Biochemical, Hematological and Immunological Parameters among Covid19 Infected Patients

Abstract: By Jan 7, 2020, Chinese scientists had isolated a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously known as 2019-nCoV), from these patients with virus-infected pneumonia, which was later designated coronavirus disease 2019 (COVID-19) in February, 2020, by WHO. Severe SARS-CoV-2-associated disease COVID-19 was declared a pandemic by the WHO in March 2020 and is characterized by cytokine storm, acute respiratory distress syndrome, and in some cases by systemic inflammation related pathology. A deeper understanding of the mechanism behind the immune dysregulation might give us clues for the clinical management of the severe cases and for preventing the transition from mild to severe stages. Thus, the aim of this review was to assess the values of biochemical, hematological and Immunological among COVID-19 infected patients. It’s imperative to regulate innate and adaptive immunity for better control of immune response consequence, predict treatment outcomes and for development of drug or vaccine. Biochemical and hematological parameters could also serve for diagnosis, prognosis or monitoring especially for hospitalized patients of the COVID-19 infection. Besides, monitoring of biochemical and hematological parameters is essential and can assist in the identification of patients who will need care in the ICU, and could discriminate survivors and non-survivors too. Finally, the contribution of asymptomatic cases in the transmission deserve further studies to examine the extent of occurrence and the role in transmission, and also the immunity status of those individuals should be assessed very well.

Keywords: Covid19, Immunological, Hematological, Biochemical.

INTRODUCTION

In December 2019, a cluster of fatal pneumonia cases presented in Wuhan, China. They were caused by a previously unknown coronavirus. The virus spread rapidly and public health authorities in China initiated a containment effort (Rabi, F. A. et al., 2020). On 31 December 2019, the World Health Organization (WHO) was alerted to the emergence of cases of pneumonia of unknown etiology detected in Wuhan city, China. Within days, Chinese health authorities identified 44 more cases (WHO, 2020).

On 30 January 2020, the Emergency Committee of the WHO, under the 2005 International Health Regulations, declared COVID-19 acute respiratory disease a public health emergency of international concern (Lee, A. 2020), by this time as of September 5, 2020 more than 26 million cases and 881,000 deaths were reported worldwide and it’s pandemic throughout all countries except Antarctica. By January 7, 2020, Chinese scientists had isolated a novel coronavirus, severe acute respiratory syndrome coronavirus 2 from these patients with virus-infected pneumonia, which was later designated coronavirus disease 2019 (COVID-19) in February, 2020, by WHO (Zhou, F. et al., 2020). Based on clinical criteria and available serological and molecular information, the new disease was called coronavirus disease of 2019 (COVID-19), and the novel coronavirus was called SARS Coronavirus-2 (SARS-CoV-2), emphasizing its close relationship to the 2002 SARS virus (SARS-CoV) (Rabi, F. A. et al., 2020).

Evidence has shown that there are asymptomatic carriers of COVID-19 who can transmit the disease to others. The virus incubation time shows a wide range (0–24 days) and the virus displays a high infectivity. It is therefore urgent to develop an effective therapy to treat patients with COVID-19 and to control the spread of the causative agent, severe respiratory syndrome (Zhong, J. et al., 2020). Asymptomatic infections cannot be recognized if they are not confirmed by RT-PCR or other laboratory testing, and symptomatic cases may not be detected if they do not seek medical attention. Estimates such as this therefore provide important insight by using a targeted population to assess the prevalence of asymptomatic viral shedding (Nishiura, H. et al., 2020). The contribution of asymptomatic persons with MERS-CoV or SARS-CoV-2 to the transmission is not well characterized. The contribution of asymptomatic cases in the transmission of these viruses is not well known and

Available: https://iarconsortium.org/journal-info/iajabms
deserves further studies to examine the extent of occurrence and the role in transmission. These studies should examine the clinical course of those individuals, viral dynamics, viral loads and contribution to the transmission (Al-Tawfiq, J.A. 2020).

Innate immune sensing serves as the first line of antiviral defense and is essential for immunity to viruses. To date, our understanding of the specific innate immune response to SARS-CoV-2 is extremely limited (Vabret, N. et al., 2020). In recent years, profound understandings of the innate immune response to viruses have been made. This type of immune response inhibits virus replication, promotes virus clearance, induces tissue repair, and triggers a prolonged adaptive immune response against the viruses. In most cases, pulmonary and systemic inflammatory responses associated with CoVs are triggered by the innate immune system when it recognizes the viruses (Li, G. et al., 2020).

