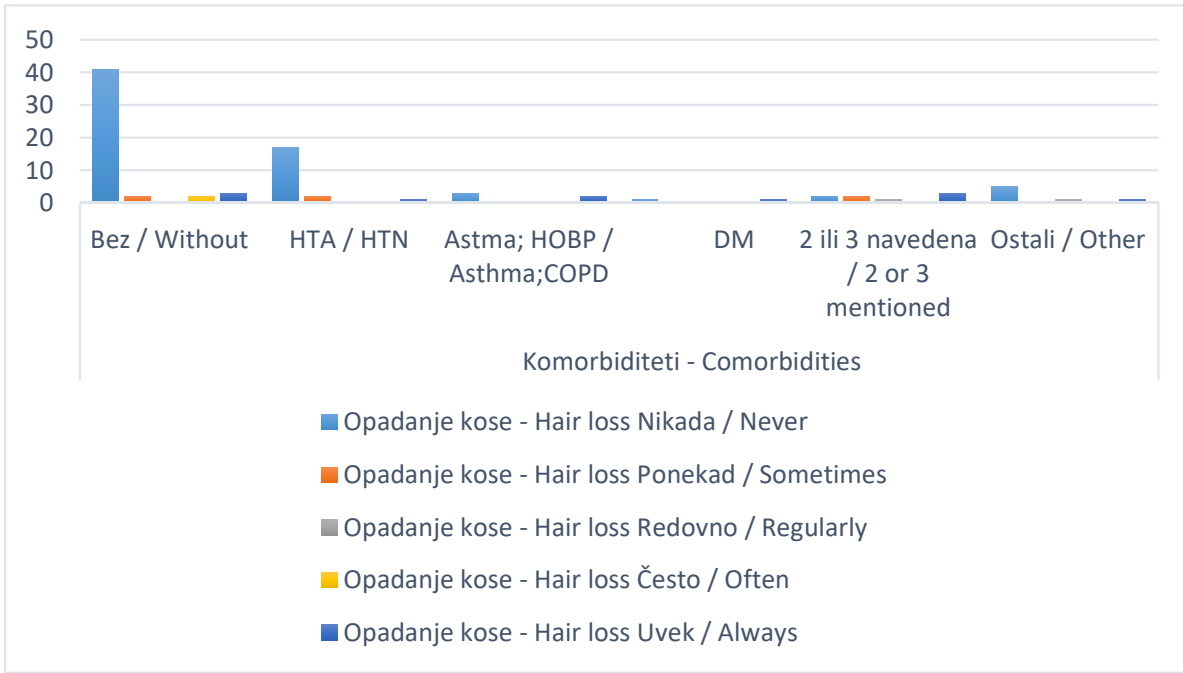
Grafikon 11. Pojava bola u stomaku u zavisnosti od pušačkog statusa
Figure 11. The occurrence of abdominal pain depending on smoking status



Grafikon 12. Pojava dijareje u zavisnosti od pušačkog statusa
Figure 12. The occurrence of diarrhea depending on smoking status

U odnosu na prisustvo komorbiditeta, postojala je statistički značajna razlika za opadanje kose kod ispitanika sa prisustvom dva ili tri sledeća komorbiditeta: HTA, DM, astma/HOBP, u odnosu na ispitanike sa prisustvom samo HTA (p=0,012), kao i u odnosu na ispitanike bez komorbiditeta (p=0,004) (Grafikon 13).

In terms of comorbidities, there was a statistically significant difference in hair loss between participants with two or three comorbidities (hypertension, diabetes mellitus, asthma/COPD) compared to those with only hypertension (p=0.012) as well as those without comorbidities (p=0.004) (see Figure 13).



Grafikon 13. Opadanje kose u zavisnosti od prisustva koomorbiditeta
Figure 13. Hair loss in relation to the presence of comorbidities

