Hematological Parameters as Indicators of COVID-19 Severity in Sudanese Patients at Khartoum State

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Abstract

Background: COVID-19 is a pandemic viral illness that has impacted people all over the world. The severity of COVID-19 might be assessed by looking at various blood parameters, primarily wbcs, platelet, and neutrophil to lymphocyte ratio (NLR). Objectives: The goal of this work was to identify indicators of severity in COVID-19 patients by examining their hematological parameters at various severity stages.

Method: Cross-sectional retrospective observational research was conducted; COVID-19 tests were positive for every patient. Age, gender, and complete blood count were among the information acquired. Patients were divided into three groups according to disease severity: Mild group (21%), moderate group (ER patients), and severe group (isolated in ICU) 49%.

Results: Hematological parameters did not significantly differ between males 59% and females 41%. All the ICU patients were more than 60 years. Most of the mild patients were below 45 years. Of patients above 60 years: 91.2 % had Neutrophilia, 93.9 % had Lymphopenia, 64% had Thrombocytopenia and 80 % had Low Hb concentration and trbcs count. Among ICU patients 91.8% showed Neutrophilia, 93.8% had Lymphopenia and 55% showed Thrombocytopenia. Of the ER patients 63.3% revealed Neutrophilia, and 66.7%

had Lymphopenia. All the mild group patients had normal wbcs count. There was significant variation among the disease severity groups in neutrophils, lymphocytes, and platelets with P value (0.00). All the patients in different severity stages had high neutrophil lymphocyte ratio.

Conclusion: For the purpose of determining the severity and mortality of COVID-19, certain blood parameters must be monitored continually. These variables, including lymphocyte, neutrophil, white blood cell, and platelet counts, could be used as appropriate biomarkers for COVID-19 illness prognosis. Due to the simplicity and accessibility of regular blood tests, the significant change in the above parameters can be simply used to assess the severity and mortality of COVID-19.

Keywords: COVID-19, Blood Parameters, RNA, RT-PCR, mortality, ICU.

Introduction

Corona virus disease is a respiratory tract infection, caused by the novel corona virus (SARS-cov-2) that is belonging to the Coronaviridae family. It was seen to be extremely homologous to the SARS coronavirus (SARS-cov), which was responsible for the respiratory pandemic during the 2002–2003 period.[1]

COVID-19has been reported in Sudan since 13 March 2020, and up to 3ed of July 2020 there had been 9894 confirmed cases and 616 deaths, with a 6.6% case fatality rate. The highest number of confirmed cases and mortality rates appeared in the Khartoum State. About 35% of confirmed cases were over 45 years old, and this age group showed the highest mortality rate (6%) and the majority were male (58%). [5]According to Sudanese ministry of health the final update of COVID-19 in Sudan revealed 38824 cases (recovered cases were 32395 and 2967 deaths).[6]Approximately 80% of infected

individuals have mild to moderate symptoms. The remainder have severe enough disease to necessitate hospitalization. Among severely ill individuals, the most severe complications are acute respiratory distress syndrome/ diffuse alveolar damage and sometime metabolic acidosis multi-organ failure, and shock in severe COVID-19 cases. These worsen conditions of patients may lead to death.[23, 24]

The severity of disease associated with age and clinical status of patient (12). COVID-19 primary target lung and it can damage other organs according to the severity of the disease; about half of patients are a symptomatic.

According to the WHO clinical management of COVID -19 patients were categorized into 4 group based on disease severity. Mild symptoms: no signs of pneumonia and no need for hospital care. Moderate symptoms: have fever and cough and dyspenia fast breathing and no severe pneumonia. Severe symptoms: have clinical sign of pneumonia and severe sign of respiratory distress. Critical acute respiratory distress syndrome (ARDS) : complicated with organ dysfunction such as heart failure and renal failure ,DIC and septic shock .In the initial of the disease ranged from mild nonspecific symptoms of acute respiratory syndrome affected upper and lower respiratory tract (mainly fever ,cough and dyspena) to acute distress and some case leading to death.[41]

Elaborative studies regarding relationship between severity of disease and hematological abnormalities are limited in different countries, also the severity and mortality of COVID -19 infection vary from country to country according to mutation of virus in various geographical location. COVID-19 plays a critical role in the host immune response in disease pathogenesis and clinical manifestation. It triggers the antiviral immune

system to produce an uncontrolled inflammatory response that may lead to cause hematological abnormalities such as lymphopenia, lymphocytes, and abnormalities in granulocyte and monocyte.[26]

