SaRS-CoV-2: EPIDEMIOLOGICAL CHARACTERISTICS, CLINICAL CHARACTERISTICS, DIAGNOSIS AND PREVENTION – A REVIEW OF CURRENT KNOWLEDGE

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UVOD
Bolest SARS-Cov-2 se pojavila krajem decembra 2019. godine u Vuhanu, Kina, kada je zapažena serija slučajeva pneumonija nepoznatog prouzrokovala. Nekoliko nedelja kasnije potvrdeno je da je novi korona virus uzročnik oboljenja. U Srbiji je, polovinom marta 2020. godine, nakon registriranja prvih slučajeva i proglašenja pandemije od strane Svetske zdravstvene organizacije, uvedeno vanredno stanje [1,2,3,4]. Na početku epidemije, lekari primarne zdravstvene zaštite su bili u komunikaciji sa pacijentima putem telefona i u obavezi da u skladu sa anamnestičkim i epidemiološkim podacima koje dobiju od pacijenta, pruže sve neophodne savete i odrede potrebnu simptomatsku i/ili suportivnu terapiju, odgovarajući higijensko-dijeteškom režim.

INTRODUCTION
The SARS-Cov-2 disease appeared towards the end of December 2019, in Wuhan, China, when a series of pneumonia cases of unknown cause was registered. Several weeks later it was confirmed that a new coronavirus was the cause of the disease. In mid-March 2020, after the first cases had been registered and the pandemic had been declared by the World Health Organization, a state of emergency was declared in Serbia [1,2,3,4]. At the beginning of the epidemic, doctors in primary health care were in communication with patients by phone, and were obliged, in accordance with the anamnestic and epidemiological data received from the patients, to offer all necessary advice, as well as to prescribe necessary symptomatic and/or supportive therapy, to recommend the appropriate hygiene and dietary regimen, to provide advice on staying at home, and, if need be, to instruct the patient on necessary home isolation. Later, as the epidemic progressed, and the number of infected and sick people increased, Covid clinics were established, at the level of primary health care, where, for each patient with suspected SARS-Cov-2 infection, the doctor was required to examine them, and perform laboratory analyses, a lung X-ray, a nasopharyngeal swab test; and after that, to instruct the patient to go into self-isolation, to treat the patient, or, if necessary, to refer the patient to the next-level triage center for hospitalization. In order to prevent the spread of the infection, guidelines were established by the Ministry of Health and the Institute for Public Health, for the purpose of early detection and control of infection sources and the application of standard precautionary measures related to: hand hygiene and respiratory hygiene, maintaining physical distance, the importance of the use of personal protective equipment, isolation of suspected Covid cases, their treatment and their transport to Covid hospitals, if necessary [5,6]. The spreading of the SARS-Cov-2 infection can be slowed down by early detection, isolation, contact tracing and monitoring, and mass vaccination.

The goal of this paper is to give an overview of the research conducted so far regarding the epidemiological characteristics, causes, clinical presentation, diagnostics, prevention and control of the new coronavirus disease, the SARS-Cov-2 infection.

ETIOLOŠKE KARAKTERISTIKE
Koronavirusi su prvi put identifikovani kao patogeni za ljude krajem šezdesetih godina prošlog veka [7]. Novi SARS-Cov-2 virus pripada rodu beta-koronavirusa. Čestice su okrugle, ovalne, često i polimorfne, prečnika od 60 – 140 nm i imaju omotač. Među funkcijama strukturalnih proteina, omotač ima presudnu ulogu u patogenosti virusa. Do sada dostupni podaci ukazuju na to da ova virusna infekcija može izazvati prekomernu imunološku reakciju kod domaćina, a koja se u celini označava kao “citokinska oluja”, a čiji efekat je obimno oštećenje tkiva [8,9]. Novi koronavirus pokazao je mogućnost prenošenja sa životinja na čovjeka i sa čovjeka.
 According to the latest guidelines, three main transmission routes of the COVID-19 virus have been described: 1) transmission through droplets, 2) transmission through direct contact, 3) transmission via aerosol. 

Droplet transmission occurs when respiratory droplets are inhaled or swallowed by healthy individuals who find themselves in close proximity to infected persons, who expel these droplets during speech, coughing or sneezing [11]. Touching surfaces or objects contaminated with the virus, and then touching one’s nose, mouth or eyes, is also a route of transmission of the disease. As the SARS-Cov-2 can be isolated from urine and feces of infected persons, attention should be paid to the possibility of orofecal transmission of the infection [12]. It has been estimated that the expected number of cases that one infected person could produce in the population would be 2.2 [13]. Chinese scientists have discovered that the feces of SARS-Cov-2 positive patients was positive for the virus in 6.5% of the cases [10,14,15]. Infectious droplets can also easily contaminate the epithelium of the conjunctiva of the eye [16]. Epidemiological studies have confirmed that half of the diseased patients also suffered from some chronic disease (51%) [17]. The age distribution of patients was published in some studies, ranging from 25 to 89 years. Most of the adult patients were in the 35 to 55 age group, although there were also cases identified amongst children and newborns [18]. The average age of the patients was 59 years; most of them (59%) were male [19]. A study including nine babies born to infected or sick mothers did not discover Covid-19 positivity in the newborns [20,21]. However, there are data on newborn babies being infected [22]. The possibility of vertical transmission requires further research.

