PERINATAL JOURNAL

Original Article

Perinatal Journal 2017;25(1):32–37

A new marker for the prediction of mean platelet volume, placenta previa and placental invasion anomalies

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Abstract

Objective: The aim of this study is to evaluate the relationship between some parameters of complete blood count and placenta previa and placental invasion anomalies.

Methods: In this study, 70 cases with placenta previa and 70 control cases who admitted to the Department of Obstetrics and Gynecology of Mustafa Kemal University between September 2015 and December 2016 were reviewed retrospectively. The sociodemographic data and the numbers of previous cesarean section of the patients were recorded. Before the cesarean section, the counts of preoperative lymphocyte, neutrophil and platelet, mean platelet volume (MPV), neutrophil/lymphocyte rate, platelet/lymphocyte rate, and hemoglobin and hematocrit values were recorded. It was analyzed whether these parameters were able to predict placenta previa and placental invasion anomalies or not.

Results: There was no difference between two groups in terms of sociodemographic (age, gravida, parity, living fetus and the number of previous cesarean section) data. The week of gestation during delivery and birth weight were significantly low in placenta previa group. Postoperative hemoglobin and hematocrit values were also significantly low in previa group. Considering the complete blood parameters, MPV was significantly low in previa group (p=0.042). Placental invasion anomaly was confirmed histopathologically in 24 of 27 cases in previa group who underwent cesarean hysterectomy. When the group with invasion anomaly was compared to the control group, MPV was also significantly low (p=0.047).

Conclusion: In addition to the ultrasound images, simple blood count parameters can be used to confirm placenta previa and placental invasion anomalies in particular. Among these parameters, MPV seems to be the most potent predictor.

Keywords: Placental invasion anomalies, placenta previa, mean platelet volume.

Özet: Ortalama trombosit hacmi, plasenta previa ve plasenta invazyon anomalilerini öngörmede yeni bir belirteç

Amaç: Bu çalışmanın amacı bazı tam kan sayımı parametreleri ile plasenta previa ve plasenta yapışma anomalileri arasındaki ilişkiyi değerlendirmektir.

Yöntem: Bu çalışmada Eylül 2015 – Aralık 2016 tarihleri arasında Mustafa Kemal Üniversitesi Kadın Hastalıkları ve Doğum Kliniği'ne başvuran 70 plasenta previa ve 70 kontrol olgusu retrospektif olarak tarandı. Hastaların sosyodemografik özellikleri, önceki sezaryen sayıları kaydedildi. Sezaryen öncesi tüm olguların preoperatif lenfosit sayısı, nötrofil sayısı, trombosit sayısı, ortalama trombosit hacmi (MPV), nötrofil/lenfosit oranı, trombosit/lenfosit oranı, hemoglobin ve hematokrit değerleri kaydedildi. Bu parametrelerin plasenta previa ve plasenta yapışma anomalilerini öngörüp öngöremeyeceği analiz edildi.

Bulgular: Her iki grupta olguların sosyodemografik (yaş, gravida, parite, yaşayan, geçirilmiş sezaryen sayısı) verileri açısından fark yoktu. Doğumdaki gestasyonel yaş ve doğum ağırlığı plasenta previa grubunda anlamlı düşük bulundu. Postoperatif hemoglobin ve hematokrit değerleri previa grubunda anlamlı düşük idi. Tam kan parametrelerine bakıldığında previa grubunda MPV anlamlı düşük bulundu (p=0.042). Previa grubundaki sezaryen histerektomi uygulanan 27 olgunun 24 tanesinde histopatolojik olarak plasenta invazyon anomalisi konfirme edildi. İnvazyon anomalisi olan grup ile kontrol grubu karşılaştırıldığında MPV yine anlamlı düşük bulundu (p=0.047).

Sonuç: Sonografik görüntülere ek olarak basit kan sayımı parametreleri plasenta previa ve özellikle de plasenta invazyon anomalilerini konfirme etmek için kullanılabilir. Bu parametreler içinde MPV en güçlü prediktör gibi görünmektedir.

