Laboratory Abnormalities in Pregnant Women with Novel Coronavirus Disease 2019

Li Shi, BM¹ Ying Wang, BM¹ Haiyan Yang, MD, PhD¹ Guangcai Duan, MD, PhD¹ Yadong Wang, MD, PhD²

¹Department of Epidemiology, School of Public Health, Zhengzhou University, Zhengzhou, China
²Department of Toxicology, Henan Center for Disease Control and Prevention, Zhengzhou, China

Address for correspondence Haiyan Yang, MD, PhD and Guangcai Duan, MD, PhD, Department of Epidemiology, School of Public Health, Zhengzhou University, No. 100 of Science Avenue, Zhengzhou 450001, China (e-mail: yhy@zzu.edu.cn; gcduan@zzu.edu.cn).

Am J Perinatol 2020;37:1070–1073.

Novel coronavirus disease 2019 (COVID-19), sustained by the causative agent called severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), is highly contagious.¹,² At present, above 2 million confirmed cases and over 170,000 deaths of COVID-19 have occurred in the world according to the World Health Organization.³ Pregnant women, because of their special physiological conditions, are susceptible to the virus and put themselves at greater risk.⁴ Timely control and treatment of pregnant women with COVID-19 infection are a major concern.⁵ Moreover, laboratory medicine plays a vital role in this process.⁶ Therefore, the purpose of this article is to identify the most common laboratory abnormalities in pregnant women with COVID-19.

PubMed, Chinese National Knowledge Infrastructure (CNKI), and Wanfang databases were reviewed by two independent authors, using the keywords “coronavirus” OR “Wuhan coronavirus” OR “SARS-CoV-2” OR “2019 novel coronavirus” OR “2019-nCoV” OR “COVID-19” AND “pregnancy” OR “pregnant woman” OR “pregnant women” OR “vertical transmission” (up to April 20, 2020). There were no country, race, or language restrictions. We included articles reporting laboratory data in pregnant women with confirmed COVID-19 by reading titles, abstracts, and full texts. Besides, the lists of references for all articles were also screened to identify potentially additional articles. A descriptive statistical analysis was applied to summarize their findings. A random-effects model meta-analysis was then carried out to calculate the pooled prevalence and 95% confidence interval (95% CI) to assess the prevalence of laboratory abnormalities in pregnant women with COVID-19. Double arcsine method was implemented to make original data conform to normal distribution, and then we analyzed them in software Stata version 11.2 to obtain initial results. Final results were restored by the formula \( P = \sin^2 \left( \frac{t}{2} \right) \).⁷ Begg’s test and Egger’s test were utilized to evaluate publication bias.

A total of 244 articles were reviewed, among which 223 were removed due to a lack of laboratory data about pregnant women. Although eight articles reported laboratory data in pregnant women with COVID-19, they were eliminated because of duplicated data. In addition, two articles that did not clearly report laboratory abnormalities were also excluded. Overall, a total of 11 articles with 173 pregnant patients were included⁸–¹⁸ among which 11 women had severe disease, and 2 women had critical disease. Most of the patients came from China, and one each came from Korea, the United States, Sweden, Iran, Peru, and Canada. The stages of pregnancy ranged from the first trimester to the third trimester. The characteristics of these patients are indicated in Table 1.

Four articles were included in the meta-analysis.⁹,¹⁰,¹⁵,¹⁶ Our results indicated that among all laboratory parameters of pregnant women with COVID-19, the incidence of elevated D-dimer was 82% (95% CI: 75–89%), elevated neutrophil count was 81% (95% CI: 69–91%), elevated C-reactive protein was 69% (95% CI: 58–79%), and decreased lymphocyte count was 59% (95% CI: 41–75%). Begg’s test and Egger’s test showed that no publication bias existed (Table 2). No other laboratory parameters showed apparently consistent changes due to the limitation of available data.

Considering the relatively high-sequence identity of SARS-CoV-2 and SARS-CoV and the effects of SARS-CoV on pregnant women, we must pay great attention to the group of pregnant women infected with COVID-19.¹⁹,²⁰ Our review suggests that the most frequent abnormalities are elevated D-dimer (82%), elevated neutrophil count (81%), elevated C-reactive protein (69%), and decreased lymphocyte count (59%). However, a meta-analysis of adult COVID-19 infection reported that...
| Characteristics | Wang et al<sup>17</sup> | Li et al<sup>14</sup> | Lee et al<sup>13</sup> | Iqbal et al<sup>12</sup> | Gidlöf et al<sup>11</sup> | Zamanian et al<sup>18</sup> | Alzamora et al<sup>8</sup> | Vlachodimitropoulou Koumoutsea et al<sup>16</sup> | Chen et al<sup>10</sup> | Liu et al<sup>15</sup> | Chen et al<sup>9</sup> |
|-----------------|------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|------------------------|---------------------|---------------------|---------------------|
| Location        | China                  | China               | Korea               | USA                 | Sweden              | Iran                | Peru                | Canada                 | China               | China               | China               |
| Number of cases | 1 (severe)             | 1                   | 1                   | 1                   | 1 (critical)        | 1 (severe)          | 2                   | 5                      | 41                  | 118 (9 severe and 1 critical) |
| Age (y)         | 28                     | 30                  | 28                  | 34                  | 34                  | 22                  | 41                  | 40/23                  | 29 (median)         | 30 (median)         | 31 (median)         |
| Gestational age (wk) | 30                  | 35                  | 37                  | 39                  | 36                  | 32                  | 33                  | 35/35                  | 38–41               | 22–40               | N/R                 |

