Can mean platelet volume predict abortion?

Murat Eroglu¹, Ugur Keskin², Ali Osman Yildirim¹, Icel Anil Saygi³, Ismet Gun⁴, Samet Topuz⁴

¹Department of Emergency Medicine, Haydarpasa Teaching Hospital, Gulhane Military Medical Academy, Istanbul, ²Department of Obstetrics and Gynecology, Gulhane Military Medical Academy, Ankara, ³Department of Obstetrics and Gynecology, Haydarpasa Teaching Hospital, Gulhane Military Medical Academy, ⁴Department of Obstetrics and Gynecology, Faculty of Medicine, Istanbul University, Istanbul, Turkey

Corresponding author:
Samet Topuz
Department of Obstetrics and Gynecology, Faculty of Medicine, Istanbul University
Selimiye Mahallesi, Tıbbiye Caddesi, 34668, Istanbul, Turkey
Phone: +90 532 563 75 97;
Fax: +90 216 348 78 80;
E-mail: drismetgun@gmail.com

ABSTRACT

Aim To investigate whether any mean platelet volume (MPV) changes detectable with simple complete blood count (CBC) precede abortion development.

Methods In this retrospective study, patients were divided into three groups according to the miscarriage type. Group 1 was threatened miscarriage (n=54), group 2 was missed abortion (n=46) and group 3 was control (n=40). Samples were collected from all pregnant women visiting Gulhane Military Medical Academy, Haydarpasa Training Hospital, between January 1, 2012 and December 31, 2012, from venous blood during the bleeding time for threatened miscarriage and at the first diagnosis of missed abortion.

Results One hundred and forty patients were included. Mean age, gravidity, parity and previous miscarriage histories were similar in study groups. There was no statistical difference (p= 0.125) between groups in terms of mean platelet volume.

Conclusion It is not considered to use MPVs as a diagnostic test for unsuccessful pregnancies at present time.

Key words: missed, threatened, embryo loss, platelet aggregation
INTRODUCTION

Threatened miscarriage (TM) is an important event that can have psychological consequences for many parents (1), which occurs in 20 to 40 percent of pregnant women (2), and is associated with a 10-14% risk of complete abortion (3,4). The pathophysiologic mechanism of TM is related to bleeding from uteroplacental vessels at the margin of the placenta with blood accumulating between the chorionic membrane and uterine wall (5). If the subchorionic hematoma expands to the rest of the placenta, it will induce complete abortion within a week of the first symptoms (6). If the bleeding is limited, the pregnancy may continue. Several factors have been explored as possible predictors of pregnancy outcome in TM. Among these predictors age, smoking, serum hormone levels and the presence of retroplacental hematoma have been suggested (1,3).

Platelets have a key role in haemostasis. It has been indicated that platelet size reflects platelet activity and is measured using mean platelet volume (MPV). Large platelets are more reactive and produce more prothrombotic factors (7,8). Small platelets have lower functional capabilities than larger ones and bleeding diathesis is seen more frequently in patients with low platelet size (9). It has been known for a long time that increase in platelet volume is an indicator of increased platelet synthesis (10,11). In normal pregnancies, an increase in the platelet aggregation has been detected, which is compensated for with increased synthesis and increased platelet volume (12,13). In the evaluation of platelet functions during a normal pregnancy, the sensitivity of the variations in the platelet volume was found to be higher than variations in the platelet number (14).

There are limited data investigating the relationship between miscarriage and mean platelet volume. To our knowledge, there was one study which evaluated MPV changes in missed abortion cases compared with normal pregnancies (15), however, there were no reports in the existing literature regarding the predictive value or usefulness of MPV in patients with threatened miscarriage. The aim of this study is to examine whether any MPV changes detectable by simple complete blood count (CBC) precede abortion development and to consider the diagnostic value of this marker in clinical practice for the prediction of abortion.

PATIENTS AND METHODS

This retrospective study was conducted at Gulhane Military Medical Academy, Haydarpasa Training Hospital, Istanbul, Turkey, during the period from January till December 2012. The investigation was approved by the Institutional Review Board. All subjects provided written informed consents to participate in the study.

The patients were divided into three groups according to the miscarriage type. Group 1 was threatened miscarriage (n=54), group 2 was missed abortion (n=46) and group 3 was control (n=40). Threatened miscarriage is described as uterine bleeding in the presence of a closed cervix and sonographic visualization of an intrauterine pregnancy with detectable fetal cardiac activity. Missed abortion is described as in-utero death of the embryo or fetus prior to the 20th week of gestation, with retention of the pregnancy for a prolonged period of time. The control group is described as having uncomplicated pregnancies.

