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A Retrospective Study of Absolute Lymphocyte Count as a Marker of Covid 19 Disease Severity in Tertiary Care Center

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Abstract

Introduction: Coronavirus disease 2019 (Covid-19) is a predominantly respiratory illness caused by the SARS-CoV-2 virus. Data regarding prognostic factors are currently scarce given the novelty of the disease. Prognostic information would aid clinicians in managing patients, who are often left without data-driven guidelines to make important clinical decisions. It is known that lymphocytopenia, defined as an absolute lymphocyte count (ALC) < 1000 cells/µL, occurs in Covid-19 and may correlate with increased disease severity.**Materials and Methods:** Data were obtained for patients admitted to one local, academic, community-based Hazaribag Medical College and hospital, Hazaribag. Patients were included if they had a positive diagnosis of Covid-19 based on a polymerase chain reaction-based assay to detect the SARS-CoV-2 virus or had been diagnosed in the community, were over the age of 18, and were admitted and discharged from the hospital between 03/01/2020 and 30/07/2020. **Results:** We obtained 114 patients who were admitted to and discharged from the hospital between 03/01/2020 and 30/07/2020. The cohort was predominantly male (59%), obese (average BMI of 32.3 ± 1.19 kg/m^2) with an average age of 58.2 ± 2.08 years. Our cohort consisted mostly of patients with minority backgrounds (86%). Thirty-one percent of patients (N = 36) were admitted to the ICU and mortality was 16% (N = 18). Of note, 4 patients had a diagnosis of Human Immunodeficiency Virus (HIV) infection. The median Charlson comorbidity index was 4 (1.5-6), indicating an median 10-year survival rate of 53%. In our study, we found that 50% (18/36) of patients admitted to the ICU required intubation and 38% (14/36) required vasopressors. Thus, patients admitted to the ICU were classified as having severe disease given the relatively common occurrence of hemodynamic instability and respiratory failure in this population.**Conclusion:** In summary, we find that lymphocytopenia and anemia are more common in patients admitted to the ICU, with an odds ratio of approximately 3.4 and 3.6, respectively. Additionally, patients with lymphocytopenia are more likely to develop an AKI relative to those without lymphocytopenia by an odds ratio of 4.2. Thus, it appears likely that lymphocytopenia is related to disease severity and clinical outcomes in Covid-19.
Keywords: Coronavirus disease, ICU, AKI, absolute lymphocyte count.

Introduction

Coronavirus disease 2019 (Covid-19) is a predominantly respiratory illness caused by the SARS-CoV-2 virus[1]. Data regarding prognostic factors are currently scarce given the novelty of the disease. Prognostic information would aid clinicians in managing patients, who are often left without data-driven guidelines to make important clinical decisions[2].It is known that lymphocytopenia, defined as an absolute lymphocyte count (ALC) < 1000 cells/µL, occurs in Covid-19 and may correlate with increased disease severity[3].Lymphocytopenia is a common systemic manifestation of many viral illnesses; in particular, other coronaviruses like Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle Eastern Respiratory Syndrome coronavirus (MERS-CoV) have been demonstrated to cause lymphocytopenia[4]. However, few studies have examined whether lymphocytopenia found at the time of admission to the hospital is helpful in understanding the disease course[5]. Here, we set out to study a cohort of patients admitted to the hospital diagnosed with Covid-19 to determine whether lymphocytopenia,

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found at the time of admission to the hospital, was associated with disease severity and other clinical outcomes.
Materials and Methods
Study design: A Retrospective Study
Study location: Hazaribag Medical College and hospital, Hazaribag.
Study duration: 3-January-2020 to 30- July 2020 (7 months).
Data were obtained for patients admitted to one local, academic, community-based Hazaribag Medical College and hospital, Hazaribag. Patients were included if they had a positive diagnosis of Covid-19 based on a polymerase chain reaction-based assay to detect the SARS-CoV-2 virus or had been diagnosed in the community, were over the age of 18, and were admitted and discharged from the hospital between 03/01/2020 and 30/07/2020. Data were collected and extracted from an electronic medical record system and included many variables, such as demographic, clinical outcomes, and laboratory data. We define severe disease as those patients who required admission to the ICU; non-severe disease is classified as those admitted to the hospital, but did not require ICU admission. Admission to the ICU was determined by clinical factors, namely respiratory failure and hemodynamic instability. Lymphocytopenia was not part of these criteria. Acute Kidney Injury (AKI) is defined as a rise in serum creatinine > 0.3 mg/dL from baseline within 48 hours at any time during admission (if baseline data were unavailable, the lowest value during admission was presumed to be the baseline; if only one value was available, the patient was not presumed to have an AKI).All laboratory data were collected within

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24 hours of admission. Laboratory data were analyzed by our hospital's hematology laboratory. All laboratory samples are typically processed within hour of receipt.

