Eosinopenia: An early diagnostic marker of COVID-19

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INTRODUCTION

Coronaviruses have led to the outbreak of diseases in East Asia and the Middle East in the past decades. Lately, a new coronavirus virus has emerged in Wuhan, China, whose genome sequencing differs from previous strains and has been named severe acute respiratory syndrome CoV-2 (SARS-CoV-2) [1]. This virus strain causes COVID-19 (coronavirus disease 2019), which emerged at the end of 2019 [1]. COVID-19 was declared a global pandemic by the WHO on March 11, 2020 [2]. As of February 8, a total of 106,765,682 cases and 2,328,912 deaths have been reported by the WHO [3]. Previous studies have suggested an association between a decrease in the eosinophil count and acute respiratory diseases seen in COVID-19 infection [4-7]. The aim of our study was to find the association between the eosinophil count and COVID-19 in patients admitted as confirmed cases of COVID-19.

Eosinophils constitute 6% of bone marrow nucleated cells [8]. Eosinophils are potent proinflammatory cells, mainly because of the granules that contain cytotoxic proteins [9]. Although a blood cell, it is also present in various tissues, such as the gastrointestinal tract and the lungs [9,10]. Eosinopenia is the decrease in eosinophils, less than 0.01 × 109/L [11]. It has been found that the eosinophil count decreases during acute inflammation and increases during recovery from infection [12]. Since the emergence of COVID-19, there have been numerous reports of biomarkers involved in the disease, including C-reactive protein (CRP), interleukin-6 (IL-6), an increased ferritin level, the white cell count (WBC), lactate dehydrogenase (LDH), D-dimer, the platelet count, ALT, AST, an increased prothrombin time, high-sensitivity troponin, and renal markers [11]. Previous studies suggest that eosinopenia occurs as a response to acute inflammation or due to another systemic reaction
induced by its virtue. The initial decrease in the eosinophil count was attributed to the sequestration of circulating eosinophils. Migration may happen in an inflammatory site due to the release of chemotactic factors [11].

METHODS

Study Design and Participants

This was a cross-sectional study that included 35 patients with COVID-19, confirmed either by RT-PCR or HRCT, prior to the initiation of any treatment. Patients with a CO-RADS score of 4, 5, and 6 in HRCT were considered positive. Critically ill patients and patients who were suspected cases of COVID-19 were excluded. The study was approved by the institutional ethical committee. Informed consent was not taken as this study included only routine evaluation. Information regarding demographics, clinical manifestations, vitals, laboratory data, and clinical progression of the disease and treatment were collected.

Statistical Analysis

Categorical variables were reported as numbers and percentages.

RESULTS

All 35 patients collected were cases of COVID-19, confirmed either by RT-PCR or HRCT. The median age was 62 years. Among them, 7 patients belonged to the age group of 30–49 years, 16 to the age group of 50–69 years, and 10 to the age group of 70–89 years (Fig. 1). 27 were males and the remaining 8 were females (Fig. 2). A majority of the patients presented with fever, dry cough, and myalgia. Other symptoms included a sore throat, dyspnea, and anosmia. 26 patients (74.3%) were found to have an eosinophil count of zero, 6 (17.1%) were found to have an eosinophil count of 1–2, and 1 (2.9%) had an eosinophil count of 4 (Fig. 3).

DISCUSSION

Coronaviruses are highly enveloped, positive-sense RNA viruses with a high mutation rate and infectivity [1]. They are important zoonotic pathogens infecting animals and humans [1]. The clinical features may vary from asymptomatic through severe acute respiratory distress to multiorgan failure and death [13,14]. Even if the patient is asymptomatic, they are still capable of transmitting the virus [13]. The clinical manifestations include fever, myalgia, dry cough, a sore throat, headache, dyspnea [13,14], as well as severe manifestations such as hypoxemia, confusion, chest pain, and pneumonia, with some cases requiring intensive care unit (ICU) admission and mechanical ventilation. Diarrhea, anosmia, and ageusia have also been reported in several studies [15,16].

