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Clinical immunity and medical cost of COVID-19 patients under grey relational mathematical model

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ABSTRACT

This study was to explore the performance of immune function and compositions of hospitalization cost for patients with COVID-19 as well as the application of a grey relational mathematical model (GRMM). A total of 100 COVID-19 patients diagnosed by nucleic acid test and chest CT examination in our hospital were collected in this study. They were divided into 2 groups: non-severe group (mild and moderate patients, n = 57 cases), and severe group (severe and critical patients, n = 43 cases) based on the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) published by the World Health Organization (WHO). The general clinical data, blood routine indexes, cellular immune and humoral immune function test indexes, and the composition of hospitalization costs of the two groups of patients were collected and analyzed. The results showed that the average age, proportion of males, smoking history, and the number and proportion of patients in the non-severe group were smaller than those in the severe group (P < 0.05); the severe group had significantly more shortness of breath patients than the non-severe group (P < 0.05). Compared with the non-severe group, the number of white blood cells (WBC), the number and proportion of neutrophils, and the count of neutrophils/lymphocytes in the severe group increased obviously (P < 0.05), and the number of lymphocytes and the proportion of monocytes decreased dramatically (P < 0.05); the number and proportion of CD3+, CD4+, CD8+, and CD19+ in the severe group were much lower in contrast to those in the non-severe group (P < 0.05), while the ratio of CD4+/CD8+ was greatly higher in contrast to that of non-severe patients (P < 0.05). Compared with the non-severe group, the bed fee, laboratory test fee, diagnosis fee, and medicine fee of the severe group were increased observably (P < 0.05). The changes in hospitalization cost of patients in the severe group was related to bed fees, laboratory fees, and expenses of proprietary Chinese medicines, while the hospitalization cost of patients in the severe group was related to bed fees, laboratory fees, and examination fees. The results revealed that elderly COVID-19 patients with basic diseases were prone to develop severe disease, immune cell depletion may be one of the reasons for the development of severe patients, and the medical insurance policy greatly reduced the hospitalization costs of COVID-19 patients.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) broke out in Wuhan for the first time in December 2019, and then rapidly developed throughout the country. The COVID-19 infected by SARS-CoV-2 broken out in China and even the world, the WHO announced it as a sudden public health emergency of international concern on January 30, 2020 [1]. After the outbreak, the number of newly diagnosed COVID-19 patients dropped from a maximum of 14,109 cases to 206 cases after March 1st due to the effective anti-epidemic measures and treatments adopted by China. By the end of April, the number of daily newly diagnosed COVID-19 patients was 4, and a total of 84,385 cases were diagnosed, 4643 cases (5.5%) died, and 78,845 cases (93.4%) were cured. However, since March 1st, the
The epidemic situation in foreign countries has developed rapidly. The number of newly diagnosed cases per day is up to more than 100,000, and even as high as 43,885 a day in the United States. Currently, the number of newly diagnosed cases in foreign countries is still increasing at a rate of more than 100,000. As of April 30, there were 3.22 million cases diagnosed abroad, 229,000 cases (7.1%) died, and 967,000 cases (30%) were cured. This indicates that SARS-CoV-2 is highly contagious.

Studies have shown that SARS-CoV-2 is more susceptible to infection of elderly male patients with basic diseases [2,3], who are often immunocompromised. COVID-19 is a highly contagious new disease, and its highly pathogenic pathophysiological mechanism has not been fully understood. Several studies have shown that the increase in serum proinflammatory cytokines is related to lung inflammation and large-scale lung injury caused by severe acute respiratory syndrome (SARS) [4] and MERS-CoV infection [5], and even to recent COVID-19 [6]. However, there is little studies on correlation between the lymphocyte subsets and the immune responses of COVID-19 patients. In addition, the Ministry of Finance announced clearly that the financial support will be implemented by 60% subsidence from the central government for the personal expenses of patients diagnosed with COVID-19, and issued related documents to request local governments to refine the policy measures for epidemic prevention funds. By analyzing the hospitalization costs composition of COVID-19 patients, it can provide a reference for the medical insurance to determine the subsidy standards and formulate related subsidy policies. The GRMM could measure the relational degree of factors according to the similarity or difference of the development trend of factors. Therefore, it was intended to analyze the degree of correlation between total hospitalization cost and various expenses.

