Hematological and Coagulation Features of COVID-19Patients in Hodeidah, Yemen

Abstract :

Background : The blood parameters are very important for progressive of infection and predicator for severity .

Objectives: Therefore, the study aimed to describe the hematological and coagulation featuresof coronavirus disease 2019 (COVID-19) infection .**Methodology**: The study was designed in descriptive study (a case series). The study included 49 patients that were diagnosed clinically and confirmed by the real time – polymerase chain reaction (RT-PCR)with COVID-19. The study group were severe and critical cases that treated in isolation center (inpatient) .

Results :The results of 42/49 cases (85.7 %) patients had that leukocytosis pre - treatment with average of WBC 15.24 ± 6.18 ($\times 10^{9}$/L) . On the other hand, the WBCs count, which had reached a peak of 34 ($\times 10^{9}$/L) as maximum value . Also, lymphocytes decreased (lymphopenia) with COVID -19 infection to 1 % with average (8.75±6.92%). The neutrophils increased (neutrophilia) to 98 % with average (87.40±8.45%). In addition , the thrombocytopenia was reported in 2/49 cases (4.08 %), and low in hemoglobin (severe anemia) was reported in 5/49 case (10.20 %) . The coagulation tests revealed increased in d-dimer levels ($p< 0.05$) in severe and critical patients. On the other hand , the results showed normal in prothrombin time (PT) and partial thromboplastin (PTT) ($p> 0.05$).

Conclusion: The study concluded that neutrophils - lymphocytes ratio is good predicator for progressive and severity illness in COVID-19 infection .

Keywords :COVID-19 , Hematological, Hodeidah,Yemen

1.INTRODUCTION

The hematological parameters is very important for progressive of infection and predicator for severity.The highly contagious novel coronavirus, also known as coronavirus disease 2019

(COVID-19), was first reported in Wuhan, China, in December 2019[1]. COVID-19 is a disease caused by a novel coronavirus related to the virus that caused the SARS (severe acute respiratory distress syndrome) outbreak in 2002 (SARS-CoV) and Middle East respiratory syndrome (MERS) outbreak in 2012. It should be regarded as a systemic disease involving multiple systems, including cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic and immune system[2].Full blood count (FBC) is inexpensive and not difficult to perform. Included in the FBC are various values, including counts of leucocytes (neutrophils and lymphocytes) and thrombocytes, indices of erythrocytes, and certain ratios of these values. Of leucocytes, the neutrophils are the most distinctive and essential component of the immune system. The role of lymphocytes in infections is well evidenced. Moreover, thrombocytes have a crucial role in the regulation ofseveral inflammatory processes[3.4].

The clinical hematology laboratory plays an important role by providing the clinical team a number of useful prognostic markers [4]. Although information is in some cases based on the results of limited amount of data and should be validated with additional studies, the available findings clearly establish the clinical hematology laboratory as an important partner in the triage and management of affected patients.The results of a CBC can provide information about not only the number of cell types but can also give an indication of the physical characteristics of some of the cells. Also, these parameters play an important role in helping doctors to know these values in a true way so that they can come to a sound diagnosis [5].Therefore , the study aimed to describe the hematological features of COVID-19 infection .

2. METHODOLOGY

3.1. Study area

Center of Tropical Medicine and Infectious Diseases (CTMID), Al Thawara Public Hospital Authority, Hodeidah, Yemen from 1st June to 31st December 2020. Note : The area is endemic of vector – borne diseases (VBDs) such as the malaria , dengue and vaccine – preventable diseases (VBDs) that cause other infection (coinfection) to effect on hematological parametric [6-10].

3.2. Study design

This study was designed in a case series. It focuses on the patients who sought care at the emergency team, COVID-19 isolation department.

3.3. COVID-19 confirmation

49 severe and critical patients were confirmed and admitted in the COVID-19 isolation department, which was located at CTMID. Nasopharyngeal swabs were collected and confirmed by Real Time - Polymerase Chain Reaction (RT-PCR), oxygen saturation, radiological and hematological finding were tested [11-16].

3.4. Samples collection

Whole blood samples namely 49 (40 male and 9 female) were taken before treatment and collected into the ethylenediaminetetraacetic acid (EDTA) tube, and then sent to the clinical laboratory for analysis of standard clinical tests within two hours.

