

# Učestalost smanjenja PCT (plateletkrit ili trombokit) kod COVID-19 pozitivnih pacijenata – dijagnostički i epidemiološki značaj

# Incidence of PCT (plateletcrit) decrease in COVID-19 positive patients – diagnostic and epidemiologic value

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## Sažetak

**Uvod:** Trombociti imaju važnu ulogu u patogenezi COVID-19, te im parametri variraju u različitim fazama bolesti. Značaj plateletkrita u COVID-19 je nedovoljno poznat.

**Cilj:** Ispitati dijagnostički značaj trombokitima u COVID-19.

**Metode:** U periodu od januara do marta i od septembra do decembra 2021. godine, analizirano je 440 pacijenata koji su se prvi put javili na pregled u COVID ambulantu Doma zdravlja Niš zbog sumnje na COVID-19, gde im je nakon pregleda urađena analiza krvne slike. Testom je potvrđena infekcija COVID-19. Analiziran je plateletkrit iz analize krvi pri prvom pregledu. Kontrolnu grupu su činili pacijenti iz “zelene zone”, i to 60 bolesnika u periodu januar–decembar 2021. godine, i još 48 pacijenata iz perioda pre COVID-19, pre 2020. godine.

**Rezultati:** U prvom periodu snižen plateletkrit je imalo 48,4% žena i 63,3% muškaraca, a ukupno od 111 pacijenata, snižen plateletkrita je imalo 54,9%. U drugom periodu snižen plateletkrit je imalo 72,2% žena i 85% muškaraca, a ukupno od 329 pacijenata snižen plateletkrit je imalo 78,7%.

**Zaključak:** Trombokrit je smanjen kod značajnog broja pacijenata koji se prvi put javljaju zbog simptoma COVID-19, te bi na osnovu samo analize plateletkrita sa velikom verovatnoćom moglo da posumnja da se radi o infekciji COVID-19.

**Ključne reči:** trombocit, infekcija, D-dimer, virus

## Abstract

**Introduction:** Platelets play an important role in the pathogenesis of COVID-19. Therefore, their parameters vary in different stages of the disease. The importance of plateletcrit in COVID-19 is not well known.

**Objective:** To examine the diagnostic value of plateletcrit in COVID-19.

**Methods:** From January to March and September–December 2021. during their initial visit to the COVID outpatient clinic at the Primary Healthcare Center Nis, we examined 440 patients who were experiencing possible COVID-19 symptoms. Following the examination, a complete blood count was performed, and they tested positive for COVID-19. We analyzed the plateletcrit in every lab sample collected during their first visit. The control group consisted of 60 patients from the “green zone” from January to December 2021, as well as 48 patients from the pre-COVID period, before 2020.

**Results:** Lower plateletcrit was found in 48,4% of women and 63,3% of men in the first period. Out of the total of 111 patients, lower plateletcrit was found in 54,9%. In the second period lower plateletcrit was found in 72,2% of women and 85% of men. Out of the total number of 329 patients, lower plateletcrit was found in 78,7%. In the control group, from the “green zone” lower plateletcrit was found in 8,3% of 60 patients, and no decrease in plateletcrit levels was observed in 48 patients from the pre-COVID-19 era.

**Conclusion:** Plateletcrit levels are decreased in many patients during their initial visit due to COVID-19. Symptoms. Therefore, variations in plateletcrit levels could raise concerns about potential COVID-19 infection.

**Keywords:** platelets, infection, D-dimer, virus

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## Uvod

U proteklom periodu smo mnogo toga čuli i naučili od naučnika o virusu Sars-CoV-2, izazivaču bolesti COVID-19. O dijagnozi, patogenezi i lečenju bolesti takođe, a možda najviše o epidemiološkim merama za sprečavanje i suzbijanje ove zarazne bolesti koja se raširila u formi pandemije. Nesumnjivo je da su mnoge stvari vezane za ovu bolest još uvek nepoznanica i da ćemo ih u budućnosti otkrivati, što će nam omogućiti da pobedimo ovu pandemiju i da se COVID-19 bolest svede na pojedinačne i retke slučajeve sa minimalnom stopom oštećenja zdravlja i smrtnosti. Dok se ceo svet vakciniše, što nam je za sada jedina sigurna opcija da se virus kontroliše, nije na odmet malo se osvrnuti i na svakodnevnu kliničku praksu i analizirati iskustvo stečeno na prvoj liniji odbrane u ordinaciji COVID ambulante i ordinaciji izabranog lekara, tj. celokupnog zdravstvenog osoblja ambulanti na primarnom nivou zdravstvene zaštite. Oni su podneli i podnose najveći teret u ovoj pandemiji, a nekako su, čini se, retko pominjani kao heroji, uvek u senci zaposlenih na višim nivoima zdravstvene zaštite, koji su uvek u prvom planu kada je reč o rezultatima i borbi protiv kovida.

U svakodnevnoj kliničkoj praksi je veoma brzo primećeno da COVID-19 dovodi do neuobičajeno većeg broja tromboza i plućne embolije<sup>1,2</sup> i da to može često da bude uzrok teške kliničke slike i smrtnosti, kao i povećane sklonosti ka trombozi<sup>3</sup> i kod bolesnika koji su preležali COVID, kao deo tzv. postcovid sindroma<sup>4</sup>.

Brojna istraživanja pokazala su da je COVID-19 zapravo prokoagulantno stanje<sup>5-11</sup>. U stanjima povećane koagulabilnosti krvi i povećane verovatnoće za pojavu tromboze kod obolelih od COVID-19, jednu od ključnih uloga imaju trombociti. Trombociti imaju veliku ulogu u patogenezi bolesti izazvanoj Sars-CoV-2 virusom zbog stvaranja mikrotromboembolusa i prekomernog i ubrzanog "trošenja", te su zbog toga njihovi parametri u krvnoj slici izmenjeni.

U svakodnevnoj kliničkoj praksi u našim uslovima u COVID ambulanti i ordinaciji izabranog lekara, analizom krvne slike automatskim hematološkim analizatorom određuju se sledeći parametri trombocita: PLT - broj trombocita i MPV - srednja zapremina trombocita koji se mere direktno brojačem, i drugi parametri koji su dobijeni matematičkim postupcima, indeksi, koji bliže određuju morfologiju i odstupanje od normalne populacije trombocita. Najčešći indeksi koji se tako dobijaju su PDW - širina krivulje raspodele trombocita po volumenu i PCT - plateletkrit ili trombokrit - trombocitni pokazatelj koji predstavlja volumni procenat trombocita, odnosno udeo ukupnog volumena trombocita i volumena aspiriranog uzorka pune krvi. Određuje se isključivo matematički. Normalne vrednosti kreću se od 0,158 do 0,425%, a razlikuju se kod različitih tipova brojača.

## Introduction

In recent years we have heard and learned from various scientists about the Sars-CoV-2 virus which causes COVID-19 disease. There were data about diagnosis, pathogenesis, and treatment but most of all epidemiological measures for prevention and containing of this infectious disease that spread in the form of a pandemic. Undoubtedly many issues concerning this disease still remain unknown and will probably be revealed in the future. It will enable us to beat this pandemic and reduce COVID-19 disease to singular and rare cases with minimal rates of health hazards and death. While the whole world is getting vaccinated, which is a surefire way to control the virus, it doesn't hurt to take a look at everyday clinical practice and analyze current experiences from the frontlines of COVID and GP outpatient clinics but also all the health workers from the primary healthcare level. They took and are still taking the brunt of the pandemic and somehow it seems they are rarely mentioned as heroes, always in the shadow of those working on the higher levels of the healthcare system and they are the front liners when it comes to results and the fight against COVID.

Fairly soon, it was noticed in everyday clinical practice that COVID-19 causes an unusually high number of thrombosis and pulmonary embolism cases<sup>1,2</sup> which in turn causes severe clinical presentations and often leads to death. Also, greater affinity to thrombosis<sup>3</sup> was noticed in patients who had COVID, as a part of so-called post-covid syndrome<sup>4</sup>.

Numerous studies showed COVID-19 is actually a procoagulation condition<sup>5-11</sup>. In the state of increased blood coagulation and a higher probability of thrombosis occurrence in COVID-19, platelets play an important role.

Platelets' role is important in the pathogenesis of the Sars-CoV-2 virus caused disease due to the formation of micro emboli and fast and excessive "spending". Therefore, their parameters in CBC are changed.

In everyday practice, in our COVID and GP clinics, CBC analysis performed with an automatic hematological analyzer produces these platelet parameters: PLT - platelet count and MPV - mean platelet volume, both measured directly by the counter, other parameters are obtained through mathematics calculations, and indexes, which more closely define morphology and aberrations from the usual platelet population. The most common indexes are PDW - platelet distribution width and PCT - plateletcrit which represents platelet volume percentage or the share of total platelet volume and volume of the aspirated blood sample. It is calculated solely mathematically. Reference ranges from 0,158 to 0,425%, and it varies in different types of counters.

**Cilj rada** je bio da se pokaže da određene karakteristike analize trombocita (PCT - plateletkrit ili trombokrit) mogu i u kojoj meri da ukažu na infekciju Sars-CoV-2 virusom. Ideja je da se pokaže povezanost između karakteristika trombocita dobijenih u rutinskoj analizi kompletne krvne slike i verovatnoće da se na osnovu tih parametara odredi da li je pacijent, koji ispunjava kriterijume definicije slučaja, zaista i COVID-19 pozitivan, tj. da li je inficiran virusom.

