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Review Article

Hematological Parameters in Pregnant Women with COVID-19: A Systematic Review

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ABSTRACT

Background: In the COVID-19 pandemic, the prevention and control of COVID-19 infection are extremely important. Therefore, laboratory indicators are needed that can detect pregnant patients with mild symptoms or no symptoms at the time of admission to the hospital and ensure that these patients are separated from the healthy population. This study aimed to review hematologic parameters in pregnant women with COVID-19 and evidence for their prognostic and diagnostic value.

Methods: We searched PubMed/Medline, Scopus, and Google Scholar for the term "pregnancy" in combination with "COVID-19," "coronavirus 2019" and "SARS-CoV-2" in studies published in the English literature between March 2020 and January 2021 and identified a number of studies. Studies that reported complete blood cell counts in pregnant patients with COVID-19 infection were selected. Both retrospective and prospective studies were included in this review, whereas case reports, cohort studies with less than 10 participants, and duplicate reports were excluded. A power analysis was not performed in any of the included studies.

Results: Fourteen studies were found that evaluated hematologic parameters in pregnant women with COVID-19. A review of these studies revealed conflicting findings in terms of the potential diagnostic and prognostic value of following hematologic parameters in healthy pregnant women versus pregnant COVID-19 patients on admission to the hospital: the White Blood Cell (WBC) count, neutrophil, platelet, eosinophil and lymphocyte counts, and Neutrophil-to-Lymphocyte Ratio (NLR). WBC count in pregnant women with COVID-19 infection was significantly higher than that in non-pregnant women with COVID-19 infection. There was no difference in the lymphocyte counts of the pregnant and non-pregnant population with COVID-19, suggesting that lymphopenia may be a prognostic factor independent of pregnancy.

Conclusion: In terms of their diagnostic value, the hematologic parameters evaluated did not distinguish healthy pregnant women from those with COVID-19 infection.

Keywords: COVID-19; SARS-CoV-2; Pregnancy; Hematology; White blood cells; Platelets; Lymphocytes

INTRODUCTION

COVID-19 is a highly contagious disease caused by the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). On 11 March 2020, the World Health Organization declared a COVID-19 pandemic due to the worldwide spread of the virus [1]. The symptoms of COVID-19 range from mild to severe, with acute respiratory distress syndrome, septic shock, and multiorgan failure. Mild symptoms and signs of COVID-19 are very similar to those of upper respiratory infections caused by other viruses, and they need to be differentiated through the use of biological markers [2].

Pregnant women are more susceptible to respiratory pathogens due to variables, such as increased oxygen consumption, an elevated diaphragm, and edema of the respiratory tract mucosa [3]. Furthermore, the pregnancy-related state of immune adaptation increases maternal susceptibility to intracellular pathogens, such as viruses [3,4]. Higher numbers of complications and intensive care unit (ICU) admissions have been reported in pregnant women with viral infections (H1N1 influenza, Zika virus, and SARS-CoV) than in the general population [5-10].

Many studies have reported the course of COVID-19 in pregnant women and adverse pregnancy outcomes among these patients

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[9-12]. Based on these studies, the effects of COVID-19 related pneumonia on pregnant women appear to be less severe than those of SARS-CoV and MERS-CoV [12], with several authors reporting no or mild respiratory symptoms in pregnant women with COVID-19 [12,13]. According to the literature, the most common symptom of COVID-19 in pregnant women is a fever [13].

In the COVID-19 pandemic, the prevention and control of COVID-19 infection are extremely important. Therefore, laboratory indicators are needed that can detect pregnant patients with mild symptoms or no symptoms (i.e., asymptomatic) at the time of admission to the hospital and ensure that these patients are separated from the healthy population.

A complete blood count is a common blood test ordered by physicians and interpreted in clinical laboratories. The diagnostic and prognostic value of hematologic parameters in a complete blood count for different diseases has been demonstrated previously [14,15]. A recent review of the literature suggested that hematologic abnormalities in COVID-19 patients may serve as a diagnostic and prognostic tool for predicting illness severity and mortality [16].

Given the severity of the COVID-19 pandemic and the lack of sufficient evidence on the utility of specific markers, the present study aimed to review the main hematologic parameters in pregnant women with COVID-19 and the evidence for their prognostic and diagnostic value.

LITERATURE SEARCH

In this systematic review, using MeSH-compatible keywords, we searched PubMed/Medline, Scopus, and Google Scholar for the term "pregnancy" in combination with "COVID-19," "coronavirus 2019," and "SARS-CoV-2" in studies published in the English literature between March 2020 and January 2021 and identified a number of studies. Only full-text studies that reported complete blood cell counts in pregnant patients with COVID-19 infection were selected. The titles, abstracts, and full-text articles were screened to identify all relevant articles published in English. The reference lists were reviewed to identify additional references to eligible studies.

Two researchers analyzed the search results separately. Disagreements on the inclusion of studies were resolved by a third independent reviewer. Both retrospective and prospective studies were included in the review. Case reports, cohort studies with less than 10 participants, and duplicate studies were excluded.

Statistical analysis

Power analysis has not been performed in any of these studies. There were not enough research data among the studies on this subject.

RESULTS AND DISCUSSION

Fourteen studies were found that evaluated hematologic parameters in pregnant women with COVID-19. The following hematologic parameters were used in determining the diagnosis, severity, course, and complications of COVID-19: white blood cell (WBC), platelet, lymphocyte, neutrophil, and eosinophil counts; neutrophil-to-lymphocyte ratios (NLRs); and hemoglobin values [16,17]. However, hematologic findings in pregnant patients with COVID-19 should be interpreted with caution because during normal pregnancy, physiological changes in hematological indices occur, making it difficult to define reference ranges for a complete blood count [18-20].

WBC count

WBCs, also called leukocytes, are a heterogeneous group of cells in the immune system responsible for protecting the body from infections and other diseases. Table 1 provides information on the WBC counts of the healthy pregnant women and pregnant women with COVID-19 upon admission to the hospital. As can be seen from the data in the table, the evidence on the possible diagnostic and prognostic value of WBC counts was conflicting.

Table 1: Summary of studies that compare white blood cell counts.

