

Kliničke karakteristike i dijagnostika COVID-19 kod pacijenata u COVID-ambulantama u opštoj medicini

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Clinical characteristics and diagnosis of the COVID-19 in patients in COVID outpatient clinics

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Sažetak

Cilj rada. Ispitati koje su kliničke manifestacije, rezultate PCR testiranja i ishod posete kod pacijenata u COVID-ambulantama u opštoj medicini.

Metod. Istraživanje je sprovedeno upitnikom februara 2021. god. među pacijentima u četiri COVID-ambulate u Beogradu i jednoj u Subotici. Dobijeni su podaci o polu, starosti, postojećim simptomima i komorbiditetima, PCR-testiranju i ishodu posete. Podaci su obrađeni softverskim statističkim paketom SPSS 17. Statistička značajnost je definirana za nivo $p < 0,05$.

Rezultati. Obuhvaćeno je 676 ispitanika oba pola, prosečne starosti 49 godina. Lekarima su se javljali 1-3 dana nakon pojave simptoma. Najčešći simptomi su bili povišena temperatura i kašalj, zatim umor i bolovi u mišićima. Hipertenzija i gojaznost su najčešći komorbiditeti, većinom kod starijih od 65 godina ($p=0,000$). Testirano je 92% ispitanika PCR testom, i od njih 676, 60,95% je bilo PCR pozitivno, najčešće stariji od 50 godina ($p=0,010$). Zbog težine kliničke slike, 17,3% ispitanika upućeno je na bolničko lečenje, najčešće > od 51 do 65 godina, ali razlika nije statistički značajna ($p=0,183$).

Zaključak. Najčešći simptomi COVID-19 su povišena temperatura i kašalj, a ispitanici su se lekarima javili, u proseku, nakon 1 do 3 dana od pojave simptoma. Od komorbiditeta, najčešća su bili hipertenzija i gojaznost, češće kod ispitanika starijih od 65 godina. Kod više od polovine ispitanika PCR test je bio pozitivan, najčešće kod starijih od 50 godina.

Ključne reči: Simptomi COVID-19, PCR test, ishodi, opšta medicina

Abstract

Objective. Examine clinical manifestations, PCR test results, and visit outcomes in patients in COVID-outpatient clinics.

Method. The survey was performed using the questionnaire, in February 2021. in patients in four COVID-outpatient clinics in Belgrade and one in Subotica. We got the data about their jobs, gender, age, present symptoms and comorbidities, PCR-testing, and visit outcomes. The data were processed using the software statistical package SPSS 17. Statistical significance was defined for level $p < 0,05$.

Results. We included 676 participants, of both genders, with an average age of 49. They visited the doctor 1-3 days after symptoms onset. The most common symptoms were fever and cough, followed by fatigue and muscle aches. Hypertension and obesity were the most common comorbidities, mostly in patients over 65 ($p=0,000$). We tested 92% of the participants, using PCR tests, and out of 676, 60,95% tested PCR positive, mostly those over 50 ($p=0,010$). Due to the disease severity, 17,3% of the participants were referred to the hospitals, mostly those aged 51 to 65, but the difference wasn't statistically significant ($p=0,183$).

Conclusion. The most common symptoms of the COVID-19 were high temperature and cough, and the participants visited the doctor 1 to 3 days after symptoms onset. Hypertension and obesity were the most common comorbidities, more often in participants over 65. The PCR tests were positive in more than half of the participants, mostly in those over 50.

Keywords: COVID-19 symptoms, PCR test, visit outcome, general medicine

Uvod

U kineskom gradu Vuhanu decembra 2019. godine, primećeni su prvi slučajevi oboljenja nazvanog *COVID-19* i utvrđen je uzročnik - novi virus iz grupe koronavirusa *SARS-CoV2*. Svetska zdravstvena organizacija - *WHO* je 11.03.2020. proglasila pandemiju koja još uvek traje, s velikim brojem obolelih i značajnim mortalitetom¹. Ovaj respiratorni virus ima veliku sposobnost prenošenja. Sprovedena epidemiološka istraživanja su potvrdila da je velika pokretljivost ljudi, ekonomske, trgovačke i druge socijalne veze i komunikacije prisutne među ljudima, doprineli da se virus proširi na ceo svet^{2,3}. Kliničke manifestacije variraju od najčešće blagih oblika infekcije do teških oblika bolesti s brojnim akutnim, ozbiljnim komplikacijama koje, nekada, dovode i do smrtnog ishoda. Najčešći simptomi bolesti su bili slični gripu: umor, povišena temperatura, suv kašalj⁴⁻⁸, mada su pojedina istraživanja pokazala da mogu postojati i brojni drugi simptomi - glavobolja, bolovi u mišićima, dispneja, mučnina, povraćanje⁹, a gubitak mirisa je izdvojen kao četvrti izolovani simptom¹. Samo na osnovu simptoma i kliničke slike ne može se postaviti dijagnoza *COVID-19*¹⁰. Brzo postavljanje dijagnoze omogućuje da se bolest prepozna i oboleli izoluju kako bi se njeno širenje stavilo pod kontrolu. Među najčešće preporuke za dijagnostikovanje *COVID-19* su *Rtg* pluća, ultrazvuk, kompjuterizovana tomografija pluća i PCR test¹¹. Zlatni standard za dijagnostiku ovog oboljenja je test lančane reakcije polimeraze - PCR test, koji se jednostavno izvodi i pogodan je za masovna testiranja^{12,13}, koja brzim dijagnostičkim testovima predstavljaju važan instrument za upravljanje svim zaraznim bolestima¹⁴. U početku je smatrano da virus napada samo respiratorni trakt, ali su rezultati sprovedenih istraživanja pokazali da može da dovede do oštećenja i drugih organa i organskih sistema, posebno kardiovaskularnog sistema^{6,15-18}. U svetu je sprovedeno niz istraživanja radi sagledavanja epidemioloških i kliničkih karakteristike ove pandemije i pronašla rešenja da se spreči dalje održavanje virusa u zajednici i njegovo dalje prenošenje i širenje^{1,4,5,9,19,20}. U Srbiji su do danas bila četiri talasa epidemije. Primenuju se nefarmakološke mere prevencije, sprovodi se masovna vakcinacija, ali novootkrivenih slučajeva još uvek ima. Lekari opšte medicine, koji rade u *COVID* ambulantama, prvi su u kontaktu s pacijentima kod kojih se sumnja na *COVID-19* infekciju. Naučni odbor Sekcije opšte medicine Srpskog lekarskog društva osmislio je ovo istraživanje, a sprovedli su ga lekari koji su radili u *COVID* ambulantama, kako bismo utvrdili koje su karakteristike i specifičnosti ove pandemije u našoj sredini.

