

Eosinopenia could be a relevant prognostic biomarker in patients with coronavirus disease 2019

Letters to Editor,

The Editors underlined the extraordinary challenge provided by coronavirus disease 2019 (COVID-19) for the allergist/immunologist.¹ In particular, COVID-19 induces a particular immune response characterized by a specific pattern. In this regard, an intriguing relationship seems to exist among type 2 inflammations, including eosinophils, Angiotensin converting enzyme 2 (ACE2) expression, asthma, and allergic diseases. Consistently, eosinopenia has been proposed as a reliable biomarker in the triage of patients with COVID-19.² Eosinophils play a crucial role in orchestrating the immune response to fight viral infections, *viz.*, SARS-CoV-2.

Different mechanisms have been proposed, including the release of cytotoxic proteins, amplification of type 1 response, recruitment of CD8⁺ T lymphocytes, and clearance of viral load, so promoting recovery from viral infection.³ Interestingly, it has been demonstrated that allergic reaction was inversely related to ACE2 expression, such as allergen challenge reduced ACE2 expression.⁴ All these outcomes suggest that allergy, characterized by eosinophilia, could be a protective condition for COVID-19. In this regard, we recently reported that children and adolescents with COVID-19 are rarely allergic.⁵ Based on this background, we tested the hypothesis that the peripheral eosinophil count could be a reliable biomarker in patients with suspected COVID-19 during the preliminary clinical assessment in the hospital.

To this purpose, we retrospectively analyzed the clinical records of all patients with COVID-19 evaluated at the emergency department (ED) of the San Matteo Hospital, the hub hospital placed in the area where the first Italian COVID-19 pandemic cluster occurred. The time of observation lasted from the end of February to early May 2020. Globally, 909 patients (555 men; mean age, 69 years; interquartile range, 54–79 years) were evaluated. The patients were stratified according to intensity of care, such as discharged as paucisymptomatic, hospitalized in low-intensity care, in sub-intensive and intensive care, and deceased in the ED. The characteristic of patients and data concerning blood eosinophil count are shown in Table 1. Notably, the

median and mean values of peripheral eosinophils were very low in most patients with COVID-19. We also considered all the patients with COVID-19 during hospitalization (Table 2).

Further, mixed ordinal and logistic models were fitted with eosinophil count, age, and gender as explicatory variables in the fixed part, and with week of admission as a random intercept to take into account unmeasured confounders. The fixed part of the model is reported in Table 3. The eosinophil count was positively associated with being discharged from the ED (odds ratio 1.002) and negatively associated with higher-complexity ward admission (odds ratio 0.997), but they are not associated with death. Men and older patients had the worst outcome. The random part shows that random variability across the week was significant.

These outcomes underlined the reliable account provided by the blood eosinophil count during the admission procedure in the ED, mainly in discharged patients and patients who required high-intensity care. Impressively, eosinopenia was a common feature in most patients with COVID-19.

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Table 1 Comparison among the five groups of patients: did not require hospitalization, admitted to low-intensity care unit, admitted to subintensive care unit, admitted to intensive care unit, deceased in the emergency department

	Not Hospitalized (n = 300)	Low Intensity Care (n = 199)	Subintensive Care (n = 284)	Intensive Care (n = 83)	Deceased in the Emergency Department (n = 43)
Men, n (%)	161 (54)	122 (61)	180 (63)	67 (80)	25 (58)
Age, median (1st, 3rd quartiles), y	55 (45, 72)	77 (65, 85)	72 (60, 79)	65 (59, 69)	84 (79, 88)
Blood eosinophils, median (1st, 3rd quartiles), cells/ μ L	0 (0, 17.5)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Blood eosinophils, mean \pm standard deviation, cells/ μ L	26.73 \pm 59.49	23.12 \pm 93.90	10.49 \pm 32.5	11.08 \pm 35.89	16.74 \pm 56.35
Patients with eosinopenia (<20 eosinophils/ μ L), n (%)	225 (75)	170 (85)	250 (88)	71 (85)	38 (88)
Patients with complete absence of eosinophils, n (%)	184 (61)	163 (81)	242 (85)	68 (81)	36 (83)

Table 2 All deceased patients (in the emergency department plus after hospitalization) (n = 197)

Men, n (%)	132 (67)
Age, median (1st, 3rd quartiles), y	80 (73, 86)
Blood eosinophils, median (1st, 3rd quartiles), cells/ μ L	0 (0, 0.010)
Blood eosinophils, mean \pm standard deviation, cells/ μ L	16.90 \pm 90.75
Patients with eosinopenia (<20 eosinophils/ μ L), n (%)	180 (91)
Patients with complete absence of eosinophils, n (%)	172 (87)

Table 3 Effect of gender, age, and eosinophil count as outcome predictors

	Discharged		Higher Complexity Ward Admission		Death	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Men	0.56 (0.41–0.77)	<0.001	1.50 (1.16–1.94)	<0.001	1.69 (0.96–2.99)	0.073
Age	0.95 (0.94–0.97)	<0.001	1.04 (1.03–1.05)	<0.001	1.06 (1.04–1.09)	<0.001
Eosinophils ($\times 1000$) cells/ μ L	1.002 (1.000–1.005)	0.046	0.997 (0.995–0.999)	0.014	0.999 (0.995–1.001)	0.79

The data in bold represent the statistically significant results.

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