Prognostic analysis of neutralizing antibody levels in patients with COVID-19

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Research

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Abstract

Background

In the high incidence period of COVID-19, it is very important to quickly classify and evaluate the prognosis of patients through limited clinical antibody data.

Methods

Chemiluminescence immunoassay was used to detect serum IgM and IgG concentrations in 1951 patients diagnosed with COVID-19, and R language was used to analyze the influence of factors such as antibody, age, gender and concomitant diseases on the prognosis of SARS-CoV-2 patients.

Results

The results showed that the incidence of COVID-19 was consistent with the characteristics of the elderly, and patients with hypertension, diabetes, stroke, hypoalbuminemia and anemia were at increased risk of critical illness ($p < 0.05$). The analysis of antibodies results showed that there were no significant difference in antibodies concentration between COVID-19 patients of different ages. While there were no significant difference in antibodies concentration between mild and severe patients, the expression levels of serum IgM and IgG in critically ill patients decreased ($p = 0.000$ and 0.013), and high IgM and IgG concentration could reduce the incidence of critical illness ($p = 0.003$ and 0.015). Except in the 41–60 and 91–100 age groups, the simultaneous low expression of IgM and IgG in COVID-19 patients was significantly positively correlated with the severity of illness ($p = 0.000$).

Conclusions

IgM and IgG were important prognostic factors for COVID-19 patients. It was hence vital to carry out special clinical classification for the management and early intervention for patients with low IgM/IgG concentrations and with concomitant diseases.

Background

The novel coronavirus disease (COVID-19) pandemic started in December 2019 and broke out worldwide in the following year. According to the latest WHO data, as of February 2021, approximately 110 million people were infected with the disease and recording more than 2.5 million deaths. Real-time reverse transcription PCR (rRT-PCR) was the main method to diagnose SARS-CoV-2, but sensitivity and specificity problems were the main pitfalls of this method [1]. Given the high false negative rate of virus detection, the latest Diagnostic and Therapeutic Protocol for New Coronavirus Pneumonia in China included the presence of SARS-CoV-2 specific IgM and IgG antibodies as part of its diagnostic criterion since March 3,

2020, which could be used for collaborative judgment of suspected cases. Compared with viral RNA detection, antibody detection was simpler, faster, and the specimen was more stable and convenient for preservation. Nevertheless, serological testing also faced the problems of delayed antibody detectability, host immune function difference and cross-reaction of antibodies with other coronaviruses. Therefore, antibody testing was an important complement to the clinical diagnosis of SARS-CoV-2[2]. In addition, given the important role of the production and maintenance of SARS-CoV-2 neutralizing antibodies in resisting host virus infection, the combined detection of IgM and IgG could not only be used for the early diagnosis of infectious diseases, but also for staging of infection; Studies have shown that the levels of IgG and total antibodies in hospitalized patients were related to the severity of the disease[3]. The SARS-CoV-2 antibody response determined the severity of the disease in patients infected with COVID-19, which once again confirmed the correlation between clinical manifestations and immune response [4]. It could be seen that real-time monitoring of IgM and IgG levels could play a very important role in evaluating patient prognosis and guiding pharmacologic/timely and relevant clinical interventions.

The existing data showed that the risk of death was higher in the elderly infected with SARS-CoV-2, especially in male patients[5]. In addition, the presence of concomitant diseases in COVID-19 patients were also important factors leading to death. For example, Zhang et al. showed in an analysis of the clinical characteristics of 82 COVID-19 patients that deaths were mainly male, and more than 80% of fatalities were older than 60 years old, and more than 75% had comorbidities, including hypertension, heart disease, diabetes, cerebrovascular disease or cancer[6]. Wang et al. also reported that cardiovascular and cerebrovascular diseases and COPD can aggravate the condition of patients with COVID-19[7]. Through meta-analysis, Taneri PE et al. showed that when compared with clinically moderate COVID-19 patients, the hemoglobin level of severe stage patients was significantly decreased, while the ferritin content was significantly increased, which indirectly indicated that anemia can lead to poor prognosis of COVID-19 patients[8]. Merugu GP also confirmed that low hemoglobin leads to high mortality in COVID-19 patients[9]. However, there was no direct report of anemia leading to poor prognosis of COVID-19 patients.

Although various factors affecting the prognosis of COVID-19 patients have been reported from time to time, few studies had systematically analyzed reports on disease risk assessment, patient classification management, and early preventive treatment of COVID-19 confirmed patients based on antibody test results and related physiological indicators. This article analyzed the impact of different factors on the prognosis of COVID-19 patients, including age, gender, SARS-CoV-2 specific IgM and IgG levels, and presence of concomitant diseases. The results of this study will provide a new clinical reference for the disease risk assessment, divisional management and early prevention and treatment of patients with COVID-19.

