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Original Article

The association between in vitro fertilization outcome and the inflammatory markers of complete blood count among nonobese unexplained infertile couples

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ABSTRACT

Objective(s): The purpose of our study was to evaluate whether the inflammatory parameters of complete blood count (CBC), including white blood cell (WBC), neutrophil-to-lymphocyte-ratio (NLR), platelet-to-lymphocyte-ratio (PLR), and mean platelet volume (MPV), had potential roles in the etiopathogenesis of unexplained infertility (UI) among nonobese women. We also aimed to investigate whether there could be an association between these markers and in vitro fertilization (IVF) success among nonobese women with UI.

Materials and methods: This was a retrospective clinical trial, including a total of 246 nonobese patients undergoing IVF procedures, 121 diagnosed as UI and 125 were age and body mass index (BMI) matched infertile controls who received IVF for tubal factor and male factor. Only normoweight (BMI<25 kg/m^2) participants were recruited to our study to rule out the effect of obesity on inflammation. CBC parameters were evaluated before ovarian stimulation protocol.

Results: All of the inflammatory parameters of CBC were distributed homogenously between groups. Platelet and lymphocyte count were positively correlated with fertilization rate (FR) among UI patients. Embryo count was positively correlated with platelet and negatively correlated with MPV. PLR was also positively correlated with luteinizing hormone on day 3 of cycle. After adjustment for age and BMI, there was a positive association between lymphocyte count and FR and a negative association between PLR and implantation among UI patients. None of the inflammatory markers of CBC were predictive for clinical pregnancy, take home baby, and clinical and biochemical abortion rates among nonobese UI patients.

Conclusion: Increased levels of CBC inflammation markers may have a negative impact on IVF outcomes among nonobese women with UI.

Introduction

Unexplained infertility (UI) refers to the condition of infertility in which the results of standard investigations, including ovulation tests (midluteal serum progesteron level), tubal and uterine patency (hysterosalpingogram), and semen analysis (spermiogram), are all normal [1]. The prevalence of UI ranges from 15 to 25% among infertile couples after their diagnostic procedures [2]. Although the etiopathogenetic mechanisms underlying UI are unclear, several mechanisms have been proposed, such as abnormalities related to oocyte, tubal, or sperm function, which cannot be diagnosed by standard diagnostic procedures [3–5].

In vitro fertilization (IVF) is an effective and successful therapeutic option for UI patients when other infertility treatments have failed to achieve a pregnancy. Moreover, IVF may provide additional diagnostic information regarding gamete function [6]. However, studies have shown lower success rates of IVF in women with UI than in other infertile women [6]. Higher failure rates of IVF in UI couples suggest that there may be other key factors which play essential roles in the absence of known infertility.

Low-grade chronic inflammation is defined as an elevation of several inflammatory markers, such as C-reactive protein (CRP), tumour necrosis factor-α (TNF-α), and interleukins (IL) [7–10]. Low-grade chronic inflammation is commonly blamed for the etiopathogenetic mechanisms of infertility due to the altered levels of inflammatory markers in unexplained infertile patients [11,12]. Studies have demonstrated an association between IL and proinflammatory

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factors and higher failure rates of IVF, especially in the implantation stage, among UI women [13]. Some complete blood count (CBC) parameters, such as white blood cell (WBC), neutrophil, and neutrophil-to-lymphocyte ratio (NLR), are thought to be inflammatory markers [14–17]. In recent years, the platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV) are also increasingly used as markers of chronic inflammation [17–19]. It has been found that PLR could serve as a biological marker of both thrombosis and inflammation [20]. It is believed that increased proliferation of platelets is the result of an ongoing proinflammatory state [20]. MPV is also a marker of platelet activation because there is a close relationship between platelet size and platelet activation [20].

