The Association between Platelet Parameters and Unexplained Recurrent Miscarriagea

Original Article

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ABSTRACT

Objectives: The purpose of this study was to determine whether there is a correlation among the PLT parameters of mean platelet volume (MPV), platelet crit (PCT), and platelet (PLTs) distribution width (PDW) and unexplained RM.

Patients and Methods: This case-control study was conducted on 70 women, ranging in age from 18 to 30 years, who had a history of Recurrent Miscarriagea (RM) (defined as two or more consecutive miscarriages). There were two equal categories of women: Group A: with history of recurrent unexplained miscarriage and Group B: without history of RM and has been delivered at least once before. All were subjected to MPV, PCT, and PDW measurements.

Results: The mean age in the case category was 28.89±5.69 years, while in the control category was 31.26 ± 5.30 years. The mean of BMI in the case category was 25.44 ± 2.77 kg/m^2, whereas in the control category, was 25.26 ± 2.44 kg/m^2. Both categories showed significantly different gravidity and parity (P <0.05). No statistically significant differences were seen in the PLT count, MPV, PDW, or PCT among the two categories.

Conclusions: In women with unexplained RM, PLT count, and indices were shown to be like those in women without RM.

Key Words: Mean platelet volume, platelet distribution width, plateletcrit, recurrent miscarriage.

Received: 29 September 2024, **Accepted:** 18 November 2024

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ISSN: 2090-7265, 2025, Vol. 15

INTRODUCTION

Two or more clinical pregnancies that were unsuccessful, as confirmed by ultrasonography (US) or histopathologic investigation, are referred to as recurrent pregnancy loss (RPL). The incidence of spontaneous miscarriage rises with the mother's age and affects between 15%-25% of pregnancies[1]. Both spontaneous miscarriage and recurrent miscarriagea are described by the royal college of obstetricians and gynaecologists. The former occurs when a pregnancy ends before the fetus reaches viability, while the latter occurs when a woman has had the loss of three or more pregnancies in a row[2].

Loss of a clinical pregnancy prior to 20 completed weeks of gestational age (18 weeks following conception) is also characterized as a miscarriage. The weight (the loss of an embryo or fetus<400 grams) was used in cases when the gestational age was not known[1]. Pregnancies involving ectopic, molar, or biochemical factors are thus excluded[3]. The occurrence of a miscarriage prior to the tenth week of gestation is known as embryonic loss or early miscarriage[1]. There is a great challenge for clinicians to differentiate between sporadic miscarriage and RM. As the etiology of RM is multifactorial. Its diagnosis needs more workup starting from full history to investigations, which as consecutive spontaneous miscarriages include testing for thyroid stimulating hormone (TSH), glycated hemoglobin (HBA1C), Anticardiolipin antibody (immunoglobulin G (IgG), immunoglobulin M (IgM), and lupus anticoagulant antibodies. US for genital tract, hysteroscopy, and karyotyping which is cost-effective for couples (European Society of human reproduction and Embryology, 2017). Couples with RM experience psychological issues as a result of this[4,5].

Unfortunately, there is no available proven test that can predict RM[6]. Blood components such as platelets (PLTs) are quick to activate and offer an early response to vascular damage[7]. The average volume of thrombocytes, or mean platelet volume (MPV), is evaluated by analysers and expressed in femtoliters (fL) with normal reference values in females ranging from (8-11.6 Fl). The normal reference values for platelet distribution width (PDW) in females range from 7.8 to 16.2 fL, and it is a measure of the volume variability in platelet size. Plateletcrit (PCT) is the volume occupied by PLTs in the blood and its unit is percentage (%) and its normal reference values in females are (0.13-0.33%)[2].

DOI:10.21608/EBWHJ.2024.324146.1363

This study aimed to find the possible connection between unexplained RM and the PLT parameters namely MPV, PCT and PDW.

