

SaRS-CoV-2: EPIDEMIOLOŠKE KARAKTERISTIKE, KLINIČKA SLIKA, DIJAGNOSTIKA I PREVENCIJA – PREGLED DOSADAŠNJIH SAZNANJA

AKTUELNA TEMA

CURRENT TOPIC

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

Marina B. Fišeković-Kremić¹, Snežana P. Stojanović-Ristić²

¹ Dom zdravlja Novi Beograd, Beograd, Srbija

¹ Health Care Center New Belgrade, Belgrade, Serbia

² Zavod za zdravstvenu zaštitu studenata, Beograd, Srbija

² Institute for Student Health Care, Belgrade, Serbia

SAŽETAK

Bolest SARS-Cov-2 se pojavila decembra meseca 2019. godine, kada je potvrđeno da je novi korona virus uzročnik oboljenja. Cilj ovog rada je da rezimira dosadašnja istraživanja o epidemiološkim karakteristikama, uzrocima, kliničkoj slici, dijagnostici, prevenciji i kontroli nove bolesti uzrokovane koronavirusom. SARS-Cov-2 virus pripada rodu beta-koronavirusa, jednolančanim RNK virusima. Omotač ima presudnu ulogu u patogenosti virusa. Virusna infekcija može izazvati prekomernu imunološku reakciju kod domaćina, koja je označena kao "citokinska oluja", čiji efekat je obimno oštećenje tkiva. Opisana su tri glavna puta prenosa virusa: kapljičnim putem, direktnim kontaktom i aerosolom. Smatra se da inkubacioni period iznosi 1-14 dana. Klinička slika može da varira od asimptomatske, preko blage, do teške forme, koja se može završiti i smrtnim ishodom. Glavne kliničke manifestacije uključuju povišenu telesnu temperaturu, kašalj i kratak dah. Nazalna kongestija, curenje iz nosa, gušobolja, glavobolja, bolovi u mišićima, prolivaste stolice, gubitak čula ukusa i/ili mirisa se takođe prijavljuju. Dijagnostički postupci su: klinička slika, radiografija pluća, biohemijske analize, epidemiološka anamneza. Za postavljanje etiološke dijagnoze služi pozitivan nalaz nazofaringealnog ili orofaringealnog brisa (brzi Ag test, i/ili reverzna transkriptaza-lančana reakcija polimeraze (RT-PCR)). SARS-Cov-2 infekcija je pogodila veliki broj ljudi i zemalja širom sveta. Primena preventivnih mera, vakcinacija, rano prepoznavanje inficiranih osoba i njihova izolacija, za sada su najefikasniji način borbe sa ovim virusom. Po završetku pandemije, moći će da se proceni zdravstveni, socijalni i ekonomski uticaj infekcije ovim virusom.

Cljučne reči: SARS-Cov-2, virus, pandemija, prevencija

ABSTRACT

The SARS-Cov-2 disease appeared in December 2019, when the new coronavirus was confirmed to be the cause of the disease. The objective of this article is to summarize previous research on the epidemiological characteristics, etiology, clinical characteristics, diagnosis, prevention, and control of the new SARS-Cov-2 infection. The SARS-Cov-2 virus belongs to the group of betacoronaviruses, which are single-stranded RNA viruses. The envelope has a crucial role in the pathogenicity of the virus. A viral infection can cause an excessive immune response in the patient, which is labeled as a "cytokine storm," and whose effect is extensive tissue damage. Three main routes of the transmission of the virus are: droplets, direct contact, aerosol. The incubation period is considered to be 1-14 days. The clinical manifestation ranges from asymptomatic, mild, to severe, and some cases end in death. The main clinical manifestations include fever, cough, and 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. The diagnostic procedures are the following: clinical manifestation, chest X-rays, biochemical analyses, epidemiological anamnesis. A positive nasopharyngeal or oropharyngeal swab (Ag test, and/or reverse transcription polymerase chain reaction (RT-PCR)) is used for etiological diagnosis. The SARS-Cov-2 infection has affected a large number of people and countries around the world. The application of preventive measures, early identification of infected persons, their isolation, and vaccination are currently the most effective mode in the battle against this virus. After the conclusion of the pandemic, it will be possible to estimate the health, social and economic impact of the virus.