Although it has been documented that infertility involves chronic inflammation, it remains to be seen whether an increased inflammatory response affects IVF success rates. There are some reports about NLR, MPV, and PLR in infertile women with PCOS [20]; however, there is no report regarding CBC parameters in women with UI. Concerning the possible role of inflammation in infertility and IVF success, we aimed to investigate whether CBC inflammation markers are one of the etiopathogenetic mechanisms of UI and whether there is an association between these markers and IVF success among women with UI.

Material-method

This was a retrospective case control study performed in the IVF Unit of Suleyman Demirel University Faculty of Medicine, between January 2012 and December 2016. The study was approved by the Local Ethics Committee with the protocol number 72867572- 050-5026. Data were collected from the hospital files of infertile women who administered to our clinic for an IVF cycle.

Patients selection

We scanned all the files of patients undergoing IVF treatment. A total of 246 infertile patients were randomly selected for the study. *The unexplained group* was comprised of 121 women, and *the control group* was comprised of 125 infertile women, who were matched by age and body mass index (BMI). All the women in the sample were between the ages of 21 and 44 years old. Only normoweight (BMI<25 kg/m^2) participants were recruited to our study to rule out the effect of obesity on inflammation. All participants had normal ovarian morphology, demonstrated normal ultrasonographic examinations, and had regular ovulatory cycles.

Patients were diagnosed with UI after being evaluated based on standard infertility tests, according to the guidelines of the Practice Committee of the American Society for Reproductive Medicine [2]. These tests included assessments of spermiogram, ovulation, hysterosalpingogram, and, if indicated, ovarian reserve tests and laparoscopy. If the results of all these tests were normal, patients were accepted as UI. The inclusion criteria for the study group were a minimum of one-year infertility duration, a regular menstrual cycle of 21–35 days, evidence of ovulation (midluteal serum progesterone (PG) level >5 ng/ml), levels of the day 2 follicle stimulating hormone (FSH) being <10 IU/L, normal tubal patency confirmed with hysterosalpingogram, and normal sperm parameters (sperm density >15 million/mL; progressive motility >40%; and normal forms >4%; or total progressive motile sperm count >5 million according to World Health Organization criteria) [21].

The control group included women who underwent IVF for male or tubal factor related infertility. However, patients with hydrosalpinx, severe pelvic adhesions, endometriosis or pelvic inflammatory disease, severe male factor (azoospermia and severe oligoasthenospermia), and diminished ovarian reserve were not included as controls.

Exclusion criteria for all participants were systemic diseases (hypertension, diabetes, asthma, liver/kidney disease, etc), endocrinological abnormalities (hyper/hypothyroidism, hyperprolactinemia, etc), evidence of postmenopausal FSH levels, ovarian disease (endometrioma, etc), hematologic disorders (haemophilia, etc), malignancy, presence of infectious disease, autoimmune diseases, history of splenectomy, use of anti-inflammatory drugs or glucocorticoids, and other chronic inflammatory conditions (arthritis, etc). Patients who had a BMI of >25 kg/m^2 and demonstrated smoking and alcohol use were also excluded.

Data collection

We recorded the demographic features of patients, including age; partner's age; BMI; cycle count (if performed); duration of infertility; and day 3 basal hormone levels, including FSH, LH, and estradiol (E_2) levels. Moreover, thyroid stimulating hormone (TSH) and prolactin (PRL) levels that had been measured on a random day were recorded from the patients' files.

Stimulation protocol (agonist/antagonist), type of gonadotropin (recombinant/urinary), type of human chorionic gonadotropin (hCG) (recombinant/urinary), and starting dose of gonadotropin were also recorded from the patients' files.