Diskusija

U našem uzorku 37,8% ispitanika je koristilo antivirusnu terapiju tokom infekcije SARS-CoV-2, dok je približno tri četvrtine ispitanika bilo vakcinisano protiv virusa. S obzirom da je približno polovina naših ispitanika vakcinisana nakon zaražavanja SARS-CoV-2, nije ispitivan uticaj vakcinalnog statusa za nastanak post-COVID. Potrebu za hospitalizacijom je imalo 8,9% ispitanika, a polovini od njih je bila neophodna terapija kiseonikom, što je znatno manje od podatka iz literature gde se navodi da približno oko 20% pacijenata obolelih od COVID-19 razvija hipoksiju[19]. Vodeći komorbiditet je bio hipertenzija (22,2%), što je i očekivano s obzirom da je zastupljenost u opštoj populaciji 34,5%[20]. Najviše je bilo ispitanika starosti od 66 do 76 godina, približno jedna četvrtina od ukupnog broja. Kod starije populacije post-COVID je u određenoj meri zanemaren, jer simptomi mogu biti maskirani ili pripisani postojećim hroničnim bolestima što značajno pogoršava kvalitet života i ima za posledicu dekondicioniranost kod ovih osoba[21]. Interesantno, u našem istraživanju post-COVID tegobe kao što su znojenje, tahikardija, opstipacija su bile manje zastupljene u populaciji starijoj od 66 godina. U skladu sa tim, treba posebno obratiti pažnju i na mlađe osobe sa određenim simptomima, a koje su pre COVID infekcije bile zdrave.

Približno četvrtina naših ispitanika je imala post-COVID tegobe koje su trajale duže od šest meseci, dok su post-COVID simptomi prijavljeni od izuzetno velikog broja ispitanika (84,4%). Slično je zabeleženo i u istraživanju sprovedenom na Filipinima kod kojih je prevalencija post-COVID iznosila 71,4%[22]. Međutim, najčešći podatak u literaturi koji se odnosi na prevalenciju post-COVID je u opsegu od 10% do 30%[9]. Simptomi u post-COVID su obično udruženi i smatra se da 80% pacijenata ima više od jednog simptoma, što je u skladu i sa našim rezultatima[5]. Uporedili smo naše rezultate sa rezultatima meta-analize koja je obuhvatila 21 istraživanje, od čega je 10 studija bilo iz Evrope[23]. Post-COVID simptomi koji su imali sličnu distribuciju kao u našem istraživanju bili su: hronični umor, slabije pamćenje/demencija, pojava ospe i pojačano opadanje kose, dok su kod naših ispitanika bili učestaliji sledeći simptomi: znojenje, dispneja, kašalj, anksioznost, nesanica, tinitus, bol u grudima, gubitak telesne težine, poremećaj čula mirisa i ukusa, artralgije, mijalgije, smanjeno raspoloženje[23]. Rezultati našeg istraživanja sugerišu da su brzo zamaranje, hronični umor, mijalgija, slabije pamćenje i smanjena koncentracija najučestalije post-COVID tegobe što je u skladu sa podacima iz literature[5,22,24,25]. Meta-analiza u kojoj su analizirane publikacije iz 2020. godine i prve polovine 2021. godine, identifikovala je hronični umor i kognitivno oštećenje kao najučestalije post-COVID tegobe, sa sličnom zastupljenošću i kod hospitalizovanih i nehospitalizovanih pacijenata[26]. Sindrom hroničnog umora uključuje više patofizioloških mehanizama, a jedna od hipoteza je da je umor

Discussion

In our sample, 37.8% of the participants used antiviral therapy during SARS-CoV-2 infection, while approximately three-quarters were vaccinated against the virus. Considering that almost half of our participants were vaccinated after contracting SARS-CoV-2, we haven't examined the influence of vaccination status on the occurrence of post-COVID. We found that 8.9% of the participants needed to be hospitalized, and half of them needed oxygen therapy, which is significantly lower than the literature data claiming that approximately 20% of COVID-19 patients developed hypoxia[19]. The most common comorbidity was hypertension (22.2%), which is expected given its incidence in the general population (34.5%)[20]. The majority of the participants were between 66 and 76 years of age, making up around a quarter of the total number. Post-COVID symptoms are often overlooked in older populations because they may be masked or attributed to existing chronic diseases, significantly worsening the quality of life and health conditions of these individuals[21]. Interestingly, in our research, post-COVID symptoms such as sweating, tachycardia, and constipation were less frequent in the group over 66. Therefore, we should pay closer attention to younger people with specific symptoms who were healthy before contracting COVID.