In this study, the differences in blood routine, immune indexes, and hospitalization costs components of 100 COVID-19 severe and non-critical cases diagnosed by nucleic acid test were retrospectively analyzed, the clinical immune characteristics and features of hospitalization costs components of COVID-19 patients were explored by using the GRMM, aiming to provide reference for the prevention and treatment of COVID-19 patients and the formulation of the medical insurance policies.
Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)

Materials and methods

Research objects and grouping

100 cases of COVID-19 patients diagnosed by nucleic acid test and chest CT examination in our hospital from February 1 to March 1, 2020 were selected as the research objects in this study. All patients met the diagnosis standard given in the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) published by the WHO [7] after rescreening based on such standard. The clinically initial symptoms were fever and respiratory symptoms, chest CT showed viral pneumonia, and the respiratory throat swab specimens were positive for SARS-CoV-2 nucleic acid by the real-time quantitative PCR. Among all patients, there were 64 male patients, with an average age of 53.7 ± 8.2 years old, and 36 female patients, with an average age of 50.1 ± 7.6 years old.

The patients were divided into 2 groups: non-severe group (mild and moderate patients, n = 57 cases), and severe group (severe and critical patients, n = 43 cases) based on the clinical grading criteria under the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) published by the WHO. There were 33 males and 24 females in the non-severe group and 31 males and 12 females in the severe group.

The age, gender, medical history, clinical symptoms, blood routine, immune function test, and hospitalization costs and other data of all patients were collected.

White blood cells could be divided into granulocytes, monocytes, and lymphocytes. Granulocytes could be divided into neutrophils, eosinophils, and basophils. Lymphocyte was composed by T cells, B cells, and suicide cells. The classification of white blood cells was shown in Fig. 1. The routine indexes of fasting venous blood in this study mainly included the white blood cell count, neutrophil count and percentage, lymphocyte count and percentage, neutrophil count/lymphocyte count (NLR), monocyte count and percentage, eosinophil count and percentage, and basophil count and percentage.

Immune function test indexes of venous blood mainly included the cellular immune function test indexes (CD3 count and percentage, CD4 count and percentage, CD8 count and percentage, CD4/CD8, CD19 count and percentage, and the count and percentage of other lymphocyte) and humoral immune function test indexes (IgG, IgM, IgE, IgA, complement C3 and C4). The immune response process mediated by T cells and the roles of CD3+, CD4+, and CD8+ were shown in Fig. 2.

The hospitalization costs mainly included bed fees, laboratory fees, examination fees, expenses of proprietary Chinese medicines, materials costs, nursing charging, treatment expenses, and medicine expenses.

Results

Comparison on general basic data of patients in two groups

As shown in Table 1 and Fig. 3, the average age of patients in non-severe group was 48.4 ± 6.9, and the average age of patients in severe group was 59.1 ± 9.5, so the difference was statistically significant (P < 0.05). There were 33 males in the non-severe group patients, accounting for 57.9%, and 31 males in severe group patients, accounting for 72.1%, so the difference was statistically significant (P < 0.05). Compared with the non-severe group, the number and proportion of patients in severe group with smoking history and basic diseases were significantly higher, and the difference was statistically significant (P < 0.05).

In the clinically initial symptoms, there was no obvious difference on the number and proportion of patients in non-severe group and severe group for fever, dry cough, sputum, hemoptysis, myalgia, headache, dizziness, and fatigue. Compared with the non-severe group, the number and proportion of patients with shortness of breath in the severe group were significantly higher, and the difference was statistically significant (P < 0.05).

Comparison on blood routine indexes of patients in two groups

As shown in Table 2 and Fig. 4, compared with non-severe group, the white blood cell count, neutrophil count proportion, NLR of patients in the severe group were significantly increased, and the differences were statistically significant (P < 0.05); while the number and proportion of lymphocytes in severe group were significantly reduced, and the difference was statistically significant (P < 0.05). There was no significant difference in the number of monocytes between the two groups, but the proportion of monocytes in patients in the severe group was significantly lower than that in the non-severe group (P < 0.05). Eosinophils and basophils were not detected in the blood of patients in both groups.

