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Evaluation of some biochemical and complete blood count parameters in pregnant women with COVID-19

COVID-19'lu gebelerde bazı biyokimyasal ve tam kan sayımı parametrelerinin değerlendirilmesi

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ABSTRACT

Aim: Prediction of severity of COVID 19 infection in pregnant population is very important to management. The aim of this study was to investigate the relationship between COVID 19 infection severity and routine hematologic/biochemical laboratory tests.

Materials and Methods: In this retrospective study the hematologic parameters of pregnant women with COVID 19 were investigated. The patients were allocated into 5 subgroups as asymptomatic, mild, moderate, severe and critical. Presenting symptoms were identified. Laboratory test results detected at the first admission were compared between groups.

Results: A total of 343 patients were included in the study. The most common symptoms were cough (n=74, %21.6) and fatigue (n=46, %13.4). Statistically significant differences observed at following parameters. The mean Hb level was lower (p=0.001) and WBC, neutrophil, AST, ALT, GGT, LDH, direct bilirubin and total bilirubin levels were higher in critical group (p=, 0.005, 0.001, 0.000, 0.015, 0.000, 0.000, 0.000, 0.007 respectively). The mean lymphocyte and monocytes levels in the severe group were lower (p=0.000, 0.01, respectively). Furthermore, the mean eosinophil levels in the asymptomatic group was higher (p=0.002).

Conclusion: There is a relationship between changes in routine laboratory examinations performed in clinical practice and the severity of COVID 19 disease. Monitoring of these tests may provide guidance for the prediction of the severity of the COVID 19 infection among pregnant women.

Keywords: Complete blood count, COVID 19, laboratory, pregnancy, symptom.

ÖZ

Amaç: *Gebe popülasyonda COVID 19 enfeksiyonunun şiddetinin öngörülmesi, yönetim için çok önemlidir. Bu çalışmanın amacı, COVID 19 enfeksiyon şiddeti ile rutin hematolojik/biyokimyasal laboratuvar testleri arasındaki ilişkiyi araştırmaktır.*

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Gereç ve Yöntem: *Bu retrospektif çalışmada COVID 19'lu gebe kadınların hematolojik parametreleri araştırıldı. Hastalar asemptomatik, hafif, orta, şiddetli ve kritik olarak 5 alt gruba ayrıldı. Başvuru semptomları tespit edildi. İlk başvuruda tespit edilen laboratuvar test sonuçları ve gruplar arasında karşılaştırıldı.*

Bulgular: *Çalışmaya toplam 343 hasta dahil edildi. En sık görülen semptomlar öksürük (n=74, %21.6) ve halsizlik (n=46, %13.4) idi. Aşağıdaki parametrelerde istatistiksel olarak anlamlı farklılıklar gözlendi. Kritik grupta ortalama Hb düzeyi daha düşük (p=0,001), WBC, nötrofil, AST, ALT, GGT, LDH, direkt bilirubin ve total bilirubin düzeyleri daha yüksekti (p= 0,005, 0,001, 0,000, 0,015, 0,000, 0,000, 0.000, 0.007). Şiddetli grupta ortalama lenfosit ve monosit seviyeleri daha düşüktü (sırasıyla p=0.000, 0.01). Ayrıca asemptomatik grupta ortalama eozinofil düzeyleri daha yüksekti (p=0,002).*

Sonuç: *Klinik pratikte bakılan rutin tetkiklerdeki değişimlerle COVID 19 hastalığının şiddeti arasında ilişki vardır. Bu testlerin izlenmesi, hamile kadınlar arasında COVID 19 enfeksiyonunun ciddiyetinin tahmin edilmesi için rehberlik sağlayabilir.*

Anahtar Sözcükler: *Tam kan sayımı, COVID 19, laboratuvar, gebelik, semptom.*

INTRODUCTION

COVID 19 infection, which emerged in December 2019 and spread all over the world, still maintains its importance as a serious health problem. By March 2023, there were approximately 761402282 proven cases and 6887000 million deaths (1). The emergence of new variants increases the severity of the pandemic and poses management challenges for clinicians.

Studies examining the effects of COVID 19 infection in the pregnant population have yielded very alarming results. Poor obstetric outcomes are observed in pregnant women infected with COVID 19 (2, 3). These data show that COVID 19 infection poses a serious risk for both the fetus and the pregnant women. Pregnancy also seems like as a risk factor for developing more serious disease of COVID 19 infection (4).

