Analysis of absolute lymphocyte count in patients with COVID-19

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ABSTRACT

Introduction: Symptoms of COVID-19 vary in severity and presentation. When admitting patients to the hospital, it is desirable to isolate patients with COVID-19 from those without the disease. However, reliably identifying patients with COVID-19 in the emergency department before hospital admission is often limited by the speed and availability of testing. Previous studies determined a low lymphocyte count is commonly found in patients with COVID-19. We sought to explore the sensitivity of absolute lymphocyte count in patients presenting to the emergency department requiring subsequent hospitalization who were found to have COVID-19.

Methods: A retrospective chart review was performed on 312 patients with laboratory-confirmed COVID-19 who were admitted to the hospital from the emergency department. The absolute lymphocyte count for these patients was used to calculate sensitivities at various cut-off values. The relationships between absolute lymphocyte count and variables, including age, sex, need for intubation, and mortality, were also explored.

Results: Cut-off values for absolute lymphocyte count ranged from 1.1 K/μL to 2.0 K/μL, with sensitivities of 72% and 94%, respectively. Additionally, lower mean absolute lymphocyte counts were identified in males, patients who required intubation, and patients who died.

Conclusion: Knowing the sensitivity of absolute lymphocyte count in patients with COVID-19 may help identify patients who are unlikely to have the disease. Additionally, absolute lymphocyte count can be used as a marker of disease severity in patients with COVID-19.

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1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus that causes coronavirus disease (COVID-19) [1]. Symptoms of COVID-19 vary in severity and presentation, and many patients with COVID-19 may be asymptomatic or have only mild symptoms [2]. When admitting patients to the hospital, it is desirable to isolate patients with COVID-19 from those without the disease. However, reliably identifying patients with COVID-19 in the emergency department (ED) before hospital admission is often limited by the speed and availability of SARS-CoV-2 testing.

Current research suggests that lymphopenia, defined as a low lymphocyte count, is commonly present in patients with COVID-19 [3,4]. There is also evidence that the degree of lymphopenia correlates with illness severity in patients with COVID-19 [5-7]. The converse may also be true; those without lymphopenia may be unlikely to have COVID-19, but currently, there is a paucity of data to support this.

Turn-around-time for absolute lymphocyte count (ALC) is much quicker than SARS-CoV-2 testing, with results obtained while the patient is in the ED. We explore the relationship between lymphopenia and COVID-19 in patients who present to the ED and require hospitalization.

2. Methods

2.1. Design

A retrospective chart review was performed to assess the relationship between ALC and infection from SARS-CoV-2 in patients with laboratory-confirmed COVID-19 who were admitted to the hospital from the ED. We hypothesized that in patients presenting to the ED requiring subsequent hospitalization, ALC cut-off values could be used to help physicians identify patients who are unlikely to have COVID-19. ALC and secondary variables, including age, sex, need for intubation (either in the ED or during hospitalization), and mortality, were of interest.
Comparing absolute lymphocyte count

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
<th>Kruskal-Wallis P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>164</td>
<td>1.06 (0.71)</td>
<td>0.80 (0.6, 1.3)</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>147</td>
<td>0.90 (0.62)</td>
<td>0.80 (0.5, 1.1)</td>
<td></td>
</tr>
<tr>
<td>Intubated</td>
<td>No</td>
<td>228</td>
<td>1.01 (0.66)</td>
<td>0.80 (0.6, 1.2)</td>
<td>0.048</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>83</td>
<td>0.91 (0.72)</td>
<td>0.80 (0.4, 1.1)</td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>No</td>
<td>226</td>
<td>1.01 (0.66)</td>
<td>0.80 (0.6, 1.2)</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>85</td>
<td>0.91 (0.72)</td>
<td>0.76 (0.5, 1.02)</td>
<td></td>
</tr>
<tr>
<td>Severity</td>
<td>Death with Intubation</td>
<td>51</td>
<td>0.96 (0.83)</td>
<td>0.76 (0.4, 1.1)</td>
<td>0.093</td>
</tr>
<tr>
<td></td>
<td>Intubation without death</td>
<td>34</td>
<td>0.85 (0.51)</td>
<td>0.75 (0.5, 1.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neither death or intubation</td>
<td>194</td>
<td>1.04 (0.67)</td>
<td>0.80 (0.6, 1.3)</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td>&lt;50</td>
<td>47</td>
<td>1.08 (0.63)</td>
<td>1.00 (0.7, 1.3)</td>
<td>0.145</td>
</tr>
<tr>
<td></td>
<td>50–59</td>
<td>49</td>
<td>0.92 (0.50)</td>
<td>0.80 (0.5, 1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60–69</td>
<td>70</td>
<td>0.89 (0.67)</td>
<td>0.70 (0.5, 1.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>70–79</td>
<td>59</td>
<td>0.90 (0.53)</td>
<td>0.80 (0.5, 1.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>80+</td>
<td>86</td>
<td>1.11 (0.84)</td>
<td>0.80 (0.6, 1.2)</td>
<td></td>
</tr>
</tbody>
</table>

