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*Original Article*

# The relationship between mean platelet volume and other platelet indices with testicular artery blood flow and fertility: a preliminary study

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**Abstract:** Objectives: To examine the relationship between platelets (PLT) and platelets indices such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) as noninvasive biomarkers with testicular artery blood flow and fertility. Methods: Fifty-seven healthy and fertile men with normal semen values and 52 patients with abnormal semen values were included in the study. The participants' PLT, MPV, PDW and PCT values were analyzed. Four different levels of the testicular artery, peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) were measured using color Doppler ultrasound. Results: There was no significant difference in terms of platelet and platelet indices (MPV, PDW and PCT) between the fertile and infertile group. There were no between group differences in the RI values of the testicular- and intra-testicular artery. When all fertile and infertile participants were considered together, there was no statistically significant correlation between the parameters of the testicular artery blood flow (PSV, EDV and RI) and platelet and platelet indices (MPV, PDW and PCT) ($P > 0.05$). Conclusions: There is not statistically significant correlation between any of the following parameters: platelets and platelet indices such as MPV, PDW and PCT, RI of the testicular artery, and fertility.

**Keywords:** Platelets, testicles, blood supply, infertility

## Introduction

In recent times, platelets (PLT) and platelets indices such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) have emerged to be important markers for disease pathophysiology. Platelet activity is associated with the initiation of coagulation cascades. When a blood vessel is damaged, the sub-endothelial surface becomes the primary target site of platelet action, where it establishes hemostasis [1].

In various diseases, platelet hyperactivity provokes adverse effects. The role of platelets has been investigated in many atheroscleroses, especially in the coronary artery. However, to our knowledge, no studies have investigated the effects of platelets and platelet indices on testicular arteries. We aimed to investigate it for the first time in this study.

## Material and methods

After obtaining approval from the local ethics committee, 109 men (aged 23-43 years, 206 testicles) were prospectively investigated between December 2014, and May 2015. Fifty-two men who were admitted to the urology clinic with infertility or with abnormal semen values were assigned to the 'infertile' group. Three semen samples were obtained from these patients for analysis. Fifty-seven healthy and fertile men with normal semen values with a similar age group were included in the control group (fertile group). After the study was designed, written informed consent was obtained from all participants.

Patients were included into the infertile group if their primary concern was infertility after 12 months of regular sexual intercourse without use of contraception. In accordance with the World Health Organization (WHO) guidelines,

**Table 1.** Demographic and clinical characteristics of the fertile and infertile patients

| Variables | Fertile Group | Infertile Group | *p*-value |
|---|---|---|---|
| *n* | 57 | 52 | |
| Age (years) | 29.7±5.1 | 29.5±6.8 | 0.826† |
| Age of wife (years) | 27.4±6.1 | 28.6±6.9 | 0.438† |
| Duration of infertility (years) | - | 4 (1-21) | - |
| BMI (kg/m$^2$) | 24.4±3.1 | 24.8±2.9 | 0.689† |
| Previous varicoselectomy | 8 (15.4%) | 5 (10.4%) | 0.461‡ |
| Presence of varicocele | 21 (45.7%) | 31 (67.4%) | 0.035‡ |
| Varicocele grades | | | 0.088¶ |
| Grade I | 4 (8.7%) | 2 (4.3%) | |
| Grade II | 11 (23.9%) | 17 (37.0%) | |
| Grade III | 6 (13.0%) | 12 (26.1%) | |
| Testicular volume (cm$^3$) | 19.1 (12.5-29.0) | 16.7 (10.0-23.5) | 0.035$ |
| Testicular parenchymal disorder | 3 (6.0%) | 5 (11.4%) | 0.467# |
| Vein diameter of pampiniform plexus | 1.8 (0.9-4.0) | 2.4 (0.9-5.5) | 0.002$ |
| FSH (mIU/mL) | 2.6 (0.8-19.6) | 4.3 (0.5-19.5) | 0.011$ |
| LH (mIU/mL) | 3.6 (1.0-9.1) | 3.3 (1.0-10.3) | 0.720$ |
| Testosteron (ng/mL) | 5.2 (1.1-10.1) | 4.0 (1.7-8.9) | 0.066$ |

†Student's t-test. ‡Pearson's Chi-square test. ¶Likelihood Ratio test. $Mann-Whitney U test. #Fisher's exact test.

each patient provided three complete semen analyses at three-week intervals [2]. The values of the best semen sample results were examined in the study. Semen samples were obtained after 2-5 days of sexual abstinence.