## Metode

U periodu januar-mart i septembar-decembar 2021. godine obavljena je retrospektivna analiza laboratorijskih rezultata krvne slike 440 pacijenata koji su se prvi put javili na pregled u COVID ambulantu Doma zdravlja Niš zbog sumnje na COVID-19. Nakon pregleda urađena je analiza kompletne krvne slike. Testom je potvrđena infekcija COVID-19. Analiziran je plateletkrit iz analize krvi pri prvom pregledu.

Korišćena je medicinska dokumentacija 440 COVID-19 pozitivna pacijenta starijih od 18 godina, kod kojih je testom potvrđen COVID-19. U kontrolnoj grupi analizirani su parametri krvne slike kod 108 pacijenata. Kontrolnu grupu su činili pacijenti iz "zelene zone", i to 60 bolesnika u periodu januar-decembar 2021. odnosno pacijenti koji su se iz drugih razloga javljali lekaru), i još 48 pacijenata iz perioda pre COVID-19, pre 2020. godine.

## Rezultati

Kovid pozitivni pacijenti su praćeni u dva vremenska razmaka i to: januar-mart 2021. godine (111 pacijenata) i septembar-decembar 2021. godine (delta soj - 329 pacijenata) (Grafikon 1).

**We aimed** to show that certain characteristics of platelet analysis (PCT - plateletcrit) may, and to a certain degree, point to the Sars-CoV-2 virus infection. Our idea was to show the connection between platelet characteristics obtained from the routine CBC tests and the probability that based on these parameters we can decide if the patient, fitting the criteria of the case definition, is indeed COVID-19 positive, that is to say infected with the virus.

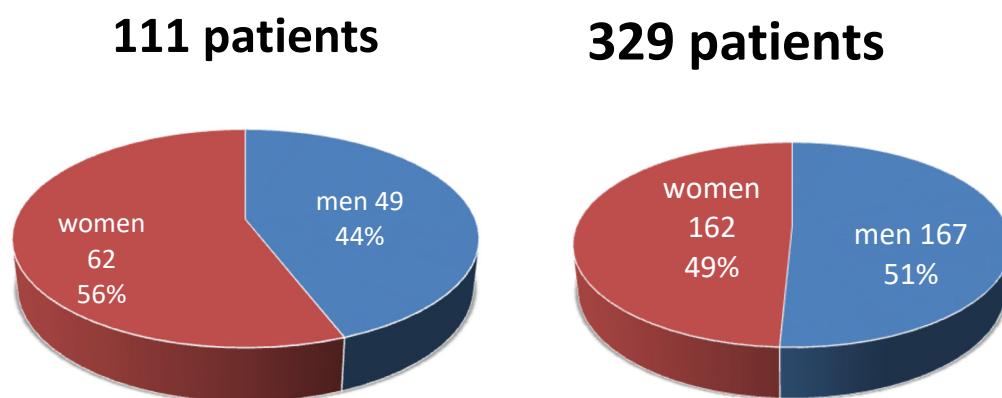
## Methods

In the period January-March and September-December 2021, a retrospective analysis of the laboratory results of the blood count of 440 patients who came to the COVID clinic of the Niš Health Center for suspected COVID-19 was performed for the first time. After the examination, a complete blood count was analyzed. The test confirmed the infection of COVID-19. The plateletcrit from the blood test at the first examination was analyzed.

The medical documentation of 440 COVID-19 positive patients over the age of 18, in whom the test confirmed COVID-19, was used. In the control group, blood count parameters were analyzed in 108 patients. The control group consisted of patients from the "green zone", namely 60 patients in the period January-December 2021, i.e. patients who visited the doctor for other reasons), and another 48 patients from the period before COVID-19, before 2020.

## Results

COVID positive patients were followed in two periods: from January to March 2021. (111 patients) and from September to December 2021. (Delta strain - 329 patients) (Figure 1).



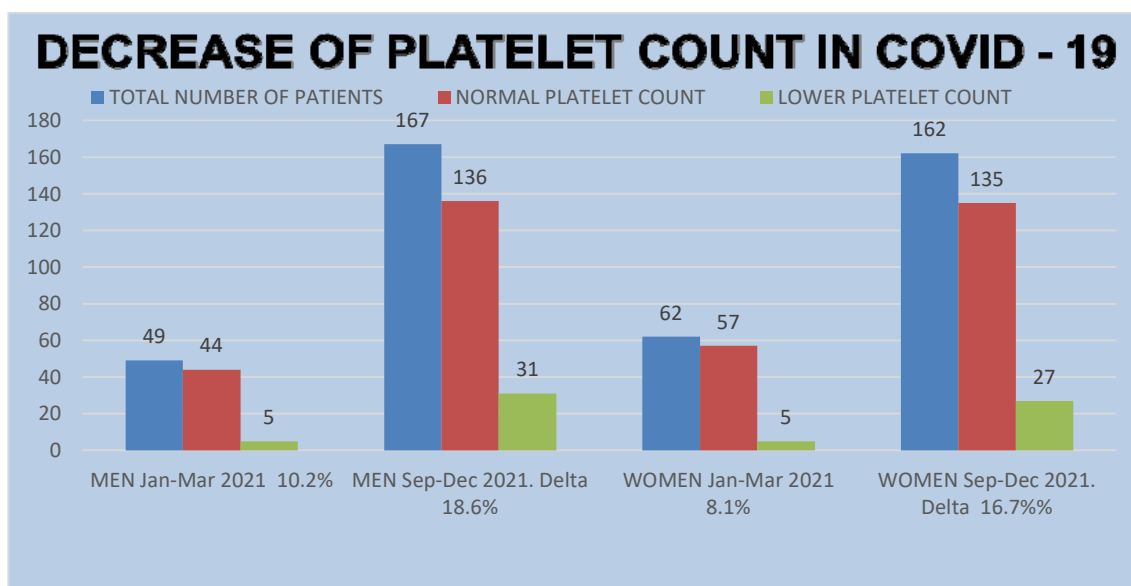
**Grafikon 1.** 111 pacijenata u periodu januar-mart 2021. i 329 pacijenata u periodu septembar-decembar 2021. (delta soj)  
**Figure 1.** 111 patients from January to March 2021. and 329 patients from September to December 2021. (Delta strain)

U pitanju su pacijenti koji se zbog simptoma koji ukazuju na COVID-19 prvi put javljaju lekaru, te im se nakon fizikalnog pregleda radi i analiza kompletne krvne slike, a kod kojih je zatim testom potvrđena infekcija COVID-19.

Ukupan broj pacijenata sa sniženjem broja trombocita kod COVID-19 u periodu januar–decembar 2021. godine prikazan je na Grafikonu 2.

Those were the patients who paid a visit to a doctor due to symptoms consistent with COVID-19 and after a physical examination CBC was performed. After this, they were tested and were positive for COVID-19.

The total number of patients with a decrease in the number of platelets due to COVID-19 in the period January–December 2021 is shown in Chart 2.



**Grafikon 2.** Sniženje broja trombocita kod COVID-19 pacijenata u periodu januar–decembar 2021.

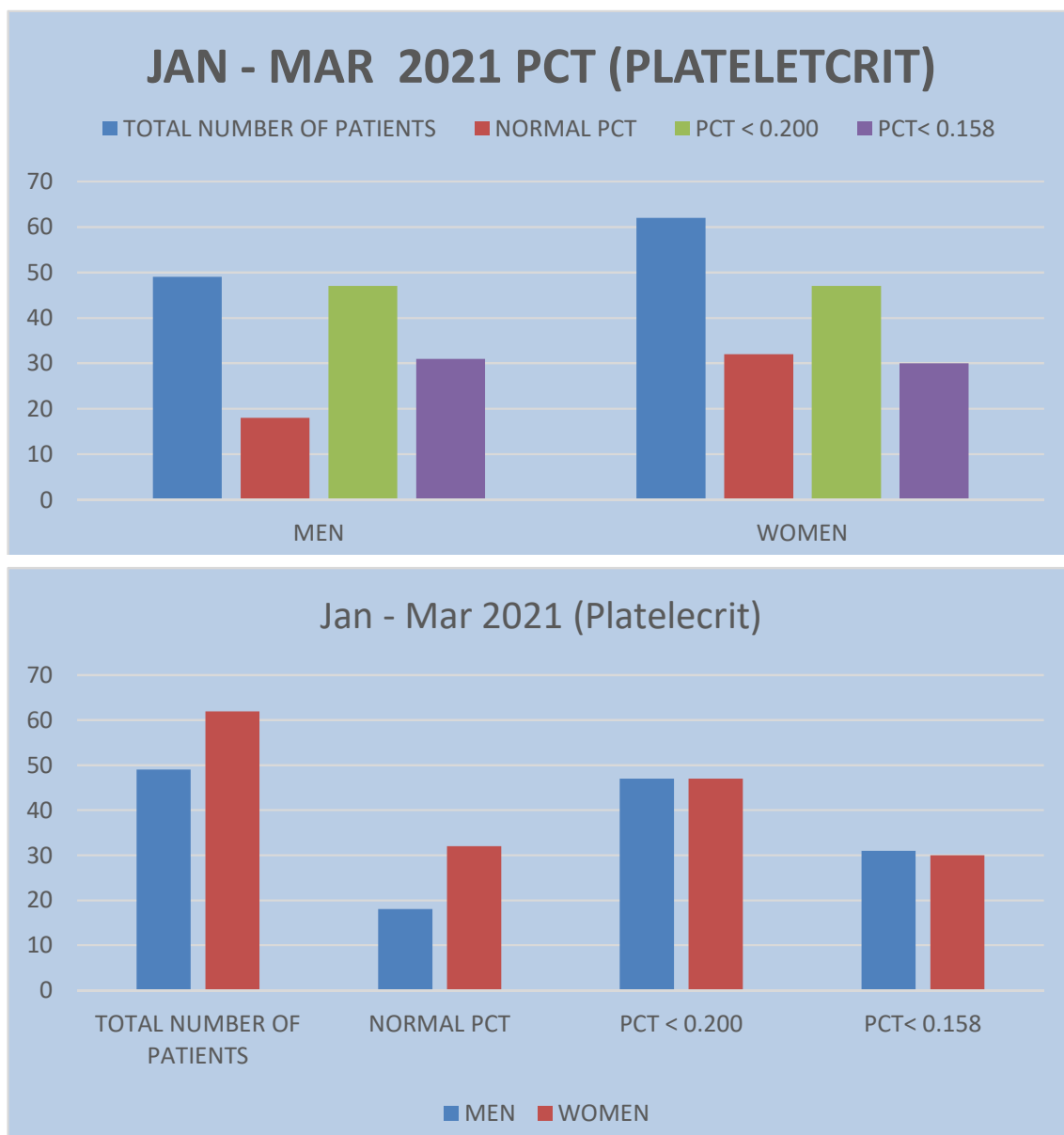
**Figure 2.** Decrease of platelet count in COVID-19 patients, January–December 2021.