Methods

Study design and participants

Huoshenshan Hospital was a designated hospital for COVID-19 treatment in Wuhan. This article analyzed the laboratory test results and clinical physiological indicators of 1951 COVID-19 patients admitted to the hospital from 4th March to 24th March . All the patients infected with SARS-CoV-2 were diagnosed by nucleic acid testing or imaging studies, the serum of hospitalized patients was collected and used for IgM and IgG detection. The first antibody test results of hospitalized patients were selected for this studyto prevent the influence of factors such as drugs and hormones on antibodies response. According to WHO standards[10], patients are divided into 3 categories based on the following clinical symptoms: (1) Mild/Moderate, if they had clinical signs of pneumonia (fever, cough, dyspnea, fast breathing(tachypnea) but no signs of severe pneumonia, including SpO2 ≥ 90% on room air; (2) Severe, if they had signs of pneumonia (fever, cough, dyspnea, fast breathing(tachypnea)) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 < 90% on room air; (3) Critical, if a diagnosis of acute respiratory distress syndrome (ARDS) was made. The clinical characteristics and laboratory examination results of all patients were extracted from the hospital electronic medical records. The study is based on the principles of the Helsinki Declaration, and this study was approved by the Medical Ethics Committee of Huoshenshan Hospital (approval No.: 202013) with each patient receiving written informed consent.

Determination of SARS-CoV-2 antibody in serum

Chemiluminescence method was used to determine the SARS-CoV-2 IgM or IgG concentration in 1951 cases. The magnetic beads of the kit were coated respectively with recombinant anti-SARS-CoV-2 antibodies (Shenzhen Yahuilong Biotechnology Co., Ltd.). Briefly, blood samples were centrifuged at room temperature, supernatant was then removed and incubated separately with magnetic beads coated with SARS-CoV-2 antibody. The antigen-antibody complex captured in the slurry was precipitated by a magnetic separator. The pellets were then incubated with acridinium ester-labeled mouse anti-human IgM or IgG antibodies and reacted with hydrogen peroxide in the excitation buffer. The relative luminous intensity was recorded in the iFlash 3000-A chemiluminescence analyzer (Shenzhen Yahuilong Biotechnology Co., Ltd.). The relative luminescence intensity is converted to represent antibody level in the unit of AU/mL. According to the manufacturer's instructions, the cutoff for seropositivity was set at an > 10.00 AU/mL for IgM and 10.00 AU/mL for IgG, respectively; in turn, all samples below these thresholds were considered as negative.

Statistical Analysis

The clinical characteristics and laboratory examination results of all patients were anonymized and extracted from the hospital electronic medical records. MASS library and nnet library of R language were employed for data analysis, namely chisq.test and wilcox.test to analyze the impact of different antibody concentrations on gender, age, and disease severity. In experimental statistics, $p < 0.05$ is considered to be of statistical significance. GraphPad Prism 8 (GraphPad Software Company) was used for graph plotting.

Results

Analysis of the correlation between patient characteristics and illness

This article analyzed the laboratory test results and clinical physiological indicators of 1951 COVID-19 patients admitted to Huoshenshan Hospital from 4th March to 24th March 2020. Table 1 summarized the general sociodemographic characteristics and the presence of clinical concomitant diseases in these patients. There were 769 patients (39.4%) with concomitant diseases, among which hypertension (460, 59.8%) and type 2 diabetes (228, 29.6%) were the most common. There were 406 patients (52.8%) with more than 2 concomitant diseases. Multiple regression analysis was performed on the differences in gender, age and condition of the cases that met the statistics. The results showed that independent of age, hypertension (p = 0.000), diabetes (p = 0.000), stroke (p = 0.000), anemia (p = 0.000) and hypoproteinemia (p = 0.000) were positively correlated with the severity of the illness, Benign Prostatic Hyperplasia also increases the risk of severe illness (p = 0.025). In addition, patients with COPD (chronic obstructive pulmonary disease) and coronary atherosclerotic disease had a tendency of aggravation (p = 0.069 and 0.074), while other factors had no significant influence on the progression of the illness (Table 1, Fig. 1a). In patients with concomitant diseases, age will further increase the risk of disease deterioration (p = 0.000) (Fig. 1b). Age structure analysis showed a normal distribution (mean age 59.3±14.3 years), and the peak prevalence was 61-70 years old (Fig. 1c), age was positively correlated with disease progression, the age of patients with mild symptoms was significantly lower than that of severe illness (57.3 ± 14.5 *vs* 63.8 ± 12.5, p = 0.000), but there was no significant difference between severe and critical patients (Table 1, Fig. 1d). The proportion distribution of different age groups further confirmed that the disease progressed with age (p = 0.000) (Fig. 1e). Gender difference analysis showed that the overall gender distribution of COVID-19 patients was close to 1:1 (977:974). However, the proportion of men in the 21-40 and 71-80 age groups was relatively higher, while the proportion of women in the 51-60 age group was relatively higher (p = 0.043) (Fig. 1f). In addition, men were more likely to experience aggravation of disease than women (p = 0.000) (Table 1, Fig. 1g).