3.5. Hematological and blood coagulation assays

Hematological parameters namely RBC , WBC and Platelets were analyzed by Sysmex XE-5000 automated hematology analyzer (Sysmex, Japan).Also ,Prothrombin time (PT) , Partial Prothrombin Time (PTT) , International Normalized Ratio (INR) and d-Dimer were measured based on standards methods

3.6. Data analysis

The variables studied namely age and gender that were collected from triage area. Data on clinical symptoms , hematological and coagulation parameters by patients with severe and critical COVID-19 were recorded. Data were checked and entered in Statistical Package for Social Science (SPSS) and Microsoft Excel. The data were subsequently visualized using tables, graphs and text. Data were described through calculations of medians, ranges, frequencies and percentages. Comparisons between qualitative variables were analyzed using Chi-squared test.

1. RESULTS

3.1. Patients Characteristics

The background information of personal data on the 49 patients that were admitted in COVID-19 isolation department , CTMID , AL Thawarah Public Hospital Authority in Hodeidah, Yemen and summarized in Table 1.

Table 1. Patients Characteristics of COVID-19

Variables	(n)	(%)	X^2	*p* – value
Gender				
Male	40	81.16	19.62	0.00001*
Female	9	18.36		
Total	49	100		
Age				
<15	3	6.12		
15-29	2	4.10		
30 -49	11	22.44	20.29	0.00044 *
50-59	17	34.69		
60+	16	32.65		
Total	49	100		
Clinical symptoms				
• Difficulty breathing	42	85.7		
• Fever	30	61.2		
• Cough	20	40.8	NA	
• Joints pains	16	32.65		
• Sore throat	14	28.6		
• Headache	3	6.12		
Total	49	100		
Severity illness				
Severe cases	21	42.85	NA	
Critical cases	28	57.14		
Total	49	100		
* Significant (*p* - value < 0.05)				

3.2. Hematological Characteristics

3.2.1. Red Blood Cells and Hemoglobin

Anemia was reported in 50 % of cases (10.4 ± 3.5) and bloodtherapy was transfused into 10.20 % of cases in their treatment ; however, the RBC don't changein response.

Table 2. Results of RBC count , Hb and PCV

Parameters	Mean ± SD (n = 49)	*p* value
RBC ($\times 10^{12}$/L)	4.34±0.95	
Median	4.45	$p< 0.05$
Rang	2.1-5.93	
Normal values	5.5±1.0	
Hb(g/dl)	10.84 ±2.16	
Median	10.8	$p<0.05$
Rang	6.4 -16.5	
Normal values	15.5 ± 2.5	
PCV (%)	34.19 ±5.94	
Median	34.01	$p< 0.05$
Rang	20.8 -46.3	
Normal values	37.5 ± 47.5	

3.2.2. White Blood Cells and Differential Count

The results of 42/49 cases (85.7 %) patients had that leukocytosis pre - treatment with average of WBC 15.24 ± 6.18 ($\times 10^{9}$/L). On the other hand, the WBCs count, which had reached a peak of 34 ($\times 10^{9}$/L) as maximum value . Also, lymphocytes decreased (lymphopenia) with COVID -19 infection to 1 % with average (8.75±6.92%). In addition, neutrophils increased (neutrophilia) to 98 % with average (87.40±8.45%).

Table 3. Results of WBC and Differential Count Parameters

Parameters	Mean ± SD (n = 49)	*p* value
WBC($\times 10^{9}$/L)	15.24±6.18	$p<0.05$
Median	14.7	
Rang	5.6-34.0	

Normal values	3.5±7.5	
Neutrophil (%)	87.40 ± 8.45	$p<0.05$
Median	90	
Rang	60-98	
Normal values	40-75	
Lymphocyte (%)	8.75 ± 6.92	$p<0.05$
Median	6	
Rang	1-32	
Normal values	20-45	
Monocyte (%)	2.61 ± 2.32	$p> 0.05$
Median	3	
Rang	00-12	
Normal values	2-10	
Eosinophil (%)	1.02 ± 1.13	$p> 0.05$
Median	1	
Rang	0-5	
Normal values	1-6	
Basophil (%)	0.06±0.31	$p> 0.05$
Median	0	
Rang	0-2	
Normal values	0-1	

3.2.3. Platelets Count

Platelet count was found in normal range in 40/49 case (81.63 %) of COVID-19 patients. 3/49 (6.12 %) of patients indicated into severe thrombocytopenia (death).On the other hand , 6/49 of cases (12.24) had increase in the platelets .

