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Evaluation of Hematologic Inflammatory Indices in Relation to IgG Avidity Status in Pregnant Women with *Toxoplasma gondii* IgM Positivity

Toxoplasma gondii IgM Pozitif Gebelerde Hematolojik Enflamasyon İndekslerinin IgG Avidite Durumu ile İlişkisinin Değerlendirilmesi

Erkan Yergin[1], İbrahim Taşkum[1], Seyhun Sucu[2], Fatma Didem Yücel Yetişkin[2], Erkan Şimşek[1], Selcan Sınacı[2]

[1]University of Health Sciences Turkey, Gaziantep City Hospital, Department of Obstetrics and Gynecology, Gaziantep, Turkey
[2]University of Health Sciences Turkey, Gaziantep City Hospital, Department of Obstetrics and Gynecology, Division of Perinatology, Turkey

Abstract

Objective: This study aimed to evaluate hematologic inflammatory indices in pregnant women with *Toxoplasma gondii* (*T. gondii*) immunoglobulin (Ig)M positivity and to investigate whether these markers could help predict low or intermediate IgG avidity, which indicates a recent or ongoing infection.

Method: This retrospective case-control study included 192 pregnant women admitted to the Obstetrics and Gynecology Department of University of Health Sciences Turkey, Gaziantep City Hospital between November 2023 and April 2025. Ninety-six women with *T. gondii* IgM positivity and 96 seronegative controls were analyzed. Hematologic parameters were obtained from complete blood counts, and inflammatory indices—including neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV)—were calculated. Patients were further categorized according to IgG avidity (high vs. low/intermediate).

Results: No significant differences were found in inflammatory indices between IgM-positive and control groups (p>0.05). However, among IgM-positive women, those with low or intermediate IgG avidity exhibited significantly lower monocyte (p=0.018), neutrophil (p=0.034), and white blood cell counts (p=0.023), along with reduced MLR (p=0.036), SIRI (p=0.014), and PIV (p=0.020) values compared

Öz

Amaç: Bu çalışma, *Toxoplasma gondii* (*T. gondii*) immünoglobulin (Ig)M pozitifliği bulunan gebelerde hematolojik enflamasyon indekslerini değerlendirmeyi ve bu belirteçlerin, yakın zamanda geçirilmiş veya devam eden enfeksiyonu gösteren düşük ya da orta düzey IgG aviditesini öngörmede yardımcı olup olamayacağını araştırmayı amaçladı.

Yöntem: Bu retrospektif olgu-kontrol çalışmasına, Kasım 2023 ile Nisan 2025 tarihleri arasında Sağlık Bilimleri Üniversitesi, Gaziantep Şehir Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'ne başvuran toplam 192 gebe dahil edildi. *T. gondii* IgM pozitifliği olan 96 kadın ile 96 seronegatif kontrol incelendi. Hematolojik parametreler tam kan sayımı sonuçlarından elde edildi ve nötrofil/lenfosit oranı, monosit/lenfosit oranı (MLR), trombosit/lenfosit oranı, sistemik immün-enflamasyon indeksi (SII), sistemik enflamasyon yanıt indeksi (SIRI) ve pan-immün-enflamasyon değeri (PIV) hesaplandı. Hastalar ayrıca IgG avidite düzeylerine göre yüksek ve düşük/orta aviditeli olarak sınıflandırıldı.

Bulgular: IgM pozitif ve kontrol grupları arasında enflamasyon indeksleri açısından anlamlı fark saptanmadı (p>0,05). Ancak IgM pozitif gebeler arasında, düşük veya orta IgG aviditesine sahip olanlarda monosit (p=0,018), nötrofil (p=0,034) ve lökosit (p=0,023) sayıları ile MLR (p=0,036), SIRI (p=0,014) ve PIV (p=0,020) değerleri yüksek aviditeli gruba göre anlamlı olarak daha düşük bulundu.

Address for Correspondence: İbrahim Taşkum, MD, University of Health Sciences Turkey, Gaziantep City Hospital, Department of Obstetrics and Gynecology, Gaziantep, Turkey
E-mail: ibrahimtaskum@gmail.com **ORCID:** orcid.org/0000-0001-5260-2087
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Abstract

with the high-avidity group. Logistic regression analysis identified SIRI [area under the curve (AUC) =0.66, p=0.023] and PIV (AUC =0.65, p=0.047) as significant predictors of low/intermediate avidity.

