

## Platelet indices in evaluation of patients with recurrent pregnancy loss

Abeer Abdul-Rahman Al-Aghbary<sup>1✉</sup>, Mohammed Abdul Wahid Almorish<sup>2</sup>, Dikra Waheeb Mohamed Jaffar<sup>3</sup>, Wael Mohmed Al-Kahiry<sup>4</sup>

<sup>1</sup>Department of Gynecology and Obstetrics, Taiz University, Yemen

<sup>2</sup>Department of Hematology, Sanaa University, Yemen

<sup>3</sup>Department of Gynecology and Obstetrics, Aden University, Yemen

<sup>4</sup>Department of Hematology Oncology, Aden University, Yemen

### ARTICLE INFO

#### Article history:

Received 28 October 2017

Revision 7 November 2017

Accepted 27 November 2017

Available online 1 January 2018

#### Keywords:

Pregnancy loss

Platelets

Platelet distribution width

Mean platelet volume

Plateletcrit

### ABSTRACT

**Objective:** To explore the change of platelet indices namely plateletcrit, platelet distribution width and mean platelet volume among patients with recurrent pregnancy loss (RPL). **Methods:** The medical records of 45 women with a history of RPL and 45 women who gave birth without RPL were reviewed retrospectively from three governmental hospitals in Yemen. The personal, obstetric and complete blood count reports were analyzed. **Results:** Platelets' count and indices were significantly higher among RPL patients when compared to the control and the receiver operating characteristic curve for each platelet index showed significant area under the curve, with higher area for plateletcrit followed by platelet distribution width and then mean platelet volume. While the multiple logistic regression analysis for all platelets indices revealed that the platelet distribution width was the significant predictor for RPL in this study. **Conclusions:** The use of platelet indices may help gynecologists in predicting high risk pregnancy (pregnancy loss) in the low resources areas in Yemen.

## 1. Introduction

Human reproduction is characterized by its inefficiency. Recurrent pregnancy loss (RPL) is defined as two or more failed clinical pregnancies as documented by ultrasonography or histopathologic examination before 20 weeks gestation, ectopic, molar, and biochemical pregnancies are not included[1]. The loss of at least two consecutive pregnancies occurs in up to 5% of women at reproductive age[2] and only 1% experience three or more[1].

The estimated incidence of early pregnancy loss is 15% of conceptions with a significant age variability[3]. Late losses between 12 and 22 weeks occur less frequently and constitute around 4% of pregnancy outcomes[4].

The etiology of RPL is multifactorial, however, the underlying cause cannot be clarified in 50%–60% of all RPL[5,6]. Early pregnancy loss, particularly those occurring within 12th to 14th weeks has been suggested to be due to maternal thrombophilia which interferes with placental development and implantation of the fertilized egg in the uterine deciduas[7].

The mean platelet volume (MPV), plateletcrit, and platelet distribution width (PDW) have been investigated as the markers of platelet activation and predictors of thrombophilic disorders[8–10]. Moreover, the combination of MPV and PDW could predict activation of coagulation more efficiently[11–12].

This study was conducted to determine the change of platelet

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 3.0 License, which allows others to remix, tweak and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

©2018 Asian Pacific Journal of Reproduction Produced by Wolters Kluwer- Medknow  
**How to cite this article:** Abeer Abdul-Rahman Al-Aghbary, Mohammed Abdul Wahid Almorish, Dikra Waheeb Mohamed Jaffar, Wael Mohmed Al-Kahiry. Platelet indices in evaluation of patients with recurrent pregnancy loss. *Asian Pac J Reprod* 2018; 7(1): 15-18.

✉First and corresponding author: Abeer Abdul-Rahman Al-Aghbary, Department of Gynecology and Obstetrics, Taiz University, Yemen.  
 E-mail: abeerlaghbary@gmail.com  
 Tel: +967 733721012

indices namely plateletcrit, PDW and MPV among patients with RPL.

## 2. Materials and methods

A total of 45 women with a history of RPL (2 or more), and a control group of 45 women who gave birth without RPL (2 or more) were included. All the included women were between 20 and 35 years old. The medical records were taken from the gynecology departments of three governmental hospitals in three governorates: Al-Sadaka Teaching Hospital in Aden, Al-Thawra Hospital in Sana'a, and Gebla Hospital in Ibb, Republic of Yemen, for a period of two years (May 2015-April 2017). Patients with a known history of chronic diseases, immobilization, surgery, trauma during pregnancy, uterine abnormalities, fever or proven infection in the first trimester were excluded; smokers and those used non-steroid anti-inflammatory drugs or anti-coagulants were also excluded. Data of personal, obstetric and complete blood count reports were collected from medical records.

