Utjecaj pandemije COVID-19 na oboljele od shizofrenije

/ The Impact of COVID-19 Pandemic on Patients with Schizophrenia

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Strah od prijenosa zaraze COVID-19 pridonio je pojavi anksioznosti i depresije kod osoba koje do sada nisu bolovale od mentalnih bolesti, te do pogoršanja simptoma u osoba s prethodno dijagnosticiranim mentalnim bolestima. Pokazano je da oboljeli od shizofrenije imaju povećan rizik od zaraze COVID-19 kao i da su češće hospitalizirani te imaju veću smrtnost, što se povezuje s velikim brojem komorbiditeta, pušenjem te korištenjem velikog broja lijekova. Uočena je i veza između imunološkog i upalnog profila COVID-19 i shizofrenije. Problem su također nejednakost zdravstvene skrbi i stigma koji doprinose lošijem ishodu COVID-19 kod osoba oboljelih od mentalnih bolesti. Pandemija COVID-19 može dovesti do pogoršanja psihotičnih simptoma i pojave relapsa u osoba s prethodno dijagnosticiranim mentalnim bolestima. Nadalje, uočena je veza između socijalne izolacije i pogoršanja mentalnog zdravlja u smislu razvoja stresa i anksioznosti. Kako bi se nastavila pružati kontinuirana skrb oboljelima od shizofrenije, a smanjio rizik od zaraze, telemedicina pruža najbolje moguće riješenje, no za teže slučajeve fizički posjeti ostaju i dalje ključni. Oboljeli od shizofrenije su vulnerabilna skupina u smislu zaraze COVID-19 i mogućeg smrtnog ishoda i potrebno ih je zaštititi senzibiliziranjem društva i medicinskih djelatnika kako bi se uklonila stigma i smanjile nejednakosti u pružanju zdravstvene skrbi.

/ The fear of transmission of COVID-19 infection has contributed to the occurrence of anxiety and depression in individuals who have not previously suffered from mental illness, and to the worsening of symptoms in patients previously diagnosed with mental illness. It has been shown that patients with schizophrenia have an increased risk of contracting COVID-19, are more often hospitalized and have a higher mortality rate. This is correlated with many comorbidities, tobacco consumption, and extensive use of medications. It has been noted that there is a connection between the immune and inflammatory response of COVID-19 and schizophrenia. Healthcare inequality and stigma result in a poorer outcome of COVID-19 in persons suffering from mental illness. The COVID-19 pandemic can cause a worsening of psychotic symptoms and the reoccurrence of relapses in those with a prior mental illness diagnosis. Additionally, it has been noted that social seclusion can cause a decline in psychological wellbeing, leading to increased levels of stress and anxiety. To ensure that patients with schizophrenia receive uninterrupted care and minimize the risk of infection, telemedicine offers an optimal solution; however, for more severe cases, physical visits remain imperative. Patients with schizophrenia are particularly exposed to contraction and potential death from COVID-19 and require the support of society and medical professionals to help eliminate the stigma they often face, and guarantee equal access to healthcare.

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COVID-19 I MENTALNO ZDRAVLJE

Veliki broj slučajeva atipične upale pluća uzrokovane novim koronavirusom koji je kasnije identificiran kao virus SARS-CoV-2, opažen je u Wuhanu u Kini u prosincu 2019. godine (1). Bolest se naglo proširila diljem svijeta pa je Svjetska zdravstvena organizacija 11. ožujka 2020. proglasila pandemiju COVID-19 (2). Strah od prijenosa bolesti COVID-19 pridonio je pojavi depresije, stresa i anksioznosti među pojedincima koji do sada nisu bolovali od mentalnih bolesti (3). Anksioznost se može javiti kao posljedica straha od zaraze te zbog nedovoljno jasnih uputa vezanih za socijalno distanciranje i manje pouzdanim informacijama iz medija koje doprinose strahu (4). Osim što strah u pandemiji povećava razinu anksioznosti i stresa kod psihički zdravih osoba, zapaženo je i da pojačava simptome kod osoba s ranije dijagnosticiranim psihijatrijskim poremećajima. Skupine koje su posebno ranjive u pandemijama su osobe starije dobi, imunokompromitirani bolesnici te bolesnici s ranije dijagnosticiranim psihijatrijskim bolestima (5). Pojedinci s ranije dijagnosticiranom mentalnom bolešću imaju povećan rizik od zaraze COVID-19 te su i pod povećanim rizikom od negativnih tjelesnih i psiholoških učinaka koji proizlaze iz pandemije (6). Smatra se da u tih bolesnika čimbenici rizika poput pušenja, pretilosti te neaktivnosti pridonose razvoju bolesti i posljedično tome povećanom morbiditetu i mortalitetu. U pojedinaca

COVID-19 AND MENTAL HEALTH

In December 2019, Wuhan, China, reported a great number of unusual pneumonia cases due to the novel coronavirus, later identified as the SARS-CoV-2 virus (1). The World Health Organization proclaimed a pandemic of COVID-19 on March 11, 2020 as the disease spread quickly around the world (2). The fear of transmitting COVID-19 has led to the emergence of depression, stress, and anxiety in individuals who were not already suffering from mental illness (3). Anxiety is a possible consequence of fear of infection, with unclear social distancing instructions and a lack of reliable sources from the media intensifying the fear (4). Fear of the pandemic not only raises the levels of stress and anxiety in people with sound mental health, but it has also been seen to exacerbate the symptoms of those already struggling with psychiatric disorders. Elderly individuals, those who are immunocompromised, and those who have existing psychiatric illnesses are especially at risk from pandemics (5). Individuals with a history of mental health difficulties are more likely to contract COVID-19 and are more vulnerable to physical and psychological impacts resulting from the pandemic (6). It is thought that risk factors such as smoking, obesity and inactivity are implicated in the onset of the disease, resulting in higher morbidity and mortality rates in these patients. For indi-

kojima je dijagnosticirana teška mentalna bolest opaženo je smanjenje životnog vijeka za 13 do 30 godina. Najčešće su u komorbiditetu prisutne kardiovaskularne bolesti, koronarna bolest te šećerna bolest tip 2 (7). S obzirom da je tijekom pandemije medicinska pomoć usredotočena na liječenje oboljelih od COVID-19, starije osobe te bolesnici s kroničnim bolestima koje nisu povezane s COVID-19 suočeni su s promjenama ranije dostupnih zdravstvenih usluga što ima za posljedicu smanjenu zdravstvenu skrb. Nadalje, u tih je ranjivih skupina zabilježen veći rizik od negativnih posljedica socijalnog distanciranja na njihovo mentalno zdravlje. Osim toga brzi prijenos zaraze i veći broj smrtnih slučajeva u tim skupinama mogu povećati rizik od psihičke dekompenzacije i pogoršati već prisutne psihijatrijske poremećaje (8). Ograničavanje socijalnih kontakata može imati negativan utjecaj na psihijatrijske bolesnike, budući da je održavanje međuljudskih odnosa ključna komponenta u postupku njihovog zbrinjavanja i liječenja. Isto tako, negativan utjecaj može imati i smanjen pristup psihijatrijskim pregledima koji su često puta otkazani jer se ne smatraju nužnima, iako su korisni za bolesnika (4). Standardne preporuke za sprječavanje širenja zaraze poput pranja ruku, pokrivanja usta i nosa pri kihanju i kašljanju te izbjegavanja bliskog kontakta s ljudima koji pokazuju simptome respiratorne bolesti, mogu biti teško provedive u mentalno oboljelih pojedinaca, koji osim što imaju povećani rizik od razvoja infekcije, mogu pridonijeti samom prijenosu bolesti. Nadalje, potrebne mjere samoizolacije, koje su inače teško provedive, mogu dodatno pogoršati mentalno stanje ovih bolesnika što uključuje razvoj osjećaja ljutnje i anksioznosti četiri do šest mjeseci nakon izlaska iz karantene (7). S pojavom pandemije COVID-19 pojavila se i stigma. Stvara se odbojnost prema skupinama koje karakterizira visoka stopa infekcije što kod njih rezultira stigmom, a ona je dalje povezana s povećanom anksioznošću i depresijom. Kombinacija stigme prema mentalnim bolestima i stigme prema COVID pozitivnim bolesnicima