CLINICAL CHARACTERISTICS

The incubation period is 1-14 days, with the average being 5.2 days [19]. A long incubation period is the reason why there is high transmission of the virus from the infected person onto his/her environment. The complete
clinical manifestation of the disease is not as yet completely clear, since the symptoms range from those typical for the mild clinical presentation to those characteristic of severe clinical presentation, which may sometimes end in death, while, on the other hand, there are also asymptomatic cases. The guidelines for defining a case of Covid-19 state the following: elevated body temperature, decreased leukocyte and/or lymphocyte count, an abnormal finding on lung X-ray. Based on a study including 44,500 cases with confirmed infection, the mild form of the disease was present in 81% of the cases, serious and severe forms of the disease in 14% of the cases, the critical form with disturbed pulmonary gas exchange, state of shock, failure of other organs, was present in 5% of the cases, and in 2.3% – 5% of the cases, the disease ended in death [23]. The main clinical manifestations include elevated body temperature, coughing, shortness of breath. Nasal congestion, a runny nose, a sore throat, headache, myalgia, diarrhea, loss of the sense of taste and/or smell, have also been reported. In patients with hypoxia, confusion is possible. The average duration of the symptoms is estimated to be 8 days [24]. In a research of early clinical manifestations, 87% patients had a fever, 60% had a dry cough, and around 39% experienced fatigue and weakness [25,26]. In asymptomatic cases, the X-ray finding is normal, while the SARS-Cov-2 test is positive. Mild clinical presentation is characterized by symptoms of acute upper respiratory tract infection, including elevated body temperature, fatigue, myalgia, a sore throat, a runny nose, sneezing, and coughing. Some of the patients experienced symptoms related to the digestive tract: nausea, vomiting, pain in the abdomen, diarrhea. On examination, these patients presented only with hyperemia of the pharynx, while the auscultatory finding was normal. Pulmonary X-ray showed know signs of pneumonia. Moderate clinical presentation is accompanied by fever, subfebrile body temperature, dry irritating cough, and blood oxygen levels above 94%. Further exacerbation of symptoms typical of the moderate clinical presentation leads to severe clinical presentation. Febrility continues, there is dyspnea, central cyanosis; the blood oxygen level drops below 90%, and specific changes visible on a CT scan occur. There is a need for supplemental oxygen. Critical clinical presentation is accompanied by signs of respiratory distress syndrome (RDS), respiratory arrest, state of shock, encephalopathy, and there is a need for mechanical ventilation. Laboratory findings related to the cytokine storm show elevated levels of fibrinogen, C-reactive protein, D-dimer, and IL-6.

DIJAGNOZA

Za pacijente sa sumnjom na SARS-Cov-2 infekciju, dijagnoza se postavlja na osnovu kliničkih slika, radiografskog nalaza pluća, i biohemijskih analiza. Kliničke manifestacije su u vidu akutnih respiratornih simptoma, povišene telesne temperature, i nalaza radiografije pluća, koji pokazuje znake pneumonije. Od značaja su i pozitivni epidemiološki podaci o putovanjima ili kontaktima sa osobama obolelim od SARS-Cov-2 infekcije. Etiološka dijagnoza se postavlja na osnovu pozitivnog nalaza nazofaringealnog ili orofaringealnog brisa, RT-PCR metodom i/ili Ag brzim testom. Od laboratorijskih
analiza krvi, u ranim fazama bolesti, broj perifernih le-
ukocita je smanjen ili normalan, broj limfocita je sman-
jen, dok je povišen nivo sedimentacije eritrocita, od-
nosno CRP-a.

Broj trombocita je niži kod oboljelih sa težom klinič-
kom slikom, a trombocitopenija je nezavisni prediktor mortaliteta kod oboljelih sa težom kliničkom slikom [27]. Kod težih slučajeva, broj limfocita se progresivno smanjuje, a povišeni su D-dimer, serumski kalcitonin, troponin i ferrorit, naročito kod onih pacijenata koji zah-
tevaju smeštaj u jedinice intenzivne nege [17,28]. Zbog promena na plućima, važno je uraditi i radiografiju pluća. Najčešće promene, vidljive na rentgenskom snimku pluća, su zadebljanja intersticijuma, dominantno perifer-
o i u donjim plućnim poljima, retikularne promene i konsolidacije. Ukoliko su prisutni respiratorni simptomi, a rentgenski nalaz pluća je normalan, ukoliko je došlo do kliničkog pogoršanja, ili da bi se isključile potencijal-
ne komplikacije, preporučen je CT pluća. Neprozirnost plućnog parenhima u vidu mlečnog stakla i konsola-
dacije, sa ili bez vaskularnog uvećanja, kao i zadebljana interlobularnih septi, su uobičajeni CT nalazi SARS-Cov-2 pozitivnih pacijenata. Pleuralni izliv je redak [29,30,31].

