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# Prognostic Value of Lymphopenia among Sudanese Patients with COVID-19 Infection

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## Abstract

**Background:** The COVID-19 is highly contagious infection caused by single strand positive sense RNA virus. Laboratory findings are very important during pandemic situation to predict disease morbidity and mortality.
**Objective:** In this article we evaluate the clinical implication of haematological parameter particularly lymphocytes count in determining the severity and outcome of COVID-19 disease.
**Method:** Data was collected during the period from April to June 2020 using the laboratory database of Jabra Hospital for Emergency and Injuries; all patients were tested positive for COVID-19. The data included age, gender, and full blood count. Information regarding patient outcomes was also analysed.
**Result:** The study cohort comprises of 65 patients positive for SARS-CoV-2 RNA. 39 (60%) patients were male while 26 (40%) were female. Of the 65 patients, 28 died due to the infection and 37 had recovered. Haematological markers were evaluated on both died and recovered patients. The result of haemoglobin concentration and platelet count shows no effect on the COVID-19 infection outcome. The mean of Absolute lymphocyte count (ALC) was shown to be $0.73 \pm 0.50 \times 10^3$ cell/µl in the Covid-19 died group which is significantly lower than that of recovered group $1.58 \pm 0.89 \times 10^3$ cell/µl with P. value 0.00. None of those patients over 60 years and having ALC less than $0.6 \times 10^3$ cell/µl survive after COVID-19 infection.
**Conclusion**: These findings highlight the prognostic value of lymphopenia at time of admission, which can be helpful in tailoring a prompt response for early interventions in Covid-19 disease patients.

**Keywords:** COVID-19; Lymphocytes; Prognosis; Died group; Recovered group

## Introduction

The novel coronavirus SARS-CoV-2 also known as COVID-19 is highly contagious infection caused by single strand positive sense RNA virus belong to genus Beta coronavirus, in subgenus Sarbecovirus [1]. In December 2019 the disease was first identified in Wuhan, China. The World Health Organization regard the covid19 as pandemic in March 2020. Based on WHO data, there have been 53,766,728 confirmed cases of COVID-19, including 1,308,975 deaths by the end of 13 November 2020 [2]. COVID-19 is transmitted mainly through the air via small droplets or aerosols when people are coming to cluster each other long enough. It can be transmitted as early as 2 days before infected persons possess symptoms and even from asymptomatic patients [3]. Although most patients with COVID-19 are asymptomatic or have mild symptoms, a few portions could develop severe pneumonia and eventually lead to acute respiratory distress syndrome. Some patients however may go so far in disease progression to mount multi-organ failure and death [4]. Clinical remarks and laboratory findings are very important during pandemic situation to predict disease morbidity and mortality. Viral infection is well established cause of abnormal haematological parameters and COVID-19 is not exception of the general rule. Many studies have demonstrated that COVID-19 is associated with lymphopenia as well as cytokine storm syndrome. Additionally, Autopsy of patients who passed due to COVID-19 revealed shrunken spleen organ with reduced lymphocyte, macrophage proliferation, and phagocytosis. These features could reveal that the immune system particularly lymphocytes could play a key role in determining COVID-19 infection prognosis [5-7]. In this article we evaluate the clinical implication of haematological parameter particularly lymphocytes count in determining the severity and outcome of COVID-19 disease.

## Method

### Ethics approval and consent to participate

All the protocol has approved and carried out according to ethical guidelines of the declaration of Helsinki for human research. Ethics Review Committees Jabra Hospital for Emergency and Injuries also provided the authorization. Participant informed consent was not obtained since the study performed in retrospective manner as granted by the ethical committees.

### Data collection and analysis

Data was collected during the period from April to June 2020 using the laboratory database of Jabra Hospital for Emergency and Injuries; all patients who tested positively for COVID-19 were included and monitored in this study. However, all patients tested negative for COVID-19 are excluded from this study. The data included age, gender, and full blood count. Information regarding patient outcomes was also analysed. The statistical analysis was performed by using SPSS version 20. A comparison of lymphocyte counts in each group (dead group, recovered group) was carried out using chi-squared test.

## Results

The study cohort comprises of 65 patients. All of them tested positive for SARS-CoV-2 RNA. 39 (60%) of the patients are male and 26 (40%) are female. Of the 65 patients, 28 died from the infection, while 37 had recovered. The mean age of our cohort was 52.87 ± 16.033 years with a minimum of 23 years and maximum of 82 years old.