COVID-19 causes a large-scale spread around China and the world. The vast majority of patients are mild or common type. Early finding, diagnosis and treatment have a certain extent of positive effect on the prognosis. Old age, chronic basal diseases and smoking history may be risk factors to a poor prognosis. In addition, based on certain laboratory results such as lymphocytes and other biomarker we may be able to judge the severity of the illness in a timely manner (10). Many aspects of the virus and disease are still not understood. A better understanding will be needed to provide improved guidance. For example: Viral dynamics: optimal timing and type of clinical material to sample for molecular testing, Dynamic of immunological response, Disease severity in various populations, e.g.by age, the relationship between viral concentration and disease severity, etc. are the main area that need further studies for better understanding about the virus (WHO. 2020).

Immunological response for Covid19

The emerging epidemiological observation that significant proportions of individuals are asymptomatic despite infection not only reflects our current understanding that SARS-CoV-2 has a longer incubation period and higher rate of transmission than other coronaviruses, but also speaks to significant differences in the host immune response (Vabret, N. et al., 2020). It is crucial to evaluate the burden of asymptomatic individuals. Such studies will enhance the understanding of the pathogenesis of these emerging viruses and will inform policy makers to make scientifically sound recommendations (Al-Tawfiq, J.A. 2020).

It is imperative that immune responses against SARS-CoV-2 and mechanisms of hyper inflammation driven pathology are further elucidated to better define therapeutic strategies for COVID-19 (Vabret, N. et al., 2020). In this regard, treatments addressing the immunopathology of SARS-CoV-2 infection have become a major focus. Notably, while a rapid and well-coordinated immune response represents the first line of defense against viral infection, excessive inflammatory innate response and impaired adaptive host immune defense may lead to tissue damage both at the site of virus entry and at systemic level (Catanzaro, M. et al., 2020).

The pathology of severe cases of COVID-19 does indeed resemble certain immunopathologies seen in SARS-CoV-1 and MERS-CoV infections, like Cytokine related syndrome (CRS). However, in many other ways, immune responses to SARSCoV-2 are distinct from those seen with other coronavirus infections (Vabret, N. et al., 2020). Severe SARS-CoV-2-associated disease (coronavirus disease 2019 (COVID-19)) was declared a pandemic by the WHO in March 2020 and is characterized by cytokine storm, acute respiratory distress syndrome (ARDS), and in some cases by systemic inflammation related pathology. The innate immune system is therefore a potentially important target for therapeutic treatment of COVID-19, but experimental studies are needed, and SARS-CoV-2 presents unique challenges for preclinical and mechanistic studies in vivo (Fence, B.D. 2020).

In 2003, glucocorticoid was widely used in SARS treatment to control pulmonary infection by regulating inflammatory responses. Similarly, in COV pneumonia cases, it is important to control cytokine production and inflammatory response, given that they are responsible for the accumulation of cells and fluids (Li, G. et al., 2020). Several studies highlight relevant changes occurring both in innate and adaptive immune system in COVID-19 patients. In particular, the massive cytokine and chemokine release, the so-called “cytokine storm”, clearly reflects a widespread uncontrolled dysregulation of the host immune defense. A deeper understanding of the mechanism behind the immune dysregulation might give us clues for the clinical management of the severe cases and for preventing the transition from mild to severe stages (Catanzaro, M. et al., 2020). Notable achievements have been made in analyzing detrimental and protective mechanisms. For instance, completely blocking a proximal event in the immune response seems unwise considering its general role in regulating the host defense. In contrast, more limited and specific effector arms, such as controlled production of oxygen radicals, NET formation, IL - 1, IL - 4, IL - 6, IL - 8, and IL - 21 production, are probably practicable targets (Li, G. et al., 2020).