Reference; country	Study design	Number of patients and controls; age	WBC count, × 10^9 cells/L	Results		p value	Comment
	Pregnant women are grouped			Healthy Pregnant women without Covid-19	Pregnant women with Covid-19		
Yang H, et al. China	Retrospective Single center January 20 to March 5, 2020.	Pregnant women with Covid-19 (n=13) 30.2 ± 2.3 yrs, Healthy pregnant controls (n=42) 29.8 ± 3.4 yrs	On admission for delivery	10.0 ± 2.9	8.9 ± 1.5	0.201	None of the patients developed severe COVID-19 or died.
Norooznezhad AH et al. Iran	Retrospective Multicentre March 3 to May 10, 2020.	Pregnant women with Covid-19 (n=20) 31.4 ± 5.8 yrs, Healthy pregnant controls (n=38) 32.6 ± 5.4 yrs	PreCeserian	10.0 ± 2.2 (9.3–10.7)	9.6 ± 3.8 (7.7–11.4)	0.64	No comorbidities. %75 symptomatic.
Sun G, et al. China.	Retrospective Single center Case control January 24 to March 14, 2020.	Pregnant women with Covid-19 (n=60) 30.97 ± 4.13 yrs, Healthy pregnant controls (n=120) 29.97 ± 3.43 yrs	All research subjects were recruited in the third trimester	9.6 ± 3.0	10.68 ± 3.9	0.077	Patients with comorbidities were included. Mild Covid 19 Only 15 % reported respiratory symptoms

Li N, et al. China	Retrospective Single center Case control January 24 to February 29, 2020.	Pregnant women with Covid-19 (n=16) 30.9 ± 3.2 yrs Suspected cases (n=18) 29.8 ± 2.3 yrs, Healthy pregnant controls (n=121) 29.3 ± 2.6 yrs	All research subjects were recruited in the third trimester Reference range 3.5-9.5	10.3 ± 3.1	8.6 ± 1.8	0.021	Patients with comorbidities were included. Pregnant women had no or mild respiratory symptoms.
Yazihan N, et al., Turkey	Prospective Single center Case control May 11, 2020 to August 30, 2020.	Pregnant women with Covid-19 (n = 95) 29(7) yrs Healthy pregnant controls (n = 92) 28 (7.7) yrs		8.88 (3.09)	6.07 (3.48)	<0.001	Each group was divided into trimesters. Patients have comorbidities. Only 2 patients had severe disease.
Anuk AT, et al. Turkey.	Prospective Single center May 11, 2020 to August 30, 2020.	Pregnant women with Covid 19 (n = 100) 17-41 yrs Healthy pregnant controls (n = 100) 17-41 yrs					Each group was divided into trimesters
			1st Trimester	(n=33) 8.30 (3.63–12.86)	(n=34) 5.38 (3.2–15.62)	<0.010	
			2nd Trimester	(n=32) 9.43(4.04–15.03)	(n=33) 5.97(3.49–10.81)	<0.001	
			3rd Trimester	(n=35) 9.22 (5.40–14.14)	(n=33) 8.05 (3.93–14.38)	<0.001	
Erol Koç EM, et al. Turkey.	Prospective Single center March 20 and July 25, 2020,	Pregnant women with COVID-19 (n=39) 27. ± 4.9 yrs Healthy pregnant controls (n=69) 27.8 ± 6.0 yrs		8.08 ± 1.57	9.73 ± 3.51	0.14	None of the patients developed severe COVID-19 or died.
Tanacan A, et al. Turkey.	Prospective Single center June 1 and August 30, 2020,	Pregnant women with COVID-19 (n=90) 28 (6) yrs Healthy pregnant controls (n=90) 27 (5) yrs	Equal number of patients for each pregnancy trimester were recruited.	8.8 (3.1)	6.1 (3.4)	<0.001	Pregnant women with Covid-19 have more comorbidities than control group (16.6% vs 3.3%)
	Women with Covid-19 are grouped			Non-pregnant women with Covid-19	Pregnant women with Covid-19		
Cheng B, et al. China.	Retrospective Single center January 15 to February 23, 2020	Pregnant women with Covid-19 (n=31) 29.0 (24.0-41.0) yrs Nonpregnant women with Covid-19 (n=80) 33.0 (22.0-41.0) yrs	Normal range 3.5-9.5	4.6 (3.5–6.1)	6.9 (5.6–9.1)	<0.001	Pregnant patients had a significantly lower percentage of severe disease (3.2% vs 14.4%) Patients (%13.5) have comorbidities
Mohr-Sasson A, et al. Israel.	Retrospective cohort study Single center March to April 2020.	Pregnant women with Covid-19 (n=11), 28 (24–35) yrs Non-pregnant women with Covid-19 infection (n=25) 40 (27–46) yrs	Normal range during third trimester 5.6–16.9 Nonpregnant normal range 4.0–10.8	6.23 (4.64–7.58)	9.2 (6.80–12.00)	0.001	All enrolled pregnants were in the third trimester Hospitalization was less common in the pregnant group compared to controls (63.6% vs 80%) Leukopenia was observed in 44% of pregnant women.
Wang Z, et al. China.	Retrospective Single center December 8, 2019 to April 1, 2020.	Pregnant women with Covid-19 (n=30) 29.9 (26.8–33.3) yrs Nonpregnant women with COVID 19 (n=42) 30.0 (27.0–34.0) yrs	Normal range 3.5–9.5	5.6 (4.1-7.3)	7.5 (6.4-10.3)	0.01	Pregnant patients had milder disease

Wei L, et al. China	Retrospective Single center January 19 to March 2, 2020	Pregnant women with Covid-19 (n=17) median age 33.0 yrs Non pregnant women with COVID-19 (n=26) median age 33.5 yrs		5.2 (3.8-7.6)	7.8 (6.6-10.2)	<0.001	Pregnant patients not have any underlying comorbidities due to a chronic disease. More leukocytosis (24 % vs 0%) was detected in pregnant group. Only 1 pregnant woman in her first trimester and 3 in their second trimester.
Qiancheng X, et al. China	Retrospective Single center January 15 to March 15, 2020	Pregnant women with Covid-19 (n=28) 30.0 (26.7-32) yrs Nonpregnant women with Covid-19 (n=54) 31.0 (28.0 -35.0)		4.69 (3.87–5.77)	7.54 (6.58–10.26)	<0.001	Patients have comorbidities 7.1% pregnant, 1.9% non-pregnant have severe disease More leukocytosis (37.5% vs 3.7%) was detected in pregnant group.
				Non-ICU hospitalization	**ICU hospitalization**		
Vivanti AJ et al. France	Retrospective Multicenter March 12 to April 13, 2020	Non ICU hospitalization (n=90) ICU hospitalization (n=10) 33.7 (29–36.7) yrs		7.2 (5.4-8.9)	6.6 (6.1-7.2)	0.68	Patients have comorbidities Women with a high BMI (30.7 kg/m2 [IQR 29.8–33.1 kg/m2]) were more likely to be hospitalized in ICUs than women with lower BMIs