viduals with severe mental illness, there was a noted decrease in life expectancy of between 13 and 30 years. Cardiovascular disease, coronary disease, and type 2 diabetes mellitus tend to occur together (7). With the pandemic, medical resources being dedicated to the treatment of COVID-19, elderly and those with chronic diseases unrelated to COVID-19 were experiencing a shift in available health services, leading to a decline in healthcare. Additionally, these at-risk populations have experienced greater odds of detrimental effects on their mental health as a result of social distancing. Furthermore, swift transmission of the virus and higher mortality rates in these populations can lead to psychological decompensation and worsen existing mental health issues (8). A restriction in social interaction can detrimentally affect psychiatric patients, since sustaining human contact is an essential element in the process of their recovery. Similarly, limited access to psychiatric assessments can have an adverse effect. These are frequently cancelled since they are not considered necessary, despite the fact that they are beneficial for the patient (4). It can be challenging to get mentally ill individuals to adhere to standard preventive measures for infection control such as hand washing, covering the nose and mouth when sneezing and coughing, and staying away from people who manifest signs of respiratory illness. Aside from the greater risk of infection, they can facilitate its transmission. Moreover, the necessary self-isolation protocols, which are hard to put into practice, can further worsen the mental state of these patients, like creating anger and anxiousness four to six months after the quarantine is finished (7). The emergence of the COVID-19 pandemic brought with it an issue of stigma. An antipathy to groups with a high rate of infection develops, causing a stigma, which is then associated with augmented anxiety and depression. Stigmatization of both mental illness and COVID-positive patients creates a double stigma. Thus, the patient's compliance with psychiatric treatment

ima kao posljedicu dvostruku stigmu. To negativno utječe na suradljivost bolesnika u psihijatrijskom liječenju što dovodi do povećanog morbiditeta (9). Stigma prema ranjivim pojedincima može biti dodatno produbljena socijalnom deprivacijom te neadekvatnim informacijama i može rezultirati marginalizacijom, ali i povećanim institucionaliziranjem tih pojedinaca (8).

COVID-19 I SHIZOFRENIJA

Stopa zaraze od COVID-19

Oboljeli od shizofrenije mogu imati povećan rizik od zaraze COVID-19 zbog niza razloga. Naime, oboljeli od shizofrenije susreću se s poteškoćama oko provođenja preporučenih protuepidemijskih mjera poput pranja ruku i fizičke distance, što može biti posljedica slabijeg kognitivnog funkcioniranja, smanjene svijesti o riziku te smanjene sposobnosti prosuđivanja i donošenja odluka. Osim toga, često ih karakterizira život u skupini ili domovima, što zbog loših higijenskih uvjeta i gužve ima povišeni rizik od zaraze. To ujedno podrazumijeva i izloženost većoj količini virusa što korelira s težinom bolesti i stopom mortaliteta (10-12). Nadalje, shizofrenija je rizični čimbenik za institucionalno zbrinjavanje, što također može pridonijeti većem riziku od zaraze (13).

Istraživanja su pokazala da je među populacijom beskućnika povećana prevalencija shizofrenije i, prema meta-analizi koja je obuhvatila 31 studiju, iznosi 10,29 % (14). Veliki broj beskućnika ima kronične mentalne i tjelesne bolesti, povezuje ih se s višom stopom zloporabe droga te imaju smanjen pristup zdravstvenoj skrbi što znatno otežava provođenje probira, mjera karantene te liječenje onih koji razviju COVID-19 (15). Beskućnici koji imaju mentalnu bolest nalaze se pod povećanim rizikom od zaraze COVID-19 zbog toga jer žive u lošim higijenskim uvjetima, imaju otežan pristup zdravstvenim informacijama (a time i otežanu primjenu preventivnih zaštitnih mjera) declines, which increases morbidity (9). Social deprivation and lack of information can worsen the stigma faced by vulnerable individuals and may lead to their exclusion from society, as well as greater institutionalization (8).

COVID-19 AND SCHIZOPHRENIA

COVID-19 infection rate

The risk of contracting COVID-19 may be heightened for patients with schizophrenia due to a range of reasons. Patients with schizophrenia have a hard time following the suggested anti-epidemic measures like handwashing and physical distancing, which can be caused by impaired cognitive functioning, lack of risk awareness, and decreased capacity to assess and decide. Additionally, they are usually found in groups or homes, which, due to inadequate hygiene and overcrowding, increases the risk of infection. This suggests that increased exposure to the virus is connected to a more extreme form of the disease and a higher mortality rate (10-12). Additionally, schizophrenia is a risk factor that can lead to institutional care, raising the risk of infection (13).

Research has revealed that the rate of schizophrenia among individuals without permanent housing has grown, and a meta-analysis of 31 studies concluded that it is 10.29% (14). Homeless individuals, many of whom suffer from chronic mental and physical health problems, have a higher propensity for drug use, and limited access to healthcare, leading to difficulties in screening, isolating and treating individuals with COVID-19 (15). Mentally ill homeless people are especially susceptible to COVID-19 due to inadequate hygiene, lack of access to health information (and thus difficulty applying preventive protective measures), and weaker immune systems (16). Conversely, a study carried out in Israel did not demonstrate a higher prevalence of infection among

i slabiji imunološki sustav (16). S druge strane, rezultati studije koja je provedena u Izraelu nisu potvrdili povećanu stopu zaraze među oboljelima od shizofrenije u odnosu na opću populaciju, što može biti posljedica obveznog testiranja u psihijatrijskim institucijama i domovima te u klinikama pri prijmu na liječenje (17). Osim toga, dodatni čimbenik koji bi mogao biti odgovoran za nižu stopu zaraze je činjenica da većina oboljelih od shizofrenije nije u braku, a upravo je zaraza preko člana obitelji jedan od glavnih načina infekcije.

Smrtnost od COVID-19

Oboljeli od shizofrenije i COVID-19 imaju povećani rizik od hospitalnog liječenja za više od dva puta te čak tri puta veću smrtnost od COVID-19 u odnosu na zdravu populaciju (17).