Key words: SARS-Cov-2, virus, pandemic, prevention

Autor za korespondenciju:

Marina B. Fišeković Kremić

Dom zdravlja Novi Beograd, Beograd, Srbija

Đorđa Čutukovića 48a/6, 11080 Zemun, Beograd, Srbija

E-mail: marina.b.fisekovic@gmail.com

Corresponding author:

Marina B. Fišeković Kremić

Health Care Center New Belgrade, Belgrade, Serbia

48a/6 Đorđa Čutukovića Street, 11080 Zemun, Belgrade, Serbia

E-mail: marina.b.fisekovic@gmail.com

Primljeno • Received: February 13, 2021; **Revidirano • Revised:** May 23, 2021; **Prihvaćeno • Accepted:** June 4, 2021; **Online first:** June 25, 2021.

DOI: 10.5937/smclk2-30845

UVOD

Bolest SARS-Cov-2 se pojavila krajem decembra 2019. godine u Vuhanu, Kina, kada je zapažena serija slučajeva pneumonija nepoznatog prouzrokovača. Nekoliko nedelja kasnije potvrđeno je da je novi korona virus uzročnik oboljenja. U Srbiji je, polovinom marta 2020. godine, nakon registrovanja 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-dijetetski režim, savet da se ostane kod kuće, pa i kućnu izolaciju, ako je neophodna. Kasnije, kako je epidemija odmicala, a broj zaraženih i obolelih osoba se povećavao, formirane su Kovid ambulante na primarnom nivou, u kojima je lekar bio u obavezi da pacijenta sa sumnjom na SARS-Cov-2 infekciju pregleda, uradi mu laboratorijske analize, radiografiju pluća, kao i nazofaringealni bris, i nakon toga ga uputi u izolaciju, leči, ili, ako je neophodno, uputi u dalji trijažni centar, radi hospitalizacije. Kako bi se sprečilo prenošenje infekcije, sledile su smernice Ministarstva zdravlja i Instituta za javno zdravlje Srbije, u cilju ranog otkrivanja i kontrole izvora infekcije i primene standardnih mera predostrožnosti, u smislu higijene ruku i mera respiratorne higijene, fizičke distance, važnosti upotrebe lične zaštitne opreme, izolacije sumnjivih slučajeva, i njihovog lečenja i transporta u Kovid bolnice, ako je neophodno [5,6]. Širenje SARS-Cov-2 infekcije može biti usporeno ranim otkrivanjem, izolacijom, praćenjem kontakata, i masovnom vakcinacijom.

Cilj ovog rada je da rezimira dosadašnja istraživanja o epidemiološkim karakteristikama, uzrocima, kliničkoj slici, dijagnostici, prevenciji i kontroli nove koronavirus bolesti, SARS-Cov-2 infekcije.

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 strukturnih 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, koja je u celini označena kao "citokinska oluja", a čiji efekat je obimno oštećenje tkiva [8,9]. Novi koronavirus pokazao je mogućnost prenošenja sa životinja na čoveka i sa čoveka

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, 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.

ETIOLOGICAL CHARACTERISTICS

Coronaviruses were first identified as pathogens affecting humans in the late 1960s [7]. The new SARS-Cov-2 virus belongs to the betacoronavirus genus. The particles are spherical, oval, and often polymorphous, 60 – 140 nm in diameter, with an envelope. Amongst the functions of the structural proteins, the envelope has a crucial role in the pathogenicity of the virus. Data available so

na čoveka. Prema istraživanju koje su sproveli Nanšan i Zonga (*Nanshan and Zhonga*) na 1.099 pacijenata koji su imali potvrđenu SARS-Cov-2 infekciju, više od dve trećine pacijenata je imalo kontakt sa inficiranim ljudima, a svega 1,18% pacijenata je imalo podatak o izloženosti divljim životinjama [10].

EPIDEMIOLOŠKE KARAKTERISTIKE

Prema poslednjim smernicama, opisana su tri glavna puta prenosa virusa COVID-19:

- 1) kapljicama,
- 2) direktnim kontaktom,
- 3) aerosolom.

