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Effect of complete blood count parameters on the clinical course of COVID-19 in pregnant women

Zehra YILMAZ[1], Huri GÜVEY[2,*], Canan SOYER ÇALIŞKAN[3], Samettin ÇELİK[3]

[1]Private Clinic, Samsun, Turkey
[2]Department of Gynecology and Obstetrics, Private Parkhayat Hospital, Kütahya, Turkey
[3]Department of Gynecology and Obstetrics, University of Health and Sciences, Samsun Training and Research Hospital, Samsun, Turkey

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Abstract

Coronavirus Disease-19 (COVID-19) pandemic, affected pregnant women as well as many people. Aim of this study is to compare complete blood count (CBC) parameters of pregnant women infected with COVID-19 to that of healthy pregnant women and determine their prognostic features. 142 pregnant women infected with COVID-19 and 46 healthy pregnant women, included in this retrospective case-control study. Patients infected with COVID-19 were grouped as mild, moderate and severe, according to the findings of oxygen saturation and lung involvement. Age, gestational age, gravida, hospitalization length and CBC parameters of the participants were compared, according to the groups. CBC test revealed that uninfected pregnant women had statistically lower level of white blood cell count (WBC, p=0.001), platelet count (p=0,024), neutrophil count (p=0,001), lymphocytes (p=0,005), monocytes (p=0,001) and platelecrit (p=0.007) than from infected pregnant women. Evaluation of pregnant women with COVID-19 grouped into 3 categories as mild, moderate and severe showed that age, gravida and hospitalization length were comparable between groups, WBC (p=0.012) and neutrophile (p=0.001) counts of mild group were significantly lower than moderate group and there was no significant difference between moderate and severe groups regarding WBC and neutrophile counts (respectively p=0,281, p=0.542). CBC analysis is simple, applicable, widely used and cheap laboratory method. CBC parameters seem as a candidate for predicting COVID-19 clinical course. However, larger sample sized prospective studies supporting this idea are required.

Keywords: COVID-19, pregnancy, complete blood count, disease severity

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes acute respiratory distress syndrome, defined in December 2019 in Wuhan city of China and caused a rapidly emerging endemic disease. Disease caused by this newly emerged virus is named coronavirus disease by World Health Organization at 11.02.2020 and announced as pandemic one month later (1). Diagnosis is usually based on identifying SARS-CoV-2 from respiratory tract secretions with real time polymerase chain reaction (rt-PCR) (2).

Physiological and anatomical changes, including suppression of cellular immunity which occurs to prevent fetal rejection during pregnancy, increased oxygen consumption, heart rate, stroke volume, and decreased lung capacity, may increase the likelihood for severe maternal disease (3). It has been suggested that the course and symptoms of COVID-19 in pregnancy do not differ from the normal population, in some studies (4, 5). In a systematic review performed by Zaigham (6), it is noted that most of the pregnant women with Covid-19 discharged without any major complication, but there are serious maternal morbidity and perinatal mortality in some cases.

Inflammation develops due to infectious diseases, and there are evidences suggests that it has an important role in the development of viral pneumonias, like COVID-19 (7). Heavy inflammation suppresses adoptive immunity, whereas causes imbalance on immune response (8). In these circumstances, circulating biological markers reflecting inflammation and immune system may also be candidates to be indicators for COVID-19 prognosis. Lymphopenia and neutrophilia have been identified as prognostic factors for severe cases of COVID-19, according to Australian and New Zealand guidelines (9). According to the study of Huang et al. (10), white blood cell count (WBC), neutrophil and lymphocyte count were determined as risk factors for intensive care needs of COVID-19 patients. Neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and lymphocyte to monocyte ratio (LMR) are also useful indicators in the prognosis of patients with viral pneumonia and an indicator of the systemic inflammatory response (11).

Complete blood count (CBC) examination is an inexpensive method that is widely available in many countries of the world. The aim of this study is to determine how CBC

*Correspondence: huriguvey@gmail.com

parameters change in pregnant women with covid 19 and their prognostic features.

2. Materials and Methods

This study designed in retrospective case control settings. 200 consecutive pregnant women admitted to Samsun Education and Research hospital with headache, cough, dyspnea diarrhea, diminished taste and smell perception, fever, myalgia included to the study. Presence of SARS-CoV-2 was investigated with rt-PCR method from nasopharyngeal and oropharyngeal swab samples and pregnant patients were hospitalized. All patients who had positive rt-PCR result included study group otherwise who had negative rt-PCR results included control group. Patient who had any known hematological disorders (n=5) or infected with other pathogens (n=7) were excluded from study. The patient who had negative test results discharged if their complaints did not worsen follow up continued in outpatient settings. SARS-CoV-2 patient classified with pulse oximetry and chest X-Ray findings as follow; oxygen saturation 94% and above without lung involvement cases were mild, oxygen saturation below 94% and involved lung areas lower than 50% were moderate, oxygen saturation lower than 94% and involved lung areas bigger than 50% were severe.

