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Eosinopenia in COVID-19 Patients

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ABSTRACT

Background: COVID-19 is diagnosed primarily by direct detection of SARS-CoV-2 RNA by Nucleic Amplification Tests, most commonly Reverse Polymerase Chain Reaction (RT-PCR) from the upper respiratory tract. The reporting of the result has been time consuming due to the global crisis during this pandemic. In this study, the complete blood count of COVID positive patients showed Eosinopenia. It appeared as a low-cost warning test for COVID-19. Eosinopenia as a biomarker is a promising observation in COVID-19 infection and requires further exploration.

Objective: To study the relationship between Eosinophil count and COVID-19 in patients admitted at Dr. B.R Ambedkar Medical College and Hospital, Bangalore.

Material and methods: This is an observational study conducted on COVID-19 patients in Dr. B.R Ambedkar Medical College and Hospital, Bengaluru. Eosinophil count was calculated using Coulter method.

Results: Eosinopenia was observed in 146 out of 186 COVID- 19 patients.

In patients with mild disease 68% had Eosinopenia, 93% with moderate disease, 97% with severe disease and all of them i.e 100% with very severe disease had Eosinopenia. In patients who succumbed to COVID-19, the count was very low. As the patients improved, they showed an increase in the count.

Conclusion: Eosinopenia can provide an early aid in the diagnosis of COVID 19. Our study showed Eosinopenia in 78.5% of the COVID-19 positive cases. As the disease severed, there was no increase in the count. Patients whose condition improved showed an increase in the count which suggested that Eosinophil count can be used as a biomarker for disease progression.

Keywords: COVID-19, Early Biomarker, Eosinopenia.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), was first noted as a cluster of cases of pneumonia of unknown cause in Wuhan City, Hubei Province, China, in December 2019.[1] COVID-19 has spread globally and was declared a pandemic by the World Health Organization on March 11, 2020.[2]

The clinical diagnosis of COVID-19 is confirmed by laboratory testing with a reverse-transcription polymerase chain reaction (RT-PCR) assay, which remains a challenge due to limited test availability, variable turnaround time, and the unreliable availability of rapid RT-PCR kits. In many hospitals, test results may take days to return.

Other laboratory values that shows strong indications in COVID-19 infection include lymphopenia,

prolonged prothrombin time (PT), elevated lactate dehydrogenase (LDH), elevated alanine aminotransferase (ALT), elevated IL-6 and elevated ferritin levels. Elevated elevated D-dimer, elevated neutrophils, Eosinopenia, elevated C-reactive protein (CRP), aspartate aminotransferase (AST), and elevated troponin (including high sensitivity troponin had been implicated in most cases.

In our study, Eosinopenia was considered as a marker for the study and it was observed that 146 patients out of 186 had Eosinopenia.

A similar study conducted by Li Ka Shing, Faculty of Medicine, The University of Hong Kong, Hong Kong, SAR, China observed Eosinopenia as an early diagnostic marker of COVID-19 at the time of the epidemic[3].

Due to low cost and turn over time, this marker was used for prognosis as well. Patients with very low Eosinophil count had a poor prognosis, in patients who improved , there was a raise in the Eosinophil count.

MATERIALS AND METHOD:

Study subjects: The study was conducted in 186 confirmed COVID-19 cases admitted in Dr. B.R Ambedkar Medical College and Hospital, Bengaluru.

Inclusion criteria:

All the patients above 18 years of age

Exclusion criteria:

Below 18 years of age

Subjects non willing to participate in the study

METHOD:

Eosinophil count were determined by the Coulter counter method.

Blood samples for Eosinophil count were collected on admission for all the patients.

Repeat blood sample for determining the Eosinophil count was drawn weekly for all the patients admitted in ICU.

Normal range of Eosinophil count as per our lab: 1% to 6% per high power field. <1% is considered as Eosinopenia

RESULTS:

A total of 186 COVID 19 patients' data was collected.

