Original article

Can Hemogram Parameters Predict a Positive PCR Result in COVID-19?

Abdurrahman Sarmis[1], Mehmet Agirbasli[2], Esra Kocoglu[3], Hasan Guclu[4], Tuncer Ozekinci[5], Zafer Habip[6]

Abstract

Objective: Quick diagnosis of COVID-19 has been an important factor to manage the ongoing pandemic at hospitals and other health facilities.We aimed to investigate the effects of PCR test on hemogram parameters in COVID-19 patients. ***Materials and Methods:*** We collected hemogram data of 120 nasopharyngeal and oropharyngeal combo swab PCR positive and 119 PCR negative patients admitted to our hospital's COVID-19 clinics with COVID-19 symptoms between 1 April 2020 and 24 June2020. ***Results:*** Age, MPV and NLR were found to be higher; hemoglobin, neutrophil, lymphocytes, basophil, platelet, PCT, WBC levels were lower in PCR positive cases.The highest sensitivity, 75 % is found on WBC count with cut off 7.15. ***Conclusion:*** Lower leukocyte count than 7.15, lower neutrophil count than 4.91, greater NLR than 2.95, lower platelet than 221.5 may give an idea about the diagnosis of SARS-CoV-2 infection.

Keywords: PCR; COVID-19; infectious disease; pandemics; hemogram

Bangladesh Journal of Medical Science, Special Issue on COVID-19. 2021. Page : 118-124
DOI: https://doi.org/10.3329/bjms.v20i5.55404

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)was identified in early 2020 and has caused more than 145 million confirmed cases and more than 3.000.000 deaths all over the world during the COVID-19 pandemic outbreak[1]. "Confirmed case" is defined by WHO (World Health Organization)as "a person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms"[2]. It seems like to affect plenty of people from all over the world for some more time according to modelling studies for the pandemic outbreak[3]. WHO suggests real time reverse transcription polymerase chain reaction quantification RT-PCR (qRT-PCR) test to identify SARS-CoV-2[4]. RT-PCR is the gold standard test to determine SARS-CoV-2 infection presently5. Time consuming manual process, expensive kits and biosafety environment necessities and false negative results are disadvantages of RT-PCR tests during pandemic outbreak. Time is very important to detect cases, contacts and to stop the transmission of the virus earlier.

COVID-19 starts a cascade of events related to inflammation and thrombosis. Quantifying some blood cell subtype proportions like white blood

1. Abdurrahman Sarmis, Department of Medical Microbiology Laboratory, Goztepe Prof. Dr. SuleymanYalcin City Hospital, Istanbul, Turkey.
2. Mehmet Agirbasli, Department of Cardiology, Istanbul Medeniyet University Faculty of Medicine,Uskudar, Istanbul, Turkey.
3. Esra Kocoglu, Department of Medical Microbiology, Istanbul Medeniyet University Faculty of Medicine, Uskudar, Istanbul, Turkey.
4. Hasan Guclu, Biostatistics& Medical informatics, Istanbul Medeniyet University Faculty of Medicine, Uskudar, Istanbul, Turkey.
5. Tuncer Ozekinci, Department of Medical Microbiology, Istanbul Medeniyet University Faculty of Medicine, Uskudar, Istanbul, Turkey.
6. Zafer Habip, Department of Medical Microbiology, Istanbul Medeniyet University Faculty of Medicine, Uskudar, Istanbul, Turkey.

Correspondence: Abdurrahman Sarmis, Department of Medical Microbiology Laboratory, Goztepe Prof. Dr. SuleymanYalcin City Hospital, Kadikoy, Istanbul, Turkey
E- mail address: asarmis@gmail.com

cell(WBC) count, neutrophil (N) count, lymphocyte (L) count, the neutrophil-lymphocyte ratio (NLR), the mean platelet volume (MPV), the platelet-lymphocyte ratio level (PLR) and red blood cell distribution width (RDW) may give idea about the diagnosis and prognosis of the infection. NLR, PLR and MPV are progressively being utilized as biomarkers of chronic inflammation recently[6]. NLR is being used as a pointer of systemic inflammation inpreeclampsia, coronary artery disease and ulcerative colitis[7,8]. PLR may give an idea about the status of thrombosis and inflammation[9].