Anahtar sözcükler: Riskli gebelik, normal gebelik, sağlıklı yaşam biçimi davranışı.

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Received: January 26, 2017; **Accepted:** March 18, 2017

Please cite this article as: Soylu Karapınar O, Gözükara İ, Hakverdi AU, Güngören A. A new marker for the prediction of mean platelet volume, placenta previa and placental invasion anomalies. Perinatal Journal 2017;25(1):32–37.

Available online at:
www.perinataljournal.com/20170251007
doi:10.2399/prn.17.0251007
QR (Quick Response) Code:

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Introduction

Placenta previa is defined as the condition that placenta tissue is placed above or very close to internal cervical os. Its estimated incidence at term is 1/200 and the worldwide incidence varies.[1] Placenta accreta is the attachment of trophoblasts to uterine wall and it may invade at various levels including myometrium and serosa. The term 'placenta accreta' comprises entire spectrum including accreta, increta and percreta, and it is also called as morbid invasive placenta.[2] Placenta accreta is seen in 1 out of 300 pregnancies and its incidence has increased about 10 times in the last 5 decades.[3,4] It is a life-threatening clinical condition due to unexpected catastrophic complications during delivery such as severe hemorrhage, cesarean hysterectomy or bladder injury, and intestinal and vascular trauma.[5]

The connections between maternal inflammatory cells in basal layer, maternal desidual tissue and fetal extravillous trophoblast cells may lead to morbid invasive placenta. However, the underlying pathogenic mechanism of morbid invasive placenta is still unclear.[6] Although defective decidualization in implantation area is one of the significant underlying etiological factors of placenta previa and morbid invasive placenta, some studies histopathologically showed uteroplacental vascular anomalies in basal layer,[7] decidual hemosiderosis and infarction,[8] and acute and chronic inflammation.[9] Various studies reported that the invasion of cancerous cells had common characteristics with trophoblast invasion.[10] Neutrophil/lymphocyte rate (NLR), platelet/lymphocyte rate (PLR) and mean platelet volume (MPV) values are the most recent markers to evaluate the inflammatory response, and they are successfully used in various gynecological cancer and inflammatory diseases as predictive marker and prognostic factor.[11–13] In this study, we aimed to evaluate the relationship between complete blood count and their parameters and placenta previa and placental invasion anomalies, which are inflammatory and invasive.

Methods

This study was conducted through the retrospective review of the cases who admitted to the Department of Obstetrics and Gynecology of Mustafa Kemal University between September 2015 and December 2016. For this study, we obtained the approval of head physician of Health Application and Research Hospital of Mustafa Kemal University.

The study group included 70 cases who were suspected to have complete placenta previa and placental invasion anomaly according to the ultrasonography examination. The control group had 70 cases who had normally located placenta with previous or repeating cesarean section. Cases with multiple pregnancies, those with infectious and hemorrhagic problems in current pregnancy, cases with systemic diseases such as cardiovascular, endocrinologic, metabolic, inflammatory and autoimmune diseases, cases with smoking habit, and those with maternal obesity were excluded from the study. By reviewing the files of cases, their demographic data (age, gravida, parity, living fetus, week of gestation, birth weight, and previous deliveries) and preoperative hematologic parameters before cesarean section were recorded. Since the cases had placenta previa and with previous cesarean section, all patients delivered by cesarean section. In previa group, cesarean hysterectomy was performed in 27 cases who had placental invasion anomaly and developed postpartum hemorrhage.

Among the hematologic parameters, preoperative hemoglobin, hematocrit, and postoperative hemoglobin and hematocrit values were recorded. Preoperative neutrophil count, lymphocyte count, platelet count and MPV values were recorded. NLR and PLR were calculated by proportioning neutrophil to lymphocyte and platelet to neutrophil, respectively. The demographic data and hematologic parameters of the patients were compared. SPSS 21 was used for statistical analysis. The groups were compared by independent t-test. $p<0.05$ was considered significant.

