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Characteristics of peripheral Leukocyte in moderate infection of COVID-19

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Abstract:

Background: Blood leukocytes are an important part of the body's defense system, and infection status can be predicted by measuring WBC levels. COVID-19 may involve many organ systems in its host. Studies suggest that hematological profiles change during SARS-CoV-2 illness. **Patients and methods:** This study included 504 mild infected patients with confirmed COVID-19 infection, these study subjects were randomly selected irrespective of the age group and both genders were included, EDTA blood sample was collected for performing total and differential white blood cells (Diagon D-cell 60 hematology analyzer Europe-Diagon Ltd. Hungary). **Results:** The present study included patients aged from14 years to 75 years mean age was 44.5 ±30.5 who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, female gender was more frequent (n=280, 55.6%) than Male gender (n=224, 44.4%). This study reveals normal total WBCs count in 320 patients (63.5%), neutrophilia with a sensitivity of 77.8%, and lymphopenia with a sensitivity of 73%. **Conclusion:** Neutrophilia has a sensitivity of 77.8% and lymphopenia has a sensitivity of 73% for diagnosis or prognosis of mild infection of COVID-19 patients (Outpatients and patients under home observation).

Keywords: COVID-19, WBCs, neutrophilia, lymphopenia, biomarker.

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1. Introduction:

The coronavirus disease 2019 (COVID-19) outbreak began in early December 2019 in Wuhan, China [(1)], the WHO officially named the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as COVID-19 and then officially declared the COVID-19 outbreak a pandemic on March 11, 2020 (WHO, 2020) [(2)].

The previous study mainly focused on the immune dysfunction caused by severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), respectively. Coronavirus infections (SARS and MERS) are confirmed to activate both innate and adaptive immune responses [(3,4)]. Simply it means that the changes in peripheral blood cells could reflect the immune damage caused by virus infection.

In mild cases, immune responses were efficiently established to curb the viral replication, while in severe cases, uncontrolled inflammation and microcirculation

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dysfunctions together lead to viral sepsis with immunologic impairment [5]. As components of blood routine tests available for almost all hospitalized patients, PBICs usually serve as practical markers in infectious diseases. Indeed, leukocytosis, leukopenia, and lymphopenia have been reported to be commonly seen in COVID-19 patients [6].

Blood leukocytes are an important part of the body's defense system, and infection status can be predicted by measuring WBC levels [7]. COVID-19 may involve many organ systems in its host. Studies suggest that hematological profiles change during SARS-CoV-2 illness. Neutrophils are involved in early anti-viral defense. However, during severe pneumonia, neutrophils become cytotoxic through degranulation and lysis [8]. Studies have suggested that neutrophil recruitment may exacerbate COVID-19 immunopathology [9].

Lymphocytes play a crucial role in maintaining immune homeostasis during virus infection, especially SARS-CoV-2[10], among hematological parameters, lymphopenia is associated with disease severity; patients who have died from COVID-19 have had significantly lower lymphocyte counts than survivors. Repletion of lymphocytes may be an important factor for recovery [11] (Henry, 2020).

Thus, the differentiation of peripheral white blood cells may indicate the immunologic impairment at the early stage of the disease. So, this study was performed to assess the value of peripheral total white blood cells, neutrophils, and lymphocyte cells in mild infection of COVID-19 patients, this study included outpatients and patients under home observation, while hospitalized patients are not included in this study.

2. Patients and methods

2.1. **Study population Patients**

This study included 504 hospitalized patients with confirmed COVID-19 infection, these study subjects were randomly selected irrespective of the age group and both genders were included.

It was performed following the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All the studied population was informed about the purpose of sample collection. Patients were free to refuse to include in this study.

2.2. Data collection

In this cross-sectional study, we obtained data regarding 504 hospitalized patients with confirmed COVID-19 via real-time reverse transcription-polymerase chain reaction (PCR), they came to Alyameny laboratory in Alexandria, Egypt for biomarkers and complete blood count investigations**,** and reviewed the medical records and compiled data between August 12 and December 30, 2020.

2.3. Collection and processing of blood samples:

EDTA blood sample was collected for performing complete blood count and platelet count (Diagon D-cell 60 hematology analyzer Europe-Diagon Ltd. Hungary) on 504 Positive COVID-19 patients for individuals matching in age and gender.

2.4. Assay procedure as manufactory instructions:

Diagon D-cell 60 hematology analyzer Europe-Diagon Ltd. Hungary was used for white blood cell count, considered normal WBCs count: $4 – 10 \times 10^9$/L, normal neutrophils: 45- 70%, and normal lymphocytes: 20-45%

2.5. Statistical analysis

Data were analyzed using SPSS statistical software, version 20.0(SPSS, Chicago, Illinois, USA). All continuous data are presented as means and standard deviations, while categorical data are presented as numbers and percentages. A sensitivity analysis was performed to analyze relationships between COVID-19 infected patients and WBCs, neutrophils, and lymphocytes count.

3. Results:

The present study included patients aged from14 years to 75 years mean age was 44.5 ±30.5 who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, the female gender was more frequent (n=280, 55.6%) than the Male gender (n=224, 44.4%).

Table (1): shows the percentage of COVID-19 mild infected patients (out hospitalized and home observation Patients) concerning total white blood cells count, this study reveals normal WBCs count in 320 patients (63.5%), low WBCs count in 40 patients (7.9%), and high WBCs count in 144 patients (28.6%).

