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Clinical characteristics of COVID-19 patients combined with allergy

To the Editor,

Coronavirus disease 2019 (COVID-19) is a highly contagious disease that could affect not only the lung but also many other systems and has already infected over 2 471 000 and with more than 169 000 deaths worldwide.[1] Large numbers of clinical studies so far have shown that changes in inflammatory factors and cellular immune function of COVID-19 patients may lead to impaired immune function with an unknown specific mechanism. Allergy is an immune response to antigen stimulation, inducing the release and production of various inflammatory mediators which cause allergic symptoms of different organs, such as allergic rhinitis, bronchial asthma, allergic gastrointestinal disorders, and drug allergy. Whether there is specificity in the evolvement of COVID-19 in allergic patients remains to be explored.

Accordingly, we obtained the medical records and compiled data for 110 patients with laboratory-confirmed COVID-19, between February 1, 2020, and March 8, 2020, in Renmin Hospital of Wuhan University, eliminating those who had uncomplete clinical information or SARS-CoV-2 nucleic acid (nasopharyngeal swabs) test still representing positive. We eliminated 45 patients with underlying disease or operation history among which 3 patients were combined with allergic disease history and were all with drug allergy. Thus, 65 patients were included in our study: 21 patients with combined allergy history (7 males and 14 females; aged from 41 to 88; including 15 patients with a history of drug allergy, 2 patients with asthma, 1 patient with allergic rhinitis, 1 patient with asthma combined with drug allergy, 1 patient with allergic rhinitis combined with drug allergy, and 1 patient with food allergy) were screened out as observation group and 44 patients without combined allergy history were screened out as control group (23 males and 21 females; aged from 30 to 81). We designed a single-center retrospective review, and all the enrolled patients met the criteria of the Chinese Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Provisional 7th Edition).[2]

Wendan and Ziang contributed equally to this work.

From the manifestations of the lung CT taken on admission, bilateral lesions were dominant in both groups, but the proportion of bilateral lesions in the observation group (14 cases, 66.7%) was lower than that in the control group (39 cases, 88.6%), $P < .05$, as shown in Table 1. Compared with the control group, LY (lymphocyte) and MO (monocyte) count in the observation group showed an increasing trend ($P < .05$). T cells in the observation group were significantly increased, with statistical significance ($P < .05$), as shown in Table 2. The proportion of severe patients was significantly lower in the observation group (Table 2), and in severe patients, the count of LY and the levels of CD3+, CD4+, and CD8+ T cells in the observation group also showed an increasing trend compared with the control group ($P < .05$) (Table S1).

In this study, we found that the rate of combined allergy was low in COVID-19 patients. The ratio of combined asthma and allergic rhinitis was far lower than those of domestic morbidity,[3] which might suggest that asthma and AR may not be a susceptibility factor for SARS-CoV-2.

Imbalance of immune function has a serious impact on the occurrence and development of COVID-19. According to the Chinese Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Provisional 7th Edition), in the early stages white blood cells were normal or decreased, and lymphocytes might have a decrease. Especially in severe and critical patients, a decrease in lymphocytes was more significant and correlated with the severity of illness.[4-6] We thus speculated that SARS-CoV-2 may reduce the body's immune function by inhibiting lymphocyte generate and killing existing lymphocytes. Our conclusion is consistent with the result of the negative correlation between the lymphocyte number and illness severity. These findings indicate that resistance to SARS-CoV-2 by high-sensitivity state may result in a lighter attack on lymphocytes and thus induce the severity of the initial condition of COVID-19 patients.

Lymphocytes are an important component of immune response and are composed of three subgroups of T cells, B cells, and NK cells. The status of lymphocyte subgroups is an important indicator to reflect the immune response.[7] T cells play an important role in cellular immunity. Pathological examinations of the COVID-19 autopsy revealed a significant reduction in the number of lymphocytes in bone marrow, peripheral immune organs, and peripheral blood.[8]

TABLE 1 General conditions of 65 COVID-19 patients

Items	Observation group/patients combined with allergy (n = 21)	Control group/patients without underlying diseases (n = 44)	*P*
Age, median (range, y)	64 (56.5, 77)	57 (50.25, 64)	.005
Male (n, %)	7(33.3%)	23(52.2%)	.152
Lung CT (n, %)			.044
Unilateral lesion	7 (33.3%)	4 (9.1%)	.03
Bilateral lesion	14 (66.7%)	39 (88.6%)	.045
Regular	0	1 (2.3%)	>.999
Severity (n, %)			.04
Moderate	7 (33.3%)	4 (9.1%)	.03
Severe	12 (57.2%)	37 (84.1%)	<.001
Critical	2 (9.5%)	3 (6.8%)	.523
First negative nucleic acid results during hospitalization (d)	8.7 ± 5.3	12.1 ± 7.2	.036
Incipient symptoms (n, %)			
Fever	11 (52.4%)	35(79.5%)	.014
Dry cough	11 (52.4%)	25 (56.8%)	.6
Expectoration	5 (23.8%)	4 (9.1%)	.135
Dyspnea	8 (38.1%)	19 (43.2%)	.697
Diarrhea	2 (9.5%)	0	.101
Vomiting	1 (4.8%)	4 (9.1%)	>.999
Headache	1 (4.8%)	0	.323
Fatigue	4 (19%)	3 (6.8%)	.2
Rhinorrhea	0	1 (2.3%)	>.999
No symptoms	0	0	-