Viral antigen tests have also been tried to detect SARS-CoV-2 antigens during the pandemic outbreak. Immunochromatographic assay and biosensor based tests have been developed. The sensitivity of immunochromatographic assays vary from 16 % to 85 %[10].

Antibody testing against SARS-CoV-2 has also been used for the diagnosis of recent and past COVID-19 infection. Specific Ig M antibody against SARS-CoV-2 can be produced within the first 5-7 days of the infection and could be used to demonstrate recent infection, while it takes 10-15 days to develop Ig G antibody which may persistperceptible for months[11]. Ig A can be established in mucosal secretions within thefirst 6-8 days, but the importance of it remains unclear[12]. Antibody tests are usually not enough to diagnose as a single test.

Hemogram test is cheap and very widely used all over the world and displays the numbers of many different cell types related to the human immune system. Hematological complications caused by COVID-19 also increases the importance of hemogram. Here in this article, we aimed to investigate the effects of PCR test on hemogramparameters in COVID-19 patients.

Materials and Methods

Data collection

Patients' nasopharyngeal and oropharyngeal combo swab samples for SARS-CoV-2 detection were collected after admission and physical examination in Emergency Room. Patients with critical, serious, fair general situation and radiologic examination were hospitalized, blood samples for hemogram and biochemistry tests were collected routinely. Hemogram data of PCR positive and negative patients were collected from Laboratory Information Management System of our hospital.

We collected hemogram data of 120 nasopharyngeal and oropharyngeal combo swab PCR positive and 119 PCR negative patients admitted to our hospital's COVID-19 clinics with COVID-19 symptoms between 1 April 2020 and 24 June2020. PCR and hemogram tests were performed on the same day or the next day of the former.

PCR tests were performed with RT-PCR test kits provided by the Turkish Health Ministry (Biospeedy COVID-19 RT-qPCR version 1 and 2).Swab samples including viral transport medium were studied with RT-qPCR method according to the manufacturer instructions (Bioeksen, Istanbul, Turkey). The Test kit detects the RdRp (RNA dependent RNA polymerase) single gene fragment of SARS-CoV-2 specifically. World Health Organisation (WHO) published a document which declares that single discriminatory target in RT-PCR tests is acceptedadequate in areas where COVID-19 virus is widely spread on 19th March 2020 at the beginning of the pandemic outbreak[13]. Internal control is provided by the human RNase P gene in the test kit. The LightCycler 480 System (Roche Diagnostics GmbH, Mannheim, Germany) is used to perform gene amplification reactions and signal detections. Specimens indicating positive signal in internal control and RdRp region were regarded as positive while specimens indicating a positive signal in internal control and negative result in RdRp region were regarded as negative. If the cycle threshold (Ct) values detected below 40 with appropriate curves, the test isregarded as positive, if the Ct value was 0, the test was regarded as negative. PCR tests were concluded in approximately 16 hours after the test was ordered. Hemogram tests were performed on Mindray Hematology Analyzer (Shenzhen, P. R. China) and concluded on the same day. 120 PCR positive and 119 PCR negative patients with hemogram data were randomly chosen and parameters in the hemogram test were compared with biostatistical methods. 11 parameters of the hemogram test were collected to analyze. These parameters are;

White Blood Cell, neutrophil, lymphocytes, neutrophil/lymphocytes ratio (NLR), basophil, platelet count, Hemoglobin, Red Cell Distribution Width (RDW), Mean Corpuscular Hemoglobin (MCH),Mean Platelet Volume (MPV), plateletcrit (PCT).

Statistical methods:

We compared numerical data from two independent groups by using Mann-Whitney U test. We used chi-square test for categoric variables. We used ROC analysis and logistic regression for each parameter to predict the existence of the disease as a dependent outcome. We used the Python programming language (14) and IBM SPSS for Mac OS, Version 22 (15)to prepare and analyse the data.

