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Predictive value of hematological parameters in testicular torsion: retrospective investigation of data from a high-volume tertiary care center

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Abstract

Objective: To investigate the use of hematological parameters in the differential diagnosis of testis torsion and epididymo-orchitis, and to determine the predictive value of these parameters in the diagnosis of testis torsion.

Methods: This study retrospectively reviewed the medical data of patients who presented to our institute with the complaint of acute scrotal pain. Eighty-five patients who had undergone orchiectomy or surgical detorsion due to testis torsion and 72 patients with epididymo-orchitis were included in the study. The control group comprised 78 healthy males. The groups were compared with respect to age, hematological parameters, neutrophil to lymphocyte ratio (NLR), monocyte to eosinophil ratio (MER), and platelet to lymphocyte ratio (PLR).

Results: The monocyte count significantly differed between testis torsion and epididymo-orchitis, and was useful in the differential diagnosis. The mean neutrophil, platelet, and white blood cell counts, and the NLR, MER, and PLR values in the control group were significantly lower than those in the torsion and epididymo-orchitis groups.

Conclusion: The sensitivity and specificity of NLR in predicting testis torsion were as high as the sensitivity and specificity of doppler ultrasonography, suggesting the possible use of this parameter in the diagnosis of testis torsion.

Keywords

Testis torsion, neutrophils, epididymo-orchitis, monocytes, eosinophils, blood platelets, orchiectomy, leukocyte count, doppler ultrasonography

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Introduction

Testis torsion is a clinical condition characterized by the rotation of the spermatic cord around its own axis, which results in reduced blood flow to the testicles; the condition requires emergency treatment to avoid loss of the testes. Importantly, testicular loss may be avoided by an intervention within the first 6 hours following the onset of acute scrotal findings.[1] Testis torsion has an incidence of 1:4000 in males younger than 25 years of age.[2] Epididymo-orchitis is the most common pathology considered in the differential diagnosis. A rapid and accurate differential diagnosis is essential to reduce testis loss and unnecessary surgical interventions. Although clinical findings have been used in the differential diagnosis, scrotal power doppler ultrasonography, which has 63% to 86% sensitivity and 97% to 100% specificity, is currently the most common approach.[3] New diagnostic methods have been investigated owing to the operator-dependent nature of ultrasonography, the 30 to 40 minute duration of the procedure (even in well-equipped health centers), and the diagnostic difficulties in some circumstances.[4] Notably, there is no consensus regarding definitive diagnosis of testis torsion. Additionally, there have been many investigations of methods to reduce testis loss and unnecessary exploration rates.[1,5] Because testis torsion is an inflammatory process, hematological parameters of systemic inflammation have been investigated for diagnosis and differential diagnosis; however, the number of such studies in the literature is insufficient.

The aim of this study was to investigate the role of hematological parameters in the differential diagnosis of testis torsion and epididymo-orchitis, and to determine the predictive value of these parameters in the diagnosis of testis torsion.

Materials and methods

Patients and study design

This study retrospectively reviewed the medical data of patients, 12 to 81 years of age, who had presented to the urology clinics or emergency unit of our institute with the complaint of acute scrotal pain, during the period between 2006 and 2018. Patients who had undergone orchiectomy or surgical detorsion due to testis torsion, as diagnosed by scrotal power doppler ultrasonography, and patients with epididymo-orchitis, as diagnosed by scrotal ultrasonography, were included in the study. Excluded patients were those with a duration of more than 6 hours between the onset of scrotal pain and admission to the hospital, those who had undergone manual detorsion and subsequent surgical fixation, those with appendix testis torsion, hepatic or renal function failure, and those with hematological disease. The control group comprised healthy males who had presented to the urology clinics for any reason, and who had no diagnosis of epididymo-orchitis, testicular trauma, hepatic, renal or hematological disease, or previous scrotal surgery.