These hematological abnormalities can facilitate the infection by other microorganisms, septic shock, and multiorgan dysfunction. Moreover, individuals with comorbid diseases such as hypertension, obesity, diabetes, etc., are at higher risk of corona virus infection. Most comorbidities are frequently associated with excessive body fat mass.[27]

Hematological abnormalities in COVID-19 are related with disease progression, severity and mortality. Lymphopenia, thrombocytopenia, abnormal coagulation profile and sepsis leading to disseminated intravascular coagulation (DIC) is very well documented in patients of COVID-19.[32]These changes in parameters are different from case to case and level of the disease severity. Lymphopenia has been previously reported in about 35%–85% of patients and was the most common blood count abnormality.[10-12] Moreover, knowledge about the risk of infections along with other comorbid conditions would provide valuable insights on risk stratification and making a clinical decision in severe COVID-19 patients.[15] According to different studies, NLR in severe patients was raised as compared to those with mild or moderate disease.[4,16] Further, Liu et al[16] found out in hospitalized patients that NLR serves as an independent risk factor for mortality. Cbcs are the most appropriate and potent laboratory examination. The major objective of this study to evaluate and review the differences among CBC level of COVID-19 patients with the disease severity level and how the CBC level changes after the onset of disease to recognize the stage and

disease's key indicator to provide information for the diagnosis and treatment basis for health professionals.

Materials and methods

This was a cross sectional retrospective observational study conducted at Khartoum state. A structured questionnaire was used to obtain data. 2.5 ml blood was taken from each participant in EDTA containers for hematological profile, blood counter Sysmex Kx-21 was used for hematological profile. PCR exipreptmdx Viral DNA\RNA Kit was used for RNA extraction and exiprep™16 Dx instrument was used to perform the RTPCR. Population of the study was were categorized into 3 groups based on disease severity. Mild: Positive covid-19 patients with no signs of pneumonia, have clinical sign near to influenza and don't need hospital care. Moderate (Emergency room stage ER): Positive covid-19 patients with no history of chronic disease who showed fever, cough and dyspenia fast breathing and no severe pneumonia. They have good prognosis to COVID-19 treatment protocol and didn't need intensive care unit ICU admission. Sever (ICU group of patients) : Positive covid-19 patients who have chronic disease and clinical signs of pneumonia and severe signs of respiratory distress .These patient had critical acute respiratory distress syndrome (ARDS), complicated with organ dysfunction such as heart failure and renal failure ,DIC and septic shock .

Result

Background characteristic of study participants: This is study conducted in Royal Care Hospital to investigate the hematological parameters in patients with COVID-19 and compare CBC results in different severity stages of the disease. A number of one hundred patients with COVID -19 [59 male and 41 female] were included (Figure 1). Relatively, the patients were evenly

distributed into three age groups: up to 45 yrs (31) %, 46- 60 yrs (35) %and more than 60 yrs (34) %(Figure 2). According to the records, patients were divided into three severity stages: 21% of patients had mild disease ,30% were in emergency room while 49% were in intensive care unit ICU (Figure 3).

The distribution of age groups among different severity stages revealed the presence almost all the patients more than 60 years (30% of the study population) were in ICU group of patients. Most of patients below 45 years (19 % of the study population) were in the mild group of patients. (Figure 4).

There was no significant variation between the male and female in all hematological parameters in this study except in platelets count (Table 1).

According to normal ranges[47, 48], Leukocytosis was found in 50% and more of the patients whose age is above 45 years and those in ICU and ER groups. Neutrophilia was observed in 91.2% of the patients above 60 years, 91.8% of the ICU patients, and 63.3 % of the ER patients. Lymphopenia was found in 93.9 % of the patients above 60 years, 93.8% of the ICU patients, and 66.7 % of the ER patients. Thrombocytopenia was detected in 64 % of the patients above 60 years and 55 % of the ICU patients. Low Hb concentration and trbcs count was observed in 80% of the patients whose age is above 60 years and more than 70% of the ICU and ER groups. All the mild group patients had normal wbcs count, 50% had low Hb and 38.1% had low trbcs count. (Table 2), (Table 3) All the patients in different severity stages had high neutrophil lymphocyte ratio. (Table 3). Based on these results significant variation between the means of different hematological parameters among severity stages was found: twbcs, neutrophils, lymphocytes, absolute neutrophils, absolute lymphocytes, and platelets with P value (0.00) and (0.04) for Hb concentration. (Table 4)

Discussion

A new wave of COVID-19 is expeted any time and cases could increase around the globe. There is a need to assess thedisease severity and mortality risk associated with COVID-19 for the optimal management of the patients. Several inflammatory and hematological parameters are thought to associate with the severity of COVID-19[31].