Conclusion: Although no significant differences were observed between IgM-positive and control groups, certain hematologic indices such as SIRI and PIV may serve as supportive tools for identifying recent or ongoing *T. gondii* infection during pregnancy.

Keywords: Hematologic indices, IgG avidity, pregnancy, systemic inflammation, *Toxoplasma gondii*

Öz

Lojistik regresyon analizinde, düşük/orta aviditeyi öngörmede SIRI [eğri altında kalan alan (AUC) =0,66, p=0,023] ve PIV (AUC =0,65, p=0,047) anlamlı prediktörler olarak belirlendi.

Sonuç: IgM pozitif ve kontrol grupları arasında genel olarak anlamlı fark bulunmamakla birlikte, SIRI ve PIV gibi bazı hematolojik indeksler, gebelikte yakın zamanda geçirilmiş veya devam eden *T. gondii* enfeksiyonunu belirlemede destekleyici araçlar olarak kullanılabilir.

Anahtar kelimeler: Gebelik, hematolojik indeksler, IgG aviditesi, sistemik enflamasyon, *Toxoplasma gondii*

Introduction

Toxoplasma gondii is an obligate intracellular protozoan parasite that infects nearly one-third of the global population, making toxoplasmosis one of the most prevalent zoonotic infections worldwide (1-5). Human infection is primarily acquired through ingestion of food or water contaminated with oocysts shed by cats, or by consumption of undercooked meat containing tissue cysts (3). The parasite exhibits remarkable adaptability and can persist in host tissues by evading immune surveillance and forming latent cysts that may reactivate under immunosuppression (4). Although most infections are subclinical in immunocompetent individuals, toxoplasmosis can cause devastating disease in immunocompromised patients and during pregnancy.

Primary maternal infection may lead to intrauterine fetal death, stillbirth, or congenital toxoplasmosis, resulting in neurological, ocular, and developmental sequelae (1-3,5). Current treatment with pyrimethamine-sulfadiazine remains the gold standard for acute infection, and spiramycin prophylaxis during pregnancy has been shown to reduce vertical transmission, yet no therapy effectively eradicates latent cysts (5). Given its global burden and potential for severe fetal outcomes, prevention, early diagnosis, and timely management remain key public health priorities (2,5).

Serologic testing remains the mainstay for diagnosing *Toxoplasma gondii* infection in pregnancy. Detection of *Toxoplasma*-specific IgG and IgM antibodies helps determine maternal immune status and the risk of fetal transmission. However, IgM antibodies may persist for months or yield false-positive results, making it difficult to distinguish recent from past infections (6,7). The IgG avidity test improves diagnostic accuracy: High avidity indicates infection more than three months earlier, whereas low avidity suggests a recent infection (7). Yet intermediate ("gray-zone") results remain difficult to interpret and require clinical and serologic follow-up (6,7).

These limitations highlight the need for additional objective markers to aid in differentiating recent from past infections during pregnancy. Several hematologic indices, including the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV), are considered practical indicators of systemic inflammation. These parameters have been widely used in obstetric research as accessible tools for assessing inflammatory status and predicting adverse pregnancy outcomes (8,9). However, their potential association with *Toxoplasma gondii* infection and IgG avidity levels during pregnancy has not been clearly established.

Therefore, this study aimed to evaluate hematologic inflammatory indices in pregnant women with *Toxoplasma gondii* IgM positivity and to investigate whether these markers could help predict low or intermediate IgG avidity, potentially reflecting recent maternal infection.

Materials and Methods

Study Design and Patient Selection

This retrospective case-control study included a total of 192 pregnant women who were admitted to the Obstetrics and Gynecology Department of University of Health Sciences Turkey, Gaziantep City Hospital between November 2023 and April 2025. The study population consisted of 96 patients with positive *Toxoplasma gondii* IgM tests and 96 healthy pregnant women serving as the control group. Control subjects were selected from women who presented for routine antenatal follow-up during the same period, had negative *Toxoplasma* serology, and exhibited no

signs of systemic infection or inflammation. Among the *Toxoplasma* IgG avidity positive patiens, all had singleton pregnancies and complete medical records available for review.