It was observed that, 78.5% COVID-19 positive patients had Eosinopenia (i.e., 146 out of 186)

Distribution of the 146 patients with Eosinopenia with different disease category can be seen in "Table 1: Patients distribution as per severity of Disease".

Out of 186 COVID-19 patients, 111 were with mild disease. Out of these 111 patients, 75 (68%) had Eosinopenia & the remaining 36 (32%) did not have Eosinopenia as shown in "Figure 1: Patients with Mild Disease".

40 Patients had moderate disease. Among them, 37 (93%) had Eosinopenia & the remaining 3(7%) had no Eosinopenia as shown in "Figure 2: Patients with Moderate Disease".

29 Patients had Severe Disease. Among them, 28 (97%) had Eosinopenia & the remaining 1 patient had no Eosinopenia as shown in "Figure 3: Patients with Severe Disease".

6 Patients had Very Severe Disease. 100% of them had Eosinopenia as shown in "Figure 4: Patients with Very Severe Disease".

It was observed that, as the disease severity progressed among the patients, the Eosinophil count decreased.

The ICU patients with very severe disease who succumbed to death did not have any improvement in their Eosinophil count.

We also observed that, there was no correlation between the Age of the patients and Eosinopenia as shown in "Graph 1: Age v/s Eosinopenia correlation".

DISCUSSION:

Eosinophils are circulating and tissue-resident leukocytes that have potent proinflammatory effects in a number of diseases. Recently, Eosinophils have been shown to have various other functions, including immunoregulation and antiviral activity.

Eosinophil level is clinically relevant because Eosinophils are potent proinflammatory cells, primarily due to their preformed granules, which are packed with cytotoxic proteins, including major basic protein (one of the most basically charged molecules

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in the body), Eosinophil peroxidase, and 2 RNAses (Eosinophil cationic protein and Eosinophil neurotoxin). In addition to their proinflammatory effects, evidence is emerging, albeit primarily in mice, that Eosinophils have pleotropic roles as regulatory cells involved in protective immunity, including antiviral responses and shaping diverse physiological responses, such as organ development and metabolism. Although Eosinophils are normally considered blood cells, they reside in various tissues. Most notably, Eosinophils reside in the gastrointestinal tract, which is their primary residence, and the lung, where a population of regulatory Eosinophils, which have unique features compared with inflammatory Eosinophils, has been identified .[4]

The role of Eosinophils in mucosal immune responses in the respiratory tract has largely focused on the detrimental impact that these cells can have in inflammatory responses due to their potent proinflammatory function. However, preclinical studies (mainly in mice) have shown that Eosinophils are equipped with an assortment of molecular tools that enable them to recognize, respond, and orchestrate antiviral responses to respiratory viruses.

Human Eosinophils express several endosomal Toll-like receptors (TLRs), including TLR3, TLR7, and TLR9, that detect viral microbe– associated molecular patterns [6,7,8]

TLR7 enables Eosinophils to recognize single-stranded RNA viruses such as Coronavirus and stimulating this receptor in human Eosinophils triggers Eosinophil cytokine production, degranulation, superoxide and nitric oxide (NO) generation, and prolonged cellular survival.

Eosinopenia is defined as a decrease in the number of circulating Eosinophils.

Eosinopenia has been shown to be a reliable maker of sepsis on admission to intensive care units, which is highly sensitive in distinguishing between non infection and infection which is more specific than C-reactive protein [9].

The pathophysiology for Eosinopenia in COVID-19 remains unclear but is likely multifactorial, involving inhibition of Eosinophil egress from the bone marrow, blockade of Eosinophilopoiesis, reduced expression of chemokine receptors/adhesion factors, and/or direct Eosinophil apoptosis. Postmortem analysis of lung tissue from a patient who died from COVID-19 demonstrated signs of acute respiratory distress syndrome that was dominated by inflammatory infiltrates.[10]

We categorized the patients into Mild, Moderate, Severe & Very Severe based on the criteria explained under "Table 2: Disease Category". We observed that Eosinophil count dropped in most of the patients. Further to that, it was observed that, the drop was more dramatic in patients with moderate and severe to very severe disease. We did not observe an improvement in the Eosinophil count in patients who had critical illness and in those who succumbed to death. In patients who were discharged, there was an improvement in the count. So this suggested that Eosinophil count could be used as a biomarker for disease progression.

