



LABORATORY DIAGNOSTIC SIGNIFICANCE OF COVID-19

Saidov F.A.

Department of Hematology and Clinical Laboratory Diagnostics
Bukhara State Medical Institute, Bukhara, Uzbekistan

ANNOTATION

The ongoing COVID-19 pandemic forces many scientists around the world to fight to prevent and address its dire consequences and complications. Despite the current active development of methods for specific laboratory diagnosis of a new coronavirus infection, there are many difficulties in identifying asymptomatic carriers of SARS-CoV-2. Given the high variability of COVID-19 and the different ability of mutated coronaviruses to affect human immunity and cause disruption of the organs and systems of the body, it is necessary to determine the level of laboratory parameters of blood serum, which are closely related to the assessment of the development of a secondary bacterial infection, as well as the nature of the course, severity and prognosis in patients with COVID-19.

Keywords: COVID-19, PCR analysis, SARS-CoV 2, CT, antiviral antibodies

ЛАБОРАТОРНО ДИАГНОСТИЧЕСКАЯ ЗНАЧИМОСТЬ COVID-19

Саидов Ф.А.

Кафедра гематологии и клиническая лабораторная диагностика
Бухарского государственного медицинского института, Бухара, Узбекистан

АННОТАЦИЯ

Продолжающаяся пандемия COVID-19 заставляет многих ученых во всем мире бороться за предотвращение и устранение ее тяжелых последствий и осложнений. Несмотря на активное развитие в настоящее время методов специфической лабораторной диагностики новой коронавирусной инфекции остаётся немало сложностей для выявления бессимптомных носителей SARS-CoV-2. Учитывая высокую изменчивость COVID-19 и различную способность мутированных коронавирусов воздействовать на иммунитет человека и вызывать нарушения работы органов и систем организма, необходимо определение уровня лабораторных показателей сыворотки крови, которые имеют тесную взаимосвязь с оценкой развития вторичной бактериальной инфекции, а также характером течения, тяжестью и прогнозом у больных COVID-19





Ключевые слова: COVID-19, ПЦР-анализ, SARS-CoV-2, КТ, противовирусные антитела

COVID-19 LABORATOR DIAGNOSTIK AHAMIYATI

Saidov F.A.

Gematologiya va klinik laboratoriya diagnostikasi bo'limi
Buxoro davlat tibbiyot instituti, Buxoro, O'zbekiston

Annotatsiya

Davom etayotgan COVID-19 pandemiyasi butun dunyo bo'ylab ko'plab olimlarni uning dahshatli oqibatlari va asoratlarning oldini olish va bartaraf etish uchun kurashishga majbur qilmoqda. Yangi koronavirus infeksiyasining aniq laboratoriya diagnostikasi usullari faol ishlab chiqilayotganiga qaramay, SARS-CoV-2 ning asimptomatik tashuvchisini aniqlashda ko'plab qiyinchiliklar mavjud. COVID-19 ning yuqori o'zgaruvchanligini va mutatsiyaga uchragan koronaviruslarning inson immunitetiga ta'sir qilish va tananing a'zolari va tizimlarining buzilishiga olib keladigan turli xil qobiliyatini hisobga olgan holda, qon zardobining laboratoriya ko'rsatkichlari darajasini aniqlash kerak, bu ikkilamchi bakterial infeksiyaning rivojlanishini baholash, shuningdek, COVID-19 bilan og'rigan bemorlarda kursi, zo'ravonligi va prognozi bilan chambarchas bog'liq.