Correlation analysis of COVID-19 patients' antibodies and illness

The IgM and IgG of COVID-19 patients were grouped according to a 2-fold concentration gradient. Analysis of differences in age groups showed that the IgM concentration in the 81-90 ages group was significantly lower than that in the 41-80 group (p < 0.05), the characteristic was similar in different genders, but there was no significant difference in IgM concentration among other age groups (Fig. 2a). While the differences of IgG in different gender and age groups were not statistically significant (Fig. 2b). Analysis of the difference in antibodies concentration of different genders showed that the IgG concentration in males was slightly lower than that in females (median 135.5 *vs* 142.5 AU/ml, p = 0.028), while there was no significant difference in IgM concentration among different genders (Fig. 2c); The overall analysis of antibody levels with different severity showed that, compared with mild and severe patients, the levels of IgM ($p = 3.59\times10^{-08}$) and IgG (p = 0.013) in critical patients decreased (Fig. 2d).

Table 1 The characters of 1951 patients with COVID-19

	All patients	Mild	Severe	Critical	*p*-value
No.	1951	1369	557	25	-
Age（year）	59.3 ± 14.3	57.3 ± 14.5	63.8 ± 12.5	67.6 ± 14.9	M *vs* S, *p*=0.000; M *vs* C, *p*=0.002; S *vs* C, *p*=0.519
Female,n(%)	974(49.9%)	696(50.8%)	269(48.3%)	9(36%)	0.00
Type Ⅱ diabetes, n(%)	228(11.7%)	129(9.4%)	88(15.8%)	11(44%)	0.000
Hypertension, n(%)	460(23.6%)	269(19.6%)	180(32.3%)	11(44%)	0.000
COPD,n(%)	16(0.8%)	8(0.6%)	7(1.3%)	1(4%)	0.069
Stroke, n(%)	55(2.8%)	25(1.8%)	28(5.0%)	2(8.0%)	0.000
Rheumatism, n(%)	27(1.4%)	17(1.2%)	10(1.8%)	0	0.537
AD, n(%)	14(0.7%)	7(0.5%)	7(1.3%)	0	0.195
Anemia, n(%)	31(1.6%)	12(0.9%)	16(2.9%)	3(12%)	0.000
Tumor, n(%)	33(1.7%)	19(1.4%)	13(2.3%)	1(4%)	0.230
CAC, n(%)	89(4.6%)	53(3.9%)	34(6.1%)	2(8%)	0.074
Hypoproteinemia, n(%)	25(1.3%)	8(0.6%)	14(2.5%)	3(12%)	0.000
Chronic bronchitis, n(%)	25(1.3%)	15(1.1%)	9(1.6%)	1(4%)	0.313
Hepatitis B virus, n(%)	17(0.9%)	14(1%)	3(0.5%)	0	0.523
Hypothyroidism, n(%)	24(1.2%)	15(1.1%)	9(1.6%)	0	0.550
BPH, n(%)	15(0.8%)	6(0.4%)	9(1.6%)	0	0.025
Chronic Gastritis, n(%)	14(0.7%)	11(0.8%)	3(0.5%)	0	0.751
Gallstone, n(%)	15(0.8%)	9(0.7%)	6(1%)	0	0.574

AD: Alzheimer's disease; BPH: Benign Prostatic Hyperplasia; CAC: Coronary atherosclerotic cardiopathy; COPD: chronic obstructive pulmonary disease; M: mild patients; S: severe patients; C: critical patients

Analysis of the correlation between IgM and IgG concentrations in patients showed that there was a slight correlation between IgM and IgG concentrations in the same individual (Pearson correlation, *r* =