 The current study was aimed to examine the different blood parameters in the confirmed positive COVID-19 patients. We analyzed several blood parameters and their linkage with the severity of the COVID-19 disease. In this study, patients were classified into different categories based on disease severity. The patients were categorized into mild, moderate (emergancy room ER patients), and sever ICU patients groups.

Among the previously reported mortality predictors for COVID-19, the increasing age was an important factor and associated with the poor outcomes.[31] This is suporyed by our results that revealed almost all the elder patients in our study were in the sever ICU patients groups.

There was no significant association between the severity of COVID-19 and gender in our study.

A significant increase in the wbcs level in elder and ICU individuals was observed. It has been previously reported that the wbcs count increased with the severity of the COVID-19 disease.[49]Our study observed neutrophilia, lymphopenia and low absolute lymphocytes in elder and ICU individuals. It could be speculated that the lymphocytes count depletion is directly associated with the COVID-19 disease severity and the survival rate of the disease could be linked with

the ability of T lymphocytes which are essential for the destruction of infected viral particles[50] Our observation supports the previous investigations which documented differential diagnostic criteria for COVID-19 patients based on the increased WBC count along with lymphopenia.[31, 51]We observed the decreased lymphocytes count and increased granulocytes in the most sever diseased individuals (ICU patients)which could be attributed to increased inflammation and suppression of the immune system caused by SARS-cov-2 infection. The elevation in granulocytes and decrease in lymphocytes can be, therefore, easily used for severity and mortality analysis of COVID-19 as routine blood tests are easy and readily available.[36, 52] The lymphopenia has been reported to be common events in the previous coronavirus outbreaks that is, MERS and SARS.[53] Our results are in accordance with the previous investigation where the lymphopenia was common in MERS-cov and SARS-cov infection.[11]Various studies have supported lymphopenia as a reliable and effective biomarker for the severity of COVID-19 disease.[53, 54]

Thrombocytopenia was increased in more than 50 % of the elder and ICU indivduals with more than 90% in the mild patients. Our findings are consistent with the previous studies in which thrombocytopenia was associated with severely diseased individuals and dead patients. Therefore, thrombocytopenia could be used as a useful indicator for disease progression.[51] The mechanism of thrombocytopenia in COVID-19 and other coronavirus diseases is still unknown which needs to be explored.[36]The platelet count was decreased in the severe and critical patients which could be linked to thrombin generation, immunological destruction of platelets, impaired megakaryopoiesis, and inappropriate platelet consumption.[11] Examination of the platelet could be a suitable biomarker for recognition of coagulopathy and its severity[31].

All the patients in different severity stages had high neutrophil lymphocyte ratio.

As COVID-19 causes a systemic inflammatory response, neutrophils are activated by virus-induced inflammatory markers IL-6 and IL-8, GCSF, IFN-ϒ, TNF-α formed by lymphoid and endothelial cells. Conversely, the immune response is considerably depressed notably the helper T lymphocytes. Hence, NLR is elevated as a result and it is associated with disease progression. Previous investigations have also reported neutrophil to lymphocytes and platelets to lymphocytes ratio as important prognostic factors for disease progression.[52, 55]Additionally, patients with severe COVID-19 infection were reported to have a higher NLR than those with non-severe COVID-19 infection.[56-59]