Some of the included studies reported similar WBC counts among healthy pregnant women and pregnant women with COVID-19 on admission [21-24], whereas other reported slightly lower WBC counts in pregnant women with COVID-19 [12,25-27]. WBC count in pregnant women with COVID-19 infection was significantly higher than that in non-pregnant women with COVID-19 infection [28-32]. Nevertheless, pregnant women had lower disease severity, combined with an increased inflammatory response and cell immunity, compared to non-pregnant patients [28].

Collin et al. reported that the risk of admission to the intensive care unit (ICU) was higher in pregnant women with COVID-19 infection than in non-pregnant women with COVID-19 infection of similar age. Evaluation at the time of diagnosis is very important to determine the risk level of the disease progressing to an adverse form. Early identification of COVID-19 patients at risk of severe outcomes can enable timely interventions and improved outcomes [33].

In adult patients, baseline leukocytosis was associated with a higher mortality rate [34,35]. Vivanti et al conducted a retrospective study to identify prognostic factors associated with adverse outcomes in pregnant women with COVID-19 at the time of their diagnosis [36]. They detected no statistically significant difference in the WBC count of two groups. Hence, the WBC count cannot be used to distinguish severity and progression early in the infection course in pregnant women with COVID-19.

Neutrophil count

Neutrophils constitute 50%–70% of WBCs in healthy adults. In pregnant women, neutrophils increase and account for up to 95% of peripheral blood leukocytes [37]. Various phenotypic and functional properties of neutrophils, as well as the responsiveness of circulating neutrophils to pro-inflammatory stimuli, change during pregnancy [38]. Some studies suggested that neutrophils exhibited an intense response to the virus, with increased organ damage in COVID-19 through infiltration of tissues, which contributed to widespread thrombosis [39,40].

In the present review, the neutrophil counts in pregnant women with COVID-19 were similar [12,21,22,24], or higher than those in pregnant women without COVID-19 (Table 2) [23,25,27]. In terms of the neutrophil counts in non-pregnant women with COVID-19 and those in pregnant women with COVID-19, the studies reported contradictory findings (Table 2) [28-32]. However, it should be noted that other factors, such as underlying viral and bacterial infections, may impair the accuracy of observed neutrophil results [41].

Table 2: Summary of studies that compare lymphocyte counts.

Reference country	Study design	Number of patients and controls; age	Lymphocyte, × 10^9/L	Results		P value	Comment
	Pregnant women are grouped			Healthy pregnant women without Covid-19	Pregnant women with Covid-19		
Yang H, et al. China.	Retrospective Single center January 20 to March 5, 2020.	Pregnant women with Covid-19 (n=13) 30.2 ± 2.3 yrs, Healthy Pregnant controls (n=42) 29.8 ± 3.4 yrs		1.6 ± 0.5	1.4 ± 0.4	0.48	Lymphocyte count did not differ between healthy pregnant women and pregnant women with Covid-19. The sample size was small
Norooznezhad et al. Iran	Retrospective Multicentre March 3 to May 10, 2020.	Pregnant women with Covid-19 (n=20) 31.4 ± 5.8 yrs, Healthy p regnant controls (n=38) 32.6 ± 5.4 yrs	Pre-Ceserian	2.2 ± 0.6 (2.0–2.4)	1.6 ± 0.7 (1.2–1.9)	0.004	Pregnant women with COVID-19 had significantly lower lymphocyte count.
			Lymphocyte ratio (%)	22.5 ± 6.1 (20.5–24.5)	17.7 ± 5.6 (15.1–20.3)	0.005	Pregnant women with COVID-19 had significantly lower lymphocyte count.
Sun G, et al. China.	Retrospective January 24 to March 14, 2020.	Pregnant women with Covid-19 (n=60) 30.97 ± 4.13yrs, Healthy Pregnant controls (n=120) 29.97 ± 3.43 yrs		1.66 ± 1.18	1.25 ± 0.53	0.001	Lymohocytopenia among Covid-19 patients were higher than control group (43.33% vs 15.83%,p=0.0003)
Li N, et al. China	Retrospective Case control 01-01-2024 to February 29, 2020	Pregnant women with Covid-19 (n=16) 30.9 ± 3.2yrs, Suspected cases (n=18) 29.8 ± 2.3yrs Healthy Pregnant controls (n=121) 29.3 ± 2.6yrs	1.1-3.2	1.5 ± 0.5	1.5 ± 0.4	0.622	Lymphocyte count did not differ between healthy pregnant women and pregnant women with Covid-19. The sample size was small
Yazihan N, et al. Turkey	Prospective Single center Case control May 11, 2020 to August 30, 2020.	Pregnant women with Covid-19 (n = 95) 29(7) yrs Healthy Pregnant controls (n = 92) 28 (7.7) yrs		1.83 (0.59)	1.24 (0.66)	<0.001	Pregnant women with COVID-19 had significantly lower lymphocyte count.
Anuk AT, et al. Turkey	Prospective Single center May 11, 2020 to August 30, 2020.	Pregnant women with Covid-19 infection(n = 100) 17-41 yrs Healthy Pregnant controls (n = 100) 17-41 yrs					Pregnant women with COVID-19 had significantly lower lymphocyte count.
			1st Trimester	1.9 (0.46–2.85)	1.27 (0.52–2.60)	<0.001	
			2nd Trimester	1.82 (0.9–3.20)	1.16 (0.36–2.22)	<0.001	
			3rd Trimester	1.7 (0.36–2.22)	1.28 (0.36–2.22)	<0.001	