The demographic characteristics of the patients and complete blood count (CBC) on admission were recorded. For CBC, 3 mL peripheral venous blood samples were collected into tubes containing 5.4 mg ethylenediaminetetraacetic acid. CBC analysis was performed using the Coulter LH-780 hematology blood analyzer (Beckman Coulter Inc, Brea, CA, USA). The neutrophil to lymphocyte ratio (NLR), monocyte to eosinophil ratio (MER), and platelet to lymphocyte ratio (PLR) were calculated. The groups were compared with respect to age, hematological parameters, NLR, MER, and PLR. The success of NLR, MER, and PLR in predicting the diagnosis of testicular torsion was evaluated.

Consent from the ethics committee was not required because of the retrospective nature of this study. Written informed consent to undergo surgery was routinely obtained from each surgical patient. Written and verbal informed consent was obtained from all subjects in the control group.

Statistical analysis

Descriptive statistics are reported as mean, minimum value, and maximum value. The Kolmogorov–Smirnov test was used to determine whether data exhibited normal distributions. For the continuous dependent variables, the Kruskal-Wallis test was used for comparisons between groups, for all dependent variables following a non-normal distribution. The post hoc Dunn-Bonferroni test was applied to any Kruskal-Wallis test results that were significant. Receiver operating characteristic (ROC) curves were analyzed to assess the optimal cut-off values of potential predictive factors. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated for the chosen cut-off values. The probability of a Type I error (alpha) was designated as 5% in all tests. Data analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA); a p value of <0.05 was considered significant.

Results

The medical data of a total of 235 patients were retrospectively evaluated in this study. The torsion, epididymo-orchitis, and control groups comprised 85, 72, and 78 patients. The mean ages in the torsion, epididymo-orchitis, and control groups were 19 (range: 12–81), 28 (range: 15–79), and 31 (range: 15–45) years, respectively; the age difference was statistically significant ($p<0.001$). The demographic and hematological data of the patients are presented in Table 1. Significant differences were present between the torsion and epididymo-orchitis groups with regard to age and monocyte count ($p<0.001$ for both). The mean neutrophil, platelet, and white blood cell counts, and the NLR, MER, and PLR values in the control group were lower than those in the torsion and epididymo-orchitis groups; these differences were statistically significant ($p<0.001$ for all). No significant difference was observed among any groups with regard to the mean MPV value. No significant difference was observed between the torsion and epididymo-orchitis groups with regard to the NLR, MER, or PLR values (Figures 1–3). However, significant differences were observed between the torsion and epididymo-orchitis groups with regard to the NLR, MER, and PLR values ($p<0.001$ for all). The success of NLR, MER, and PLR values in predicting the diagnosis of testis torsion was evaluated using the ROC curve (Figure 4), and the cut-off values were calculated (Table 2).

Discussion

This study investigated the role of hematological parameters in the differential diagnosis of testis torsion and epididymo-orchitis, and assessed the predictive value of these parameters in the diagnosis of testis torsion, using 12 years of data from cases of testis torsion treated in our high-volume clinics. Our study is the largest among the literature on this subject. Although there have been studies regarding the use of systemic inflammatory parameters in the differential diagnosis of testis torsion and epididymo-orchitis (these conditions elicit an inflammatory response), the number of these studies has been insufficient.

Various studies have shown that the leukocyte count is increased in patients

Table 1. Patients' hematological parameters among the groups.

