

Do Ectopic Pregnancy Treatment Choices Affect the Risk of COVID-19 Transmission?

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Abstract

BACKGROUND/AIMS: To investigate the effects of treatment choices in ectopic pregnancy (EP), either surgery or single-dose methotrexate approaches, to see whether it leads to the incidence of coronavirus disease-19 (COVID-19) disease after discharge, as well as to determine any correlations in changes in cell blood counts (CBC) with the progress of COVID-19 infections.

MATERIALS AND METHODS: This study was conducted with 95 patients who were diagnosed as having EP at University of Health Sciences Türkiye, Etlik Zübeyde Hanım Gynaecology Training and Research Hospital. COVID-19 swabs were taken from the patients with EP before hospitalization. Demographic parameters, CBCs, post-discharge COVID-19 disease occurrence rates, and infection progress were evaluated.

RESULTS: Ninety-five patients with tubal EP were separated into two groups; 20 patients who underwent surgical intervention (Group 1), and 75 patients who underwent single-dose methotrexate treatment (Group 2). There was no difference between the groups in terms of their demographic characteristics ($p>0.05$). The mass size was measured using transvaginal ultrasound and the mean mass diameter in Group 2 was significantly smaller than in Group 1 ($Z=4.123$; $p<0.001$). The hospital stay of Group 2 was longer than in group 1 ($Z=4.451$; $p<0.001$). No patients were infected with COVID-19 before the hospitalization period; however, three (3.1%) patients were COVID-19-positive in the 90-day post-treatment period, two of whom had surgical treatment, and the other who received medical treatment. The patient who had medical treatment went into self-isolation and used favipiravir medication at home and completely recovered. By contrast, the patients who had surgical treatment needed hospital care. The mean neutrophil-lymphocyte ratio (NLR) values were significantly higher for those patients with EP in Group 1 compared with Group 2, both pre-treatment and post-treatment ($Z=4.108$, $p<0.001$; $Z=4.783$; $p<0.001$). Also, significant differences were detected between the groups regarding their haemoglobin levels, and white blood cell, platelet, and neutrophil counts ($p=0.005$, $p=0.001$, $p=0.008$, and $p=0.001$ respectively).

CONCLUSION: Variances in EP treatment modalities and durations of hospitalization days did not increase the transmission of disease or mortality scores. It was concluded that methotrexate treatment could be chosen as the first-line treatment for ectopic pregnancy during the COVID-19 pandemic for patients. However, healthcare professionals must be aware that medical or surgical treatment approaches for patients with EP may change the NLR, which is an independent prognostic factor in COVID-19.

Keywords: COVID-19, ectopic pregnancy, methotrexate treatment, neutrophil-lymphocyte ratio

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INTRODUCTION

In ectopic pregnancy (EP), the fertilized ovum most frequently implants in the fallopian tubes (95%). The incidence of EP is 1% in patients aged 24-44 years.¹ Approaches for diagnosis [serum human chorionic gonadotropin (β -hCG) sensitive values, high-resolution ultrasounds (USG)] and treatment (experienced surgeons frequently use laparoscopic approaches) in EP are crucial for improving maternal morbidity and mortality. Treatment options for stable patients include expectant management, surgical treatment, and methotrexate (single or multiple-dose) administration. Methotrexate treatment is a non-invasive treatment approach used in patients with stable hemodynamics and smaller mass sizes. It is effective in the early stages of pregnancy as a folic acid antagonist, but it can cause anomalies immunodeficiency.² After administration, approximately 92% of methotrexate is excreted in the urine within the first 24 hours and 1-2% remains in the body.³ The obstetrician's treatment approach selection can change because the benefits and harms of methotrexate must be balanced.

The coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in January, 2020 in a group of patients who developed severe acute respiratory symptoms (fever, cough, shortness of breath) in Wuhan Province, China. Although approximately 81% of patients with COVID-19 have mild symptoms such as a dry cough and fever, which do not require hospitalization, 14% have severe symptoms, and 5% have rapid-developing acute respiratory distress syndrome.⁴ On March 11th, 2020, the first COVID-19 case in our country, Türkiye, was seen. As of September 26th, 2021, the mortality rate was almost 0.89%.⁵ Governments had to focus on and change hospitalization advice for gynaecologic surgeries because of the intensity levels in hospitals. Governments had to change their recommendations for hospitalization for gynaecologic surgeries because of the COVID-19-related intensity levels of hospitals. Due to the hospital occupancy of patients during the COVID-19 pandemic, appropriate methods were determined in surgical indications to prevent mortality due to emergency surgeries and to manage oncological patients.⁶ Although most patients exhibit mild symptoms, some patients have a worse prognosis⁷ and studies focused on prognostic factors such as laboratory data.⁸

Severe inflammatory responses can provide a weak adaptive immune response, resulting in imbalances in the immune response. Therefore, circulating biomarkers which can represent inflammation and immune status may predict the likelihood and prognosis of COVID-19.⁹ The peripheral white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio are commonly investigated indicators of the systematic inflammatory response.⁹ Also, NLR can be used as a prognostic marker for COVID-19 given the significant difference in NLR between those patients who died and those who recovered from COVID-19.¹⁰

Given the rapid spread and severe damage of COVID-19, it is important to improve and enrich clinical diagnostic and therapeutic research. Using methotrexate, which is an immunosuppressive agent, in the treatment of EP, has provoked the notion of the possibility of increased COVID-19 infections and transmission. In this study, our primary aim was to determine the effects of primary methotrexate or surgical treatment choices on patients with EP regarding the probability of having COVID-19 after treatment and its clinical severity, along with alterations in their descriptive laboratory parameters.

MATERIAL AND METHODS

This retrospective single-cohort study included patients who were admitted to University of Health Sciences Türkiye, Ankara Etlik Zübeyde Hanım Training and Research Hospital early pregnancy department with a diagnosis of EP and seronegative COVID-19 results between June 1st, 2020, and January 1st, 2021. Approval from the Ankara Etlik Zübeyde Hanım Training and Research Hospital Local Ethics Committee (approval number: 03, date: 26.02.2021) was received.

Selection and Description of Participants

This study included 95 patients with tubal EP who received either methotrexate or surgical treatment. All women were followed up through transvaginal USG and measurements of beta-hCG (β -hCG) and those with a diagnosis of EP received medical or surgical treatment. Maternal age, parity, gravidity, mode of conception (natural or assisted reproduction method), gestational age, smoking habits, ultrasonographic measurements, and previous EP history were recorded. We compared the effects of single-dose methotrexate treatment with surgical treatment for tubal EP with regards to the length of hospital stay, and CBC parameters. In addition, the effect of treatment types on whether patients had COVID-19 after discharge was evaluated retrospectively.

Methotrexate treatment was given to hemodynamically stable patients, if there were no contraindications for methotrexate administration, with β -hCG levels of <6,000 IU/L at the time of diagnosis, tubal EP diagnosis with an ectopic pregnancy mass size <45 mm, no history of tubal surgery, and no foetal heartbeat. Patients with a decline of 15% in β -hCG levels between days 4 and 7 were accepted as having a positive response and monitored on an outpatient basis weekly until their β -hCG levels were below 5 mU/mL. Surgery was performed on those patients who did not meet these criteria, whose hemodynamics deteriorated due to tubal rupture during follow-up, had a 15% decrease in β -hCG between the fourth and seventh day, and those who had hepatic or renal disease and did not respond to medical treatment. According to these criteria, the patients were separated into two groups, those who had success with methotrexate treatment, and those who required surgery. In addition, CBCs were performed after both methotrexate treatment and surgical treatment. All hematologic laboratory parameters were compared between the groups.