Kao kontrolna grupa služe rezultati 60 pacijenata iz „zelene zone“ u istom periodu i 48 pacijenata pre 2020. godine, tj. pre pojave COVID-19.

U grupi januar-mart 2021. godine bilo je 49 muškaraca i 62 žene (Grafikon 3).

The control group consisted of 60 patients from the „green zone“, from the same period, and 48 patients from the period before 2020., that is before COVID-19.

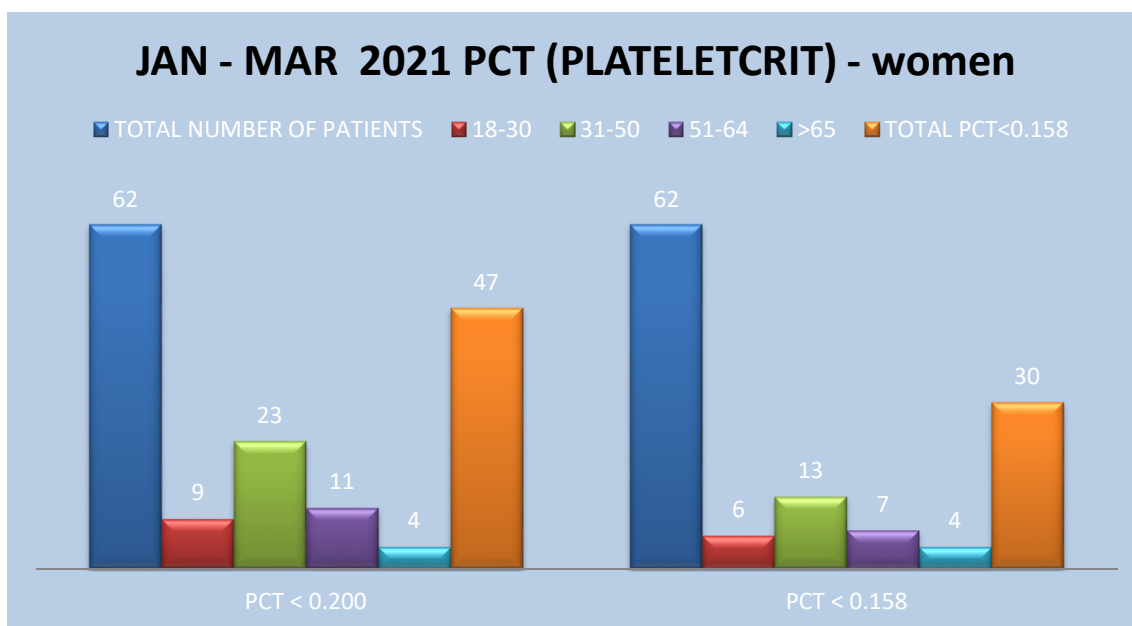
In the group from January to March 2021. there were 49 men and 62 women (**Figure 3**).



**Grafikon 3.** Sniženje PCT (plateletkrit) u periodu januar–mart 2021.  
**Figure 3.** Decrease in PCT (plateletcrit) during January–March 2021.

Od 62 žene, snižen broj trombocita je imalo pet žena, što je 8,1%. Snižen PCT je imalo 30 žena, što je 48,4% (Grafikon 4).

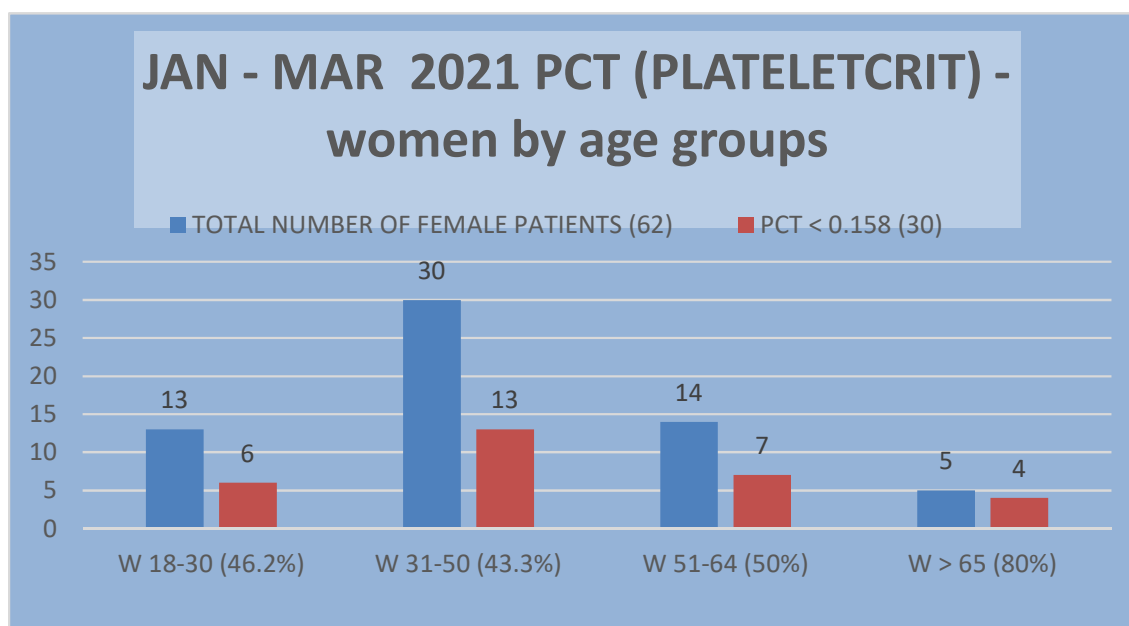
Out of 62 women, a lower platelet count was found in five, which makes 8,1%. Lower PCT was found in 30 women, which makes up 48,4% (**Figure 4**).



**Grafikon 4.** Snižen PCT kod ženskog pola za period januar–mart 2021.  
**Figure 4.** Reduced PCT in the female sex for the period January-March 2021.

Gledano po starosnim grupama 18–30, 31–50, 51–64 i >65 godina, najveći procenat sniženja PCT imaju žene starije od 65 godina, i to 4 od 5 pacijentkinja, što je 80% (Grafikon 5).

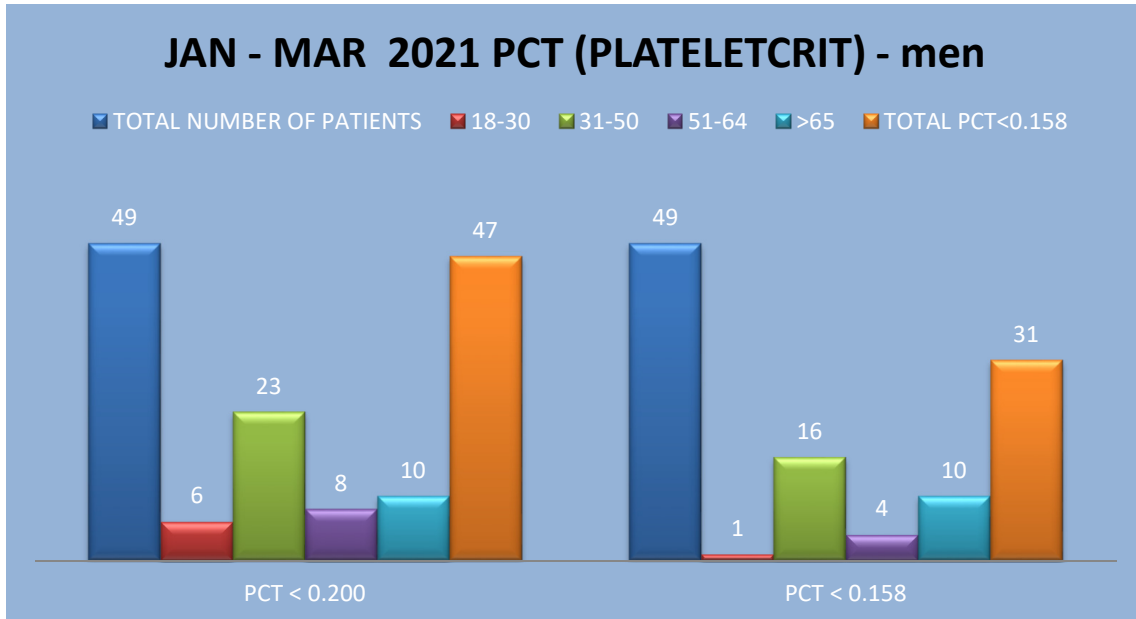
Viewed by age groups, 18–30, 31–50, 51–64, and >65, the highest percentage of PCT lowering was found in women over 65, 4 out of 5 patients, which makes up 80% (**Figure 5**).