Patients were further categorized based on their *Toxoplasma* IgG avidity results: High avidity (n=68) and low/intermediate avidity (n=28). Although 15 patients had low and 13 had intermediate avidity, these categories were combined into a single group because their clinical management and follow-up protocols are identical, both reflecting a recent or ongoing infection status. Among the initially identified patients, four with body mass index ≥30 kg/m² (obesity), four using low-molecular-weight heparin, and three with incomplete data were excluded from the study. No cases of multiple pregnancy, fetal anomalies, preeclampsia, gestational diabetes mellitus, thyroid dysfunction, autoimmune or rheumatologic diseases, hematologic disorders, infectious or inflammatory conditions, coagulopathies, malignancy, or corticosteroid/immunomodulatory drug use were identified in the dataset. This study was approved by the University of Health Sciences Turkey, Gaziantep City Hospital Clinical Research Ethics Committee (approval no: 215/2025, dated: May 21, 2025). A comprehensive review of the patients' medical records was conducted to gather clinical data, patient characteristics, and follow-up information. Due to the retrospective design of the study, informed consent was waived.

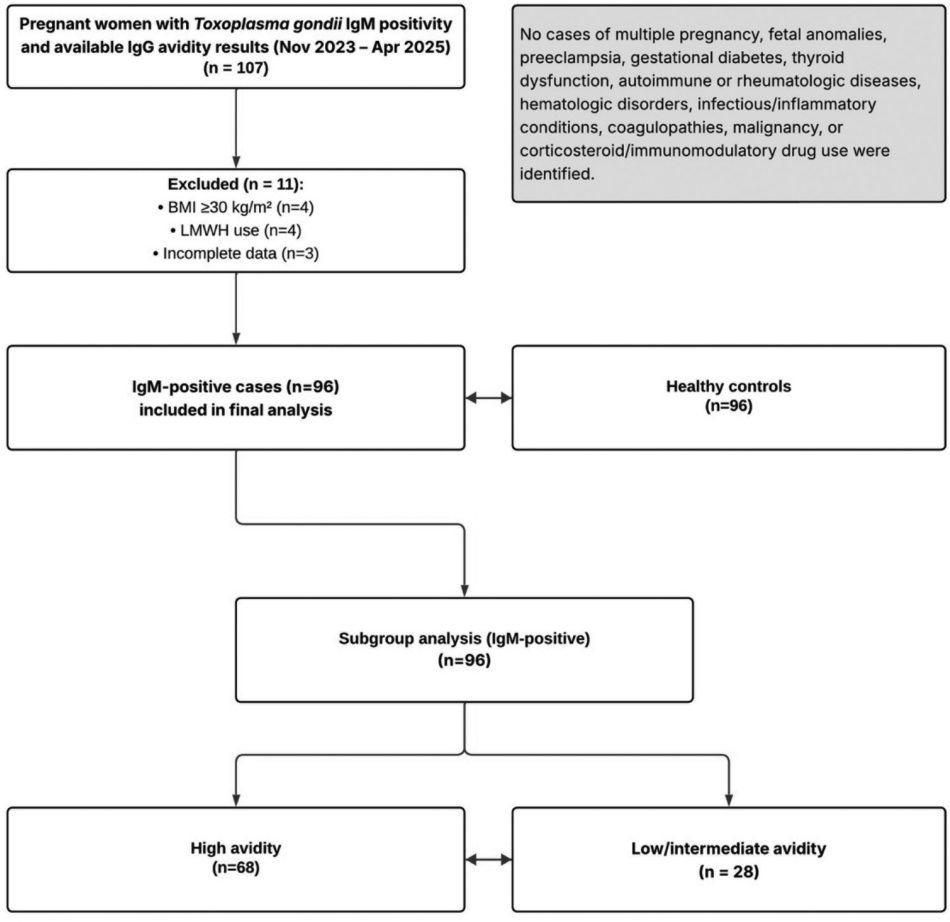

Figure 1. Flow diagram of patient selection and subgroup classification

Among 107 pregnancies with *Toxoplasma gondii* IgM positivity and available IgG avidity results, 11 were excluded due to obesity (n=4), LMWH use (n=4), or incomplete data (n=3). The final analysis included 96 IgM-positive patients and 96 healthy controls. The IgM-positive group was further divided into high and low/intermediate avidity subgroups for comparative analysis

LMWH: Low-molecular-weight heparin, Ig: Immunoglobulin, BMI: Body mass index

All procedures were conducted in accordance with the ethical standards of the institutional and national research committees and with the principles outlined in the Declaration of Helsinki. The selection process of the study population is summarized in Figure 1.