Technical Information

Methotrexate reversibly inhibits the enzyme dihydrofolate reductase. Further pregnancy attempts are allowed 3 months after methotrexate treatment. Patients with EP between January 1st, 2020 and January 1st, 2021 were included in this study. All patients were followed up until April 1st, 2021 (3 months later due to the continuation of the effects of methotrexate) to determine whether they had had COVID-19. The patients were screened retrospectively for COVID-19 test results via the report system after hospital discharge. After discharge from the hospital, COVID-19 test results were scanned via the Hospital Information Management System (HIMS) or by phone to inquire whether the patients had had COVID-19. Those patients whose personal data could not be accessed, who had positive COVID-19 test results when hospitalized, with systemic diseases which were contraindicated for methotrexate treatment and multiple-dose methotrexate regimes, and those who required methotrexate treatment after surgical treatment because of treatment failure were not included in this study.

Statistical Analysis

The data obtained within the scope of this research were statistically analysed using the IBM SPSS Statistics program Ver. 23.0 software package (IBM Corp. IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.). The normality of the data distribution was examined graphically and the Shapiro-Wilk test. Frequency (n) and percentage (%) values were calculated in the definition of categorical variables related to the medical history, and median [interquartile range (IQR)] values were used for the measurement variables. The Mann-Whitney test was used to compare non-normally distributed continuous variables and the chi-squared test was used for categorical variables. Pre-treatment and post-treatment comparisons in each group were made using the Wilcoxon signed-rank test. The level of significance was accepted as $p < 0.05$ in all analyses.

RESULTS

This study included 95 patients with tubal EP who were divided into two groups: Group 1, those treated with single-dose 50 mg/m² intramuscular methotrexate therapy (n=75), and Group 2, patients who underwent surgery (n=20). The mean age of the patients was 31.8±6.0 (range, 19-46) years. Their mean BMI was 26.96±4.53 kg/m². Six (6.3%) patients had chronic diseases (asthma n=2, type 2 diabetes mellitus n=2, epilepsy n=1, multiple sclerosis n=1). Twenty-eight (29.5%) patients had undergone previous surgery. The most common surgery was caesarean section (22.1%). Twenty-two patients were smokers and none had allergies. None of the patients had received in vitro fertilization treatment before. Twenty-seven (28.4%) patients were

nulliparous. Eight (8.4%) patients had had elective abortions (Table 1). In our study, the median overall hospital length of stay was 5 (IQR 3) (min: 3 max: 21) days. A statistically significant difference was detected between the groups in terms of hospital stay ($p < 0.01$).

Most tubal masses were visualized in the right adnexal region (n=51; 60%); the left adnexal region was n=34, 40%. Ten patients with EP tubal masses were not detected using transvaginal USG. The mean tubal mass diameter was 21 (IQR=13) (range, 6-40) mm. Free abdominal fluid was visualized in 35 patients. The mean volume of abdominal free fluid was 41 (IQR=29) (range, 16-140) mm³. The number of patients who had ruptured ectopic pregnancies was 22 (23.2%). The ASA PS classification of all 26 (27.4%) patients who underwent surgery was ASA II. Ten (50%) of these patients underwent left salpingectomy and the other 10 (50%) underwent right salpingectomy.

The masses, which were measured using transvaginal USG diameter, in Group 1 were significantly smaller than in Group 2 ($Z=4.123$; $p < 0.001$). The hospital stay in Group 1 was longer than in Group 2 ($Z=4.451$; $p < 0.001$). There was no difference between the groups in terms of the other demographic characteristics ($p > 0.05$) (Table 2). Three (3.1%) patients had COVID-19 positive tests after their treatments. Table 3 shows which types of treatment were received by those patients who became COVID-19 positive, the progress of their infection, their survival rates, and their treatment modalities. The mean NLR values were significantly higher for those patients with EP in Group 2 compared with Group 1 both before and post-treatment ($Z=4.108$, $p < 0.001$; $Z=4.783$; $p < 0.001$). Although NLR decreased after treatment in