Variables	Torsion (a)	Orchitis (b)	Control (c)	P value
Age	19 (12–81)[b,c]	28 (15–79)	31 (15–45)	<0.001
White blood cells ($\times 10^3\ \mu L^{-1}$)	12.3 (5.2–20.7)	12.6 (4.7–31.5)	7 (3.9–16.2)[a,b]	<0.001
Neutrophils ($\times 10^3\ \mu L^{-1}$)	9.7 (2.7–68)	10.15 (2.8–27.3)	4 (0.1–9.5)[a,b]	<0.001
Lymphocytes ($\times 10^3\ \mu L^{-1}$)	1.9 (0.5–51.4)	1.8 (0.7–6.3)	2.35 (0.1–6)[a,b]	<0.001
Monocytes ($\times 10^3\ \mu L^{-1}$)	0.6 (0.1–10)	0.8 (0.1–5)[a,c]	0.6 (0.1–2.1)	<0.001
Eosinophils ($\times 10^3\ \mu L^{-1}$)	0.1 (0–9.8)	0.1 (0–1.3)	0.2 (0–1.6)	0.825
Basophils ($\times 10^3\ \mu L^{-1}$)	0.1 (0–0.8)	0.1 (0–0.5)	0 (0–0.5)	0.940
Red blood cells ($\times 10^3\ \mu L^{-1}$)	4.9 (2.7–5.9)	4.7 (2.4–6.1)	4.99 (4.2–6.6)	0.724
Hemoglobin (g/dL)	14.3 (7.7–16.1)	13.3 (7.4–16.5)	15.2 (12.1–16.8)[a,b]	0.434
Hematocrit (%)	42.3 (23.6–49.8)	40.3 (21.5–49.3)	43.65 (36.2–50.5)[a,b]	0.546
MCV	86.7 (61.3–97.4)	85.7 (56.3–97)	88.05 (49.7–96.3)	0.137
MCH	29 (19.8–33.8)	29 (15.7–32.8)	30 (20.6–33.4)	0.879
MCHC	33.7 (23.9–36.2)	33.65 (27.9–37.6)	34.3 (25–36.4)	0.675
RDW	13.3 (11.2–20.4)	13.65 (11.8–20.8)	13.4 (11.5–20.4)	0.245
Platelets ($\times 10^3\ \mu L^{-1}$)	255 (69.5–481)	272 (139–592)	226.5 (90–360)[a,b]	<0.001
MPV	8.1 (5.5–12.3)	8.15 (6.4–12.5)	8.3 (5.1–12.7)	0.541
NLR	4.91 (1–28.4)	5.74 (0.73–32.3)	1.696 (0.75–4.08)[a,b]	<0.001
MER	5 (0.6–370)	6 (0.73–27)	3 (0.44–50)[a,b]	<0.001
PLR	145.7 (6.44–676)	136.7 (57.3–845.7)	89.32 (35.2–2300)[a,b]	<0.001

MCV, mean corpuscular volume; MCH mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; NLR, neutrophil to lymphocyte ratio; MER, monocyte to eosinophil ratio; PLR, platelet to lymphocyte ratio; a, b, c: the difference between the groups have been expressed with letters as superscripts within the table.

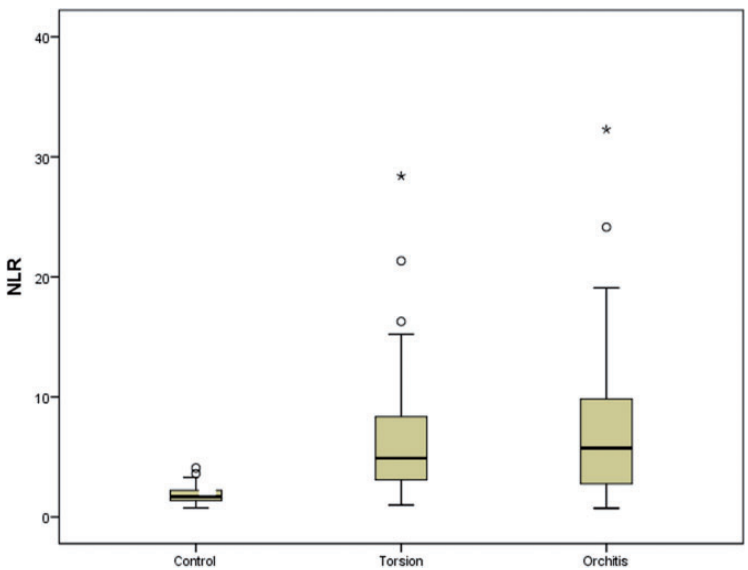

Figure 1. Box graph of neutrophil to lymphocyte ratio (NLR) among the groups.

