Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Autoantibodies in COVID-19: frequency and function

Dear Editor

COVID-19 pandemic that induced by SARS-CoV-2 has been going on for more than ten months, and shows no sign of abating. Numerous COVID-19 cohort studies have been reported. In addition to the common clinical feature, multiple similar symptoms between COVID-19 and autoimmune diseases were found, including vascular inflammation, endothelial dysfunction and lung manifestations and occurrence of autoantibodies [1–3]. This paper provide an overview on the autoantibodies in COVID-19 patients.

Antinuclear antibodies (ANAs) were found in COVID-19 patients. First, Zhou Y and colleagues investigated the ANAs in 8 severe and 12 critical ill COVID-19 patients [4]. Their results showed that ANAs was positive in 50% of these patients. Both the positive rate (37.5% vs 58.5%, $P = 0.361$) and ANAs level (98.60 ± 142.77 vs 184.83 ± 191.24 AU/mL, $P = 0.298$) were not significant different between severe and critical patients. Second, Vlachoyiannopoulos PG et al. found that 10 patients (34.5%) were positive for ANAs in 29 severely ill COVID-19 patients. And moreover, the outcome of ANAs positive patients (3 patients in ICU and 2 patients death) were worse than that of the autoantibody negative patients (all alive) [5]. Third, Pascolini S and colleagues found that 11 patients were positive (33.3%) for ANAs in 33 consecutive patients with COVID-19 [6]. And moreover, the outcome of ANAs positive patients were worse than ANA negative patients: the death rate of ANAs positive patients were 36.4% (4 death among 11 ANAs positive patients), while the death rate of ANAs negative patients were 13.6% (3 death among 22 ANAs negative patients). However, the difference of death rate was not statistically significant ($P = 0.292$). Taken together, the positive rate for ANAs were similarly among three independent cohorts. A total of 82 patients were included in these studies (Table 1), 31 patients were tested positive for ANAs (36.4%). Notably, although no definite conclusion can be drawn due to the small sample size, the positive of ANAs might be associated with poor prognosis, and this possibility need further verification in larger cohorts.

COVID-19 patients are at a high risk for thrombotic arterial and venous occlusions. Antiphospholipid antibodies (aPL) are pathogenic autoantibodies targeting phospholipids and phospholipid-binding proteins, that can cause so called Antiphospholipid Syndrome, characterized by a rapidly occurring multiorgan thrombotic damage. The aPL are including anticardiolipin (aCL), anti-beta-2 glycoprotein I (aβ2GPI), anti-phosphatidylserine/prothrombin (aPS/PT) and lupus anticoagulant (LA). Nine studies that have tested the aPL in COVID-19 were reviewed (Table 2) [5–13]. These studies showed that: aPL is frequent in COVID-19 patients. The positive rate ranged from 24%–57% in different case series. The positive rate of LA even reached 90% in COVID-19 patients with a prolonged activated partial-thromboplastin time (aPTT) [9]. And moreover, Bertin D et al. showed that aCL IgG autoantibody level (>15 U/mL) is an independent risk factor for COVID-19 severity [OR (95% CI): 6.5 (1.76–31.77); $P = 0.009$)], while the aCL IgM and aβ2GPI are not [14]. Thus, these studies suggested that the occurrence of aPL might be involved in COVID-19 associated coagulopathy. However, Galeano-Valle F et al. showed that aPL is not frequent (8.3%) among COVID-19 patients who suffer venous thromboembolism (VTE), suggesting that aPL might not be involved in the pathogenesis of VTE in severe COVID-19 pneumonia [15]. Notably, the prevalence of aPL in non-VTE patients is not provided. Therefore, further studies were needed to determine the association between aPL and COVID-19 severity and coagulopathy.

Type I IFNs are ubiquitously expressed cytokines that contribute to both innate and cell-intrinsic immunity against viral infections. Bastard P et al. found that at least 10.2% patients (101 in 987) with life-threatening COVID-19 had neutralizing IgG autoantibodies against type I IFNs, including IFN-ω and IFN-α [16]. These autoantibodies were not found in 663 individuals with asymptomatic or mild COVID-19. Thus, the occurrence of anti-IFNs autoantibodies were associated with the life-threatening, via neutralize the ability of the corresponding type I IFNs to block SARS-CoV-2 infection. The results suggested that convalescent plasma with anti-IFNs positive should be excluded from treatment for ongoing clinical trial.