Approximately a quarter of our participants experienced post-COVID symptoms lasting longer than six months, with 84.4% reporting post-COVID symptoms. A similar study in the Philippines found a prevalence of 71.4% for post-COVID symptoms[22]. However, the literature generally cites a prevalence range of post-COVID symptoms from 10% to 30%[9]. Post-COVID symptoms often occur together, with around 80% of patients experiencing more than one symptom, which is in line with our results[5]. Our results align with a meta-analysis of 21 studies, 10 of which were from Europe[23]. Symptoms such as chronic fatigue, poor memory/dementia, rash occurrence, and increased hair loss were found to have a similar distribution in both our study and the meta-analysis. However, our participants reported more frequent symptoms including sweating, dyspnea, cough, anxiety, insomnia, tinnitus, chest pain, weight loss, taste and smell disorders, joint pain, muscle pain, and low mood[23]. The results of our research indicate that rapid fatigue, chronic fatigue, myalgia, poor memory, and low concentration are the most common post-COVID symptoms, which is in line with findings in the literature[5,22,24,25]. A meta-analysis of publications from 2020 to the first half of 2021 identified chronic fatigue and cognitive impairment as the most frequent post-COVID symptoms, with a similar incidence in hospitalized and non-hospitalized patients[26]. Chronic fatigue syndrome involves several pathophysiological mechanisms. One hypothesis is that fatigue results from mitochondrial structural changes and decreased energy production within muscle tissue[13]. Fatigue, along with

posledica promene u strukturi mitohondrija i proizvodnje energije unutar mišićnog tkiva[13]. Zajedno sa neurokognitivnim simptomima, umor ima veliki uticaj na ograničenje radne aktivnosti[5]. Takođe, poznato je da je dispneja česta tegoba u okviru post-COVID [27], što dokazuje i 34,4% ispitanika u našem uzorku sa ovom tegobom. Srčane manifestacije su takođe definisani poremećaj u okviru post-COVID[27], što je potvrđeno i našim istraživanjem s obzirom da je tahikardija bila prisutna kod 37,8% ispitanika, a bol u grudima kod 25,6% ispitanika.

Perzistentni post-COVID simptomi povezani su sa značajnim uticajem na mentalno zdravlje. U našem uzorku smanjeno raspoloženje i anksioznost prijavilo je 32,2% ispitanika, pospanost 30%, a nesanicu 38,8%. Slično sindromu hroničnog umora, etiologija i patofiziologija neuropsihijatrijskih simptoma (glavobolja, nesanica, anksioznost, depresija, poremećaj čula, poremećaj spavanja) u post-COVID su multifaktorijalni i još uvek nedovoljno razjašnjeni[24]. Aktuelnim terminom „moždana magla" uz širok spektar kliničkog ispoljavanja, opisuje se stanje umora i zaboravnosti/konfuznosti, a po rečima pacijenata predstavlja „osećaj kao da nisi sasvim svoj"[28]. Procena mentalnog zdravlja je važna u post-akutnoj fazi COVID-19, jer i dermatološki simptomi kao što su pojačano opadanje kose ili hiperhidroza mogu dovesti do emocionalnog distresa[23,29]. Trihoskopijom je potvrđena visoka prevalencija opadanja kose u post-COVID [30]. Kod naših ispitanika, opadanje kose značajnije više je registrovano kod osoba koje su imale dva ili tri komorbiditeta (HTA, DM, astma/DM). Rezultati meta-analize ukazuju da prisustvo komorbiditeta povećava rizik za razvoj post-COVID sindroma[18].

Poznato je da mukocilijarni epitel deluje kao primarna linija odbrane od patogena. Ova barijera je ugrožena kod pušača i čini ih podložnim infekcijama[31]. Pušenje/*vaping* indukuje oksidativni stres i inflamatorne odgovore koji mogu dodatno doprineti komplikacijama vezanim za COVID-19 kod pušača/vejpera. Brar i saradnici sugerišu da su adolescenti koji koriste elektronske cigarete podložniji za nastanak težih respiratornih simptoma ako razviju multisistemski inflamatorni sindrom (MIS-C) nakon obolevanja od COVID-19[31]. Smatra se da su tradicionalno pušenje cigareta, kao i korišćenje elektronskih cigareta faktori rizika za nastanak post-COVID tegoba[32]. U našem istraživanju pušački status je imao uticaj na razliku u ispoljavanju neuropsihijatrijske i gastrointestinalne patologije u sklopu post-COVID.