0.563) (Fig. 3a). The analysis showed that the levels of IgM and IgG antibodies in 136 patients were both very low at the same time (IgM < 32 AU/ml; IgG < 8 AU/ml) (Fig. 3a). The age structure analysis of this group showed that the proportion of low-concentration antibodies in 21-40 and 61-100 years old was the most (p = 0.001) (Fig. 3b). The incidence of low level antibody in men was slightly higher, but the difference was not significant (p = 0.061) (Fig. 3c). In addition, the simultaneous lower expression of IgM and IgG reduced the ratio of severity in 41-60 and 91-100 age groups (p = 0.000), but increased the severity of the disease in the remaining age groups (Fig. 3d). Gender and severity analysis of 19 patients with low IgM and IgG antibodies in the 20-40 age group showed that the number of male patients in this group was twice that of females, and the proportion of men with moderate to severe disease increased significantly (p = 0.014) (Fig. 3e). Although the presence of low antibody levels were slightly higher in critically ill patients, overall, there was no significant correlation between low antibodies and the severity of the illness (p = 0.88). In contrast, the analysis of 91 cases of high IgM (> 256 AU/ml) and 265 cases of high IgG (> 200 AU/ml) patients showed that the proportion of illnesses with mild cases increased, while the proportion in critical patients decreased (Fig. 3f). Multiple regression analysis showed that although the increase of IgG was positively correlated with the incidence of severe illness (p = 0.016), the increased expression of IgM (p = 0.003) and IgG (p = 0.015) reduced the incidence of critical illness (p = 0.003) (Fig. 3g). Analysis of IgM and IgG levels in patients with hypertension, diabetes, anemia and stroke showed that there was a poor correlation between the prsence of concomitant diseases and the levels of IgM/IgG in COVID-19 patients (data not shown).

Discussion

Medical resources were in short supply during the COVID-19 pandemic. Hence classified management and treatment of admitted patients will potentially save substantial manpower and material resources leading to improved medical efficiency. It is extremely important to accurately assess the progression of the patient's condition through limited admission data.

Although there were many clinical reports on COVID-19, there was no systematic analysis report on admission assessment. The analysis of antibody levels and clinical characteristics of 1951 COVID-19 patients in this study shows that the overall age of the patients was normally distributed, with the peak value at 61 to70 years old, considering the age distribution characteristics of the normal population, it could be seen that the incidence of COVID-19 conforms to the characteristics of susceptibility to the elderly, which was consistent with previous studies[5]. It has been reported that men were more susceptible to COVID-19[11], but the sex ratio of COVID-19 patients in this study was close to 1:1, and there was no statistical difference in the COVID-19 infection rate of different genders, but men were more likely to experience aggravation of the disease than in women. It was worth noting that the proportion of male patients with COVID-19 in the 21–40 age group was significantly higher, which might be related to the irregular dietary habits, sub-optimal lifestyle and stresses in males of this age group; as for the 71–80 age group, the proportion of males was also relatively higher, which may be related to weaker immunity of males in this stage. In addition, although the proportion of men and women in the 81–100 age group

was similar, given that there were more women in this age group, older men might be more susceptible to the disease. Interestingly, the proportion of COVID-19 female patients in women from the 51–60 age group of was significantly higher, which may be related to the relatively low immune function of women at this stage of due to menopause. However, when compared with gender of patients, age has a more obvious influence in the degree of disease with severity gradually worsens with age.

Although the severity and pathogenicity of patients infected with COVID-19 were not as serious as SARS virus, the patients with other chronic diseases before infection would get worse(deteriorate) and even become fatal after infection. Such common diseases include cardiovascular diseases, diabetes and hypertension, etc.[12], in which patients with hypertension and diabetes usually needed to be treated with Angiotensin Converting Enzyme(ACE) inhibitor or Angiotensin Receptor Blocker (ARB), but these two drugs both lead to an increase in the expression of ACE2, the key guidance factor for COVID-19 to invade the body of patients where the up-regulation of ACE2 expression will lead to increase susceptibility of COVID-19, and then aggravate the disease [13]. The recognition and combination of SARS-CoV-2 and ACE2 could promote the expression of angiotensin II, which induced inflammatory factors and vasoconstriction, and promoted organ damage and stroke[14] which was another poor prognostic factor for COVID-19[15]. Anemia and hyperlipidemia were also important fatal factors. Anemia not only leads to an increase in ferritin and inflammation of the body, but also leads to insufficient oxygen supply, eventually leading to multiple organ failure[16]. In addition, limited studies showed that hypoalbuminemia was also an adverse factor for COVID-19[17]. Our analysis showed that common diseases such as hypertension, diabetes, stroke, hypoalbuminemia and anemia could aggravate the condition of patients with COVID-19, which were important factors to evaluate the prognosis of patients with COVID-19. However, atherosclerosis, Alzheimer's disease, liver disease, COPD and cancers had no obvious effect on the disease. The main reason was due to the minute number of cases. In this study, there were 6 patients with rheumatic diseases (3 severe and 3 mild cases), and 3 with systemic lupus erythematosus, including 2 severe cases and 1 mild disease, although the above data could not be statistically analyzed. However, these two diseases tend to aggravate the condition of patients with COVID-19. Because elderly patients account for a higher number in those with the above diseases, the prognosis of elderly patients with COVID-19 infection might be worse.