Gestational age was determined based on first day of last menstrual period or ultrasonographic findings at the first trimester. Venous blood samples analyzed with Coulter 180 hematology analyzer (Beckman Coulter Ireland Inc, Galway, Ireland). Following parameters were calculated, NLR, PLR and platelet to neutrophil ratio (platelet/neutrophil, PNR). Gestational age, gravida, length of hospital stays, oxygen saturation, chest X-ray and CBC parameters data of participants was obtained from hospital records.

Study performed with approval of Samsun training and research hospital noninvasive clinical research ethic committee (27.01.2021, 2021/2/2) and guidance of Helsinky declaration criteria.

2.1. Statistics

SPSS 25 (Statistical Package for Social Sciences) package program is used to analyze data. Descriptive statistics were presented as mean ± standard deviation and median (minimum-maximum) for continuous-measure variables, and number of observations and (%) for nominal variables. Whether the distribution of continuous-measure variables was normal or not was investigated by Kolmogorov Smirnov test and Shapiro-Wilks test. Mann-Whitney U test and Kruskal-Wallis test were used to determine whether there was a statistically significant difference between the groups in terms of continuous measurement variables that were not normally distributed; Whether there was a statistically significant difference in terms of normally distributed continuous measurement variables was evaluated with the independent samples T test and One-Way ANOVA. Nominal variables were evaluated with Chi-Square test, Fisher's Exact test and Fisher-Freeman Halton Exact test. In order for the differences to be considered statistically significant, the p value set to be less than 0.05. Bonferroni correction was performed to find out the source of significance for nominal variables found to be significant and for variables found to be significant by Kruskal-Wallis test, and those with p <0.017 were considered significant.

3. Results

Totally 188 pregnant women included to the study. The ages of 46 pregnant women with negative rt-PCR test were between 19 and 40, and the ages of 142 pregnant women with positive rt-PCR test were between 18 and 44 (p=0.002) (Table 1). While there was no difference between the groups in terms of gestational age (p=0.618) and gravida (p=0.552), hospitalization lengths of pregnant women with positive rt-PCR test were significantly longer (p<0.001). WBC (p<0.001), platelet count (p=0.024), neutrophil count (p<0.001), lymphocyte count (p=0.005), monocyte count (p=0.001), eosinophil count (p<0.001) and platelecrit (PCT) (p=0.007) levels of rt-PCR negative pregnant women were significantly higher than from rt-PCR positive group (Table 2).

Table 1. Comparison of variables according to rt-PCR results

Variables	rt-PCR (-) (n=46)	rt-PCR (+) (n=142)	p
Age (years)	26 (19-40)	30.50 (18-44)	**0.002**
Gestational age (weeks)	30.5 (5-41)	32 (5-41)	0.618
Gravida	2 (1-5)	2 (1-5)	0.552
Hospitalization length (days)	2 (1-9)	6 (1-16)	**<0.001**

Values are given as minimum-maximum median. Kruskal-Wallis test was applied.

Table 2. Comparison of complete blood count parameters of groups according to rt-PCR results

Variables	rt-PCR (-) (n=46)	rt-PCR (+) (n=142)	p
NLR	5.1 (0.53-17.80)	4.59 (0.82-25.33)	0.516*
PLR	163.22 (25.54-378.89)	176.08 (52.81-846.67)	0.201*
PNR	30.83 (9.86-76.67)	34.55 (9.19-209.52)	0.100*
WBC ($x10^3/\mu L$)	10.19 (6.70-17.80)	8.35 (2.66-22.30)	**<0.001$^{\delta}$**
RBC ($x10^6/\mu L$)	3.95 (2.92-5.66)	3.97 (2.22-5.24)	0.718*
Hemoglobin (g/dL)	11.7 (6.90-16.70)	11.55 (6.60-15)	0.382*
Platelet count ($x10^3/\mu L$)	257 (125-477)	215.50 (109-880)	**0.024***
Neutrophil count ($x10^3/\mu L$)	7.95 (4-15.40)	6.23 (1.80-17.50)	**<0.001***
Lymphocyte count ($x10^3/\mu L$)	1.60 (0.50-13.90)	1.20 (0.20-3.60)	**0.005***
Monocyte count ($x10^3/\mu L$)	0.60 (0.20-7.30)	0.40 (0.10-4)	**0.001***
Eosinophil count ($x10^3/\mu L$)	0.10 (0-1.10)	0 (0-0.30)	**<0.001***