Data Collection and Calculation of Inflammatory Indices

Demographic and laboratory data were retrospectively retrieved from the hospital's electronic medical records. The following variables were collected for each patient: Maternal age (years), gravida, parity, number of abortions, and gestational week at the time of testing. Hematologic parameters included hemoglobin (g/dL), white blood cell count ($\times 10^3/\mu L$), neutrophils ($\times 10^3/\mu L$), lymphocytes ($\times 10^3/\mu L$), monocytes ($\times 10^3/\mu L$), and platelets ($\times 10^3/\mu L$). All hematologic measurements were performed using the Beckman Coulter DxH 800 automated hematology analyzer in the hospital laboratory. Systemic inflammatory indices were calculated using parameters obtained from the complete blood count.

The NLR was determined by dividing the neutrophil count by the lymphocyte count, while the platelet-to-lymphocyte ratio (PLR) and MLR were computed by dividing the platelet and monocyte counts, respectively, by the lymphocyte count. The SII was calculated by multiplying the platelet count by the neutrophil count and dividing the result by the lymphocyte count. Similarly, the SIRI was obtained by multiplying the neutrophil and monocyte counts and dividing the product by the lymphocyte count. Finally, the PIV was calculated as the product of the neutrophil, platelet, and monocyte counts divided by the lymphocyte count. All indices were computed automatically from laboratory data and used for subsequent statistical analyses.

Statistical Analysis

All statistical analyses were performed using R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria). The normality of distribution for continuous variables was evaluated using the Shapiro-Wilk test and visual inspection of histograms. Continuous variables were expressed as median (minimum-maximum) values, whereas categorical variables were presented as counts (percentages). Comparisons between the *Toxoplasma* IgM-positive group and the control group, and subsequently between the low/intermediate and high avidity subgroups, were conducted using the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. Univariate logistic regression analyses were performed to assess the association between each inflammatory index (NLR, PLR, MLR, SII, SIRI, and PIV) and the presence of low/intermediate avidity. Variables with a p-value <0.10 in univariate analysis were entered into a multivariate logistic regression model adjusted for maternal age. Results were reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs) and p-values. The discriminatory performance of each index and the multivariate model was evaluated by calculating the area under the curve (AUC) values obtained from receiver operating characteristic (ROC) analysis. A two-tailed p-value <0.05 was considered statistically significant.

Results

A total of 192 pregnant women were analyzed, including 96 (50%) with *Toxoplasma gondii* IgM positivity and 96 (50%) healthy controls with negative serology. All participants had singleton pregnancies and complete medical data. Among the IgM-positive group, 68 (70.8%) had high IgG avidity and 28 (29.2%) had low or intermediate avidity.

The demographic and hematological characteristics of the study groups are presented in Table 1. There were no statistically significant differences between the groups regarding maternal age, gravida, parity, number of abortions, or gestational week (p>0.05 for all). Similarly, white blood cell, neutrophil, monocyte, hemoglobin, and platelet counts were comparable between the groups (p>0.05). However, the lymphocyte count was significantly higher in the IgM-positive group compared with controls [2.1 (0.5-4.29) vs. 2.0 (0.1-15.0); p=0.033].

The comparison of systemic inflammatory indices between the study groups is summarized in Table 2. No statistically significant differences were observed in any of the hematologic inflammation markers between IgM-positive and IgM-negative pregnant women. Median values of NLR, PLR, MLR, SII, SIRI, and PIV were comparable across groups (p>0.05 for all).

In the univariate logistic regression analysis evaluating the predictive performance of hematologic inflammatory indices for Toxoplasma IgM positivity, none of the parameters demonstrated a statistically significant association (Table 3). NLR, PLR, MLR, SII, SIRI, and PIV showed ORs close to 1, and all p-values exceeded 0.05. Therefore, multivariate regression and ROC curve analyses were not performed.