Demographic data of the patients were obtained from their antenatal follow-up cards. In our department, the demographic data and obstetric histories are recorded on antenatal follow-up cards and an ultrasound scan is carried out during antenatal periods. Maternal features such as age, method of conception (spontaneous or assisted conception requiring IVF), cigarette smoking during pregnancy (yes or no), gravidity, parity (parous or nulliparous if no delivery beyond 23 weeks), blood type and Rh status, menstrual cycle and date of the last menstrual period (LMP) were recorded.

Diagnosis of pregnancy was based on ultrasonography. Gestational age was calculated from the first day of the last menstrual period and confirmed by ultrasonography. If the pregnant woman had been admitted to the antenatal unit on more than one occasion, she was selected for the first sonographic findings demonstrating a live embryo and the first MPV and platelet values. To avoid potential contradiction, patients who had severe uterine anomalies, thyroid dysfunction, chronic diseases, haematological disease, a history of thrombosis, autoimmune diseases such as systemic lupus erythematosus, multiple pregnancies, or who were receiving anticoagulant therapy were excluded from the study.
Samples were collected from all pregnant women from venous blood during the bleeding time for threatened miscarriage and at the first diagnosis of missed abortion. The MPV was studied in the biochemistry laboratory of the hospital. In all cases, complete blood counts were measured by an automatic blood counter (CELL-DYN Sapphire, Abbott, Illinois, United States) within two hours of 4.5 ml of blood having been drawn from the antecubital vein into tubes containing ethylene diamine tetra acetic acid (K3EDTA). The MPV values of the patients were recorded. The expected MPV values in our laboratory ranged between 6.0 and 9.5 fl.

Data analyses were carried out using SPSS for Windows version 13.0. One-sample Kolmogorov-Smirnov test was used to analyze the normality of the continuous variables. Comparisons between proportions were made using chi-square test. Continuous variables were compared by using Kruskal Wallis Test and analyses of variance, where appropriate. Pearson and Spermann correlation analysis was used for evaluating the association between variables. Data were expressed as a mean ± standard deviation, number and percentage, according to the variables. Differences were considered significant when p<0.05 for the two tails.

RESULTS

One hundred and forty patients were included in the study. Mean age, gravidity, parity and previous miscarriage histories were similar in the study groups (Table 1). The median age of the groups was 31, 32 and 29 years, respectively. The median parity of the groups was 0. The median MPVs were 8.10 and 7.66 fl, respectively. There was no significant difference between groups (p=0.20) (Table 3).

Table 2. Comparison of the mean platelet volume and other haematological parameters in patients with missed abortion, threatened miscarriage and control group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1 (Missed Abortion)</th>
<th>Group 2 (Threatened Miscarriage)</th>
<th>Group 3 (Control)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=46)</td>
<td>(n=54)</td>
<td>(n=40)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Mean +/- SD)</td>
<td>(Mean +/- SD)</td>
<td>(Mean +/- SD)</td>
<td></td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>8.64 (1.35)</td>
<td>8.16 (1.05)</td>
<td>8.18 (1.10)</td>
<td>0.12</td>
</tr>
<tr>
<td>Platelet (x103/l)</td>
<td>251 (56)</td>
<td>238 (57)</td>
<td>278 (65)</td>
<td>0.20</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>12.30 (1.15)</td>
<td>12.21 (1.24)</td>
<td>12.22 (1.28)</td>
<td>0.99</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>35.60 (3.25)</td>
<td>35.61 (3.55)</td>
<td>34.04 (3.28)</td>
<td>0.09</td>
</tr>
<tr>
<td>PDW (fl)</td>
<td>15.69 (1.41)</td>
<td>16.52 (1.18)</td>
<td>15.82 (0.72)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

In the threatened miscarriage group, 10 patients had complete spontaneous abortion during pregnancy. In analysis of the TM with ongoing pregnancy and with complete spontaneous abortion, the median MPVs were 8.10 and 7.66 fl, respectively. There was no significant difference between groups (p=0.20) (Table 3).

Table 3. Comparison of the MPV and other haematological parameters in patients with threatened miscarriage and ongoing pregnancy, and those who underwent complete spontaneous abortion

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TM with ongoing pregnancy (Median (Range) (n=44))</th>
<th>TM with complete spontaneous abortion (Median (Range)) (n=10)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPV (fl)</td>
<td>8.10 (5.9-10.8)</td>
<td>7.66 (6.2-9.4)</td>
<td>0.200</td>
</tr>
<tr>
<td>Platelet (x103/l)</td>
<td>230 (124-371)</td>
<td>234 (95-325)</td>
<td>0.705</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>12.30 (8.9-14.5)</td>
<td>12.44 (9.6-13.4)</td>
<td>0.608</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>35.90 (26.3-42.0)</td>
<td>36.35 (28.4-40.2)</td>
<td>0.929</td>
</tr>
<tr>
<td>PDW (fl)</td>
<td>13.20 (11.1-34.0)</td>
<td>13.40 (12.4-16.2)</td>
<td>0.533</td>
</tr>
</tbody>
</table>

