Letter to the Editor

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Serum prealbumin deserves more significance in the early triage of COVID-19 patients

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To the Editor

Recently, comprehensive analyses of laboratory findings in COVID-19 have been reported in *Lancet* [1] and *JAMA* [2]. According to these findings, C-reactive protein (CRP) has been reported as a sensitive inflammatory biomarker for the initial screening of COVID-19. Clinical practice guidelines indicated that routine blood tests and CRP should be performed first in COVID-19 suspected cases on admission [3]. However, CRP is highly aspecific to effectively identify the COVID-19 patients among patients with fever or cough [4].

Given that fever and cough are the earliest common symptoms of COVID-19 [5, 6], the hospital has established rigorous procedures to segregate patients with fever or cough and to prevent a further outbreak of COVID-19 in China. According to our previous study, we found that serum prealbumin, a negative acute phase protein, exhibited a significant change in the early stage of SARS-CoV-2 infection [7]. Prealbumin, which is also known as transthyretin, is mainly produced by the liver, and is consumed in inflammatory responses [8, 9]. Prealbumin levels are significantly downregulated when stimulated by acute

phase cytokines, such as interleukin-6 (IL-6), which increase the synthesis of the positive acute-phase reactants, including CRP, serum amyloid-A and α 1-antitrypsin [10]. Thus, we suspect that prealbumin may be a good indicator in SARS-CoV-2 infection.

Here, we enrolled in 51 non-COVID-19 cases (patients merely had fever or cough symptoms) as the control group, and 31 confirmed COVID-19 patients. Prealbumin and CRP values from COVID-19 patients on admission were analyzed and compared with those of the control group. Baseline characteristics of patients in the two groups are shown in Table 1. Although the difference in serum CRP concentrations does not reach statistical significance between the groups (4.1 [1.31–14.69] mg/L vs. 15.2 [1.08–34.4] mg/L, Mann–Whitney U test, $p>0.05$), serum prealbumin was significantly decreased in COVID-19 patients on admission compared with the control group (141.4 [123.5–153.67] mg/L vs. 228 [193–263.5] mg/L, $p<0.001$, Mann–Whitney U test) (Figure 1A and B). Furthermore, prealbumin concentration had recovered to normal range after the patients recovered (Supplemental Table S1).

In addition, the ROC curve was used to analyse the clinical predictive value of prealbumin and CRP in COVID-19 patients (Figure 1C). The ROC curve results showed that prealbumin was more effective in predicting COVID-19 with an AUC of 0.94 at the best cut-off value of 176.5 mg/L, a sensitivity of 0.903, and a specificity of 0.863 (Supplemental Table S2). These findings suggest that prealbumin has a potential to be an effective biomarker and is more sensitive than CRP, for the early triage of COVID-19 patients.

In the early stage of SARS-CoV-2 infection, serum prealbumin decreased markedly in COVID-19 patients compared with the control group. Combined with common symptoms and epidemiology, prealbumin could act as a surrogate biomarker for the early triage of COVID-19. However, the reliability of this approach should be verified with more clinical data. This inflammation-related biomarker could be helpful to prevent the COVID-19 from spreading and it can be even more reliable and economical once widely applied in clinical laboratory.

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Table 1: Baseline characteristics of patients in COVID-19 group and control group.

	COVID-19 group (n=31)	Non-COVID-19 group (n=51)	p-Value ^a
Age, years			
Mean (SD)	40.45 (12.8)	29.3 (14.9)	0.001
≤39	14 (45%)	42 (82%)	
40–59	15 (48%)	6 (12%)	
≥60	2 (7%)	3 (6%)	
Sex			
Female	16 (52%)	26 (51%)	0.956
Male	15 (48%)	25 (49%)	
Common symptoms			
Fever	21/31	40/51	0.282
Cough	20/31	13/51	<0.001
Laboratory findings			
CRP, median (IQR) (0–5 mg/L)	4.1 (1.31–14.69)	15.2 (1.08–34.4)	0.1
>5 mg/L	15/31 (48.39%)	36/51 (70.59%)	
Prealbumin, median (IQR) (180–400 mg/L)	141.4 (123.5–153.67)	228 (193–263.5)	<0.001
<180 mg/L	28/31 (90.32%)	7/51 (13.73%)	

^ap-Values indicate differences between COVID-19 group and non-COVID-19 group. $p < 0.05$ was considered statistically significant.

Figure 1: Prealbumin and CRP in COVID-19 patients.

(A, B) Distribution of results of prealbumin and CRP in the two groups. © Prealbumin and CRP for diagnosing COVID-19 patients.

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Ethical approval: Research involving human subjects complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as revised in 2013), and has been approved by the authors' Institutional Review Board.

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