Data were processed and analyzed by computer facilities using the statistical package of social science program version 24. Quantitative variables were found with parametric distribution, presented as means  $\pm$  standard deviations and tested by the Student *t*-test. To explore the role of platelets indices in RPL, the receiver operating characteristic (ROC) curve was obtained for the each index and the multiple logistic regression analysis was conducted for all using enter method. The statistical tests were conducted with the 95% confidence interval and  $P < 0.05$  was considered as statistically significant difference.

This study was conducted retrospectively after taking the consent of each hospital director and archivist who was requested to code personal data to numbers and accordingly no psychological or any type of harm was on the patients with RPL and the control in this study.

## 3. Results

The demographic data obtained for the studied population showed that no significant difference between RPL patients and the control in regard to patients' age, body weight and gestational age. Only parity was statistically significantly higher among the control (Table 1).

**Table 1**

Demographic data of studied patients and control (Mean  $\pm$  SD).

Item	Patients (n=45)	Control (n=45)	P-value
Age (years)	26.70 $\pm$ 3.20	27.50 $\pm$ 4.10	0.305
Parity	2.10 $\pm$ 0.89	3.40 $\pm$ 1.30	0.001*
Body weight (kg)	72.45 $\pm$ 7.09	70.15 $\pm$ 7.75	0.145
Gestational age (weeks)	8.50 $\pm$ 1.42	7.90 $\pm$ 2.28	0.138

\*Statistically significant  $P < 0.05$ .

Platelets' count and indices were significantly higher among RPL patients when compared to the control (Table 2).

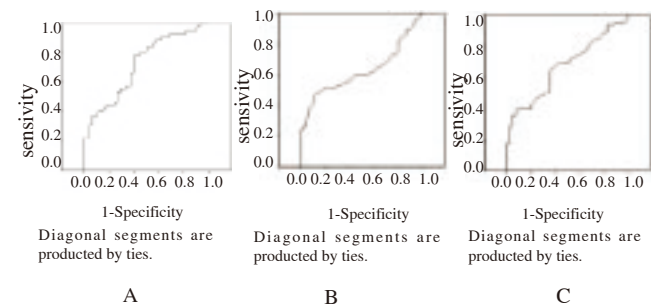
**Table 2**

Platelet indices of studied patients and control (Mean  $\pm$  SD, Min.-Max.).

Item	Patients (n=45)	Control (n=45)	P-value
Platelets count ( $\times 10^9/L$ )	253.80 $\pm$ 64.60 (164-395)	213.60 $\pm$ 71.90 (115-410)	0.006*
Platelet distribution width (fl)	14.48 $\pm$ 2.25 (11.50-18.90)	13.19 $\pm$ 1.44 (11.50-16.90)	0.002*
Mean platelet volume(fl)	10.59 $\pm$ 3.10 (5.80-15.90)	9.12 $\pm$ 1.90 (5.60-13.50)	0.009*
Plateletcrit (%)	0.27 $\pm$ 0.10 (0.12-0.52)	0.19 $\pm$ 0.06 (0.10-0.35)	0.001*

\*Statistically significant  $P < 0.05$ .

The ROC curve for each platelet index showed significant area under the curve, with higher area for plateletcrit followed by PDW and then MPV (Figure 1).



**Figure 1.** ROC curve for plateletcrit (A), MPV (B), PDW (C) between RPL and control.

A: AUC= 0.721,  $P=0.001$ ; B: AUC= 0.625,  $P=0.042$ ; C: AUC= 0.667,  $P=0.006$ .

While the multiple logistic regression analysis for all platelets indices revealed that the PDW was the significant predictor for RPL in this study (Table 3).

**Table 3**

Multiple logistic regression analysis for risk factors of RPL.

Predictors	Standardized beta coefficients	t	P-value
Platelets count ( $\times 10^9/L$ )	- 0.291	- 0.789	0.432
Platelet distribution width (fl)	- 0.295	- 3.108	0.003*
Mean platelet volume(fl)	- 0.274	- 0.775	0.440
Plateletcrit (%)	0.017	0.034	0.973

The test was performed by using the enter method ( $F=6.99$ ,  $P < 0.0001$ ).