Presently, it is considered that IgM was the first line of defense for adaptive immune response after virus infection, and although IgM was produced earlier than IgG, it was the latter which provided long-term immunity and immunological memory[18]. Therefore, IgM antibodies produced in the early stage of virus infection could indicate current or recent infection, while IgG antibodies were an important antibody produced by the immune system. The appearance of IgG in patients means that the disease was in the middle and late stage or has a history of infection. Therefore, the combined detection of IgM and IgG was not only used for the early diagnosis of infectious diseases, but also for the evaluation of infection stages[19]. In theory, adaptive immunity was the best way to deal with all types of infections. The good contribution of innate and adaptive immune response could quickly control the virus and eliminate infectious particles in the body. Antibodies played an important role in virus neutralization, Fc receptor-

mediated phagocytosis, antibody dependent cytotoxicity (ADCC), complement dependent cytotoxicity (CDCC) and subsequent pathogen clearance. However, ADCC and CDCC could cause harmful systemic pro-inflammatory response, resulting in serious pathophysiological consequences. The disproportionate immune response can lead to virus transmission, multiple organ failure and high mortality[20]. At present, there were still debates whether antibodies in COVID-19 patients activate protective or destroy the immune response of the host[21]. Compared with the contribution of host antibodies in COVID-19 patients to resist and eliminate the virus, people paid more attention to the correlation between the level of SARS-CoV-2 antibody and the disease severity of patients with COVID-19. Although it had been reported that the weak correlation between antibody titers and neutralizing activity in COVID-19 patients[22], some literatures showed that IgG and total antibody levels of hospitalized patients were positively correlated with disease severity, and positively correlated with the patient's age and gender. This phenomenon can explain that severe COVID-19 infection was more common in elderly men[23]. Hansen even pointed out that the antibody concentration, especially the IgG level, was related to specific symptoms such as fever, sore throat, shortness of breath and nausea. The SARS-CoV-2 antibody response determined the disease severity of patients infected with COVID-19 [24]. The unnecessary immune response to SARS-CoV-2 might be one of the mechanisms leading to overactive macrophages and monocytes, leading to a fatal cytokine storm, which seemed to be a marker of COVID-19 [25]. Nevertheless, some studies have shown that low IgG levels in COVID-19 patients were associated with poor prognosis of severe and critically ill patients[26]. This conclusion was partly consistent with the results of our analysis. Our study of 136 patients with COVID-19 with low IgG and IgM concentrations showed that most of the patients with low IgG and IgM concentrations were male patients aged 20–40 years old, and the low expression of antibodies was related to the poor prognosis of patients with severe and critical diseases, the severity of disease was closely correlated ($p = 0.061$); In addition, 136 cases of COVID-19 patients with low IgG and IgM were analyzed in different age groups. The results showed that the proportion of patients with severe diseases in the age group of 21–40 years increased significantly, the proportion of patients with severe diseases in the range of 41–60 years was relatively reduced, and the proportion of patients with severe diseases in the 71–80 years old group increased again. This contradiction in different age groups may explain the phenomenon that some studies have reported that COVID-19 antibodies have made the disease worse. This contradiction itself explains the complex evolution of antibody levels and diseases: On the one hand, continuous viral infection will lead to the consumption of antibodies and thus the decrease of antibody levels. On the other hand, the virus itself was the raw material for stimulating the immune response, and the antibody level often reflects the degree of immune response. Although low antibody concentration did not necessarily aggravate the disease, the expression levels of IgM and IgG in critical illness were significantly lower than those in mild or severe patients. Consistent with our analysis of 265 patients with high IgG concentration, the results showed that although the proportion of patients with mild illness increased and the proportion of patients with critical illness decreased in patients with high concentration of IgG, this phenomenon was consistent with the overall low level of IgM and IgG in critically ill patients, which further illustrated the duality of the effects of high concentrations of antibodies. Although there was no case data of children aged 0–10 years in this study, we detected the

antibody concentration of children aged 11–20 years. The results show that the IgG level of COVID-19 patients in this age group was the highest than that in other age groups, which may also be an important reason for the low infection rate and high cure rate of juveniles with COVID-19. These results suggest that high concentration of COVID-19 antibodies tends to benefit patients.