Result shows that there was insignificant difference between male and female in the COVID-19 infection outcome since the P. value was (0.438) (Table 1). However, the mean of age for the COVID-19 died group 65.86 ± 6.87 years was significantly higher than that of the COVID-19 recovered group 42.89 ± 13.7 with P. value 0.00 (Table 1). When we categorized the patients into age groups, we found a highly significant difference between the age groups in the death and recovery rates P. value 0.00. The death occurrence was 0 (0%) among patients aged below 40 years old, while the highest prevalence 18 (78.6%) of death was found among patients over 60 years old compared to only 5 (13.6%) patients recovered in the same group (Table 1). Amongst patients aged between 40 to 60 years the recovery rate 6 (21.4%) was higher than the death rate 14 (37.8%). Haematological markers, including haemoglobin concentration (g/dl) white cell count (WBC) ($\times 10^3$ cell/µl) and lymphocyte count ($\times 10^3$ cell/µl) as well as platelet count ($\times 10^3$ cell/µl) were evaluated on both died and recovered patients. The result of haemoglobin concentration and platelet count shows no effect on the COVID-19 infection outcome with P. Value of 0.754 and 0.10 respectively. The results show that In the Covid-19 died group 32.1% (n=9) had normal WBC, 7.2% (n=2) had leucopoenia, and 60.7 % (n=17) leucocytosis. On the other hand, in the Covid-19 recovered group, 48.6% (n=18) had normal WBC and 27.3 % (n=9) had leucocytosis and 24.1 % (n=10) had leucopoenia. There was statistically significant difference between groups in the WBC with P. value of 0.008 and the mean of WBC was significantly higher 13.429 ± 6.17 among died group than recovered group 8.281 ± 3.67. The result show that amongst the COVID-19 died group 85.7% (n=24) had lymphocyte percentage less than 10% and 14.3% (n=4) hade lymphocyte percentage more than 10%. In contrast, amongst COVID-19 recovered group 27.0% (n=10) had lymphocyte percentage less than 10% and 73.0% (n=27) hade lymphocyte percentage more than 10% with P. value of 0.00

(Table 1). On the other hand, 35.7% (n=10) of a died group had Neutrophil percentage less than 85% and 64.3% (n=18) in the same group had neutrophil percentage more than 85% while amongst recovered group, 81.1% (n=30) had Neutrophil percentage less than 85% and 18.9% (n=7) in the same group had Neutrophil percentage more than 85% with P. value 0.00. The degree of lymphopenia, using absolute lymphocyte count ×103 cell/µl (ALC), was also assessed on admission. The mean ALC was shown to be 0.73 ± 0.50 $\times 10^3$ cell/µl in the Covid-19 died group which is highly significantly lower than that of recovered group 1.58 ± 0.89 $\times 10^3$ cell/µl with P. value 0.00.

***Table 1:*** *Summary of the epidemiological and hematological characteristics of the cohort.*

| Parameter | COVID-19 disease out come | | P. value |
|---|---|---|---|
| | Died | Recovered | |
| **Gender** | | | |
| Male | 16 (57.1%) | 23 (62.2%) | 0.438 |
| Female | 12 (42.9%) | 14 (37,8) | |
| **Age groups / years** | | | |
| Less than 40 | 0 (0%) | 18 (48.6%) | 0.00 |
| 40 – 60 | 6 (21.4%) | 14 (37.8%) | |
| More than 60 | 22 (78.6%) | 5 (13.6%) | |
| Age mean | 65.86 ± 6.87 | 42.89 ± 13.7 | |
| **Hemoglobin group g/dl** | | | |
| Less than 8.0 | 1 (3.6%) | 1 (2.7%) | 0.754 |
| 8.0 – 11.0 | 9 (32.1%) | 9 (24.3%) | |
| More than 11.0 | 18 (64.3%) | 27 (73.0%) | |
| mean of hemoglobin | 11.282 ± 1.40 | 12.424 ± 2.33 | |
| **WBC group** $\times 10^3$ cell/µl | | | |
| Less than 4.0 | 2 (7.2%) | 10 (24.1%) | 0.008 |
| 4.0 – 11.0 | 9 (32.1%) | 18 (48.6%) | |
| More than 11.0 | 17 (60.7%) | 9 (27.3%) | |
| mean of WBC | 13.429 ± 6.17 | 8.281 ± 3.67 | |
| **Plate lets group cell/µl×$10^3$ cell/µl** | | | |
| Less than 150 | 6 (23.4%) | 4 (10.8%) | 0.10 |
| 150 - 450 | 14 (50%) | 28 (75.7%) | |