Cilj rada

Ispitati koje su kliničke manifestacije, rezultate PCR testiranja i ishod posete kod pacijenata u *COVID*-ambulantama u opštoj medicini.

Introduction

The first cases of the disease, soon to be known as *COVID-19*, were spotted in the Chinese city of Wuhan in December 2019. The cause was the new virus, from the coronavirus family, *SARS-CoV2*. The World Health Organization - *WHO* declared a pandemic on March 11th, 2020, and it's still ongoing, with huge morbidity and mortality¹. This respiratory virus is hugely transmissible. The epidemiological surveys confirmed people's movement, economic, trade, and other social connections, and inter-personal communication led to spreading the virus all around the world^{2,3}. Clinical manifestations vary from mostly mild forms of infection to severe with numerous acute complications which sometimes lead to deathly outcomes. The most common symptoms of the disease are similar to flu: fatigue, fever, dry cough⁴⁻⁸, although some researches show there could be other numerous symptoms, as well – headache, muscle pain, dyspnea, nausea, vomiting⁹, and the loss of smell is singled out as the fourth isolated symptom¹. It's not possible to make the diagnosis of *COVID-19* based only on the symptoms and clinical presentation¹⁰. Fast diagnosis enables disease recognition and isolation of the diseased in order to control the spreading. The most common methods for *COVID-19* diagnosis are chest X-ray, ultrasound, computerized tomography of the chest, and PCR test¹¹. The gold diagnostic standard for the disease is the polymerase chain reaction test - PCR test, which is easily performed and is convenient for mass testing^{12,13}. These fast diagnostic tests are an important tool in the management of all infectious diseases¹⁴. At first, it was believed the virus affects only the respiratory tract but the research results showed it can damage other organs and systems, especially the cardiovascular system^{6,15-18}. There are numerous researches worldwide on epidemiological and clinical characteristics of the pandemic and finding solutions to prevent the virus transmission and spreading, and its presence in the community^{1,4,5,9,19,20}. There were four disease waves in Serbia until now. We practice nonpharmacological preventive measures, mass vaccination but there are still new-found cases. General practitioners working in the *COVID* – outpatient clinics are the first to come into contact with the patients suspected of *COVID-19* infection. The Scientific Board of the Section of General Medicine of the Serbian Medical Society devised the survey, and the GPs working in the *COVID* – outpatient clinics carried it out, so we could identify the characteristics and specificities of the pandemic in our community.

Objective

We aimed at researching clinical manifestations, PCR test results, and visit outcomes in patients visiting *COVID* – outpatient clinics in general practice.

Metod

Ovo multicentrično istraživanje sprovedli su lekari u februaru 2020. godine, koji su radili u COVID-ambulantama u četiri doma zdravlja u Beogradu (Dom zdravlja Novi Beograd, Dom zdravlja Palilula, Dom zdravlja Zvezdara, Dom zdravlja Lazarevac) i u Domu zdravlja u Subotici. Lekari uključeni u istraživanje, popunjavali su upitnik tokom 5 uzastopnih dana, obuhvatajući sve pacijente starije od 18 godina koji su se javili na prvi pregled. Upitnikom su dobijeni podaci o: polu, starosti, postojećim simptomima, drugim oboljenjima i stanjima, podaci o vremenu koje je proteklo od pojave simptoma do javljanja lekaru, o rezultatu PCR testa i kakav je bio ishod ove posete lekaru, odnosno da li je ispitanik upućen na kućno ili bolničko lečenje. Simptome COVID infekcije smo podelili na *glavne simptome*: povišena telesna temperatura, suvi kašalj i gušenje; *ostale simptome*: poremećaj čula mirisa i ukusa, glavobolja, bolovi u mišićima i zglobovima, umor, bolovi u grlu, proliv i povraćanje i *simptom "alarm"* koji bi ukazivali na teži stepen infekcije koja može da ugrozi život pacijenta: dispneja i ortopneja, bol u grudima, hemoptizije, oligurija i anurija, nemogućnost pacijenta da samostalno ustane i stoji i poremećaj svesti.

Statistička obrada i analiza podataka

Podatke dobijene upitnikom statistički smo obradili koristeći softverski paket SPSS 20.0. U obradi podataka korišćena je deskriptivna analiza u obliku učestalosti i procenata za prikazivanje uzorka i odgovora na svako postavljeno pitanje. Rezultati su prikazani tabelarno i grafički, gde je učestalost posmatranih parametara izražena u procentima. Pearsonov (*Pearson*) χ^2 -test je korišćen za utvrđivanje postojanja statistički značajne razlike između individualnih karakteristika ispitanika. Ukoliko je u nezavisnoj promenljivoj prisutno više različitih grupa, korišćena je jednofaktorska analiza varijansi - ANOVA različitih grupa sa naknadnim testovima, kako bi se utvrdilo između kojih grupa je razlika statistički značajna. Statistička značajnost je definisana za nivo $p < 0,05$.

Rezultati

Istraživanjem je obuhvaćeno 676 ispitanika oba pola (338 muškaraca), od 31 do 50 godina, prosečne starosti $48,97 \pm 18,56$ (muškarci $49,26 \pm 21,11$ i žene $48,67 \pm 15,61$), (Tabela 1).