Comparison on cellular immune indexes between two groups of patients

As shown in Table 3 and Fig. 5, cellular immune function test indexes mainly included CD3 count and percentage, CD4 count and percentage, CD8 count and percentage, CD4/CD8, CD19 count and percentage, and lymphocyte count and percentage. Compared with the non-severe group, the CD3+ cell count and proportion, CD4+ cell count and proportion, CD8+ cell count and proportion, and CD19+ cell count and proportion of patients in the severe group were significantly reduced, and the differences were statistically significant (P < 0.05). The ratio of CD4+/CD8+ in patients in the severe group was significantly higher than that in the non-severe group (P < 0.05).

Comparison on humoral immune indexes of patients in two groups

As shown in Table 4 and Fig. 6, the humoral immune function test indexes mainly included IgG, IgM, IgE, IgA, complement C3 and C4. The
results showed that there were no significant differences in the levels of IgG, IgM, IgE, IgA, complement C3 and C4 between the patients in two groups (P greater than 0.05).

**Comparison on hospitalization costs composition of patients in two groups**

As shown in Table 5 and Fig. 7, the hospitalization costs mainly included bed fees, laboratory fees, examination fees, expenses of proprietary Chinese medicines, materials costs, nursing charging, treatment expenses, and medicine expenses, of which the laboratory fees, medicine expenses, and examination fees accounted for high proportions. Compared with the non-severe group, the bed fees, laboratory fees, examination fees, and medicine expenses of patients in severe group increased significantly (P < 0.05), but the proportion of them did not change significantly. Expenses of proprietary Chinese medicines in the severe group were significantly higher than those in non-severe group (P < 0.05). There was no significant difference between the two groups in terms of materials costs and treatment expenses.

GRMM analysis can be used to study the influencing factors of dynamic process changes. It was used in this study to analyze the correlation between the total hospitalization costs and various costs, so as to reflect the main factors that affect the total hospitalization costs. The total hospitalization costs of the two groups of patients were used as the reference sequence, and the other costs were used as the comparison sequences. The resolution coefficient was 0.5. As shown in Fig. 8, the changes in hospitalization costs in patients in severe group were related to bed fees, laboratory fees, and expenses of proprietary Chinese medicines, while those in the non-severe group were related to bed fees, laboratory fees, and examination fees.

**Discussion**

COVID-19 has infectious and epidemic characteristics and is an acute infectious disease. SARS-CoV-2 is a kind of β coronavirus. It is reported that the virus is extremely similar to the bat coronavirus, thus, it is speculated that bat is the main source of transmission [8], which has to be further confirmed. Among the 100 patients in this study, the age, male proportion, smoking history, and basic diseased of patients in the severe group were higher than those in the non-severe group (P < 0.05). There was no significant difference between the two groups in terms of materials costs and treatment expenses.
may be more likely to occur in some elderly male patients with basic diseases, which is closely related to its low autoimmune function.

It is found based on the blood routine indexes that white blood cells and lymphocytes in the patients in severe group are significantly reduced, while neutrophils are significantly increased, and the ratio of NLR is significantly increased. The total number of leukocytes in normal adults is \((3.5–9.5) \times 10^9/L\). Leukocytes can be classified as granulocytes, monocytes, and lymphocytes based on their morphology, function, and origin, and participate in the body’s defense response [10]. Lymphocytes participate in the immune response. In this study, the lymphocytes of patients in the severe group were significantly reduced, suggesting that the immune function of the patient was significantly reduced. NLR is an important index to judge the occurrence of systemic infection and inflammation. Studies have shown that it is also a predictive index of bacterial infections (including pneumonia) [11,12]. In this study, patients in the severe group had significantly increased NLR, which was consistent with the results of Wang et al. on patients with COVID-19 [13]. This study showed that neutrophils increased significantly and lymphocytes decreased significantly during the severe stage of COVID-19. Such data and research showed that the internal environment of the severe COVID-19 cases is seriously unbalanced, which mainly manifested as impaired immune system balance and increased inflammation. Therefore, immune impairment and high inflammation may play an important role in the pathogenesis of COVID-19.