Kalit so'zlar: COVID-19, PSR tahlili, SARS-CoV 2, КТ, antivirus antitelalar

At the end of 2019, humanity encountered a new representative of the Coronaviridae family, SARS-CoV 2 (subgenus Sarbecovirus, genus Betacoronavirus) [1,4,5], which, like SARS-CoV, is most closely related to bat viruses (88% similarity of nucleotide sequences), but at the same time it has a lower degree of similarity with SARS-CoV – 79% [2,7,9]. The emergence of this virus led to serious consequences for humanity, causing a pandemic of severe respiratory disease COVID 19, which swept all countries and continents, claimed and continues to claim hundreds of thousands of human lives. In the course of effectively countering this unprecedented biological threat, the global medical community is striving to develop various strategies for the treatment and prevention of COVID 19, the success of which directly depends on the effectiveness of the approaches, methods and technologies used for laboratory diagnosis of infection. Laboratory diagnostic methods are a key component in diagnosing and monitoring the course of COVID-19. Reliable tests should be used to





detect active infections with varying degrees of clinical symptoms, evaluate immune response and monitor cure, and diagnose and differentiate characteristic comorbid conditions and complications. In this regard, laboratory diagnostics for COVID-19 is complex and includes specific tests aimed at detecting the virus itself and the immune response to its invasion, markers used for the differential diagnosis of viral and bacterial infections, as well as general clinical studies that allow monitoring of the inflammatory reaction, organ dysfunction, the state of the blood coagulation system, etc [3,6,8]. In the case of bacterial co- and superinfection, microbiological diagnostic methods are important. There is also the possibility of obtaining false positive responses when setting up PCR. Despite the decrease in the risks of DNA (RNA) contamination when performing real-time PCR, compared with the electrophoretic format for recording results, this problem remains significant and requires a high level of organization of laboratory studies, especially with their significant volumes. It should be borne in mind that positive PCR responses do not mean the presence of a live virus in the sample, since the method detects only RNA fragments - SARS-CoV-2 markers. The issues of accuracy of laboratory research are inextricably linked with the peculiarities of performing the preanalytical and analytical stages of diagnostics. We can distinguish the following factors that largely determine the accuracy of diagnostic analysis, which must be taken into account when planning and performing the preanalytical stage of work[10,12,16].

The main method is real-time RT-PCR. The material for the study is the combined nasopharyngeal and oropharyngeal smears placed in 1 test tube with a transport medium. If the result is negative and at a later date of sampling, it is better to use sputum samples or bronchoalveolar lavage in patients with severe disease. The absence of a positive result in RT-PCR against the background of typical clinical signs of a new coronavirus infection does not allow us to reliably exclude the etiological role of the SARS CoV 2 coronavirus, and in this case, serodiagnostic methods are appropriate. When performing serodiagnostic studies, it is necessary to use the most sensitive and specific diagnostic tools, which primarily include tests for total (total) antiviral antibodies (IgM / IgG / IgA), as well as IgG (from 8–14 days after clinical manifestations). Separate determination of IgM and IgG is considered less justified, since the effectiveness of detection of total antibodies to SARS-CoV 2 exceeds that of detection of individual classes of antiviral immunoglobulins [11,13,17]. The detection of isolated IgM in patients is characterized by lower sensitivity [19] and may also lead to false positive results [21] due to their lability and relatively lower specificity compared to other classes of antiviral antibodies. Rapid tests may have low sensitivity



[21], are screening, and are not recommended for the etiological laboratory diagnosis of COVID 19 [14,20].

The humoral immune response in COVID-19 is formed along a universal path and consists in the sequential synthesis of IgM, which appear on days 5–7, reach a peak by the 14th day of the disease and leave the circulation over the next two weeks, IgA with similar kinetics, and IgG, which begin be determined from 2–3 weeks of the disease and circulate indefinitely, presumably providing acquired immunity to this disease. To determine the presence and level of antibodies, test systems based on immunochromatographic, immunochemiluminescent, and enzyme immunoassay methods are used [6,15]. The simplest is a high-quality immunochromatographic method, implemented in the form of test strips, which allow within 10-15 minutes. detect the presence or absence of antibodies in whole blood (venous or capillary), serum or plasma. Currently, a number of test systems using this method are registered in our country. All these systems are built according to a universal principle using specific antibodies labeled with colloidal gold to the corresponding immunoglobulins and differ in the type of antibodies detected (only IgG, total antibodies, IgM and IgG separately), in their kit, ease of use, and also in the ease of reading the result (visibility).). Test systems using the immunochromatographic method are characterized by the speed of obtaining results, have high specificity with satisfactory sensitivity, do not require high qualifications of the personnel using them, do not impose special requirements on storage conditions and can be implemented everywhere for the purpose of primary screening, being true tests "point of care". A relative disadvantage is the impossibility of obtaining a quantitative result that allows assessing the dynamics of changes in the level of immunoglobulins. Interest in the widespread use of serological tests is increasing, but there are still many questions and uncertainty regarding the extent and duration of immunity caused by SARS-CoV-2 infection, the frequency of false positive and false negative test results. According to WHO, laboratory tests that detect antibodies to SARS-CoV-2 in humans need further validation to determine their accuracy and reliability [14, 16].