In view of the limited medical conditions and insufficient knowledge of the SARS-CoV-2 virus in the early stage of the COVID-19 outbreak, this study itself had many shortcomings. For example, most patients admitted to Wuhan Huoshenshan Hospital were admitted after a period of infection. Case analysis showed that most patients admitted to Huoshenshan Hospital had been sick for nearly one month, there might be more asymptomatic and mildly infection in patients, while there were relatively few severely and critically infected patients. As a result, some results of this study may be inconsistent with other reports; In addition, in view of the short half-life of IgM, there was only a slight correlation between IgM and IgG in this study. A separate analysis of the correlation between low IgM and disease prognosis might be of little significance; Finally, due to the limitations of experience and conditions, the 1951 patients in this study lacked biochemical testing such as interleukin 6 (IL6) and C-reactive protein (CRP). If these indicators could be detected at the same time, it might play a more accurate role in guiding the prognosis of COVID-19 patients.

Conclusions

In summary, the elderly were prone to being infected with COVID-19 and the disease was more serious. In addition, hypertension, diabetes and other accompanying diseases often increased the severity of COVID-19 patients. Most critically ill patients had relatively low levels of IgM and IgG indicating increased tendency of disease progression. Thus, comprehensive assessment including the age, presence or absence of concomitant diseases and antibody concentration could predict the progression of COVID-19 patients, and provided valuable references for clinical management and disease prevention.

Abbreviations

COVID-19: Corona Virus Disease 2019; COPD: chronic obstructive pulmonary disease; AD: Alzheimer's disease; BPH: Benign Prostatic Hyperplasia; CAC: Coronary atherosclerotic cardiopathy; WHO: World Health Organization; No.: number; ACE2: Angiotensin Converting Enzyme 2; ARB: Angiotensin Receptor Blocker; ARDS: acute respiratory distress syndrome; ADCC: antibody dependent cytotoxicity; CDCC: complement dependent cytotoxicity; IL6: interleukin 6; CRP: C-reactive protein; RT-qPCR: Real-time quantitative PCR; M: mild patients; S: severe patients; C: critical patients;

Declarations

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Author's contribution

XL, LJX and BY wrote the first draft. XHC offered the clinical data, All authors designed the study, analyzed the data and contributed in writing and reviewing the manuscript.

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Availability of data and materials

The datasets supporting the results of this article are included within the article and its additional files.

Consent for publication

Informed consent for publication was obtained from all participants.

Ethics approval and consent to participate

The study design and protocol were reviewed and approved by the Institutional Review Committee of Huoshenshan Hospital and Southern Theater Command General Hospital (approval number: 202013).

Competing interests

The authors report no declarations of interest.