Table 1. Comparison of demographic and hematological parameters between groups

Variable	IgM positive (group 1)	IgM negative (group 2)	p-value
Age (years)	25.0 (18-40)	26.0 (18-42)	0.079
Gravida (n)	2.0 (1-9)	2.5 (1-8)	0.065
Parity (n)	1.0 (0-5)	1.0 (0-5)	0.051
Abortus (n)	0.0 (0-6)	0.0 (0-5)	0.154
Gestational week (weeks)	8.14 (4.71-16.0)	9.14 (5.14-16.29)	0.305
White blood cell ($\times10^9$/L)	8.2 (3.6-14.75)	8.35 (5.1-14.4)	0.767
Neutrophil ($\times10^9$/L)	5.45 (1.8-11.4)	5.75 (2.7-11.2)	0.404
Lymphocyte ($\times10^9$/L)	2.1 (0.5-4.29)	2.0 (0.1-15.0)	**0.033**
Monocyte ($\times10^9$/L)	0.6 (0.3-1.0)	0.5 (0.3-1.0)	0.578
Hemoglobin (g/dL)	12.5 (10.0-14.8)	12.75 (7.1-15.1)	0.593
Platelet ($\times10^3$/µL)	272.5 (141-479)	268.0 (96-456)	0.474

Values are presented as median (minimum–maximum), p<0.05 was considered statistically significant, Ig: Immunoglobulin

Table 2. Comparison of inflammatory indices between groups

Index	IgM positive (group 1)	IgM negative (group 2)	p-value
NLR	2.74 (0.64-12.20)	2.83 (0.62-29.00)	0.054
PLR	130.83 (65.86-514.00)	137.13 (17.60-2310.00)	0.118
MLR	0.27 (0.13-0.60)	0.29 (0.05-3.00)	0.332
SII	738.71 (169.71-3135.40)	766.22 (163.68-6699.00)	0.155
SIRI	1.47 (0.26-4.17)	1.56 (0.49-8.70)	0.379
PIV	392.14 (67.89-1490.44)	410.72 (103.94-2009.70)	0.502

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, PIV: Pan-immune inflammation value, Ig: Immunoglobulin

Table 3. Univariate logistic regression analysis of inflammatory indices for predicting *Toxoplasma* IgM positivity

Variable	OR	95% CI	p-value
NLR	0.841	0.672-1.053	0.13
PLR	0.998	0.994-1.002	0.372
MLR	0.255	0.021-3.177	0.289
SII	1.0	0.999-1.000	0.195
SIRI	0.828	0.612-1.120	0.22
PIV	1.0	0.999-1.001	0.509

In univariate logistic regression analysis, none of the hematologic or inflammatory indices were significantly associated with *Toxoplasma* IgM positivity (all p>0.05). Therefore, multivariate modeling and ROC analysis were not further performed. NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, PIV: Pan-immune inflammation value, CI: Confidence interval, OR: Odds ratio, Ig: Immunoglobulin, ROC: Receiver operating characteristic

When the IgM-positive patients were further categorized according to IgG avidity levels, 68 (70.8%) were classified as having high avidity, whereas 28 (29.2%) had low or intermediate avidity. The comparison of demographic and hematologic parameters between these subgroups is presented in Table 4. Patients with low or intermediate avidity were significantly younger than those with high avidity [21.0 (17-40) vs. 26.0 (17-38); p=0.015]. In addition, white blood cell, neutrophil, and monocyte counts were significantly lower in the low/intermediate avidity group (p=0.023, 0.034, and 0.018, respectively). No significant differences were found regarding gravida, parity, gestational week, lymphocyte count, hemoglobin, or platelet levels (p>0.05 for all).

The comparison of inflammatory indices according to IgG avidity levels is presented in Table 5. Among the parameters analyzed, MLR, SIRI, and PIV were significantly lower in the low/intermediate avidity group compared with the high avidity group (p=0.036, 0.014, and 0.020, respectively). No significant differences were observed for NLR, PLR, or SII values between the groups (p>0.05 for all).