| | | | |
|---|---|---|---|
| More than 450 | 8 (28.6%) | 5 (13.5%) | |
| Plate lets mean | 353.54 ± 252.1 | 294.27 ± 126.6 | |
| **LYMPH% group** | | | |
| Less than 10% | 24 (85.7%) | 10 (27.0%) | 0.00 |
| More than 10% | 4 (14.3%) | 27 (73.0%) | |
| LYMPH% mean | 6.257 ± 5.0 | 21.681 ± 13.6 | |
| **Neutrophil% group** | | | |
| Less than 85% | 10 (35.7%) | 30 (81.1%) | 0.00 |
| More than 85% | 18 (64.3%) | 7 (18.9%) | |
| Neutrophil% mean | 87.004 ± 7.6 | 70.395 ± 15.4 | |
| **ALC $\times 10^3$ cell/µl** | | | |
| Less than 0.6 | 15 (53.6%) | 0 (0%) | 0.00 |
| 0.6 - 1.0 | 9 (32.1%) | 13 (35.1%) | |
| More than 1.0 | 4 (14.3%) | 24 (64.9 %) | |
| ALC mean | 0.73 ± 0.50 | 1.58 ± 0.89 | |
| **ANC Group$\times 10^3$ cell/µl** | | | |
| Less than 3.0 | 0 (0%) | 9 (24.3%) | 0.00 |
| 3.0 - 6.0 | 3 (10.7%) | 11(29.7%) | |
| More than 6.0 | 25 (89.3%) | 17 (45.9%) | |
| ANC mean | 11.896 ± 6.1 | 6.207 ± 3.65 | |

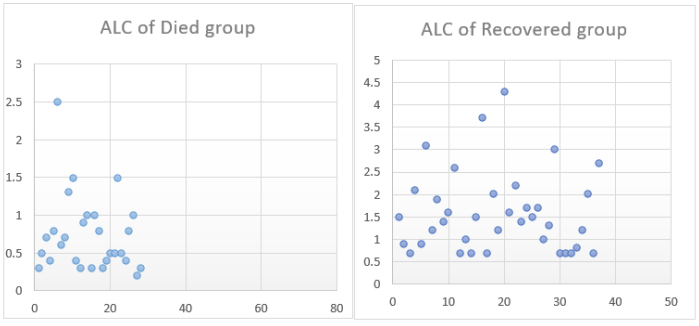


***Figure 1:*** *Show the distribution of patients ALC. Y axis = ALC 103 cell/µl. X axis= patients. The left the figure show that with exception of 4 cases, all died group patients shows ALC less than 1.0×103 cell/µl. In the right figure majority of recovered group have ALC more than 1.0×103 cell/µl.*

The result also demonstrated that amongst COVID-19 died group 53.6% (n=15) had ALC less than 0.6×$10^3$ cell/µl, 32.1% (n=9) had ALC between 0.6 – 1.0 ×$10^3$ cell/µl, and 14.3% (n=4) had ALC more than 1.0 ×$10^3$ cell/µl. Furthermore, amongst COVID-19 recovered group 0% (n=0) had ALC less than 0.6 × $10^3$ cell/µl, 35.1% (n=13) had ALC between 0.6 – 1.0 ×$10^3$ cell/µl, and 64.9% (n=64) had ALC more than 1.0 ×$10^3$ cell/µl. There was significant effect of ALC in predication of COVID-19 infection outcome with P. value of 0.00. The result show that a mortality of Covid-19 died group 89.3% (n =25) had Absolute neutrophil count (ANC) more than 6.0 ×$10^3$ cell/µl and none of them 0%

(n=0) had ANC less than 3.0. In contrast 45.9% (n=17) of COVID-19 recovered group had ANC more than 6.0 $\times 10^3$ cell/µl, 29.7% (n=11) had ANC between 3.0-6.0 $\times 10^3$ cell/µl and 24.3% (n=9) had ANC less than 3.0. There was also significant effect of ANC in predication of COVID-19 infection outcome with P. value of 0.00 (Table 1) (Figure 1).