Erol Koç EM, et al. Turkey	Prospective Single center March 20 and July 25, 2020	Pregnant women with COVID-19 (n=39) 27. ± 4.9 yrs Healthy pregnant controls (n=69) 27.8 ± 6.0 yrs		1.38 ± 5.92	1.18 ± 5.16	0.1	Lymphocyte count did not differ between healthy pregnant women and pregnant women with Covid-19.
Tanacan A, et al. Turkey.	Prospective Single center June 1 and August 30, 2020	Pregnant women with COVID-19 (n=90) 28 (6) yrs Healthy pregnant controls (n=90)		1.8 (5.8)	1.2 (6.6)	<0.001	Pregnant women with COVID-19 had significantly lower lymphocyte count.
	Women with Covid-19 are grouped			Non-pregnant women with Covid-19	Pregnant women with Covid-19		
Cheng B, et al. China	Retrospective January 15 to February 23, 2020	Pregnant women with Covid-19 (n=31) 29.0 (24.0-41.0) yrs Nonpregnant women with Covid-19 (n=80) 33.0 (22.0-41.0)		4.6 (3.5–6.1)	6.9 (5.6–9.1)	<0.001	Lymphopenia occured in 32.4% patients
Mohr-Sasson A, et al. Israel.	Retrospective cohort study March to April 2020.	Pregnant women with Covid-19 (n=11), 28 (24–35) yrs 28 (24–35) yrs Non-pregnant women with Covid-19 (n=25) 40 (27–46) yrs		1.49 (0.92–1.93)	1.13 (0.64–1.68)	0.11	Lymphopenia was observed in 45.5% and 32% of the pregnant and control groups, respectively.
			Lymphocyte (%)	26.50 (15.70–29.90)	13.60 (4.50–19.37)	0.003	The relative lymphocyte count to WBC was significantly reduced in the pregnant group compared to the controls.
Wang Z, et al. China.	Retrospective study, December 8, 2019 to April 1, 2020.	Pregnant women with Covid-19 (n=30) 29.9 (26.8–33.3) yrs Nonpregnant women with Covid-19 (n=42) 30.0 (27.0–34.0) yrs		1.6 (1.3–2.0)	1.4 (1.1–2.0)	0.13	Lymphocyte counts did not differ between pregnant women with Covid-19 and control group.
			Lymphocyte %	31.5 (21.5–37.5)	16.1 (11.5–23.6)	<0.001	Median lymphocyte percentage was significatly lower in pregnant women compared with nonpregnant women
Wei L, et al. China.	Retrospective January 19 to March 2, 2020	17 COVID-19 pregnant women 26 COVID-19 median age 33.0 yrs nonpregnant women 33.5 years		1.4 (1.0-2.0)	1.1 (0.9-1.6)	0.21	Small sample size. Lymphopenia occurred in pregnant and non pregnant women (41% vs 38%)

Qiancheng X et al. China.	Retrospective January 15 to March 15, 2020	Pregnant women with Covid-19 (n=28) Nonpregnant women with Covid-19 (n=54)	1.54 (1.09–2.03)	1.29 (0.91–1.71)	0.148	Lymphocyte count did not differ between pregnant women with Covid-19 and control group.
			Non-ICU hospitalization	ICU hospitalization		
Vivanti AJ et al. France.	Retrospective Multicenter March 12 to April 13, 2020	Non ICU hospitalization (n=90) ICU hospitalization (n=10) 33.7 (29–36.7) yrs	1.15 (0.9-1.6)	0.77 (0.7-1)	0.01	Sample size of patients admitted to the ICU was too small. The proportion of women with lymphocytopenia at diagnosis was higher in the ICU group than the rest of the cohort (89% vs 36% p=0.008)

Lymphocyte count

SARS-CoV-2 directly infects lymphocytes, the primary immune barrier against viral infections, and causes a profound cytopathic effect that damages lymphocytes [42]. In addition, the release of pro-inflammatory cytokines and chemokines draws immune cells, such as monocytes and T lymphocytes, from the blood to the infected area, causing lymphopenia in COVID-19 patients [43-47]. In some of the studies, lymphopenia was present to a variable extent in almost all symptomatic patients and was considered a sensitive and reliable marker of disease severity and outcomes in COVID-19 infection [46-48].

In terms of the diagnostic and prognostic value of the lymphocyte count, the evidence based on the included studies is conflicting (Table 3) [21-32]. As shown in Table 3, there was no difference in the lymphocyte counts of the pregnant and non-pregnant population with COVID-19, suggesting that lymphopenia may be a prognostic factor independent of pregnancy [28-32].

The disease course in COVID-19 infection appeared to depend on differences in lymphocyte regeneration in response to lymphocyte destruction by the virus [45]. In the study by Vivanti et al. pregnant COVID-19 patients had lymphopenia upon admission, and lymphocyte counts were particularly low in severe cases hospitalized in ICUs [36]. They noted that the lymphocyte count could help to identify the likelihood of disease progression and severity in COVID-19 and therefore aid patient risk stratification and medical management.

NLR

The NLR is recognized as a systemic marker of the inflammatory response that is superior to individual levels of neutrophils and lymphocytes in assessing disease progression in some viral infections [49]. The NLR is less affected by a number of physiological conditions and represents two complementary immunological pathways. Accumulating evidence suggests that the NLR increases significantly in patients with more severe COVID-19 infection and that this is associated with poor outcomes, such as acute respiratory distress syndrome [50-52].

The NLR increases in accordance with gestational age and has been used as a predictor of pregnancy-related complications [53]. In this review, we excluded studies that did not calculate NLR values. There are limited data comparing the NLR in healthy pregnant women with that in pregnant women with COVID-19, and the results were inconsistent. The results of the six studies were inconsistent, possibly due to the small sample sizes in the studies, pointing to the need for further studies (Table 4) [22,24,26].

Eosinophil count

A low eosinophil count in a symptomatic patient is an indicator of COVID-19 infection [54]. In addition to other functions, eosinophils play a role in adaptive immunity by producing molecules with antiviral activity against particular respiratory viruses [55,56]. It should be noted that many aspects of serious illness are specific to COVID-19 and that severe lymphopenia and eosinopenia and widespread lung tissue damage due to a cytokine storm are rare in other respiratory viral infections [57].

Few publications have focused on the eosinophil count in pregnant women with COVID-19 [12,29]. Mohr-Sasson et al. found no difference in the eosinophil counts of pregnant and non-pregnant women with COVID-19 (Table 5) [29]. In contrast, Li et al. found lower eosinophil counts in pregnant women with COVID-19 as compared to those in pregnant women without COVID-19 on admission [12].