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Figures

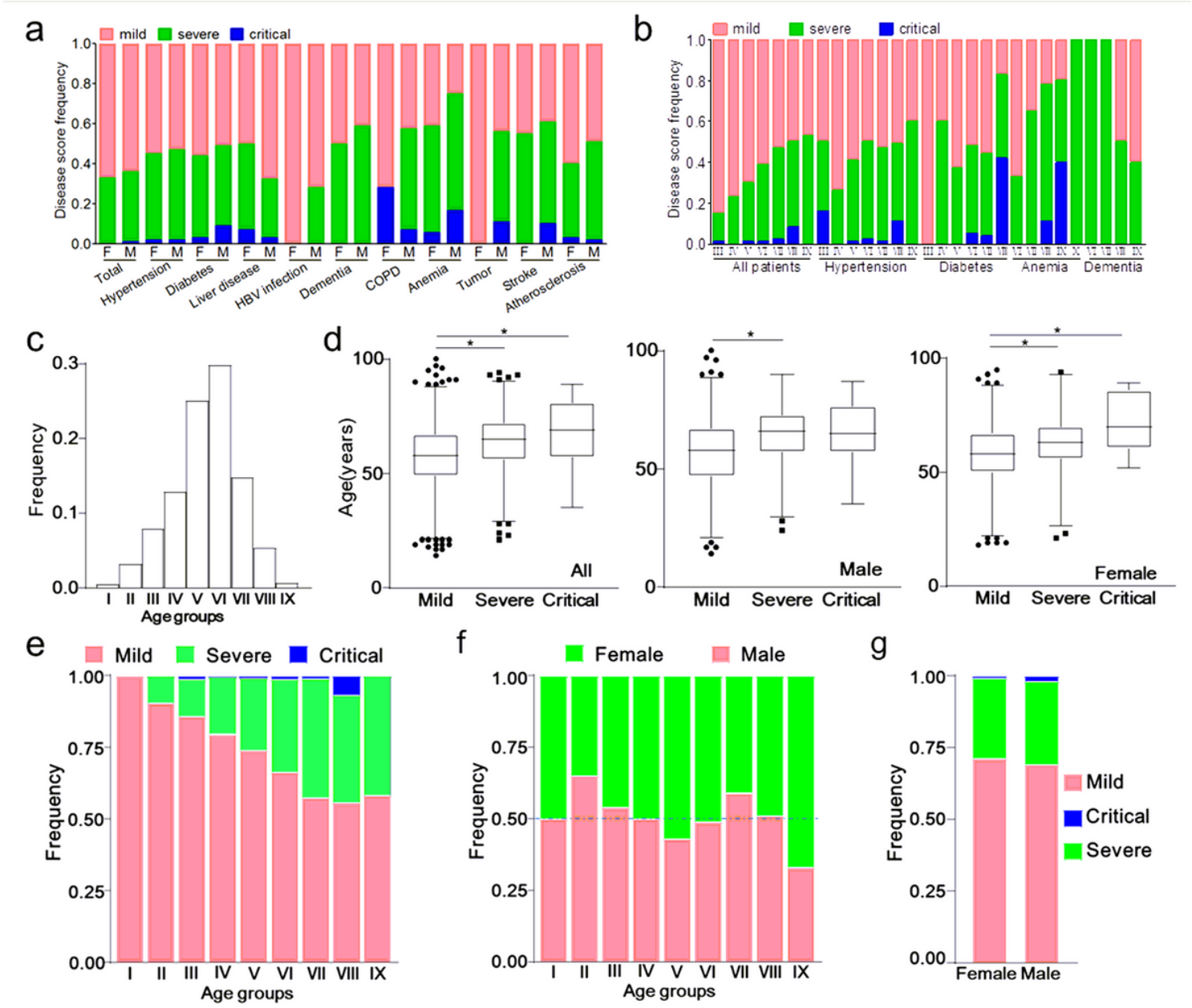

Figure 1

Analysis of characteristics of 1951 COVID-19 patients. a. Analysis of the difference in the condition of patients with concomitant diseases between different genders. b. Analysis of the difference of patients with concomitant diseases in different age groups. c. The overall age distribution of COVID-19. d. Analysis of age difference of patients with different diseases severity and genders. e. Relative proportion of COVID-19 patients of different severity in respective age groups. f. Sex ratio of COVID-19 patients in different age groups. g. Disease severity ratio of COVID-19 patients with different gender. F: female; M: male; age groups from to represent sequential increase in age groups of patients, for example, represents patients in the 11-20 age group; represents patients in the 91-100 age group. *p < 0.05.

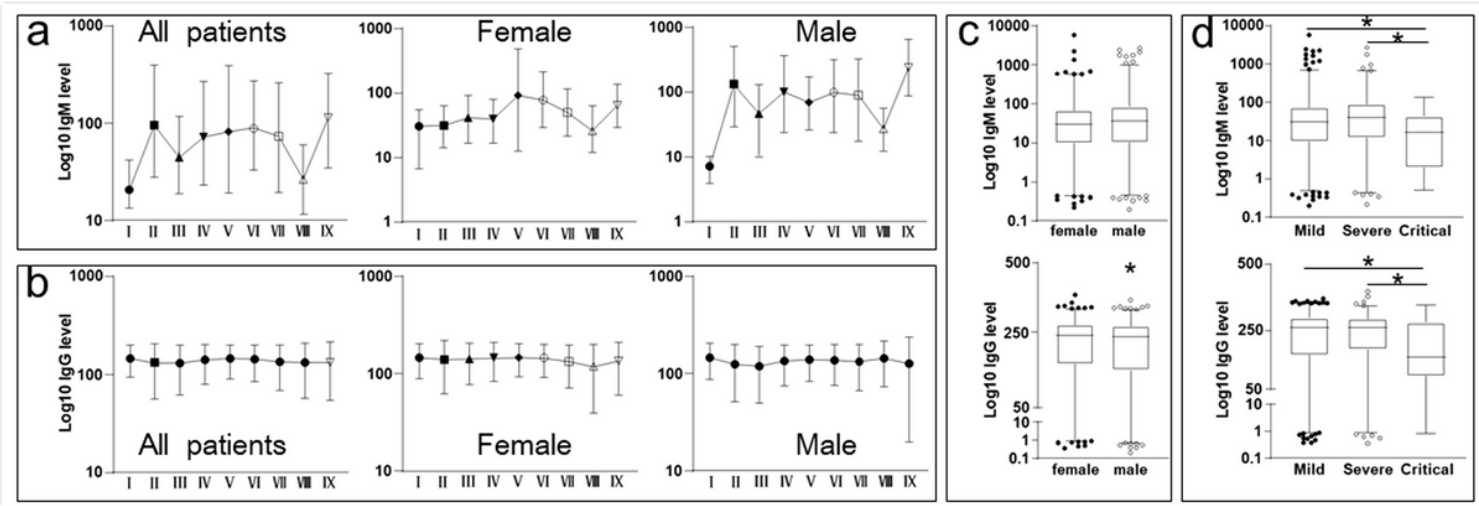

Figure 2

Analysis of antibody characteristics of COVID-19 patients with different gender and age. a. Analysis of the difference of IgM concentration in COVID-19 patients of different genders and ages. b. Analysis of the difference of IgG concentration in COVID-19 patients of different genders and ages. c. Analysis of antibody concentration difference in patients of different genders. d. Concentration differences of IgM and IgG in COVID-19 patients with different severities. *p < 0.05.