Table 4. Results of Platelets Parameters

Parameters	**Mean ± SD (n = 49)**	***p* value**
Platelets ($\times 10^3$/ul)	313.55 ± 139.48	
Median	277	$p> 0.05$
Rang	75-450	
Normal values	150-400	

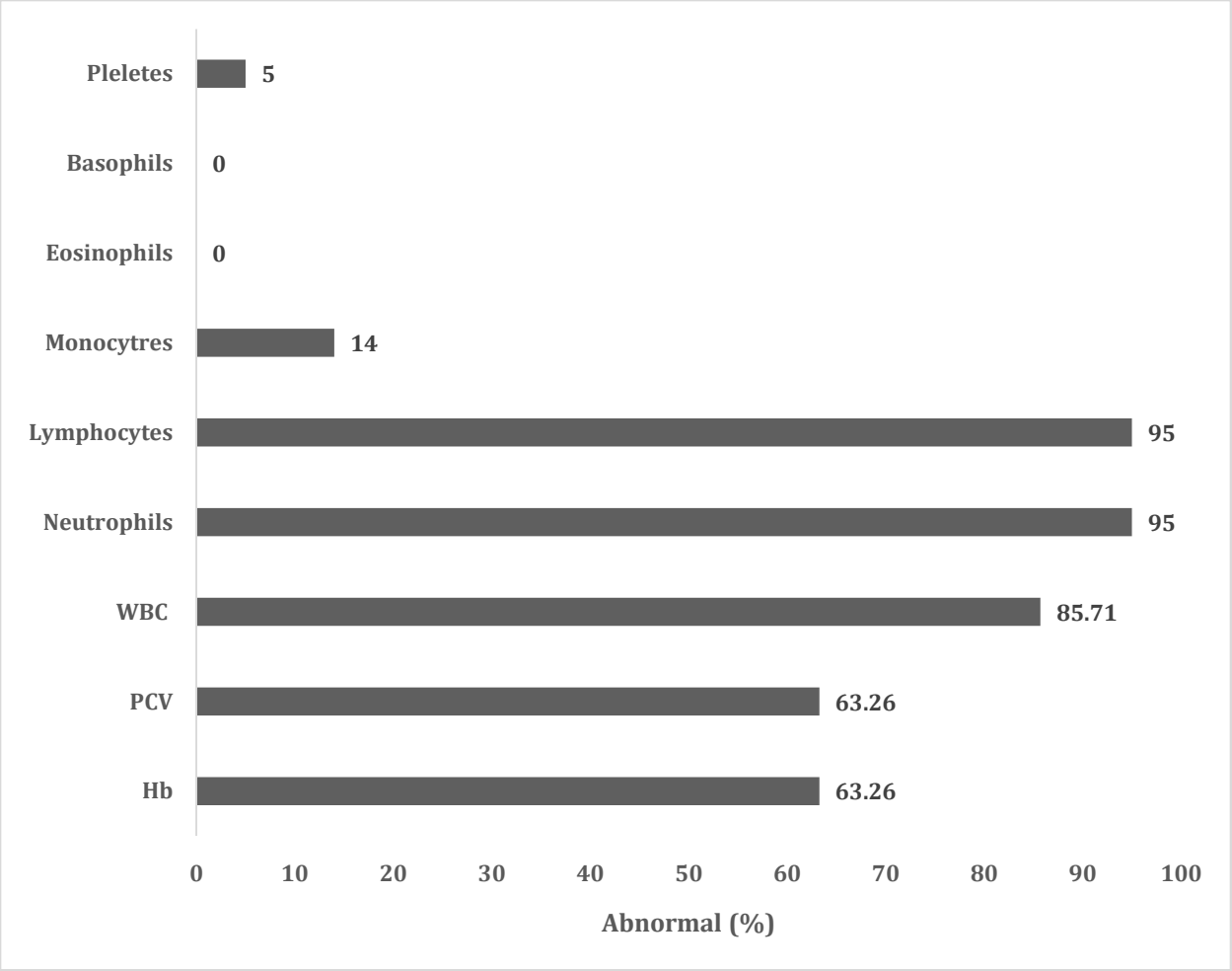

Figure (1) : Abnormalities change percentage of hematological parameters

3.4. Coagulation Parameters

The coagulation tests revealed increased in d-dimer levels ($p< 0.05$) in severe and critical patients. On the other hand , the results showed normal in prothrombin time (PT) and partial thromboplastin (PTT) ($p> 0.05$).