Lošijoj prognozi COVID-19 pridonosi veliki broj komorbiditeta prisutnih među ovom populacijom, no isto tako čimbenici povezani s liječenjem osnovne bolesti. Osim toga, oboljelima od shizofrenije nije jednako dostupna zdravstvena skrb kao ostalim bolesnicima, što ima za posljedicu zakašnjelo dijagnosticiranje i liječenje drugih bolesti, što dodatno negativno utječe na prognozu COVID-19. Povećani rizik od lošijeg ishoda posljedica je nepovoljnog životnog stila, lošeg stambenog zbrinjavanja te slabijeg društvenog života oboljelih od shizofrenije (10).

Oboljeli od shizofrenije u dobi od 65 do 80 godina mogu imati povećani rizik smrtnog ishoda od COVID-19 u odnosu na osobe iste dobi koje nemaju dijagnosticiranu težu mentalnu bolest što se može povezati s ubrzanim biološkim starenjem koje je izraženo kod oboljelih od shizofrenije (18). Kod njih je ubrzano starenje i tijela i mozga, pa tako i stanica imunološkog sustava, što je vrlo značajno u kontekstu COVID-19.

Komorbiditeti

Oboljeli od shizofrenije imaju povećani rizik od smrtnog ishoda u odnosu na opću populaciju zbog lošijeg fizičkog zdravlja (11). U više od

patients with schizophrenia in comparison to the general population, which may be due to the mandatory testing done in mental health facilities, care homes and clinics upon admittance to care (17). Additionally, another factor that could be the cause of the reduced infection rate is that the majority of schizophrenia patients are not married, and contagion through a family member is a major source of infection.

COVID-19 mortality

Those suffering from schizophrenia and having COVID-19 have more than double the risk of hospitalization and three times the risk of death from COVID-19 when compared to a healthy population (17).

The presence of multiple comorbidities among this population leads to a worse prognosis for COVID-19, as well as factors related to the management of the underlying disease. Schizophrenia patients have less access to health care than other patients, leading to a delayed diagnosis and treatment of other diseases, worsening the prognosis of COVID-19. Patients with schizophrenia are more likely to experience a poorer outcome because of an unfavourable lifestyle, inadequate housing care, and lacking social life (10).

Individuals aged 65-80 with schizophrenia could be at greater risk of death from COVID-19 than the individuals of similar age without more serious mental illness, due to the accelerated biological aging seen in schizophrenia (18). Accelerated aging of the body, brain, and the cells of the immune system is observed in them, which is of great significance to COVID-19.

Comorbidities

Compared to the general population, schizophrenia patients have a higher probability of death due to diminished physical health (11). In more than 70% of patients with schizophrenia, at least one comorbidity is present, such as car-

70 % bolesnika oboljelih od shizofrenije prisutan je barem jedan komorbiditet, poput kardiovaskularnih bolesti, bolesti dišnog sustava te šećerne bolesti. Upravo su te bolesti povezane s lošijom prognozom kod oboljelih od COVID-19 (10,13). Također, u 27 % bolesnika oboljelih od shizofrenije u usporedbi s općom populacijom (21 %) prisutan je nedostatak vitamina D, što doprinosi lošijem ishodu u oboljenih od COVID-19 (19,20). U jednom je istraživanju uočena povezanost između shizofrenije i demencije u smislu da je 25,2 % ispitanika oboljelih od shizofrenije imalo demenciju, pogotovo žene, a demencija je prepoznata kao čimbenik rizika za smrtnost kod bolesnika s COVID-19 (21).

Pušenje i lijekovi

Prevalencija pušenja u oboljelih od shizofrenije iznosi 50 % do 90 % (13). Nikotin povećava aktivnost i ekspresiju angiotenzin konvertirajućeg enzima 2 u plućima (ACE-2), a budući da je ACE-2 mjesto ulaza virusa SARS-CoV-2 u stanice, očito je da pušenje povećava rizik od progresije bolesti te doprinosi teškim komplikacijama COVID-19 utječući na imunološki odgovor i stanje pluća (13). Pušenje čini bolesnike podložnima za razvoj bolesti koje su inače povezane s pušenjem poput kronične opstruktivne plućne bolesti, a ona je sama rizični čimbenik za smrtnost od COVID-19 (17). Uočena je povezanost polifarmakoterapije s povećanim rizikom od razvoja COVID-19, a psihotropna polifarmakoterapija česta je u bolesnika koji boluju od teške mentalne bolesti (18). Nema provedenih istraživanja o tom problemu na bolesnicima koji boluju isključivo od shizofrenije, ali su provedena na bolesnicima koji boluju od teških mentalnih bolesti što uključuje i shizofreniju. Naime, prema jednom takvom istraživanju 25 % bolesnika koji boluju od različitih psihičkih poremećaja uključujući i shizofreniju, a kojima su propisani antipsihotici, u terapiji su imali dva ili više antipsihotika (18). Barcella i sur. pokazali su da je broj prodiovascular diseases, respiratory diseases and diabetes mellitus. It is these diseases that are associated with a less favourable prognosis for COVID-19 patients (10,13). In comparison to the 21% of the general population, 27% of those with schizophrenia have lower levels of vitamin D, resulting in a worse outcome if they contract COVID-19 (19, 20). A study established a link between schizophrenia and dementia, whereby 25.2% of those with schizophrenia also had dementia, particularly amongst women, and dementia was identified as a risk factor for mortality in those affected by COVID-19 (21).

Smoking and medication

The prevalence of smoking in people with schizophrenia is 50% to 90% (13). Nicotine increases the activity and expression of angiotensin converting enzyme 2 in the lungs (ACE-2). Since ACE-2 is the primary access for SARS-CoV-2 virus to enter cells, it is no surprise that smoking increases the risk of disease progression and worsens the complications of COVID-19 by impacting the immune system and lung health (13). Smoking makes people more likely to contract diseases typically associated with smoking, like chronic obstructive pulmonary disease, and it raises the risk of death from COVID-19 (17). There has been an association of polypharmacotherapy with an increased risk of developing COVID-19, and psychotropic polypharmacotherapy is common in patients suffering from severe mental illness (18). No research has been conducted on this issue specifically for individuals with schizophrenia, however, studies have been done on people with serious mental illness, schizophrenia included. A study revealed that out of patients with different mental health issues, such as schizophrenia, who were given antipsychotics, 25% were on two or more antipsychotics (18). It was demonstrated by Barcella et al. that the amount of prescribed psychotropic drugs was linked to an increased risk of severe forms of

pisanih psihotropnih lijekova korelirao s povišenim rizikom od teških oblika COVID-19 i smrti, sugerirajući vezu između težine bolesti i lošijeg ishoda COVID-19 (12). Liječenje klozapinom može biti povezano s povećanim rizikom od lošijeg ishoda COVID-19. Naime, kao nuspojava primjene klozapina primijećeni su otežano gutanje, sedacija, hipersalivacija te kao posljedica aspiracijska upala pluća (10,11). Liječenje klozapinom povezano je s oko dva puta većim rizikom od razvoja upale pluća. Osim toga djeluje na prirođenu imunost u obliku prolazne eozinofilije, oslobađanja citokina te vrućice u ranoj fazi liječenja, a rjeđe uzrokuje neutropeniju i agranulocitozu, koja je vjerojatni čimbenik rizika COVID-19. Nadalje, liječenje klozapinom povezano je i sa smanjenom razinom cirkulirajućih imunoglobulina IgM, IgA i IgG. Također, tijekom imunološkog odgovora dolazi do porasta koncentracije klozapina, što dodatno povećava rizik od nuspojava. Rezultati istraživanja upućuju na veći rizik od zaraze COVID-19 u bolesnika koji su liječeni klozapinom (13,22).