Results

Age, MPV and NLR were found to be significantly higher; hemoglobin, neutrophil, lymphocytes, basophil, platelet, PCT, WBC levels were lower in PCR positive cases than those of PCR negative cases. There were no statistical differences between two groups concerning RDW and MCH values. Gender did not have any statistically significant effect on being tested positive.

Cut off points, specificity and sensitivity of Hemogram parameters are shown in Table 1. The highest sensitivity, 75 % is found on WBC count with cut off 7.15. According to these results, a patient with WBC count lower than 7.15 is PCR positive with probability 0.75, and a patient with WBC count more than 7.15 is PCR negative with probability 0.61. The second highest sensitivity, 67 % is found on neutrophil count with cut off 4.91. So a patient with neutrophil count less than 4.91 is PCR positivewith probability 0.67, and a patient with neutrophil count more than 4.91 is PCR negativewith probability 0.62. Best predicting parameters are WBC, neutrophil, lymphocyte, basophil and PLT counts.

Table 1. Cut off points, specificity and sensitivity of Hemogram parameters

Parameters	Cut off	Sensitivity %	Specificity %	p Value
RDW	13.55	54.2	54.8	0.357
MPV	9.85	42.5	69.6	**0.026***
NLR	2.95	60	57.4	**0.045***
Hemoglobin	14.45	36.5	80	**0.018***
Neutrophil	4.915	67	62.5	**0.001****
Lymphocyte	1.85	64.3	78.3	**0.001****
Basophil	0.025	65.2	70	**0.001****
PLT	221.5	63.5	67.5	**0.001****
PCT	0.255	37.4	82.5	**0.002****
WBC	7.15	75.7	61.7	**0.001****
MCH	28.85	66.1	43.3	0.489

* p<0.05, statistically significant, ** p<0.005, statistically very significant

Logistic Regression

A logistic regression was executed to understand the impacts of age, basophil, RDW, and MCH on the likelihood that the participants have COVID-19 (Table 2). The logistic regression model was statistically significant by Hosmer-Lemeshow test, $\chi2(8)=20.01$, $p<0.01$. Collinearity was observed among neutrophil, lymphocyte, and WBC, but their contribution to the logistic regression was not significant. The model explained 38.2% (Negelkerke R2) of the variance in COVID -19 and correctly classified 73.7% of cases (Table 3). Increasing age was associated with a slight increase in the likelihood of having COVID -19, but increasing MCH or RDW was associated with a decrease in the likelihood of having COVID -19.

Table 2: Logistic regression analysis results

	B	SE β	Wald χ^2	df	p	OR Exp(β)
Constant	12.028	4.281	7.894	1	**0.005***	NA
BAS#	-29.803	13.106	5.171	1	**0.023***	0
RDW	-0.38	0.118	10.452	1	**0.001****	0.684
MCH	-0.223	0.077	8.399	1	**0.004****	0.8
Age	0.018	0.009	4.389	1	**0.036***	1.018

* p<0.05, statistically significant, ** p<0.005, statistically very significant

Table 3. The observed and predicted frequencies by logistic regression with the cutoff 0.50

	Predicted		
	PCR		
Observed	Negative	Positive	% Correct
PCR Negative	79	35	69.3
PCR Positive	26	92	78.0
Overall % correct			**73.7**

Discussion and Conclusion

Fast and accurate confirmation of COVID-19 cases with or without symptoms has a very crucial importance to stop the current spread of infection. The basic reproduction number (R0) of SARS-coV-2 varies from 2 to 4 at different studies which means that a carrier or a patient may spread the virus two to four persons on average(16). This highly contagious

disease increases the importance of fast and accurate confirmation of cases to isolate them and to stop the spread. The clinicians may need additional parameters to predict a PCR positivity in COVID-19 suspected cases.