Oocyte retrieval parameters, including the number of total retrieved oocytes, methaphase II (MII), MI, germinal vesicle (GV), oocytes with anomaly, and oocytes with empty zona (EZ), were noted from embryologic data. “An oocyte with anomaly” was defined on the basis of cytoplasmic (such as presence of abnormal cytoplasmic granulation, dark cytoplasm, vacuolization, inclusion body, refractile body and smooth endoplasmic reticulum) and extracytoplasmic (such as differences in size, anomaly in shape, thickness of zona pellucida, wideness of perivitelline space, presence of debris in perivitelline space, fragmented polar body) features of an oocyte. Fertilization (defined as the presence of two pronuclei one day after intracytoplasmic sperm injection), embryo number, and embryo quality were also recorded. In our IVF unit, the quality of embryos was evaluated on day 3 when the embryos were at least at the 8-cell stage, according to their morphological characteristics. The embryos were classified from Grade 1 (best quality) to Grade 3 (poor quality). Embryos with even-sized blastomeres and/or <5% fragments were classified as Grade 1; embryos with slightly-moderate size differences in blastomeres and/or 5–50% fragments were classified as Grade 2 (moderate quality); and embryos with markedly different-sized blastomeres and/or >50% fragments were classified as Grade 3.

We calculated the *fertilization rate (FR)* as the ratio of fertilized oocytes to MII oocytes. The results were classified as ‘*low FR*’ and ‘*normal FR*’, if the FR was <60% and ≥60%, respectively.

IVF outcomes, including implantation, clinical pregnancy (CP), take-home baby, biochemical abortion (BA), and clinical abortion (CA), were noted from the patient's file. *Implantation* was determined as positive hCG 14 days following embryo transfer. *CP* was established as the identification of an intrauterine gestational sac via transvaginal ultrasonographic examination. The *take-home baby* rate was determined by identifying whether the patients delivered or not. *BA* referred to a pregnancy that was diagnosed only by the detection of hCG in serum or urine and that did not develop into a clinical pregnancy. *CA* was defined as the disappearance of an initially proven gestational sac according to a transvaginal ultrasound.

Laboratory evaluation

We also scanned the CBC parameters of all the patients in the sample. In our IVF unit, we routinely scanned the CBC of all the

patients before conducting the controlled ovarian stimulation protocol to determine whether the patients had any disorder or not and to prepare for the administration of anaesthesia. Venous blood samples were taken into the ethylene diamine tetra acetic acid (EDTA) possesing tubes between 08: 00 and 09: 00 AM, after an overnight 12 h fasting. The CBC was performed using an auto blood analyser (Cell-Dyn 3700.Abbott®, USA). WBC, neutrophil, lymphocyte, platelet, MPV levels and NLR and PLR were recorded.

Statistical analysis

The Statistical Package for Social Sciences for Windows (SPSS 20, Chicago, IL, USA) was used for statistical analyses. A p value < 0.05 was considered statistically significant. The distribution of data were evaluated by Kolmogrow–Smirnow test. Student's *t*-test or Mann Whitney *U* test and Chi-square or Fischer's exact test were used for comparisons. Data were expressed as mean ± SD. Correlations between continous variables were evaluated using Pearson's correlation analysis or Spearman's rank test. Logistic regression analysis was used to evaluate the association between dependent and independent variables.

Results

A total of 246 nonobese infertile patients were recruited to our study. *The unexplained group* was comprised of 121 women diagnosed as UI, and *the control group* was comprised of 125 BMI-matched controls. Only the normoweight (BMI<25 kg/m^2) participants were recruited to rule out the effect of obesity on inflammation.

Baseline characteristics

The mean age of the UI group was 30.09 ± 4.59, and the mean age of the control group was 29.72 ± 5.09. The BMI of the unexplained group was 23.58 ± 3.37 kg/m^2, and the BMI of the control group was 23.16 ± 2.81 kg/m^2. As shown in Table 1, there were no significant differences in age range and BMI (p = 0.54 and p = 0.28, respectively) between the two groups. Partner's age, duration of infertility, and cycle count were distributed homogenously between the unexplained and control groups (p = 0.052, p = 0.14, and p = 0.58, respectively). Day 3 basal hormone levels, TSH levels, and PRL levels were also similar between the two groups. A comparison of the baseline characteristics between the unexplained and control groups is presented in Table 1.

Table 1
The comparison of basal characteristics between unexplained and control groups.