Results

Both groups were similar in terms of age distribution (31.4±5.3 years in previa group, and 29.8±4.7 years in control group) and obstetric history (except gravida) (**Table 1**). Statistically significant low results were found in previa group compared to the control group in terms of week of gestation during delivery (36.0±2.4 weeks in previa group and 37.6±1.0 weeks in the control group) and birth weight (2802.28±590.31 g in previa group and 3090.00±477.00 g in the control group) (**Table 1**).

While preoperative hemoglobin levels (10.7±1.6 in previa group and 11.2±1.4 in the control group) were similar in previa and control groups, hematocrit level was

Table 1. Demographic data of previa and control groups.

	Placenta previa (n=70) (mean±SD)	Control group (n=70) (mean±SD)	p value
Age (year)	31.4±5.3	29.8±4.7	0.058
Gravida	3.8±1.3	3.1±1.1	**0.002**
Parity	2.1±1.0	1.9±0.9	0.236
Living fetus	2.0±1.0	1.8+0.9	0.121
Number of previous cesarean section	1.87±0.97	1.72±0.81	0.349
Week of gestation during delivery	36.0±2.4	37.6±1.0	**0.000**
Birth weight (g)	2802.28±590.31	3090.00±477.99	**0.002**

lower in previa group (32.5±4.8 in previa group and 34.5±3.8 in the control group; p=0.008) which was statistically significant. Postoperative hemoglobin (9.4±1.4 in previa group and 10.0±1.1 in the control group; p=0.016) and hematocrit values (28.8+4.4 in previa group and 31.1+3.5 in the control group; p=0.001) were significantly lower than control group. Procedure duration was significantly higher in previa group compared to the control group (88.2±32.9 hours in previa group and 44.0±4.1 hours in the control group; p=0.000).

Lymphocyte count, neutrophil count, and NLR and PLR were similar in both groups. Thrombocyte count was higher in previa group, which was statistically significant (226.3±56.5 in previa group and 201.8±62.9 in the control group; p=0.017) (**Table 2**). MPV was found significantly lower in previa group than the control group (8.9±1.2 in previa group and 9.4±1.6 in the control group; p=0.042) (**Table 2**).

All patients in our study underwent cesarean section. Cesarean hysterectomy was performed in 27 cases in previa group due to placental invasion anomaly and postpartum hemorrhage. It was found that 8 cases had perioperative bladder injury. There was no postoperative complication. It was recorded that there was no neonatal death. When we considered that the cases who underwent hysterectomy in previa group were positive for invasion, MPV, NLR and PLR values of cases who were positive for invasion (n=27) and negative for invasion (n=43) were similar. When the cases who underwent only cesarean hysterectomy were confirmed with pathology results, placental invasion was positive in a total of 24 cases, of which 10 had increta and 9 had percreta. Since all cases in previa group underwent protective uterine surgery gradually (hypogastric artery ligation in 20 cases, uterine artery ligation in 5 cases, and uterine square sutures in 14 cases), the cases who were positive for invasion and confirmed pathologically were compared with the cases in the control group in terms of lymphocyte count, neutrophil count, platelet count and MPV, NLR and PLR values. Only the MPV value (8.7±1.2 in the invasion-positive group and 9.4±1.6 in the control group; p=0.047) was lower in the invasion-positive group, which was statistically significant (**Table 3**).

Table 2. The analysis of hematological parameters in previa and control groups.

	Placenta previa (n=70) (mean±SD)	Control group (n=70) (mean±SD)	p value
Lymphocyte count $\times 10^3/mm^3$	1.8±0.6	1.7±0.8	0.158
Neutrophil count $\times 10^3/mm^3$	9.1±3.3	8.7±2.8	0.485
Platelet count $\times 10^3/mm^3$	226.3±56.5	201.8±62.9	**0.017**
MPV (femtoliter)	8.9±1.2	9.4±1.6	**0.042**
NLR	5.9±4.4	6.0±3.0	0.875
PLR	135.4±62.9	140.7±74.5	0.648

MPV: mean platelet volume, **NLR:** neutrophil/lymphocyte rate, **PLR:** platelet/lymphocyte rate

Table 3. The analysis of hematological parameters in previa group (positive for invasion) and control group.