**Grafikon 5.** Snižen PCT kod ženskog pola za period januar–mart 2021. po starosnim grupama  
**Figure 5.** Decreased PCT in women, January-March 2021., by age groups

Od 49 muškaraca, snižen broj trombocita je imalo pet pacijenata, što je 10,2%. Snižen PCT je imao 31 pacijent, što je 63,3% (Grafikon 6).

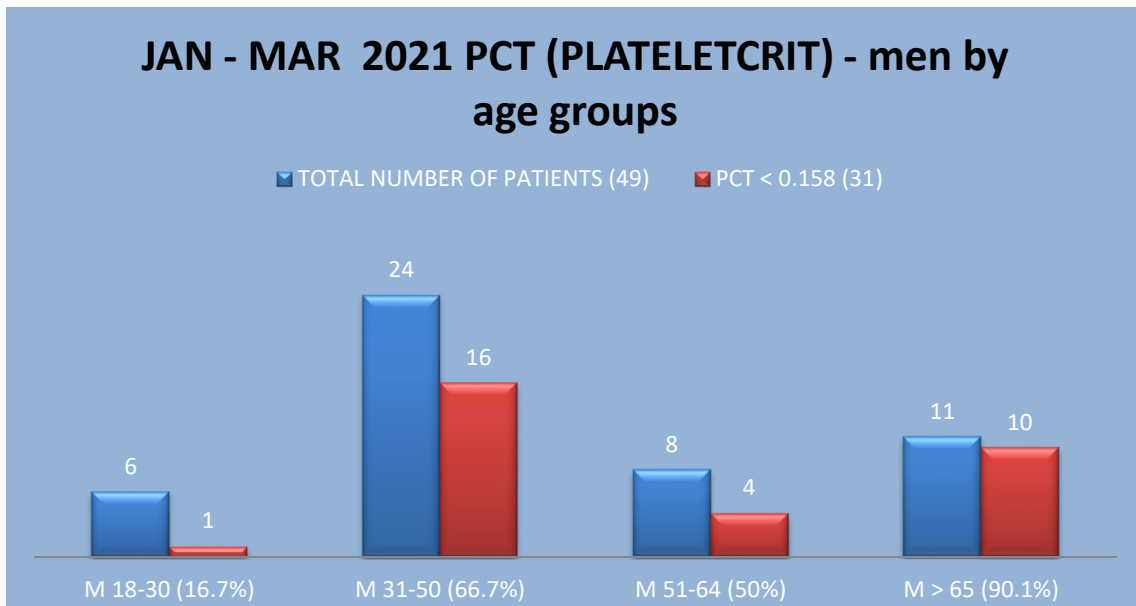
Of the 49 men, five had a decreased platelet count patients, which is 10.2%. 31 patients had decreased PCT, which is 63.3% (Figure 6).



Grafikon 6. Snižen PCT kod muškog pola za period januar–mart 2021.  
 Figure 6. Decreased PCT in men, January–March 2021.

Gledano po starosnim grupama 18–30, 31–50, 51–64 i >65 godina, najveći procenat sniženja PCT imaju muškarci stariji od 65 godina, i to 10 od 11 pacijenata, što je 90,1% (Grafikon 7).

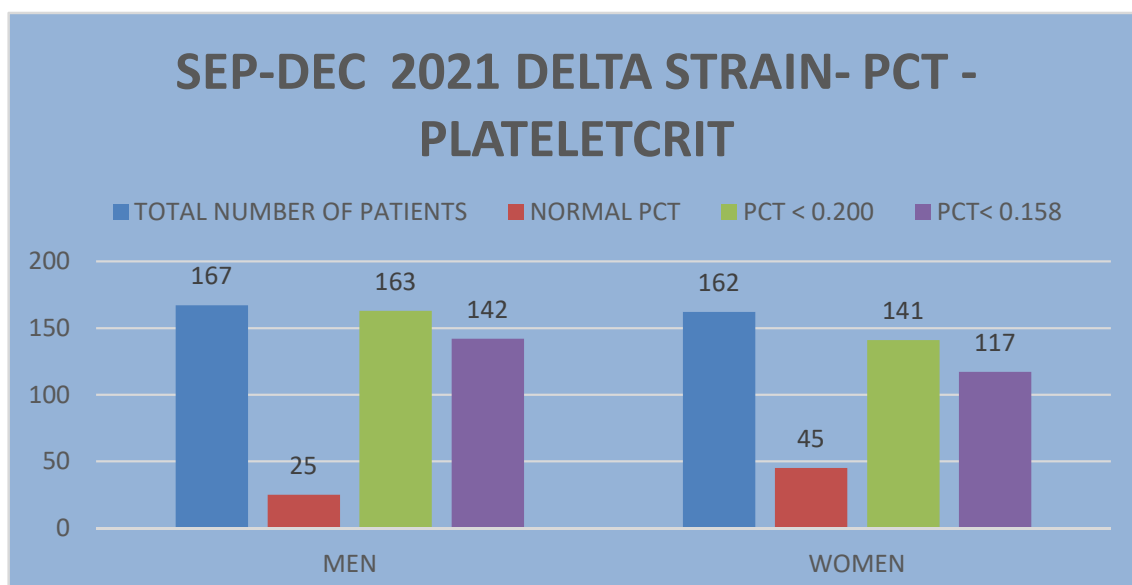
Viewed by age groups, 18–30, 31–50, 51–64, and >65, the highest percentage of PCT lowering was found in men over 65, 10 out of 11 patients, which makes up 90,1% (Figure 7).



Grafikon 7. Snižen PCT kod muškog pola za period januar–mart 2021. po starosnim grupama  
 Figure 7. Decreased PCT in men, January-March 2021., by age groups

U grupi od septembra do decembra 2021. bilo je 167 muškaraca i 162 žene (Grafikon 8).

In the group from September to December 2021. there were 167 men and 162 women (Figure 8).

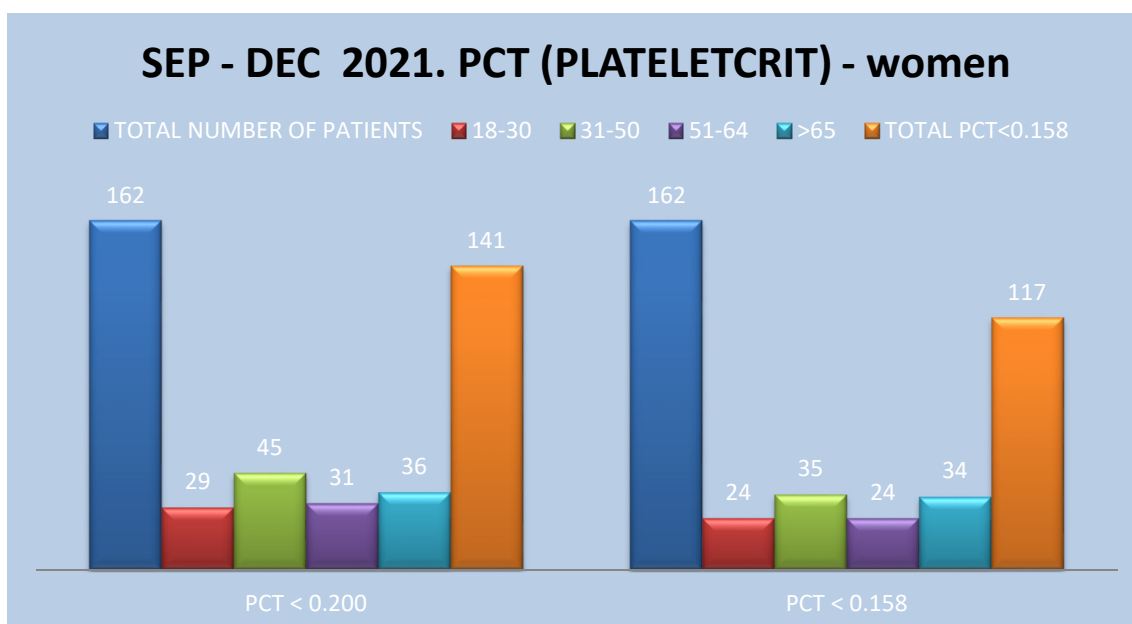


Grafikon 8. Sniženje PCT (plateketkrit) u delta soju - period septembar–decembar 2021.

Figure 8. Decrease of PCT (plateletricit) in Delta strain, September-December 2021.

Od 162 žene, snižen broj trombocita je imalo 27 žena, što je 16,7%. Snižen PCT je imalo 117 žena, što je 72,2% (Grafikon 9).

Out of 162 women, a lower platelet count was found in 27, which makes 16,7%. Lower PCT had 117 women, which makes up 72,2% (Figure 9).