Nejednakosti u zdravstvenoj skrbi

Stigma povećava rizik za COVID-19 u oboljelih od shizofrenije jer su često diskriminirani i nailaze na teškoće u ostvarivanju zdravstvene skrbi. Stoga je manje vjerojatno da će dobiti odgovarajuću dijagnostičku obradu te će sukladno tome somatske bolesti biti pogrešno dijagnosticirane ili uopće neće biti dijagnosticirane (23). Stigma može pridonijeti nižoj stopi prijema u jedinice intenzivnog liječenja (JIL) oboljelih od shizofrenije iz domova ili sa psihijatrijskih odjela. Ponekad je premještaj oboljelih od shizofrenije s psihijatrijskih odjela u jedinice intenzivne skrbi otežan zbog potencijalnog poremećaja ponašanja i agresivnosti te smanjene mogućnosti adekvatnog monitoriranja (21).

Stigma mentalnih bolesti dovodi do pojave autostigme i gubitka samopouzdanja što oboljeCOVID-19 and death, implying a correlation between the severity of the disease and a worse outcome of COVID-19 (12). Clozapine treatment may be associated with an increased risk of a more severe outcome of COVID-19. Clozapine use was associated with side effects such as difficulty swallowing, sedation, and hypersalivation, leading to aspiration pneumonia (10,11). The use of clozapine has been associated with around a twofold increase in the risk of pneumonia. Additionally, it has an effect on congenital immunity in the form of transient eosinophilia, production of cytokines and fever in the early stages of treatment, and infrequently triggers neutropenia and agranulocytosis, which is a potential risk factor of COVID-19. Furthermore, clozapine treatment is also associated with reduced levels of circulating immunoglobulins IgM, IgA and IgG. Furthermore, during an immune response, clozapine concentrations increase, which in turn amplifies the potential of side effects. The results of the study suggest a higher risk of contracting COVID-19 in patients treated with clozapine (13,22).

Inequalities in health care

The stigma associated with schizophrenia makes it harder for those affected to receive proper health care, increasing their risk of COVID-19. As a result, they are less likely to receive appropriate diagnostic treatment and thus somatic diseases can be misdiagnosed or not diagnosed in any way (23). Stigma can contribute to a lower rate of admission to intensive care units (ICU) of patients with schizophrenia from homes or psychiatric wards. Sometimes the transfer of schizophrenia patients from psychiatric wards to intensive care units can be difficult due to a potential behavioural disorder, aggressiveness and a compromised capacity to adequately assess (21).

The stigma surrounding mental illness creates autostigma and a decrease in self-esteem, which

lima od shizofrenije dodatno otežava traženje zdravstvenih usluga. Nadalje, stigma koja prati mentalne bolesti često puta može biti prisutna i među medicinskim djelatnicima, iako na nesvjesnoj razini. Često se događa da čak ni liječnici se shvaćaju ozbiljno tjelesne simptome kod oboljelih od shizofrenije te ih nastoje objasniti kao njihova sumanuta uvjerenja. Općenito govoreći, medicinsko osoblje manje učinkovito i manje temeljito liječi tjelesne bolesti u osoba sa psihičkim bolestima u usporedbi sa psihički zdravim osobama (24).

Udio broja prijmova u bolnicu ili na hitnu pomoć zbog akutne tjelesne bolesti uvelike otpada i na bolesnike s teškim mentalnim bolestima. Prije pandemije je među ovom populacijom uočena niska razina kvalitete skrbi akutnih stanja poput akutnog koronarnog sindroma te kronične opstruktivne bolesti pluća. Opterećenje koje COVID-19 stavlja na zdravstvene ustanove nesrazmjerno može utjecati na bolesnike koji boluju od teških mentalnih bolesti u smislu da bi njihov dolazak na prijam zdravstveni djelatnici mogli percipirati kao nepotreban, odnosno da bi se mogao izbjeći, što bi moglo rezultirati dodatnom stigmom i diskriminacijom prema ovoj skupini bolesnika (25).

U odnosu na predpandemijsko razdoblje, uočene su značajne razlike u korištenju zdravstvenih usluga među psihijatrijskom populacijom što se očitovalo u smanjenju hitnih prijmova (14 %), kao i ukupnog broja prijmova (30,7 %) kod oboljelih od shizofrenije, demencije i afektivnih poremećaja u odnosu na neke druge dijagnostičke kategorije poput bolesnika s mentalnim poremećajima povezanima s alkoholom i psihoaktivnim tvarima te intelektualnim poteškoćama (26). To je smanjenje korištenja zdravstvenih usluga među oboljelima od shizofrenije bilo vidljivo već u prvom valu pandemije COVID-19 (27). Rezultati ovih istraživanja ukazuju da veliki broj oboljelih od shizofrenije nije dobio adekvatnu zdravstvenu zaštitu tijekom trajanja pandemije.

makes it even more difficult for patients with schizophrenia to access health care services. Moreover, the stigma related to mental health can sometimes be found among health care providers, even if they are not aware of it. It often happens that even doctors do not take physical symptoms seriously in patients with schizophrenia, trying to explain them as delusions. Overall, medical personnel tend to be less effective and comprehensive in their treatment of physical illnesses in patients with mental illnesses as compared to mentally healthy people (24).

A large percentage of the admissions to the hospital or emergency room for acute physical illness is attributed to patients suffering from severe mental illness. Prior to the pandemic, this population received an inadequate level of care for critical conditions like acute coronary syndrome and chronic obstructive pulmonary disease. The burden that COVID-19 places on health institutions can disproportionately affect patients suffering from severe mental illness in the sense that their arrival at admission could be perceived by health care professionals as unnecessary, i.e. that it could be avoided. This could in turn result in additional stigma and discrimination against this group of patients (25).

Compared to the pre-pandemic period, significant differences were observed in the use of health services among the psychiatric population, which was manifested in the reduction of emergency admissions (14%), as well as the total number of admissions (30.7%) in patients with schizophrenia, dementia and affective disorders compared to some other diagnostic categories such as patients with mental disorders associated with alcohol and psychoactive substances and intellectual disabilities (26). This decrease in the use of health services among schizophrenia patients was evident already in the first wave of the COVID-19 pandemic (27). The results of these studies indicate that many schizophrenia patients did not receive adequate health care during the pandemic.

Potreba za liječenjem u JIL-u

Kod oboljelih od shizofrenije zapažene su više stope prijmova u jedinice intenzivnog liječenja, više stope akutnog respiratornog zatajenja, mehaničke ventilacije te bolničke smrtnosti u usporedbi s većinom bolesnika tijekom liječenja plućnih bolesti. Također, tijekom hospitalizacije u jedinicama intenzivnog liječenja, neovisno o uzroku, u oboljelih od shizofrenije prisutan je veći rizik od akutnog organskog zatajenja u odnosu na opću populaciju (28). Nadalje, potreba za mehaničkom ventilacijom, liječenje u JIL-u te smrtni ishod veći su za 63,8 % u oboljelih od COVID-19 koji su imali dijagnosticiranu mentalnu bolest. To može biti posljedica sumanutih ideja i obmana osjetila koje u tih bolesnika pridonose kognitivnom oštećenju što rezultira izostankom traženja skrbi ili liječenja (29).