Method

This multicentric research was carried out by the physicians working in four COVID – outpatient clinics in Belgrade (PHC Novi Beograd, PHC Palilula, PHC Zvezdara, PHC Lazarevac) and PHC Subotica in February 2020. The physicians participating in the research were filling out the questionnaires during five consecutive days, including all patients over 18 who came for their first medical check-up. The questionnaire included data on: gender, age, existing symptoms, comorbidities and other health issues, time from symptoms onset to doctor's visit, PCR test results, and visit outcomes (whether the patient was sent home or to the hospital). COVID symptoms were divided into *main symptoms*: fever, dry cough, and dyspnea; *other symptoms*: a sense of smell and taste disorder, headache, muscle and joint aches, fatigue, sore throat, diarrhea, vomiting, and *"alarm" symptoms* indicating the severe form of the infection that can endanger the patient's life: dyspnea and orthopnea, chest pain, hemoptysis, oliguria and anuria, patient's inability to get up and stand up on his own and loss of consciousness.

Statistical processing and data analysis

The obtained data were statistically processed using the software package SPSS 20.0. We used descriptive analysis in data processing, in the form of frequencies and percentages, for showing sample and answer for each question asked. Results were presented in tables and figures, and the frequency of the observed parameters was shown in percentages. Pearson's χ^2 -test was used for deducing statistically significant differences between individual participants' characteristics. If there were several different groups in the independent variable, we used one-factorial analysis of variance - ANOVA of different groups with additional tests to identify the statistically significant difference between the groups. Statistical significance is defined for level $p < 0,05$.

Results

The survey included 676 participants of both genders (338 males), from 31 to 50 years, of average age $48,97 \pm 18,56$ (males $49,26 \pm 21,11$ and females $48,67 \pm 15,61$), (Table 1).

Tabela 1. Struktura ispitivane populacije
Table 1. Structure of the survived population

Ispitanici/Participants	N	%
Pol/Gender:		
Muškarci/Males	338	50.0
Žene/Females	338	50.0
Starost/Age:		
≤ 30 godina/years	98	14.50
31-50 godina/years	274	40.53
51-65 godina/years	201	29.73
>65 godina/years	103	15.24
Ukupno/Total	676	100.0

Od ukupno 676 ispitanika, 72,63% se javilo lekaru nakon 1 do 3 dana od pojave simptoma (Tabela 2). Nije bilo statistički značajne razlike u odnosu na pol ($p=0.994$) i starost ispitanika ($p=0.111$).

Out of the total of 676 participants, 72,63% visited the doctor after 1 to 3 days from symptoms onset (Table 2). There was no statistically significant difference concerning gender ($p=0.994$) and age of the participants ($p=0.111$).

Tabela 2. Vreme proteklo od pojave simptoma bolesti do javljanja lekaru
Table 2. The time-lapse between disease symptoms onset to a doctor visit

Karakteristike ispitanika/ Participants` characteristics	Pojava tegoba pre dolaska lekaru/ Symptoms onset before doctor visit N/%			Od ukupno 676 ispitanika/Out of the total of 676 participants N/%	Statistička značajnost/ Statistical significance*
	1-3 dana/days	4-5 dana/days	> 5 dana/days		
Pol/Gender:					
Muškarci/Males	245 72.49	38 11.24	55 16.27	338 50.0	p=0.954
Žene/Females	246 72.78	38 11.24	54 15.98	338 50.0	
Starost/Age:					
≤ 30 godina/years	81 82.65	5 5.10	12 12.24	98 14.50	p= 0.111
31-50 godina/years	202 73.72	29 10.58	43 15.69	274 40.53	
51-65 godina/years	140 69.65	29 14.43	32 15.92	201 29.73	
> 65 godina/years	68 66.02	13 12.62	22 21.36	103 15.24	
Od ukupno 676 ispitanika/Out of the total of 676 participants	491 72.63	76 11.24	109 16.12	676 100.0	

* Statistička značajnost je definisana za nivo $p<0,05$ /Statistical significance is defined for level $p<0,05$.

Od glavnih simptoma, najčešće je postojala povišena telesna temperatura (35.21% ispitanika). Kod više od polovine ispitanika glavni simptomi su se javljali udruženo, najčešće istovremeno povišena temperatura i suv kašalj (29,88% ispitanika). Sva tri glavna simptoma najčešće su bila kod starijih od 50 godina, a kod starijih od 65 godina najčešće je, uz povišenu telesnu temperaturu, postojala dispneja ($p=0.000$). U zasupljenosti glavnih simptoma nije bilo statistički značajne razlike u odnosu na pol ($p=0.375$). Svaki četrnaesti ispitanik nije imao nijedan od glavnih simptoma, (Tabela 3).

As far as the main symptoms go, the most frequent was fever (35.21% of the participants). In more than half of the participants, the main symptoms appeared collectively, most often at the same time - fever and dry cough (29,88% of the participants). All three main symptoms were mostly present in people over 50, and in those over 65, alongside high fever, dyspnea was mostly present ($p=0.000$). There was no statistically significant difference concerning gender ($p=0.375$). Every fourteenth participant had none of the main symptoms. (Table 3).

Tabela 3. Prisustvo glavnih simptoma kod ispitanika
Table 3. Presence of the main symptoms in the participants