We evaluated the diagnostic value of hemogram parameters which is one of the cheapest and most common tests available in almost every hospital all over the world. The gold standard RT-PCR tests require expensive equipment and biosafety conditions which may not be available widely at especially undeveloped countries[17]. However hemogram itself is widely available and may give an idea to isolate patients. Isolation is a key point to stop the spread. WHO pays attention to exposure during 2 days before and 14 days after the onset of symptoms of a probable or confirmed case to determine the term contact[2]. Therefore, we suggest that careful review of hemogram parameters can provide useful clues until accurate molecular test results are available.

Hemogram parameters are valuable biomarkers in infectious diseases as an indicator of immune system activation. We found some interesting findings from our analysis of hemogram data which may give idea to clinicians and make them gain time before PCR test results. Especially white blood cell (Leukocyte) count with cut off 7.15, neutrophil count with cut off 4.91, lymphocyte count with cut off 1.85, basophil count with cut off 0.025 and platelet count with cut off 221.5 would give an idea about PCR positivity if results are lower than cut off values.

First of all, in our study, we found age was greater among positive patients. Natale et al., found older people to be more infected in Spain and Italy while in China and Korea middle or younger age groups seemed to be more infected[18]. This result may be obtained due to difference in average age of populations and more widely testing executed in China and Korea than other countries. At the time of study, in our country, only symptomatic patients were being tested with PCR at early stages of pandemic outbreak. This situation would explain our finding which reveals symptomatic patients who required to be tested were at higher ages.Also elderly people are at more risk due to being vulnerable to mental health issues and chronic diseases, therefore we need to pay more attention to them during the pandemic outbreak[19].

We secondly found that NLR were greater in PCR positive patients. NLR has been promising toforesee the prognosis of COVID-19 in a few months after pandemic outbreak started. Ai-Ping Yang et al. studied the diagnostic and predictive role of age, NLR, Platelet to Lymphocyte Ratio (PLR) in COVID-19 patients and they found NLR as the best predictive parameter at the disease. They concluded that elevated age and NLR can be regarded as distinct biomarkers for poor prognosis[20]. Neutrophil (NEU) is a major element of immune system, which destroys the infected cell and release the virus from the cells. Therefore, virus in outer part of the cell may be destroyed, cell-specific and humoral immunities may be stimulated[21]. Then again, lymphocyte is the main factor of human immune response in viral infections[22], whereas CD4+ T lymphocytes decreases and CD8+ suppressor T lymphocyte increases in systematic inflammation[23]. As a result NLR increases in a virus activated inflammation. In our study, NLR value with cut off 2.95 demonstrates PCR positivity with 60 % sensitivity, 54% specificity (Table 1).

WBC count lower than 7.15 has the biggest under the curve area according to ROC curves of our hemogram parameters (Fig 1). Gita Vita Soraya et al. studied a meta-analysis about the effect of important laboratory tests in COVID-19 diagnosis and prognosis and they have found significantly lower leukocyte, neutrophil and platelet counts in COVID-19 patients with pneumonia compared to non-COVID-19 patients with pneumonia in seven studies[24]. They have also found that significantly lower lymphocyte and thrombocyte counts and significantly higher leukocyte, neutrophil, D-dimer, and CRP in severe COVID-19 patients compared to non-severe COVID-19 patients in twenty-six studies. In our study, we analysed these parameters at the beginning of the disease to indicate the diagnosis. In that mentioned meta-analysis, their findings about lower parameters are compatible with our findings, but higher leukocyte and neutrophil are found in severe COVID-19 patients which may have coinfections or comorbidities after being hospitalised. These findings also indicate the importance of hemogram sampling at the beginning and in different stages of the disease. They also concluded that thrombocyte count plays a key role in both diagnosis and prognosis, low leukocyte and neutrophil counts point

out COVID-19 infection, but contrastingly higher counts reveal continuous COVID-19, and although lymphocyte, D-dimer and CRP levels did not have diagnostic measure, all may be increased in severe COVID-19[24]. This conclusion supports our findings about low leukocyte, neutrophil counts which we have found best predictor parameters of hemogram in diagnosis.