Rizik od tromboembolijskih incidenata

U bolesnika koji boluju od psihotičnih poremećaja poput shizofrenije, opažen je dva do tri puta veći rizik od razvoja duboke venske tromboze ili plućne embolije. Naime, pretilost, ateroskleroza i kardiovaskularne bolesti koje su česte u oboljelih od shizofrenije, povezane su s poremećajem protoka krvi i pridonose tromboembolijskom riziku. Također, uočena je povezanost između shizofrenije i endotelne disfukcije. Smatra se da povišenom riziku od tromboembolijskih incidenata doprinosi i liječenje antipsihoticima, no nije jasno je li povišen rizik posljedica terapijskog učinka lijeka ili pak tome pridonose drugi učinci, poput sediranosti ili dobivanja na težini (30,31). Nadalje, postoje dokazi koji ukazuju na povezanost psihoze i abnormalnosti u sastavu krvi u smislu hiperkoagulabilnog stanja (30). Budući da je u COVID-19 bolesnika zapažena visoka incidencija tromboembolijskih incidenata u vidu arterijske i venske tromboze (32), smatra se da su oboljeli od psihotičnih poremećaja koji

The need for ICU treatment

In patients with schizophrenia, admissions to intensive care units, rates of acute respiratory failure, mechanical ventilation and mortality during hospital treatment for lung disease were found to be higher than in most other patients. During ICU hospitalization, patients with schizophrenia are more likely to experience acute organic failure than the general population, regardless of the cause (28). Furthermore, the need for mechanical ventilation, ICU treatment and death increased by 63.8% in COVID-19 patients who had been diagnosed with mental illness. Cognitive decline in these patients can be attributed to delusions and hallucinations which leads to an absence of seeking medical help (29).

Risk of thromboembolic incidents

Patients with psychotic disorders like schizophrenia have a two to three times greater risk of developing deep vein thrombosis or pulmonary embolism. Specifically, obesity, atherosclerosis and cardiovascular diseases that are common in people with schizophrenia, are associated with a blood flow disorder and contribute to thromboembolic risk. Also, an association between schizophrenia and endothelial dysfunction has been observed. Treatment with antipsychotics is also considered to contribute to an increased risk of thromboembolic incidents, but it is not clear whether the increased risk is due to the therapeutic effect of the drug or whether other effects, such as sedation or weight gain, contribute to this (30,31). Furthermore, there is evidence suggesting an association between psychosis and abnormalities in blood composition in terms of hypercoagulable condition (30). Since a high incidence of thromboembolic incidents in the form of arterial and venous thrombosis (32) has been observed in COVID-19 patients, it is considered that patients with psychotic disorders and

se zaraze COVID-19 pod povećanim rizikom od razvoja tromboembolijskih komplikacija (30).

Imunološke osobitosti

Varijacija u kompleksu humanog leukocitnog antigena (engl. *human leukocyte antigen*, HLA) jedan je od najdosljednijih nalaza u cijelogenomskim asocijacijskim studijama (engl. *genome-wide association studies*, GWAS) kod oboljelih od shizofrenije i bipolarnog poremećaja. HLA pretežno sudjeluje u regulaciji virusne infekcije, posebno COVID-19. Varijabilnost među genima HLA klase I može doprinijeti razlikama u imunološkom odgovoru na COVID-19, a neodgovarajući odgovor T-stanica opažen je kod nepovoljnih ishoda COVID-19 (20).

U prethodnim pandemijama respiratornih virusa uočen je utjecaj neuroinvazije i pojave upalnog odgovora na razvoj psihoze, a sposobnost neuroinvazije i razvoj upale uočeni su i kod COVID-19 (33). Poznato je da je ACE-2 mjesto ulaza virusa SARS-CoV-2 u stanice (13). Iako je ekspresija ACE-2 u središnjem živčanom sustavu niska, ipak postoje područja veće ekspresije, točnije dopaminergičke i serotoninergičke jezgre, glutamatergički neuroni, lateralne komore i *substantia nigra*. Ta su područja strukturno i neurokemijski povezana sa shizofrenijom i smatra se da njihova povećana osjetljivost na infekciju može imati ulogu u razvoju psihopatologije. COVID-19 također dovodi do masivnog sistemskog upalnog odgovora, poznatog kao citokinska oluja, te je povezan s indikatorima sistemske upale kao što je aktivacija komplementa, povišena razina C reaktivnog proteina te brzina sedimentacije eritrocita i feritina. Poznato je da su sistemski upalni parametri u shizofreniji povišeni uz mogućnost razvoja neuroupalnog odgovora (33). Iako su akutne neurološke manifestacije COVID-19 potaknule na razmišljanje o dugotrajnim neuropsihijatrijskim posljedicama, upalni profil

infected with COVID-19 are at increased risk of developing thromboembolic complications (30).

Immune system characteristics

In patients with schizophrenia and bipolar disorder, a variation in the human leukocyte antigen (HLA) is one of the most consistent findings in all-genome association studies (GWAS). HLA predominantly participates in the regulation of viral infection, especially COVID-19. Variability between HLA class I genes may contribute to differences in immune response to COVID-19 while an inadequate T-cell response has been observed in adverse COVID-19 outcomes (20).

Previous pandemics of respiratory viruses have exhibited the impact of neuroinvasion and inflammatory response on the progress of psychosis. Neuroinvasion and an increase in inflammation have been observed in cases of COVID-19 (33). Research has revealed that ACE-2 is the point of entry for SARS-CoV-2 into cells (13). Despite the low expression of ACE-2 in the central nervous system, there are nevertheless areas of greater expression, namely dopaminergic and serotoninergic nuclei, glutamatergic neurons, lateral ventricles and *substantia nigra*. These areas are structurally and neurochemically correlated to schizophrenia and it is thought that their increased susceptibility to infection may play a role in the development of psychopathology. COVID-19 also leads to a massive systemic inflammatory response, known as a cytokine storm, and is associated with indicators of systemic inflammation such as complement activation, elevated reactive protein C levels, and erythrocyte sedimentation rate and ferritin. There is evidence to suggest that people with schizophrenia have higher levels of inflammation in their body, potentially causing a neuroinflammatory reaction (33). Although the acute neurological manifestations of COVID-19 have prompted reflection on the long-term neu-

COVIDa-19 može biti relevantniji za razvoj shizofrenije (33).

Utjecaj COVID-19 na stopu relapsa shizofrenije

Pandemija COVID-19 posebno je utjecala na osobe s prethodno dijagnosticiranim mentalnim poremećajima rezultirajući pojavom recidiva ili pogoršanjem već postojećeg stanja zbog povećane osjetljivosti tih bolesnika na stres, u usporedbi s općom populacijom. Populacija koja pati od teških mentalnih poremećaja, poput psihotičnih osoba, osjetljiva je na restriktivne mjere i na promjene u dnevnoj rutini. Stresori koji tome doprinose tijekom karantene jesu njeno trajanje, strah od zaraze, gubitak aktivnosti i manjak informacija (34). Oboljelima od shizofrenije može biti otežan pristup liječenju što također povećava rizik od relapsa (35). Strah od zaraze u oboljelih od shizofrenije može pogoršati paranoju kao i sumanute ideje. Dodatno pogoršanje kod ove vrste bolesnika u smislu strahova i neizvjesnosti mogu potencirati shizotipske, neurotične i anksiozne osobine (36). Bitno je napomenuti da egzacerbaciji psihotičnih simptoma može doprinijeti i prisutna infodemija. Kao korisna intervencija smatra se smanjena izloženost medijima i vijestima o stresnim situacijama koje imaju štetan učinak na mentalno zdravlje (10).