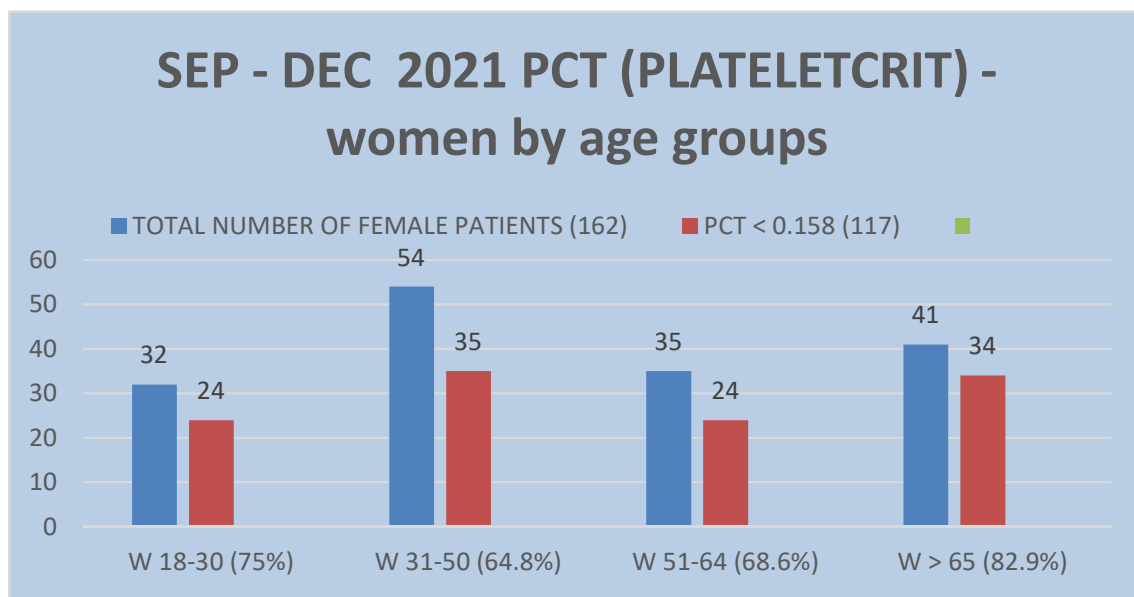
Grafikon 9. Snižen PCT kod ženskog pola za period septembar–decembar 2021.

Figure 9. Decreased PCT in women from September–December 2021.



Gledano po starosnim grupama 18–30, 31–50, 51–64 i >65 godina, najveći procenat sniženja PCT imaju žene starije od 65 godina, i to 34 od 41 pacijentkinje, što je 82,9% (Grafikon 10).

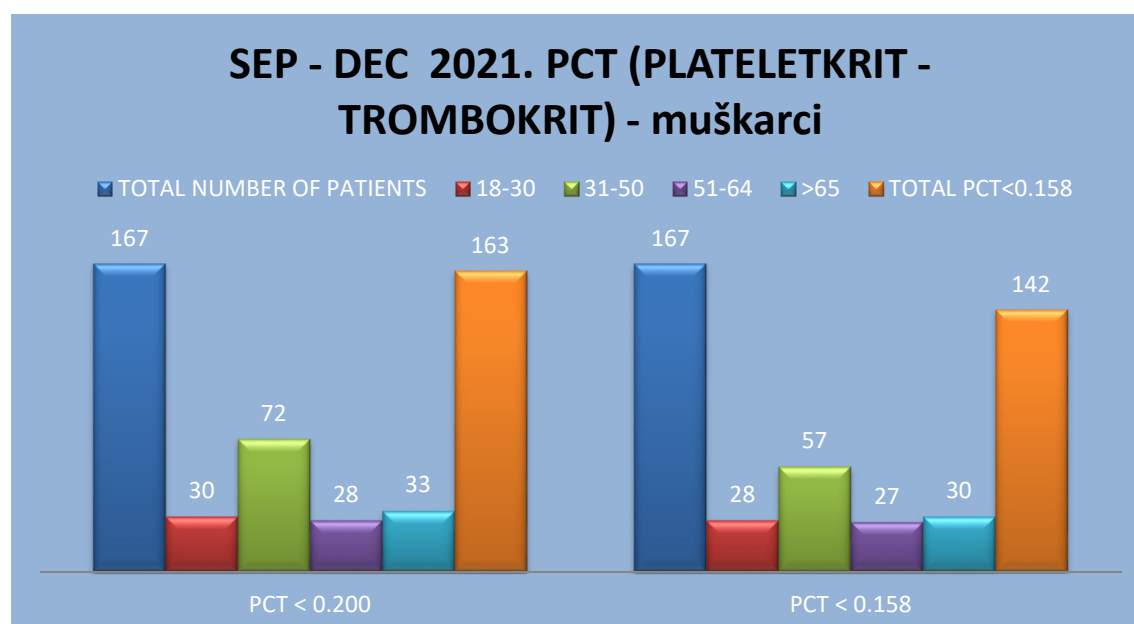
Viewed by age groups, 18–30, 31–50, 51–64, and >65, the highest percentage of PCT lowering was found in women over 65, 34 out of 41, which makes up 82,9% (Figure 10).



Grafikon 10. Snižen PCT kod ženskog pola za period septembar–decembar 2021. po starosnim grupama  
 Figure 10. Decreased PCT in women from September–December 2021. by age groups

Od 167 muškaraca, snižen broj trombocita je imao 31 pacijent, što je 18,6%. Snižen PCT su imala 142 pacijenta, što je 85% (Grafikon 11).

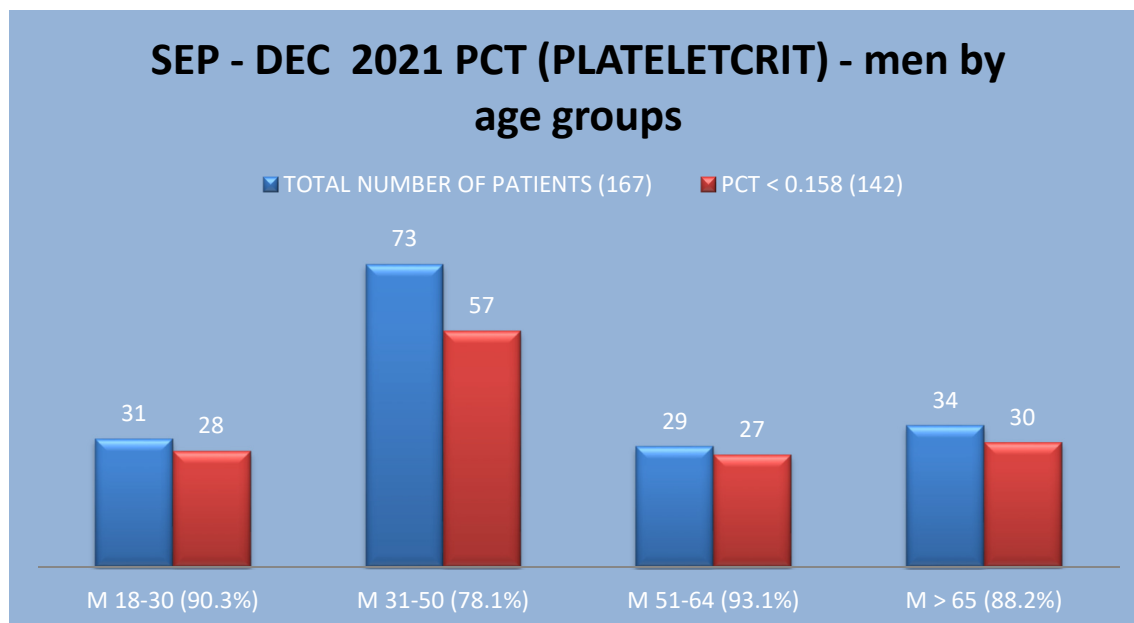
Out of 167 men, a lower platelet count was found in 31 patients, which makes 18,6%. Lower PCT was found in 142 patients, which makes up 85% (Figure 11).



Grafikon 11. Snižen PCT kod muškog pola za period septembar–decembar 2021.  
 Figure 11. Decreased PCT in men from September–December 2021.

Gledano po starosnim grupama 18–30, 31–50, 51–64 i >65 godina, najveći procenat sniženja PCT imali su muškarci od 51 do 64 godine, i to 27 od 29 pacijenata, što je 93,1% (Grafikon 12).

Viewed by age groups, 18–30, 31–50, 51–64, and >65, the highest percentage of PCT lowering was found in men aged 51 to 64, 27 out of 29, which makes up 93,1% (Figure 12).