Prenos kapljicama se dešava kada respiratorne kapljice udišu ili gutaju zdrave osobe koje se nađu u blizini zaraženih osoba, koje te kapljice izbacuju pri govoru, kašljanju ili kijanju [11]. Dodirivanjem površina ili predmeta kontaminiranih virusom, a potom usta, nosa ili očiju, takođe predstavljaju put prenošenja infekcije. Kako se virus SARS-Cov-2 može izolovati iz mokraće i stolice inficirane osobe, treba obratiti pažnju na mogućnost fekalno-oralne infekcije [12]. Procenjeno je da bi očekivani broj slučajeva koje bi direktno proizvela jedna zaražena osoba u populaciji bio 2,2 [13]. Kineski naučnici otkrili su da je izmet pacijenta pozitivnih na SARS-Cov-2 u 6,5% slučajeva bio pozitivan na virus [10,14,15]. Infektivne kapljice lako mogu kontaminirati i epitel konjunktive očiju [16]. Epidemiološke studije su potvrdile da je polovina obolelih imala neku hroničnu bolest (51%) [17]. Neke studije su objavile starosnu distribuciju pacijenata, koja se kretala između 25 i 89 godina. Većina odraslih pacijenata je bila između 35 i 55 godina, mada je bilo identifikovanih slučajeva među decom i novorođenčadima [18]. Prosečna starost pacijenata bila je 59 godina; većina (59%) su osobe muškog pola [19]. Studija koja je sprovedena na devet novorođenih beba inficiranih ili obolelih majki, nije otkrila pozitivnost na virus kod novorođenčadi [20,21]. Međutim, ima podataka i da su novorođene bebe bile inficirane [22]. Mogućnost vertikalnog prenosa zahteva dalja istraživanja.

KLINIČKE KARAKTERISTIKE

Inkubacioni period iznosi 1-14 dana, prosečno 5,2 dana [19]. Dug inkubacioni period je razlog za veliku prenosivost virusa sa inficirane osobe na njenu okolinu. Kompletna klinička manifestacija bolesti još nije u potpunosti jasna, budući da se simptomi kreću od blage do teške kliničke slike, koja se ponekad može završiti i letalno, dok sa druge strane postoje i asimptomatski slučajevi. Smernice za definiciju slučaja pominju sledeće: povišenu telesnu temperaturu, smanjenje leukocita

far indicate that this viral infection may cause an excessive immune response in the host, which is, as a whole, marked as a "cytokine storm", whose effect is massive tissue damage [8,9]. The new coronavirus has demonstrated the ability of being transmitted from animal to human and from human to human. According to the research conducted by Nanshan and Zhonga on 1,099 patients with confirmed SARS-Cov-2 infection, more than two thirds of the patients had been in contact with infected people, and as few as 1.18% of patients had the data on exposure to wild animals in their medical history [10].

EPIDEMIOLOGICAL CHARACTERISTICS

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

i/ili limfocita, radiografski nalaz na plućima. Na osnovu studije koja je obuhvatila 44.500 slučajeva potvrđene infekcije, blagi oblik bolesti bio je u 81%, ozbiljni i teški oblici oboljenja u 14%, kritičan oblik oboljenja sa poremećajem razmene gasova u plućima, šokno stanje, popuštanje i drugih organa u 5%, a 2,3 % do 5% obolelih sa smrtnim ishodom [23]. Glavne kliničke manifestacije uključuju povišenu telesnu temperaturu, kašalj, kratak dah. Nazalna kongestija, curenje iz nosa, gušobolja, glavobolja, bolovi u mišićima, prolivaste stolice, gubitak čula ukusa i/ili mirisa su takođe prijavljeni. Kod bolesnika sa hipoksijom moguća je konfuznost. Prosečno trajanje simptoma procenjeno je na 8 dana [24]. U istraživanju ranih kliničkih manifestacija, 87% pacijenata je imalo groznicu, 60% suv kašalj i oko 39% malaksalost [25,26]. Kada se radi o asimptomatskim slučajevima, rentgen nalaz pluća je normalan, test na SARS-Cov-2 je pozitivan. Blagu kliničku sliku karakterišu simptomi akutne infekcije gornjih disajnih puteva, uključujući povišenu temperaturu, umor, bolove u mišićima, bol u guši, curenje iz nosa, kihanje, kašalj. Neki od pacijenata su imali i simptome oboljenja digestivnog trakta: muku, povraćanje, bol u trbuhu, prolivaste stolice. Pregled ovih pacijenata je samo pokazivao hiperemiju ždrela, dok je auskultatorni nalaz na plućima bio normalan. Na radiografiji pluća nije bilo znakova pneumonije. Umerena klinička slika praćena je groznicom, subfebrilnom temperaturom, suvim nadražajnim kašljem i zasićenjem krvi kiseonikom višim od 94%. Produblivanjem simptoma umerene kliničke slike nastaje teška klinička slika. Nastavlja se febrilnost, dispneja, centralna cijanoza, zasićenje kiseonikom koje je niže od 90%, i javljaju se specifične promene viđene na skeneru pluća (CT). Postoji potreba za kiseoničkom potporom. Kritična klinička slika praćena je znacima respiratornog distres sindroma (RDS), respiratornim zastojem, stanjem šoka, encefalopatijom, i postoji potreba za mehaničkom ventilacijom. Laboratorijski nalazi usled citokinske oluje pokazuju porast fibrinogena, C reaktivnog proteina, D-dimera, i IL-6.