It occurs almost simultaneously (a similar feature of seroconversion was previously shown for the SARS-CoV coronavirus) or sequentially, with a short interval of 2–3 days [17]. Moreover, in some patients, IgM is first detected, in others - IgG, and after 17-23 days they are detected in 100%. Within 3 weeks from the onset of clinical symptoms, a gradual quantitative increase in IgM and Ig G is observed. After 3 weeks, there is a decrease in IgM titers, while IgG remain high. Taking into account these features, the detection of total antibodies in the blood provides the maximum diagnostic sensitivity [18]. In parallel with the study of the immune response to





infection, studies aimed at studying the kinetics of virus release during the infectious process were carried out [19]. It has been established that the seroconversion of IgM and IgG, which occurs almost simultaneously, is not associated with the cessation of virus isolation: in most patients whose blood contains IgM and IgG to the SARS CoV 2 coronavirus, RNA of this pathogen is found in the respiratory tract [19].

In the first scientific publications about the course of COVID-19, an unprecedented prevalence of complications caused by a violation of the hemostasis system was noted almost immediately. Thrombotic complications (TO) and the development of consumption coagulopathy (DIC) often accompanied the severe course of the disease, and also caused the death of patients. Thus, according to a number of studies in ICU patients, even against the background of thromboprophylaxis, the frequency of TO ranged from 23% to 69%, while 71% of patients who developed DIC died [30]. It should be noted that in later publications such a high frequency of coagulopathy was no longer described, which may be due to the beginning of the routine use of heparins for the correction of hypercoagulable states. According to a meta-analysis, hemostasis parameters in hospitalized patients with COVID-19 predominantly demonstrate mild thrombocytopenia, an increase in D-dimer levels, a prolongation of prothrombin time, and an increase in fibrinogen levels. Statistically significant differences between surviving and deceased patients were observed in the levels of D-dimer (≈ 3 times) and fibrin degradation products (≈ 2 times), as well as in a significant prolongation of prothrombin time (by 14%) [21]. Changes in various parts of the hemostasis system in COVID-19 are multidirectional, and therefore the diagnostic and prognostic significance of individual hemostasis tests may be unobvious and contradictory. Making clinical decisions based on changes in individual parameters can lead to the wrong choice of therapy. So, for example, with the aggravation of the course of the disease, as well as with the onset of coagulopathy of consumption, the level of fibrinogen decreases, as well as the level of antithrombin III, which is not measured routinely [20]. These changes affect the hemostasis system in different ways, so defining one parameter without the other can lead to false conclusions. That is why multifactorial changes in the hemostasis system that occur against the background of the course of coronavirus infection, especially during the development of critical conditions, are most effectively assessed using global tests that show the resulting state of the patient's hemostasis, taking into account all factors, including the effect of therapy. Thus, it has been shown that in patients with COVID-19 and acute respiratory failure, compared with the control group of healthy volunteers, hypercoagulation is recorded according to the parameters of thromboelastometry/-graphy, which may indicate a tendency of this group of patients to develop TO-PCR.