	Cases with placental invasion anomaly (n=24) (mean±SD)	Control group (n=70) (mean±SD)	p value
Lymphocyte count $\times 10^3/mm^3$	1.8±0.6	1.7±0.8	0.599
Neutrophil count $\times 10^3/mm^3$	9.2±4.0	8.7±2.8	0.541
Platelet count $\times 10^3/mm^3$	225.0±59.3	201.8±62.9	0.118
MPV (femtoliter)	8.7±1.2	9.4±1.6	**0.047**
NLR	6.5±5.6	6.0±3.0	0.578
PLR	140.6±62.0	140.7±74.5	0.993

MPV: mean platelet volume, **NLR:** neutrophil/lymphocyte rate, **PLR:** platelet/lymphocyte rate

Discussion

Placenta previa and morbid invasive placenta are the most common reasons for cesarean hysterectomy. Although the underlying pathogenic mechanism of morbid invasive placenta is unclear, the greatest and most systematic histopathological study performed on this matter considerably associated morbid invasive placenta with chronic inflammation, low maternal vascular blood supply and hemorrhage. Presence of chronic inflammation may lead to abnormal immune response on maternal fetal surface, and this chronic inflammation may have a role in the progress of trophoblastic tissue or in controlling the invasion of placenta.[14] Also, the studies performed on trophoblasts showed that there are similarities between placental cells and cancerous cells in terms of proliferation, migration and invasion.[15]

It was confirmed that some inflammation markers such as neutrophil/lymphocyte and platelet/lymphocyte rates predict malignancy and even they have both diagnostic and prognostic values according to the meta-analyses of some other studies. NLR and PLR values are cheap screening markers calculated from complete blood parameters which show simple systemic inflammatory response in peripheral blood. NLR has diagnostic value in some pathologies characterized by systemic and local inflammatory responses such as diabetes, coronary artery disease, ulcerative colitis and inflammatory arthritis. The rate of these two cell types provides the estimation to identify inflammation.[16–18] PLR, on the other hand, is used to show elevating endogenous residual anticancer preinflammatory and precoagulative responses in malignancies. PLR is currently a prognostic and sensitive marker for breast, ovarian and colorectal cancers.[19] MPV, which is a routine component of complete blood count, is the marker of platelet function and activity. It was reported that decreased MPV values showed disease activity and inflammation in various inflammatory diseases. It was shown that MPV values decreased in high-grade inflammation such as active rheumatoid arthritis, acute attack of familial Mediterranean fever and active chronic obstructive pulmonary disease.[20] İncebıyık et al. reported low MPV values in pelvic inflammatory disease.[21] Due to the similarities between tumor metastases and placental invasion and the presence of chronic inflammation in cases with placenta previa and percreta, they developed the hypothesis that these markers might be significant to identify abnormal placentation. In our study, we found no difference between control and previa groups in terms of age, parity, living fetus and number of previous cesarean section. Similarity of such demographic data between the groups increased the validity of this comparison. Birth weight and week of gestation during delivery were significantly lower in previa group compared to the control group, and these results are associated with preterm labor due to the fact that these pregnancies are among the high-risk pregnancy group and particularly due to hemorrhagic complications. Postoperative hemoglobin and hematocrit levels were significantly low in placenta previa group compared to the control group, and this is the result of severe hemorrhage of these perioperative patients, and procedure durations were significantly higher in previa group than the control group.