PATIENTS AND METHODS

This case-control study was conducted on 70 women aged from 18 to 30 years old, with history of RM (two or more consecutive miscarriages) according to American society for reproductive medicine (ASRM) [Two or more consecutive miscarriages, miscarriages must be clinically documented, meaning that they have been confirmed by ultrasound or by the passage of fetal tissue and miscarriages must have occurred before 20 weeks of gestation]. The research took place from December 2021 to June 2022 at Tanta University Hospitals in Tanta, Egypt, with the blessing of the Ethical Committee. The cases' written informed consent was acquired.

Study exclusion criteria included women who were pregnant, had certain medical conditions (such as antiphospholipid syndrome, hyperprolactinemia, or uncontrolled diabetes mellitus), were known to have uterine anomalies (as detected by ultrasound, hysterosalpingogram, or hysteroscopy), were overweight (BMI >30%), smoked, consumed 3–5 drinks per week of alcohol, or used cocaine; and their body mass index affected the study's parameters.

Each case was randomly assigned to one of two categories: Group A consists of women who have experienced many unexplained miscarriages in a row, and Group B consists of women who have given birth at least once before and do not have a history of RM.

The patients underwent a thorough evaluation that included taking their medical history, performing a physical exam, and running a battery of tests, including [complete blood count (CBC), TSH, HbA1C, anticardiolipin antibody IgG, IgM, lupus anticoagulant antibodies and serum prolactin level] and radiological investigations [transvaginal US].

Blood Sampling

A 10 ml blood sample was drawn from each patient. Samples were divided into four groups: 1st group 2ml for CBC with ethylenediaminetetraacetic acid (EDETA) tube and tested by ABX Micros 60. 2nd group 2ml for HBA1C with EDETA tube and tested by MISPA I2 machine. 3rd group 2ml for lupus anticoagulant with sodium citrate tube then the tube put in centrifuge for 10 min then use plasma in Co-date machine. 4th group 4ml for TSH, prolactin and anticardiolipin antibody with tube for 7:10 min then put in centrifuge and the serum test for TSH and prolactin in Mindray hormones machine and Immulyte machine. A PLT count is the number of PLTs in a given amount of blood, measured in PLTs per cubic millimeter of whole blood. The typical range for PLT counts is 150–400 x 109/liter, or 150,000–400,000 per microliter. MPV: thrombocyte volume measured in fL; (8 -11.6) fL. Variation in platelet volume, expressed as PDW and measured in fL, ranges from 7.8 to 16.2 fL. PCT: The proportion of blood volume that is occupied by PLTs, expressed as a percentage: (0.13-0.33%).

Sample Size Calculation

Using with the use of a t-test for equal variance on both sides of the sample[8]. When the population effect size is 0.70 (moderate to large) and the significance level (alpha) is 0.050, a group sample size of 35 per group achieves 80% power to reject the null hypothesis of zero effect size. To determine the sample size, the PLT indices' means were utilized.

Statistical analysis

We used SPSS v26 (IBM Inc., Chicago, IL, USA) for our statistical analysis. To determine if the data was normally distributed, the Shapiro-Wilks test and histograms were employed. We used an unpaired Student's t-test for comparing the two categories for quantitative parametric variables, which were given as means and standard deviations (SD). Our quantitative non-parametric data was evaluated using the Mann Whitney-test and provided as median and interquartile range (IQR). Frequency and percentage (%) were used to present qualitative variables, which were examined using either the Chi-square test or Fisher's exact test as applicable. Statistical significance was determined by a two-tailed *P value* less than 0.05.

RESULTS

Eighty-two people met the investigation's inclusion criteria. They underwent a full blood profile as part of the PLT indices test. Twelve samples had inconclusive results because of technical issues with the samples given. It was determined that 70 women met the ASRM criteria. The following diagram shows the distribution of the two groups of women: category A, consisting of 35 women with unexplained RM, and category B, consisting of 35 women who had given birth at least once and had no history of miscarriage (Figure 1).

