Research Letter

# Lymphopenia and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection Among Hospitalized Obstetric Patients

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## INTRODUCTION

Significant concern exists regarding asymptomatic infections in the ongoing coronavirus disease 2019 (COVID-19) pandemic.[1–3] Reports from New York City demonstrate considerable prevalence of asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among pregnant patients and several cases of extensive health care worker exposure during deliveries.[4–6] Lymphopenia has been described as a common and early laboratory test abnormality associated with COVID-19 infection.[7] Given an inability to perform universal testing at our institution secondary to supply chain limitations, we explored a strategy of obtaining white blood cell (WBC) count differentials for all patients admitted to our obstetric unit. We sought to examine whether lymphopenia identified asymptomatic SARS-CoV-2 infection and to assess whether lymphopenia could discriminate the presence of infection in symptomatic patients under investigation for COVID-19.

## METHODS

We implemented a policy of universal automated WBC count differential testing for all obstetric patients from April 1 through April 14, 2020. Patients with lymphopenia (defined as absolute lymphocyte count less than $0.8 \times 10^3$/microliter[8,9]) underwent COVID-19 testing using a nasopharyngeal swab test (PANDAA qDx real-time polymerase chain reaction), as did all symptomatic patients. To assess whether lymphopenia could predict COVID-19 infection status among symptomatic individuals, all patients with suspected or confirmed COVID-19 infection who underwent an obstetric inpatient evaluation or admission from March 10 through April 14, 2020, were analyzed. The study was approved by our institutional review board.

## RESULTS

From April 1 through April 14, 2020, there were 213 admissions to obstetric services. Of those patients with complete blood count results, 172 (84.3%) had a WBC count differential performed. The absolute lymphocyte count ranged from 0.5 to $6.0 \times 10^3$/microliter

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**Table 1.** **Maternal Demographics and Blood Count Characteristics of Obstetric Patients With a Complete Blood Count and White Blood Cell Count Differential Performed on Admission (N=172)**

| Characteristic | Value |
|---|---|
| Age (y) | 33.0 (30.4–36.3) |
| Race | |
| White | 69 (40.1) |
| Black | 17 (9.9) |
| Hispanic | 17 (9.9) |
| Asian | 20 (11.6) |
| Other or unknown | 49 (28.5) |
| Insurance | |
| Public | 10 (5.8) |
| Private or self-pay | 161 (93.6) |
| Unknown | 1 (0.6) |
| Laboratory values | |
| RBC count (m/microliter) | 4.0 (3.7–4.2) |
| Hematocrit (%) | 36.1 (33.7–38.4) |
| Hemoglobin (g/dL) | 11.9 (11.0–12.7) |
| Platelet count ($\times 10^3$/microliter) | 211.5 (178.0–263.0) |
| WBC count ($\times 10^3$/microliter) | 10.8 (8.9–12.8) |
| Lymphocytes (%) | 17.1 (13.4–23.1) |
| Less than 19 | 99 (57.6) |
| Absolute lymphocytes ($\times 10^3$/microliter) | 1.8 (1.3–2.3) |
| Less than 0.8 | 8 (4.7) |
| Less than 1.0 | 16 (9.3) |

RBC, red blood cell; WBC, white blood cell.
Data are median (interquartile range) or n (%).

(median $1.8\times 10^3$/microliter, interquartile range 1.3–2.3, Table 1). Nine patients had lymphopenia; six of these had suspected or known COVID-19 infection. The remaining three patients were asymptomatic and had negative COVID-19 test results. None of these patients developed symptoms during admission.

From March 10 through April 14, 2020, 37 symptomatic patients with known or suspected COVID-19 infection presented for inpatient evaluation or admission. All underwent COVID-19 testing. Of the 37 patients, one had an insufficient sample, 15 (41%) had positive test results, and 21 (57%) had negative test results. Of the 36 patients with test results, 31 had an absolute lymphocyte count performed at admission, with a COVID-19 infection prevalence of 48% (15/31). There was no difference in median absolute lymphocyte count in symptomatic patients with and without COVID-19 infection (1.1 vs $1.4\times 10^3$/microliter, $P$=.11). Among 15 patients with confirmed COVID-19 infection, 33% had an absolute lymphocyte count less than $0.8\times 10^3$/microliter, compared with 25% among the 16 patients with negative test results ($P$=.70). Of note, all three patients who required critical care for hypoxia in our cohort had an initial absolute lymphocyte count less than $0.8\times 10^3$/microliter. Test performance characteristics for three definitions of lymphopenia to identify COVID-19 infection are shown in Table 2. At a COVID-19 infection prevalence of 48%, the positive predictive value for each definition was less than 60%.

## DISCUSSION

Lymphopenia (defined as absolute lymphocyte count less than $0.8\times 10^3$/microliter) was an uncommon finding among obstetric inpatients and was not a useful screening strategy for identifying asymptomatic SARS-CoV-2 infection. Moreover, absolute lymphocyte count did not meaningfully discriminate those with and without infection among patients under investigation. Lymphopenia is a common feature of many viral infections, including including infection with SARS-CoV-2, and may result from direct infection of lymphocytes or immunologically mediated cell apoptosis.[10] Although lymphopenia was more common in symptomatic patients with confirmed COVID-19 infection, this was not a great marker of disease. We did observe that lymphopenia was consistently present in patients presenting with severe disease, an association that has been reported frequently in nonpregnant patients with COVID-19 infection (Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of

**Table 2.** **Test Characteristics of Primary and Alternative Definitions of Lymphopenia in Predicting Coronavirus Disease 2019 (COVID-19) Infection Among 31 Symptomatic Patients, With COVID-19 Infection Prevalence of 48%**

| Lymphopenia Definition | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|
| ALC ($\times 10^3$/microliter) | | | | |
| Less than 0.8 | 33 (12–62) | 75 (48–93) | 56 (21–86) | 55 (32–76) |
| Less than 1.0 | 47 (21–73) | 69 (41–89) | 58 (28–85) | 58 (34–80) |
| Lymphocytes less than 19% | 87 (60–98) | 19 (4–46) | 50 (30–70) | 60 (15–95) |

PPV, positive predictive value; NPV, negative predictive value; ALC, absolute lymphocyte count.
Data are % (95% CI).

COVID-19: a descriptive and predictive study [letter] [published erratum appears in Signal Transduct Target Ther 2020;5:61.]. Signal Transduct Target Ther 2020;5:33.).[11–13] Our results should be interpreted in the context of our small sample size and unknown community disease prevalence but do add to the limited studies of WBC count indices in pregnancy.[14–16]

Labor units continue to care for high volumes of patients, and the care provided involves close and frequent contact with health care workers and the possibility of unanticipated emergency surgery. Universal COVID-19 testing may be necessary to identify asymptomatic infections in areas with active community transmission. The decision to implement universal testing may require knowledge of local prevalence rates given the possibility of false-positive results in the setting of low prevalence.

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