There are also other autoantibodies were found in COVID-19, such as autoantibodies against red blood cell [17], anti-neutrophil cytoplasmic antibodies (ANCA) [5], anti-cyclic peptide containing citrulline (CCP) antibody [18]. Taken together, various autoantibodies were found in COVID-19, the existing autoantibodies might be associated with the severity of illness and autoimmune symptoms. The convalescent plasma should be tested for autoantibodies before their plasma donations are accepted. Notably, due to the multiple peptide sequence sharing between SARS-CoV-2 spike glycoprotein and the human proteins have been found, molecular mimicry has been proposed as a cause of the autoimmune phenomena observed in COVID-19 [19]. Therefore, one of the potential side effects of giving a mass vaccine could be an mergence of autoimmune diseases especially in individuals who are genetically prone for autoimmunity [20]. Thus, these peptide epitopes which are similarities to the human constiuantes should be consider or avoid in vaccine production.

Declaration of Competing Interest

The authors declared that there are no conflicts of interests.

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Table 1
The information of ANAs data in COVID-19 patients from different cohorts.

Male/ Female	Age range	Hospital / Country	Positive rate	Patients type
12/8	42–85	Huangshi Central Hospital, Hubei / China	50%	critical ill COVID-19 patients
21/8	43–85	Evangelismos Hospital, Athens /Greece	34.5%	severely ill covid-19 patients
17/16	22–90	Azienda Ospedaliero-Universitaria Bologna / Italia	33.3%	consecutive patients with COVID-19

Table 2
The information of aPL data in COVID-19 patients from different cohorts.

Male/ Female	Age range	positive rate of aPL and its subtypes	Patients type
10/9	36–80	aPL: 52.6%; LA: 5.3%; aCL: IgA 31.6%; IgG 10.5%; IgM:5.3% aβ2GPI: IgA 36.8%; IgG 31.6%	Critically ill COVID-19 [7]
Total: 56	Not provided	aPL: 48.2%; LA: 45%; aCL or aβ2GPI: 10%	COVID-19 patients [8]
24/11	19–83	LA: 91%	COVID-19 patients with a prolonged aPTT (≥30s) [9]
97/75	25–95	aPL:52%; aPS/PT: IgG: 24%; IgM 18%; aCL: IgG 4.7%; IgM 23%; IgA 3.5% aβ2GPI: IgG 2.9%; IgM 5.2%; IgA 4.1%	COVID-19 patients [10]
60/62	Age (mean ± SD): 54.3 ± 19.3	aPL: 43.4%; LA: 22.2%; aCL: IgG 13.4%; IgM 2.7%; IgA 1.7% aβ2GPI: IgG 6.3%; IgM 7.1%; IgA 3.3%	53 hospitalised and 69 home-quarantined patients [11]
9/12	54–67	aPL: 57.1%; aPS: IgG 0; IgM 0; aCL: IgG 9.5%; IgM 14.3% aβ2GPI: IgG 4.8%; IgM 0; aPT: IgG 0; IgM 14.3%	severe or critical COVID-19 [12]
34/34	LA negative 50.45 ± 20.19; LA positive: 64.77 ± 13.84	LA: 44.1%; aCL: IgG 0; IgM 1.6% aβ2GPI: IgG 0; IgM 1.7%	COVID-19 patients [13]
21/8	43–85	aPL: 55.2%; aCL: IgG 24.1%; IgM 10.3%; aβ2GPI: IgG 17.2%; IgM 27.6%	severely ill covid-19 patients [5]
17/16	22–90	aPL: 24.2%; aCL: IgG 9.1%; IgM 15.2%; aβ2GPI: IgG 6.1%; IgM 6.1%	consecutive COVID-19 patients [6]

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Zhao-wei Gao, Hui-zhong Zhang, Chong Liu, Ke Dong*
Department of Clinical Diagnose, Tangdu Hospital, Air Force Medical University, Xi'an, Shanxi 710038, China

* Corresponding author.
E-mail address: tdjyk3@fmmu.edu.cn (K. Dong).