Table 1. Demographic features and obstetric histories of patients

	Surgery (n=20)	Methotrexate (n=75)	Group comp.
	Median (IQR)	Median (IQR)	Z; p
Age (year) ^a	31.00 (8.75)	32.50 (9.00)	Z:0.347; p=0.728
BMI (kg/m ²) ^a	28.58 (6.07)	26.50 (5.68)	Z=1.753; p=0.080
	n (%)	n (%)	Z; p
Chronical disease ^b	1 (5.0)	5 (6.7)	Z=0.78; p=0.780
Previous surgery ^b	2 (10.0)	26 (34.7)	Z=4.622; p=0.032
Smoker ^b	5 (25.0)	17 (22.7)	Z=0.048; p=0.826
Gravida^b			
1	3 (15.0)	15 (17.6)	Z=0.257; p=0.612
2+	17 (85.0)	60 (82.4)	
Parity^b			
0	5 (25.0)	21 (28)	Z=0.071; p=0.789
1+	15 (75.0)	54 (72.0)	
Before ectopic pregnancy^b			
0	17 (85.0)	65 (86.7)	Z=0.037; p=0.847
1+	3 (15.0)	10 (13.3)	
Adnexal mass*	Median (IQR)	Median (IQR)	Z; p
Average size (mm) ^a	28.00 (17.00)	18.00 (10.25)	Z=4.123 p<0.001
Ectopic pregnancy site^b	n (%)	n (%)	
Right	12 (60.0)	NA	
Left	8 (40.0)	NA	
Hospitalization	Median (IQR)	Median (IQR)	Z, p
Hospitalizations (day)	4.50 (1.75)	7.00 (3.00)	Z=4.451; p<0.001

^a: Mann-Whitney test, ^b: Chi-squared test, BMI: Body mass index, IQR: Interquartile range

both groups, it did not change significantly during treatment ($p=0.108$ and $p=0.431$, respectively). Also, significant differences were detected between the groups regarding their haemoglobin levels, and WBC, platelet, and neutrophil counts ($p=0.005$, $p=0.001$, $p=0.008$, and $p=0.001$ respectively).

DISCUSSION

To the best of our knowledge, this study is the first to compare treatment options for EP, the probability of contracting the disease according to changes in blood parameters, and the length of hospital stay, and to calculate the COVID-19 positivity rates. The post-treatment COVID-19 rate was 3.1% for our patients with EP (two patients underwent surgery, and another who had methotrexate treatment). The methotrexate-treated patient went into self-isolation, only used favipiravir medication

at home, and completely recovered. By contrast, the surgically treated patients required hospitalization. NLR values were significantly higher in those patients with EP in Group 2 compared with Group 1, both before and after treatment.

Medical treatment with methotrexate is used as an alternative to surgical treatment because of its potency, cost-effectiveness, and safer characteristics in EP.¹¹ Methotrexate reversibly inhibits the enzyme dihydrofolate reductase, preventing the conversion of purine and pyrimidine synthesis, inhibiting cell growth.¹² It is hypothesized that patients who receive methotrexate treatment may be more prone to infection during the pandemic owing to their immunocompromised condition. Patients who use this treatment often need hospital monitoring. It may alter hematologic and biochemical parameters, and