Table 5 Results of Coagulation Parameters

Parameters	Mean ± SD (n = 49)	*p* value
d-dimer (mg/L)	3.5	
Median	4	$p<0.05$
Rang	1.2 -10	
Normal values	0-0.5	
PT (Second)	11	
Median	10	$p> 0.05$
Rang	10-21	
Normal values	11-14	
PTT(Second)	28	
Median	32	$p> 0.05$
Rang	25-55	
Normal values	25-35	
INR	1.3	
Median	1.1	$p> 0.05$
Rang	1-1.8	
Normal values	Up to 1	

4.DISCUSSION

Hematologic manifestations of COVID-19 were initially reported in case series and descriptive studies of COVID-19 patients from China and other countries. Yang et al from China reported that infected with COVID-19 changed the levels of lymphocyte, neutrophil, LMR, and NLR in the blood, and these analyzing items were significantly different between the non-severe and severe groups. Furthermore, the dynamic changes of lymphocyte and NLR levels may help discriminate the severe group from the non-severe group [17,6].Study in Pakistan was reported by Taj et al and concluded that leukocytosis, neutrophilia, elevated NLR , APTT, D-dimer, LDH and serum ferritin and CRP are associated with severity of covid-19 disease[18,7].Javadi et al in Iran found that hemoglobin, WBCs , neutrophil, lymphocytes, and platelets count together with chest tomography score might be beneficial for expedition the diagnosis, assessment the severity of the disease, and outcome in the hospitalized cases, while CRP and LDH might be considered as the consequence of lung involvement[19,8]. Bhandary et al India reported to the known hematologic parameters implicated in COVID-19 illness such as NLR, eosinopenia and D-dimer, platelet parameters (MPV, PDW and PCT) can also be used as biomarkers that indicate the severity of the disease[20,9].Szklanna et al in Ireland“ proof-of-concept study shows that a combination of activated partial thromboplastin time, white cell count-to-neutrophil ratio, and

platelet count can predict subsequent severity of COVID-19 with high sensitivity and specificityat the time of the patient's hospital admission. These data, pending further validation, indicate that a decision tree model with hematological parameters could potentially form the basis for a rapid risk stratification tool that predicts COVID-19 severity in hospitalized patients[21,10].Usul et al in Turkey concluded a statistically significant difference was found between the test groups regarding platelet, hemoglobin, leukocyte, neutrophil, NLR and SII values. Leukocyte, neutrophil, platelet count, NLR and SII values can be used in the diagnosis of COVID-19 [22,11].

Other study by Suryawanshi et al in India concluded a significant decrease in lymphocytic counts was found among severe and critical patients. Hemoglobin level was found to demonstrate higher decrease among severe and critical patients. Platelet count was found in normal range in all COVID-19 patients [23,12].Terpos et al in Grace reported that lymphopenia may be considered as a cardinal laboratory finding, with prognostic potential. NLR and peak PLR may also have prognostic value in determining severe cases. Elevated d- Dimer levels are consistently reported, whereas their gradual increase during disease course is particularly associated with disease worsening. Other coagulation abnormalities such as PT and aPTT prolongation, fibrin degradation products increase, with severe thrombocytopenia lead to life- threatening disseminated intravascular coagulation (DIC), which necessitates continuous vigilance and prompt intervention. So, COVID- 19 infected patients, whether hospitalized or ambulatory, are at high risk for venous thromboembolism, and an early and prolonged pharmacological thromboprophylaxis with low molecular weight heparin is highly recommended. Last but not least, the need for assuring blood donations during the pandemic is also highlighted[24,13].Rahi et al in USA reported that hematologic manifestations constitute a significant area of concern. Severe acute respiratory syndrome coronavirus 2 infects monocytes and endothelial cells leading to a complex downstream cascade, cytokine storm, and eventual intravascular thrombosis. Coronavirus disease 2019 causes lymphopenia, neutrophilia, and thrombocytopenia. Prophylactic anticoagulation is vital in patients with coronavirus disease 2019, as its effect on the coagulation system is associated with significant morbidity and mortality. The disease can cause both arterial and venous thromboses, especially pulmonary embolism and pulmonary microthrombi. A high index of suspicion is indispensable in