Platelet count

The number of platelets in pregnant women is slightly lower than that in non-pregnant women of the same age and decreases as pregnancy progresses [58]. Multiple physiological changes that occur during pregnancy can contribute to lower platelet counts [59].

Previous research reported that thrombocytopenia was very common in COVID-19 patients. In patients with severe COVID-19, the platelet count is markedly reduced, suggesting that changes in platelet levels may be predictive of the patient's prognosis [60]. Thrombocytopenia may be directly due to infection of bone marrow precursors, resulting in abnormal hematopoiesis of platelets, or a cytokine storm destroying progenitor cells. Thrombocytopenia may also be associated with platelet destruction by the immune system as a result of an auto-immune response or by increased platelet consumption due to lung damage [61,62].

As shown in Table 5, the studies revealed no difference in the platelet counts in non-pregnant patients with COVID-19 versus those in pregnant patients with COVID-19 [28-32]. Norooznezhad et al. compared platelet counts in pregnant controls without COVID-19 with those in pregnant with COVID-19 and found no difference in the counts (Table 5) [22]. However, in some of the studies, platelet counts were lower in in pregnant with COVID-19 [26,27].

Table 3: Summary of studies that compare lymphocyte counts.

	Pregnant women are grouped		NLR	Healthy pregnant women without Covid-19	Pregnant women with Covid-19	p	Comment
Norooznezhad et al. Iran	Retrospective Multicentre March 3 to May 10, 2020.	Pregnant women with Covid-19 (n=20) 31.4 ± 5.8 yrs, Healthy Pregnant controls (n=38) 32.6 ± 5.4 yrs		3.6 ± 2.2 (2.8–4.3)	5.0 ± 2.3 (3.9–6.1)	0.027	A non significant increase in NLR after CD in pregnant patients diagnosed with COVID-19 should not concern the clinicians
Yazihan N et al ; Turkey	Prospective Case control May 11, 2020 to August 30, 2020.	Pregnant women with Covid-19 infection (n = 95) 29(7) yrs Healthy Pregnant controls (n = 92) 28 (7.7) yrs		3.3 (1.8)	3.5 (3.1)	0.55	The NLR value did not differ between healthy pregnant women and pregnant women with Covid-19.
Erol Koç, et al. Turkey		Pregnant women with Covid-19 infection (n = 39) 27.5 ± 4.9 yrs 27.5 ± 4.9 yrs Healthy Pregnant controls (n = 69) 27.8 ± 6.0 yrs		5.12 ± 2.7	6.46 ± 3.5	0.043	Optimal cut off value of NLR was 6.23 With a sensitivity 45.9 and specifity 75.4
Tanacan A, et al. Turkey.	Prospective Single center June 1 and August 30, 2020,	Pregnant women with COVID-19 (n=90) 28 (6) yrs 28 (6) yrs Healthy pregnant controls (n=90) 27 (5) yrs		3.4 (1.8)	3.7(3)	0.56	The NLR value did not differ between healthy pregnant women and pregnant women with Covid-19.
	Women with Covid-19 are grouped			Non-pregnant women with Covid-19	Pregnant women with Covid-19		
Cheng B, et al. China	Retrospective January 15 to February 23, 2020	Pregnant women with Covid-19 (n=31) 29.0 (24.0-41.0) yrs Nonpregnant women with Covid-19 (n=80) 33.0 (22.0-41.0) yrs		1.9	4.4	<0.001	Median NLR value was significaltly higher in pregnant women compared with nonpregnant women
Mohr-Sasson A, et al. Israel	Retrospective cohort study March to April 2020	Pregnant women with Covid-19 (n=11), 28 (24–35) yrs Non-pregnant women with Covid-19 Non-pregnant women with Covid-19 (n=25) 40 (27–46) yrs	Lymphocyte to neutrophil ratio	13.6 (4.5-19.3)	26.5 (15.7-29.9)	0.003	Median NLR value was significaltly higher in pregnant women compared with nonpregnant women

Table 4: Summary of studies that compare eosinophil counts.

Reference; country	Study design	Number of patients and controls; age	WBC count, × 10^9 cells/L	Results		p value	Comment
	Pregnant women are grouped			Healthy pregnant women without Covid-19	Pregnant women with Covid-19		
Li N, et al. China	Retrospective Single center Case control 01-01-2024 to February 29, 2020	Pregnant women with Covid-19 (n=16) 30.9 ± 3.2 yrs, Suspected cases (n=18) 29.8 ± 2.3 yrs, Healthy pregnant controls (n=121) 29.3 ± 2.6 yrs	All research subjects were recruited in the third trimester Reference range (0.02-0.52)	0.08 ± 0.02	0.04 ± 0.05	0.008	Significantly lower eosiophil count was found in the Covid-19 group
	Women with Covid-19 are grouped			Non-pregnant women with Covid-19	Pregnant women with Covid-19		
Mohr-Sasson A, et al. Israel.	Retrospective cohort study Single center March to April 2020.	Pregnant women with Covid-19 (n=11), Non-pregnant women with Covid-19 infection (n=25) 40 (27–46) yrs	Normal range during third trimester 0-0.6 Nonpregnant normal range 0-0.6	0.01(0.005-0.05)	0.02(0.001-0.05)	0.097	Eosinophil count did not differ between pregnant women with Covid-19 and control group.
			%	0.20(0.10-1.00)	0.20(0.001-0.50)	0.46	

Table 5: Summary of studies that compare haemoglobin values.