	Unexplain group (n = 121) Mean ± SD	Control group (n = 125) Mean ± SD	p value
Age (years)	30.09 ± 4.59	29.72 ± 5.09	0.54
Partner's age (years)	34.82 ± 5.35	33.48 ± 5.37	0.052
BMI (kg/m^2)	23.58 ± 3.37	23.16 ± 2.81	0.28
Duration of infertility (years)	7.09 ± 4.1	6.31 ± 4.28	0.14
Cycle count (if performed)	1.47 ± 0.82	1.52 ± 0.8	0.58
TSH (mIU/ml)	2.06 ± 1.17	1.82 ± 0.88	0.06
E_2 (pg/ml)	50.43 ± 34.31	60.7 ± 57.09	0.09
FSH (mIU/ml)	7.72 ± 2.65	7.66 ± 3.5	0.88
LH (mIU/ml)	5.36 ± 3.14	5.33 ± 3	0.92
PRL (ng/ml)	14.53 ± 8.22	14.59 ± 11.63	0.96

BMI: Body mass index; TSH: Thyroid stimulan hormon; E_2: Estradiol; FSH: Follicle stimulating hormone; LH: Luteinizing hormone; PRL: Prolactin.

Oocyte retrieval parameters and IVF outcome between unexplained and control group

Gonadotropin releasing hormone antagonists were used for down-regulation of the pituitary gland in all the patients. Most of the patients were stimulated by both the recombinant and the urinary FSH. There were no significant differences in terms of the starting dose and type of gonadotropin used for each of the groups. Recombinant hCG was used in all the patients for final maturation of oocytes. Single fresh embryo transfer was performed in all patients according to the rules of Turkish reproduction. All the oocyte retrieval parameters except the number of oocytes with anomaly were distributed homogenously between the unexplained and control groups. The UI group had a higher number of oocytes with anomaly (0.13 ± 0.53) than the control group had (0.08 ± 0.38, p = *0.04*). Among the 246 initiated cycles, five cycles had no oocytes retrieved, and only three cases had immature oocytes for which ICSI could not be performed; therefore, fertilization was assessed among the remaining 238 cycles. Total fertilization failure occurred in 16 cases (13.2%) in the UI group and in 11 cases (8.8%) in the control group. Embryo transfer could be performed in 99 cases of the UI group and 93 cases of the control group. MII rate, FR, embryo number, and embryo quality were distributed homogenously between the two groups (p = 0.88, p = 0.15, p = 0.38, and p = 0.5, respectively).

Implantation was 14.1% in the UI group and 21.5% in the control group (p = 0.18). Although implantation, CP, and take-home baby rates were all lower in the unexplained group than in the control group, this difference was not statistically significant. BA and CA rates were also comparable between the UI and control groups (Table 2).

Table 2
Oocyte retrieval parameters and IVF outcome between unexplained and control groups.

	Unexplain group (n = 121)	Control group (n = 125)	p
Type of gonadotrophins			
r-FSH (%)	42/121 (34.7%)	34/125 (27.2%)	0.2
u-FSH+r-FSH (%)	79/121 (65.3%)	91/125 (72.8%)	
r-FSH dosage per day (IU)	239.15 ± 53.49	235.6 ± 64.46	0.63
u-FSH dosage per day (IU)	128.57 ± 47.39	133.96 ± 37.35	0.40
Oocyte retrieval parameters			
Total oocyte retrieved	9.12 ± 4.96	9.91 ± 6.38	0.28
MII oocyte number	6.33 ± 3.57	6.88 ± 4.38	0.28
MI oocyte number	1.35 ± 1.32	1.55 ± 1.92	0.34
GV oocyte number	1 ± 1.91	1.06 ± 1.52	0.79
Oocyte with anomaly	0.13 ± 0.53	0.08 ± 0.38	***0.04***
Degenere oocyte number	0.07 ± 0.36	0.2 ± 0.64	0.46
EZ	0.14 ± 0.45	0.12 ± 0.39	0.71
MII rate (%)	71.24 ± 21.97	71.61 ± 19.09	0.88
FR (%)	55.09 ± 30.97	49.2 ± 31.24	0.15
Embryo number	3.78 ± 2.88	3.45 ± 2.75	0.38
Embryo quality			
Grade 1	92/102 (90.2%)	83/95 (87.4%)	0.5
Grade 2	9/102 (8.8%)	9/95 (9.5%)	
Grade 3	1/102 (1%)	3/95 (3.2%)	
IVF outcomes			
Implantation (%)	14/99 (14.1%)	20/93 (21.5%)	0.18
Clinical pregnancy (%)	12/99 (12.1%)	16/93 (17.2%)	0.31
Take home baby (%)	11/99 (11.1%)	12/93 (12.9%)	0.7
Biochemical abortion (%)	1/99 (1%)	3/93 (3.2%)	0.28
Clinical abortion (%)	1/99 (1%)	3/93 (3.2%)	0.28