CONCLUSION:

Our study showed 146 out of 186 COVID 19 patients had Eosinopenia. As the severity of the diseased progressed there was no improvement in the Eosinophil count and in discharged patients, there was an improvement in the Eosinophil count.

Early diagnosis of Coronavirus disease 2019 (COVID-19) and patient isolation are important for both individual patient care as well as the disease containment. The diagnosis by testing the viral RNA with a Polymerase Chain Reaction Assay, has a limited availability, variable turnaround time but the Eosinophil count, which is readily obtained from a routine complete blood cell count (CBC), may provide actionable clinical information to aid in the early recognition of COVID-19 in patients, and as well provide prognostic information.

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TABLES:

Disease Category	No. of Patients with Eosinopenia
Mild	75 out of 111
Moderate	37 out of 40
Severe	28 out of 29
Very Severe	6 out of 6
Grand Total	146

Table 1: Patients distribution as per severity of Disease

Disease Category	Symptoms	Respiratory Rate Cycles /Minute	SpO2 % at Room Air
Mild	Fever, URTI symptoms, Anosmia, Loss of Taste, Myalgia	< 24	>94%
Moderate	Pneumonia, No signs of severe disease	>24 & <30	> 90% & < 94%
Severe	Respiratory distress requiring mechanical ventilation	>30	<90%
Very Severe	Endotracheally intubated, Sepsis	>30	<90%