Sample testing for SARS-CoV-2 was similarly acquired by an ED nurse or physician during a patient’s ED encounter using a nasal or nasopharyngeal swab. Samples obtained from March 15, 2020, through March 26, 2020, were analyzed using the Centers for Disease Control and Prevention (CDC) RT-PCR assay on a Roche LC480 thermocycler at Henry Ford Hospital in Detroit, Michigan. From March 27, 2020, through the end of the study period, the RT-PCR assay was analyzed on a NeuMoDx, Diasorin Simplexa, or Cephelid GenXpert automated RT-PCR platform. The results from all samples were expressed as either positive or negative. A positive result was defined by the expression of one of two genetic targets on the SARS-CoV-2 genome in quantity greater than the predetermined fluorescence threshold.

2.2. Setting

This study took place at Henry Ford Wyandotte Hospital (HFWH), a 360-bed community-based teaching hospital located in the Detroit Metropolitan area whose ED receives approximately 60,000 visits a year.

2.3. Sample

The sample population consisted of adult patients who presented to the HFWH ED between March 20, 2020, and May 5, 2020, required hospital admission and had a positive SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) result. A positive SARS-CoV-2 RT-PCR result was found either in the ED or during hospitalization. Inclusion criteria included patients aged ≥18 years, hospital admission, COVID-19 as confirmed by SARS-CoV-2 RT-PCR, and a complete blood count (CBC) with ALC obtained in the ED or during hospitalization. Exclusion criteria included patients aged <18 years, discharged from the ED, negative SARS-CoV-2 RT-PCR testing, and no ALC obtained during ED encounter or hospitalization duration. A total of 312 patients were eligible for inclusion in our study based on inclusion criteria. One patient was excluded from data analysis due to a pre-existing diagnosis of chronic lymphocytic leukemia with an ALC of 72.16 K/uL. As such, 311 patients were included for data analysis.

2.4. Data Collection & Measurement

Blood samples for laboratory evaluation were collected at the patient’s bedside by ED nurses or physicians while in the ED. Only data from the first blood draw that included ALC was included in our analysis. All patients in our study had a CBC with ALC drawn in the ED; thus, no blood samples acquired upon hospitalization were used for data analysis due to a pre-existing diagnosis of chronic lymphocytic leukemia with an ALC of 72.16 K/uL. As such, 311 patients were included for data analysis.

Table 2

<table>
<thead>
<tr>
<th>ALC sensitivity at cutoff values</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALC cutoff</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>1.1 (K/uL)</td>
</tr>
<tr>
<td>1.25 (K/uL)</td>
</tr>
<tr>
<td>1.5 (K/uL)</td>
</tr>
<tr>
<td>2.0 (K/uL)</td>
</tr>
</tbody>
</table>
A total of 311 patients with COVID-19, as confirmed by SARS-CoV-2 RT-PCR, were included in the data analysis. Patient ages ranged from 18 to 97 years, with the mean age being 67.1 years (SD = 16.9). Breakdown of the variables analyzed were as follows: 147 (47.3%) patients were male, 83 (26.7%) patients were intubated, 85 (27.3%) patients died, 51 (16.4%) patients died while intubated, 34 (10.9%) patients died without intubation, and 194 (62.4%) patients survived without intubation.