The direct cytopathic effect caused by viruses and the viral escape of

| Table 2 | Comparison on blood routine indexes of patients in non-severe group and severe group. |
|---------|-------------------------------------------------------------------------------------|
| Normal value | Non-severe group (n = 57) | Severe group (n = 43) | t | P |
| White cell count \((10^9/L)\) | 3.5–9.5 | 4.8 ± 1.2 | 5.7 ± 1.6 | 0.139 | 0.007 |
| Neutrophil count \((10^9/L)\) | 1.8–6.3 | 3.1 ± 1.5 | 4.5 ± 1.4 | 0.230 | 0.005 |
| Neutrophil proportion (%) | 40–75 | 66.3 ± 12.5 | 79.6 ± 14.2 | 0.118 | 0.001 |
| Lymphocyte count \((10^9/L)\) | 1.1–3.2 | 1.0 ± 0.2 | 0.7 ± 0.1 | 0.434 | 0.009 |
| Lymphocyte proportion (%) | 20–50 | 21.5 ± 5.3 | 12.9 ± 3.8 | 0.127 | 0.000 |
| NLR | 3.1 ± 1.1 | 6.5 ± 1.9 | 0.103 | 0.000 |
| Monocyte count \((10^9/L)\) | 0.1–0.6 | 0.4 ± 0.1 | 0.4 ± 0.2 | 1.514 | 0.425 |
| Monocyte proportion (%) | 3–10 | 8.3 ± 1.7 | 7 ± 1.2 | 0.572 | 0.004 |
| Eosinophil count \((10^9/L)\) | 0.02–0.52 | 0 | 0 | – | – |
| Eosinophil proportion (%) | 0.4–8 | 0 | 0 | – | – |
| Basophil count \((10^9/L)\) | 0.00–0.10 | 0 | 0 | – | – |
| Basophil proportion (%) | 0–1 | 0 | 0 | – | – |

Table 3
Comparison on cellular immune indexes of patients in non-severe group and severe group.

| Normal value | Non-severe group (n = 57) | Severe group (n = 43) | t | P |
|--------------|-------------------------|---------------------|---|---|
| CD3 \((\text{count/} \mu\text{L})\) | 955–2860 | 1264.5 ± 407.7 | 356.1 ± 164.9 | 0.276 | 0.000 |
| CD3 (%) | 40.0 ± 5.63 | 17.3 ± 3.85 | 0.136 | 0.000 |
| CD4 \((\text{count/} \mu\text{L})\) | 450–1440 | 657.4 ± 237.9 | 218.5 ± 145.1 | 0.313 | 0.000 |
| CD4 (%) | 20.8 ± 3.57 | 10.6 ± 2.14 | 0.145 | 0.000 |
| CD8 \((\text{count/} \mu\text{L})\) | 320–1250 | 406.2 ± 189.7 | 113.8 ± 75.4 | 0.249 | 0.000 |
| CD8 (%) | 12.9 ± 2.62 | 5.5 ± 1.05 | 0.231 | 0.000 |
| CD4/CD8 | 1.00–2.87 | 1.62 ± 0.44 | 1.92 ± 0.37 | 0.962 | 0.043 |
| CD19 \((\text{count/} \mu\text{L})\) | 0–500 | 238.1 ± 126.8 | 94.6 ± 67.5 | 0.241 | 0.000 |
| CD19 (%) | 7.5 ± 1.12 | 4.6 ± 0.84 | 0.338 | 0.004 |

**Fig. 4.** Comparison on blood routine indexes of patients in non-severe group and severe group. Left figure: count \((10^9/L)\), right figure: proportion (%), * indicated that the difference was obvious in contrast to the non-severe group \(P < 0.05\).
immune responses of the host are considered to play the major role in the occurrence and development of viral infection diseases [14]. The first line of defense for viral infection is a rapid and coordinated innate immune response. Once the immune response is unregulated, it can lead to excessive inflammation and even death [15]. Lymphocyte is a kind of white blood cell that exerts an important role in specific immunity, including T lymphocytes, B lymphocytes, and natural killer (NK) cells [16]. The results of this study showed that the counts and proportions of

CD3⁺, CD4⁺, CD8⁺, and CD19⁺ of patients in severe group were less than those in non-severe group, and there was no significant difference in humoral immune indexes between the two groups. It was not different from the previous SARS, which suggests that the count of CD3⁺, CD4⁺, and CD8⁺ cells in the peripheral blood of SARS patients is significantly reduced [17]. CD3⁺, CD4⁺, and CD8⁻ T cells are widely involved in the immune response of the body, and CD19 is an important membrane antigen involved in the activation and proliferation of B cells to play an immune role [18]. The initial CD4⁺ T cells can be differentiated into the memory cell subsets of effector cells, and is the most basic feature of T cells to mediate the immune response. The balance between the initial T cells and memory CD4⁺ T cells is essential to maintain an effective immune response. In addition, during the viral infection, T cells (especially CD4⁺ T cells and CD8⁻ T cells) play important roles in