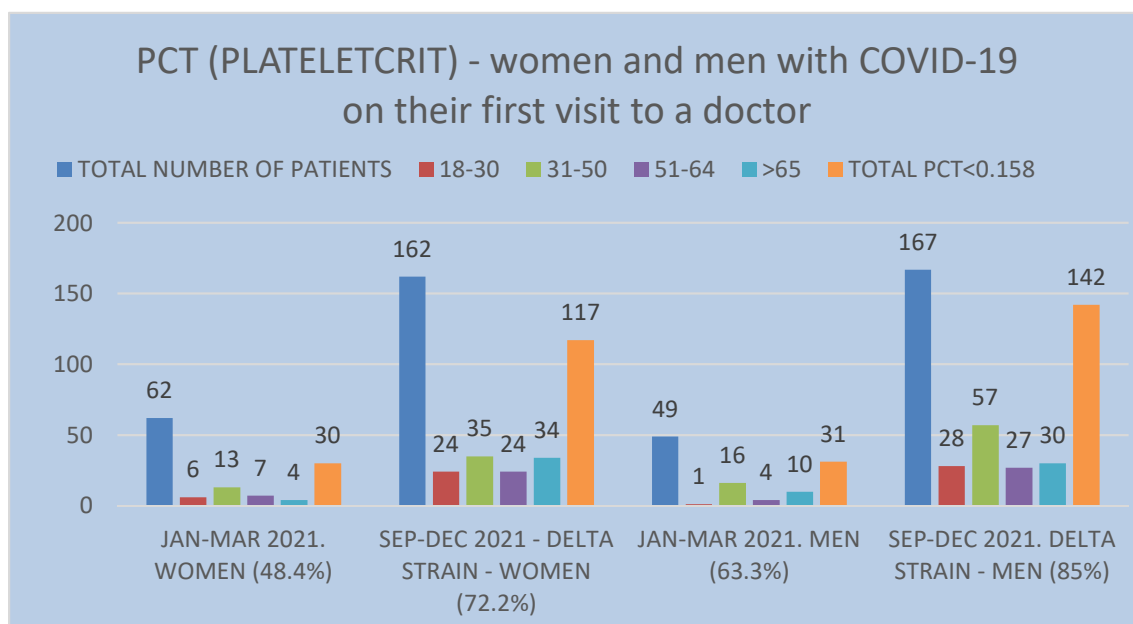
**Grafikon 12.** Snižen PCT kod muškog pola za period septembar–decembar 2021. po starosnim grupama  
**Figure 12.** Decreased PCT in men from September–December 2021. by age groups

Pedeset sedam od 63 kovid pozitivna muškarca starija od 51 godine imali su snižen PCT, što je 90,5% uzorka. Ako donju granicu referentne vrednosti za PCT “pomerimo” do 0,200 (što je opet blizu donje vrednosti), dobijamo da 163 od 167 posmatranih muškaraca ima tu vrednost, što je 97,6%.

Ukupno gledano, snižen PCT u posmatranom uzorku zaraženih delta sojem je kod 78,7% pozitivnih pacijenata (Grafikon 13).

Fifty-seven out of 63 COVID positive men, over 51, had lower PCT, which makes up 90,5% of the sample. If we were to “move” the lower threshold of the reference range for PCT to 0,200 (which is near the lower threshold), we get 163 out of 167 observed men with this result, which makes 97,6%.

In total, a lower PCT in the observed sample of those infected with the Delta strain was found in 78,7% of positive patients (Figure 13).



**Grafikon 13.** Snižen PCT kod žena i muškaraca u dva posmatrana perioda u procentima  
**Figure 13.** Decreased PCT in women and men in two observed periods in percentages

U kontrolnoj grupi pacijenata koji su se javljali u „zele-  
 nu zonu“ kod izabranog lekara zbog nekog drugog zdravstve-  
 nog problema koji nije vezan za COVID-19, u 2021. godini  
 bilo je 60 pacijenata - 28 muškaraca i 32 žene. Od toga je pet  
 imalo snižen PCT i to tri muškarca i dve žene, što je 8,3%.  
 Kod 48 pacijenata koji su radili laboratorijske analize krvne  
 slike pre pojave COVID-19, tj. pre 2020. godine (25 žena i 23  
 muškarca), nije pronađeno sniženje PCT.

Parametar koji se pominje u vodičima za COVID-19  
 je broj trombocita, koji može da bude smanjen. U periodu  
 januar–mart 2021, kod 10 pacijenata oba pola je pronađen  
 snižen broj trombocita. Kod pet od ispitivane 62 žene je na-  
 đen snižen broj trombocita, a to je 8,1%, dok ostalih 57 žena,  
 tj. 91,9% ima normalan broj trombocita. Kod pet od ispitiva-  
 nih 49 muškaraca je snižen broj trombocita, a to je 10,2%,  
 dok su ostali imali normalan broj trombocita, njih 89,8%.  
 Sniženje broja trombocita kod pacijenata u periodu septem-  
 bar–decembar 2021. kada preovladava delta soj je izraženije.  
 Od 162 žene, snižen broj trombocita je imalo 27 žena, što je  
 16,7%, a od 167 muškaraca, snižen broj trombocita je imao  
 31 pacijent, što je 18,6%.

U grupi od januara do marta 2021. bilo je 49 muškaraca  
 i 62 žene. Od 62 žene, snižen PCT je imalo 30 žena, što je  
 48,4%. Ako donju granicu referentne vrednosti za PCT “po-  
 merimo” do 0,200 (što je blizu donje vrednosti), dobijamo da  
 47 od 62 posmatranih žena ima tu vrednost, što je 75,8%. Od  
 49 muškaraca, snižen PCT je imao 31 pacijent što je 63,3%.  
 Ako donju granicu referentne vrednosti za PCT “pomerimo”  
 do 0,200 (što je blizu donje vrednosti), dobijamo da 47 od 49

In the control group, the patients who visited their GPs  
 in the „green zone“ for some other health problem other than  
 COVID-19, in 2021., there were 60 patients - 28 men and  
 32 women. Out of them, five had a lower PCT, three men  
 and two women, which makes up 3%. In 48 patients who did  
 CBC before the COVID-19 era, that is to say before 2020.,  
 (25 women and 23 men), no PCT lowering was found.

The parameter mentioned in the COVID-19 guidelines  
 is the platelet count and it may be decreased. From January to  
 March 2021., in 10 patients, of both genders, a lower platelet  
 count was found. In five out of 62 women decreased platelet  
 count was found, and it made up 8,1%, while the rest of 57  
 women, making up 91,9%, had normal platelet count. In five  
 out of 49 men, platelet count was decreased, which made up  
 10,2%, while others had normal platelet count, making up  
 89,8%. A decrease in platelet count, in patients followed from  
 September to December 2021., when Delta strain prevailed,  
 was more prominent. Out of 162 women, a lower platelet  
 count was found in 27 women, which made up 16,7%, and  
 out of 167 men, a lower platelet count was found in 31, ma-  
 king up 18,6%.

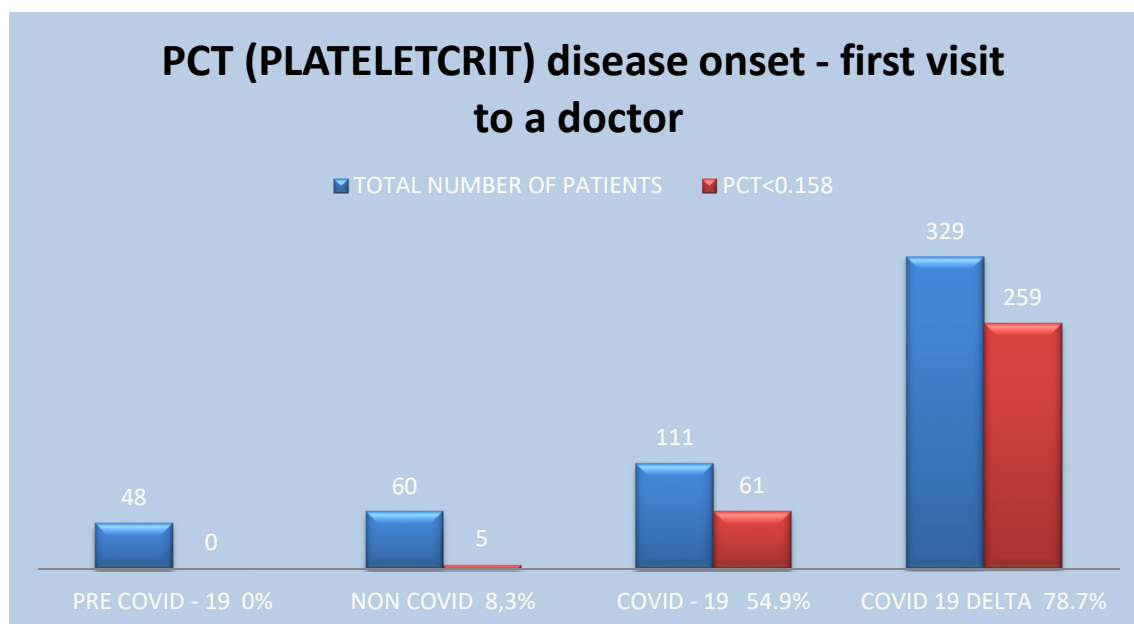
In January to March 2021. group, there were 49 men  
 and 62 women. Out of 62 women, lower PCT was found in  
 30, which made up 48,4%. If the lower threshold of the refe-  
 rence range for PCT is “moved” to 0,200 (which is close to  
 the lower lower reference range), we get 47 out of 62 obser-  
 ved women for this value, making up 75,8%. Out of 49 men,  
 decreased PCT was found in 31, which made up 63,3%. If  
 the lower threshold of a reference range for PCT is “moved”

posmatranih muškaraca ima tu vrednost, što je 95,9%. Ukupno gledano, snižen PCT, ispod 0,158, u posmatranom uzorku pre pojave delta soja je kod 54,9% pozitivnih pacijenata.