Adjusted *r* square = 0.498.

\* Statistically significant  $P < 0.05$ .

#### 4. Discussion

It is well known that pregnancy is a hypercoagulable state attributing to alterations of coagulation proteins[13,14]. It is associated with changes in platelets functions and during pregnancy loss, and thrombocytic functions return to normal after 12 weeks[15].

In the study of Van Dreden *et al*[16], they observed an increasing level of platelet activating factors in serum samples from women who have suffered two or more RPL and they attributed its implications to placental function and fetal growth.

Several studies have reported a positive correlation between RPL and the heritable thrombophilic defects. It is suggested that the mutations of factor V leiden and prothrombin gene (*G20210A*) mutation might aggravate the hypercoagulable state of pregnancy resulting in placental thrombosis and infarcts, thus playing an important role in implantation failure and pregnancy loss[17-20].

Since most of the diagnostic tests for RPL evaluation are costly and time-consuming, the question that when the tests are needed is raised. Some gynecologists recommend the tests after two consecutive pregnancy losses, while others recommend tests until three pregnancy losses.

There are several studies on platelets indices among RPL. In the study of Rai *et al*[21], they reported that a relationship between platelet indices and the increased risk of thrombosis.

In Yemen, the facilities for PCR testing for such mutations are scarce and most gynecologists manage RPL randomly. They need simple, easy and cheap methods to evaluate Yemeni patients with RPL, because of that we decided to conduct the current study to determine the level of these simple platelets indices among Yemeni patients with RPL.

In the current study, platelets count and indices were significantly higher among RPL patients, which might suggest a role in the etiology of their RPL. These differences are similar to that recently reported in India by Meena *et al*[22], in Turkey by Avciolu *et al*[23], and Dundar *et al*[24].

Furthermore, the ROC curve was drawn for each index alone and the result was significant area under the curve for the three indices and was associated with plateletcrit. Plateletcrit was reported recently by Aynioglu *et al*[25] as a low-cost, widely available marker for prediction of RPL in patients with a history of at least 1 abortus.

When the multiple logistic regression analysis for all platelets indices was conducted among the studied pregnant women, it revealed that the PDW was the significant predictor for RPL in this study. Similar finding was reported by Dundar *et al*[24], where the elevation in PDW and red blood cell distribution width values was found to be associated with RPL among their patients.

The platelet count may physiologically decrease during pregnancy. It is considered as multifactorial and is related to hemodilution, increased platelet consumption and increased platelet aggregation driven by the increased level of thromboxane A<sub>2</sub>[26]. It is suggested that during evaluation of first trimester pregnant women who suffer two or more early pregnancy loss, it is wise to use platelet indices instead of platelet count in patients with history of RPL.

This study indicates that the use of platelet indices may help gynecologist in predicting high risk pregnancy (pregnancy loss) in

the low resources areas in Yemen. Since these indices are simple, easy, cost-effective test, complete blood count including platelets' indices in following any pregnant during her first trimester is strongly recommended.

#### Conflict of interest statement

In this study, there is no conflict of interest.