r-FSH: Recombinant follicle stimulating hormone; u-FSH: Uriner follicle stimulating hormone; MII: Methaphase II; MI: Methaphase I; GV: Germinal vesicle; EZ: Oocyte with empty zona; FR: Fertilization rate; IVF: In vitro fertilization.

Table 3
The comparison of inflammatory markers of CBC between unexplained and control groups.

	Unexplained group (n = 121) Mean ± SD	Control group (n = 125) Mean ± SD	p value
WBC (10^3/μl)	9.12 ± 2.14	8.99 ± 2.31	0.64
Platelet (10^3/μl)	258.86 ± 63.97	266.08 ± 60.78	0.36
Neutrophil (10^3/μl)	6.23 ± 1.87	5.98 ± 1.66	0.27
Lymphocyte (10^3/μl)	2.15 ± 0.57	2.26 ± 1.25	0.37
NLR	3.05 ± 1.21	2.88 ± 0.94	0.22
PLR	126.01 ± 37.98	130.08 ± 42.62	0.43
MPV(fL)	8.62 ± 0.94	8.59 ± 0.93	0.82

WBC: White blood cell; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; MPV: Mean platelet volume.

The comparison of CBC inflammation markers between unexplained and control groups

There was no difference between the two groups in terms of CBC inflammation markers, including WBC, platelet, neutrophil, and lymphocyte, as well as NLR, PLR, and MPV. WBC, neutrophil, NLR, and MPV were higher whereas platelet, lymphocyte, and PLR were lower in the unexplained group than in the control group; however, the differences were not statistically significant. Data related to the comparison of inflammatory markers between the unexplained and control groups is presented in Table 3.

Correlation between the inflammatory parameters of CBC and basal hormone levels and IVF outcomes among unexplained group

There was no correlation between age, BMI, and inflammatory markers in the UI group. There was also no correlation between the CBC inflammation markers and the FSH and E_2 levels in the UI group. However, LH levels were positively correlated with PLR ($r = 0.22$, $p = 0.01$). In terms of IVF outcomes, we found a positive correlation between FR and platelet ($r = 0.27$, $p = 0.003$) as well as between FR and lymphocyte ($r = 0.23$, $p = 0.01$). Embryo number was positively correlated with platelet ($r = 0.22$, $p = 0.01$) and negatively correlated with MPV ($r = -0.18$, $p = 0.04$). The correlation CBC inflammation markers with basal hormone levels and IVF outcome among UI women is shown in Table 4.

Table 5
Predictive effect of inflammatory markers of CBC on fertilization rate.

	B	p value	OR	95% CI for OR	
				Lower	Upper
Lymphocyte (10^3/μl)	0.99	0.012	2.69	1.243	5.844
Constant	−2.14	0.012	0.11		

Covariates: Age, body mass index, white blood cell, platelet, neutrophil, lymphocyte, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, mean platelet volume.