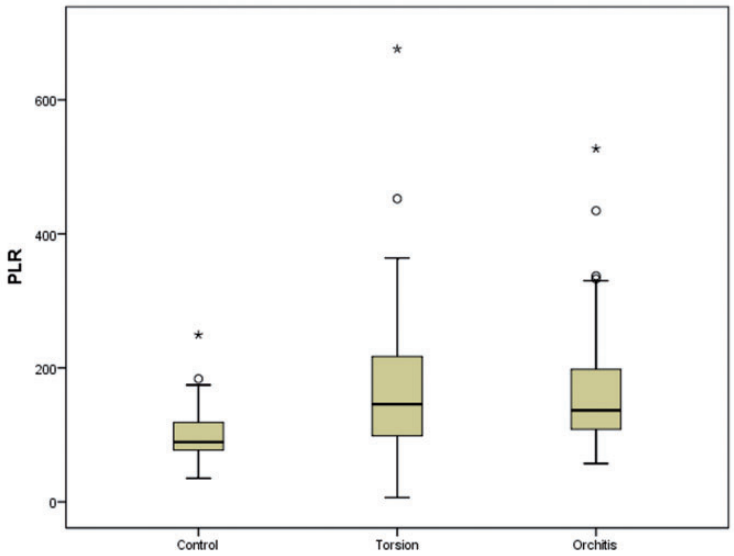

Figure 2. Box graphs of platelet to lymphocyte ratio (PLR) among the groups.

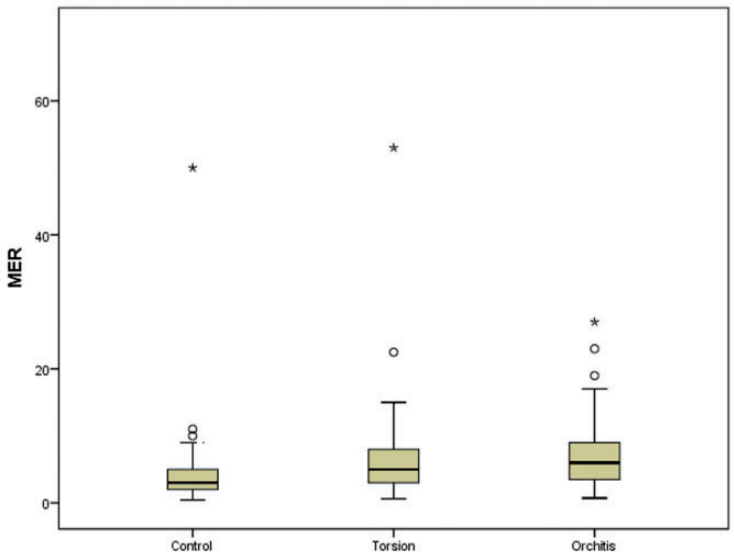

Figure 3. Box graphs of monocyte to eosinophil ratio (MER) among the groups.

with the diagnosis of testis torsion; it serves as an indicator of the inflammatory response.[6] A study in rats showed that testis torsion leads to an increased leukocyte count within the muscular tissue of the cremaster muscle, which surrounds the testicular tissue; moreover, that study showed deteriorating hypoxia, reduced microperfusion, and reduced capillary vessel function.[7]

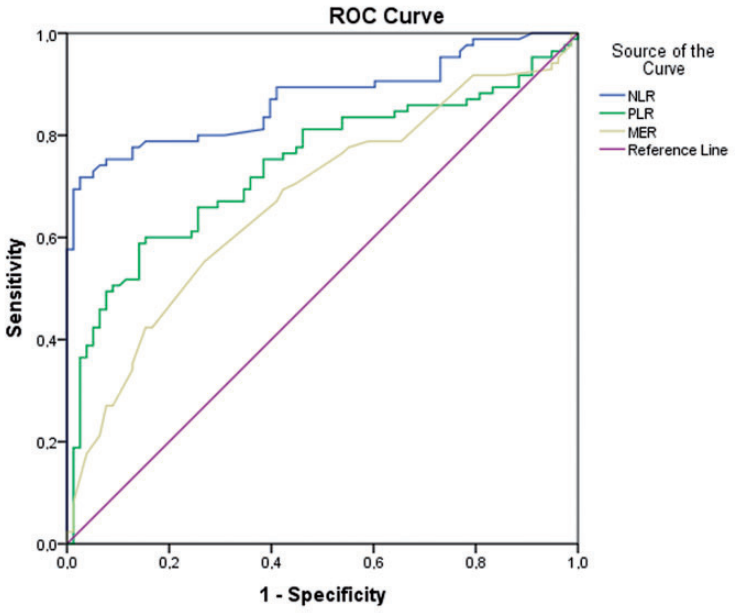

Figure 4. Receiver operating characteristic (ROC) curve analysis of neutrophil to lymphocyte ratio (NLR), monocyte to eosinophil ratio (MER), and platelet to lymphocyte ratio (PLR) in the torsion group.