The involvement of immune hyperactivation and acute respiratory distress syndrome in fatal cases of COVID-19 has been confirmed by pathological examination, as a result several disease-modifying anti-
rheumatic drugs (DMARDS), such as hydroxychloroquine and tocilizumab, have been proposed as potential therapies for the treatment of COVID-19 (Zhong, J. et al., 2020). Some early observations as well as previous knowledge from epidemic SARS-CoV-1 suggest that monocytes and pulmonary monocyte derived macrophages play an early and key role in the progression to severe COVID-19 by promoting cytokine storm, ARDS, and disseminated peripheral tissue damage. Pathological monocyte responses in COVID-19 bear some similarities to those in aging, suggesting that monocytes may be a contributor to the disproportionate severity of COVID-19 in older adults (Pence, B.D. 2020).

The study highlighted hypotheses that interrogate mechanisms for viral escape from innate sensing, for hyperinflammation associated with CRS and inflammatory myeloid subpopulations, for lymphopenia marked by T cell and NK cell dysfunction, and for correlates of protection and their duration, among others (Vabret, N. et al., 2020). Adverse outcome is associated with depletion of CD3+ T lymphocytes that is tightly linked to bursts of cytokines such as IL-6 & IL-8 (Zhang, X. et al., 2020). Asymptomatic group had a significantly longer duration of viral shedding than the symptomatic group (log-rank \( P = 0.028 \)). The virus-specific IgG levels in the asymptomatic group were significantly lower (\( P = 0.005 \) ) relative to the symptomatic group in the acute phase. In addition, asymptomatic individuals had a reduced inflammatory response characterized by low circulating concentrations of cytokines and chemokines. These data suggest that asymptomatic individuals had a weaker immune response to SARS-CoV-2 infection (Long, Q. X. et al., 2020). Hence, the difference between asymptomatic and symptomatic population is immune response to the virus specifically inflammatory response accompanied by cytokine and chemokines.

Different immunological parameters could be used to diagnosis, predict risk and/or monitor the disease. High level of IL-6, CRP and hypertension were independent risk factors for the severity of COVID-19. The risk model based on IL-6, CRP and hypertension had the highest area under the receiver operator characteristic curve (AUROC). Additionally, the baseline IL-6 was positively correlated with other immune-inflammatory parameters and the dynamic change of IL-6 in the severe cases were parallel to the amelioration of the disease that indicates IL-6 played a pivotal role in the severity of COVID-19 and had a potential value for monitoring the process of severe cases (Zhu, Z. et al., 2020). Evaluation of cytokine profiles and immune cell subsets has important implications for selecting appropriate immunosuppressants. Also, the severity of the hyperinflammation and viral load or replication status needs to be taken into consideration. One way to avoid the suppression of anti-viral immunity is to choose selective instead of broad immunosuppressive drugs. The timing of treatment is also crucial to reduce the side-effects of immunosuppression (Long, Q. X. et al., 2020).

**Biochemical and Hematological parameters among Covid19 infected patients**

Several risk factors have been identified for death in adults in Wuhan who were hospitalized with COVID-19, accordingly older age, d-dimer levels greater than 1 µg/mL, and higher Sequential Organ Failure Assessment (SOFA) score on admission were associated with higher odds of in-hospital death. Additionally, elevated levels of blood IL-6, high-sensitivity cardiac troponin I, and lactate dehydrogenase (LDH) and lymphopenia were more commonly seen in severe COVID-19 illness (4). Also, other finding confirmed Serum LDH or CK decline may predict a favorable response to treatment of COVID-19 infection (Yuan, J. et al., 2020). Serum urea creatinine (CREA), cystatin C (CysC), direct bilirubin (DBIL), cholinesterase (CHE) and lactate dehydrogenase (LDH) could be used to distinguish severe COVID-19 cases from mild COVID-19 cases. In particular, serum biomarkers, including urea, CREA, CysC, which reflect glomerular filtration function, may have some significance as potential indicators for the early diagnosis of severe COVID-19 and to distinguish it from mild COVID-19 (Xiang, J. et al., 2020), although COVID doesn’t behave the same among infected individuals these biochemical parameters could be used as diagnosis and prognosis biomarkers.

Besides, hematological parameters were used to predict treatment outcomes and for monitoring further including in ICU. Because Covid-19 is a respiratory infection with a significant impact on the hematopoietic system and hemostasis leading to several cardiovascular complications. Hematologic consequences of this new infection allowed medical community to start new treatment approaches concerning infection going from targeted anti-inflammatory drugs to anticoagulation or stem cell therapies (Debuc, B., & Smajda, D.M. 2020). It has been proposed that laboratory tests of ferritin, lymphocyte or leukocyte counts, platelet counts, erythrocyte counts, and sedimentation rate could be used to screen patients at high risk of hyperinflammation (Long, Q. X. et al., 2020).