Table 2. Biochemical parameters changes for the treatment modalities

Parameters	Surgery treatment (group 1) (n=20)			Methotrexate medication (group 2) (n=75)			Group 1 vs. group 2	
	Before treatment	After treatment	Before vs. after treatment	Before treatment	After treatment	Before vs. after treatment ^a	Before treatment ^b	After treatment ^b
Neutrophil to lymphocyte ratio (NLR)	5.87 (8.07)	4.7 (4.28)	Z=1.605; p=0.108	2.44 (1.53)	2.03 (1.41)	Z=0.787; p=0.431	Z=4.108; p<0.001	Z=4.783; p<0.001
Platelet to lymphocyte ratio (PLR)	167.92 (107.7)	116.89 (51.7)	Z=2.987; p=0.003	130.73 (61.83)	123.53 (62.26)	Z=0.158; p=0.874	Z=3.295; p<0.001	Z=0.529; p=0.596
Hb (gr/dL)	12.05 (2.43)	11.2 (2.3)	Z=1.755; p=0.079	12.5 (2.2)	12 (1.9)	Z=4.944; p<0.001	Z=1.845; p=0.065	Z=2.790; p=0.005
RDW (%)	13.3 (1.28)	13.3 (1.08)	Z=0.698; p=0.485	13.6 (1.7)	13.4 (1.7)	Z=3.039; p=0.002	Z=0.859; p=0.390	Z=0.324; p=0.746
MPV (fL)	9.6 (1.35)	9.65 (1.03)	Z=0.311; p=0.756	9.8 (1.6)	9.6 (1.4)	Z=1.514; p=0.130	Z=0.539; p=0.590	Z=0.005; p=0.996
WBC ($\times 10^9/L$)	11.675 (7.740)	11.675 (5.875)	Z=0.728; p=0.467	7.870 (3.090)	7.170 (2787.5)	Z=3.130; p=0.002	Z=4.802; p<0.001	Z=4.434; p<0.001
Lymphocyte (%)	1.520 (1.347)	1.925 (787.5)	Z=1.232; p=0.218	2.110 (750)	2.040 (800)	Z=1.240; p=0.93	Z=2.698; p=0.007	Z=1.269; p=0.204
Platelet ($\times 10^9/L$)	290.500 (79.000)	213.500 (71.500)	Z=3.734; p<0.001	273.000 (80.000)	256.500 (91.000)	Z=2.189; p=0.029	Z=0.854; p=0.393	Z=2.657; p=0.008
Neutrophil (%)	8.470 (7082.5)	8.690 (6.835)	Z=0.243; p=0.808	5.030 (2.340)	4.460 (2.150)	Z=2.735; p=0.006	Z=4.364; p<0.001	Z=5.194; p<0.001

^a: Wilcoxon signed rank test, ^b: Mann-Whitney test, RDW: Red distribution width, MPV: Mean platelet volume, WBC: White blood cell

Table 3. Patients characteristics who contracted COVID-19 after EG treatment

Patient	Age (years)	BMI (kg/m ²)	Smoking habits	Additional disease	Treatment type	Hospitalisation duration day	Time between COVID-19 diagnosis and treatment	Intensive care unit admission	Medical treatment for COVID-19	Progress	Recovery time (days)
1	30	25.9	No	No	Surgery	10	60	Yes	Favipiravir enoxaparine sodium	Complete recovery	18
2	34	28.5	No	No	Methotrexate	0	10	No	Favipiravir enoxaparine sodium	Complete recovery	12
3	35	28.6	No	No	Surgery	5	56	No	Favipiravir enoxaparine sodium	Complete recovery	10

BMI: Body mass index, COVID-19: Coronavirus disease-19

hence they may be at risk of COVID-19. Some studies which compared the clinical and laboratory components of methotrexate and surgical treatments showed that NLR was significantly increased in the surgical group.^{13,14} Raised NLR is a prognostic marker for severe COVID-19, indicating immediate admission to the intensive care unit (ICU).¹⁵ A meta-analysis of 15 studies including 1,653 patients with severe COVID-19 and non-survivor patients showed increased ICU admittance rates of RR 2.74 (95% CI: 0.98-7.66) compared with those patients with non-severe COVID-19 and those patients who recovered.¹⁶ Yang et al.⁹ also showed that NLR was an independent prognostic factor in COVID-19. According to Eslamijouybari et al.¹⁰, NLR used as a prognostic marker for COVID-19 showed that an increase in NLR could be a marker for those who died from COVID-19 when blood analyses were compared between those who died and those who recovered from COVID-19. It may be the result of the discharge of numerous cytokines which cause tissue and/or organ damage; this situation reduces cellular immunity and alters the ability to contract COVID-19 and prevents disease progression.⁹ In our study, the incidence of COVID-19 was 3.1% (n=3 patients). Two patients had surgical treatment and the other had medical treatment. The mean NLR values were significantly higher for those patients with EP in the surgical group compared with the methotrexate group both before and after treatment ($Z=4.108$, $p<0.001$; $Z=4.783$; $p<0.001$). None of these 3 patients were smokers or had additional disease. The patient who had medical treatment went into self-isolation, took Favipiravir medication at home, and completely recovered. By contrast, both surgically treated patients needed hospitalization. However, no patients died and there was no ICU need. The EP patients who were diagnosed with COVID-19 after surgical and medical treatment recovered completely and their medications were regulated to Favipiravir and Enoxaparin sodium. COVID-19 polymerase chain reaction (PCR) positivity was identified postoperatively on the 56th and 60th days after treatment. Since it is known that the incubation period of COVID-19 infection is approximately two weeks,¹⁷ these infections diagnosed more than 30 days after surgery may be a community-acquired infection.