Reference; country	Study design	Number of patients and controls; age	Hemoglobin,g/dL	Results		p value	Comment
	Pregnant women are grouped			Healthy pregnant women without Covid-19	Pregnant women with Covid-19		
Norooznezhad AH et al. Iran	Retrospective Multicentre March 3 to May 10, 2020.	Pregnant women with Covid-19 (n=20) 31.4 ± 5.8 yrs, Healthy pregnant controls (n=38) 32.6 ± 5.4 yrs	Pre-Ceserian	12.3 ± 1.2 (11.9–12.7)	12.5 ± 1.0 (12.0–13.0)	0.674	
Yazihan N, et al.Turkey	Prospective Single center Case control May 11, 2020 to August 30, 2020.	Pregnant women with Covid-19 (n = 95) 29(7) yrs Healthy pregnant controls (n = 92) 28 (7.7) yrs		12.5 (1.5)	11.7 (1.8)	0.004	Significantly lower hemoglobin value was found in the Covid-19 group
Anuk AT, et al. Turkey.	Prospective Single center May 11, 2020 to August 30, 2020.	Pregnant women with Covid 19 (n = 100) 17-41 yrs Healthy pregnant controls (n = 100) 17-41 yrs	Median(range)				
			1st Trimester	12,86 (1,04)	12,46 (1.08)	>0.5	
			2nd Trimester	12,05 (0,99)	11,20 (1.14)	<0.05	
			3rd Trimester	11,46 (0,98)	10,96 (1.16)	<0.01	
Erol Koç EM, et al. Turkey.	Prospective Single center March 20 and July 25, 2020,	Pregnant women with COVID-19 (n=39) 27. ± 4.9 yrs Healthy pregnant controls (n=69) 27.8 ± 6.0 yrs		13.2 ± 1.45	11 ± 2.16	0.34	

Tanacan A, et al., Turkey.	Prospective Single center June 1 and August 30, 2020,	Pregnant women with COVID-19 (n=90) 28 (6) yrs Healthy pregnant controls (n=90) 27 (5) yrs		12 (1.5)	11.5(1.7)	0.003	Pregnant women with COVID-19 had significantly lower Hb value.
	Women with Covid-19 are grouped			Non-pregnant women with Covid-19	Pregnant women with Covid-19		
Cheng B, et al., China.	Retrospective Single center January 15 to February 23, 2020	Pregnant women with Covid-19 (n=31) 29.0 (24.0-41.0) yrs Nonpregnant women with Covid-19 (n=80) 33.0 (22.0-41.0) yrs	Normal range 11.5-15.0	12.7 (11.7-13.3)	12.0 (11.2-13.0)	0.779	
Mohr-Sasson A, et al. Israel.	Retrospective cohort study Single center March to April 2020.	Pregnant women with Covid-19 (n=11), 28 (24–35) yrs Non-pregnant women with Covid-19 infection (n=25) 40 (27–46) yrs	Normal range during third trimester 9.5–15.0 Nonpregnant normal range 11.7–15.7	12.55 (11.50–14.07)	12.06 (11.00–12.80	0.29	Hemoglobin levels were within normal range in both groups.
Wang Z, et al. China.	Retrospective Single center December 8, 2019 to April 1, 2020.	Pregnant women with Covid-19 (n=30) 29.9 (26.8–33.3) yrs Nonpregnant women with COVID‐19 (n=42) 30.0 (27.0–34.0) yrs	Normal range 13.0-17.5	13.2 (12.1-14.1)	11.7 (10.8-12.9)	0.002	
Wei L, et al. China	Retrospective Single center January 19 to March 2, 2020	Pregnant women with Covid-19 (n=17) median age 33.0 yrs Non pregnant women with COVID-19 (n=26) median age 33.5 yrs	median (IQR)	12.3 (11.7-12.7)	11.7(11.1-13.2)	0.86	
Qiancheng X, et al. China	Retrospective Single center January 15 to March 15, 2020	Pregnant women with Covid-19 (n=28) 30.0 (26.7-32) yrs Nonpregnant women with Covid-19 (n=54) 31.0 (28.0 -35.0)		12.6 (12.1-13.5)	11.7 (10.6-12.9)	0.018	Baseline hemoglobin level was lower in pregnant patients compared with nonpregnant women.
				Non-ICU hospitalization	ICU hospitalization		
Vivanti AJ et al. France	Retrospective Multicenter March 12 to April 13, 2020	Non ICU hospitalization (n=90) ICU hospitalization (n=10) 33.7 (29–36.7) yrs	Median (IQR)	11.4 (10.5-12.2)	9.8 (9.3-11.3)	0.02	Hemoglobin count at diagnosis was lower in women who needed hospitalization in ICUs

Previous research reported that the platelet to lymphocyte ratio (PLR) was an indicator of the severity of COVID-19 infection [63]. Others presented conflicting data on the diagnostic and prognostic value of the PLR in adult patients with COVID-19 [64-66]. A scientist team has evaluated the PLR in 39 pregnant women with a clinical diagnosis of COVID-19 and 69 pregnant women without COVID-19 and detected no significant difference in the platelet count or PLR [24].

Hemoglobin

SARS-CoV-2 attack bone marrow erythroblasts leading to infection of progenitor cells, which impaired the function of mature red blood cells. In severe cases of COVID-19, this can lead to impaired hemoglobin production [65].

In the present review, a number of studies compared hemoglobin levels in healthy pregnant women without COVID-19 with those in pregnant women with COVID-19.

Some of these studies reported similar levels in the two groups [22,24], whereas others reported decreased hemoglobin levels in the pregnant group with COVID-19 infection [25-27].

Decreased hemoglobin levels might be an indicator of disease progression in COVID-19, and it would be more valuable to focus on the decline in hemoglobin levels rather than anemia [66]. Vivanti et al. reported that hemoglobin levels at the time of a COVID-19 diagnosis was lower in severe cases who required admission to the ICU than in pregnant patients with COVID-19 who did not require admission to ICUs [36].

CONCLUSION

According to the present review, the evidence for the potential diagnostic and prognostic value of WBC, neutrophil, lymphocyte, eosinophil and platelet counts, as well as the NLR and hemoglobin, is conflicting.

Thus, at present, hematologic indices do not appear to be able to distinguish between COVID-19 and non-COVID-19 cases in the obstetric setting. Such information is needed to prevent cross-contamination in the obstetric department.

Despite the rapid increase in the number of COVID-19 cases, there is limited data on laboratory findings in pregnant women. There is considerable heterogeneity in relevant published studies due to a number of variables, such as the number of patients enrolled in the study, gestational age, differences in patient exposure to the virus, and reference intervals of hematologic parameters.

In terms of illness severity in COVID-19 patients, there are different definitions of this parameter. The aforementioned has implications for subgroup analyses of COVID-19 patients.

Furthermore, the majority of reported studies are retrospective and single center. In addition, some studies have not elucidated underlying comorbidities, and it was unclear when in the disease course, the hematologic parameters were measured.

Thus, it is difficult to compare the findings of the various studies and to determine the validity of the results.