Additionally, 2 (0.6%) patients had ALC values above the normal range, 99 (31.8%) patients had ALC values within the normal range, and 210 (67.5%) patients had ALC values below the normal range. The normal range used for ALC was 1.10–4.00 K/uL, as this was the range used by the HFWH laboratory for reporting normal versus abnormal results. The mean ALC of patients in our study was 0.99 K/uL (SD = 0.67), while the median ALC was 0.80 K/uL (IQR = 0.61, 1.2).

ALC values were compared among the various subgroups analyzed (Table 1). Male patients had a lower ALC than female patients, with means of 0.90 K/uL and 1.06 K/uL, respectively (p = 0.041). Patients with severe disease had a lower ALC (0.91 K/uL) than those who did not (1.01 K/uL) (p = 0.048). Patients who died had a lower ALC (0.91 K/uL) than those who survived (1.01 K/uL) (p = 0.047). Age groups (p = 0.850). There were no significant differences in ALC based on the combination of intubations and death (p = 0.093) and age groups (p = 0.145).

The sensitivity of ALC in our patient population was assessed using different cut-off values, as outlined in Table 2. Cut-off values ranged from 1.1 K/uL to 2.0 K/uL, with sensitivities of 72% and 94%, respectively.

The sensitivity of ALC in patients with COVID-19 may help physicians identify patients who are unlikely to have the disease, allowing patients who benefit from AGPs to receive timely treatment in the ED without exposing nurses, physicians, and respiratory therapists to infectious pathogens. Furthermore, expeditious cohorting of patients unlikely to have COVID-19 allows for the early removal of isolation precautions, reducing hospital costs and resource utilization through diminished personal protective equipment use.

Our data also demonstrates the degree of lymphopenia correlates with COVID-19 severity, specifically, the need for intubation and death. As such, ALC may serve as a diagnostic indicator in patients with COVID-19, allowing physicians to pursue more aggressive treatment regimens in patients at risk for severe disease.

### 4.1. Limitations

All patients requiring admission to HFWM during the study dates underwent SARS-CoV-2 RT-PCR testing, regardless of symptoms or reason for hospital admission. Cases of a positive SARS-CoV-2 RT-PCR result after resolution of COVID-19 have been reported [9]. As such, patients included in our study might have had a positive SARS-CoV-2 RT-PCR without active COVID-19 and required admission for an alternate reason (i.e., acute surgical issue), resulting in the inclusion of patients without active COVID-19 in our study.

Our study only included patients who required hospital admission. It did not include patients who were discharged from the ED with confirmed or suspected COVID-19. As such, further studies should be conducted to determine if the ALC cut-off values found in our study extend to this population.

There are a multitude of variables and disease processes that lead to lymphopenia. These include bacterial and fungal sepsis, corticosteroid use, chemotherapy and radiation therapy, and trauma [10]. Patients in our study may have had factors independent of COVID-19 that contributed to a decreased ALC.

Our study was designed to assess the sensitivity of ALC in patients with COVID-19. As such, only patients with COVID-19 were included in our study. Additional studies are needed to determine the specificity and positive and negative predictive values of ALC as it relates to COVID-19.

### 5. Conclusion

Knowing the sensitivity of ALC in patients with COVID-19 may help identify patients who are unlikely to have the disease upon hospital admission, allowing for rapid cohorting of patients and safe utilization of procedures that may increase the risk of viral transmission.
AGPs in place of SARS-CoV-2 RT-PCR testing. Additionally, ALC can be used as a marker of disease severity in patients with COVID-19.

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**CRediT authorship contribution statement**

**Zachary Illg**: Conceptualization, Methodology, Investigation, Data curation, Writing - original draft, Writing - review & editing. **Gregory Muller**: Methodology, Investigation, Writing - original draft. **Matthew Mueller**: Methodology, Writing - original draft, Writing - review & editing. **Justin Nippert**: Investigation, Writing - original draft, Writing - review & editing. **Brian Allen**: Conceptualization, Methodology, Investigation, Writing - original draft.

**Declaration of Competing Interest**

None.

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None.

**References**