All participants' detailed medical and surgical history was assessed. Cryptorchidism, genital infections, trauma, surgical history, and lifestyle habits especially, were investigated. Body mass indexes (BMI) were calculated. On physical examination, the position of external genital organs and the presence of varicocele received particular attention. Reproductive hormones, complete blood count, semen analyses, scrotal grey-scale and color Doppler ultrasonography (CDUS) were investigated. An experienced radiologist (MAS) measured testicular blood flow of all participants using scrotal ultrasonography at four different levels of the testicular artery. Peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) values were measured.

The serum concentration of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were determined using chemiluminescent immunoassays in accordance with the manufacturer's instructions, and the serum concentration of total testosterone was measured using a radioimmunoassay (Abbott Architect C16000, USA). The normal reference ranges for men are specified as: FSH 1.27-19.26 mIU/mL, LH 1.14-8.75 mIU/mL, and testosterone 1.74-8.43 ng/mL.

Platelet and platelet indices (MPV, PDW and PCT) were measured using Abbott CELL-DYN Ruby Hematology System. The normal reference ranges were specified as: PLT 154-400 K/uL, MPV 0-99.9 fL, PDW 0-99.9 fL, and PCT 0.17-0.7%.

Scrotal ultrasonography and CDUS were undertaken in a warm room with the patient in a supine position. Testicular volume was calculated through measurements taken in three dimensions. Doppler flow was measured in each testis using a trans-scrotal approach with a 14-MHz linear array probe (Sequoia 512, Acuson Siemens, Germany). PSV, EDV, and RI were calculated bilaterally and expressed in cm/s. The examined intratesticular artery had to have ≥ 0.5 cm visualized. The RI was calculated as (PSV-EDV)/PSV×100. Testicular artery blood flow was measured at four different locations, 2 cm prior to entering the testicle and in the intra-testicular artery in the middle of the testicle and at the upper and lower poles.

*Statistical analysis*

Data analysis was performed using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, United States). The continuous variables were determined as to whether they were normally distributed using the Kolmogorov-Smirnov test. Data are shown as mean ± SD or median (min-max), where applicable.

While the mean differences between groups were compared using Student's t-test, the Mann-Whitney U test was applied for comparisons of the medians. Categorical data were

**Table 2.** Investigation of sperm parameters of the patients according to groups

| Variables | Fertile Group | Infertile Group | *p*-value† |
|---|---|---|---|
| MSC | 30.0 (11.0-155.0) | 4.0 (0.0-64.5) | < 0.001 |
| Volume | 3.0 (1.5-8.0) | 3.0 (0.6-11.6) | 0.074 |
| Sperm concentration (million/mL) | 37.8 (17.2-229.0) | 9.2 (0.0-93.3) | < 0.001 |
| Total motility (%) | 66.8 (29.4-97.2) | 34.5 (0.0-96.5) | < 0.001 |
| Progressive motility | 51.0 (15.6-89.1) | 18.2 (0.0-84.6) | < 0.001 |

†Mann-Whitney U test, MSC = Motile Sperm Count.

**Table 3.** Platelets and platelet indices parameters of the patients according to groups

| Variables | Fertile Group | Infertile Group | *p*-value† |
|---|---|---|---|
| MPV (fL) | 8.2 (5.6-15.7) | 9.3 (6.1-20.6) | 0.199 |
| PLT (K/uL) | 228.0 (117.0-347.0) | 236.0 (155.0-465.0) | 0.260 |
| PDW (fL) | 17.6 (9.6-23.7) | 17.5 (8.2-22.2) | 0.453 |
| PCT (%) | 0.19 (0.11-0.32) | 0.20 (0.11-0.42) | 0.052 |

†Mann-Whitney U test.

analyzed using Pearson's Chi-square test, Fisher's exact or Likelihood Ratio test, where applicable. Degrees of association between continuous variables were evaluated with Spearman's correlation test.

A *p* value less than 0.05 was considered statistically significant. Bonferroni correction was conducted to reduce the chances of obtaining Type I errors in all possible multiple comparisons.

## Results

The demographic and clinical characteristics of the fertile and infertile patients are shown in **Table 1**. The varicocele rate in the infertile group was higher than in the fertile group (46% and 67%, respectively). In the infertile group, the mean testicular volume was lower and the mean diameters of the pampiniform veins was higher, significantly. In the infertile group, the median FSH levels were significantly higher than in the fertile group. The groups were similar in terms of other parameters.