The association between the CBC inflammation markers and IVF outcome among unexplained group

Regression analyses were performed to evaluate the association between the CBC inflammation markers and FR, implantation, CP, take home baby rate, BA, and CA in the unexplained group. Age, BMI, WBC, platelet, neutrophil, lymphocyte, NLR, PLR, and MPV were the independent variables to analyse the dependent variables. Lymphocyte was the only positive predictive marker [$p = 0.01$; $\beta = 0.99$, OR (95% CI) = 2.69 (1.24–5.84)] for normal FR in the unexplained group. Related data is shown in Table 5. For implantation, PLR was the only negative predictive marker [$p = 0.047$, $\beta = -0.016$, OR (95% CI) = 0.98 (0.96–1)] in the unexplained group. There was no predictive effect of investigated parameters on CP, take home baby rate, BA, and CA.

Discussion

In this study, we investigated CBC inflammation markers, including WBC, neutrophil, lymphocyte, NLR, PLR, and MPV in nonobese UI women undergoing IVF treatment compared to age and BMI-matched controls and also investigated the relationship between these markers and IVF outcomes among women with UI. Adipose tissue can secrete hormones, adipokines, and cytokines [22], and studies have shown that inflammation can caused by obesity. Therefore, to exclude the impact of obesity on inflammation, only the participants with a BMI of <25 kg/m^2 were recruited to our study.

There was no difference between the unexplained and control groups in terms of CBC inflammation markers, including WBC, platelet, neutrophil, lymphocyte, NLR, PLR, and MPV. Growing evidence supports that infertility is associated with low-grade chronic

Table 4
Correlation between the inflammatory parameters of CBC and basal hormone levels and IVF outcome.

		Age	BMI	Total oocyte	MII	MII rate	FR	Embryo	E_2	FSH	LH
WBC	r	−0.08	−0.11	0.1	0.14	0.05	0.1	0.12	−0.07	−0.05	−0.07
	p	0.34	0.2	0.24	0.1	0.54	0.24	0.19	0.39	0.55	0.4
Platelet	r	−0.01	0.17	0.04	0.03	−0.007	***0.27***	***0.22***	−0.17	0.02	0.1
	p	0.9	0.05	0.61	0.69	0.94	***0.003***	***0.01***	0.06	0.76	0.26
Neutrophil	r	−0.09	−0.12	0.12	0.16	0.06	0.03	0.07	−0.007	−0.04	−0.02
	p	0.32	0.18	0.18	0.07	0.48	0.71	0.41	0.93	0.59	0.82
Lymphocyte	r	0.03	0.03	−0.02	−0.003	0.01	***0.23***	0.13	−0.1	0.06	−0.17
	p	0.72	0.7	0.81	0.97	0.84	***0.01***	0.14	0.25	0.47	0.05
NLR	r	−0.15	−0.09	0.13	0.16	0.05	−0.11	−0.02	0.09	−0.02	0.08
	p	0.09	0.28	0.14	0.07	0.52	0.19	0.79	0.3	0.82	0.36
PLR	r	−0.04	0.1	0.04	−0.01	−0.05	0.03	0.03	0.008	−0.01	***0.22***
	p	0.62	0.23	0.6	0.91	0.52	0.72	0.68	0.92	0.91	***0.01***
MPV	r	0.08	−0.11	−0.11	−0.12	−0.006	−0.15	***−0.18***	−0.06	−0.05	−0.15
	p	0.36	0.2	0.21	0.17	0.95	0.1	***0.04***	0.46	0.57	0.09

WBC: White blood cell; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; MPV: Mean platelet volume; FR: Fertilization rate; MII: Methaphase II; E_2: Estradiol; FSH: Follicle stimulating hormone; LH: Luteinizing hormone.
Bold and italic characters represent the statistical significance.

