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Role of Biomarkers in COVID-19: an Updated Review

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Abstract. Biomarkers can identify viral infection before the onset of symptoms or at an early stage, which can facilitate early diagnosis and isolation of patients, thereby reducing the spread of the virus. In addition, the monitoring of biomarker levels allows the assessment of disease severity, progression, and treatment response, thereby providing key information for making clinical decision. This document provides a comprehensive review of various COVID-19 biomarkers. It discusses how biomarkers can enable early detection of viral infection, monitoring of disease severity and progression, and assessment of treatment effectiveness. This article reviews and evaluates the biomarkers of COVID-19. Key biomarkers included serologic measures, such as IgM and IgG antibodies, and general hematologic measures, such as white-cell count, lymphocyte count, procalcitonin, C-reactive protein, lactate dehydrogenase, and interleukin-6. These markers are usually closely related to virus infection, replication, and the body's immune response. The potential for using salivary biomarkers, such as albumin, for COVID-19 diagnosis is also mentioned in this document.

Keywords: COVID-19; biomarkers; diagnosis.

1. Introduction

Biomarkers can detect viral infection before or at an early stage of symptoms, which helps in early diagnosis and isolation of patients and reduces the spread of the virus. Moreover, by monitoring the level of biomarkers, the severity, progression and treatment effect of the disease can be assessed, which provides important information for clinical decision-making. Treatment regimens are adjusted to ensure that patients receive optimal care. The number of cases of SARS-CoV-2 infection was 8,246 in June and 18,384 in July, according to the Guangdong Provincial Bureau for Disease Control and Prevention [1]. Therefore, this article aims to comprehensively discuss the main biomarker species of COVID-19.

2. COVID-19 Current Situation

COVID-19, or 2019 novel coronavirus disease, is a global public health crisis caused by SARS-CoV-2. Since its first appearance in human beings, the epidemic has rapidly swept the world, having a profound impact on human society, economy and even lifestyle, and has become a brand that cannot be ignored in an era. SARS-CoV-2, as a member of the β-coronavirus family, shows its unique biological characteristics. Its particles are small and variable in morphology, and can tightly bind to host cells through the envelope under suitable conditions, especially through the specific recognition of spike protein and ACE2 receptor, to achieve efficient invasion and replication. The virus is not only sensitive to environmental factors, such as ultraviolet light and high temperature, which can significantly impair its activity, but also shows vulnerability to a variety of chemical disinfectants, providing valuable scientific basis for prevention and control. The understanding of the clinical manifestations of COVID-19 and the best management strategies has evolved, particularly with the emergence of SARS-CoV-2 variants [2]. In addition to pneumonia and septic syndrome, a smaller proportion of patients have also developed severe gastrointestinal and/or cardiovascular symptoms as well as neurological manifestations after SARS-COV-2 infection [3].

3. Biomarkers

A biomarker represents a distinct, measurable molecular, cellular, or biochemical perturbation that serves as a precise and reproducible tool for the identification and surveillance of physiological fluctuations, pathological cascades, as well as the consequences of pharmacological manipulations. Essentially, these markers transcend mere disease diagnosisand occupy a pivotal role in the exploration of potential therapeutic avenues, evaluation of disease progression and regression, and assessment of outcomes subsequent to interventions.

Encompassing a broad spectrum of entities including but not limited to carbohydrates, proteins, lipids, genetic material like DNA and RNA, platelets, enzymes, hormones, and a myriad of others, biomarkers constitute a versatile class of indicators. Anything that facilitates the detection of a disease state, be it a metabolite, an alteration in biological architecture or functioning, or a characteristic signature, qualifies as a biomarker. Categorization of biomarkers is multifaceted, reflecting their diverse nature and wide-ranging applications [4].

4. Blood Molecular Markers

The use of blood tests to identify key biomarkers of SARS-CoV-2 virus infection is extremely important in the current medical field.

4.1. Serological Indicator ——The Specific Antibodies were IgM and IgG

The section headings are in boldface capital and lowercase letters. Second level headings are typed as part of the succeeding paragraph (like the subsection heading of this paragraph).

4.1.1. Immunoglobulin M (IgM).

As a specific antibody that is first produced within 3-5 days after SARS-CoV-2 infection, is the initial product of the immune response. This antibody exists as a pentamer, has high antigen-binding capacity, and is one of the largest types of immunoglobulins by molecular weight. IgM does not have the ability to cross the placenta and is mainly distributed in the blood. It shows strong bactericidal, complement activation, immune regulation and agglutination of viral particles.

Although the specificity of IgM antibody is strong, its sensitivity may be affected by individual differences, infection duration and other factors, which should be considered in clinical application. In the assessment of the disease, only relying on IgM test results may not be comprehensive, so it is particularly important to combine other clinical indicators and medical history information for comprehensive analysis. IgM mainly marks the acute infection stage, and its concentration changes can reflect the dynamic changes and prognostic trends of the disease. However, the in-depth research in this field is still in the development stage, and it is expected to provide more guidance for clinical practice in the future.