DIJAGNOZA

Za pacijente sa sumnjom na SARS-Cov-2 infekciju, dijagnoza se postavlja na osnovu kliničke slike, 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

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 levels, C-reactive protein, D-dimer, and IL-6.

DIAGNOSIS

For patients suspected to be infected with SARS-Cov-2, diagnosis is determined on the basis of clinical

analiza krvi, u ranim fazama bolesti, broj perifernih leukocita je smanjen ili normalan, broj limfocita je smanjen, dok je povišen nivo sedimentacije eritrocita, odnosno CRP-a.

Broj trombocita je niži kod obolelih sa težom kliničkom slikom, a trombocitopenija je nezavisni prediktor mortaliteta kod obolelih sa težom kliničkom slikom [27]. Kod težih slučajeva, broj limfocita se progresivno smanjuje, a povišeni su D-dimer, serumski kalcitonin, troponin i feritin, naročito kod onih pacijenata koji zahtevaju 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 zadebljao intersticijum, dominantno periferno 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 potencijalne komplikacije, preporučen je CT pluća. Neprozirnost plućnog parenhima u vidu mlečnog stakla i konsolidacija, sa ili bez vaskularnog uvećanja, kao i zadebljanja interlobularnih septi, su uobičajeni CT nalazi SARS-CoV-2 pozitivnih pacijenata. Pleuralni izliv je redak [29,30,31].

Analizirana je dinamika antitela kod inficiranih pacijenata. IgM antitelo se otkriva u krvi pacijenata od 3 do 6 dana od početka bolesti, dok se prisustvo IgG antitela beleži od osmog dana. Kako početak bolesti odmiče, titar IgM antitela se postepeno smanjuje, od druge nedelje bolesti. IgG antitela dostižu titar od najmanje četvorostrukog porasta tokom perioda rekoalescencije, što ukazuje da imaju zaštitnu ulogu [32]. Istraživanja su pokazala snažnu povezanost titra 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 izbegavanje izlaganja virusu. Lekari opšte medicine, kao i drugi 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 sapunom ili dezinfekcionim sredstvom, kao i da izbegavaju dodirivanje lica prljavim rukama, te da poštuju fizičku distancu.

Asimptomatski kontakti se upućuju u kućnu izolaciju, u trajanju od 14 dana. Pacijenti sa blagim simptomima se upućuju na kućno lečenje i pod zdravstvenim nadzorom su lekara primarne zdravstvene zaštite iz Kovid ambulanti. Pacijenti sa težim kliničkim formama bolesti upućuju se na konsultativno lečenje u Kovid bolnice.

presentation, pulmonary X-ray findings, and biochemical laboratory analyses. Clinical manifestations are in the form of acute respiratory symptoms, elevated body temperature, and a pulmonary X-ray finding indicating signs of pneumonia. Positive epidemiological data on travel or contact with patients afflicted with the SARS-CoV-2 infection, are also relevant. Etiological diagnosis is established on the basis of a positive nasopharyngeal or oropharyngeal swab, tested with the RT-PCR method and/or the Ag rapid test. As far as laboratory blood analyses are concerned, in the early stages of the disease, the peripheral leukocyte count is either decreased or normal, the lymphocyte count is decreased, while the erythrocyte sedimentation rate and the level of CRP are elevated.