We also found lower platelet counts at PCR positive patients with cut off 221.5 which has 63.5 % sensitivity and 67.5 % specificity. Lippi et al. found thrombocytopenia is related to severe COVID-19[25]. This study also supports the diagnostic value of thrombocyte counts in COVID-19 infections, regardless of severity. Steady thrombocytopenia is discovered in the two COVID-19 reported cases originally suspected of dengue infection in a report from Singapore[26]. The reason of thrombocytopenia is not accurately known but could be depended on many factors that inhibit thrombocyte synthesis, activation, or consumption in both beginning and severe part of the COVID-19 infection[27]. SARS-CoV which is the member of the same coronavirus family with SARS-CoV-2 invade and infect progenitor cells in bone marrow, therefore thrombocyte production from megakaryocytes is inhibited and thrombocytopenia develops(28). SARS-CoV-2 may have same mechanism resulting with thrombocytopenia which should be researched profoundly.

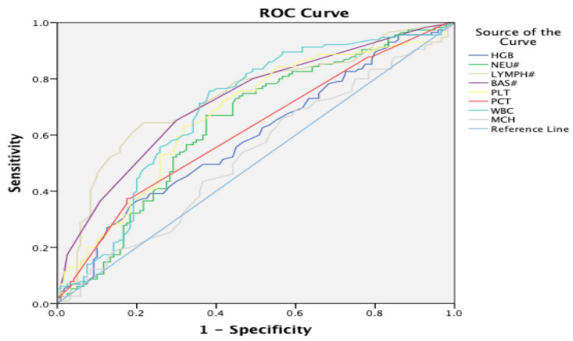

Fig 1: ROC Curves of Hemogram parameter

Logistic regression analysis indicates that a model with basophil, RDW, MCH, and age explains 38.2% of the variance in COVID-19 test result and correctly predicts nearly 3 quarters of the test positive cases. These results implicate that careful analysis of routine test results provide valuable insights in evaluating COVID- 19 suspected patients.

There are several limitations in our study. First, data is obtained from one center in one city, multicentral studies from different parts of world may give better idea about the virus and the reaction of human immune system to the virus. Secondly, PCR test kit used in our study targets one gene region of the virus which may also cause some a bit more percentage false negative results than PCR kits targets two gene region. WHO accepted "one gene region target" in regions where COVID-19 virus is extensively dedected and many test kits were able to detect one gene region in our country at the beginning of the pandemic outbreak. Almost all of test kits detect at least two gene region nowadays in our country. Thirdly, we did not have a chance to check computer tomography results of patients, especially PCR negative patients. We also know that PCR negative patients with computer tomography findings exist. If such patients are excluded from PCR negative control list, parameters of hemogram may have higher sensitivity and specificity. In spite of these limitations, our findings are compatible with current researches in the literature[24,25,26].

Pandemic outbreak is still going on all over the world, keeping causing severe acute respiratory syndrome which leads some patients to be intubated and die. Detailed and urgent studies have been establishing to understand the disease. It is also a requirement to raise the awareness of public about the severity of the COVID-19 pandemic outbreak globally[29]. Hemogram is a cheap, widely available test all over the world whereas PCR test kits are expensive and needs too much consumption material. According to hemogram results in our study, lower leukocyte count than 7.15, lower neutrophil count than 4.91, greater NLR than 2.95, lower platelet than 221.5 may give idea about the diagnosis of SARS-CoV-2 infection, and may make the clinician gain time to isolate the patient and stop the spread and start the treatment earlier. More detailed researches could be established especially with COVID-19 suspected PCR negative patients who have computer tomography findings.

Acknowledgments

This study was performed in Istanbul Medeniyet University Goztepe Education and Research Hospital which is known as Goztepe Prof. Dr.SuleymanYalcin City Hospital since 5th September 2020. We thank all of healthcare staff working devotedly from all

over the world since the beginning of COVID-19 pandemics.

Conflicts of Interest

The authors declare no conflicts of interest.

Funding/Support

We received no funding from any organization for this research.