4.1.2. Immunoglobulin G (IgG).

It constitutes the main part of immunoglobulin in the human immune system and occupies the highest proportion in the human body. After an individual is infected with the SARS-CoV-2 virus, IgG production typically begins within the first week to two weeks after infection and gradually increases with the duration of infection, reaching peak levels that can be maintained for months or even years. Notably, IgG is the only immunoglobulin that can cross the placental barrier, meaning that maternal IgG produced is able to be delivered to the fetus, thus providing a temporary passive immune protection to the newborn. In addition, IgG plays multiple roles in the immune response, such as activating the complement system, promoting bacterial lysis, and triggering cytotoxic effects. IgG antibodies play a key role in the retrospective diagnosis of COVID-19 because they emerge late in infection and persist for a long time.

At the same time, high levels of IgG antibodies often indicate that the individual may have been infected or vaccinated against SARS-CoV-2. The concentration of IgG antibody may also be closely

related to the severity of the disease and the prognosis of the patient. Generally, higher IgG levels reflect a stronger individual immune response and a relatively optimistic prognosis. Nevertheless, this idea still needs to be further verified by more research data. The detection of IgG antibodies is also a crucial indicator in the assessment of the effectiveness of vaccination, as it can help us understand the immunogenicity of the vaccine and the protection it provides. By monitoring the level of IgG antibody in the population after vaccination, we can scientifically evaluate the immune efficacy of the vaccine.

4.2. Detection of General Hematological Indicators

In addition to pathogen-specific antibody tests, hematologic tests also play a crucial role in assessing the severity of SARS-CoV-2 infection and its prognosis. These indexes covered a variety of parameters, such as the total number of white blood cells, the number of lymphocytes, the level of C-reactive protein (CRP), the concentration of procalcitonin (PCT), the activity of lactate dehydrogenase (LDH), the content of interleukin-6 (IL-6) and the value of D-dimer. These hematological parameters play an integral role in monitoring the progression of viral infections and assessing the health status of patients.

4.2.1. White Blood Cell Count (WBC).

Leukocyte is a key component of the immune system, which is responsible for the defense against the invasion of external pathogens. In patients with COVID-19, changes in white-cell counts can vary from person to person. Some patients may present with a decreased number of white blood cells, which may be triggered by myelosuppression due to viral infection or by a reconfiguration of the immune system.

However, other patients may present with normal or elevated white blood cells, which may be related to the severity of the disease, the resulting complications, or co-infection. Changes in white blood cell count can help doctors assess the patient's immune status and the degree of infection. A reduced white-cell count may indicate compromised immune function, which warrants close attention to the patient's risk of infection and the potential for complications. In contrast, an increase in the white-cell count may indicate coexisting bacterial infection or further exacerbation of inflammation, at which point the treatment regimen should be adjusted accordingly.

4.2.2. Lymphocyte Count.

Lymphocytes are a crucial cellular component of the immune system, and they actively participate in the process of humoral and cellular immunity. In patients with COVID-19, there is often a marked reduction in lymphocyte counts, a key feature of the disease. The decrease of lymphocyte number may be associated with direct infection of lymphocytes by the virus, induction of apoptosis of lymphocytes, or inhibition of proliferation of lymphocytes. The degree of lymphocyte count reduction is closely related to the severity and prognosis of the disease. A low lymphocyte count may indicate a more severe condition, which requires more active treatment and intensive monitoring. In addition, the dynamic changes of lymphocyte count can also be used as an important indicator to evaluate the therapeutic effect and the development trend of the disease.

4.2.3. Procalcitonin (PCT).

PCT is a biomarker mainly used to detect systemic infections, and its serum concentration is significantly increased in bacterial infections. Although less specific in COVID-19 than in bacterial infections, elevated PCT is still strongly associated with disease severity and mortality. Detection of PCT level can help to determine whether COVID-19 patients have bacterial infection at the same time, so as to guide the rational use of antibiotics. An increase in PCT concentration may indicate a co-bacterial infection or an exacerbation of systemic inflammatory response that may require consideration of antibiotic therapy. However, it is important to note that the increase in PCT levels may be affected by a variety of factors, including the age of the patient, renal function, etc. Therefore, comprehensive evaluation is needed.

4.2.4. C-reactive Protein (CRP).

C-reactive protein (CRP) is an acute phase protein whose serum concentration increases rapidly in pathological states such as infection, inflammation and tissue damage. CRP can interact with DNA and histones and it may scavenge nuclear material released from damaged circulating cells [5].

CRP-levels are often significantly elevated in patients and correlate strongly with disease severity and poor prognosis. By measuring the CRP level, the intensity of the inflammatory response and the severity of the condition can be assessed in patients. High CRP concentrations may indicate an exacerbation of systemic inflammation, and close monitoring of vital signs and organ functional status is required.