Posljedice socijalne izolacije u oboljelih od shizofrenije

Socijalna izolacija je rizični čimbenik za povećan morbiditet i mortalitet poput pušenja, pretilosti, sjedilačkog načina života te povišenog krvnog tlaka. Dokazano je da je socijalna izolacija povezana s pogoršanjem mentalnog zdravlja. Jun Ma i sur. istraživali su utjecaj socijalne izolacije na psihološke karakteristike bolesnika oboljelih od shizofrenije koji su zbog bliskog kontakta s COVID-19 pozitivnim bolesnicima bili izolirani i pokazali da u izoliranih bolesnika

ropsychiatric consequences, the inflammatory profile of COVID-19 may be more relevant to the development of schizophrenia (33).

The impact of COVID-19 on the rate of relapse in schizophrenia

The COVID-19 pandemic has particularly affected people with previously diagnosed mental disorders resulting in the appearance of a relapse or worsening of a pre-existing condition having in mind that these patients are more prone to stress than the general population. A population suffering from severe mental disorders, such as psychotic individuals, is vulnerable to restrictive measures and to changes in their daily routine. The stressors that contribute to this during quarantine include its duration, fear of contagion, lack of activity and lack of information (34). Individuals with schizophrenia may find it difficult to access medical care, which also increases the risk of relapse (35). Fear of infection in people with schizophrenia can exacerbate paranoia as well as delusional ideas. A decrease in mental wellbeing amongst this patient group can cause an intensification of schizotypic, neurotic and anxiety traits (36). It is important to note that the infodemia can also contribute to the exacerbation of psychotic symptoms. It is beneficial to reduce the amount of media and news about disturbing events that can have a negative effect on mental health (10).

Consequences of social isolation in patients with schizophrenia

Social isolation is a risk factor for increased morbidity and mortality similar to smoking, obesity, sedentary lifestyle and high blood pressure. Research has demonstrated a link between social isolation and a decrease in mental wellbeing. Jun Ma et al. investigated the impact of social isolation on the psychological characteristics of patients with schizophrenia who were isolated due to a close contact with

postoji viša razina psihološkog stresa, teži oblik anksioznosti, lošija kvaliteta spavanja i viša razina CRP-a, u odnosu na skupinu koja nije bila izolirana (37). Socijalna izolacija je, kao oblik stresa, povezana s mentalnom bolešću. Ona dovodi do razvoja oksidativnog stresa i aktivacije osi hipotalamus-hipofiza-nadbubrežna žlijezda te do smanjene ekspresije gena koji kontroliraju upalu i sudjeluju u regulaciji glukokortikoidnog odgovora. Poznato je da taj biološki mehanizam potencijalno sudjeluje u razvoju shizofrenije (37). Socijalna izolacija je povezana s lošijom kvalitetom života i paranojom te je rizični čimbenik za samoubojstvo u oboljelih od shizofrenije. Također, pretpostavlja se da tijekom izolacije raste uporaba sredstava ovisnosti što može dodatno pogoršati zdravstveno stanje ove populacije (10).

U istraživanju Iasevoli i sur. pokazano je da su ispitanici s teškim mentalnim bolestima nakon jednomjesečne karantene imali četiri puta veću razinu stresa povezanu s pandemijom, kao i dva do tri puta veći rizik od razvoja teških simptoma anksioznosti i depresije u usporedbi s kontrolnom skupinom (38).

POTENCIJALNA RJEŠENJA U PRISTUPU ZBRINJAVANJA

Telemedicina može biti korisna pomoćna metoda za zdravstveni sustav i društvo općenito te pomoći u smanjenju stope zaraze COVID-19. Telekomunikacija kao što je *FaceTime* dobar je način da se pojedinci povežu s obitelji tijekom socijalne izolacije. Iako postoje telekomunikacijski alati, nepovjerenje ili nepoznavanje tehnologije može biti prepreka za starije osobe oboljele od shizofrenije (36). Postoje dokazi da e-kognitivno biheviоralna terapija ima sličan učinak kao i terapija uživo kod psihijatrijskih poremećaja (39). Telemedicina i e-mentalno zdravlje mogli bi poslužiti za održavanje kontinuiteta skrbi za oboljele od shizofrenije bez povećanja rizika od zaraze i širenja virusa fi-

COVID-19 positive patients. They showed that those who were isolated experienced more psychological stress, a worse form of anxiety, worse sleep quality, and higher CRP than those who were not isolated (37). Social isolation, a source of stress, has a correlation to mental illness. It leads to the development of oxidative stress and activation of the hypothalamic-pituitary-adrenal axis and to reduced expression of genes that control inflammation and participate in the regulation of the glucocorticoid response. This biological mechanism is known to potentially participate in the development of schizophrenia (37). Social isolation is associated with poorer quality of life and paranoia and is a risk factor for suicide in individuals with schizophrenia. It is also thought that during times of quarantine, addiction to certain substances is more prominent, which can further compromise the health of this population (10).

In their study, Iasevoli et al. discovered that subjects with serious mental illnesses post-one month quarantine had quadruple the amount of pandemic-induced stress, and two to three times the risk of developing extreme symptoms of anxiety and depression as opposed to the control group (38).

POTENTIAL SOLUTIONS FOR CARE APPROACH

Telemedicine can be a helpful supplemental tool for the health system and society in general to help reduce the rate of COVID-19 infection. Social network telecommunication such as *FaceTime* is a good way for individuals to connect with families during social isolation. Although there are many telecommunication tools, distrust or lack of knowledge about technology can be a barrier for older patients with schizophrenia (36). There is evidence that e-cognitive behavioural therapy has a similar effect to live therapy in psychiatric disorders (39). Telemedicine and e-mental health could

zičkim posjetima. Međutim, u liječenju oboljelih od shizofrenije, fizički posjeti i dalje ostaju ključni pri procjeni slučajeva prve epizode bolesti, pogoršanja bolesti kod osoba koje su se prethodno nalazile u remisiji te bolesnika s više komorbiditeta i općenito složenih slučajeva (40).

Što se tiče primjene antipsihotika klozapina treba imati na umu da se simptomi COVID-19 kod bolesnika koji uzimaju klozapin mogu teško razlikovati od miokarditisa. U Ujedinjenom Kraljevstvu, bolesnicima koji uzimaju klozapin, a imaju povišenu tjelesnu temperaturu, savjetuje se da se odmah testiraju na koronavirus i da obave pretrage za agranulocitozu, pogotovo ako se žale na kašalj, grlobolju, kratkoću daha i curenje iz nosa. Preporuča se u bolesnika s COVID-19 dozu klozapina smanjiti za oko 25 % uz daljnje praćenje. Ako se nizak broj leukocita javi u kombinaciji s normalnom razinom neutrofila smatra se da se liječenje klozapinom može normalno nastaviti. Također, simptome povezane s COVID-19 treba razlikovati od malignog neuroleptičkog sindroma, pogotovo u slučaju dispneje, vrućice, promjene stanja svijesti te autonomne disfunkcije (39).