The mean of age in case group was 28.89±5.69 years, while in control group was 31.26 ± 5.30 years. The mean of BMI in cases group was 25.44 ± 2.77 kg/m^2, whereas in the control group, was 25.26 ± 2.44 kg/m2 (Table 1).

Gravidity and parity were significantly different between both categories (P <0.05). PLT count, MPV, PDW and PCT were insignificantly different between both categories (Table 2).

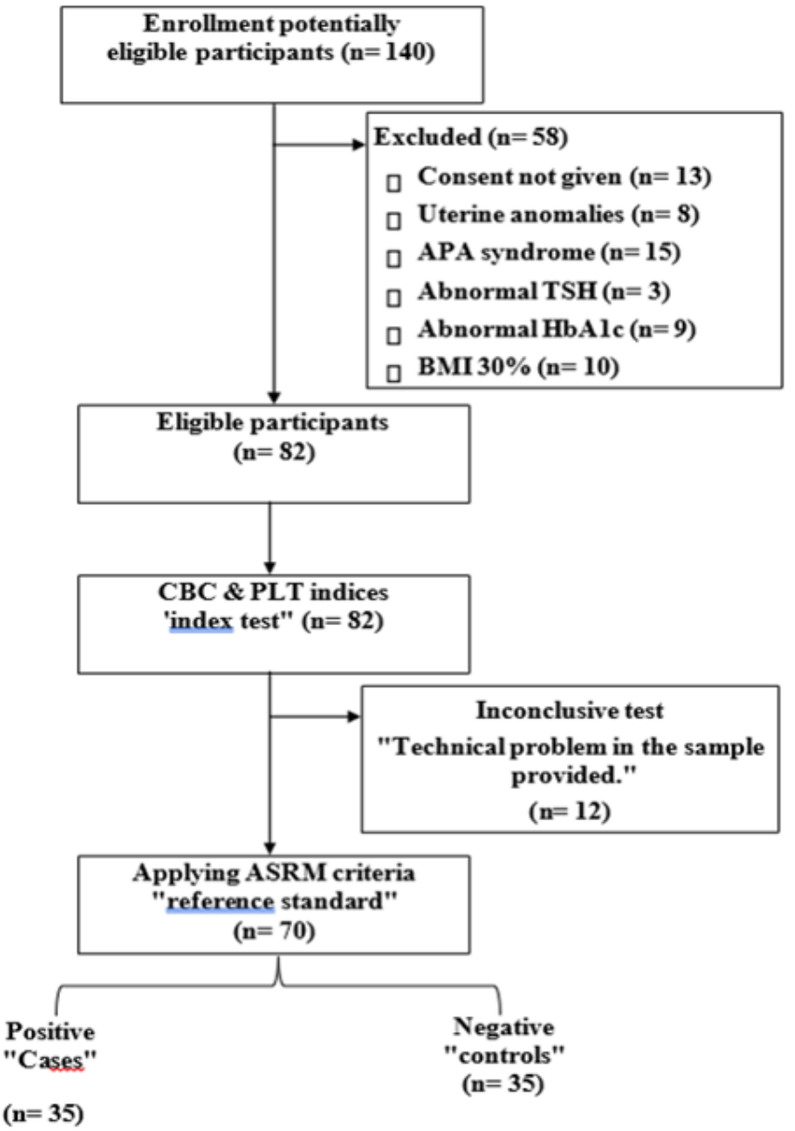

Fig. 1: Flowchart of the enrolled participants

Table 1: Demographic data of the cases and control group

	Cases group (n=35)	Control group (n=35)
Age (years)	28.89±5.69	31.26±5.30
BMI (kg/m^2)	25.44±2.77	25.26±2.44

Data are presented as mean ± SD. BMI: body mass index.