Statistical Analysis: For continuous variables, a Welch's two-sided *t* test was performed, assuming variances were unequal between samples. To correct for multiple comparisons, a Bonferroni test was performed to adjust *P*-values. For categorical data, a Fisher Exact test was used to make comparisons. For all analyses, a *P*-value < .05 was used to reject the null hypothesis that either there was no difference between two samples tested or that samples were independent.

Results

We obtained 114 patients who were admitted to and discharged from the hospital between 03/01/2020 and 30/07/2020. The cohort was predominantly male(59%),obese(average BMI of 32. 3 ± 1.19 kg / m^2) with an average age of 58.2 ± 2.08 years. Our cohort consisted mostly of patients with minority backgrounds (86%). Thirty-one percent of patients (N = 36) were admitted to the ICU and mortality was 16% (N = 18). Of note, 4 patients had a diagnosis of Human Immunodeficiency Virus (HIV) infection. The median Charlson comorbidity index was 4 (1.5-6), indicating an median 10-year survival rate of 53%. In our study, we found that 50% (18/36) of patients admitted to the ICU required intubation and 38% (14/36) required vasopressors. Thus, patients admitted to the ICU were classified as having severe disease given the relatively common occurrence of hemodynamic instability and respiratory failure in this population.

Table 1: The relationship between lymphocytopenia and clinical outcomes

	ALC < 1000, Count (%)	ALC > 1000, Count (%)	P Value
Need for intubation in the ICU	12 (54), N=22	6 (43), N=14	1.0
ICU stay > 7 d	12 (54), N=22	6 (43), N=14	1.0
Need for vasopressors in the ICU	12 (54), N=22	4 (28), N=14	0.36
Developed AKI during admission	30 (68), N=44	22 (33), N=66	0.01
Mortality	12 (26), N=46	6 (9), N=66	0.13

Table 2: Basic hematological laboratory values collected at the time of admission to the hospital of patients based on the need for ICU admission at any time during hospitalization

	Non-ICU	ICU	P Value
Sample size, N	78	36	0.01
ALC	1.4 ± 0.15	0.8 ± 0.11	0.01
Hemoglobin	12.9 ± 0.37	11.3 ± 0.54	0.08
Hematocrit	38.5 ± 1.38	35.4 ± 1.30	0.55
Platelet count	202.8 ± 11.84	274.7 ± 20.22	0.02
WBC	8.8 ± 0.73	10.4 ± 1.13	1.00

Table 3: Frequency of laboratory results and corresponding odds ratios based on ICU admission status

	Non-ICU	ICU	P Value
Sample Size	78	36	--
Lymphocytopenia Frequency	24(32), N = 76	22 (61)	0.04
Anemia Frequency	28 (49)	28 (78)	0.04
Thrombocytopenia Frequency	12 (15)	2 (5)	0.41
Leukopenia Frequency	10 (13)	0	-
Leukocytosis Frequency	18 (23)	12 (33)	0.5

Discussion

In this study, we focused on admission laboratory values, given that these values are often the first to shed light on disease severity. However, other groups have found that patients with persistent lymphocytopenia during the Covid-19 disease course may be more likely to have severe outcomes[6].This is interesting, given that persistent lymphocytopenia is associated with poor outcomes after diagnosis with sepsis; Drewery et al (2014) hypothesized that this could be due to an anti-inflammatory response in later stages of sepsis[7].Thus, it is possible that lymphocytopenia causes an immune-suppressive environment, causing more profound illness in Covid-19, necessitating ICU admission. Future studies should examine the course of pro- and anti-inflammatory markers and lymphocytopenia in Covid-19 patients to see whether there are different phenotypes that result. Additionally, prospective trials are needed to evaluate the predictive ability of lymphocyte count in determining disease severity[8].Regarding clinical outcomes, it is interesting that patients that developed an AKI at any time during admission seemed to be more common in patients with than those without lymphocytopenia in Covid-19. Recently, SARS-CoV-2 viral load was detected in human kidney samples, thus confirming that this virus can directly infect renal tissue. Additionally, it has been reported that mortality is higher in patients with Covid-19 and AKI compared to those without AKI. Although lymphocytopenia was not seen to be associated with mortality in this study, the finding of an association with AKI warrants further research. Nevertheless, it is apparent here that lymphocytopenia may serve as a prognostic marker for AKI in Covid-19 patients[8].Finally, although lymphocytopenia was not found to be statistically related to other clinical outcomes, such as mortality and need for intubation, the trend was largely in favor of a correlation; our sample size was likely small to demonstrate this association; Indeed, mortality is higher in patients with lower lymphocyte counts, thus confirming the trends observed here. Future studies should address ICU outcomes such as the need for intubation based on lymphocytopenia with appropriate statistical power to validate these findings.

Conclusion

In summary, we find that lymphocytopenia and anemia are more common in patients admitted to the ICU, with an odds ratio of approximately 3.4 and 3.6, respectively. Additionally, patients with lymphocytopenia are more likely to develop an AKI relative to those without lymphocytopenia by an odds ratio of 4.2. Thus, it appears likely that lymphocytopenia is related to disease severity and clinical outcomes in Covid-19.

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