There is the emergence of interest in the topic of eosinopenia as a biomarker of COVID-19 infection [11]. A response to acute inflammation causes the release of chemotactic factors into circulation, leading to a rapid and persistent decrease in circulating eosinophils [11,14,17]. There is also an association of adrenal corticosteroids and epinephrine, as it increases in acute stress, with the occurrence of eosinopenia [13].
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Human eosinophils may express toll-like receptors (TLR) such as TLR3, TLR7, and TLR9 that can detect molecular patterns [9,18]. TLRs may help eosinophils to identify coronaviruses and lead to degranulation, the release of cytokines, and nitric oxide (NO) production [9]. Previous studies show a direct antiviral effect of nitric oxide on parainfluenza virus and RSV [9,19]. Eosinophils may also produce extracellular DNA traps in response to viral diseases such as RSV [9]. Eosinophils may mobilize preformed granules of Th1 cytokines, such as IL-12 and IFN-g, which helps in the antiviral immune response [9,20]. Human eosinophils express MHC-II molecules and costimulatory molecules and may also act as antigen-presenting cells for viral antigens, thereby causing T-cell activation and the release of cytokines [9].

EOSINOPENIA IN COVID-19

The cause of the decrease in eosinophils in COVID-19 is multifactorial [9]. The development and maturation of eosinophils occur in the bone marrow under exposure of myeloid precursors to IL3, GM-CSF, and IL5 [11]. The suggested pathophysiology of eosinopenia includes the decrease in IL-3, IL-5, and GM-CSF, leading to a decrease in the eosinophil count, as these three cytokines regulate the production of white blood cells, and resulting in sepsis [11]. Other mechanisms are the inhibition of eosinophils from the bone marrow and eosinophil apoptosis due to type 1 interferon release during acute infection [9]. Coronaviruses target IL-33, which is responsible for the activation of eosinophil in the airways, bone marrow, and ciliated epithelial cells. IL-33 is also involved in group 2 innate lymphoid cell activation, which in turn produces IL-5 and IL-13 [21]. Previous studies have found no increase in the eosinophil count in the lung tissue in COVID-19 patients [9,22].

Li et al. conducted a study on 989 confirmed cases of COVID-19, in which eosinopenia (<0.02109/L) was present in 74.7%, compared to the controls (31.3%) [4]. Bass et al., by using chemotactic factors of acute inflammation, were able to induce a decrease in the eosinophil count in rabbits and in humans. In a study conducted by Hu Yun et al., out of 32 COVID-19 patients, 66% showed a decreased eosinophil count [7].

CONCLUSION

Because COVID-19 follows an unpredictable course and may lead to deadly complications, there is a need for its early identification. The eosinophil count may be used as its early and low-cost indicator. In our study, around 71.4% of the hospitalized patients had an eosinophil count of zero at the time of admission. The estimation of the eosinophil count may help in early therapeutic management. However, only several studies have been done in this regard. The relationship between the eosinophil count and COVID-19 infection needs more exploration.

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Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.
ABBREVIATIONS

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
COVID-19: coronavirus disease 2019
WHO: World Health Organization
RT-PCR: reverse transcriptase polymerase chain reaction
HRCT: high-resolution computed tomography
CO-RADS: COVID-19 Reporting and Data System
CRP: C-reactive protein; WBC: white blood cell; LDH: lactate dehydrogenase; ALT: alanine transaminase; AST: aspartate aminotransferase
RNA: ribonucleic acid; DNA: deoxyribonucleic acid
TLR: toll-like receptor; NO: nitric oxide; IFN-γ: interferon gamma; GM-CSF: granulocyte-macrophage colony-stimulating factor; IL: interleukin
RSV: respiratory syncytial virus
MHC: major histocompatibility complex

REFERENCES