Conclusion

Several blood parameters need to be continuously screened to assess the severity and mortality of COVID-19. Thes parameters such as lymphocytes, neutrophils, white blood cells, and platelet count could be used as suitable biomarkers for prognosis of COVID-19 disease. The great change in the mentioned parameters can be easily used for severity and mortality analysis of COVID-19 as routine blood tests are easy and readily available. The topic needs to be explored further for the early target of treatment options and optimal management of the COVID-19 patients during the pandemic. Evaluating NLR can aid clinicians to identify potentially severe cases at early stages, initiate effective management in time, and conduct early triage which may reduce the overall mortality of COVID-19 patients.
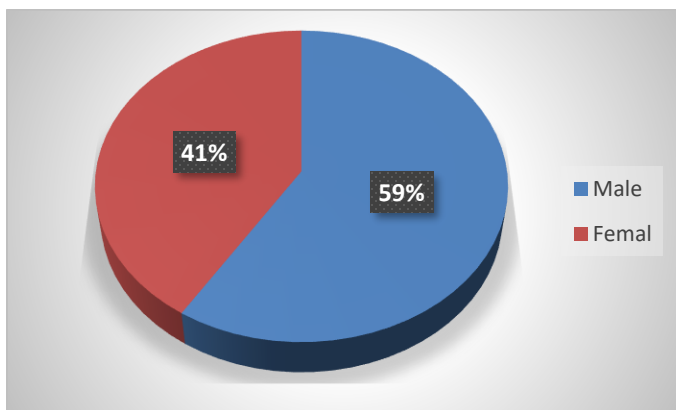
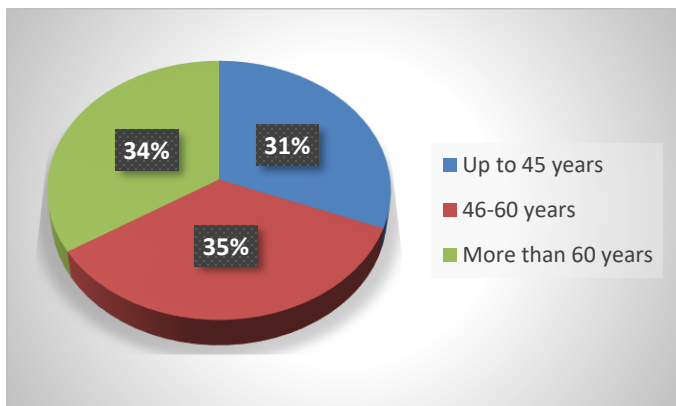Figure1: Distribution of gender among study population

Figure 2: Age distribution among study population
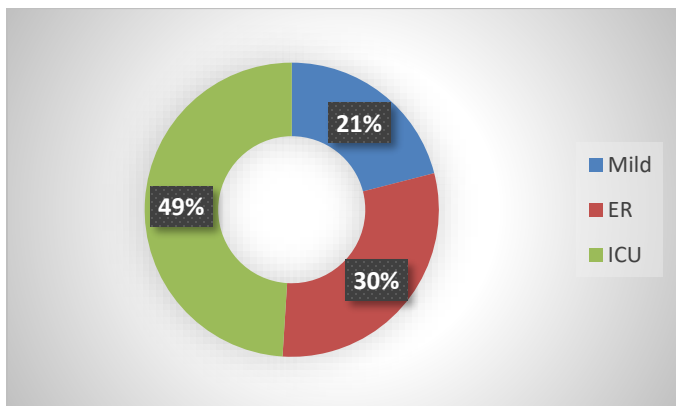
Figure 3: Distribution of disease severity stages among study population
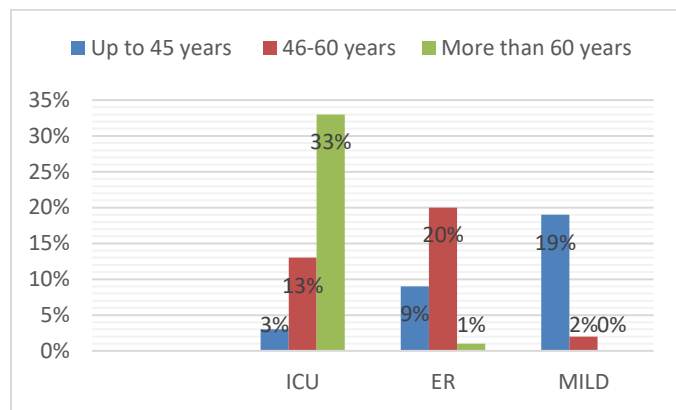
Figure 4: The distribution of age groups among different severity stages

Table 1: Distribution of hematological parameters among male and female of study population

Parameter	Gender	Mean	Significance
Twbcs	Male	11.7	0.8
	Female	12.1	
Neut.	Male	77.0	0.9
	Female	74.9	
Lymph.	Male	16.4	0.2
	Female	16.0	
Ab. Neut.	Male	9.8	0.8
	Female	10.3	
Ab. Lymph.	Male	1.1	0.2
	Female	1.5	
Trbcs	Male	4.3	1.6
	Female	4.2	
Hb	Male	12.4	0.2
	Female	11.2	
HCT	Male	36.7	0.9
	Female	33.1	
Plts	Male	214	0.04
	Female	249	
Neut./Lymph. Ratio.	Male	1.24	1.000
	Female	3.25	