Table 4
Comparison on humoral immune indexes of patients in non-severe group and severe group.

|                | Normal value | Non-severe group (n = 57) | Severe group (n = 43) | t  | P    |
|----------------|--------------|----------------------------|-----------------------|----|------|
| IgG (g/L)      | 7.51–15.60   | 12.9 ± 5.1                 | 13.0 ± 4.4            | 4.238 | 0.952 |
| IgM (g/L)      | 0.46–3.04    | 1.2 ± 0.4                  | 1.3 ± 0.5             | 4.011 | 0.837 |
| IgE (g/L)      | 20–200       | 80.63 ± 14.7               | 78.97 ± 2.052         | 0.163 |      |
| IgA (g/L)      | 0.82–4.53    | 2.2 ± 0.9                  | 2.3 ± 0.6             | 4.957 | 0.894 |
| Complement C3  | 0.65–1.39    | 0.9 ± 0.2                  | 0.8 ± 0.1             | 3.263 | 0.285 |
| (g/L)          |              |                            |                       |      |      |
| Complement C4  | 0.16–0.38    | 0.2 ± 0.0                  | 0.2 ± 0.1             | 6.681 | 1.067 |

Fig. 5. Comparison on cellular immune indexes of patients in non-severe group and severe group. Left figure: count (count/mL), right figure: proportion (%), * indicated that the difference was obvious in contrast to the non-severe group (P < 0.05).

Fig. 6. Comparison on humoral immune indexes of patients in non-severe group and severe group (g/L).

Table 5
Comparison on hospitalization costs composition of patients in non-severe group and severe group.

|                      | Non-severe group (n = 57) | Severe group (n = 43) | t    | P    |
|----------------------|---------------------------|-----------------------|------|------|
| Bed fees (ten thousand Yuan) | 5.2 ± 1.3                | 7.3 ± 1.6             | 0.735 | 0.006 |
| Bed fees proportion (%)       | 4.95 ± 1.05              | 4.83 ± 0.93           | 3.624 | 0.361 |
| Laboratory fees (ten thousand Yuan) | 42.5 ± 3.7             | 59.7 ± 3.9            | 1.044 | 0.007 |
| Laboratory fees proportion (%) | 40.46 ± 4.82           | 39.48 ± 4.08          | 4.225 | 0.443 |
| Examination fees (ten thousand Yuan) | 15.8 ± 2.8             | 21.1 ± 2.3            | 0.427 | 0.003 |
| Examination fees proportion (%)       | 15.04 ± 1.88            | 13.96 ± 1.36          | 0.964 | 0.071 |
| Expenses of proprietary Chinese medicines (ten thousand Yuan) | 0.05 ± 0.00            | 1.3 ± 0.16            | 0.337 | 0.000 |
| Proportion expenses of proprietary Chinese medicines (%)       | 0.05 ± 0.00             | 0.86 ± 0.03           | 0.314 | 0.001 |
| Materials costs (ten thousand Yuan) | 1.1 ± 0.08              | 2.0 ± 0.13            | 2.054 | 0.131 |
| Materials costs proportion (%)       | 1.05 ± 0.05             | 1.32 ± 0.08           | 1.635 | 0.059 |
| Nursing charging (ten thousand Yuan) | 2.8 ± 0.4                | 6.9 ± 0.7             | 0.582 | 0.006 |
| Nursing charging proportion (%)       | 2.67 ± 0.62             | 4.56 ± 0.87           | 0.425 | 0.005 |
| Treatment expenses (ten thousand Yuan) | 8.2 ± 1.5                | 9.7 ± 1.3             | 1.399 | 0.064 |
| Treatment expenses proportion (%)       | 7.81 ± 1.21             | 6.42 ± 1.76           | 1.613 | 0.061 |
| Medicine expenses (ten thousand Yuan) | 28.4 ± 3.2              | 40.2 ± 4.0            | 0.142 | 0.000 |
| Medicine expenses proportion (%)       | 27.03 ± 2.79            | 26.59 ± 1.8           | 1.085 | 0.118 |