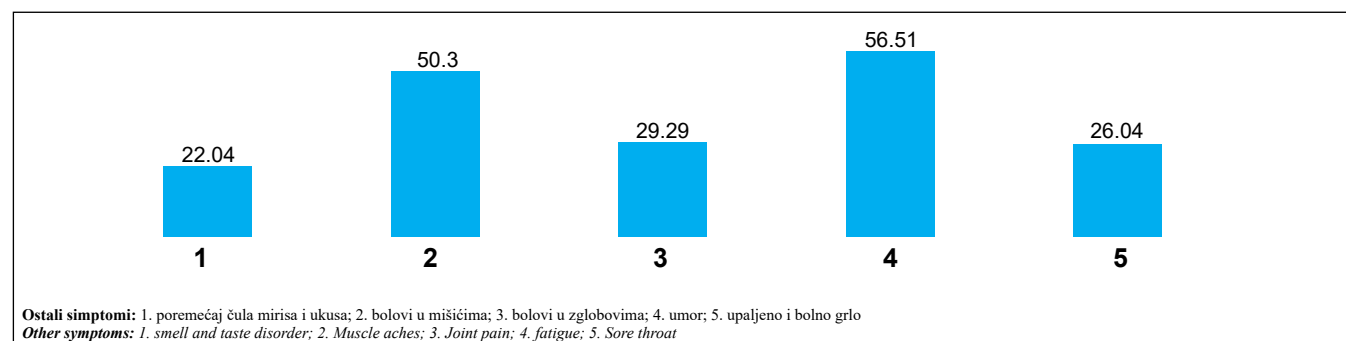
Karakteristike ispitanika/Participants' characteristics	Glavni simptomi/Main symptoms (%)								Statistička značajnost*/Statistical significance
	↑temp./ ↑fever	↑temp. i kašalj/ ↑fever and cough	↑temp. kašalj dispnea/ ↑fever, cough, dyspnea	↑temp. dispnea/ ↑fever, dyspnea	Kašalj/ cough	kašalj dispnea/ cough, dyspnea	Dispnea/ dyspnea	Bez glavnih simptoma/ No main symptoms	
Pol/Gender:									
Muški/Males	120 35.50	111 32.84	35 10.36	4 1.18	32 9.47	7 2.07	7 2.07	22 6.51	p= 0.375
Ženski/Females	118 34.91	91 26.92	34 10.06	7 2.07	47 13.91	4 1.18	10 2.96	27 7.99	
Starost/Age									
≤ 30 god./years	47 47.96	19 19.39	1 1.02	1 1.02	17 17.35	0 0	5 5.10	8 8.16	p= 0.000
31 - 50 god./ years	113 41.24	87 31.75	12 4.38	3 1.09	27 9.85	4 1.46	7 2.55	21 7.66	
51 - 65 god./ years	52 25.87	64 31.84	38 18.91	2 1.00	22 10.95	3 1.49	2 1.00	18 8.96	
> 65 god./ years	26 25.24	32 31.07	18 17.48	5 4.85	13 12.62	4 3.88	3 2.91	2 1.94	
Od ukupno 676 ispitanika/ Out of the total of 676 participants	238 35.21	202 29.88	69 10.21	11 1.63	79 11.69	11 1.63	17 2.51	49 7.25	

* Statistička značajnost je definisana za nivo $p < 0,05$ / Statistical significans is defined for level $p < 0,05$

Glavni simptomi: ↑temp. = povišena telesna temperatura; kašalj = suv kašalj; dispneja /Main symptoms: ↑fever = high fever; cough = dry cough; dyspnea

Od ostalih simptoma kod više od polovine ispitanika, najčešće je postojao umor (56,51%) i bolovi u mišićima (50,3%), (Grafikon 1).

Out of other symptoms, in more than half of the participants, the most common was fatigue (56,51%) and muscle aches (50,3%). (Figure 1).



Grafikon 1. Prisutvo ostalih simptoma (pojedinačno ili u različitim kombinacijama) izraženo u procentima

Figure 1. Presence of other symptoms (single or combined) in percentages

Ostali simptomi su se retko javljali izolovano. Od 676 ispitanika, kod 54,43% je bilo 25 različitih kombinacija simptoma, a u radu su prikazane samo najzastupljenije, (Tabela 4). Nije bilo statistički značajne razlike u odnosu na pol ($p=0,112$). Najčešće su postojali bolovi u mišićima i umor (12,57%), potom udruženost ova dva simptoma i bolova u zglobovima (10,95%), Kombinacija ova tri simptoma bila je najzastupljenija kod starijih od 65 godina (20,39%), a najređa kod mlađih od 30 godina (2,04%), ($p=0,004$). Svaki deseti ispitanik u ovom istraživanju nije imao nijedan od ovih ostalih simptoma.

Other symptoms rarely appeared on their own. Out of 676 participants, in 54,43% there were 25 different symptom combinations, and in our research, we showed only the most common ones, (Tabela 4). There was no statistically significant difference concerning the gender ($p=0,112$). The most common were muscle aches and fatigue (12,57%), followed by both of these symptoms together, and joint pains (10,95%), The combination of the three symptoms was the most frequent in those over 65 (20,39%), and the least frequent in those under 30 (2,04%), ($p=0,004$). Every tenth participant in our research had none of these symptoms.

Tabela 4. Prisustvo ostalih simptoma (pojedinačno i udruženo) kod ispitanika u odnosu na starost i po
Table 4. Presence of other symptoms (single or collective) in participants, in relation to age and gender

Karakteristike ispitanika/Participants' characteristics	Ostali simptomi/Other symptoms N/%							Od ukupno 676 ispitanika N%/Out of the total of 676 participants	Statistička značajnost*/Statistical significance *
	1	2,3,4	2,4	4	5	Ostale komb./Other combinations	Bez simptoma/No symptoms		
Pol/Gender									
Muški/Males	20 5.92	33 9.76	46 13.61	54 15.98	21 6.21	132 39.05	32 9.47	338 50.0	p= 0.112
Ženski/Females	24 7.10	41 12.13	39 11.54	38 11.24	37 10.95	121 35.80	38 11.24	338 50.0	
Starost/Age									
≤ 30 god./years	4 4.08	2 2.04	8 8.16	16 16.33	14 14.09	44 48.90	10 10.20	98 14.50	p= 0.004
31 do 50 god. /years	20 7.30	24 8.76	31 11.31	24 8.76	26 9.49	120 43.80	29 10.58	274 40.53	
51 do 65 god. /years	14 6.97	27 13.43	31 15.42	29 14.43	14 6.97	63 31.34	23 11.44	201 29.73	
> 65 god. /years	6 5.83	21 20.39	15 14.56	23 22.33	4 3.88	26 25.24	8 7.77	103 15.24	
Od ukupno 676 ispitanika/ Out of the total of 676 participants	44 6.51	74 10.95	85 12.57	92 13.61	58 8.58	253 37.42	70 10.36	676 100	

* Statistička značajnost je definisana za nivo $p<0,05$ /Statistical significance is defined for level $p<0,05$

Ostali simptomi: 1. poremećaj čula mirisa i ukusa; 2. bolovi u mišićima; 3. bolovi u zglobovima; 4. umor; 5. upaljeno i bolno grlo

Other symptoms: 1. Smell and taste disorder; 2. Muscle aches; 3. joint pains; 4. fatigue; 5. Sore throat

Od ukupno 676 ispitanika, kod 60% nisu evidentirani *simptomi alarma*, najčešće dispneja sa ortopnejom (kod 14,94%) i bol u grudima (kod 12,43%). Nije postojala povezanost sa polom, a dispneja sa ortopnejom je najređe bila prisutna kod ispitanika ≤ 30 godina, a najčešće kod starijih od 65 godina (21,36%) ($p=0.000$), (Tabela 5).