With the exception of semen volume, all sperm levels were lower in the infertile group compared with the fertile group (P < 0.001) (**Table 2**).

There was no statistically significant difference between the fertile and infertile groups in terms of platelet and platelet indices (MPV, PDW, and PCT) (**Table 3**).

In the infertile group, the median PSV and EDV in the testicular artery were lower (P = 0.039 and P = 0.016) but there was no differences between the RI values (**Table 4**). There was no statistically significant difference between the groups in testicular blood flow indicators at any level of the intra-testicular artery.

When all participants (fertile and infertile) were considered together, there was no statistically significant correlation between parameters of testicular blood flow (PSV, EDV, and RI) with platelet and platelet indices (MPV, PDW, and PCT) (P > 0.05).

## Discussion

The effect of increased platelet activity in vascular disease has been investigated in several studies [1, 3, 4]. In addition, some studies have shown that increased MPV as a platelet index indicates risk in different diseases such as Behçet's disease, Alzheimer's disease, and familial Mediterranean fever [5-7]. On the contrary, MPV values were found to be lower in the advanced stages of endometriosis [8]. However, there is not yet a study on testicular artery, testicular blood flow, and infertility.

Most of the necessary mediators for coagulation, inflammation, thrombosis, and atherosclerosis are secreted or expressed by platelets [9, 10]. Platelets are heterogeneous in size and density, and those of larger size are more metabolically and enzymatically active and have greater prothrombotic potential [11, 12]. MPV has typically been investigated to measure platelet function. However, there are also other derivatives of platelets such as PDW and PCT that have been investigated relatively less. MPV gives an indication of the size of platelets and increased MPV relates to increased platelet diameter. PDW shows the variation of plate-

**Table 4.** Measurements of testicular blood flow parameters according to the group of patients

| Variables | Fertile Group | Infertile Group | *p*-value† |
|---|---|---|---|
| Testicular artery | | | |
| PSV | 15.1 (10.0-23.2) | 13.1 (9.6-35.0) | 0.039 |
| EDV | 3.3 (1.9-5.5) | 2.8 (1.0-12.6) | 0.016 |
| RI | 0.79 (0.66-0.88) | 0.80 (0.74-0.88) | 0.571 |
| Intra-testicular artery at upper pole | | | |
| PSV | 7.0 (4.4-11.7) | 6.8 (4.9-19.6) | 0.750 |
| EDV | 2.8 (2.0-4.6) | 2.8 (1.8-9.0) | 0.596 |
| RI | 0.60 (0.48-0.77) | 0.56 (0.47-0.69) | 0.942 |
| Intra-testicular artery at middle pole | | | |
| PSV | 9.1 (4.2-18.7) | 8.5 (5.2-14.0) | 0.715 |
| EDV | 3.4 (1.8-6.4) | 3.3 (2.0-6.4) | 0.952 |
| RI | 0.63 (0.47-0.75) | 0.61 (0.49-0.76) | 0.429 |
| Intra-testicular artery at lower pole | | | |
| PSV | 7.1 (3.4-14.7) | 6.9 (4.1-29.0) | 0.438 |
| EDV | 2.9 (1.4-5.5) | 2.4 (1.9-12.0) | 0.493 |
| RI | 0.61 (0.52-0.80) | 0.61 (0.52-0.78) | 0.900 |

†Mann-Whitney U test.

let diameter. Plateletcrit (PCT) is the ratio of total blood platelets in the blood; PCT = Plt × MPV. PDW and PCT are usually not evaluated alone.

This study has revealed a few clear results. First, this study showed that there is no relationship between platelets and platelet indices (MPV, PDW, and PCT), and testicular artery blood flow. This study also revealed the following results; there is no significant relationship between RI values of the testicular artery and the intra-testicular artery with male infertility. There was no difference in terms of platelet and platelet indices between the fertile and infertile groups, such as MPV, PDW and PCT. When considered together, no relationship was demonstrated between any of these parameters in all participants (both fertile and infertile).

There are some limitations of this study. The number of participants might have been larger. Other markers of platelet activation and aggregation exist such as platelet factor 4 and beta thromboglobulin, and these markers could also have been examined.

This study was planned as a preliminary study; however, it was decided to terminate at this stage because no results were determined that would affect clinical practice.

## Disclosure of conflict of interest

None.

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