Large multicenter studies are needed to shed light on the possible diagnostic and prognostic value of hematologic indices in pregnant patients with COVID-19.

REFERENCES

1. Chatterjee P, Nagi N, Agarwal A, Das B, Banerjee S, Sarkar S, et al. The 2019 novel coronavirus disease (COVID-19) pandemic: A review of the current evidence. Indian J Med Res.2020;51:147-159.
2. Siordia JA Jr. Epidemiology and clinical features of COVID-19: A review of current literature. J Clin Virol. 2020;127:104357.
3. Madinger NE, Greenspoon JS, Ellrodt AG. Pneumonia during pregnancy: Has modern technology improved maternal and fetal outcome? Am J Obstet Gynecol.1989;161:657-662.
4. Engels G, Hierweger AM, Hoffmann J, Thieme R, Thiele S, Bertram S, et al. Pregnancy-related immune adaptation promotes the emergence of highly virulent H1N1 influenza virus strains in allogenically pregnant mice. Cell Host Microbe.2017;21:321-333.
5. Schwartz DA, Graham AL. Potential maternal and infant outcomes from (Wuhan) coronavirus 2019-nCoV infecting pregnant women: Lessons from SARS, MERS, and other human coronavirus infections. Viruses. 2020;12:194.
6. Harris JW. Influenza occurring in pregnant women. A statistical study of thirteen hundred and fifty cases. JAMA.1919;72:978-980.
7. Jamieson DJ, Honein MA, Rasmussen SA, Williams JL, Swerdlow DL, Biggerstaff MS, et al. Novel influenza a (H1N1) pregnancy working group. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet.2009;374:451-458.
8. Rasmussen SA, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: Responding to a rapidly evolving situation. Obstet Gynecol.2020;135:999–1002.
9. Chibueze EC, Tirado V, Lopes KD, Balogun OO, Takemoto Y, Swa T, et al. Zika virus infection in pregnancy: A systematic review of disease course and complications. Reprod Health.2017;28;14:28.
10. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: A systematic review and meta-analysis. Am J Obstet Gynecol MFM.2020;2:100107.
11. Castro P, Matos AP, Werner H, Lopes FP, Tonni G, Araujo Júnior E. Covid-19 and pregnancy. Rev Bras Ginecol Obstet.2020;42:420-426.
12. Li N, Han L, Peng M, Lv Y, Ouyang Y, Liu K, et al. Maternal and neonatal outcomes of pregnant women with coronavirus disease 2019 (COVID-19) pneumonia: A case-Control Study. Clin Infect Dis.2020;71:2035-2041.
13. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. Acta Obstet Gynecol Scand.2020;99:823–829.
14. Akdoğan M, Ustundag-Budak Y, Huysal K. The association of hematologic inflammatory markers with atherogenic index in type 2 diabetic retinopathy patients. Clin Ophthalmol.2016;10:1797-1801.
15. Asan A, Üstündağ Y, Koca N, Şimşek A, Sayan HE, Parildar H, et al. Do initial hematologic indices predict the severity of COVID-19 patients? Turk J Med Sci.2020.
16. Khartabil TA, Russcher H, van der Ven A, de Rijke YB. A summary of the diagnostic and prognostic value of hemocytometry markers in COVID-19 patients. Crit Rev Clin Lab Sci.2020;57:415-431.
17. Sun S, Cai X, Wang H, He G, Lin Y, Lu B, et al. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. Clin Chim Acta.2020;507:174-180.

18. Shen C, Jiang YM, Shi H, Liu JH, Zhou WJ, Dai QK, et al. A prospective, sequential and longitudinal study of haematological profile during normal pregnancy in Chinese women. J Obstet Gynaecol.2010;30:357–361.

19. Sanci M, Töz E, Ince O, Özcan A, Polater K, Inan AH, et al. Reference values for maternal total and differential leukocyte counts in different trimesters of pregnancy and the initial postpartum period in western Turkey. J Obstet Gynaecol.2017;37:571-575.

20. Chandra S, Tripathi AK, Mishra S. Physiological changes in hematological parameters during pregnancy. Indian J Hematol Blood Transfus.2012;28:144–146.

21. Yang H, Sun G, Tang F. Clinical features and outcomes of pregnant women suspected of coronavirus disease 2019. J Infect.2020;81:e40-e44.

22. Norooznezhad AH, Eskandarion S, Akbari R, Alimohammadi S, Nabavian SM, Giti S, et al. Changes of leukocytes, neutrophils, and lymphocytes count and dependent variables in pregnant women with coronavirus disease 2019 before and after cesarean delivery. J Med Virol. 2020;17.

23. Sun G, Zhang Y, Liao Q, Cheng Y. Blood test results of pregnant COVID-19 patients: An updated case-control study. Front Cell Infect Microbiol.2020;10:560899.

24. Erol Koç EM, Fındık RB, Akkaya H, Karadağ I, Tokalıoğlu EÖ, Tekin ÖM. Comparison of hematological parameters and perinatal outcomes between COVID-19 pregnancies and healthy pregnancy cohort. J Perinatal Med.2020.

25. Anuk AT, Polat N, Akdas S, Erol SA, Tanacan A, Biriken D, et al. The relation between trace element status (Zinc, Copper, Magnesium) and clinical outcomes in COVID-19 infection during pregnancy. Biol Trace Elem Res.2020;1-10.

26. Tanacan A, Yazihan N, Erol SA, Anuk AT, Yucel Yetiskin FD, Biriken D, et al. The impact of COVID-19 infection on the cytokine profile of pregnant women: A prospective case-control study. Cytokine.2021;140:155431.

27. Yazihan N, Tanacan A, Erol SA, Anuk AT, Sinaci S, Biriken D, et al. Comparison of VEGF-A values between pregnant women with COVID-19 and healthy pregnancies and its association with composite adverse outcomes. J Med Virol.2020;27.

28. Cheng B, Jiang T, Zhang L, Hu R, Tian J, Jiang Y, et al. Clinical characteristics of pregnant women with coronavirus disease 2019 in Wuhan, China. Open Forum Infect Dis.2020;11:294.

29. Mohr-Sasson A, Chayo J, Bart Y, Meyer R, Sivan E, Mazaki-Tovi S, et al. Laboratory characteristics of pregnant compared to non-pregnant women infected with SARS-CoV-2. Arch Gynecol Obstet.2020;302:629-634.