Table 2: Distribution of hematological parameters (low, normal, high) results among different age groups of study population

Parameter %	Range	Less than 45 yrs.	45-60 yrs	More than 60 yrs	Significance P.value
TWBCs	Low	6.5%	2.9%	2.9%	
	Normal	67.7%	42.9%	47.1%	0.14
	High	25.8%	**54.3%**	**50%**	
Neut.	Low	12.9%	5.7%	0.00	
	Normal	51.6%	25.7%	8.8%	**0.00**
	High	35.5%	68.6%	**91.2%**	
Lymph.	Low	38.7%	68.6%	**93.9%**	
	Normal	32.3%	25.7%	6.1%	**0.00**
	High	29.0%	5.7%	0.00%	
Abs. Neut.	Low	9.7%	0.00%	2.9%	
	Normal	64.5%	45.7%	35.3%	**0.03**
	High	25.8%	54.3%	61.8%	
Abs.Lymph.	Low	6.5%	37.1%	**94.1%**	
	Normal	**90.33%**	62.9%	5.9%	**0.00**
	High	3.2%	0.00%	0.00%	
TRBCs	Low	41.9%/	68.6%	**85.3%**	
	Normal	54.8%	31.4%	14.7%	**0.01**
	High	3.2%	0.00	0.00	
HB	Low	60.0%	**73.5%**	**82.4%**	
	Normal	40.0%	26.5%	17.6%	0.07
	High	0.00	0.00	0.00 %	
HCT	Low	64.5%	71.4%	**88.2%**	
	Normal	35.5%	25.7%	11.8%	0.29
	High	0.00	2.9%	0.00	
PLTs	Low	9.7%	28.6%	**64.7%**	
	Normal	80.6%	65.7%	35.3%	**0.00**
	High	9.7%	5.7%	0.00%	
Neut./Lymph. Ratio.	Low	0.00	0.00	0.00	
	Normal	0.00	0.00	0.00	**0.00**
	High	**100%**	**100%**	**100%**	

Table 3: Distribution of hematological parameters (low, normal, high) results among different severity groups of study population

Parameter	Range	ICU	ER	MILD
TWBCs	Low	4.1%	6.7%	0.00
	Normal	36.7%	43.3%	**100%**
	High	**59%**	50%	0.00
Neut.	Low	0.00	3.3%	23.3%
	Normal	8.2%	33.3%	66.7%
	High	**91.8%**	**63.3%**	9.5%
Lymph.	Low	**93.8%**	**66.7%**	9.5%
	Normal	4.2%	33.3%	42.9%
	High	21%	0.00	47.6%
Abs. Neut.	Low	4.1%	0.00	9.5%
	Normal	28.6%	53.3%	85.7%
	High	**67.3%**	46.7%	4.8%
Abs.Lymph.	Low	**95.9%**	0.00	0.00
	Normal	4.1%	96.7%	100%
	High	0.00	3.3%	0.00
TRBCs	Low	**75.5%**	70.5%	38.1%
	Normal	24.5%	26.7%	61.9%
	High	0.00	3.3%	0.00
HB	Low	**79.2%**	**76.7%**	**50%**
	Normal	20.8%	23.3%	**50%**
	High	0.00	0.00	0.00
HCT	Low	81.5%	76.7%	57.1%
	Normal	16.3%	23.3%	42.9%
	High	2.0%	0.00	0.00
PLTs	Low	**55.1%**	25.7%	0.00
	Normal	44.9%	63.3%	**90.5**
	High	0.00	10.0%	9.5
Neut./Lymph. Ratio.	Low	0.00	0.00	0.00
	Normal	0.00	0.00	0.00
	High	**100**	**100**	**100**

Table 4: Mean of hematological parameters among disease severity stages

Mean of Parameter	ICU	ER	MILD	P. Value
Twbcs	13.9	12.3	6.4	.000
Neut.	89	73	51	.000
Lymph	6	16	41	.000
Abs. Neut.	13	10	3	.000
Abs . Lymph.	0.54	2	2	.000
Neu. Lymph. Ratio	3.0	7.02	1.80	.000
Trbcs	4.1	4.1	4.7	0.06
Hb	11.6	11.6	13	.042
HCT	34.6	33.9	38.6	0.06
Platelet	181	247	315	.000

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