Ethical clearance

The study protocol was affirmed by the local institutional ethical committee of Istanbul Medeniyet University Goztepe Education and Research Hospital (New name of the hospital: GoztepeProf. Dr.SuleymanYalcin City Hospital) (document number: 2020/0670).

Authors's contribution:

Data gathering and idea owner of this study: AS, MA;

Study design:AS,MA,EK;

Data gathering:AS,EK,HG;

Writing and submitting manuscript: AS,MA,EK,HG,TO,ZH;

Editing and approval of final draft: AS,MA,EK,HG,TO,ZH

References

1. https://covid19.who.int/table. [Accessed 27 April 2021]
2. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200430-sitrep-101-covid-19.pdf . [Accessed 15 November 2020]
3. Ankaralı, H., Erarslan, N., Pasin, Özge, & Mahmood, A. K. Modeling and Short-Term Forecasts of Indicators for COVID-19 Outbreak in 25 Countries at the end of March. Bangladesh Journal of Medical Science,2020; **19**: 6-20. https://doi.org/10.3329/bjms.v19i0.47611
4. Chenxi Li, Chengxue Zhao, Jingfeng Bao, Bo Tang, Yunfeng Wang, Bing Gu, Laboratory diagnosis of coronavirus disease-2019 (COVID-19), *Clinica Chimica Acta*,2020**;** **510:** 35-46. https://doi.org/10.1016/j.cca.2020.06.045
5. Zakariah, S., Tengku Jamaluddin, T. Z., Mahayidin, H., Dahari, Z., & Ibrahim, R. Laboratory Diagnostics in COVID-19: What We Know So Far. *Bangladesh Journal of Medical Science*, 2020; **19**: 93-100. https://doi.org/10.3329/bjms.v19i0.48199
6. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume:a link between thrombosis and inflammation? *Curr Pharm Des*. 2011;**17**:47-58. https://doi.org/10.2174/138161211795049804
7. Oylumlu M, Ozler A, Yildiz A, Oylumlu M, Acet H, Polat N, et al. New inflammatory markers in pre-eclampsia:echocardiographic epicardial fat thickness and neutrophil to lymphocyte

ratio. *Clin Exp Hypertens.* 2014;**36**(7):503-507. https://doi.org/10.3109/10641963.2013.863324