At the same time, the dynamic change of CRP can also be used as an important index to evaluate the therapeutic effect and disease evolution. It is important to note that the increase in CRP levels may be influenced by a variety of factors, including the patient's age, underlying health status, and so a combination of these factors should be considered when interpreting the results

4.2.5. Lactate Dehydrogenase (LDH).

Lactate dehydrogenase (LDH) is a kind of enzymatic substance that generally exists in the cytoplasm, and its increase in serum concentration often indicates cell damage or necrosis. In patients with COVID-19, the level of LDH is generally increased, which is closely related to the severity of the disease and poor health outcomes. By monitoring the level of LDH, medical staff can assess the degree of tissue damage and the severity of disease progression in patients. Elevated LDH levels may indicate impairment of multiple organ functions or necrosis of lung tissue, so it is necessary to closely monitor the vital signs and functional status of various organs of patients.

At the same time, the dynamic change of LDH level is also an important reference index to evaluate the therapeutic effect and the development trend of the disease.

4.2.6. Interleukin-6 (IL-6).

As a key inflammatory mediator, interleukin-6 (IL-6) plays a central role in the regulation of immune response and inflammatory process. It is a potent inducer of the acute phase response and plays an essential role in the final differentiation of B-cells into Ig-secreting cells [6]. In COVID-19 cases, IL-6 levels are generally increased, which is closely related to the severity of the patient's illness and potential negative health outcomes. The detection of IL-6 level is of great significance for judging the intensity of inflammatory reaction and the severity of the disease. A significant increase in IL-6 levels may signal a significant exacerbation of systemic inflammatory response or the emergence of cytokine storm, which requires clinicians to adopt timely and effective anti-inflammatory treatment strategies. In addition, IL-6 has also emerged as a potential therapeutic target in COVID-19 treatment research, such as intervention with drugs such as IL-6 receptor blocker tocilizumab.

5. Salivary Molecular Markers

Saliva detection is gradually emerging as a new field for the diagnosis of 2019-ncov. In the process of viral infection, specific biomarkers appear in saliva, providing the possibility of auxiliary diagnosis. These biomarkers, mainly specific proteins, can effectively identify the infection status of SARS-CoV-2 by saliva detection technology. This method not only simplifies the testing process and reduces the risk of exposure, but also improves the convenience of testing, which is of great significance for the prevention and control of COVID-19 epidemic.

5.1. ALB (Albumin)

Albumin is the most important protein in plasma. It has many physiological functions, such as maintaining plasma colloid osmotic pressure, transporting and binding other small molecular substances. In the process of SARS-CoV-2 infection, albumin level may be affected by the body's immune response and inflammatory response. Albumin is the most important protein in plasma. It

has many physiological functions, such as maintaining plasma colloid osmotic pressure, transporting and binding other small molecular substances. In the process of SARS-CoV-2 infection, albumin level may be affected by the body's immune response and inflammatory response. Replace the above paragraph with the same meaning without changing the original meaning and professional terms, and reduce the repetition of language and increase the number of words.

5.2. HP (haptoglobin)

Haptoglobin belongs to a group of acute phase reactive proteins that are significantly increased when activated under stress situations such as infection and inflammation, and its synthesis is mainly carried out in the liver and subsequently released into the blood circulation. The concentration of haptoglobin tends to rise sharply when attacked by COVID-19, which may be an indication of active inflammatory response and aggravation of disease severity. As a key biomarker, haptoglobin detection in saliva is of great significance for identifying severe patients with SARS-CoV-2, and its detection can promote the early diagnosis and evaluation of the disease development.

5.3. LRG1 (Leucine-rich α-2-glycoprotein 1)

LRG1 protein is ubiquitous in a variety of tissues and organs and plays a variety of physiological functions, including participating in the structure of extracellular matrix and regulating the proliferation and differentiation of cells. LRG1 expression levels may be affected during SARS-CoV-2 infection. As one of the key biomarkers to identify patients with severe COVID-19, the detection of LRG1 can help to reveal the effect of viral infection on extracellular matrix and cellular function.

5.4. Detection of Kits

At present, saliva detection kits using these biomarkers have been prepared, such as dipstick kits based on colloidal gold chromatography technology. These kits can quickly and conveniently detect SARS-CoV-2 related biomarkers in saliva, providing strong support for the prevention and control of COVID-19, SAA1, SERPING1, SERPINA3, C9, C6, LUM, TNF, CRP, SAA2, LBP and CLEC3B can also be detected in saliva, which can be used as reference biomarkers for the detection of severe COVID-19 patients using saliva. The invention discloses for the first time the role of the above substances as biomarkers in the preparation of a novel coronavirus saliva detection kit, which can rapidly detect 2019-ncov infection, has easy access to samples, high detection efficiency and speed, reduces the risk of infection of operators, and has high sensitivity and specificity [7].

6. Conclusion

This document provides a comprehensive review of various COVID-19 biomarkers. It discusses how biomarkers can enable early detection of viral infection, monitoring of disease severity and progression, and assessment of treatment effectiveness. Key biomarkers included serologic measures, such as IgM and IgG antibodies, and general hematologic measures, such as white-cell count, lymphocyte count, procalcitonin, C-reactive protein, lactate dehydrogenase, and interleukin-6. The potential for using salivary biomarkers, such as albumin, for COVID-19 diagnosis is also mentioned in this document. In conclusion, this article provides a comprehensive introduction and brief review of various COVID-19 biomarkers

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