Iz literature je poznato da je viši BMI, prediktivni faktor za razvoj post-COVID-19 sindroma, a posebno u domenu kardiovaskularnih, pulmonalnih, gastrointestinalnih tegoba, kao i tegoba u vezi sa mentalnim zdravljem[33]. U ovom istraživanju vrednost BMI je imala uticaj na ispoljavanje simptoma kao što su kašalj, bol u grudima, opstipacija i poremećaj seksualne aktivnosti.

Nedostatak našeg istaživanja je nepostojanje reprezentativne kontrolne grupe. Dodatno ograničenje studije predstavlja činjenica da nismo bili u mogućnosti da procenimo uticaj vakcinacije na pojavu post-COVID sindroma.

neurocognitive symptoms, significantly impacts work performance[5]. It is widely known that dyspnea is the most common post-COVI DD[27], affecting 34.4% of the participants in our study. Cardiac symptoms are also prevalent in post-COVID syndrome[27], as evidenced by tachycardia in 37.8% and chest pain in 25.6% of our participants.

Persistent post-COVID symptoms have a significant impact on mental health. In our sample, 32.2% of participants reported low mood and anxiety, 30% reported drowsiness, and 38.8% reported insomnia. Similar to chronic fatigue syndrome, the causes and mechanisms of neuropsychiatric symptoms (such as headache, insomnia, anxiety, depression, sensory disorders, and sleep disturbances) in post-COVID cases are multifactorial and not yet fully understood[24]. The term "brain fog" encompasses a wide range of clinical symptoms and describes a state of fatigue and forgetfulness or confusion. Patients describe it as "feeling not like themselves"[28]. Assessing mental health during the post-acute phase of COVID-19 is important because dermatological symptoms such as excessive hair loss and hyperhidrosis can cause emotional distress[23,29]. Trichoscopy has confirmed a high prevalence of hair loss in post-COVID individuals[30]. In our study, we found that the incidence of hair loss was significantly higher in individuals with two or three comorbidities (such as hypertension, diabetes, asthma/COPD). The results of a meta-analysis indicated that having comorbidities posed a higher risk for developing post-COVID syndrome[18].

The mucociliary epithelium serves as the primary defense against pathogens. However, this barrier is compromised in smokers, making them more susceptible to infections[31]. Smoking and vaping lead to oxidative stress and inflammatory responses, which may further complicate COVID-19 infections in smokers and vapers. Research by Brar et al. suggests that adolescents who use e-cigarettes are more prone to severe respiratory symptoms, particularly if they develop multisystem inflammatory syndrome (MIS-C) after contracting COVID-19[31]. Traditional cigarette smoking and e-cigarette use are considered risk factors for post-COVID symptoms[32]. Our research indicates that smoking status influences the likelihood of experiencing neuropsychiatric and gastrointestinal issues as part of post-COVID complications.

Literature confirms that a higher BMI is a predictive factor for the development of post-COVID-19 syndrome, especially in the domains of cardiovascular, pulmonary, gastrointestinal symptoms, as well as those connected to mental health[33]. In our research, BMI influenced the appearance of symptoms such as cough, chest pain, constipation, and sexual activity disorders.

The flaw in our research is the absence of a representative control group. Another limitation is that we were unable to assess the influence of vaccination on the appearance of post-COVID syndrome.

Zaključak

S obzirom na visoku prevalenciju post-COVID sindroma, ekonomski i socio-medicinski značaj ovog stanja je izuzetan. Naše istraživanje potvrđuje potrebu za multidisciplinarnim praćenjem ovih pacijenata, pri čemu primarna zdravstvena zaštita ima ključnu ulogu. S obzirom da je neophodan personaliozavan i holistički pristup pacijentu, od velikog značaja je uloga izabranog lekara. Ostaje potreba za dalja istraživanja u ovoj oblasti radi sveobuhvatnijeg uvida i boljeg razumevanja post-COVID sindroma, kao i uspostavljanja odgovarajućeg protokola za praćenje i lečenje ovih pacijenata.

Conclusion

The high prevalence of post-COVID syndrome makes it exceptionally important from economic and socio-medical perspectives. Our research confirms the necessity of multidisciplinary follow-up for these patients, with primary healthcare playing a key role. Due to the need for a personalized and holistic approach, it highlights the importance of General Practitioners in their care. Further research in this area is still needed to gain a comprehensive understanding of post-COVID syndrome and to potentially develop protocols for the follow-up and treatment of these patients.

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