Laboratory Abnormalities in Pregnant Women with Novel Coronavirus Disease 2019

Li Shi, BM[1] Ying Wang, BM[1] Haiyan Yang, MD, PhD[1] Guangcai Duan, MD, PhD[1] Yadong Wang, MD, PhD[2]

[1] Department of Epidemiology, School of Public Health, Zhengzhou University, Zhengzhou, China
[2] Department 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).

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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 ($P = [\sin (tp/2)]^2$).[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 included,[8–18] 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

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Table 1 Characteristics of the included studies

Characteristics	Wang et al[17]	Li et al[14]	Lee et al[13]	Iqbal et al[12]	Gidlöf et al[11]	Zamaniyan et al[18]	Alzamora et al[8]	Vlachodimitropoulou Koumoutsea et al[16]	Chen et al[10]	Liu et al[15]	Chen et al[9]
Location	China	China	Korea	USA	Sweden	Iran	Peru	Canada	China	China	China
Number of cases	1 (severe)	1	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	↔	N/R	↔	↓100%	N/R	↑60%	↑41%	↑15%[a] ↓5%[a]
Neutrophils	↑100%	↑100%	N/R	↔	N/R	↑100%	N/R	N/R	↑80%	↑83%	N/R
Lymphocytes	↓100%	↔	N/R	↓100%	N/R	↓100%	↓100%	↓100%	↓80%	↓61%	↓44%[a]
CRP	↑100%	N/R	↔	N/R	N/R	↑100%	↑100%	N/R	↑100%[a]	↑66%	↑67%[a]
Platelets	N/R	↓100%	N/R	↔	N/R	N/R	↓100%	↓100%	↔	N/R	↓3%[a]
Hemoglobin	N/R	↔	↓100%	↓100%	N/R	N/R	↓100%	N/R	↓40%	N/R	N/R
Procalcitonin	↔	N/R	N/R	N/R	N/R	N/R	↔	N/R	↔	N/R	↑26%[a]
ESR	N/R	N/R	↑100%	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Albumin	↓100%	N/R	N/R	↓100%	N/R	N/R	N/R	N/R	↓100%	N/R	N/R
ALT	↔	N/R	N/R	↔	N/R	N/R	↔	↑100%	↔	N/R	↑23%[a]
AST	↔	N/R	N/R	↔	N/R	N/R	↔	↑100%	↔	N/R	↑21%[a]
ALP	N/R	N/R	N/R	N/R	N/R	N/R	N/R	N/R	↑80%	N/R	N/R
Bilirubin	N/R	N/R	N/R	↔	N/R	N/R	↔	N/R	↔	N/R	N/R
Creatinine	↔	N/R	N/R	↓100%	↔	N/R	↓100%	N/R	↓20%	N/R	N/R
Creatine kinase	N/R	N/R	N/R	N/R	N/R	N/R	↓100%	N/R	↑20% ↓20%	N/R	N/R
LDH	↑100%	N/R	N/R	N/R	N/R	↔	N/R	N/R	↑20%	N/R	↑29%[a]
D-dimer	↑100%	↑100%	N/R	N/R	N/R	N/R	↑100%	↑100%	↑100%[a]	N/R	↑82%[a]
PT	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.

[a]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.

Table 2 Meta-analysis results for assessing the prevalence of laboratory abnormalities in pregnant women with COVID-19 (random-effects model)

Laboratory data	Studies	Case number	Initial results[a]	Final results[b]	Heterogeneity		Begg's test (*p*-Value)	Egger's test (*p*-Value)
					I^2 (%)	*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.
[a]The pooled prevalence and 95%confidence interval obtained by meta-analysis after adjusting the original data with the double arcsine method.
[b]The pooled prevalence and 95%confidence interval obtained after restoring the initial results with the formula ($P = [\sin(tp/2)]^2$).

decreased albumin (75.8%), high C-reactive protein (58.3%), high lactate dehydrogenase (LDH; 57.0%), lymphopenia (43.1%), and high erythrocyte sedimentation rate (ESR; 41.8%) were the most prevalent laboratory abnormalities.[21] Our study found that the incidence of increased LDH in pregnant women with COVID-19 was only 29%. A total of seven cases reported by Wang et al,[17] Iqbal et al,[12] and Chen et al[10] showed decreased albumin levels. Similarly, only Lee et al[13] described that ESR increased in the pregnant woman with COVID-19. Due to the limitation of the data, we did not further conduct a meta-analysis on these laboratory parameters. Thus, more studies with large sample size are needed to discuss this in the future. In addition, Zhang et al[22] reported that among five pregnant women with SARS-CoV infection, two cases had decreased lymphocytes. Recent studies also reported elevated D-dimer levels, elevated neutrophil count, elevated C-reactive protein levels, and decreased lymphocyte count as indicators of poor outcomes in nonpregnant individuals with COVID-19.[23] We should pay careful attention to these laboratory indicators of pregnant women with COVID-19. However, D-dimer was typically elevated during pregnancy,[24] and a comparative cross-sectional study revealed that pregnant women had significantly higher white blood cell count, neutrophil count, and lymphocyte count compared with nonpregnant women.[25] Therefore, pregnancy factors should also be considered when dynamically monitoring changes of laboratory indicators in pregnant women with COVID-19.

Of course, our review has some limitations. We included only 11 articles, including case reports and case series, and most of them were from China. Again, reference ranges for laboratory values differed between reports and several data elements were not clearly reported. In addition, most of the pregnant women with COVID-19 included in our review were mild and moderate, with only 11 cases being severe and 2 cases being critical. We were unable to compare laboratory abnormalities between pregnant women with mild and severe. So, more data from other regions are needed to better define laboratory abnormalities in pregnant women with COVID-19 infection. In our meta-analysis, 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.

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Conflict of Interest

None declared.

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