The thrombocyte count is lower in patients with severe clinical presentation, and thrombocytopenia is an independent predictor of mortality in patients with severe clinical presentation [27]. In the more severe cases, the lymphocyte count progressively decreases, while D-dimer, serum calcitonin, troponin, and ferritin are elevated, especially in patients requiring intensive care [17,28]. Due to changes in the lungs, it is important to perform a pulmonary X-ray. The changes most commonly found on pulmonary X-rays are the thickening of the interstitium, dominantly peripherally and in the inferior lung fields, as well as reticular changes and consolidations. If respiratory symptoms are present, but the pulmonary X-ray is normal, in case the patient's condition clinically worsens, or if potential complications need to be excluded, it is recommended to perform a CT scan of the lungs. Ground-glass opacity of the parenchyma of the lungs and consolidation, with or without vascular enlargement, as well as interlobular septal thickening, are common findings on pulmonary CT scans for SARS-CoV-2 positive patients. Pleural effusion is rare [29,30,31].

The dynamics of the antibodies in infected patients has been analyzed. The IgM antibody is registered in the patient's blood three to six days after the onset of disease, while the presence of the IgG antibody is registered as of the eighth day. As the disease develops, the IgM antibody titer gradually decreases, as of the second week of disease. The IgG antibody titer increases to at least its quadruple value during the period of convalescence, indicating the protective role of these antibodies [32]. Research has shown a strong connection between the SARS-CoV-2 total antibody titer and the severity of clinical presentation. Patients who had had a more severe clinical presentation had higher titers of antibodies, after the illness.

PREVENTION

The best preventive measure against the disease is vaccination and avoiding exposure to the virus. General

Trenutno je u razvoju više potencijalnih vakcina. Do sada je njih 8 administrativno prihvaćeno u svetu, a četiri vakcine su dobile 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 uticaj 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 moguće su i teške forme praćene respiratornim distres sindromom, višestrukim zastojem organa, pa čak i smrtnim ishodom. Primena preventivnih mera, rano prepoznavanje inficiranih osoba, njihova izolacija i vakcinacija, za sada su najefikasniji načini borbe sa ovim virusom. Brz napredak nauke i javnog zdravlja koji je postignut pri suočavanju sa pandemijom COVID-19 neuporediv je, ali još uvek postoji potreba za ubrzanjem protokola koji vode ka brzom 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.

LITERATURA / REFERENCES

1. Lu H, Stratton CW, Tang YW. Outbreak of Pneumonia of Unknown Etiology in Wuhan China: The Mystery and the Miracle. *J Med Virol*. 2020.
2. World Health Organization. WHO Director-General's Remarks at the Media Briefing on 2019-nCoV on 11 February 2020 [citirano: marta], dostupno na: <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020>
3. COVID-19 Coronavirus Pandemic. Reported Cases and Deaths by Country, Territory, or Conveyance. [citirano: marta], Dostupno na: <https://www.worldometers.info/coronavirus/>
4. John Hopkins Bloomberg School of Public Health. 2019 Global Health Security Index: building collective action and accountability. 2019 [cited March]. Available from: <https://www.ghsindex.org/wp-content/uploads/2019/10/2019-Global-Health-Security-Index.pdf>
5. Ministarstvo zdravlja, Republika Srbija, dostupno na: www.zdravlje.gov.rs
6. Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut“, dostupno na: www.batut.org.rs
6. McIntosh K, Dees JH, Becker WB, Kapikian AZ, Chanock RM. Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease.

practitioners, as well as other health care workers, who, at the primary health care level, treat SARS-Cov-2 patients and those suspected of being infected, should implement preventive measures, primarily, they should habitually wear face masks and wash their hands with soap or disinfectant, they should avoid touching their face with dirty hands and observe physical distance.

Asymptomatic contacts should be instructed to self-isolate at home for a period of 14 days. Patients with mild symptoms are to be directed to convalesce at home under the supervision of the doctors working at primary health care Covid facilities. Patients with more severe clinical forms of the disease are to be referred for consultative treatment in Covid hospitals.

At the moment, a number of potential vaccines are being developed. So far, eight vaccines have administratively been accepted in the world, and four vaccines have been approved for use in Serbia. At the moment when this paper is being written, the vaccines available in Serbia are the following: *BioNTech/Pfizer*, *Sinopharm BBIBP-CorV*, *Sputnik V*, *Oxford/AstraZeneca*, with currently 26.9% of the population fully vaccinated and 34.1% of the population having received the first dose [5].