## Discussion

In December 2019, COVID-19 was first identified in Wuhan, China. Science that time and during the pandemic start up many researches have been conducted of which some are focused on the clinical remarks while others described the laboratory finding characteristics of patients [8]. Our study found that gender have no significant effect on COVID-19 outcome among Sudanese patient and this was in disagreement with finding of the (Sex, Gender, and COVID-19 Project data) that most countries with available data indicate a male to female case fatality ratio higher than 1.0, ranging up to 3.5 in some cases [9]. Inclusion of only 65 cases in our study may affect the result of demographic character analysis. So, this point needs more analysis in the future studies with inclusion of large-scale population. Our result indicate that elderly patients have a great chance to develop sever type of infection and even death, since none of those under 40 years dead due to infection compared to 78.6% of death rate occur among those over 60 years. Additionally, all of those over 60 years and have ALC less than 0.6 × $10^3$ cell/µl die due to the COVID-19 infection. This is not surprise because many studies have proved that advanced age is a characteristic features of immune response dysfunction affecting all lymphocytic lineages. Reduced lymphopoiesis, impaired antigen-specific immunity, tissue-specific changes [10-12]. In this study there was no significant difference between both groups of cases in the haemoglobin concentration means. With exception of 10 cases both groups show a haemoglobin concentration more than 11.0 g/dl which exclude the presence of anaemia. Most previous studies confirm our finding [13-16]. Platelet count has been evaluated as a biomarker to predict the severity of COVID-19, and our study confirm the finding of the previous reports in which thrombocytosis and thrombocytopenia is less occasionally occur among COVID-19 patients regardless the severity of the infection [17-19]. In this study we analysed the level of WBC in both groups of patients. We find that, the mean of WBC was higher significantly among COVID-19 died group and majority of them 60% have leukocytosis compared to COVID-19 recovered group. In addition, the neutrophil is predominantly detected among COVID-19 died group compared to the survival group. These two facts may support the theory of that COVID-19 as like other respiratory viruses predispose the patients to secondary bacterial infection particularly bacterial pneumonia which is characterized by elevated WBC and neutrophil and that's why many of the treatment policies include azithromycin antibiotic as major treatment used during the COVID-19 infection starting from the symptoms onset [20]. In this study the mean of ALC and lymphocytes percentage among COVID-19 died group were significantly lower than those of survival group. Recent studies have shown an increased prevalence of low lymphocyte count in Covid-19 +ve patients, compared with the general population. However, in our study we compare a COVID-19 died group with a recovered group of patients to determine the effect of the lymphocytes in COVID-19 infection outcome, we found that none of those patients over 60 years and having ALC less than 0.6 $\times 10^3$ cell/µl survive after being infected with COVID-19. Additionally, the recovery rate is increased with improvement of lymphopenia to reach about 64.9% among those with ALC more than 1.0$\times 10^3$ cell/µl with only 14.3% death rate in the same group. These findings highlight the prognostic value of lymphopenia at time of admission, which can be helpful in tailoring a prompt response for early interventions in Covid-19 disease patients. Our finding has consistently been recorded in many recently published studies, claiming that lymphopenia is a marker of severity and poor outcome in Covid-19 +ve patients [15].

## Conclusion

Our study demonstrates that lymphopenia is most a specific prognostic marker of COVID-19 infection outcome particularly among elder patients and could help physician to predict patients with poor prognosis earlier. Based on the results of our study, we therefore propose that lymphocyte transfusion treatment should be taken into consideration when treating patient with COVID-19 infection particularly older patients. Further studies with larger cohort are required to better understand the value of lymphocytes count in diagnosis and treatment of the COVID-19 infection.

## Limitations of the Study

Our study has included a relatively smaller sample size (only 65 cohort).

## Abbreviations

**WBC:** Total White Blood cells count
**ALC:** Absolute Lymphocyte Count
**ANC:** Absolute Neutrophil Count

## Declaration

### Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

### Consent for publication

Not applicable

### Competing interests

All authors declare that they have no competing interest.

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None

## Authors' contributions

RA, FA, MS, AM, MM, MH and OM have contributed to data collection. WI, BM was accountable for data analysis, and article writing. All authors contributed to manuscript revising and editing. All authors read and approved the final manuscript.

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