In our study, there was statistical difference between previa and control groups in terms of MPV values and

platelet counts. MPV values were significantly lower in the cases with placenta previa and placenta percreta, which were characterized by inflammation, compared to the control group. This shows us that acute and chronic inflammation, which was also shown histopathologically in these cases, is confirmed by MPV values. Also, when invasion-positive hysterectomized cases were compared with the control group, significantly low MPV values were observed in the invasion-positive group. All cases gradually underwent protective uterine surgery. Some procedures such as uterine square and U sutures, uterine artery ligation, ovarian artery ligation and hypogastric artery ligation are able to control hemorrhage in some accreta and increta cases. When we want to confirm the results also with invasion-positive cases, we concluded that cases which were observed adhesion anomaly histopathologically were certainly positive for invasion and we compared them with the control group; as a result, we found MPV significantly low again. High-grade inflammation and the presence of invasion were also confirmed with MPV values. In the literature review, we found only two studies performed in 2016 on this subject. Yayla et al. compared the groups with and without invasion anomaly among the cases with placenta previa, and unlike our study, they found significantly higher MPV values in the group with invasion anomaly.[22] There was no control group in this study; they compared the cases in previa group as those with and without invasion, and they found higher MPV values in the cases with invasion anomaly, and this indicates the presence of low-grade inflammation. Since there was no control group, we cannot determine why there is no similarity with our results. In another study, Ersoy et al. compared the cases with placenta previa to the control group and found significantly low MPV values; similar to our study, they found in their retrospective study that MPV value was significantly low when they performed comparison between the groups with and without invasion anomaly, and between previa group and control group.[23]

In adhesive placental disorders, which are the most common type of complications, placenta percreta is also observed particularly. When confirmed with the previous studies, there is no ideal method to predict severe hemorrhage risk during antepartum period in cases with placenta previa, because hemorrhage volume is multifactorial including the complications associated with placenta previa. Ultrasound and magnetic resonance are useful to predict and decrease the complications of placenta previa.[23] Some studies found an association between placenta previa and hormones such as PAPP-A and MS-AFP which are secreted from fetoplacental unit.[24] Molecules, such as cell free bHCG mRNA which are more complex in maternal plasma, were used to identify placental invasion anomalies, and it was concluded that they were applicable for the prenatal diagnosis (particularly for the accreta cases who need hysterectomy).[25] However, all these markers are not always available, and therefore simpler preoperative tests, which are easy-to-use, are needed. According to our study, inflammatory process and simple blood count parameters for placental invasion anomalies with histopathologies similar to some malignancies may contribute to the confirmation of the condition during ultrasound in cases suspected to have invasion anomaly.

Conclusion

In addition to the ultrasound images, simple blood count parameters can be used to confirm placenta previa and placental invasion anomalies in particular. Among these parameters, MPV seems to be the most potent predictor.

Conflicts of Interest: No conflicts declared.

References

1. Cresswell JA, Ronsmans C, Calvert C, Filippi V. Prevalence of placenta previa by world region: a systematic review and meta-analysis. Trop Med Int Health 2013;18:712–24.
2. Silver RM. Abnormal placentation. Obstet Gynecol 2015;126: 654–68.
3. Morlando M, Samo L, Napolitano R, Capone A,Tessitone G, Maruotti GM, et al. Placenta accreta: incidence and risk factors in an area with a particularly high rate of cesarean section. Acta Obstet Gynecol Scand 2013;92:457–60.
4. Lorenz RP. What is new in placenta accreta? Best articles from the past year. Obstet Gynecol 2013;121:375–6.
5. Asicioglu O, Sahbaz A, Gungorduk K, Yıldırım G, Asıcıoglu BB, Ülker V. Maternal and perinatal out-comes in women with placenta praevia and accreta in teaching hospitals in Western Turkey. J Obstet Gynaecol 2014;34:462–6.
6. Abuhamad A. Morbidly adherent placenta. Semin Perinatol 2013;37:359–64.
7. Sherer DM, Salafia CM, Minior VK, Sanders M, Ernst L, Vintzileos AM. Placental basal plate myometrial fibers: clinical correlations of abnormally deep trophoblast invasion. Obstet Gynecol 1996;87:444–9.