30. Wang Z, Xiong G. Clinical characteristics and laboratory results of pregnant women with COVID-19 in Wuhan, China. Int J Gynaecol Obstet.2020;150:312-317.

31. Wei L, Gao X, Chen S, Zeng W, Wu J, Lin X, et al. Clinical characteristics and outcomes of childbearing-age women with COVID-19 in Wuhan: Retrospective, single-center study. J Med Internet Res.2020;22:e19642.

32. Qiancheng X, Jian S, Lingling P, Lei H, Xiaogan J, Weihua L, et al. Sixth batch of anhui medical team aiding Wuhan for COVID-19. Coronavirus disease 2019 in pregnancy. Int J Infect Dis.2020:27.

33. Collin J, Byström E. Public Health Agency of Sweden's Brief Report: Pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. AOGS.2020;99:819- 822.

34. Kiss S, Gede N, Hegyi P, Nemeth D, Foldi M, Dembrovszky F, et al. Early changes in laboratory parameters are predictors of mortality and ICU admission in patients with COVID-19: A systematic review and meta-analysis. Med Microbiol Immunol.2020;21:1-15.

35. Wang K, Zuo P, Liu Y, Zhang M, Zhao X, Xie S, et al. Clinical and laboratory predictors of in-hospital mortality in patients with COVID-19: A cohort study in Wuhan, China. Clin Infect Dis.2020;71:2079-2088.

36. Vivanti AJ, Mattern J, Vauloup-Fellous C, Jani J, Rigonnot L, El Hachem L, et al. Retrospective description of pregnant women infected with severe acute respiratory syndrome coronavirus 2, France. Emerg Infect Dis.2020;26:2069-2076.

37. Lurie S, Rahamim E, Piper I, Golan A, Sadan O. Total and differential leukocyte counts percentiles in normal pregnancy. Eur J Obstet Gynecol Reprod Biol.2008;136:16–9.

38. Aghaeepour N, Ganio EA, McIlwain D, Tsai AS, Tingle M, Van Gassen S, et al. An immune clock of human pregnancy. Sci Immunol.2017;2:946.

39. Henry B, Cheruiyot I, Vikse J, Mutua V, Kipkorir V, Benoit J, et al. Lymphopenia and neutrophilia at admission predicts severity and mortality in patients with COVID-19: A meta-analysis. Acta Bio Med.2020;91:e2020008.

40. Zuo Y, Yalavarthi S, Shi H, Gockman K, Zuo M, Madison JA, et al. Neutrophil extracellular traps in COVID-19. JCI Insight.2020;5:e138999.

41. Ye W, Chen G, Li X, Lan X, Ji C, Hou M, et al. Dynamic changes of D-dimer and neutrophil-lymphocyte count ratio as prognostic biomarkers in COVID-19. Respir Res.2020;21:169.

42. Wang X, Xu W, Hu G, Xia S, Sun Z, Liu Z, et al. SARS-CoV-2 infects T lymphocytes through its spike protein-mediated membrane fusion. Cell Mol Immunol.2020;7:1–3.

43. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet.2020;395:507–513.

44. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis.2020;13:101623.

45. Henry B. COVID-19, ECMO, and lymphopenia: A word of caution. Lancet Respir Med.2020:18.

46. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao SY. Pulmonary pathology of early-phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. J Thorac Oncol.2020;15:700-704.

47. Sun DW, Zhang D, Tian RH, Li Y, Wang YS, Cao J, et al. The underlying changes and predicting role of peripheral blood inflammatory cells in severe COVID 19 patients: A sentinel? Clin Chim Acta.2020;508:122-129.

48. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): Systematic review and meta-analysis. J Intensive Care.2020;8:36.

49. Han Q, Wen X, Wang L, Han X, Shen Y, Cao J, et al. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. J Clin Lab Anal.2020;34:e23191.

50. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. J Med Virol.2020;92:1733-1734.

51. Zhang B, Zhou X, Zhu C, Song Y, Feng F, Qiu Y, et al. Immune phenotyping based on neutrophil-to-lymphocyte ratio and IgG predicts disease severity and outcome for patients with COVID-19. Front Mol Biosci.2020;7:157.

52. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol.2020;95:834-847.

53. Ling H, Hu ZD. The clinical utility of neutrophil to lymphocyte ratio in pregnancy related complications: A mini-review. JLPM.2019;5.

54. Xie G, Ding F, Han L, Yin D, Lu H, Zhang M. The role of peripheral blood eosinophil counts in COVID-19 patients. Allergy.2020;20:14465.

55. Flores-Torres AS, Salinas-Carmona MC, Salinas E, Rosas-Taraco AG. Eosinophils and respiratory viruses. Viral Immunol.2019;32:198-207.

56. Jesenak M, Schwarze J. Lung eosinophils-A novel "virus sink" that is defective in asthma? Allergy.2019;74:1832-1834.

57. Reese JA, Peck JD, Deschamps DR. Platelet counts during pregnancy. N Engl J Med.2018;379:32-43.

58. Yang M, Ng MH, Li CK. Thrombocytopenia in patients with severe acute respiratory syndrome (review). Hematology.2005;10:101–105.

59. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta.2020;506:145–148.

60. Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. Ann Hematol.2020;99:1205-1208.

61. Yuan H, Cao X, Ji X, Du F, Zhou X, He J, et al. A current emerging respiratory infection: Epidemiological and clinical characteristics, diagnosis and treatments of COVID-19. Lancet.2019.

62. Gong J, Ou J, Qiu X, Jie Y, Chen Y. A tool to early predict severe 2019-novel coronavirus pneumonia (COVID-19): A multicenter study using the risk nomogram in Wuhan and Guangdong, China. Clin Infect Dis.2020;71:833–840.

63. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharm.2020;84:106504.

64. Wang C, Deng R, Gou L, Fu Z, Zhang X, Shao F, et al. Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters. Ann Transl Med.2020;8:593.

65. Cavezzi A, Troiani E, Corrao S. COVID-19: Hemoglobin, iron, and hypoxia beyond inflammation. A narrative review. Clin Pract.2020;10:1271.

66. Liu X, Zhang R, He G. Hematological findings in coronavirus disease 2019: Indications of progression of disease. Ann Hematol.2020;99:1421-1428.