Table (2): shows the percentage of COVID-19 mild infected patients (out hospitalized and home observation Patients) concerning neutrophils count, This study reveals normal neutrophils count in 112 patients (22.2%), there were no infected patients with low neutrophils count, and high neutrophils count in 392 patients(77.8%), then the high-level of neutrophils has a sensitivity of 77.8%, it was a significant biomarker for COVID-19 diagnosis or prognosis in out-hospitalized patients (Outpatients and patients under home observation).

Table (3): shows The percentage of COVID-19 mild infected patients (out hospitalized and home observation Patients) concerning lymphocytes count, This study reveals normal lymphocytes count in 112 patients (22.2%), low lymphocytes count in 368 patients(73%), and high lymphocytes count in 24 patients(4.8%), then the low-level of lymphocytes has a sensitivity of 73%, it was a significant biomarker for COVID-19 diagnosis or prognosis in out-hospitalized patients (Outpatients and patients under home observation).

Table (1): Association between WBCs count and mild infection of COVID-19 Patients

COVID-19 POSITIVE Patients	WBCs count						Total	
	Low level		Normal		High-level			
	No.	%	No.	%	No.	%	No.	%
Male	-	-	168	52.5	56	38.9	224	44.4
Female	40	100	152	47.5	88	61.1	280	55.6
Total	40		320		144		504	

Normal WBCs count 63.5%, low 7.9%, and high 28.5%

Table (2): Association between neutrophils count and mild infection of COVID-19 Patients

COVID-19 POSITIVE Patients	Neutrophils count						Total	
	Low level		Normal		High-level			
	No.	%	No.	%	No.	%	No.	%
Male	-	-	56	50	168	42.9	224	44.4
Female	-	-	56	50	224	57.1	280	55.6
Total			112		392		504	

High neutrophils count 77.8 %

Table (3): Association between lymphocytes count and mild infection of COVID-19 Patients

COVID-19 POSITIVE Patients	Lymphocytes count						Total	
	Low level		Normal		High-level			
	No.	%	No.	%	No.	%	No.	%
Male	152	41.3	72	64.3	-	-	224	44.4
Female	216	58.7	40	35.7	24	100	280	55.6
Total	368		112		24		504	

Low lymphocytes count 73%

4. Discussion:

COVID-19 is an acute infectious disease caused by SARS-CoV-2. Most patients experience clinical symptoms, but some patients have no symptoms and are known as asymptomatic patients, the hematological changes may reflect a homeostatic mechanism to prevent systemic over-activation of inflammation.

This study was conducted on 504 mild infected COVID-19 patients (out hospitalized and home observation Patients) who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, this study reveals a normal count for monocyte cells, eosinophil cells, and monocyte cells. But total WBCs were normal in 320 patients (63.5%), low WBCs count in 40 patients (7.9%), and high WBCs count in 144 patients (28.6%), Gao et al., 2020 reported that total white blood cell count was normal in all 43 cases (28 milds, 15 severe) [(12)], also Li et al., reported WBCs count was normal in all 54 cases [(13)], another study (meta-analysis) by Li et al., (2020b) on 1994 cases showed low WBCs count in

29% of cases[14], Huang et al., 2020 reported high WBCs count in all 13 ICU cases[15].

This study showed normal leukocyte count at 63.5%, leukopenia at 7.9%, leukocytosis at 28.6%, while neutrophilia has a sensitivity of 77.8% and lymphopenia has a sensitivity of 73% in mild COVID-19 infection which was less than CRP has a sensitivity 90.2%[16], while other biomarkers have different sensitivity in mild COVID-19 infection as ferritin which has a sensitivity of 71.4% [17], LDH has a sensitivity 67.7%[18], and D-dimer has a sensitivity 36.4%[19].

Neutrophils are immune cells that are well known to be present in various lung diseases, including viral respiratory disease [20]. As a hallmark of the pathophysiology, it is widely accepted that neutrophils can exit the circulation into the airways, either through the postcapillary venule in the systemic circulation or through the capillary in the pulmonary circulation [21,22], this study showed high neutrophils count or neutrophilia has a sensitivity of 77.8% as a biomarker for COVID-19 diagnosis or prognosis in mild infected COVID-19 patients (Outpatients and patients under home observation).

Neutrophils are involved in early anti-viral defense. However, during severe pneumonia, neutrophils become

cytotoxic through degranulation and lysis [23], Huang et al., 2020 reported neutrophilia in 13 ICU cases [15], and Wu et al., (2020) reported neutrophilia in 201 ARDS cases[24], but a study by Liu et al., showed low neutrophils count in most cases [13].

Several cohort studies have reported that lymphopenia can predict prognosis in COVID-19 patients [25,26].

A study involving 90 hospitalized COVID-19 patients reported an association between lymphopenia and

disease severity [27], this study showed lymphopenia has a sensitivity of 73%, and it was a significant biomarker for COVID-19 diagnosis or prognosis in mild COVID-19 patients (Outpatients and patients under home observation).

Other studies showed Lymphopenia is a factor related to poor prognosis in disease development (Ruan et al., 2020; Yang et al., 2020) [28,29].

Chen et al., 2020a reported lymphopenia in 69% of cases (15 mild's, 9 severe, 5 critical) [30], while Huang et al., 2020 reported low lymphocyte count in ICU cases only [15], Zhang et al., 2020 reported lymphopenia in all 140 infected cases [31], another study (meta-analysis) by Li et al., (2020b) on 1994 cases showed lymphopenia in most cases [14], Liu et al., 2020 also reported lymphopenia in most cases[13], Mo et al., 2020 showed lymphopenia in all tested cases (70 mild's, 85 severe cases)[32],

The decreased production, apoptosis, and redistribution of lymphocytes may together lead to circulating lymphopenia [33].

Conflict of interest

There are no conflicts of interest.

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