Out of the total of 676 participants, in 60% there were no obvious *alarm symptoms* – mostly dyspnea with orthopnea (in 14,94%) and chest pain (in 12,43%). There was no connection to gender, and dyspnea with orthopnea was the least present in participants ≤ 30, and the most frequent in those over 65 (21,36%) ($p=0.000$). (Table 5).

Tabela 5. Prisustvo simptoma “alarma” pojedinačno i u kombinacijama
Table 5. Presence of “alarm” symptoms – single or combined

Karakteristike ispitanika/Participants' characteristics	Simptomi alarma/ Alarm symptoms N/%					Od ukupno 676 ispitanika/Out of the total of 676 participants	Statistička značajnost*/Statistical significance*
	1	2	3	Kombinacije simptoma/Symptom combinations	Bez simptoma/No symptoms		
Pol/Gender							
Muškarci/Males	50 14.79	37 10.95	25 7.40	23 6.80	203 60.06	338 50.0	p= 0.474
Žene/Females	51 15.09	47 13.91	19 5.62	20 5.91	201 59.47	338 50.0	
Starost/Age							
≤ 30 god./years	11 11.22	10 10.20	9 9.28	/	68 69.39	98 14.50	p= 0,000
31- 50 god./years	34 12.41	35 12.77	23 8.39	8 2.19	174 63.50	274 40.53	
51- 65 god./years	34 16.92	26 12.94	6 2.99	17 8.46	118 58.71	201 29.73	
> 65 god./years	22 21.36	13 12.62	6 5.83	18 17.47	44 42.72	103 15.24	
Od ukupno 676 ispitanika/Out of the total of 676 of participants	101 14.94	84 12.43	44 6.51	43 6.36	404 59.76	676 100.0	

* Statistička značajnost je definisana za nivo $p<0,05$ / Statistical significans is defined for level $p<0,05$

Simptomi alarma: 1. dispneja sa ortopneom; 2. bol u grudima; 3. nemogućnost da bolesnik samostalno ustane i stoji.

Alarm symptoms: 1. dyspnea with orthopnea; 2. Chest pain; 3. Patient unable to stand up or stand on his own.

Upitnikom su dobijeni podaci o prisustvu drugih oboljenja i stanja kod ispitanika. U ovom istraživanju 42.46% ispitanika je bilo bez drugih oboljenja, a najređe su to bili ispitanici stariji od 65 godina (10,68%). Kod ostalih, najčešće je izolovano bila hipertenzija (10,36%), potom gojaznost (6,21%) i hronična opstruktivna bolest pluća - HOBP i/ili astma (6,07%), (Tabela 6). U odnosu na pol, nije bilo statistički značajne razlike ($p=0,161$), ali su u odnosu na starost, prema očekivanju, ispitanici mlađi od 30 godina imali statistički značajno ređe, a stariji od 65 godina značajno češće istovremeno prisustvo više oboljenja ($p=0,000$). (Tabela 6)

Using the questionnaire, we got the data on participants' other comorbidities and health issues. In our research, 42.46% of the participants were without comorbidities, and the least of them were over 65 (10,68%). In others, the most frequent health issue was hypertension (10,36%), followed by obesity (6,21%) and chronic obstructive pulmonary disease - COPD and/or asthma (6,07%). (Table 6). In relation to gender, there was no statistically significant difference ($p=0,161$), but in relation to age, as expected, participants under 30 had statistically significantly more rarely, and those over 65 had more often simultaneous presence of comorbidities ($p=0,000$). (Table 6)

Tabela 6. Postojanje drugih oboljenja kod ispitanika

Table 6. Presence of comorbidities in the participants

Karakteristike ispitanika/ Participants` xharacteristics	Prisustvo drugih oboljenja/Presence of other comorbidities N/%									Statistička značajnost*/ Statistical ignificance*
	1	2	3	4	5	1,2	2,4	Ostale kombinacije/ Other combinations	Bez drugih oboljenja/ No comorbidities	
Pol/Gender										p= 0.161
Muškarci/Males	15 4.44	36 10.65	5 1.48	21 6.21	19 5.62	15 4.44	19 5.62	63 18.94	144 42.6	
Žene/Females	10 2.96	34 10.06	6 1,78	21 6.21	22 6.51	15 4.44	19 5.62	67 20.11	143 42.31	
Starost/Age										
do/up to 30 god./years	1 1.02	3 3.06	1 1.02	5 5.10	5 5.10			1 1.02	82 83.67	p= 0.000
31-50 god./years	9 3.28	17 6.20	6 2.19	23 8.39	24 8.76	1 0.36	13 4.74	16 5.83	165 60.22	
51- 65 god./years.	11 5.47	38 18.91	3 1.49	13 6.47	10 4.98	16 7.96	22 10.95	69 34.42	29 14.43	
>65 god./years	4 3.88	12 11.65	1 0.97	1 0.97	2 1.94	13 12.62	3 2.91	56 54.27	11 10.68	
Od ukupno 676 ispitanika/Out of the total of 676 participants	25 3.70	70 10.36	11 1.63	42 6.21	41 6.07	30 4.44	38 5.62	130 19.52	287 42.46	

* Statistička značajnost je definisana za nivo $p<0,05$ /Statistical significance is defined for level $p<0,05$

Druga oboljenja: 1. kardiovaskularne bolesti; 2. hipertenzija; 3. dijabetes; 4. gojaznost; 5. HOBP i/ili astma