Mass and general vaccination could be the most effective means in the fight against the SARS-Cov-2 infection.

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, multipole 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 ways to fight this virus. 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.

Conflict of interest: The authors declare no conflict of interest.

- Proceedings of the National Academy of Sciences of the United States of America. 1967 Apr; 57(4):933.
7. Lei J, Kusov Y, Hilgenfeld R. Nsp3 of coronaviruses: Structures and functions of a large multi-domain protein. *Antiviral research*. 2018 Jan 1; 149:58-74.
 8. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B beta coronaviruses. *Nature microbiology*. 2020 Apr; 5(4):562-9.
 9. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Science China Life Sciences*. 2020 Mar; 63(3):457-60.
 10. Sabino-Silva R, Jardim AC, Siqueira WL. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. *Clin Oral Invest*. 2020 Feb 20:1-3.
 11. Zhang H, Kang Z, Gong H. The digestive system is a potential route of 2019-nCoV infection: a bioinformatics analysis based on single-cell transcriptomes [objavljeno na internetu pre štampanog izdanja, 31. januara, 2020.]. *BioRxiv*.
 12. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New England Journal of Medicine*. 2020 Jan 29.
 13. Jones DL, Baluja MQ, Graham DW, Corbishley A, McDonald JE, Malham SK, et al. Shedding of SARS-CoV-2 in feces and urine and its potential role in person-to-person transmission and the environment-based spread of COVID-19. *Sci Total Environ*. 2020 Dec 20; 749:141364.
 14. Kraay AN, Hayashi MA, Hernandez-Ceron N, Spicknall IH, Eisenberg MC, Meza R, et al. Fomite-mediated transmission as a sufficient pathway: a comparative analysis across three viral pathogens. *BMC infectious diseases*. 2018 Dec 1; 18(1):540.
 15. Lu CW, Liu XF, Jia ZF. 2019-nCoV transmission through the ocular surface must not be ignored. *Lancet (London, England)*. 2020 Feb 22; 395(10224):e39.
 16. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020 Feb 15; 395(10223):507-13.
 17. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. *World J Pediatr*. 2020 Feb 7:1-9.
 18. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020 Jan 29.
 19. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *The Lancet*. 2020 Mar 7; 395(10226):809-15.
 20. Zeng H, Xu C, Fan J, Tang Y, Deng Q, Zhang W, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. *Jama*. 2020 May 12; 323(18):1848-9.
 21. Zhang ZJ, Yu XJ, Fu T, Liu Y, Jiang Y, Yang BX, et al. Novel coronavirus infection in newborn babies under 28 days in China. *Eur Respir J*. 2020 Jan 1.
 22. Zarea Gavvani V. Infodemic in the Global Coronavirus Crisis. *Depiction of Health 2020*; 11 (1): 1-5. *Am J Prev Med*. 2011; 40 (5):S154-8.
 23. De Chang GM, Yuan X, Tao Y, Peng X, Wang FS, Xie L, et al. Time Kinetics of Viral Clearance and Resolution of Symptoms in Novel Coronavirus Infection. *Am J Respir Crit Care Med*. 2020 May 1; 201(9):1150.
 24. Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early clinical and CT manifestations of coronavirus disease 2019 (COVID-19) pneumonia. *AJR*. 2020 Mar 17:1-6.
 25. Cao Y, Liu X, Xiong L, Cai K. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2: A systematic review and meta-analysis. *J Med Virol*. 2020 Apr 3.
 26. Shang W, Dong J, Ren Y, Tian M, Li W, Hu J, et al. The value of clinical parameters in predicting the severity of COVID-19. *J Med Virol*. 2020 Oct;92(10):2188-92.
 27. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020 Apr 30; 382(18):1708-20.
 28. Li Y, Xia L. Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. *AJR*. 2020 Mar; 4:1-7.
 29. Tang YW, Schmitz JE, Persing DH, Stratton CW. Laboratory Diagnosis of COVID-19: Current Issues and Challenges. *J Clin M*. 2020 May 26; 58(6).
 30. Hong KH, Lee SW, Kim TS, Huh HJ, Lee J, Kim SY, et al. Guidelines for laboratory diagnosis of coronavirus disease 2019 (COVID-19) in Korea. *Ann Lab Med*. 2020 Mar 31;40(5):351-60.
 31. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020;71(16):2027-34.