Analizirana je dinamika antitela kod inficiranih paci-
jenata. IgM antitela se otvrda u krvi pacijenata od 3 do 6 dana od početka bolesti, dok se prisustvo IgG antitela beleži od osmg dana. Kako početak bolesti odmiče, titer IgM antitela se postepeno smanjuje, od druge ne-
delje bolesti. IgG antitela dostižu titer od najmanje če-
stvorostrukog porasta tokom perioda rekovalescencije, što ukazuje da imaju zaštitnu ulogu [32]. Istraživanja su pokazala snažnu povezanost tita ukupnih antitela na SARS-Cov-2 i težine kliničke slike. Bolesnici koji su imali težu kliničku sliku stvarali su više titrove antitela, posle preležane bolesti.

PREVENCIJA

Najbolja mera prevencije bolesti je vakcinacija i izbe-
gavanje izlaganja virusu. Lekari opšte medicine, kao i druge zdravstveni radnici, koji na primarnom nivou leče obolele ili sumnjive na SARS-Cov-2 infekciju, trebalo bi da preduzmu mere predostrožnosti, pre svega da imaju naviku nošenja maske na licu i pranja ruku sapu-
om ili dezinfekcijom sredstvom, kao i da izbegavaju dodirivanje lica prljavim rukama, te da poštuju fizičku distancu.

Asimptomatski kontakti se upućuju u kućnu izola-
ciju, u trajanju od 14 dana. Pacijenti sa blagim simpto-
mima se upućuju na kućno lečenje i pod zdravstvenim nadzorom su lekara primarne zdravstvene zaštite iz Kovid ambulant. Pacijenti sa težim kliničkim formama bolesti upućuju se na konsultativno lečenje u Kovid bolnice.
Trenutno je u razvoju više potencijalnih vakcina. Do sada je njih 8 administrativno prihvaćeno u svetu, a četiri vakcine su doble upotrebnu dozvolu u Srbiji. U trenutku pisanja ovog rada, dostupne vakcine u Srbiji su BioNTech/Pfizer, Sinopharm BBIBP-CorV, Sputnik V, Oxford/AstraZeneca, sa trenutno 26,9% potpuno vakcinisanih građana i 34,1% koji su primili jednu dozu [5].

Masovna i sveobuhvatna vakcinacija bi mogla biti najuspešnije sredstvo u borbi protiv SARS-Cov-2 infekcije.

ZAKLJUČAK

Iako ne može odražavati celokupno istraživanje o SARS-Cov-2 infekciji širom sveta, ovaj rad može pružiti informacije za buduća proučavanja i kontrolu bolesti. Tek kada se pandemija završi, moći će da se proceni zdravstveni, ekonomski i socijalni uticaji ove globalne katastrofe. COVID-19 je nova bolest izazvana koronavirusom koja je pogodila veliki broj ljudi i zemalja širom sveta. Većina pacijenata će imati blagu kliničku sliku, ali teške forme praćene respiratornim distresom, višestrukim zastojem organa, pa čak i smrtnim ishodom. Primena preventivnih mera, rano prepoznavanje inficiranih osoba, njihova izolacija i vakcinacija, zajedno sa najefikasnijim načinima borbe sa ovim virusom. Brz napredak nauci i javnog zdravlja koji je postignut pri suočavanju sa pandemijom COVID-19 ne-uporediv je, ali još uvek postoji potreba za ubrzanjem protokola koji vode ka brzoj dijagnostici, terapiji i lečenju. Korist od vakcinacije bila bi vrlo velika, ako bi obuhvat populacije bio veliki, i na taj način bi se sprečile ponovljene epidemije.

Sukob interesa: Autori nemaju sukob interesa.

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CONCLUSION

Although it cannot reflect the entire research on the SARS-Cov-2 infection worldwide, this paper can offer information for future research and disease control. It is only once the pandemic is over that the health, economic and social impact of this global catastrophe can be assessed. COVID-19 is a new disease caused by coronavirus, which has afflicted a great number of people and countries all over the world. Most of the patients will develop a mild clinical presentation, but severe forms of the disease are also possible, resulting in respiratory distress syndrome, multipolar organ failure, and even death. Enforcing preventive measures, early detection of infected persons, the isolation of such persons, and vaccination, are, at the moment, the most efficient and effective means to fight the COVID-19 pandemic. The rapid development of science and public health, which has been achieved in facing the COVID-19 pandemic, is unprecedented. However, there is still a need to accelerate the protocols leading to swift diagnosis, therapy and treatment. The benefits from vaccination could be great, provided that the scope of the population covered by the vaccine is large, thus preventing repeated outbreaks of the epidemic.

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