U grupi od septembra do decembra 2021. bilo je 167 muškaraca i 162 žene. Od 162 žene, snižen PCT je imalo 117 žena, što je 72,2%. Ako donju granicu referentne vrednosti za PCT "pomerimo" do 0,200 (što je blizu donje vrednosti), dobijamo da 141 od 162 posmatranih žena ima tu vrednost, što je 87%. Od 167 muškaraca, snižen PCT su imala 142 pacijenta, što je 85%. Pedeset sedam od 63 kovid pozitivna muškarca starijih od 51 godine imali su snižen PCT, što je 90,5% uzorka. Ako donju granicu referentne vrednosti za PCT "pomerimo" do 0,200 (što je blizu donje vrednosti), dobijamo da 163 od 167 posmatranih muškaraca ima tu vrednost, što je 97,6% (Grafikon 14).

to 0,200 (which is close to the lower lower reference range), we get that 47 out of 49 observed men had this value, making up 95,9%. In total, lower PCT, below 0,158, in the observed sample, before the occurrence of Delta strain, was found in 54,9% of COVID positive patients.

In the group observed from September to December 2021. there were 167 men and 162 women. Out of 162 women, decreased PCT was found in 117, making up 72,2%. If the lower reference range for PCT is "moved" to 0,200 (which is close to the lower reference range), we get that 141 out of 162 observed women had this value, making up 87%. Out of 167 men, lower PCT was found in 142, making up 85%. Fifty-seven out of 63 COVID positive men, over the age of 51 had decreased PCT, making up 90,5% of the sample. If the lower limit of the reference range for PCT is "moved" to 0,200 (which is close to the lower reference range), we get that 163 out of 167 observed men had this value, making up 97,6%. (Figure 14).



**Grafikon 14.** Sniženje PCT kod svih pacijenata u posmatranim periodima

**Figure 14.** Decreased PCT in all patients in the observed periods

Ukupno gledano, snižen PCT ispod 0,158, u posmatranom uzorku zaraženih delta sojem je kod 78,7% pozitivnih pacijenata.

In total, decreased PCT, below 0,158, in the observed sample of those infected with Delta strain made up 78,7% of positive patients.

## Diskusija

Karakteristike trombocita u krvnoj slici kod COVID-19 se tek u naznakama pominju u dijagnostičkim algoritmima, i to samo broj trombocita - "broj trombocita može da bude snižen", u senci broja i odnosa leukocita i parametara inflamacije (CRP, feritin, D-dimer)<sup>5,12-13</sup>. Svakako su karakteristike trombocitne loze u krvnoj slici od velikog značaja i da, u odnosu sa ostalim parametrima i nađenim stanjem kod pacijenta, mogu da budu itekako od pomoći, najpre u dijagnozi, a kasnije i u prognozi i praćenju toka i ishoda bolesti<sup>12-13</sup>. Uloga lekara u primarnoj zdravstvenoj zaštiti je od velike važnosti, jer treba savetovati pacijenta da se ponaša u skladu sa epidemiološkim preporukama u cilju zaštite sebe i drugih, i samim tim i opšte populacije.

Dakle, govorimo samo o promeni, tj. smanjenju jednog parametra koji se određuje kod trombocita, PCT (plateletkrit ili trombokrit). Vrednost trombokrita u korelaciji sa ostalim karakteristikama trombocita (MPV, RDW, broj trombocita), koji mogu da budu sniženi na početku bolesti, može biti od koristi u dijagnozi kod sumnje na postojanje bolesti izazvane virusom Sars-CoV-2. Naravno, uz klinički pregled pacijenta, anamnezu i dodatne dijagnostičke pretrage.

Mnogobrojni uzroci mogu dovesti do trombocitopenije u obolelih od bolesti COVID-19, a uključuju smanjenu proizvodnju trombocita, njihovo povećano uništavanje i potrošnju, kao i trombocitopeniju uzrokovanu lekovima<sup>12</sup>. Trombocitopenija je prisutna u prosečno 18% obolelih od bolesti COVID-19<sup>13</sup>, obično je blaga, a komplikacije u smislu krvarenja su retke.

Na osnovu našeg istraživanja sprovedenog na osnovu analize samo jednog parametra trombocita PCT (plateletkrit ili trombokrit), iz krvne slike 440 pacijenata u COVID ambulanti, za koje je kasnije Ag ili PCR testom potvrđeno da imaju COVID-19, postoji pad PCT (plateletkrita/trombokrita) kod značajnog broja pacijenata koji su inficirani virusom Sars-CoV-2, izazivačem kovid 19 infekcije. U odnosu na "non-COVID" pacijente u doba COVID-19 pandemije, kod kojih je pad trombokrita nađen kod 8,3%, u vreme COVID-19 pandemije procenat pacijenata koji su imali COVID-19 sa padom trombokrita u momentu dijagnoze je bio 54,9%, a u periodu kada je preovladavao tzv. delta soj, kod 78,7% pacijenata oba pola je bio smanjen trombokrit.

Rezultati ovog istraživanja potvrđuju pretpostavku da određene karakteristike analize trombocita mogu ukazivati na infekciju virusom Sars-CoV-2. Konkretno, vrednosti trombokrita (PCT) su se pokazale kao značajan indikator u identifikaciji COVID-19 pozitivnih pacijenata<sup>12-13</sup>. Ovi nalazi se uklapaju sa prethodnim istraživanjima koja su identifikovala COVID-19 kao prokoagulantno stanje, karakterisano povećanom sklonošću ka trombozi i promenama u parametrima trombocita<sup>5-11</sup>.

## Discussion

Platelet features in the CBC of COVID-19 patients are barely mentioned in diagnostic algorithms and merely as the platelet count - "platelet count may be lowered", often shadowed by the leukocyte count and ratio, and inflammatory parameters (CRP, ferritin, D-dimer)<sup>5,12-13</sup>. The features of platelet lineage in CBC are surely of great importance and together with other parameters and the patient's condition may be of help in diagnosing, and later on prognosis and follow-up of the disease course and outcome<sup>12-13</sup>. The role of the primary healthcare physician is of great importance because someone should advise patients how to act according to the epidemiological recommendations to protect themselves and others.

Therefore, we talk about the change, or more precisely decrease in one platelet parameter, PCT (plateletcrit). The plateletcrit value in correlation with other platelet features (MPV, RDW, platelet count), which may be low at the disease onset, may be useful in diagnosing suspected Sars-CoV-2 virus-caused disease. This, of course, doesn't exclude physical exams, history, and added diagnostic procedures.

There are many causes for thrombocytopenia in COVID-19 patients including decreased platelet production, increased platelet destruction, and consumption, as well as, the one caused by medications<sup>12</sup>. Thrombocytopenia is found in 18% of COVID-19 patients<sup>13</sup>, on average, and it's usually mild. Complications, in the form of bleeding, are rare.

Our research, based on the analysis of only one platelet parameter - PCT (plateletcrit), from the blood samples of 440 patients from the COVID outpatient clinic, that were later tested positive for COVID-19, using Ag or PCR tests, found a decrease in PCT (plateletcrit) in the significant number of patients infected with Sars-CoV-2 virus. When we surveyed "non-COVID" patients, during the COVID-19 pandemic, a decrease in plateletcrit was found in 8,3% but in those who had COVID-19, decrease in plateletcrit was found in 54,9%. During the time when Delta strain prevailed, 78,7% of COVID-19 patients had lowered plateletcrit.

The results of this research confirm the presumption that certain features of platelet analysis may indicate Sars-CoV-2 virus-caused infection. More precisely, plateletcrit (PCT) value proved to be an important indicator in identifying COVID-19 positive patients<sup>12-13</sup>. These findings are consistent with previous research that identified COVID-19 as a procoagulatory condition, prone to higher affinity to thrombosis and platelet parameter changes<sup>5-11</sup>.

U ovom istraživanju je primećeno da su vrednosti PCT-a bile značajno **niže** kod pacijenata sa potvrđenom COVID-19 infekcijom u poređenju sa kontrolnom grupom. Ovi rezultati su posebno važni u kliničkoj praksi, jer pružaju dodatni alat za ranu dijagnozu i praćenje pacijenata, naročito u situacijama gde PCR testiranje nije odmah dostupno ili je neophodno brzo donošenje odluka o tretmanu<sup>14</sup>.

Trombociti, kao ključni učesnici u hemostazi, imaju važnu ulogu u patogenezi COVID-19. Njihova povišena aktivnost i ubrzano trošenje u stvaranju mikrotromboembolusa doprinose teškim kliničkim slikama kod obolelih. Ova studija pokazuje da analiza parametara trombocita, uključujući PLT, MPV, PDW i PCT, može pružiti važne informacije o stanju pacijenta i potencijalnom riziku od razvoja ozbiljnih komplikacija.

Rezultati istraživanja pokazuju da PCT može biti koristan marker za identifikaciju COVID-19 pacijenata, što je u skladu sa radovima koji sugerišu slične promene u koagulacionom statusu pacijenata sa COVID-19<sup>12-14</sup>. Ovi nalazi mogu doprineti boljem razumevanju patofizioloških mehanizama bolesti i pomoći u razvoju novih strategija za prevenciju i lečenje.

Jedno od ograničenja ove studije je relativno mali uzorak pacijenata, što može uticati na generalizaciju rezultata. Takođe, potrebno je dalje istraživanje da bi se utvrdila specifičnost i senzitivnost PCT-a kao markera za COVID-19 u različitim populacijama i u poređenju sa drugim infektivnim i neinfektivnim stanjima koja takođe mogu uticati na trombocite. Ipak, rezultati naglašavaju važnost analize trombocitnih parametara u svakodnevnoj kliničkoj praksi. Dalja istraživanja i veći uzorci mogu dodatno potvrditi ove nalaze i unaprediti naše razumevanje i tretman COVID-19.