Table 2. Performance characteristics of NLR, PLR and MER in the torsion group.

	Cut-off value	Maximum Youden Index	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% Confidence Interval)
NLR	3.39	0.692	71.8	97.4	96.8	76.1	0.872 (0.815–0.928)
PLR	135.58	0.447	58.8	85.9	95.4	91.0	0.741 (0.663–0.818)
MER	4.5	0.284	55.3	73.1	73.9	79.3	0.673 (0.591–0.756)

AUC, Area Under Curve; PPV, Positive Predictive Value; NPV, Negative Predictive Value NLR, neutrophil to lymphocyte ratio; MER, monocyte to eosinophil ratio; PLR, platelet to lymphocyte ratio.

Bitkin et al.[3] reported that although the leukocyte count was significantly increased in both epididymo-orchitis and torsion groups, compared with the control group, it was not a significant predictor for the differential diagnosis of either condition. Similar to the data in the literature, the leukocyte counts observed in the torsion and epididymo-orchitis groups in our study were higher than the count observed in the control group. In our study, only monocyte count significantly differed in the differential diagnosis of testis torsion and epididymo-orchitis.

NLR, PLR, and MER are frequently used as indicators of the systemic inflammatory response.[8] These parameters can easily be determined using the CBC analysis routinely checked prior to surgery; moreover, they are inexpensive, easy to calculate, practical, and widely used. There are more than 60 studies in the literature regarding the clinical

importance of NLR in various cancer types.[9] Furthermore, there have been investigations of its clinical importance in hypertension, diabetes, metabolic syndrome, renal diseases, inflammatory diseases, and rheumatological diseases.[10] Gunes et al.[8] compared 75 patients with testis torsion and 56 healthy individuals; they reported that NLR had 84% sensitivity and 92% specificity for prediction of testis torsion. They also reported that PLR had 51% sensitivity and 89% specificity for prediction of testis torsion. Although another study showed no significant difference between the torsion and control groups with regard to PLR values, a significant difference was observed between the torsion and epididymo-orchitis groups.[3] In our study, no difference was observed in the NLR and PLR values between the torsion and epididymo-orchitis groups; however, both groups showed significantly higher values, compared with the control group. Our study is the first to investigate the success of MER in predicting the diagnosis of testis torsion: in our study, MER had 55% sensitivity and 73% specificity in predicting testis torsion.

In testicular torsion, testicular ischemia develops as a result of rotation of the spermatic cord, including the testicular vessels, around itself. Palmer et al.[11] demonstrated that a platelet activator antagonist reduced ischemia-related testicular damage, and that platelet activation contributed to testicular ischemia. Testicular venous congestion leads to the formation of vascular microthrombus and subsequent activation of the intrinsic coagulation pathway; notably, platelets are important in the formation of microthrombus. Gunes et al.[8] demonstrated that the platelet count was significantly higher in the testis torsion group than in the control group. Similarly, the platelet count was significantly increased in the torsion group, compared with the control group, in our study.

MPV is an indirect indicator of platelet function. Larger platelets have been shown to contain greater quantities of thromboxane A2 and P-selectin, compared with normal platelets; therefore, these larger platelets were metabolically and enzymatically more active.[12] Higher levels of MPV have been found in urological pathologies, such as varicocele and erectile dysfunction.[13,14] Cicek et al.[15] demonstrated significantly higher levels of MPV in a group of patients with testis torsion, compared with healthy individuals. Bitkin et al.[3] also reported higher levels of MPV in the torsion group. In contrast, another study showed no significant difference between the torsion and control groups with regard to MPV levels.[8] In our study, there was no difference in the MPV levels between torsion and control groups.

Testis torsion and epididymo-orchitis are known as pathologies of different age groups. To obtain more objective results, age matching was not performed between the groups. Because the control group was constructed in a randomized manner, a statistically significant difference was observed between the groups with regard to patient age.

