DOI:

POVEZANOST KOAGULACIONOG STATUSA I KONCENTRACIJE PROINFLAMATORNIH CITOKINA KOD PACIJENATA SA COVID-19 INFEKCIJOM

CORRELATION BETWEEN COAGULATION STATUS AND PROINFLAMMATORY CYTOKINE CONCENTRATIONS IN PATIENTS WITH COVID-19 INFECTION

Milica Milentijević[1], Marija Milić[1], Nataša Katanić[1]
1 Medicinski fakultet, Univerzitet u Prištini sa privremenim sedištem u Kosovskoj Mitrovici

SAŽETAK

Uvod: COVID-19 infekcija je visoko zarazno multisistemsko oboljenje oboljenje uzrokovano SARS-CoV-2 virusom. Ulazak SARS-CoV-2 virusa u ćelije pokreće imunološki odgovor domaćina, koji podrazumeva aktivaciju nekoliko zaštitnih puteva. Pre svega, dolazi do produkcije značajne količine proinflamatornih citokina i pojave hiperinflamacije odnosno citokinske oluje. Rezultati preliminarnih istraživanja sprovedenih na početku pandemije COVID-19 pandemije ukazivali su na postojanje značajne korelacije između koncentracije proinflamatornih citokina i vrednosti parametara koji odražavaju koagulacioni status ovih bolesnika.
Cilj rada: Opšti cilj ovog istraživanja bio je da se ispita prediktivni značaj proinflamatornog i antiinflamatornog citokinskog profila na koagulacioni status bolesnika sa COVID-19 infekcijom hospitalizovanih u Kliničko bolničkom centru Kosovska Mitrovica.
Metode rada: Istraživanje je sprovedeno kao panel studija koja predstavlja kombinaciju kohortne i studije preseka, a koje je realizovano u Kliničko bolničkom centru Kosovska Mitrovica tokom drugog talasa obolevanja od COVID-19 u periodu od jula do septembra 2020 godine. Istraživanjem su bili obuhvaćeni bolesnici sa dijagnozom COVID-19 potvrđenom tehnikom lančane polimerizacije, oba pola, stariji od 18 godina. Pored različitih socio-demografskih podataka, od bolesnika sa COVID-19 infekcijom je prikupljana i krv za potrebe analiziranja određenih laboratorijskih i biohemijskih parametara kao i za potrebe analize citokinskog profila. Merenje koncentracije proinflamatornih i antiinflamatornih citokina vršeno je pomoću protočnog fluocitometra u Centru za biomedicinske nauke, laboratoriji za imunologiju i biologiju ćelije na Medicinskom fakultetu u Foči, Republika Srpska. Merene su koncentracije sledećih citokina: IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17A, IL-17F, IL-21, IL-22, IFN-γ i TNF--α.Podaci su analizirani u korisničkom paketu SPSS Windows, verzije 19. Korelacija između varijabli je testirana upotrebom Spearman-ovog koeficijenta korelacije.
Rezultati: Studijom je obuhvaćeno 113 bolesnika koji su se tokom 2020. godine lečili u Zdravstvenom centru Kosovska Mitrovica sa dijagnozom COVID-19. Prosečna starost obolelih bila je 58,15±13,50 godina (srednja vrednost ± standardna devijacija (SD)). Osobe muškog pola činile su većinu 79 (69,9%) obolelih. Uočena je značajna srednje jaka negativna korelacija D-dimera sa IL-5 (r=-0,277; p=0,010) i pozitivna korelacija D-dimera sa IL-6 (r=0,223; p=0,038). Korelacija između aRTT-a i IFN-γ bila je značajna negativna i jaka (r=-0,537; p=0,003). Fibrinogen (r=0,258; p=0,033) i trombociti (r=0,189; p=0,047) su značajno pozitivno slabo korelirali sa IL-17F.
Zaključak: Poremećaji koagulacione kaskade i hiperkoagulacija krvi su važni aspekti patogeneze COVID-19 infekcije. Stoga su laboratorijski parametri koji ukazuju na poremećaje u procesu koagulacije krvi, posebno D-dimer i fibrinogen, važni prognostički prediktori kod pacijenata. Rezultati naše studije ukazuju da su vrednosti D-dimera i fibrinogena u očekivanoj korelaciji sa vrednostima pojedinih proinflamatornih citokina.
Ključne reči: COVID-19 infekcija, proinflamatorni citokini, D-dimer, fibrinogen.

ABSTRACT

Introduction: COVID-19 infection is a highly contagious multisystem disease caused by the SARS-CoV-2 virus. The entry of the SARS-CoV-2 virus into the cells triggers the host's immune response, which involves the activation of several protective pathways. First of all, there is the production of a significant amount of pro-inflammatory cytokines and the appearance of hyperinflammation, i.e., a cytokine storm. The results of preliminary research conducted at the beginning of the COVID-19 pandemic indicated the existence of a significant correlation between the concentration of pro-inflammatory cytokines and the values of the parameters that reflect the coagulation status of these patients.
Aim: The general goal of this research was to examine the predictive significance of pro-inflammatory and anti-inflammatory cytokine profiles on the coagulation status of patients with COVID-19 infection hospitalized in the Clinical Hospital Center of Kosovska Mitrovica.
Methods: The research was conducted as a panel study that represents a combination of a cohort and a cross-sectional study, which was carried out in the Clinical Hospital Center of Kosovska Mitrovica during the second wave of illness from COVID-19 in the period from July to September 2020. The research included patients with a diagnosis of COVID-19 confirmed by the chain polymerization technique, both sexes, and older than 18 years. In addition to various socio-demographic data, blood was also collected from patients with COVID-19 infection for the purposes of analyzing certain laboratory and biochemical parameters as well as for the purposes of cytokine profile analysis. The concentration of pro-inflammatory and anti-inflammatory cytokines was measured using a flow cytometer at the Center for Biomedical Sciences, the Laboratory for Immunology and Cell Biology at the Faculty of Medicine in Foča, Republika Srpska. The concentrations of the following cytokines were measured: IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17A, IL-17F, IL-21, IL-22, IFN-γ, and TNF-α. Data were analyzed in SPSS Windows user package, version 19. Correlation between variables was tested using Spearman's coefficient correlations.
Results: The study included 113 patients who were treated in the Kosovska Mitrovica Health Center in 2020 with a diagnosis of COVID-19. The average age of the patients was 58.15±13.50 years (mean value ± standard deviation (SD)). Male persons made up the majority of 79 (69.9%) patients. A significant medium-strong negative correlation of D-dimer with IL-5 (r=-0.277; p=0.010) and a positive correlation of D-dimer with IL-6 (r=0.223; p=0.038) were observed. The correlation between aRTT and IFN-γ was significantly negative and strong (r=-0.537; p=0.003). Fibrinogen (r=0.258; p=0.033) and platelets (r=0.189; p=0.047) significantly positively correlated weakly with IL-17F.
Conclusion: Disorders of the coagulation cascade and blood hypercoagulation are important aspects of the pathogenesis of COVID-19 infection. Therefore, laboratory parameters that indicate disorders in the blood coagulation process, especially D-dimer and fibrinogen, are important prognostic predictors in patients. The results of our study indicate that the values of D-dimer and fibrinogen are in the expected correlation with the values of certain pro-inflammatory cytokines.
Key words: COVID-19 infection, proinflammatory cytokines, D-dimer, fibrinogen.