In the univariate logistic regression analysis performed to assess the predictive value of hematologic indices for low or intermediate IgG avidity, SIRI and PIV were identified as significant predictors (Table 6). Both indices were inversely associated with low/intermediate avidity, with SIRI (OR: 0.481, 95% CI: 0.257-0.902, p=0.023, AUC =0.66) and PIV (OR: 0.998, 95% CI: 0.996-1.000, p=0.047, AUC =0.65) demonstrating moderate discriminative ability. Other

Table 4. Comparison of demographic and hematologic parameters according to IgG avidity levels

Variable	High avidity (n=68)	Low/intermediate avidity (n=28)	p-value
Age (years)	26.00 (18-38)	21.00 (18-40)	**0.015**
Gravida (n)	2.00 (1-8)	1.00 (1-9)	0.149
Parity (n)	1.00 (0-5)	0.00 (0-4)	0.255
Abortus (n)	0.00 (0-5)	0.00 (0-6)	0.207
Gestational week (weeks)	8.29 (4.86-16.0)	7.93 (4.71-13.0)	0.478
White blood cell ($\times10^9$/L)	8.42 (3.6-14.5)	7.70 (4.5-14.75)	**0.023**
Neutrophil ($\times10^9$/L)	5.78 (1.8-11.4)	5.20 (1.8-9.05)	0.034
Lymphocyte ($\times10^9$/L)	2.10 (0.5-3.4)	2.00 (0.9-4.29)	0.510
Monocyte ($\times10^9$/L)	0.60 (0.3-1.0)	0.50 (0.3-0.98)	**0.018**
Hemoglobin (g/dL)	12.60 (10.5-14.8)	12.30 (10.0-14.5)	0.164
Platelet ($\times10^3$/µL)	282.50 (141-419)	264.50 (191-479)	0.371

Values are presented as median (minimum-maximum), p<0.05 was considered statistically significant, Ig: Immunoglobulin

Table 5. Comparison of inflammatory indices according to IgG avidity levels

Index	High avidity (n=68)	Low/intermediate avidity (n=28)	p-value
NLR	2.90 (1.14-12.2)	2.44 (0.64-7.0)	0.111
PLR	131.55 (75.68-514.0)	129.32 (65.86-387.78)	0.939
MLR	0.29 (0.14-0.6)	0.23 (0.13-0.47)	**0.036**
SII	793.06 (221.59-3135.4)	581.53 (169.71-2443.0)	0.139
SIRI	1.69 (0.5-4.17)	1.08 (0.26-3.01)	**0.014**
PIV	437.77 (97.2-1490.44)	290.76 (67.89-990.27)	**0.020**

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, Ig: Immunoglobulin, PIV: Pan-immune inflammation value, values are presented as median (minimum-maximum), p<0.05 was considered statistically significant

Table 6. Univariate logistic regression analysis of inflammatory indices for predicting low/intermediate avidity

Index	OR	95% CI	p-value	AUC
NLR	0.769	0.499-1.185	0.233	0.60
PLR	1.0	0.993-1.007	0.989	0.49
MLR	0.005	0.000-1.308	0.062	0.64
SII	0.999	0.998-1.001	0.254	0.60
SIRI	0.481	0.257-0.902	**0.023**	0.66
PIV	0.998	0.996-1.000	**0.047**	0.65

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, PIV: Pan-immune inflammation value, p-values are two-sided; AUC refers to model with the single predictor, AUC: Area under the curve, CI: Confidence interval, OR: Odds ratio

indices, including NLR, PLR, MLR, and SII, showed no significant predictive performance (p>0.05 for all).

Discussion

Toxoplasmosis remains one of the most common parasitic infections worldwide, posing significant risks during pregnancy due to its potential for vertical transmission and fetal morbidity. Accurate differentiation between recent and past maternal infections is therefore essential for appropriate management and counseling. Although serologic testing, particularly the combination of IgM and IgG avidity assays, serves as the diagnostic cornerstone, interpretation can be challenging in cases with persistent IgM or intermediate avidity results. In this context, there is growing interest in identifying additional, easily accessible biomarkers that could assist in evaluating infection activity. The present study investigated whether hematologic inflammatory indices derived from routine blood counts could reflect the immune response associated with *Toxoplasma gondii* infection and help distinguish recent from past infections during pregnancy.

Toxoplasma gondii infection triggers a complex immune response in pregnancy that involves both pro- and anti-inflammatory pathways. Neutrophils and monocytes represent the first line of defense, acting through phagocytosis and cytokine release to limit parasite dissemination. The early activation of dendritic cells and Th1-mediated secretion of interferon-gamma (IFN-γ) play a central role in controlling tachyzoite proliferation,

whereas a subsequent Th2-dominant response supports fetal tolerance but may facilitate parasite persistence. The balance between these immune axes determines the clinical course of infection and, during pregnancy, may influence IgG avidity maturation (10).