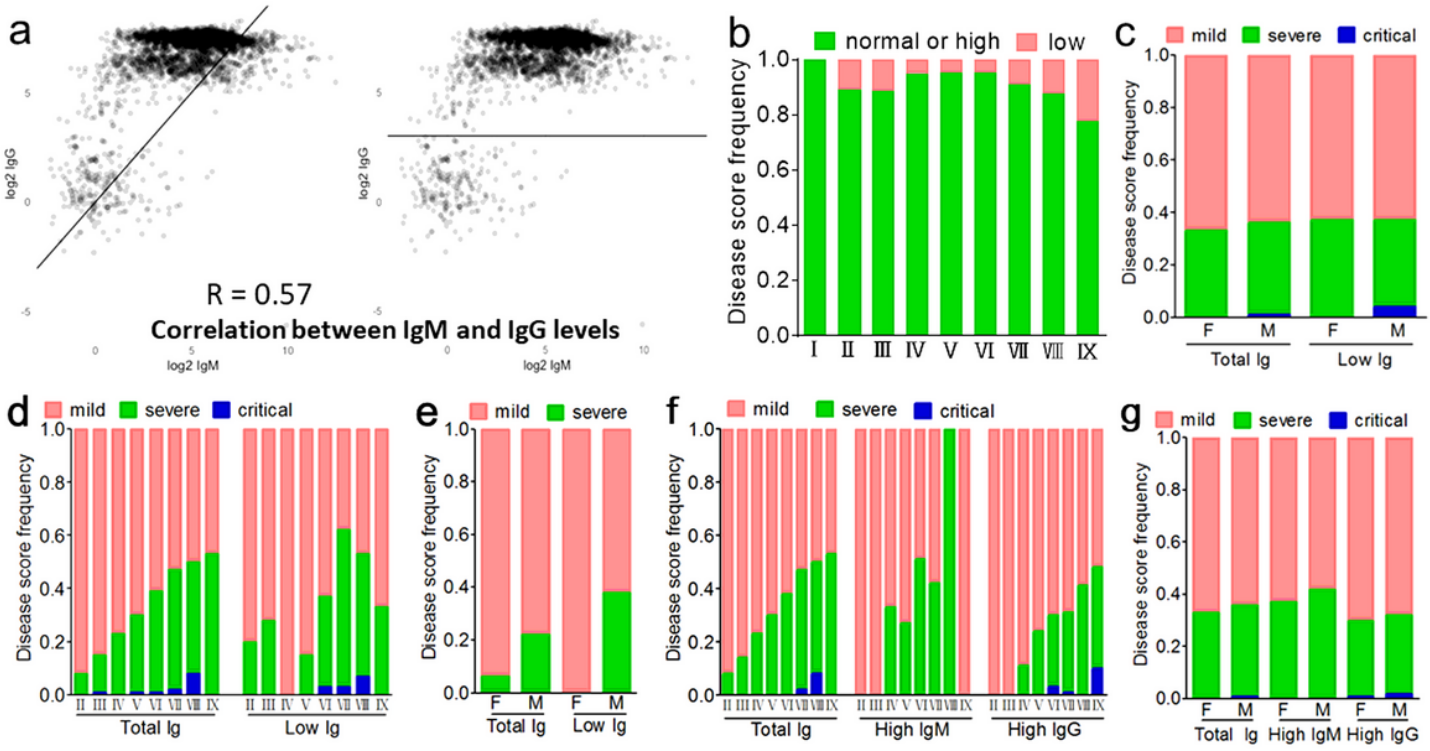

Figure 3

The role of IgM and IgG concentration in evaluating the prognosis of COVID-19 infection. a. The correlation analysis of IgM and IgG. b. The distribution of patients with low level of antibodies (LLA) in different age groups. c. The disease severity analysis of LLA patients in different genders. d. Disease severity analysis of LLA patients in different age groups. e. Distribution characteristics and disease severity analysis of LLA patients in 21-40 age groups. f. Disease severity analysis of patients with high level of antibodies in different age groups. g. Disease severity analysis of patients with high level of antibodies in different genders.