The data of scientific publications make it possible to quite fully characterize the indicators of the diagnostic accuracy of PCR analysis in detecting the SARS-CoV-2 virus and the factors influencing them. These are the timing of material sampling, with the maximum sensitivity of the test at 5-6 days after the onset of the first symptoms, the severity of the course of the disease, which correlates with the duration of detection of virus markers, the type of material being studied - a higher probability of finding the virus in bronchoalveolar lavage and sputum (during separation), compared with material from the nasopharynx and oropharynx, and low detectability in blood and urine. At the same time, even according to the most optimistic data, the diagnostic sensitivity of PCR does not exceed 90%. To date, the algorithm for diagnosing a new coronavirus infection includes instrumental (radiological) and laboratory research methods. From a clinical point of view, the results of CT, in combination with the relevant epidemiological history, can be used as a first and immediate guide for doctors to start treatment and take the necessary anti-epidemic measures, while PCR serves as a confirmation tool, its results can be used later to decide on the next steps (isolation, treatment). But at the same time, it should be noted that the health care of many countries is faced with a shortage of computed tomographs and qualified specialists, which makes this method inaccessible for full-scale research, in contrast to the laboratory molecular genetic test. PCR analysis is indispensable for examinations of contact persons, monitoring of morbidity. Thus, it is an integrated approach using PCR and CT, taking into account the factors affecting the accuracy of diagnosis, that makes it possible to obtain reliable results, correctly interpret them, which is necessary both for making a correct diagnosis for a particular patient and for obtaining objective data on the incidence of the population, timely decision-making on the necessary anti-epidemic and preventive measures. The COVID-19 pandemic, which caused unprecedented changes in the way of life around the world, showed that the usual approach to assessing a case of a disease is insufficient and required the urgent development of effective diagnostic tests that allow to identify infected and sick people with high sensitivity and specificity, determine the stage of the disease, and also to confirm the cure, which is necessary both to limit the spread of infection and to conduct appropriate treatment of the diseased. Methods have been introduced into practice to detect the presence of coronavirus in various biological substrates, as well as to evaluate the immune response to infection. Each of these methods has its advantages and disadvantages, point of application, features of application and evaluation of results. There is no universal way to diagnose COVID-19. Physicians should carefully consider the pros and cons of each method and the results of studies should be interpreted taking into





account the clinical picture of the disease and the epidemiological history. Further studies are required to assess the clinical relevance of the available methods. Of great importance is the use of a number of laboratory tests and biomarkers that can objectively support the adoption of appropriate clinical decisions in the development of concomitant COVID-19 conditions and complications. First of all, this concerns methods for monitoring violations of the hemostasis system, as well as biomarkers of bacterial infection. The seasonal increase in the incidence due to acute respiratory infections in the autumn-winter period in the context of the COVID-19 pandemic will be expected to be associated with a certain contribution of the new coronavirus to the etiological structure of ARVI pathogens. In this regard, great hopes are placed on improving the methods of diagnosis and treatment of COVID-19, where laboratory tests will be of key importance.

USED LITERATURE

1. Временные методические рекомендации «Медицинская реабилитация при новой коронавирусной инфекции COVID-19» версия 2 от 31.07.2020. URL: https://www.edu.rosminzdrav.ru/fileadmin/user_upload/specialists/COVID19/dop-materials/VMR_medreabilitacija_COVID_versija2.pdf.
2. Мещерякова Н.Н., Белевский А.С., Кулешов А.В. Легочная реабилитация пациентов, перенесших коронавирусную инфекцию COVID-19 (клинические примеры) // Пульмонология. 2020. Т.30, №5. С.715–722. <https://doi.org/10.18093/0869-0189-2020-30-5-715-722>
3. Чучалин А.Г., Айсанов З.Р., Чикина С.Ю. Черняк А.В., Калманова Е.Н. Федеральные клинические рекомендации Российского респираторного общества по использованию метода спирометрии // Пульмонология. 2014. №6. С.11–23. <https://doi.org/10.18093/0869-0189-2014-0-6-11-24>
4. Малявин А.Г., Адашева Т.В., Бабак С.Л. и др. Медицинская реабилитация больных, перенесших COVID-19 инфекцию. *Терапия*. 2020; 26(S5): 4-48 doi: 10.18565/therapy.2020.5suppl.1-48.
5. Zangrillo A, Beretta L, Silvani P, Colombo S, Scandroglio AM, Dell'Acqua A, et al. Fast reshaping of intensive care unit facilities in a large metropolitan hospital in Milan, Italy: facing the COVID-19 pandemic emergency. *Crit Care Resusc* 2020 Apr 1 [Epub ahead of print].
6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of Coronavirus disease 2019 in China. *N Engl J Med* 2020 Feb 28 [Epub ahead of print].





7. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. *Crit Care* 2020; 24: 28.
8. Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the CO-VID-19 Virus Targeting the CNS: Tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. *ACS Chem Neurosci* 2020; 11: 995–998.
9. Ulrich, H., & Pillat, M. M. (2020). CD147 as a Target for COVID19 Treatment: Suggested Effects of Azithromycin and Stem Cell Engagement. *Stem Cell Reviews and Reports*.
10. Naimova S. A. Principles of early diagnosis of kidney damage in patients of rheumatoid arthritis and ankylosing spondylarthritis // *British Medical Journal*. – 2021. – Т. 1. – №. 1.
11. Наимова Н. Ш., Хамидова Н. К., Азамов Б. З. Особенности коагуляционного и клеточного гемостаза при ревматоидном артрите у лиц с сердечно-сосудистой патологией // *Новый день в медицине*. – 2019. – №. 2. – С. 219-222.
12. Наимова Ш. А., Латипова Н. С., Болтаев К. Ж. Коагуляционный и тромбоцитарный гемостаз у пациентов с ревматоидным артритом в сочетании с сердечно-сосудистом заболеванием // *Инфекция, иммунитет и фармакология*. – 2017. – №. 2. – С. 150-152.
13. Anvarovna N. S. Features Of Kidney Damage at Patients with Ankylosing Spondylarthritis // *Texas Journal of Medical Science*. – 2021. – Т. 3. – С. 18-22.
14. Shadjanova N. S. Features of hemostasis in rheumatoid arthritis patients with ischemic hearth disease // *International Engineering Journal for Research & Development*. - 2022. - Vol. 7. - No. 1-P. - P. 1-5.
15. Tulkinjanovna S. G., Anvarovich R. A. The influence of deficiency of microelements in children with bronchial hyperreactivity// *ACADEMICIA: An International Multidisciplinary Research Journal* (ISSN: 2249-7137)–2020. April. - 2020. - Т. 10. - No. 4. - S. 846-853.
16. Boltayev K. J., Naimova S. A. Risk factors of kidney damage at patients with rheumatoid arthritis // *WJPR (World Journal of Pharmaceutical Research)*. – 2019. – Т. 8. – №. 13.
17. Болтаев К. Ж., Ахмедова Н. Ш. Характеристика феномена развития полидефицитных состояний при старении // *Проблемы биологии и медицины*. – 2020. – №. 1. – С. 24-26.





18. Boltayev K. J. et al. ASSESSMENT OF HEMODYNAMICS OF THE KIDNEYS IN YOUNG PATIENTS WITH ARTERIAL HYPERTENSION //Web of Scientist: International Scientific Research Journal. – 2022. – Т. 3. – №. 4. – С. 720-725.
19. Tulkinjanovna S. G., Anvarovich R. A. The influence of deficiency of microelements in children with bronchial hyperreactivity //ACADEMICIA: An International Multidisciplinary Research Journal (ISSN: 2249-7137)–2020. April. – 2020. – Т. 10. – №. 4. – С. 846-853.
20. Naimova N. S. et al. Features of coagulation and cellular hemostasis in rheumatoid arthritis in patients with cardiovascular pathology //Asian Journal of Multidimensional Research (AJMR). – 2019. – Т. 8. – №. 2. – С. 157-164.
21. Наимова Ш. А. The degree of secondary osteoporosis in rheumatological patients and ways of its prevention //Новый день в медицине. – 2020. – №. 1. – С. 56-58.