recognizing these complications, and timely institution of therapeutic anticoagulation is vital in treating them. Virus-induced disseminated intravascular coagulation is uncommon but shares some similarities to sepsis-induced disseminated intravascular coagulation. Marked elevations in hematologic biomarkers such as lactate dehydrogenase, D-dimer, ferritin, and C-reactive protein are associated with worse outcomes. Understanding the pathophysiology and recognizing factors associated with poor prognosis are crucial in improving patient outcomes with coronavirus disease 2019[26,14].

The available data suggest that neutrophilia is an expression of the cytokine storm and hyper inflammatory state which have an important pathogenetic role in COVID-19 and related infections such as SARS.12,18-20 Cytoplasmic and nuclear morphological anomalies, from hyposegmented nuclei to apoptosis, have been described in circulating granulocytes at the time of hospital admission, Neutrophil/lymphocyte ratio and peak platelet/lymphocyte ratio may also have prognostic value in determining severe cases. During the disease course, longitudinal evaluation of lymphocyte count and inflammatory indices, including LDH, CRP and IL-6 may help to identify cases with dismal prognosis and prompt intervention in order to improve outcomes [3].

Lymphopenia is a common finding in patients with COVID-19 infection and is believed to represent a defective immune response to the virus. In children, lymphopenia is much less common. In meta- analysis of 66 cases reported in the Chinese literature, Henry et al 17 identified lymphopenia in 3% of patients. This is in contrast to other similar viral infections, such as SARS, in which lymphopenia was a much more common finding in children [4].

Neutrophils are the most characteristic cell type among the white blood cells and are an important component of the immune system. Regulated by mast cells, epithelial cells and macrophages, neutrophils also take part in inflammatory processes. The role of lymphocytes in both inflammation and infections is evident. Additionally, thrombocytes also have importance in the regulation of various inflammatory processes. While these parameters may be used as inflammatory markers by themselves, their ratios to one another may also be indicators of early

inflammation . Circulating leukocytes respond to stress by increasing neutrophils and reducing lymphocytes; the ratio of these two parameters is also used as an inflammatory marker 4 [6].

Apart from RT-PCR testing for the organism, laboratory tests have not been assessed with regard to their sensitivity or specificity for the diagnosis of COVID-19, although their value as prognostic indicators has been established.Lymphopenia is a common finding in patients with COVID-19 infection and is believed to represent a defective immune response to the virus , leukocytosis in COVID-19-infected patients and appears to herald bacterial infection or superinfection , neutrophilia is due to bacterial superinfection, cytokine storm and thrombocytopenia is consumptive coagulopathy [26,15,3]. In addition , reduction of Hb is found from the study. These variations might be related to the case of infectious diseases, but low in nutritional values and the geographical location of Hodeidah city, Yemen [5].

Another potential application of data derived from the CBC would be to use formulas such as NLR, PLR , and MLR to act as surrogates to assess the extent of systemic inflammation [27,16] , AL Kamarany in Yemen have reported an increase in NLR in patients with severe COVID-19 infection [28,17]. In addition , SII is an easy-to-quantify parameter with high sensitivity and specificity to predict the clinical course of SARS CoV-2 infected patients. SII might be a valuable tool to improve the management of COVID-19 [29,18].

CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the authors. The raw data are secured in the Center of Tropical Medicine and Infectious Diseases (CTMID), Al-Thawara Public Hospital Authority, Hodeidah, Yemen.

ETHICAL APPROVAL

The studies involving human participants were reviewed and approved by the Ethics Committee of the Center for Tropical Medicine and Epidemiology Studies, Hodeidah University (CTMES – HU), Hodeidah, Yemen.

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