Ako bolesnici liječeni klozapinom razviju vrućicu i simptome slične gripi, pojava simptoma i znakova koji upućuju na nuspojave klozapina može zahtijevati smanjenje doze klozapina za čak 50 %. Preporuka je nastaviti s nižom dozom do 3 dana nakon nestanka vrućice, a zatim postupno povećavati do doze prije pojave vrućice (41).

U smjernicama Hrvatskog društva za shizofreniju i poremećaja iz spektra shizofrenije navodi se kako se prema dostupnim podatcima opasnost od zaraze COVID-19 ne povećava redovitom primjenom svih skupina psihofarmaka te se preporuča nastavak liječenja psihofarmacima, ako je bolest u remisiji (42).

U liječenju psihijatrijskih bolesnika tijekom pandemije može biti prikladno odabrati pse-

serve to maintain continuity of care for schizophrenia patients without increasing the risk of contracting and spreading the virus during physical visits. However, in the treatment of schizophrenia patients, physical visits still remain crucial for assessing cases of the first episode of the disorder, exacerbation in patients in remission, patients with multiple comorbidities and complex cases in general (40).

As for the use of the antipsychotic clozapine, it is important to remember that the signs and symptoms of COVID-19 in patients on clozapine can be hard to distinguish from myocarditis. In the UK, patients taking clozapine who have a fever are advised to be tested for coronavirus immediately and to perform tests for agranulocytosis, especially if they complain of cough, sore throat, shortness of breath and runny nose. It is recommended in patients with COVID-19 to reduce the dose of clozapine by about 25% with further monitoring. If a low leukocyte count occurs in combination with normal neutrophil levels, it is usually recommended to keep the clozapine treatment. Also, symptoms associated with COVID-19 should be distinguished from malignant neuroleptic syndrome, especially in the case of dyspnea, fever, change in state of consciousness and autonomic dysfunction (39).

If patients treated with clozapine develop fever and flu-like symptoms, the appearance of symptoms and signs suggesting side effects of clozapine may require a 50% reduction in the dose of clozapine. It is recommended to continue with a lower dose for up to 3 days after the fever disappears, and then gradually increase to the dose before the onset of fever (41).

The guidelines of the Croatian Society for Schizophrenia and Schizophrenia Spectrum Disorders state that according to available data, the risk of contracting COVID-19 does not increase with regular use of all groups of psychopharmaceuticals and it is recommended to continue treatment with psychopharmaceuticals, if the disease is in remission (42).

hotropne lijekove koji su pokazali antivirusna svojstva, poput haloperidola i klorpromazina. Naime, opaženo je da haloperidol smanjuje stopu smrtnosti bolesnika na mehaničkoj ventilaciji snižavanjem razine citokina i prevencijom citokinske oluje (43). S druge strane, klorpromazin je pokazao imunomodulatorno djelovanje povećanjem razine protuupalnih citokina te smanjenjem razine upalnih citokina (44). Ova se dva lijeka sada koriste rjeđe nego u prošlosti, no zbog njihovih mogućih antivirusih i anticitokinskih svojstava preporučuje se razmotriti ulogu ovih lijekova za liječenje oboljelih od shizofrenije tijekom pandemije uzimajući u obzir potencijalnu korist u odnosu na rizik od nuspojava lijeka te mogućih interakcija (45).

Potencijalni pristup liječenju rane faze COVID-19 u oboljelih od shizofrenije uključuje liječenje stanja koja su zajednička COVID-19 i shizofreniji, a utječu na težinu zaraze, kao što su pretilost i predijabetes te hiperkoagulabilno stanje i upala (46). Takav pristup uključuje korištenje antitrombocitnih i antikoagulacijskih lijekova kao što su aspirin i heparin, nesteroidne antimitotičke lijekove poput kolhicina te oralne hipoglikemike poput metformina. Treba uzeti u obzir i moguće interakcije između lijekova koji se koriste u liječenju COVID-19 te antipsihotika u smislu smanjene djelotvornosti, tolerancije i sigurnosti lijeka. Treba imati na umu da provođenje mjera samoizolacije može spriječiti bolesnike u uzimanju antipsihotika, pogotovo u slučajevima kada je riječ o primjeni dugodjelujućih antipsihotika u obliku injekcija ili kada je potrebno praćenje bolesnika prilikom primjene klozapina. Neredovito uzimanje antipsihotika može povećati rizik od relapsa psihoze (46).

Kada je riječ o mentalnim bolestima, posebice o shizofreniji, neadherentnost bolesnika u dugotrajnoj terapiji doseže visokih 75 %. Dugodjelujući antipsihotici pokazali su se superiorni-

In the treatment of psychiatric patients during the pandemic, it may be appropriate to choose psychotropic drugs that have shown antiviral properties, such as haloperidol and chlorpromazine. Specifically, haloperidol has been observed to reduce the mortality rate of patients on mechanical ventilation by lowering cytokine levels and preventing cytokine storm (43). On the other hand, chlorpromazine showed immunomodulatory activity by increasing the level of anti-inflammatory cytokines and reducing the level of inflammatory cytokines (44). These two medications are used less frequently than in the past, but due to their possible antiviral and anticytokine properties, it is recommended to consider their role in the treatment of schizophrenia during the pandemic taking into account the potential benefits in relation to side effects and possible interactions (45).

Taking care of the mutual symptoms of COVID-19 and schizophrenia, such as obesity and prediabetes, hypercoagulable condition and inflammation, which may affect the intensity of the infection, is possibly an avenue for treating the early stages of COVID-19 in schizophrenia patients (46). Such an approach involves the use of antiplatelet and anticoagulation drugs such as aspirin and heparin, nonsteroidal antimitotic drugs such as colchicine, and oral hypoglycemics such as metformin. Possible interactions between drugs used in the treatment of COVID-19 and antipsychotics in terms of reduced efficacy, tolerance and safety of the drug should also be taken into account. It should be kept in mind that self-isolation measures can stop patients from taking antipsychotics, mainly when it comes to the usage of long-acting antipsychotics in the form of shots or when tracking of patients using clozapine is needed.

Irregular use of antipsychotics may increase the risk of psychosis relapse (46).

When it comes to mental illness, especially schizophrenia, the non-adherence of patients in long-term therapy is as high as 75%.

ma nad oralnim antipsihoticima u prevenciji relapsa i smanjenju smrtnosti kod oboljelih od shizofrenije, ali se još uvijek nedovoljno primjenjuju zbog ekonomskih razloga kao i zbog straha i stigme (47). Bolesnici odbijaju taj oblik liječenja zbog načina primjene lijeka, protokola koji uključuje nadzor nakon primjene injekcije, te zbog osjećaja da više ne odlučuju o vlastitom liječenju (47).

Nakon što se u Rumunjskoj u ožujku 2020. ograničio pristup bolnicama te je sukladno tome bio zatvoren odjel za primjenu dugodjelujućih antipsihotika, 78 % bolesnika prešlo je na liječenje oralnim antipsihotikom, dok su preostali nastavili liječenje dugodjelujućim antipsihoticima. U sljedećih šest mjeseci zabilježen je relaps kod 71,4 % bolesnika koji su prešli na oralni oblik terapije, dok su bolesnici koji su nastavili s primjenom dugodjelujućih antipsihotika ostali u remisiji (48).