The outcomes of our study are clinically meaningful. Our results showed that the sensitivity and specificity of NLR in predicting testis torsion were as high as those of doppler ultrasonography, which has 63%–86% sensitivity and 97%–100% specificity;[3] this finding suggests the possible use of NLR in the diagnosis of testis torsion. Further multi-center studies, including larger sample sizes, should be conducted to better define the use of NLR in diagnosis of testis torsion.

Our study has some limitations. First, it was conducted in a retrospective manner. Second, it did not include some acute phase reactants, such as serum amyloid A level, C reactive protein level, erythrocyte sedimentation rate, and procalcitonin level, because they are not routinely checked and are expensive. Third, it could not include an assessment of smoking habits. Lastly, it

constituted a single-center study, although this was balanced by the large sample size.

Conclusion

In our study, monocyte count was the sole parameter that significantly differed in the differential diagnosis between testis torsion and epididymo-orchitis. The sensitivity and specificity of NLR in predicting testis torsion were as high as the sensitivity and specificity of doppler ultrasonography, which suggests the possible use of this parameter in the diagnosis of testis torsion. Although hematological parameters such as NLR, PLR, and MER have been suggested to predict the diagnosis of testis torsion, safe clinical use of these parameters requires prospective, multi-center studies, as well as meta-analyses with larger sample sizes.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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References

1. Boettcher M, Bergholz R, Krebs TF, et al. Clinical predictors of testicular torsion in children. *Urology* 2012; 79: 670–674.
2. Barada JH, Weingarten JL and Cromie WJ. Testicular salvage and age-related delay in the presentation of testicular torsion. *J Urol* 1989; 142: 746–748.
3. Bitkin A, Aydın M, Özgur BC, et al. Can haematologic parameters be used for differential diagnosis of testicular torsion and epididymitis? *Andrologia* 2018; 50: e12819.
4. Bader TR, Kammerhuber F and Herneth AM. Testicular blood flow in boys as assessed at color Doppler and power Doppler sonography. *Radiology* 1997; 202: 559–564.
5. Boettcher M, Krebs T, Bergholz R, et al. Clinical and sonographic features predict testicular torsion in children: a prospective study. *BJU Int* 2013; 112: 1201–1206.
6. Yang C Jr, Song B, Liu X, et al. Acute scrotum in children: an 18-year retrospective study. *Pediatr Emerg Care* 2011; 27: 270–274.
7. Boybeyi O, Yazici I, Unlu G, et al. Intravital microscopic evaluation of cremasteric microcirculation in testicular torsion evaluation. *J Pediatr Urol* 2013; 9: 940–944.
8. Gunes M, Umul M, Altok M, et al. Predictive role of hematologic parameters in testicular torsion. *Korean J Urol* 2015; 56: 324–329.
9. Yucel C, Keskin MZ, Cakmak O, et al. Predictive value of pre-operative inflammation-based prognostic scores (neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and monocyte-to-eosinophil ratio) in testicular sperm extraction: a pilot study. *Andrology* 2017; 5: 1100–1104.
10. Guthrie GJ, Charles KA, Roxburgh CS, et al. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol* 2013; 88: 218–230.
11. Palmer JS, Cromie WJ, Plzak LF, et al. A platelet activating factor antagonist attenuates the effects of testicular ischemia. *J Urol* 1997; 158: 1186–1190.
12. Kamath S, Blann AD and Lip GY. Platelet activation: assessment and quantification. *Eur Heart J* 2001; 22: 1561–1571.
13. Bozkurt Y, Soylemez H, Sancaktutar AA, et al. Relationship between mean platelet volume and varicocele: a preliminary study. *Urology* 2012; 79: 1048–1051.
14. Ciftci H, Yeni E, Demir M, et al. Can the mean platelet volume be a risk factor for vasculogenic erectile dysfunction? *World J Mens Health* 2013; 31: 215–219.
15. Cicek T, Togan T, Akbaba K, et al. The value of serum mean platelet volume in testicular torsion. *J Int Med Res* 2015; 43: 452–459.