Determining the severity of COVID 19 infection in the pregnant population is of great importance for the management of its follow-up and treatment. Detection of biomarkers that can be used to predict the prognosis and disease severity of pregnant women can improve disease prognosis by early intervention. For this purpose, determining the relationship between the changes in routine laboratory tests and the severity of infection may facilitate the management of these patients.

The aim of this study was to investigate the symptoms detected at the first admission in pregnant women infected with COVID 19 and their correlation with the severity of the disease and routine hematologic tests.

MATERIALS and METHODS

This retrospective study was conducted on the files of pregnant patients who were admitted or hospitalized due to COVID-19 between March 2020 and March 2022. The pregnant women admitted to hospital with any reason and diagnosed as Covid-19 by real-time reverse transcription-polymerase chain reaction (rRT-PCR) were included in the study. Informed consent was taken from patients. The patients included in the study were divided into 5 groups according to the diagnostic criteria of the COVID Guidelines published and updated by the Ministry of Health of the Republic of Turkey (5).

1. Asymptomatic

2. Mild clinical findings

3. Moderate; fever, respiratory symptoms, and radiological signs of pneumonia.

4. Severe; shortness of breath, respiratory rate (RR) ≥30/min, oxygen saturation ≤93% and resting ≤93% (PaO2/FiO2) ≤300 mm Hg

5. Critical cases; Patients with respiratory failure requiring mechanical ventilation, shock or organ failure

The first values at the time of admission or hospitalization of the maternal age, gravida, parity, gestational age, symptoms , complete blood count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (GGT)), blood urea nitrogen (BUN), creatinine (Crea), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), direct and total bilirubin levels were recorded and analyzed.

Inclusion criteria

Presence of a live, intrauterine pregnancy confirmed by ultrasound combined with Covid-19 infection confirmed by Covid-19 RT-PCR test

Exclusion criteria

Patients with known renal pathology, immune suppression, liver disease, diabetes mellitus, autoimmune disease, and hematological disease.

Statistical method:

Statistical Package for Social Sciences (SPSS version 22.0) program was used for statistical analysis. While evaluating study data, descriptive statistical parameters (Mean, Standard Deviation, Median, Frequency, Ratio, Minimum, and Maximum) recorded. Kruskal Wallis test was used to compare the differences between groups. Kolmogorov Smirnov test was used to determine whether the data showed normal distribution or not. Significance was evaluated at $p<0.05$ levels.

Our study was reviewed according to the "Helsinki Declaration" and "Good clinical practice guideline" and was prepared "duly" according to the guideline.

Ethical approval was obtained from the ethics committee of Recep Tayyip Erdoğan University for the study (Decision No: 2023/10).

RESULTS

A total of 343 patients were included in the study. The mean age, gravida, parity and gestational age at the time of diagnosis of COVID 19 of the patients were determined as 29.91±5.18/year, 2.41±1.46, 1.05±1.27 and 195.4±76.48/day, respectively. Demographic data of the patients and their clinical group allocations are shown in Table-1.

The most common complaint of the patients was cough (n=74, 21.6%). 80 (23.3%) of these patients were asymptomatic and 46 (8.2%) were admitted with complaints of fatigue. The distribution of the complaints of the patients is shown in Table-2.

Table-1. Demographic data of the patients.

Parameter	Mean±SD
Age	29.91±5.18
Gravida	2.41±1.46
Parity	1.05±1.27
Pregnancy day	195.4±76.48
Disease Severity Group	n (%)
Asymptomatic	120 (3498)
Mild	118(34.4)
Moderate	51(14.9)
Severe	45(13.1)
Critical	9(2.6)
Total	343(100)

Table-2. Complaints of the patients at first admission.

Symptom	Number of individuals (n)	Percentages (%)
Asymptomatic	80	23.3
Cough	74	21.6
Dyspnea	27	7.9
Myalgia	16	4.7
Fatigue	46	13.4
Fever	23	6.7
Obstetric complaints	40	11.6
Chest Pain	1	0.3
Sore throat	2	0.6
Headache	15	4.4
Runny Nose	12	3.5
Stomachache	5	1.5
Loss of smell and taste	2	0.6

Table-3. Comparison of hematologic parameters according to disease severity (SD: Standard Deviation).