DISCUSSION

To our knowledge, this is the first study that compares the mean platelet volume of patients with threatened miscarriages. This study has demonstrated that MPVs are slightly increased in threatened miscarriage and in missed abortions, although not statistically significant. Platelet volume is a specific parameter of platelet function. Larger platelets are hemostatically more active. Changes in the volume and activity of platelets play an important role in the development of intracoronary thrombus and acute myocardial infarction (AMI) (16). Patients sustaining AMI who have higher mean thrombocyte volumes at admission have been reported to have an increased mortality risk and an increased need for revascularization (16). MPV continues to increase after AMI return to nor-
mal levels within the recovery period. Higher MPV are usually associated with complications (17).

The mean platelet volume (MPV) is a parameter detected during routine blood counts to which clinicians do not often pay attention (18). Increase of MPV is due to synthesis of prothrombotic and proinflammatory agents in platelets and release of reactive platelets (19). In obstetrics, increased MPV and increased platelet aggregation have been defined as precursors to the onset of preeclampsia and intrauterine growth restriction (12). Kim et al. determined that MPV was normal in normal spontaneous vaginal delivery, but increased in abortion, in spontaneous premature rupture of membranes and in preeclampsia (20). Mean platelet volume was also greater in abnormal pregnancies when compared with normal Doppler examination results (21). Lamparelli et al. argued that platelet count decreases with advancing gestation, but that the MPV remains unchanged (22). Vagdatli et al. suggested that there was no significant increase of MPV in women in late pregnancy compared to those in early pregnancy, and that hourly measurements of MPV in random blood samples showed an increase of MPV over time (23). Tygart et al. suggested that changes in platelet volumes may be more sensitive than platelet numbers as a measure of altered function in normal pregnancy (14). Thus, in pregnancies, as a sign of platelet function, MPV is more important than platelet number. In our study, contrary to expectations, platelet counts and volumes in missed abortion and TM groups were not significantly different from normal pregnancies. We observed that platelet counts in missed abortion and TM groups were slightly low in relation to the normal pregnancies, but MPVs were not much altered. The occurrence of many shared values between the groups in terms of MPVs shows that a single measurement has no diagnostic value. Some previous studies have shown that a series of measured values is much more significant than a single value (24, 25). Similarly, we thought that the sequential measurements of MPVs may be more meaningful.

In pregnancy with missed abortion, slight increase in MPVs might reflect thrombosis or hemorrhage in the decidua basalis and inflammation in the region of implantation. The hypercoagulability and decidual vasculopathy may result in low placental perfusion and, finally, in the loss of the fetus. In pregnancies with TM, the increase of MPV levels might represent physiologic increase of bleeding from the placental bed (15, 26).

Recently automated hematological analyzers automatically measure several blood cell parameters, including platelet distribution width (PDW) and red blood cell distribution width (RDW). The reference range for PDW and RDW are not universally accepted, each laboratory defines its own reference range for both parameters. Farias et al. reported a reference range of 10.0%-17.9% (13.3%) for PDW (27). The normal reference range of the RDW typically spans between 11% and 14% (28). The meaning of elevation of PDW and RDW is not known yet. Current studies showed that PDW can be used in differentiation of thrombocytopenia from aplastic anemia, immune thrombocytopenia and thrombocytosis. The PDW also reflects disease activity as risk factors for acute coronary disease and in rheumatoid arthritis (27). High RDW is an independent risk factor for major cardiovascular events, at the same time reflects chronic events and chronic inflammatory states such as anemia, acute and chronic heart failure, peripheral artery disease, stroke, pulmonary embolism, pulmonary arterial hypertension and acute kidney injury (28). As a result, in our study, Group 2 patients had significantly higher levels of PDW and RDW compared to control and Group 1 patients. This finding may indicate a chronic vascular event or a hematological disease, that have not been detected by us. At the same time, it may be an early indicator of imminent abortion or an indicator of mortality in imminent abortion. In our study, PDW and RDW levels were not statistically different in Group 2 patients with and without continued pregnancy. However, this finding may be due to the limited number of patients in these groups. We might find a significant difference if there were more patients in the groups. Therefore, we think that these readily available simple parameters deserve more research.

Consequently, because of overlapping values between normal pregnancies and abortion cases, it is not considered to use MPVs as a diagnostic test for unsuccessful pregnancies at the present time. However, a series of MPV measurements is considered to be suggestive in terms of miscarriages. Because of the limited number of cases in our study, further studies including issues such as recurrent miscarriage, antiphospholipid syndrome,
autoimmune disorders and thrombotic disorders would help to explain the diagnostic potential of this test and explanation of the condition.

REFERENCES


FUNDING

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TRANSPARENCY DECLARATIONS

Competing interests: none to declare.