Basophil count (x10^3/µL)	0 (0-0.70)	0 (0-0.60)	0.117*
MCV (fL)	85.20 (65-94.50)	85.05 (57.80-109)	0.508*
MCH (pg)	29.60 (21.20-33.70)	29.80 (6.70-38)	0.953*
MCHC (g/dL)	34.79 (5.29-35.90)	34.90 (28.40-38)	0.212*
RDW (%)	13,95 (12-33,2)	14.30 (11.80-22.30)	0.410*
MPV (fL)	8,90 (7-15)	8.80 (7-13.80)	0.421*
PCT (%)	0.21 (0.11-0.39)	0.19 (0.06-0.50)	**0.007***
PDW (%)	17.10 (15.50-19.50)	17.05 (15.60-19.99)	0.706*

($^\delta$ One-Way ANOVA test was applied) (* Kruskal-Wallis test was applied) Values are given as minimum-maximum median. Abbreviations: NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, PNR: platelet to neutrophil ratio, WBC: White blood cell count, RBC: Red blood cell count, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width

When the group of rt-PCR positive pregnant women classified in their clinical status as mild, moderate and severe; age, gravida and length of hospital stay did not differ significantly between the groups, although the length of hospital stays, was significantly shorter in the mild group compared to the moderate group, there was no significant difference between the moderate and severe groups (p=0.099) (Table 3). Considering the hematological parameters; although the WBC (p=0.012) and neutrophil (p=0.001) values of mild clinical course group were significantly lower than from the moderate group, there was no significant difference between moderate and severe groups (p=0.281, p=0.542) (Table 4).

Table 3. Comparison of variables according to severity of the disease

Variables	Mild (n=82)	Moderate (n=44)	Severe (n=16)	p
Age (years)	31 (18-44)	28 (18-40)	31.50 (26-40)	0.061
Gestational age (weeks)	26 (5-40)	37 (11-40)	32.50 (8-41)	**0.001**
Gravida	2 (1-4)	2 (1-5)	2 (1-3)	0.464
Hospitalization length (days)	6 (1-13)	7 (1-16)	5 (1-13)	0.271

Values are given as minimum-maximum median. Kruskal-Wallis test was applied.

Table 4. Comparison of complete blood count parameters according to severity of the disease

Variables	Mild (n=82)	Moderate (n=44)	Severe (n=16)	p
NLR	4.26 (0.82-25.33)	5.45 (1.74-18.6)	5 (2.34-13.87)	0.054*
PLR	157.25 (52.81-846.67)	180.71 (60.95-397.50)	186.97 (69.40-744.4)	0.554*
PNR	37.99 (9.19-159.44)	33.25 (14.38-113.19)	32.01 (15.06-209.52)	0.205*
WBC (x10^3/µL)	7.15 (2.66-2.90)	9.30 (3.40-22.30)	8.59 (3.90-12.10)	**0.011**$^\delta$
RBC (x10^6/µL)	3.89 (2.22-5.01)	4.02 (3.20-5.24)	3.78 (2.42-4.55)	0.150$^\delta$
Hemoglobin (g/dL)	11.70 (7.70-14.10)	11.50 (9.30-14)	11.25 (6.60-15)	0.187$^\delta$
Platelet count (x10^3/µL)	211 (111-421)	222.50 (124-532)	217.50 (109-880)	0.484*
Neutrophil count (x10^3/µL)	5 (1.80-16.10)	7 (2.60-17.50)	6.28 (3.40-11.10)	**0.003***
Lymphocyte count (x10^3/µL)	1.20 (0.20-3.40)	1.25 (0.40-3.60)	1.20 (0.40-2.68)	0.494*
Monocyte count (x10^3/µL)	0.40 (0.10-4)	0.50 (0.10-1.30)	0.40 (0.10-0.70)	0.078*
Eosinophil count (x10^3/µL)	0 (0-0.30)	0 (0-0.30)	0 (0-0.20)	0.762*
Basophil count (x10^3/µL)	0 (0-0.20)	0 (0-0.60)	0 (0-0.50)	0.077*
MCV (fL)	85.10 (60.80-101)	84.40 (64.40-92.20)	87.90 (57.80-109)	0.339*
MCH (pg)	29.90 (6.70-36.50)	29.50 (21.40-33)	30 (17.70-38)	0.196*
MCHC (g/dL)	35.05 (28.40-36.29)	34.74 (31.80-37)	34.55 (30.70-38)	0.295*
RDW (%)	14.05 (11.80-22.30)	14.45 (12.40-21.90)	14.33 (12-20.70)	0.412*
MPV (fL)	8.80 (7-13.80)	8.80 (7.10-11)	8.64 (7-11.50)	0.616*
PCT (%)	0.18 (0.09-0.44)	0.20 (0.11-0.50)	0.19 (0.06-0.42)	0.465*
PDW (%)	17.10 (15.60-19.20)	17 (15.90-19)	16.89 (16-19.99)	0.777*