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Table 2: Disease Category

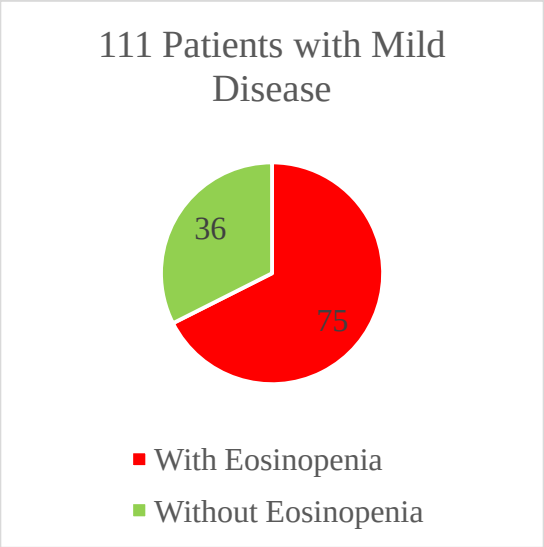

Figure 1: Patients with Mild Disease

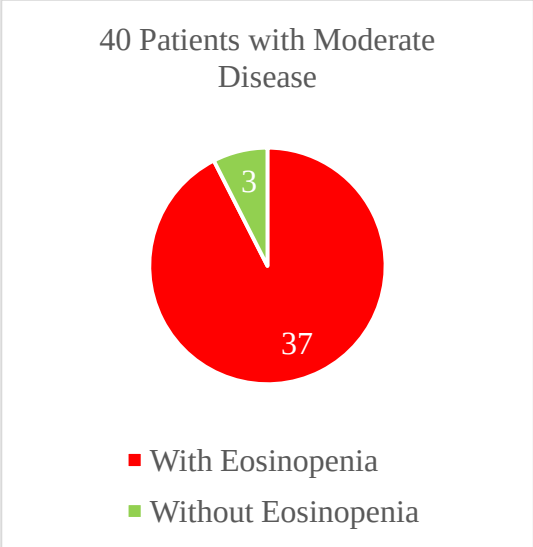

Figure 2: Patients with Moderate Disease

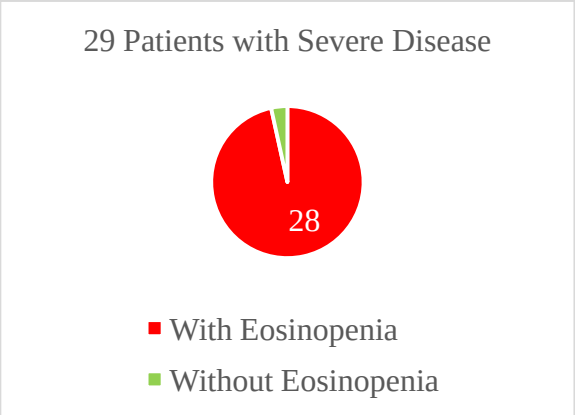

Figure 3: Patients with Severe Disease

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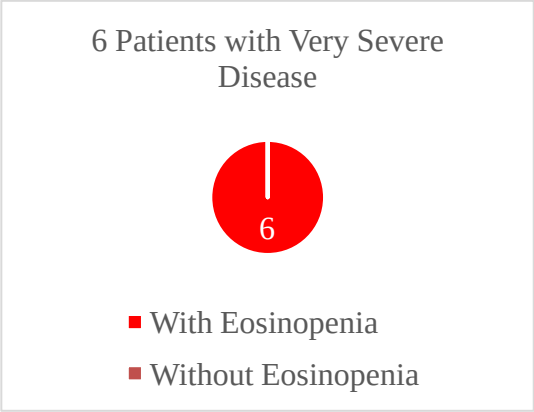
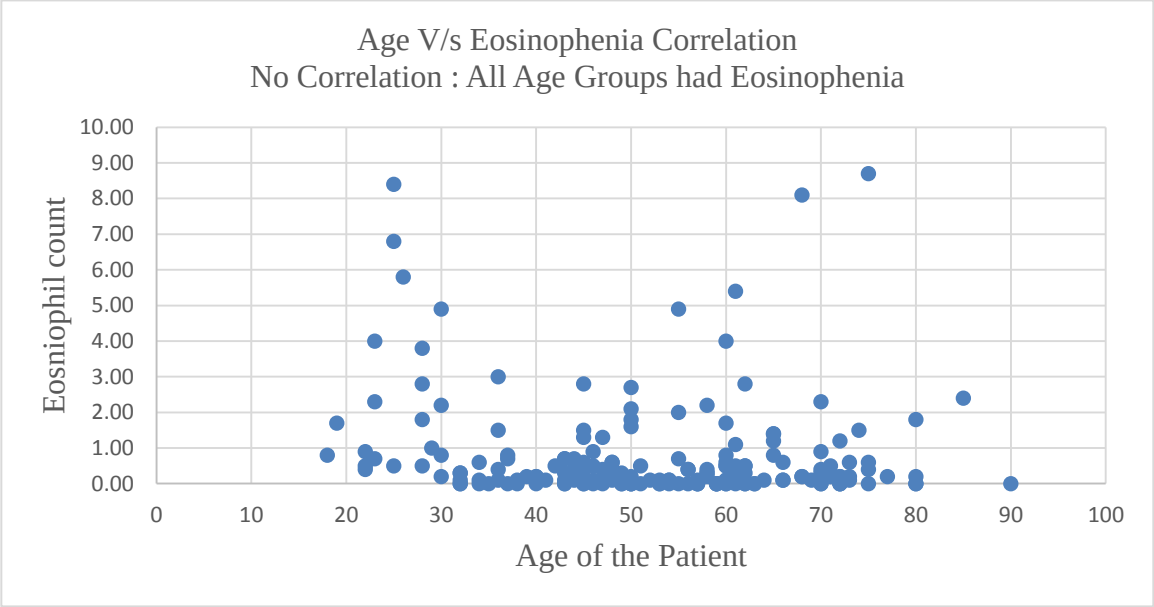


Figure 4: Patients with Very Severe Disease



Graph 1: Age v/s Eosinopenia correlation

Note: Ethical Committee Clearance obtained for this study

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