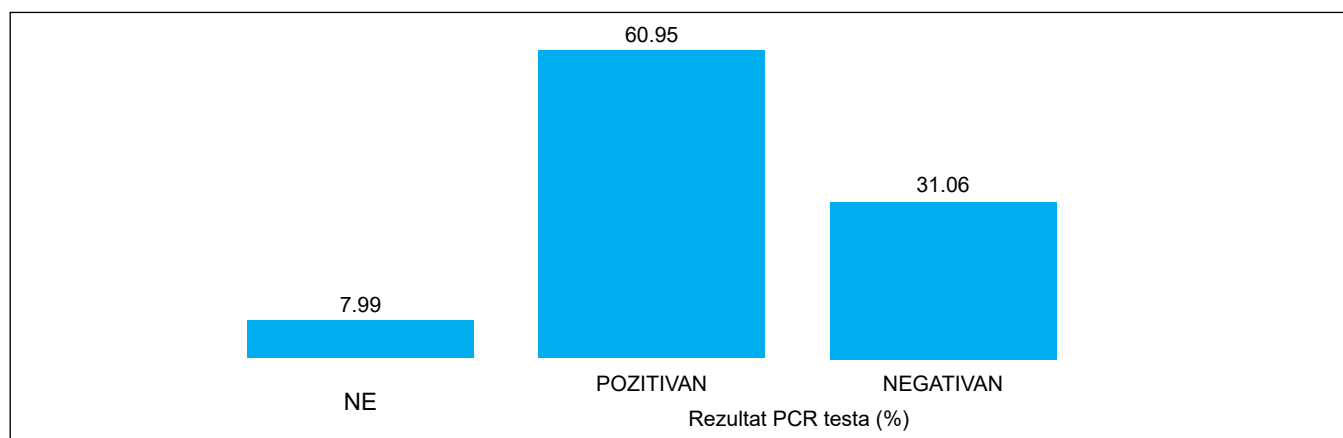
Other comorbidities: 1. Cardiovascular disease; 2. hypertension; 3. diabetes; 4. obesity; 5. COPD and/or asthma

Prema algoritmu o definiciji slučaja za potrebe nadzora, koje je izdalo Ministarstvo zdravlja Republike Srbije i Institut za javno zdravlje "Dr Milan Jovanović Batut", lekar u COVID-ambulantama, nakon uzete epidemiološke anamneze i kliničkog pregleda, donosi odluku o potrebi za PCR testiranjem, kao i odluku o ishodu posete, odnosno da li će pacijenta uputiti na dalju dijagnostiku, kućno lečenje ili na bolničko lečenje.

Poštujući kriterijume o definiciji slučaja za potrebe nadzora, od ukupnog broja ispitanika samo 8% nije testirano PCR testom, a kod 60,95% PCR test je bio pozitivan (Grafikon 2). Od 338 ispitanika muškog pola, 60,06% je PCR+ a 31,95% je PCR-, a od 338 ispitanika ženskog pola, 61,83% je PCR+ a 30,18% PCR-, te u odnosu na pol nema statistički značajne razlike ($p=0,879$), (Tabela 7). U odnosu na starosnu strukturu, među netestiranim najviše je ispitanika starosti ≤ 30 godina. Najveći procenat PCR negativnih ispitanika je od 31 do 50 godina (35,40%), a pozitivan PCR test bio češći kod starijih od 50 godina ($p=0,010$). (Tabela 7)

According to the algorithm for case definition, for the purpose of surveillance, issued by the Ministry of Health of the Republic of Serbia and the Institute for Public Health "Dr. Milan Jovanovic Batut", COVID-outpatient clinic doctor, after taking patient's history and performing the exam, decides on the PCR testing, and visit outcome – should the patient undergo further diagnostic procedures, be sent home or to the hospital.

Respecting criteria for the case definition, for the purpose of surveillance, out of the total number of the participants, only 8% were not PCR tested, and in 60,95% PCR test was positive (Figure 2). Out of 338 male participants, 60,06% were PCR+, and 31,95% were PCR-. Out of 338 female participants, 61,83% were PCR+, and 30,18% PCR-, so there was no statistically significant difference concerning the gender ($p=0,879$). (Table 7). In relation to age, among those who were not tested, the majority were ≤ 30 . The majority of PCR negative participants were from 31 to 50 (35,40%), and positive PCR tests were more frequent in those over 50 ($p=0,010$). (Table 7)



Grafikon 2, Testiranje ispitanika PCR testom sa sumnjom na COVID-19
Figure 2, COVID-19 suspected participants, PCR tested

Tabela 7. Rezultat PCR testa kod ispitanika sa sumnjom na COVID-19
Table 7. PCR test results in COVID-19 suspected participants

Karakteristike ispitanika/ Participants' characteristics	Testiranje PCR testom/PCR tested N/%			Od ukupno 676 ispitanika/Out of the total number of 676 participants N/%	Statistička značajnost*/ Statistical significance*
	Nisu testirani/ Not tested	PCR +	PCR -		
Pol/Gender					
Muški/Male	27 7.98	203 60.06	108 31.95	338 50.0	p= 0.879
Ženski/Female	27 7.98	209 61.83	102 30.18	338 50.0	
Starost/Age					
do/up to 30 god./years	16 16.33	53 54.08	29 29.59	98 14.50	P= 0.010
31 do/to 50 god./years	21 7.66	156 56.93	97 35.40	274 40.53	
51 do/to 65 god./years	12 5.97	134 66.67	55 27.36	201 29.73	
vise od/over 65 god./years	5 4.85	69 66.99	29 28.16	103 15.24	
Od ukupno 676 ispitanika/ Out of the total of 676 participants	54 7.99	412 60.95	210 31.06	676 100.0	

* Statistička značajnost je definisana za nivo p<0,05
 * Statistical significance is defined for level p<0,05

Od ukupno 676 ispitanika, 117 (17.3%) s težom kliničkom slikom upućeni su na bolničko lečenje. Samo jedan ispitanik nije bio testiran, a 92,3% je imalo pozitivan PCR test (Tabela 8). Među PCR pozitivnim ispitanicima koji su hospitalizovani, nije bilo značajne razlike u odnosu na pol (p=0,248). U odnosu na starosnu strukturu, ispitanici od 51 do 65 godina češće su upućivani u bolnicu (47%), ali razlika nije statistički značajna (p=0,183), (Tabela 8).