CD3⁺, CD4⁺, CD8⁻, and CD19⁺ of patients in severe group were less than those in non-severe group, and there was no significant difference in humoral immune indexes between the two groups. It was not different from the previous SARS, which suggests that the count of CD3⁺, CD4⁺, and CD8⁻ cells in the peripheral blood of SARS patients is significantly reduced [17]. CD3⁺, CD4⁺, and CD8⁻ T cells are widely involved in the immune response of the body, and CD19 is an important membrane antigen involved in the activation and proliferation of B cells to play an immune role [18]. The initial CD4⁺ T cells can be differentiated into the memory cell subsets of effector cells, and is the most basic feature of T cells to mediate the immune response. The balance between the initial CD4⁺ T cells and memory CD4⁺ T cells is essential to maintain an effective immune response. In addition, during the viral infection, T cells (especially CD4⁺ T cells and CD8⁻ T cells) play important roles in
weakening or reducing overactive innate immune responses [19]. The counts and proportions of CD4$^+$, CD8$^+$, and CD19$^+$ T cells of severe group patients in this study were significantly lower than those in the non-severe group, suggesting that T lymphocytes were severely depleted during the fight against SARS-CoV-2 infection, so that B cell activation was delayed, and the immune function was damaged. This is consistent with the autopsy report of COVID-19 patients. The study pointed out that the interstitial mononuclear inflammatory infiltration of lymphocytes mainly could be seen in the pathological sections of the lungs of COVID-19 patients. This is similar to the coronavirus infection of SARS and the Middle East Respiratory Syndrome (MERS).

The Ministry of Finance has announced clearly that the personal expenses of the diagnosed patients will be financed with a 60% subsidy from the central government. With the support of the subsidy policy in China, the personal expenses of patients have been greatly reduced, and most of the medical expenses are taken by the country [20,21]. The differences in hospitalization costs of patients in the non-severe group and severe-group were analyzed in this study, and the main factors affecting the total hospitalization costs were analyzed by using the GRMM analysis, with a view to providing the reference for determining the subsidy standards and formulating relevant policies for the medical insurance department. The results revealed that the bed fees, laboratory fees, examination fees, and medicine fees of patients in severe group were significantly higher than those in the non-severe group, but the proportion of them did not change significantly. Expenses of proprietary Chinese medicines in severe group patients were significantly higher than those in non-severe group patients. There was no significant difference between the two groups in terms of material costs and proportion, treatment expenses and proportion. GRMM analysis showed that changes in hospitalization costs in patients in severe group were related to bed fees, laboratory fees, and expenses of proprietary Chinese medicines, while those in the patients in non-severe group were related to bed fees, laboratory fees, and examination fees. These data suggest that bed fees, laboratory fees, examination fees, and medicine fees constitute a comparable proportion in the total cost of all patients, which is a necessary basic cost for all patients. The nursing charges for patients in the severe group was higher than that in the non-severe group, suggesting that patients in the severe group need more nursing. There is no significant difference in material costs and treatment expenses between the two groups, suggesting that with the continuous improvement of treatment capacity and medical level, the efficient use of medical resources is a beneficial part of balancing medical costs.
Conclusion

In this study, blood routine indexes and cellular immune and humoral immune function test indexes were collected from COVID-19 patients in the non-severe group (mild and moderate patients, n = 57 cases) and the severe group (severe and critical patients, n = 43 cases). In addition, the GRMM was introduced to analyze the composition of hospitalization costs. The results indicated that COVID-19 may be more likely to occur in some elderly male patients with basic diseases, which was closely related to its low autoimmune function. Depletion of white blood cells and CD3+, CD4+, CD8+ and CD19- lymphocytes was one of the important causes of imbalance of immune function in patients with COVID-19. The changes in hospitalization costs in patients in severe group were related to bed fees, laboratory fees, and expenses of proprietary Chinese medicines, and those in the non-severe group were related to bed fees, laboratory fees and examination fees. However, there were some shortcomings in this study. The number of research subjects included was small, and the influence of bacterial infection on the immune response results had not been analyzed. In future work, it will include a large sample of immune response after COVID-19 infection. Analyze the changes over time, analyze the impact of bacterial infection on the results of the immune response, and further verify the relationship between COVID-19 infection and immune system disorders. In summary, it was found that immune response disorders may be one of the pathogenesis of COVID-19. SARS-CoV-2 may mainly act on lymphocytes, especially T lymphocytes, and then induce a series of reactions in the body and damage corresponding organs. Therefore, the monitoring of NLR and lymphocyte subsets was helpful for the screening of early critical diseases and the diagnosis and treatment of COVID-19.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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