8. Stanek J, Drummond Z. Occult placenta accreta: the missing link in the diagnosis of abnormal placentation. Pediatr Dev Pathol 2007;10:266–73.
9. Fox H, Sebire NJ. Pathology of the placenta. Oxford: Elsevier Health Sciences; 2007.
10. Knöfler M, Pollheimer J. Human placental trophoblast invasion and differentiation: a particular focus on Wnt signaling. Front Genet 2013;4:190.
11. Feng Z, Wen H, Bi R, Ju X, Chen X, Yang W, et al. Preoperative neutrophil-to-lymphocyte ratio as a predictive and prognostic factor for high-grade serous ovarian cancer. PLoS One 2016;11:e0156101.
12. Akın MN, Kasap BH, Yuvacı HU. Neutrophil-to-lymphocyte ratio and platelet distribution in patients with endometrial cancer. J Obstet Gynaecol Res 2015;41:1499.
13. Kim HS, Han KH, Chung HH, Kim JW, Park NH, Song YS, et al. Neutrophil to lymphocyte ratio for preoperative diagnosis of uterine sarcomas: a case-matched comparison. Eur J Surg Oncol 2010;36:691–8.
14. Ernst LM, Linn RL, Minturn L, Miller ES. Placental pathologic associations with morbidly adherent placenta: potential insights into pathogenesis. Pediatr Dev Pathol 2017; March 20 (Epub ahead of print). doi:10.1177/1093526617698600
15. Ferretti C, Bruni L, Dangles-Marie V, Pecking AP, Bellet D. Molecular circuits shared by placental and cancer cells, and their implications in the proliferative, invasive and migratory capacities of trophoblasts. Hum Reprod Update 2007;13: 121–41.
16. Celikbilek M, Dogan S, Ozbakır O, Zararsız G, Kücük H, Gürsoy S, et al. Neutrophil-lymphocyte ratio as a predictor of disease severity in ulcerative colitis. J Clin Lab Anal 2013;27: 72–6.
17. Imtiaz F, Shafique K, Mirza SS, Ayoob Z, Vart P, Rao S. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int Arch Med 2012;5:2.
18. Tousoulis D, Antoniades C, Koumallos N, Stefanadis C. Proinflammatory cytokines in acute coronary syndromes: from bench to bedside. Cytokine Growth Factor Rev 2006;17: 225–33.
19. Proctor MJ, Morrison DS, Talwar D, Balmer SM, Fletcher CD, O'Reilly DS, et al. A comparison of inflammation-based prognostic scores in patients with cancer. A Glasgow Inflammation Outcome Study. Eur J Cancer 2011;47:2633–41.
20. Kabil Kucur S, Seven A, Yuksel KD, Sencan H, Gozukara I, Keskin N. Mean platelet volume, a novel biomarker in adolescents with severe primary dysmenorrhea. J Pediatr Adolesc Gynecol 2016;29:390–2.
21. Incebıyık A, Seker A, Vural M, Gul Hilali N, Camuzcuoglu A, Camuzcuoglu A. May mean platelet volume levels be a predictor in the diagnosis of pelvic inflammatory disease? Wien KlinWochenschr 2014;126:422–6.
22. Abide Yayla C, Ozkaya E, Tayyar A, Senol T, Senturk MB, Karateke A. Predictive value of complete blood count parameters for placental invasion anomalies. J Matern Fetal Neonatal Med 2016; Nov 2:1–5. doi:10.1080/14767058.2016.1247266
23. Ersoy AO, Ozler S, Oztas E, Ersoy E, Kırbas A, Danısman N. The association between placenta previa and leukocyte and platelet indices–a case control study. Ginekologia Polska 2016; 87:367–71.
24. Lyell DJ, Faucett AM, Baer RJ, Blumenfeld YJ, Druzin ML, El-Sayed YY. Maternal serum markers, characteristics and morbidly adherent placenta in women with previa. J Perinatol 2015;35:570–4.
25. Zhou J, Li J, Yan P, Ye YH, Peng W, Wang S, et al. Maternal plasma levels of cell-free beta-HCG mRNA as a prenatal diagnostic indicator of placenta accrete. Placenta 2014;35:691–5.