Out of the total of 676 participants, 117 (17.3%) were with severe clinical symptoms and they were sent to the hospital. Only one participant wasn't tested, and 92,3% had a positive PCR test (Table 8). Among PCR positive participants, who were hospitalized, there was no significant difference concerning the gender (p=0,248). In relation to age structure, participants from 51 to 65 were sent to the hospital more often (47%), but the difference wasn't statistically significant (p=0,183), (Table 8).

Tabela 8. Ispitanici upućeni na bolničko lečenje u odnosu na rezultat PCR testa

Table 8. Participants sent to hospital, in relation to PCR test results

Karakteristike ispitanika/ Participants' characteristics	Upućeni na bolničko lečenje/Sent to hospital N %				Statistička značajnost*/ Statistical significance*
	nije testirano/ not tested	PCR+	PCR -	Od ukupno upućenih u bolnicu/ Out of the total sent to hospital	
Pol/Gender					
Muški/Male	0	54 96.4	2 3.6	56 47.9	p= 0,248
Ženski/Female	1 1.6	54 88.5	6/9.8	61 52.1	
Starost/Age					
≤ 30 god./years	0	2 100.0	0	2 1.7	p= 0,183
31 - 50 god./years	1 5.3	15 78.9	3 15.8	19 16.2	
51 - 65 god./years	0	53 96.4	2 3.6	55 47.0	
> 65 god./years	0	38 92.7	3 7.3	41 35.0	
Ukupno upućenih u bolnicu/ Total sent to hospital	1 0.9	108 92.3	8 6.8	117 100.0	

* Statistička značajnost je definisana za nivo $p < 0,05$ / * Statistical significance is defined for level $p < 0,05$

Diskusija

Podaci o obolelima u Srbiji na početku epidemije ukazivali su da je među obolelima bilo više muškaraca, te da su uglavnom obolevale osobe starijeg životnog doba. U našem istraživanju bila je podjednaka zastupljenost oba pola, a prosečna starost ispitanika iznosila je 49 godina. Podatke o podjednakoj zastupljenosti polova nalaze u svojim istraživanjima Cheng JL i saradnici gde je: odnos muškaraca i žena bio 1,14:1, a prosečna starost 46 godina⁵, Xianguang Yang i saradnici, gde je odnos muškaraca i žena bio 1,09:1, a prosečna starost 45 godina⁴, kao i u radu Nie Y i saradnika sa učešćem 56,2% muškaraca i prosečnom starosti ispitanika od 43 godine¹⁹. U istraživanju Krishnan A i saradnika prosečna starost ispitanika sa COVID-19 bila je nešto viša, iznosila je 51 godinu²¹. Na samom početku epidemije oboleli su se često lečili sami, a lekaru su se javljali tek kada bi se bolest komplikovala. Putem medija je apelovano da se oboleli obrate lekaru s pojavom prvih simptoma. U našem istraživanju najveći broj ispitanika se javljao na pregled u COVID-ambulantu u proseku nakon 3 dana, dok je u istraživanju Nie Y i saradnika taj period bio nešto duži, 5,6 dana¹⁹. U pogledu simptomatologije, sprovedene epidemiološke studije ukazuju da su simptomi kod pacijenata sa COVID-19 veoma različiti. Obrada

Discussion

Data on the diseased patients in Serbia, at the beginning of the outbreak, showed that among them were more men, and they were mainly older persons. In our research, there were equally diseased of both genders, and the average age was 49. Data on the equal prevalence of both genders were also found in the research of Cheng JL et al. They found the ratio of men to women was 1,14:1, and the average age was 46⁵. Xianguang Yang et al. found this ratio to be 1,09:1, and the average age 45⁴, similarly Nie Y et al. found the incidence of men was 56,2% and the average age of the participants was 43¹⁹. In the research of Krishnan A et al. the average age of the participants with COVID-19 was slightly higher, 51 years of age²¹. At the very beginning of the pandemic, the diseased often medicated on their own and visited the doctor when the illness got complicated. The media urged the diseased to visit their doctors with the first sign of symptoms. In our research, we found the majority of the participants visited the doctor in the COVID outpatient clinic after 3 days of disease symptoms, on average. The research of Nie Y et al. found this period to be a bit longer - 5,6 days¹⁹. As far as symptoms go, epidemiological studies show the symptoms in COVID-19 patients vary greatly. Processing the data from our

podataka koje smo dobili u ovom istraživanju pokazala je da su od glavnih simptoma najčešće postojali povišena telesna temperatura i kašalj, što je u skladu s rezultatima *Guan W* i saradnika²², kao i rezultatima drugih istraživanja^{7,8,23}. *Mallah IS* i saradnici u svom radu kao glavne simptome navode suv kašalj i glavobolju^{6,10}. Od ostalih simptoma kod naših ispitanika, najčešće se zapaža umor i bolovi u mišićima, a poremećaj čula mirisa i ukusa (anosmija) kod 22,04%. U radu *Gane SB* i saradnika iznenadna anosmija bio je četvrti po učestalosti osnovni simptom COVID-infekcije²³. U nizu radova kao ostali simptomi navode se glavobolja, dijareja, umor, upaljeno grlo i anosmija^{2,7,21}. *Thomas Struyf Jonathan* i saradnici uradili su metaanalizu 44 studije sa 26.884 ispitanika, tražeći odgovor na pitanje da li se na osnovu znakova i simptoma pacijenata u ordinacijama primarne zdravstvene zaštite ili u bolničkim ustanovama, može utvrditi boluje li pacijent od COVID-19. Našli su da su u ovim istraživanjima identifikovana čak 84 različita znaka i simptoma, te da se samo na osnovu simptoma ne može pouzdano postaviti dijagnoza COVID-19. (7) U pogledu komorbiditeta, u našem istraživanju je nađeno da je kod 57,54% ispitanika postojalo neko drugo oboljenje ili stanje, najčešće hipertenzija, potom gojaznost. *Nie Y* i saradnici navode da su u njihovom istraživanju komorbiditeti postojali kod 22,4% ispitanika¹⁹, a *Di Salvo* i saradnici ističu da postojanje komorbiditeta predstavlja *alarm* koji ukazuje na mogućnost teže kliničke manifestacije COVID-19 i lošije prognoze²⁴. U skladu s tim, *Ahmad A* i saradnici potvrđuju da osobe sa oštećenom funkcijom jetre imaju lošiju prognozu koja češće rezultira lošijim zdravstvenim ishodom¹⁴. *Krishnan A* sa svojim saradnicima ističe da je hipertenzija najčešći zastupljen komorbiditet, ali ukazuju i na gojaznost kao značajan faktor rizika za COVID-19²¹. Do istog rezultata smo i mi došli u našem istraživanju, jer je četvrtina naših ispitanika bila gojazna (24,56%). *Hua S* i saradnici su pokazali da i metaboličke bolesti povećavaju i morbiditet i mortalitet pacijenata sa COVID-19¹⁴. Prema smernicama za dijagnostiku COVID-19, lančana reakcija reverzne transkripcije polimeraze - PCR test predstavlja zlatni standard u detekciji pacijenata zaraženih SARS-CoV-2 virusom^{1,20}, a istraživači ističu da primena ovog testa ima najvažniji uticaj na kontrolu širenja virusa^{12,25}. U našem istraživanju testirano je 92% ispitanika. Od 676 ispitanika, 60,95% je bilo PCR pozitivno. Rezultati nekih istraživanja ukazuju na mogućnost lažnopolozitivnih i lažnonegativnih rezultata. Radi dijagnostike COVID-19, preporučuje se i primena drugih vizuelnih dijagnostičkih metoda (radiografija, kompjuterizovana tomografija, pozitivna emisiona tomografija, magnetna rezonancija), uz sugestiju da istraživanja treba usmeriti na iznalaženje novih dijagnostičkih metoda koje bi imale veću pouzdanost^{9,11,13,20}. Naši ispitanici s težom kliničkom slikom upućeni su na bolničko lečenje. Među njima su, najčešće, bile osobe starije od 50 godina (mada razlika