	Mean±SD	Asymptomatic±SD	Mild±SD	Moderate±SD	Severe±SD	Critical±SD	p
Hb (g/dl)	11.77±1.4	12.08±1.34	11.76±1.24	11.63±1.15	11.49±1.78	9.93±1.83*	0.001
MCHC (g/dl)	33.59±1.35	33.59±1.77	33.54±1.11	33.59±0.92	33.78±0.9	33.28±1.77	0.329
MCV (fl)	88.73±6.2	88.91±6.59	88.78±6.5	87.23±5.47	90.1±4.9	87.37±5.45	0.121
WBC (10^3/uL)	8.23±3.24	8.44±2.48	7.75±3.14	7.4±2.58	8.85±3.7	13.36±7.48*	0.005
Neutrophil (10^3/uL)	6.28±3.06	6.18±2.26	5.86±2.85	5.45±2.28	7.44±3.57	11.72±7.41*	0.001
Lymphocyte (10^3/uL)	1.71±2.36	2.21±3.3	1.56±1.47	1.61±2.43	0.98±0.3*	1.18±0.54	0.000
Monocytes (10^3/uL)	0.493±0.411	0.557±0.623	0.462±0.201	0.521±0.255	0.388±0.218*	0.39±0.175	0.01
Eosinophil (10^3/uL)	0.101±0.285	0.129±0.33*	0.071±0.093	0.075±0.186	0.153±0.598	0.073±0.086	0.002
Basophil (10^3/uL)	0.018±0.022	0.016±0.013	0.016±0.02	0.016±0.015	0.031±0.049	0.011±0.003	0.686
Platelet (10^3/uL)	217.38±75.88	224.94±68.25	206.04±69.78	218.17±63.14	214.53±86.06	275.11±182.91	0.088
MPV (fl)	9.92±1.25	9.97±1.28	10.08±1.23	9.73±1.26	9.67±1.25	9.4±0.76	0.111
PDW (fl)	16.21±0.4	16.25±0.42	16.2±0.39	16.13±0.36	16.18±0.39	16.33±0.65	0.699
PCT (%)	0.21±0.06	0.218±0.059	0.204±0.068	0.205±0.057	0.205±0.075	0.257±0.172	0.083

Hb: Hemoglobin, WBC: White blood cell, MCHC: Mean corpuscular hemoglobin concentration, MCV: Mean corpuscular volume, PDW: Platelet distribution width, PCT: Platelet crit, MPV: Mean platelet volume.

Table-4. Statistical comparison of biochemical parameters according to disease severity (SD: Standart Deviation)

	Mean±SD	Asymptomatic±SD	Mild±SD	Moderate±SD	Severe±SD	Critical±SD	p
AST	30.46±44.61	28.65±53.2	29.68±37.49	23.94±10.58	37.46±40.06	66.66±103.99*	0.000
ALT	26.78±70.07	27.6±90.91	29.4±72.94	19.11±13.53	25.11±35.68	33.11±20.55*	0.015
GGT	18.61±20.81	16.87±15.62	17.96±26.18	16.27±11.79	20.34±13.51	54.25±36.34*	0.000
BUN	16.45±10.93	16.33±4.82	15.52±4.91	15.72±4.69	14.46±5.82	42.77±54.17	0.056
Creatinine	115.77±45.88	0.67±1.11	0.603±0.706	0.654±0.642	0.539±0.117	0.616±0.533	0.067
ALP	115.77±45.88	118±47.35	123.04±45.24	104.57±66.31	108.25±40.59	120.5±24.74	0.741
LDH	229.06±155.3	210±86.58	202.57±61.3	205.32±67.41	308.66±234.63	569.12±602.66*	0.000
Direct bilirubin	0.11±0.148	0.098±0.146	0.11±0.136	0.077±0.035	0.137±0.116	0.315±0.481*	0.000
Total bilirubin	0.431±0.352	0.402±0.282	0.418±0.291	0.345±0.129	0.578±0.59	0.728±0.752*	0.007

AST: Aspartate transaminase, ALT: Alanine transaminase, GGT: Gamma-glutamyl transferase, LDH: Lactate dehydrogenase, BUN: Blood urea nitrogen, ALP: Alkaline phosphatase

The difference between groups in the mean Hb, WBC, neutrophil, lymphocyte, monocyte and eosinophil values of the patients were found to be statistically significant (p=0.001, 0.005, 0.001, 0.000, 0.01 and 0.002, respectively). The difference between the mean MCHC, MCV, basophil, platelet, PDW, PCT and MPV values were statistically insignificant (p=0.329, 0.121, 0.686, 0.088, 0.699, 0.083 and 0.111, respectively). Statistical comparison of the hematologic parameters according to disease severity is shown in Table-3.

The difference between the mean AST, ALT, GGT, LDH, direct bilirubin and total bilirubin values were found to be statistically significant (p=0.000, 0.015, 0.000, 0.000, 0.000 and 0.007, respectively) (Table-4) The difference between the mean BUN, Creatinine and ALP values between the groups were statistically insignificant (p=0.056, 0.067 and 0.741, respectively) (Table-4).