8. Celikbilek M, Dogan S, Ozbakir O, Zararsiz G, Kucuk H, Gursoy S, et al. Neutrophil lymphocyte ratio as a predictor of disease severity in ulcerative colitis. *J Clin Lab Analysis*. 2013;**27**:72-76. https://doi.org/10.1002/jcla.21564
9. Cakiroglu Y, Vural F, Vural B. The inflammatory markers in polycystic ovary syndrome:association with obesity and IVF outcomes. *J Endocrinal Invest*. 2016;**39**:899-907. https://doi.org/10.1007/s40618-016-0446-4
10. Weitzel T, Legarraga P, Iruretagoyena M, Pizarro G, Vollrath V, Araos R et al. Comparative evaluation of four rapid SARS-CoV-2 antigen detection tests using universal transport medium. *Travel Med Infect Dis.* 2021;**39**:101942. https://doi.org/10.1016/j.tmaid.2020.101942
11. Zhou, P., Yang, XL., Wang, XG. et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020**; 579:** 270-273.
12. Padoan A, Sciacovelli L, Basso D, Negrini D, Zuin S, Cosma C, Faggian D, Matricardi P, Plebani M. IgA-Ab response to spike glycoprotein of SARS-CoV-2 in patients with COVID-19: A longitudinal study. *Clin Chim Acta.* 2020; **507**:164-166. https://doi.org/10.1016/j.cca.2020.04.026
13. https://www.who.int/publications/i/item/10665-331501. [Accessed 15 November 2020].
14. Python Software Foundation. Python Language Reference, version 2.7. Available at http://www.python.org. [Accessed 15 November 2020]
15. IBM Corp. Released 2013. IBM SPSS Statistics for MacOS, Version 22.0. Armonk, NY: IBM Corp. [Accessed 15 November 2020]
16. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W et al. The basic reproduction number of novel coronavirus (2019-nCoV) estimation based on exponential growth in the early outbreak in China from 2019 to 2020: A reply to Dhungana. *Int J Infect Dis*. 2020;**94:**148-150. https://doi.org/10.1016/j.ijid.2020.02.025
17. Haque, M., Islam, S., Iqbal, S., Urmi, U., Kamal, Z., Rahman, A.et al. Availability and price changes of potential medicines and equipment for the prevention and treatment of COVID-19 among pharmacy and drug stores in Bangladesh; findings and implications. *Bangladesh Journal of Medical Science,* 2020; **19:** 36-50. https://doi.org/10.3329/bjms.v19i0.48106
18. Natale A, Ghio D, Tarchi D, Goujon A, Conte A. COVID-19 cases and case fatality rate by age. Knowledge for policy. 2020. Available at: https://ec.europa.eu/knowledge4policy/publication/covid-19-cases-case-fatality-rate-age_en. [Accessed 15 November 2020]
19. Rahman, M. S., & Lassi, Z. Self-management for elderly during the COVID-19 pandemic. Bangladesh *Journal of Medical Science*, 2021; **20**(3), 694-695. https://doi.org/10.3329/bjms.v20i3.52820
20. Yang, A. P., Liu, J. P., Tao, W. Q., & Li, H. M. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *International immunopharmacology*, 2020; **84**, 106504. https://doi.org/10.1016/j.intimp.2020.106504
21. Kusumanto Y.H., Dam W.A., Hospers G.A.P., Meijer C., Mulder N.H. Platelets and granulocytes, in particular the neutrophils, form important compartments for circulating vascular endothelial growth factor. *Angiogenesis.* 2003; **6**(4):283-287. https://doi.org/10.1023/B:AGEN.0000029415.62384.ba
22. Rabinowich H., Cohen R., Bruderman I., Steiner Z., Klajman A. Functional analysis of mononuclear cells infiltrating into tumors: lysis of autologous human tumor cells by cultured infiltrating lymphocytes. *Cancer Res.* 1987; **47**(1):173-177.
23. Menges T., Engel J., Welters I., Wagner R.M., Little S., Ruwoldt R. et al. Changes in blood lymphocyte populations after multiple trauma: association with posttraumatic complications. *Crit. Care Med.* 1999; **27**(4):733-740. https://doi.org/10.1097/00003246-199904000-00026
24. Soraya GV, Ulhaq ZS. Crucial laboratory parameters in COVID-19 diagnosis and prognosis: An updated meta-analysis. *Med Clin* (Barc). 2020; **155**(4):143-151. https://doi.org/10.1016/j.medcli.2020.05.017
25. Lippi G., Plebani M., Henry B.M. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. *Clin Chim Acta*. 2020; **506:**145-148 https://doi.org/10.1016/j.cca.2020.03.022
26. Yan G., Lee C.K., Lam L.T., Yan B., Chua Y.X., Lim A.Y. Covert COVID-19 and false-positive dengue serology in Singapore. *Lancet Infect Dis*. 2020; **20**(5):536. https://doi.org/10.1016/S1473-3099(20)30158-4
27. Assinger A. Platelets and infection - an emerging role of platelets in viral infection. *Front Immunol.* 2014; **5**:649. https://doi.org/10.3389/fimmu.2014.00649
28. Yang M., Ng M.H., Li C.K. Thrombocytopenia in patients with severe acute respiratory syndrome. *Hematology.* 2005; **10**:101-105. https://doi.org/10.1080/10245330400026170
29. Ashiq, K., Ashiq, S., Bajwa, M., Tanveer, S., &Qayyum, M. Knowledge, attitude and practices among the inhabitants of Lahore, Pakistan towards the COVID-19 pandemic: an immediate online based cross-sectional survey while people are under the lockdown. Bangladesh Journal of Medical Science. 2020; 19:69-76. https://doi.org/10.3329/bjms.v19i0.48169