4. Discussion

Pregnant women who admitted Covid-19 related symptoms and underwent rt-PCR test, studied in this paper. WBC, platelet, neutrophil, lymphocyte, monocyte, eosinophil count results was significantly higher in rt-PCR negative patients than from positives. Another finding in this study is that WBC and neutrophil counts were higher in moderate cases than from mild cases.

Seyit et al. (12) evaluated 233 patients who admitted to the emergency department with COVID-19 related symptoms in a retrospective study. While PLR and NLR values were found significantly higher in SARS-CoV-2 positive patients, eosinophil, lymphocyte and platelet counts were found higher in SARS-CoV-2 negative patients, as in our study.

In a retrospective study which 443 patients diagnosed with COVID-19 were evaluated, it was found that NLR was significantly higher and platelet level lower in patients with severe clinical course than in non-severe patients. It has been

suggested that NLR is the most important factor determining the severity of COVID-19 and platelets are protective from severe course, with these findings (13). Presented study could not demonstrate any relation between severity of Covid-19 and NLR or platelet level, but platelet counts of SARS-CoV2 positive pregnant women found significantly lower than negatives. Although it is claimed that pregnancy has no effect on the course of COVID-19 (5), this difference may be due to the differences in the clinical classification of the severity criteria and the characteristics of the population included to the study. A retrospective study published by Yang et al. (14) which 93 patients diagnosed with COVID-19 were evaluated, has similar to our results. WBC and neutrophil counts were significantly higher in the group with severe clinical condition compared to those with non-severe, while NLR and PLR values were higher in severe COVID-19 patients' group, which differs from our results.

In the review of 18 studies conducted by Zaigham et al. (6), it was revealed that 59% of pregnant women with COVID-19 presented with lymphocytopenia. This finding supports the significantly low lymphocyte value of SARS-CoV-2 positive pregnant women in presented study. In a study conducted by Koç et al. (15) on 108 pregnant women, 39 of whom had COVID-19 and 69 of whom were healthy, and compared the hematological parameters. Unlike our results, RDW and NLO values were higher in pregnant women with COVID-19, while PCT levels were low. However, patients did not classified according disease severity in this study.

In a systematic review by Khartabil et al. (16), it was reported that while the WBC count was within normal limits or low in COVID-19 patients, it is increased in cases with a severe clinical course.

Hemogram parameters in pregnancy vary according to trimester (17). Because of this, hematological parameters of pregnant women in different trimesters and non-pregnant women with COVID-19 might have differences. For this reason, different results may have been obtained in different studies in the literature. Another issue is that although the rt-PCR test is the gold standard in the diagnosis of COVID-19, it cannot detect all cases (18). This mean that there are some COVID-19 patients who have negative rt-PCR tests.

The limitation of this paper is that it is not studied in a sufficiently large sample group because it was retrospective and single-centered. These must be considered when interpreting results and generalizing to the population. In addition, because of pregnant women in different trimesters were included to the study, our results were different from the literature.

However, as we know, there is no similar study in the literature that clinically classifies pregnant women with COVID-19 and compares hematological parameters. We think that we will first contribute to the literature on this subject.

As a result, although almost 2 years passed since the onset of the COVID-19 pandemic, there are still inadequate studies on the course of COVID-19, prognostic and diagnostic parameters in pregnant women. According to our results, WBC, platelet, neutrophil, lymphocyte, monocyte, eosinophil counts and PCT values were higher in SARS-CoV-2 negative patients, while WBC and neutrophil values were higher in moderately severe COVID-19 cases than in mild ones. CBC is an easily applicable, widely used and inexpensive laboratory method. CBC parameters appear to be candidates for predicting the course of COVID-19. However, prospective studies with larger samples are needed to support this idea.

Conflict of interest

None to declare.

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None to declare.

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