Rezultati našeg istraživanja jasno pokazuju da analiza trombocita (PCT) može pružiti korisne informacije u identifikaciji COVID-19 pozitivnih pacijenata. Naši podaci sugerišu značajne razlike u PCT vrednostima između COVID-19 pozitivnih pacijenata i kontrolne grupe, što potvrđuje hipotezu da određene karakteristike trombocita mogu ukazivati na infekciju virusom Sars-CoV-2.

U prvom periodu praćenja (januar–mart 2021. godine), 54,9% COVID-19 pozitivnih pacijenata imalo je snižene vrednosti PCT. U drugom periodu praćenja (septembar–decembar 2021. godine), kada je dominirao delta soj, taj procenat je porastao na 78,7%. Ovo povećanje može ukazivati na veću agresivnost delta soja u pogledu uticaja na koagulacione parametre.

Takođe, rezultati su pokazali da je smanjen broj trombocita bio prisutan kod manjeg broja pacijenata u poređenju sa sniženjem PCT. U periodu januar–mart 2021. godine, 10,2% muškaraca i 8,1% žena imalo je snižen broj trombocita, dok je u periodu septembar–decembar 2021. godine, taj procenat bio 18,6% kod muškaraca i 16,7% kod žena. Ovi podaci potvrđuju da snižen PCT može biti pouzdaniji marker za identifikaciju COVID-19 pozitivnih pacijenata nego sam broj trombocita.

Our research found PCT values were significantly lower in patients with confirmed COVID-19 infection, compared to the control group. These results were especially important in clinical practice because they were an added tool for early diagnosis and patient follow-up, especially when PCR testing wasn't readily available or fast medical treatment decisions were warranted<sup>14</sup>.

Platelets, as key factors in hemostasis, play an important role in COVID-19 pathogenesis. Their increased activity and fast consumption in microthromboemboli formation led to severe clinical presentations in the diseased. Our research shows the analysis of platelet parameters, including PLT, MPV, PDW, and PCT, may supply important information about the patient's condition and potential risks for developing serious complications.

Research results show PCT may be a useful marker for the identification of COVID-19 patients, which is in line with the studies suggesting similar changes in the coagulation status of these patients<sup>12-14</sup>. These findings may help in better understanding of the pathophysiological mechanisms of the disease and developing novel strategies for the prevention and treatment.

One of the limitations of our study is a relatively small sample of patients which may influence generalization of the results. Further research is necessary to affirm the specificity and sensitivity of PCT, as a COVID-19 marker in different populations but also compared to other infectious and non-infectious states that can influence platelets. Still, our results stress the importance of platelet parameter analysis in everyday clinical practice. Further research and bigger samples may additionally confirm our findings and improve our understanding and treatment of COVID-19.

The results of our research clearly show the analysis of plateletcrit (PCT) may give useful information on identifying COVID-19 positive patients. Our data suggest significant differences in PCT values between COVID-19 positive patients and the control group. This confirms the hypothesis that certain platelet features may indicate the infection caused by Sars-CoV-2 virus.

In the first follow-up period (January–March 2021), 54,9% of COVID-19 positive patients had lower PCT values. In the second follow-up period (September–December 2021), when the Delta strain was dominant, this percentage rose to 78,7%. This increase may indicate a larger aggression of the Delta strain in its influence on coagulation parameters.

Also, the results showed that lower platelet count was found in fewer patients, compared to lower PCT. During January–March 2021, 10,2% of males and 8,1% of females had a lower platelet count while from September–December 2021 this percentage was 18,6% in males and 16,7% in females. These data confirm the lower PCT may be a more reliable marker for the identification of COVID-19 positive patients than the platelet count itself.

Analiza po starosnim grupama pokazala je da su stariji pacijenti imali značajno veći procenat sniženja PCT vrednosti. Na primer, kod muškaraca starijih od 65 godina, sniženje PCT je bilo prisutno kod 90,1% u prvom periodu praćenja, dok je kod žena starijih od 65 godina taj procenat bio 80%. Ova distribucija je dodatno potvrđena u drugom periodu praćenja, gde su sniženje PCT imali 90,5% muškaraca starijih od 51 godine i 82,9% žena starijih od 65 godina. Ovi nalazi ukazuju na značajan uticaj starosne dobi na koagulacione promene izazvane COVID-19. Stariji pacijenti su podložniji promenama u PCT vrednostima, što može biti posledica opšteg pada imunološkog odgovora i povećane sklonosti ka koagulopatijama u ovoj populaciji<sup>15-16</sup>.

Kod pacijenata u kontrolnoj grupi (oni koji su se javljali zbog drugih zdravstvenih problema ili pre pojave COVID-19), snižene vrednosti PCT su bile prisutne u mnogo manjem obimu. U 2021. godini, snižen PCT je primećen kod samo 8,3% pacijenata u zelenoj zoni, dok kod pacijenata pre 2020. godine nije primećeno sniženje PCT. Ovo dodatno potvrđuje da snižen PCT može biti specifičan marker za infekciju COVID-19.

Parametri trombocitne loze u rutinskoj krvnoj slici, koja se radi kod sumnje na postojanje zarazne bolesti COVID-19, sa velikim procentom sigurnosti ukazuju da se radi o COVID-19 čak i pre testiranja. Najznačajnije je da pacijenta sa sumnjom na COVID-19 nećemo da „pustimo“ da slobodno šeta i ugrožava i sebe i druge šireći zarazu ukoliko mu testovi na COVID-19 budu negativni. Treba da uložimo dodatni trud i našim autoritetom i znanjem tim pacijentima objasnimo šta znači i koliko je potrebno da budu savesni i da se pridržavaju svih mera koje zakonski važe i za COVID-19 pozitivne pacijente. Takođe je taj zdravstveno-vaspitni rad usmeren i na pacijente koji rutinski, iz nekog razloga, rade krvnu sliku (prijem na operaciju, u bolnicu, priprema za pregled kod specijaliste). Znamo da je veliki broj zaraženih potpuno asimptomatski, pa ukoliko se javi pacijent koji ima snižene parametre trombocita, dalju dijagnostiku tog pacijenta bi trebalo usmeriti na dokazivanje, odnosno isključivanje postojanja COVID-19 infekcije. Na taj način bi se sigurno smanjila mogućnost i da se u bolnice, odnosno u sekundarne i tercijarne ustanove unese COVID-19 u „zelene zone“.

Analysis by age groups showed that older patients had a significantly higher percentage of low PCT values. For example, in males over 65, a PCT decrease was found in 90,1%, in the first period of our research while in women over 65, this percentage was 80%. This distribution was additionally confirmed in the second follow-up period when lower PCT was found in 90,5% of males over 51 and 82,9% of females over 65. These findings point to an important influence of age on coagulation changes caused by COVID-19. Older patients are more susceptible to changes in PCT values, which may be a consequence of the general downfall of the immune answer and greater affinity to coagulopathy in this population<sup>15-16</sup>.

In the patients from the control group (those who were checked for other health problems or those from the time before COVID-19), lower PCT values were found in very few. In 2021, lower PCT was found in only 8,3% of patients from the ‘green zone’ while in those from before 2020, there were none with low PCT. This additionally confirms that low PCT may be a specific marker for COVID-19 infection.

The parameters of the platelet lineage in the routine CBC performed in suspected COVID-19 disease may suggest, with great certainty, that it actually is COVID-19, even before the testing. It is of utmost importance not to allow suspected COVID-19 patients to roam around and endanger themselves and others by spreading the disease even though their tests were negative. An additional effort should be made and we should use our authority and knowledge to explain to these patients what it means and how important it is for them to be conscientious and take all measures of precaution that apply to COVID-19 positive patients. This health and educational work should be also aimed at the patients who, for some reason, do CBC (hospital admission, admission due to operation, preparation for specialist exam). We are aware that the huge number of the infected are completely asymptomatic, so if we find a patient with lower platelet parameters further diagnostics should be aimed at proving or excluding COVID-19 infection. That way, we could surely lower the possibility of bringing in COVID-19 in the ‘green zones’ of the hospitals or other secondary and tertiary healthcare institutions.

## Zaključak

Rezultati ovog istraživanja ukazuju na značajnu povezanost između sniženih vrednosti PCT i infekcije virusom Sars-CoV-2. Ovi nalazi pružaju dokaze da analiza trombokrita može biti koristan alat u dijagnostici COVID-19, posebno u kombinaciji sa drugim kliničkim i laboratorijskim parametrima. Takođe, značajan uticaj starosne dobi na koagulacione promene ukazuje na potrebu za posebnom pažnjom i praćenjem starijih pacijenata tokom pandemije. Dalja istraživanja su potrebna kako bi se bolje razumeli mehanizmi koji stoje iza ovih promena i kako bi se unapredile dijagnostičke i terapijske strategije u borbi protiv COVID-19.

## Conclusion

The results of this study indicate a significant association between reduced PCT values and Sars-CoV-2 virus infection. These findings provide evidence that thrombocrit analysis may be a useful tool in the diagnosis of COVID-19, especially in combination with other clinical and laboratory parameters. Also, the significant influence of age on coagulation changes indicates the need for special attention and monitoring of elderly patients during the pandemic. Further research is needed to better understand the mechanisms behind these changes and to improve diagnostic and therapeutic strategies in the fight against COVID-19.



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