In this context, Prescott et al. (11) demonstrated that indoleamine 2,3-dioxygenase (IDO-1) activity—a key enzyme in tryptophan catabolism induced by IFN-γ—is suppressed in chronically infected pregnant women, resulting in lower kynurenine-to-tryptophan ratios and reduced systemic inflammation. Their findings suggest that chronic *Toxoplasma gondii* infection is associated with a downregulation of Th1-mediated immunity and a shift toward metabolic and immunologic tolerance. Consistent with this, the decreased SIRI (p=0.014) and PIV (p=0.020) levels observed in our study among women with low or intermediate IgG avidity may reflect an attenuated inflammatory milieu in early or subclinical infection. The parallel reduction in monocyte (p=0.018) and neutrophil counts (p=0.034) further supports the notion of a modulated innate immune response, possibly reflecting host adaptation to maintain pregnancy while controlling parasite activity.

The results of our study are also consistent with the findings of the recent systematic review by Dos Santos et al. (12), who reported that pregnant women infected with *Toxoplasma gondii* exhibited elevated plasma concentrations of both pro-inflammatory cytokines (IL-5, IL-6, IL-8, IL-17, and CCL5) and the regulatory cytokine IL-10. The authors emphasized that the balance between inflammatory and anti-inflammatory mediators determines the maternal immune status and, consequently, the clinical course of infection. Disruption of this equilibrium—either toward excessive inflammation or excessive immune tolerance—can adversely affect the placenta and fetus. In this context, the reduced levels of SIRI, PIV, and MLR observed in our low-avidity group may reflect a predominance of regulatory rather than pro-inflammatory responses, suggesting that immune suppression necessary for fetal tolerance might also limit effective pathogen clearance in early infection.

Recent evidence has further expanded the understanding of the immunological and clinical spectrum of toxoplasmosis in pregnancy. Silva et al. (13) demonstrated that chronically infected pregnant women exhibited higher plasma levels of IL-17A and IL-33, cytokines linked to Th17 activation and neuroinflammatory signaling, along with elevated neuroserpin concentrations. These alterations were associated with mild depressive symptoms, suggesting a potential interface between inflammatory and neuroimmune pathways during chronic *Toxoplasma gondii* infection. When interpreted alongside our findings, the reduced systemic inflammatory indices in women with low or intermediate IgG avidity may represent a transient immunoregulatory phase preceding the establishment of the more stable, low-grade inflammatory profile observed in chronic infection.

Our findings may also be interpreted in light of recent mechanistic evidence implicating macrophage dysfunction in the pathogenesis of gestational toxoplasmosis. Wang et al. (14) demonstrated that *Toxoplasma gondii* infection suppresses the Trem2/Syk/PI3K signaling axis in decidual macrophages, leading to impaired trophoblast migration, increased pro-inflammatory cytokine production [IL-1β, IL-6, tumor necrosis factor (TNF)-α], and adverse pregnancy outcomes. The inhibition of this pathway compromises macrophage-mediated immune regulation at the maternal-fetal interface, thereby disrupting the delicate balance required for fetal protection and tolerance. In this context, the lower SIRI, PIV, and MLR values observed in our low- or intermediate-avidity group may reflect early macrophage dysfunction and downregulated innate immune activity, preceding the excessive inflammatory response described in severe or uncontrolled infection.

Our findings also complement population-based data linking chronic toxoplasmosis to systemic inflammation and vascular injury. Egorov et al. (15) reported that individuals with latent *Toxoplasma gondii* infection exhibited higher circulating levels of C-reactive protein, soluble intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, suggesting the persistence of low-grade inflammation even in asymptomatic stages. This chronic inflammatory state has been implicated in endothelial dysfunction and increased cardiovascular risk. In contrast, the reduced inflammatory indices observed in our study among pregnant women with low or intermediate IgG avidity likely represent an earlier phase of infection, before the establishment of sustained immune activation. Together, these findings indicate a biphasic inflammatory pattern in toxoplasmosis: an initial phase characterized by immune modulation and suppression, followed by a chronic phase marked by mild but persistent systemic inflammation.