Similarly, monitoring of hematological parameters is essential and can assist in the identification of patients who will need care in the ICU, as they presented a deeper lymphopenia, as well as a decrease in hemoglobin, absolute monocyte count and even tend to develop neutrophilia during hospitalization, with a peak in this period of ICU stay (Duarte, F.B. et al., 2020). On admission, the counts of lymphocytes, T-cell subsets, eosinophils, and platelets decreased markedly, especially in severe/critical and fatal patients. Increased neutrophil count and
neutrophils-to-lymphocytes ratio were predominant in severe/critical cases or non-survivors. During hospitalization, eosinophils, lymphocytes, and platelets showed an increasing trend in survivors, but dropped significantly afterwards in non-survivors. Non-survivors kept a high level or showed an upward trend for neutrophils, IL-6, procalcitonin, D-dimer, amyloid A protein, and C-reactive protein, but showed a downward trend in survivors (Chen, R. et al., 2020). Hematological parameters were used for predicting the treatment outcomes or for prognosis purposes especially for those who were in critical care.

Further, both biochemical and hematological parameters could also predict treatment outcome or could be used as prognosis biomarkers. For instance, patients with severe and fatal disease had significantly increased white blood cell (WBC) count, and decreased lymphocyte and platelet counts compared to non-severe disease and survivors. Biomarkers of inflammation, cardiac and muscle injury, liver and kidney function and coagulation measures were also significantly elevated in patients with both severe and fatal COVID-19. IL-6 and IL-10 and serum ferritin were strong discriminators for severe disease (Henry, B.M. 2020). During hospitalization, neutrophil-to-lymphocyte ratio (NLR) was found to have certain relevance to the hospitalization days and a role in forecasting disease prognosis for patients with COVID-19. Compared to non-severe patients, leukocyte count, neutrophil count and NLR were significantly higher, whereas lymphocyte count was declined in severe patients at each time point (Ding, X. et al., 2020).

Hematologic and immunologic parameters impairment could also serve to predict recovery or fatal outcome. These parameters impairment showed a significantly different profile between survivors and non-survivors in patients with COVID-19. A multivariate Cox regression model suggested that restored levels of lymphocytes, eosinophils, and platelets could serve as predictors for recovery, whereas progressive increases in neutrophils, basophils, and IL-6 were associated with fatal outcome (Chen, R. et al., 2020). In hospitalized patients Clinicians should consider low lymphocyte count as well as the serum levels of CRP, D-dimers, ferritin, cardiac troponin and IL-6 which may be used in risk stratification to predict severe and fatal COVID-19. It is more likely that the course of the disease will be unfavorable if some or all of these parameters are altered (Velavan, T. P., & Meyer, C. G. 2020; & Lavezzo, E. et al., 2020), thus by monitoring these parameters we can predict whether treatment outcomes will be bad or good.

Although it’s not as such convincing some studies found the association between blood types and COVID-19. The odds of COVID-19 positive vs negative test results were increased in blood types A whereas decreased in blood types O while Rh negative blood types are rare, the study find evidence of association only for Rh positive blood groups (Zietz, M., & Tatonetti, N.P. 2020). Similarly, other findings showed that blood group A was associated with a higher risk for acquiring COVID-19 compared with non-A blood groups, whereas blood group O was associated with a lower risk for the infection compared with non-O blood groups (Zhao, J. et al., 2020).

CONCLUSION
Uncontrolled dysregulation of the host immune defense that include both in innate and adaptive immune system is the major causes for symptomatic compared to asymptomatic cases among COVID-19 patients. Besides, biochemical and hematological characteristics are very importance for monitoring or prognosis purpose of hospitalized patients and/or could serve to predict recovery or fatal outcome for COVID-19 infected patients. Still many studies are expected to identify and justify the specific immune system response and biochemical & hematological parameters as well for discovery of the respective drugs or vaccine for Covid19 virus.

Authors’ Contribution: None
Ethics approval: None
Conflicts of interest: None
Funding: None

REFERENCE