DISCUSSION

Pregnancy is a physiological process in which a wide variety of changes are observed in the female body. These changes cause alterations in many organs and systems such as immunological, vascular, urinary, pulmonary and gastrointestinal systems. These physiological changes may result in altered immune responses

to infections. As a result of these differences, symptoms and biochemical findings of the same infection with different frequency and severity can be observed when compared to non-pregnant individuals (6).

The most frequently observed symptoms in COVID 19 infection have been reported as fever, cough, malaise, and dyspnea (7). Similar symptoms have been reported in the pregnant population (8). However, pregnant women are more likely to be asymptomatic (9). According to the data obtained in our study, 23.3% of pregnant women were asymptomatic, and 11.6% were patients who applied to the clinic with obstetric complaints such as nausea, vomiting, bleeding and pain. In symptomatic pregnant women, the most common symptom was cough (21.6%). fatigue (13.4%), dyspnea (7.9%), fever (6.7%) and myalgia (4.7%). The data obtained in our study are compatible with that of the literature.

Anemia appears to be associated with the severity of COVID 19 infection. This association may be due to low oxygen supply to peripheral tissues. At the same time, the infection itself may contribute to the worsening of anemia (8). In a meta-analysis, it was stated that the risk of serious COVID 19 disease in the general population increased 2.44 times in anemic patients (10). Anemia may also be associated with the formation of more serious disease in the pregnant population (11). In our study, mean hemoglobin levels were found to be lower in critically ill patients.

The number of circulating WBC is a part of the systemic inflammatory response to infections. An activated immune system may also lead to pulmonary injury (12). This situation increases the importance of monitoring the WBC count in an infection that shows its potential effect in the respiratory system, such as COVID 19 infection. Low WBC levels can be observed in non-pregnant adults with COVID 19 infection (13). WBC levels have been reported to be higher in the pregnant population (14). The data in our study showed that the number of WBCs increased in the critically ill group.

Changes reported in the literature regarding alterations in neutrophil levels vary. While neutropenia was reported in 16% of pregnant patients in a meta-analysis, neutrophil levels were reported to be higher in severe patients in another study (15, 16). In our study, high neutrophil counts were found in the critically ill patients.

Many systemic viral infections result in an increase in blood total lymphocyte count. One of the viral infections in which a decrease in lymphocyte count is observed is COVID 19 infection (17). According to our study, too, lymphopenia is observed in the group with severe infection.

The innate immune system is the first line of defense against infectious diseases. Monocytes are an important part of this system, and infiltration of macrophage produced from monocytes has been observed in the lungs of COVID19 patients (18). It has been shown that the monocyte levels in the blood of COVID 19 patients hospitalized in the intensive care unit may be lower (19). The migration of monocytes to the site of inflammation may be responsible for this decrease. The data in our study show that peripheral blood monocyte levels decrease in severe COVID 19 cases.

Eosinophils are a subgroup of granulocytes in the blood leukocyte pool mostly associated with parasitic or allergic conditions. The decrease in blood eosinophil levels was found to be inversely proportional to the severity of COVID 19. It has been reported that blood levels of eosinophils returned to normal before discharge in patients who survived (20). Eosinophil levels were found to be significantly higher in asymptomatic pregnant women in our study compared to other groups.

Since COVID 19 infection affects many tissues and organs, there are changes in many biochemical parameters in the body. AST and ALT, which are used as indicators of liver damage, are elevated in the blood as an indicator of tissue damage. With the severity of COVID 19 infection, the levels of these enzymes in peripheral blood increase (21). GGT and total bilirubin levels are also parameters that increase in liver damage, and the increase in these enzymes has been found to be associated with the severity of the disease (22). Our study shows that AST, ALT, GGT and total bilirubin levels increase with the severity of COVID 19 infection in the pregnant population.

Lactate dehydrogenase (LDH) is an enzyme that plays a role in the anaerobic glycolysis pathway. It has been reported that blood levels of this enzyme are also increased in COVID 19 infections (23). Our study shows that infection with COVID 19 also increases blood LDH levels in the pregnant population.

CONCLUSIONS

As a result, when evaluating the blood parameters of pregnant women presenting with COVID 19 infection at their first admission, determining which patients are at higher risk is of great importance in the management of patients and improving prognosis. Low Hb, lymphocyte, monocyte, eosinophil levels and high WBC, neutrophil, ALT, AST, GGT, total bilirubin and LDH levels are associated with more severe disease.

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Conflict of Interest: The authors declares no conflict of interest.

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