



## Commentary

## Eosinopenia as an early diagnostic marker of COVID-19 at the time of the epidemic

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The Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly worldwide since its outbreak in December 2019. COVID-19 may present with varying degrees of disease severity, from asymptomatic or mild upper respiratory illness to multiple organ failure with fatal outcome. SARS-CoV-2 is more contagious than SARS-CoV or the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Subsequently, isolation of suspected cases is of utmost importance to prevent the epidemic spreading. However, similar to SARS and MERS, fever and respiratory symptoms are not unique clinical manifestations of COVID-19 [1], despite that fever occurs in the majority (83% to 98%) of diagnosed COVID-19 patients [2]. While definitive diagnosis of COVID-19 requires a high degree of clinical understanding of its clinical characteristics with laboratory confirmation test of SARS-CoV-2 infection and typical pulmonary computed tomography abnormality, the initiative screening for COVID-19 mostly starts from fever clinics. Thus, it is critical for the fever clinic to efficiently triage suspected COVID-19 patients from other patients with similar symptoms, ideally to use a method that is accurate and yet be easily applicable. In this issue of EClinicalMedicine, Li and colleagues [3] reported that the combination of eosinopenia (defined as a reduction of circulating eosinophils  $<0.02 \times 10^9/L$ ) and elevated high sensitive C-reactive protein (hs-CRP,  $\geq 4.0 \text{ mg/L}$ ) can effectively triage suspected COVID-19 patients from other patients attending the fever clinic with COVID-19-like symptoms, with a positive predictive value at 72.7%. In other words, about 73% of the predicted suspected COVID-19 are true COVID-19 patients that were subsequently diagnosed via standard confirmation tests. This finding is particularly useful and helpful for patients triage at the time of an epidemic outbreak when large number of patients with COVID-19 or COVID-19-like symptoms are expecting confirmative nucleic acid tests

and/or radiographic examination, while related resources are limited. These two laboratory parameters could be particularly practical in certain underdeveloped regions and community clinics where simple blood tests may be the only available approach that can be used to help identify COVID-19 infection due to shortage of specialized equipment or reagents for nucleic acid tests, given that both eosinophil and hs-CRP can be included in routine blood tests.

It is intriguing that eosinopenia alone produced a sensitivity of 74.7% and specificity of 68.7% [3] for separating COVID-19 cases and controls (other patients with COVID-19 -like symptoms), suggesting its usefulness and presumably some kind of uniqueness for preliminary COVID-19 screening. It has been known that eosinopenia, a reduction in blood eosinophil count, typically accompanies the response to acute infection or acute stress [4] although the related mechanism remains inadequately understood. Eosinopenia has been shown to be a reliable maker of sepsis on admission to intensive care units, which is highly sensitive in distinguishing between noninfection and infection, and be more specific than C-reactive protein [5]. Similarly, in the study of Li and colleagues [3], the area under the receiver operating characteristic (ROC) curve for eosinopenia (0.717) is greater than that for hs-CRP (0.707), and the combination of the two (i.e. eosinopenia and hs-CRP) only slightly increased the area under the ROC curve to 0.730. This is indicative that eosinopenia alone may serve as a good early diagnostic marker of COVID-19 at the time of the pandemic. However, it is of note that eosinophil test was not specifically included in some early reports focusing on clinical characteristics of confirmed COVID-19 patients [1,2,6] despite that hs-CRP was usually tested. A few studies that tested eosinophil showed that eosinopenia occurred in 52% [7] to 53% [8] of confirmed COVID-19 patients. This relatively stable range of the presentation of eosinopenia (52%–53%) in confirmed COVID-19 cases may serve to further justify its usefulness in predicting COVID-19, especially when used with other parameters like hs-CRP or the optimal eosinophil cutoff value be established (e.g., eosinopenia defined as circulating eosinophils  $<0.02 \times 10^9/L$  vs.  $<0.01 \times 10^9/L$ ). While, further study is needed to answer whether or not eosinopenia may be associated with the severity or prognosis of COVID-19 [9].

It should be noted that there is currently increasing number of patients with biological drug-induced eosinopenia, during the treatment of specific diseases such as subsets of moderate and severe asthma and hypereosinophilic syndrome, and thus eosinophil responses during COVID-19 in these patients may be different [10].

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And, this particular aspect of eosinopenia was not addressed in the study of Li et al. [3] and deserves attention or further study.

#### Author contribution

Dr. Xia wrote the commentary

#### Declaration of Competing Interest

The author has nothing to disclose

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