In addition, NLR was considered a usable prognostic factor when deciding on the most suitable EP treatment. Kan et al.¹⁷ reported that patients with EP with tubal rupture had higher NLR than those without rupture, and they suggested that NLR could assist obstetricians in choosing a treatment approach. Also, in an investigation of 78 patients with EP with methotrexate treatment success and 37 with treatment failure, higher NLR was observed in those patients who had methotrexate treatment success. This study indicated that NLR was a predictor of methotrexate treatment efficacy.¹⁸ However, in our study,

NLR decreased after treatment in both groups, and did not change significantly during treatment ($p=0.108$ and $p=0.431$, respectively). Also, a significant difference was identified between the groups regarding haemoglobin levels, and WBC, platelet, and neutrophil counts.

Another problem in the treatment of EP during the COVID-19 pandemic is hospitalization. Thousands of patients worldwide have had difficulty accessing hospitals due to the high occupancy rates of hospitals and ICUs, leading to a decrease in elective procedures and outpatient visits.¹⁹ With the delays in diagnosis of EP, emergency surgical procedures have increased, causing increased morbidity and mortality as an additional adverse effect of the COVID-19 pandemic. In their retrospective study, Casadio et al.²⁰ showed an increased proportion of ruptured tubal EPs requiring emergency surgical interventions during the COVID-19 lockdown period. Furthermore, Anteby et al.²¹ reported that, in their tertiary medical centre in Israel, although the number of admissions to the emergency department considered as suspected extrauterine pregnancies did not change, the rate of ruptured extrauterine pregnancies was significantly higher during the COVID-19 pandemic (odds ratio: 2.40, 1.27-4.54). Despite there being no government restrictions in terms of emergency department presentations during the pandemic around the world, patients with EP presented later with significantly increased blood loss and were symptomatic.²² The author explained this as being due to postponements in presenting to emergency departments due to a fear of socializing and/or overburdening healthcare systems. Also, in agreement with other studies,^{23,24} significantly increased emergency surgical procedures were reportedly caused due to interruptions in routine scans and later presentations during the COVID-19 pandemic.

Another condition which changes treatment management of EP is hospital stay. Hospitalization days are accepted as relevant risk factor for COVID-19 infections because of the nature of the disease and the human-to-human contamination risk for droplet transmission.²⁵ A single institution reported that the hospital-acquired transmission rate was almost 6.7% in patients with cancer.^{25,26} In our study, the median hospital stay was 5 (IQR 3) days. Furthermore, there was a statistically significant difference detected between the groups, with the methotrexate treatment group having a longer hospital stay ($p<0.01$). The underlying longer stay using immunosuppressive treatments can be explained by patients requiring at least four days of follow-up until a decline is observed in β -hCG levels in our hospital. However, in our study, hospitalization did not increase the rate of COVID-19 illness. This may be because patients had adapted to the social isolation rules, the restrictions on visitors, and compliance with the guidelines during hospitalization.