#### References

- [1] Practice Committee of American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: A committee opinion. *Fertil Steril* 2013; **99**(1): 63.
- [2] Jauniaux E, Farquharson RG, Christiansen OB, Exalto N. Evidence-based guidelines for the investigation and medical treatment of recurrent miscarriage. *Hum Reprod* 2006; **21**: 2216-2222.
- [3] Wang X, Chen C, Wang L, Chen D, Guang W, French J. Conception, early pregnancy loss, and time to clinical pregnancy: A population-based prospective study. *Fertil Steril* 2003; **79**: 577-584.
- [4] Macklon NS, Geraedts JP, Fauser BC. Conception to ongoing pregnancy: The 'black box' of early pregnancy loss. *Hum Reprod Update* 2002; **8**: 333-343.
- [5] Lund M, Kamper-Jorgensen M, Nielsen HS, Lidegaard O, Andersen AM, Christiansen OB. Prognosis for live birth in women with recurrent miscarriage: What is the best measure of success? *Obstet Gynecol* 2012; **119**: 37-43.
- [6] Isaksson R, Tiitinen A. Present concept of unexplained infertility. *Gynecol Endocrinol* 2004; **18**: 278-290.
- [7] Grandone E, Margaglione M, Colaizzo D, Cappucci G, Paladini D, Martinelli P, et al. Factor V Leiden, C>T MTHFR polymorphism and genetic susceptibility to preeclampsia. *Thromb Haemost* 1997; **77**: 1052-1054.
- [8] Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: A simple, practical and specific marker of activation of coagulation. *Hippokratia* 2010; **14**: 28-32.
- [9] Colkesen Y, Muderrisoglu H. The role of mean platelet volume in predicting thrombotic events. *Clin Chem Lab Med* 2012; **50**: 631-634.
- [10] Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. *Indian J Hematol Blood Transfus* 2012; **28**: 144-146.
- [11] Sharma G, Berger JS. Platelet activity and cardiovascular risk in apparently healthy individuals: a review of the data. *J Thromb Thrombolysis* 2011; **32**: 201-208.
- [12] Lowe G. Can haemostatic factors predict atherothrombosis? *Intern Emerg Med* 2011; **6**: 497-501.
- [13] Gersh KC, Nagaswami C, Weisel JW. Fibrin network structure and clot mechanical properties are altered by incorporation of erythrocytes. *Thromb Haemost* 2009; **102**: 1169-1175.
- [14] Patel BG, Lessey BA. Clinical assessment and management of the

- endometrium in recurrent early pregnancy loss. *Semin Reprod Med* 2011; **29**: 491-506.
- [15] Bates SM, Greer IA, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO, et al. VTE, thrombophilia, antithrombotic therapy, and pregnancy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American college of chest physicians evidence-based clinical practice guidelines. *Chest* 2012; **141**(2 Suppl): e691S-736S.
- [16] Van Dreden P, Woodhams B, Rousseau A, Favier M, Favier R. Comparative evaluation of tissue factor and thrombomodulin activity changes during normal and idiopathic early and late foetal loss: The cause of hypercoagulability? *Thromb Res* 2012; **129**: 787-792.
- [17] Settin A, Alkasem R, Ali E, ElBaz R, Mashaley AM. Factor V Leiden and prothrombin gene mutations in Egyptian cases with unexplained recurrent pregnancy loss. *Hematology* 2011; **16**: 59-63.
- [18] Behjati R, Modarressi MH, Jeddi-Tehrani M, Dokoohaki P, Ghasemi J, Zarnani AH, et al. Thrombophilic mutations in Iranian patients with infertility and recurrent spontaneous abortion. *Ann Hematol* 2006; **85**: 268-271.
- [19] Santoro R, Iannaccaro P, Sottilotta G. Prothrombotic gene mutations in women with recurrent abortions and intrauterine fetal death. *Minerva Ginecol* 2005; **57**: 447-450.
- [20] Li TC, Makris M, Tomsu M, Tuckerman E, Laird S. Recurrent miscarriage: Aetiology, management and prognosis. *Hum Reprod Update* 2002; **8**: 463- 481.
- [21] Rai R, Shlebak A, Cohen H, Backos M, Holmes Z, Marriott K, et al. Factor V Leiden and acquired activated protein C resistance among 1000 women with recurrent miscarriage. *Hum Reprod* 2001; **16**: 961-965.
- [22] Meena R, Meena ML, Meena P, Meena R. Association of increased platelet distribution width and red cell distribution width with recurrent pregnancy loss. *Int J Reprod Contracept Obstet Gynecol* 2017; **6**(3): 1083-1086.
- [23] Avcıo lu SN, Altınkaya SÖ, Küçü M, Sezer SD, Yüksel H. The association between platelet indices and clinical parameters in recurrent pregnancy loss. *Gynecol Obstet Reprod Med* 2014; **20**(20): 146-149.
- [24] Dunder O, Pektas MK, Bodur S, Bakır LV, Cetin A. Recurrent pregnancy loss is associated with increased red cell distribution width and platelet distribution width. *J Obstet Gynaecol Res* 2015; **41**(4): 551-558.
- [25] Aynioğlu O, Isik H, Sahbaz A, Harma MI, Isik M, Kokturk F. Can plateletcrit be a marker for recurrent pregnancy loss? *Clin Appl Thromb Hemost* 2016; **22**(5): 447-452.
- [26] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Practice bulletin No.166: Thrombocytopenia in pregnancy. *Obstet Gynecol* 2016; **128**(3): e43-53.