**Laboratory data**

| Leukocytes      | ↑ 100% N/R            | ↓ 100% N/R          | N/R                 | ↓ 100% N/R          | ↓ 100% N/R          | ↓ 100% N/R          | ↓ 100% N/R          | 100% N/R          | 15%<sup>a</sup> N/R |
| Neutrophils     | ↑ 100%                 | ↑ 100% N/R          | N/R                 | ↑ 100% N/R          | ↑ 100% N/R          | ↑ 100% N/R          | N/R                 | 80% N/R            | 83% N/R            |
| Lymphocytes     | ↓ 100%                 | ↑ 100% N/R          | N/R                 | ↓ 100% N/R          | ↓ 100% N/R          | ↓ 100% N/R          | N/R                 | ↓ 80% N/R          | ↓ 61% N/R          | ↓ 44%<sup>a</sup> |
| CRP             | ↑ 100% N/R            | N/R                 | N/R                 | N/R                 | ↑ 100% N/R          | ↑ 100% N/R          | N/R                 | 100%<sup>a</sup> N/R | 66% N/R            | 67%<sup>a</sup>     |
| Platelets       | N/R                    | ↓ 100% N/R          | N/R                 | N/R                 | N/R                 | ↓ 100% N/R          | N/R                 | 100% N/R            | 3%<sup>a</sup> N/R  |
| Hemoglobin      | N/R                    | ↓ 100% N/R          | N/R                 | N/R                 | N/R                 | ↓ 100% N/R          | N/R                 | ↓ 40% N/R           | N/R                | N/R                |
| Procalcitonin   | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | 26%<sup>a</sup> N/R |
| ESR             | N/R                    | ↑ 100% N/R          | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | N/R                |
| Albumin         | ↓ 100% N/R            | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | N/R                |
| ALT             | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | 100% N/R            | N/R                |
| AST             | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | 100% N/R            | N/R                |
| ALP             | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | 180% N/R            | N/R                |
| Bilirubin       | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | N/R                |
| Creatinine      | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | N/R                |
| Creatine kinase | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | 100% N/R            | N/R                |
| LDH             | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | N/R                |
| D-dimer         | N/R                    | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                 | N/R                  | N/R                | N/R                |

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ; LDH, lactate dehydrogenase; N/R, not (clearly) reported; PT, prothrombin time.

<sup>a</sup>Data missing for patients; ‒Data within the normal reference range.

Note: laboratory data are presented as percent of patients with abnormalities defined by local reference ranges.
Laboratory Abnormalities in Pregnant Women with COVID-19

| Laboratory data          | Studies | Case number | Initial results | Final results | Heterogeneity | Begg's test (P-value) | Egger's test (P-value) |
|--------------------------|---------|-------------|-----------------|---------------|---------------|------------------------|------------------------|
| Elevated D-dimer         | 3       | 109         | 2.27 (2.09, 2.46) | 0.82 (0.75, 0.89) | 0.0           | 0.697                 | 1                      | 0.148                 |
| Elevated neutrophil count| 2       | 46          | 2.25 (1.97, 2.53) | 0.81 (0.69, 0.91) | 0.0           | 0.707                 | 1                      | –                     |
| Elevated CRP             | 3       | 151         | 1.95 (1.73, 2.18) | 0.69 (0.58, 0.79) | 31.2          | 0.234                 | 1                      | 0.317                 |
| Decreased lymphocyte count| 4     | 164         | 1.75 (1.39, 2.10) | 0.59 (0.41, 0.75) | 62.9          | 0.044                 | 0.308                  | 0.082                 |
| Elevated leukocyte count  | 3       | 162         | 1.23 (0.69, 1.78) | 0.33 (0.11, 0.60) | 86.7          | 0.001                 | 1                      | 0.392                 |
| Elevated LDH             | 2       | 84          | 1.14 (0.93, 1.35) | 0.29 (0.20, 0.39) | 0.0           | 0.796                 | 1                      | –                     |

Abbreviations: COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase.

The pooled prevalence and 95% confidence interval obtained after adjusting the original data with the double arcsine method.

The pooled prevalence and 95% confidence interval obtained after restoring the initial results with the formula \( P = \sin(tp/2) \)².

Elevated D-dimer levels, elevated neutrophil count, elevated C-reactive protein levels, and decreased lymphocyte count are the most prevalent laboratory abnormalities in pregnant women with COVID-19, which is slightly different from the characteristics in nonpregnant patients. We should consider pregnancy factors when monitoring changes in pregnant women.

**Funding**

This study was supported by a grant from the National Natural Science Foundation of China (no.: 81973105).

**Conflict of Interest**

None declared.

**References**

1. Lake MA. What we know so far: COVID-19 current clinical knowledge and research. Clin Med (Lond) 2020;20(02):124–127
2. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020;395(10223):514–523
3. World Health Organization. Coronavirus disease (COVID-19) situation reports-94. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf?sfvrsn=b304bf0_4. Accessed 23 April, 2020
4. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet 2020;395(10226):809–815
5. Qiao J. What are the risks of COVID-19 infection in pregnant women? Lancet 2020;395(10226):760–762
6. Lippi G, Plebani M. A modern and pragmatic definition of Laboratory Medicine. Clin Chem Lab Med 2020 (e-pub ahead of print). Doi: 10.1515/cclm-2020-0114
7. Sun P, Qie S, Liu Z, Ren J, Li K, Xi J. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis. J Med Virol 2020 (e-pub ahead of print). Doi: 10.1002/jmv.25735
8. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during pregnancy and possible vertical