research we found the most common symptoms were fever and cough, which is in line with the results of *Guan W* et al.²², as well as the results of some other researches^{7,8,23}. *Mallah IS* et al. found the dry cough and headache to be the main symptoms^{6,10}. Other symptoms in our participants mostly included fatigue and muscle aches, and loss of smell or taste (anosmia) was found in 22,04%. In the study of *Gane SB* et al. sudden anosmia was the fourth most frequent symptom of the COVID infection²³. In the series of studies, other mentioned symptoms were headache, diarrhea, fatigue, sore throat, and anosmia^{2,7,21}. *Thomas Struyf Jonathan* et al. performed a meta-analysis of 44 studies with 26.884 participants, looking for the answer to whether the diagnosis of COVID-19 in a patient can be made based on the symptoms and signs with which patients presented in outpatient clinics or hospitals⁹. They found 84 different signs and symptoms in these studies, and therefore COVID-19 diagnosis can't be solely made based on the symptoms⁷. As for the comorbidities, our research showed 57,54% of the participants had a comorbidity or health issue, most commonly hypertension, followed by obesity. *Nie Y* et al. showed comorbidities were present in 22,4% of the participants from their research¹⁹, while *Di Salvo* et al. pointed out the presence of the comorbidities was an *alarm* signaling the possibility of severe clinical manifestations of the COVID-19 and worse prognosis²⁴. Hence, *Ahmad A* et al. confirm the persons with liver damage had a worse prognosis resulting in worse health outcome¹⁴. *Krishnan A* et al. emphasize that hypertension is the most common comorbidity but they also point out obesity as an important risk factor for COVID-19²¹. We came to the same results in our research because the fourth of our participants were obese (24,56%). *Hua S* et al. showed metabolic diseases also raised morbidity and mortality of the COVID-19 patients¹⁴. According to the COVID-19 diagnostic guidelines, the chain reaction of the reverse polymerase transcription - PCR test is the gold standard in detecting patients infected with SARS-CoV-2 virus^{1,20}. The researchers emphasize the use of this particular test has the most important influence on the control of the virus spreading^{12,25}. In our research, 92% of the participants were tested. Out of 676 participants, 60,95% were PCR positive. The results of some other studies point out the possibility of false-positive or false-negative results. For the purpose of COVID-19 diagnosis, other visual diagnostic methods are recommended as well (chest X-ray, computerized tomography, positive emission tomography, magnetic resonance), with a suggestion that future research should be aimed at finding new diagnostic methods, with higher reliability^{9,11,13,20}. Our participants with the severe clinical presentation were sent to hospitals. Among them were mostly persons over 50 (although the difference wasn't statistically significant). *Anand U* et al. in their review pointed out, the disease susceptibility bore no relevance to

nije bila statistički značajna). Anand U i saradnici u svom preglednom radu ističu da u odnosu na podložnost infekciji nema razlike u odnosu na pol, ali da su osobe starije od 60 godina u većem riziku za razvoj teže kliničke slike zbog prisustva komorbiditeta², što potvrđuje u svom istraživanju i Alkhathami MG sa saradnicima²⁶.

Zaključak

Najčešći simptomi COVID-19 kod naših ispitanika bili su povišena temperatura i kašalj, a lekaru su se javili, u proseku, nakon 1 do 3 dana od pojave simptoma. Od komorbiditeta, najučestaliji su bili hipertenzija i gojaznost, češće kod ispitanika starijih od 65 godina. Kod više od polovine ispitanika PCR test je bio pozitivan, najčešće kod starijih od 50 godina. Kod svih posmatranih parametara nije nađena statistički značajna razlika u odnosu na pol.

Сукоб интереса

Изјављујем да аутори немају никакав сукоб интереса у писању овог рада.

gender but persons over 60 were at a higher risk for severe clinical presentation due to the comorbidities², which was confirmed in the research of Alkhathami MG et al. as well²⁶.

Conclusion

The most common symptoms of COVID-19 in our participants were fever and cough, and they visited a doctor after 1 to 3 days from symptoms onset, on average. Out of the comorbidities, the most common were hypertension and obesity, more often in those over 65. In more than half of the participants, the PCR test was positive, most commonly in those over 50. In all the looked at parameters there was no statistically significant difference in relation to gender.

Conflict of interest

I hereby confirm the authors have no conflict of interest in writing this paper.

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