inflammation. Evaluating NLR and PLR could predict systemic inflammation [23]. Consistent with our study, studies have found no differences between UI and fertile controls in terms of WBC and lymphocytes in the assessment of plasma between days 20 and 24 of the menstrual cycle [24]. Studies have found elevated interferon-γ (IFN-γ) and IL-2 levels and decreased transforming growth factor-β (TGF-β, an important endogenous anti-inflammatory mediator) [11] in the plasma of UI patients compared to fertile controls during the implantation window (luteal phase) [24]. Moreover, UI patients have demonstrated elevated serum IL-2, IL-4, IL-6, IL-21, TNF-α, and IFN-γ levels compared to fertile individuals [12]. In this study, the small sample size and other factors which affect CBC parameters, such as subclinical infections, could be the causes of the nonsignificant differences between the unexplained and control groups. Moreover, in contrast to previous studies, all the participants in our study were nonobese; therefore, the results of the current study could have been affected by the participants' BMI.

We found decreased implantation, clinical pregnancy, and take-home baby rates in the UI group; however, the differences in these measures were not statistically significant between the two groups. Consistent with our study, studies have shown lower success rates with IVF in UI patients compared in other infertile women [6].

There was no correlation between the CBC inflammation markers and FSH and E_2 levels; however, LH levels were positively correlated with PLR among women with UI. We also found a positive correlation between platelet and embryo number as well as a positive correlation between platelet and FR. Lymphocyte count was also positively correlated with FR, and MPV was negatively correlated with embryo number. A previous report found no relationship between CBC inflammation markers and FSH and E_2 levels; however, it has been demonstrated that LH levels were negatively correlated with neutrophil and lymphocyte count and positively correlated with PLR in patients with polycystic ovary syndrome (PCOS) [20]. A discrepancy in the study groups could be one cause of the dissimilarity in the results.

Lymphocyte was found to be the only positive predictive marker for normal FR in the unexplained group, and PLR was the only negative predictive marker for implantation in the unexplained group after adjusting for age and BMI. The positive predictive ability of lymphocyte regarding FR, and the negative predictive ability of PLR regarding implantation among UI patients suggests that inflammation could negatively affect IVF outcomes in UI patients. There are a few studies that concern the role of CBC parameters on IVF outcomes. MPV values were reported to be negatively correlated with CP and implantation rate, and PLR levels were found to be positively associated with miscarriages in patients with PCOS [20]. It is believed that one of primary mechanisms of implantation failure and abortion in UI is the compromised receptivity of the endometrium, and studies have highlighted the role of immune factors in implantation failure in UI women [25]. It has been suggested that elevated platelet counts and PLR, and decreased lymphocyte counts are risk indicators of both thrombosis and inflammation [17,20]. It is believed that increased proliferation of platelets is the result of an ongoing proinflammatory state [20]. Both thrombosis and inflammation via demonstrated PLR could affect implantation negatively. Inflammation is the key feature of endothelial dysfunction [14]. Endotelial dysfunction and elevated PLR could contribute to increased hemostatic functions resulting in thrombosis of spiral arterioles [19,26]. It has also been suggested that platelet activation plays a central role in the etiopathogenesis of arterial occlusion and could also cause injury to the endothelium resulting in elevated thromboxane A2 levels [20]. Therefore, a negative association between PLR and embryo implantation can be explained by thrombosis of spiral arterioles.

The main limitation of our study is its small sample size and lack of power calculation. Another limitation its retrospective design and its use of data from a single tertiary centre. This limits the ability of the results to reflect and apply to the general population. The lack of evaluation of oocyte quality, which is closely associated with fertilization, was another limitation. It should be noted that our study group was only infertile women undergoing IVF treatment, and the results could not be generalized to all UI patients experiencing spontaneous cycles or taking ovulation induction drugs without undergoing IVF. Moreover, IVF is a supraphysiologic situation in which many other factors, such as laboratory conditions, could affect its success. Despite these limitations, this was the first study that evaluated the association between CBC inflammation markers and IVF outcome in women with UI.

Conclusion

In conclusion, our data suggest that inflammation may have a negative impact on IVF outcomes among women with UI. Future prospective studies with the larger population are needed to elucidate the impact of inflammation on IVF success among UI patients.

Conflict of interest

The author declares that they have no conflict of interest.

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