TABLE 2 Blood routine examination results, and cellular and humoral immune indexes of 65 COVID-19 patients

Items	Observation group/patients combined with allergy (n = 21)	Control group/patients without underlying diseases (n = 44)	*P*	Reference range
WBC (10^9/L)	6.30 ± 1.42	5.83 ± 3.08	.069	3.5-9.5
LY (10^9/L)	1.39 ± 0.67	0.89 ± 0.40	.004	1.1-3.2
MO (10^9/L)	0.52 ± 0.17	0.39 ± 0.21	.02	0.1-0.6
EO (10^9/L)	0.11 ± 0.14	0.05 ± 0.85	.069	0.02-0.52
LY%	23.42 ± 12.13	17.99 ± 9.12	.084	20-50
MO%	8.48 ± 2.64	7.38 ± 3.56	.214	3-10
EO%[a]	0.90 (0.30, 2.30)	0.35 (0, 2.15)	.077[b]	0.4-8.0
$CD3^+$ (cells/μL)	840.20 ± 545.81	447.95 ± 278.74	.003	723-2737
$CD4^+$ (cells/μL)	561.95 ± 388.81	334.18 ± 280.54	.007	404-1612
$CD8^+$ (cells/μL)	358.33 ± 253.14	219.25 ± 165.50	.019	220-1129
$CD19^+$ (cells/μL)[a]	139 (88.5, 223)	111 (72, 159.5)	.161[b]	80-616
$CD16^+56^+$ (cells/μL)[a]	137 (90, 210.5)	98 (63.5, 165)	.114[b]	84-724
IgG (g/L)	12.87 ± 3.76	13.72 ± 14.20	.377	7.0-16.0
IgM (g/L)	0.99 ± 0.40	0.97 ± 0.45	.832	0.4-2.3
IgA (g/L)	2.77 ± 0.90	2.26 ± 0.90	.442	0.7-4.0
IgE (IU/mL)[a]	44.30 (18.30, 143.00)	53.30 (26.15, 143.25)	.388[b]	<100
Complement C3 (g/L)	1.05 ± 0.22	1.12 ± 0.16	.218	0.9-1.8
Complement C4 (g/L)	0.24 ± 0.06	0.30 ± 0.10	.404	0.1-0.4

Abbreviations: EO, eosinophil count; LY, lymphocyte count; MO, monocyte count; WBC, White blood cell count.

[a]Abnormal distribution.

[b]Mann-Whitney *U* test.

Immunohistochemical staining showed a decrease in $CD4^+$ T and $CD8^+$ T cells in the spleen and lymph nodes. In bronchoalveolar lavage fluid, the number of CTL cell ($CD8^+$ T cell) clones decreased significantly in severe COVID-19 patients.[9] These studies suggested that T lymphocytes, B lymphocytes, and NK cells might all be involved in the immune response of COVID-19, but T lymphocytes played a more important role, and the degree of their reduction might be a predictive factor on the progression from normal to the critical stage of COVID-19. In our study, compared with the control group, T cells in peripheral blood of the observation group were significantly increased ($P < .05$). In the observation group, $CD19^+$ and $CD16^+$ 56+ T cells showed an increasing trend, but there was no statistically significant difference between the two groups ($P > .05$). These findings suggested that the reduction in lymphocyte count impairment in COVID-19 patients with allergies might mainly affect T lymphocytes, rather than B lymphocytes or NK cells. In this study, there was no significant difference in the humoral immune indexes such as IgG, IgM, IgA, IgM, complement C3, and complement C4 between the two groups, which was consistent with the change in $CD19^+$.

In this study, we found that combined allergies might reduce the destructive power of SARS-CoV-2 infection. COVID-19 patients combined with allergy had less severe initial conditions and a lower degree of lung lesions, which might owe to the fact that T lymphocytes were less damaged by SARS-CoV-2. Other underlying diseases may also exist with these patients and often with the worse condition and worse prognosis. On the other hand, the interval of nucleic acid turning to negative in allergic patients was shorter, which may indicate that the history of allergy plays a positive role in the prognosis of COVID-19 patients. We speculated further that in general population allergic patients are relatively younger may be because patients with combined allergies might be more resistant to SARS-CoV-2 infection compared with nonallergic people at the same age. But this hypothesis needs further epidemiological investigation of a larger population.

There are several limitations to our study. We screened out the specific patients with entire records and eliminated those whose records were incomplete, so we are afraid that our data may not fully reflect the incidence of COVID-19 combined with allergy. This is a single-center retrospective study with a small sample size, short follow-up time, and we did not separately analyze the clinical characteristics of the patients with different illness degrees in detail and the diagnosis of allergies based on the history without performing SPT or sIgE. It is difficult to draw a definite conclusion on the relationship between allergic diseases and COVID-19, but it provides references and hints for further studies.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHORS' CONTRIBUTIONS

WDS and ZAG collected clinical data, discussed the details, and wrote this article together. Since WDS and ZAG contributed to the work equally, they should be regarded as co-first authors. YJD, TZ, and WZ analyzed and interpreted the data regarding the COVID-19. YX analyzed the data and did the modification of this manuscript, and was a major contributor in writing the manuscript. The division of labor is clear-cut, each one being charged with specific responsibilities. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

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