The clinical relevance of hematologic inflammatory indices in obstetric conditions has been increasingly recognized.

Bozbay et al. (16) demonstrated that both the SII and the lymphocyte-to-monocyte ratio measured in the first trimester were significantly higher in women who later developed gestational diabetes mellitus, indicating that subtle immune alterations may precede overt metabolic dysregulation. Similarly, a study on hyperemesis gravidarum reported that NLR, MLR, and PLR values were significantly elevated compared with healthy pregnancies and correlated positively with ketonuria severity, reflecting the degree of systemic inflammatory activation (17). Collectively, these findings, together with our results, suggest that hematologic inflammatory indices derived from routine blood counts may serve as accessible and cost-effective tools for assessing immune activation and regulation in a wide spectrum of pregnancy-related disorders, including infectious, metabolic, and inflammatory conditions.

In our cohort, although systemic inflammatory indices did not differ significantly between IgM-positive and IgM-negative pregnant women, distinct hematologic and inflammatory patterns emerged when the IgM-positive group was stratified by IgG avidity. Women with low or intermediate avidity—reflecting a recent or ongoing infection—had significantly lower monocyte, neutrophil, and white blood cell counts, as well as reduced MLR, SIRI, and PIV values compared with those with high avidity. These findings suggest that in the early phase of infection, immune activation may be attenuated, possibly reflecting adaptive modulation of the maternal immune response aimed at preserving fetal tolerance while limiting tissue inflammation. To the best of our knowledge, this is the first study in the literature to investigate the relationship between hematologic inflammatory indices and IgG avidity status in pregnant women with *Toxoplasma gondii* IgM positivity. The inclusion of a healthy control group further strengthened the comparative interpretation of our findings.

The inverse association between inflammatory indices and IgG avidity underscores the complex interaction between systemic inflammation and humoral immune maturation. Because IgG avidity reflects the functional affinity of antibody binding, a suppressed inflammatory environment may delay the development of high-avidity antibodies, consistent with the immunoregulatory milieu characteristic of early infection. Although the magnitude of differences in MLR, SIRI, and PIV was moderate, their consistent direction suggests potential clinical value for these parameters in aiding serologic interpretation, particularly in cases with equivocal or persistent IgM positivity.

From a clinical standpoint, hematologic indices are readily obtainable, inexpensive, and reproducible parameters that could complement serologic testing in the evaluation of suspected toxoplasmosis during pregnancy.

Study Limitations

However, this study has several limitations. Its retrospective single-center design may limit generalizability, and cytokine or metabolic markers such as IFN-γ, TNF-α, and IDO-1 activity were not measured, precluding direct mechanistic correlations. Furthermore, follow-up data on maternal or neonatal outcomes were unavailable. Future prospective studies integrating immunologic and clinical parameters are warranted to validate the predictive value of SIRI and PIV in distinguishing recent from chronic *Toxoplasma gondii* infections.

Conclusion

This study evaluated the association between hematologic inflammatory indices and IgG avidity status in pregnant women with *Toxoplasma gondii* IgM positivity. While no significant differences were found between IgM-positive and IgM-negative women overall, those with low or intermediate IgG avidity—representing recent or ongoing infection—exhibited lower monocyte, neutrophil, and white blood cell counts, along with significantly reduced MLR, SIRI, and PIV values. These findings indicate that systemic inflammation is attenuated in the early phase of infection and that simple hematologic indices may reflect dynamic immune modulation during pregnancy. Although these parameters cannot replace serologic assays, they may serve as supportive markers for differentiating between recent and past infections. Further prospective and mechanistic studies are needed to validate their predictive utility in clinical practice.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Gaziantep City Hospital Clinical Research Ethics Committee (approval no: 215/2025, dated: May 21, 2025).

Informed Consent: A comprehensive review of the patients' medical records was conducted to gather clinical data, patient characteristics, and follow-up information. Due to the retrospective design of the study, informed consent was waived.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Y., İ.T., S.Sı., Concept: İ.T., S.Sı., Design: E.Y., S.S., E.Ş., Data Collection or Processing: E.Y., S.S., Analysis or Interpretation: F.D.Y.Y., S.Sı., Literature Search: S.S., F.D.Y.Y., E.Ş., Writing: İ.T., F.D.Y.Y., E.Ş.

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