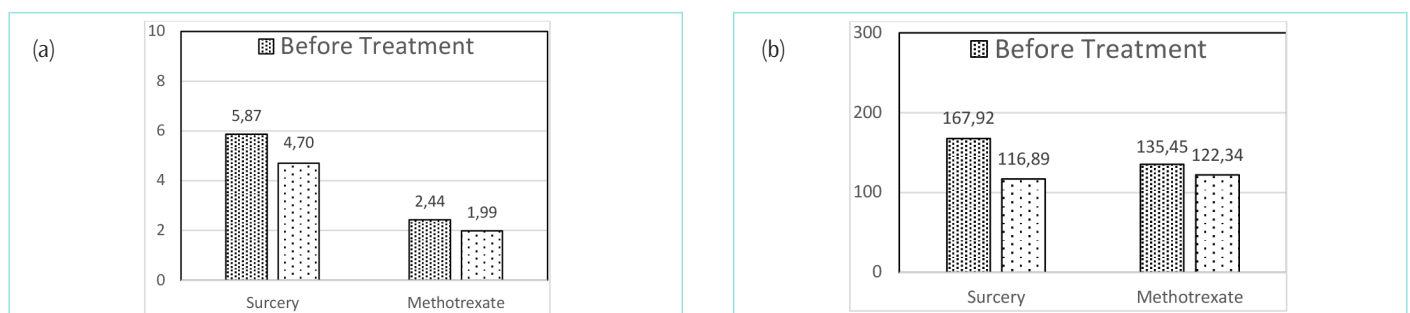


Figure 1. Relationship between NLR and PLR levels before and after single-dose methotrexate treatment and surgery. (a) Median NLR ratio in groups (before and after treatment), (b) median PLR ratio in groups (before and after treatment)

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio.

Study Limitations

There are several notable limitations to this paper. First, the data were obtained from a single clinical trial centre, not from multiple centres. Secondly, the experimental data are limited and the data analyses are retrospective from the patient records. In addition, only three patients developed COVID-19, which may differ from the results of other research. Also, pregnant patients are a special group regarding COVID-19; they may be more attentive to social distancing in order to protect themselves during the COVID-19 pandemic. Social distancing may have an impact on the volume and distribution of illness and the assessment of exposure situations for COVID-19. Also, several other factors such as whole-family characteristics may be important, for example, families of more than five people living together at home, the demographic characteristics at home, and asymptomatic patients may have been included in the population. Screening tests for COVID-19 in our hospital were performed using PCR analyses as soon as possible upon hospitalization.

CONCLUSION

Methotrexate treatment may be chosen as the first-line treatment for EP during the COVID-19 pandemic. Also, it may be useful during other infectious diseases apart from the COVID-19 pandemic. The mean NLR values were significantly higher among those patients with EP who underwent surgery compared with those who had methotrexate treatment both before and post-treatment. Although NLR decreased after treatment in both groups, it did not change significantly during treatment. The length of hospital stay and immunosuppressive treatment procedure did not negatively affect EP treatment. Healthcare professionals must be aware that medical or surgical treatment approaches in patients with EP may change NLR, which is an independent prognostic factor for COVID-19.

MAIN POINTS

- Ectopic pregnancy treatments include expectant management, surgical treatment, and methotrexate (single or multiple-dose) administration. Methotrexate treatment is a non-invasive treatment approach and it is used in patients as the first line treatment but it can cause immunodeficiency.
- The COVID-19 disease has an effect on imbalances in the immune response. Blood laboratory parameters are commonly investigated indicators of this systematic inflammatory response. NLR can be used as a prognostic marker for COVID-19.
- We discussed the ectopic pregnancy treatment choices, either surgery or single doses of methotrexate approaches, and hospitalization days effects on the risk of COVID-19 transmission. Secondly, we aimed to investigate whether the treatment approaches have an effect on the clinical severity after treatment, and compared correlations with alter cell blood counts.

ETHICS

Ethics Committee Approval: Approval from the University of Health Sciences Türkiye, Ankara Etik Zübeyde Hanım Training and Research Hospital Local Ethics Committee (approval number: 03, date: 26.02.2021) was received.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Data Collection and/or Processing: N.A., M.D., M.A., Literature Search: Y.Ü., E.Ü., Writing: N.A., M.D., E.Ü., S.E., Y.Ü.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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