Uočeno je da primjena antipsihotika može utjecati na zarazu koronavirusom te spriječiti teže oblike bolesti. Canal-Rivero i sur. pokazali su da je kod bolesnika liječenih dugodjelujućim antipsihoticima utvrđena niža prevalencija zaraze te niža stopa teških oblika bolesti (49). Međutim, nije jasno je li to posljedica farmakološke upotrebe samih antipsihotika ili su bolesnici liječeni dugodjelujućim antipsihoticima bolje slijedili javnozdravstvene smjernice. U svakom je slučaju važno kontinuirano pružanje usluga mentalnog zdravlja pojedincima koji boluju od psihotičnih poremećaja kako bi se spriječili negativni ishodi osnovne bolesti te eventualno ublažio COVID-19 te smanjila smrtnost od COVID-19 u ovoj ranjivoj populaciji (50).

ZAKLJUČAK

Oboljeli od shizofrenije imaju povećani rizik od zaraze COVID-19 zbog niza sociodemografskih i kliničkih karakteristika zastuplje-

Long-acting antipsychotics have proven to be superior to oral antipsychotics in preventing relapse and reducing mortality in schizophrenia patients, but they are still insufficiently used for economic reasons as well as fear and stigma (47). Patients refuse this form of treatment because of the route of administration of the drug, a protocol that includes supervision after injection, and because of the feeling that they no longer decide on their own treatment (47).

After access to hospitals was restricted in Romania in March 2020 and the department for the use of long-acting antipsychotics was closed accordingly, 78% of patients switched to oral antipsychotic treatment, while the remaining continued treatment with long-acting antipsychotics. In the next six months, relapse was recorded in 71.4% of patients who switched to oral therapy, while patients who continued to use long-acting antipsychotic drugs remained in remission (48).

It has been observed that the use of antipsychotics can affect coronavirus infection and prevent more severe forms of the disease. Canal-Rivero et al. demonstrated that patients treated with long-acting antipsychotics had a lower prevalence of infection and a lower rate of severe forms of the illness (49). However, it is not clear whether this is due to the pharmacological use of the antipsychotics or whether patients treated with long-acting antipsychotics followed the public health guidelines better. In any case, it is important to continuously provide mental health services to individuals suffering from psychotic disorders in order to prevent negative outcomes of the underlying disease and possibly mitigate COVID-19 and reduce COVID-19 mortality in this vulnerable population (50).

CONCLUSION

Patients with schizophrenia have an increased risk of contracting COVID-19 due to a number of sociodemographic and clinical characteristics

nih u ovoj populaciji, što rezultira otežanim provođenjem protuepidemijskih mjera. Oboljeli od shizofrenije su više od dva puta češće hospitalizirani te imaju više od tri puta veću smrtnost od COVID-19. Lošijoj prognozi COVID-19 pridonose brojni komorbiditeti prisutni kod oboljelih od shizofrenije, poglavito kardiovaskularne bolesti, bolesti dišnog sustava te šećerna bolest. Oboljeli od shizofrenije povezani su s visokom stopom pušenja i korištenjem velikog broja lijekova što se također povezuje s lošijim ishodom COVID-19. Uočen je i nepovoljan utjecaj liječenja klozapinom na stopu smrtnosti od COVID-19. Veliki problem je nejednakost u zdravstvenoj skrbi te sveprisutna stigma prema mentalno oboljelim pojedincima što često rezultira neadekvatom zdravstvenom skrbi. U bolesnika sa psihotičnim poremećajem koji razviju COVID-19 povećan je rizik od razvoja tromboembolijskih incidenata. Varijacija u HLA kompleksu čvrsto je povezana sa shizofrenijom, a HLA pretežno sudjeluje u regulaciji virusne infekcije, posebno COVID-19. Varijabilnost među genima HLA klase I može doprinijeti razlikama u imunološkom odgovoru na COVID-19, dok je neodgovarajući odgovor T-stanica opažen kod lošijih ishoda infekcije COVID-19. Pandemija utječe na osobe s već ranije dijagnosticiranim mentalnim poremećajima u obliku pojave recidiva ili pogoršanja već postojećeg stanja. Dokazano je da je socijalna izolacija povezana s pogoršanjem mentalnog zdravlja te dovodi do povišenih razina psihološkog stresa, razvoja težih oblika anksioznosti te problema sa spavanjem. Kao potencijalna rješenja nude se telemedicina i e-mentalno zdravlje koji bi mogli poslužiti za održavanje kontinuiteta zdravstvene skrbi osoba oboljelih od shizofrenije bez povećanja rizika od zaraze i širenja virusa fizičkim posjetima. Međutim, pri procjeni prve psihotične epizode bolesti i općenito složenih slučajeva, fizički posjeti i dalje ostaju nezamjenjiv oblik skrbi.

represented in this population, resulting in difficulties in implementing anti-epidemic measures. The hospitalization rate of schizophrenia patients is more than double, and their mortality rate from COVID-19 is more than triple, compared to the general population. Patients with schizophrenia who have multiple comorbidities, such as cardiovascular diseases, respiratory diseases and diabetes mellitus, tend to have a worse prognosis with COVID-19. Schizophrenia patients are associated with high rates of smoking and the use of a large number of medications, which is also associated with a worse outcome of COVID-19. An adverse effect of clozapine treatment on the COVID-19 mortality rate was also observed. A major challenge is the inequality in health care and the pervasive stigma concerning individuals with mental illness, leading to deficient health care. In patients with psychotic disorder who develop COVID-19, the risk of developing thromboembolic incidents is increased. There is a strong correlation between schizophrenia and variations in the HLA complex, and HLA predominantly participates in the regulation of viral infection, especially COVID-19. Variations in HLA class I genes may contribute to differences in immune response to COVID-19, while an inadequate T-cell response has been observed in poorer COVID-19 infection outcomes. The pandemic affects individuals with previously diagnosed mental disorders in the form of relapses or worsening of a pre-existing condition. It has been proven that social isolation is associated with deterioration of mental health and leads to increased levels of psychological stress, development of severe forms of anxiety and sleep problems. As potential solutions, telemedicine and e-mental health care are offered that could serve to maintain the continuity of health care for people suffering from schizophrenia without increasing the risk of infection and spreading the virus during physical visits. However, when assessing the first psychotic episode of the illness and generally complex cases, physical visits still remain an indispensable form of care.

Oboljeli od shizofrenije su vulnerabilna skupina s obzirom na zarazu i smrtnost tijekom pandemije COVID-19 te ih treba zaštititi ulaganjem dodatnih napora u smanjivanju nejednakosti zdravstvene skrbi, kao i provođenjem javnozdravstvenih akcija sa ciljem otklanjanja stigme prema mentalnim bolestima. Isto je tako potrebno provoditi i edukaciju oboljelih od shizofrenije kako bi se što učinkovitije moglo primijeniti mjere zaštite od infekcije COVID-19.

Schizophrenia patients are a vulnerable group with regard to infection and mortality during the COVID-19 pandemic and should be protected by making additional efforts to reduce health care inequality, as well as by conducting public health actions aimed at eliminating the stigma towards mental illness. It is also necessary to conduct education of schizophrenia patients in order to apply measures of protection against COVID-19 infection as effectively as possible.

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