Table 2: Comparison between the two studied groups according to obstetric history, PLT count, and indices

		Cases group (n=35)	Control group (n=35)	*P*
Obstetric history	Gravidity	4.0	3.0(2.0–3.0)	<0.001*
	Parity	1(0.0–2.0)	3.0(2.0–3.0)	<0.001*
PLT count		285±26.8	296±27.8	0.888
PLT indices	MPV	11.04 ±0.96	10.65±0.80	0.069
	PDW	13.37 ±2.21	12.46±1.90	0.070
	PCT	0.31±0.07	0.31±0.08	0.755

Data are presented as mean ± SD or median (IQR). *Significant *P value* <0.05. PLT: platelet, MPV: mean platelet volume, PDW: platelet distribution width, PCT: Plateletcrit.

DISCUSSION

RM is a heterogeneous multifactorial condition. Among reproductive-age couples who are fertile, its prevalence is estimated to be around 1%[8]. Although there are a number of potential reasons, between fifty and sixty percent of the time, the exact reason is unknown[9]. Because coagulation proteins undergo changes during pregnancy, the body becomes hypercoagulable. The hemostatic equilibrium in placental vasculature is altered due to an elevation in prothrombotic factors and a reduction in antithrombotic factors. This leads to insufficient placental perfusion and feto-maternal circulation insufficiency[10].

Many diseases affecting the female reproductive system, including RM, have recently been linked to inadequate inflammatory responses[11]. Immunopathological evaluations of abortus material at placental implantation sites show inflammation, fibrin accumulation in the decidua, and thrombosis in decidual arteries, suggesting that coagulation abnormalities and inflammation play a role in the pathogenesis of RM[12].

No comparison of miscarriage rates was needed between study groups due to predefined selection criteria. The control group consisted solely of women who had delivered at least once without a history of miscarriage. Consequently, an implicit assumption was made that these control subjects did not have any miscarriages to report, in contrast to the RM group.

In most cases, a high PLT count indicates inflammation. Our research found no statistically significant difference in PLT count among the two sets of participants. alongside the most recent case-control investigation by Desoky *et al*.[13] found no significant differences in PLT count, PCT, MPV, or PDW among the two groups. Also, Najjar *et al*.[14] reported no significant differences between cases and controls in PLT parameters, antinuclear antibodies, or thyroid markers. In contrast, Alaghbary *et al*.[15] reported a significant difference in PLT count between women with RPL compared to controls.

PCT reflects the total PLT mass in a given volume of blood[16]. Our study found no significant difference in PCT among women with a history of RM and control women. This aligns with findings by Desoky *et al*.[13] reported no significant PCT difference between RM cases and controls in their research. However, a conflicting investigation by Sever Erdem *et al*.[17] showed highly significant differences in PCT values between RPL cases and controls.

MPV reflects the average PLT size and can indicate PLT activation and function[18]. Some research suggests that increased PLT aggregation and clotting during early placental development is associated with high MPV and may lead to pregnancy loss[19]. Thus, MPV may have value as a biomarker for conditions causing abnormal PLT destruction and low PLT count, like immune thrombocytopenia, preeclampsia, sepsis, and certain inherited PLT disorders such as Bernard-Soulier syndrome[20]. High MPV alongside thrombocytopenia can signify underlying PLT abnormalities contributing to RM risk. More research is needed to determine the practical use of MPV in RPL prediction and management[21]. This finding conflicts with a study by Amin *et al*.[20] detected a remarkably distinct variation in MPV throughout the categories.

The present study found no significant PDW difference between RM cases and controls. This agrees with Desoky *et al*.[13] findings. However, three recent conflicting studies dispute our findings. Sever Erdem *et al*.[17] identified no statistically significant variations in PLT indicators, including PDW, among the control group and the patients Additionally, Anter *et al*.[22] found highly significant PDW differences between cases and controls, with PDW significantly predicting RPL Moreover, a recent meta-analysis of 11 case-control studies by Shi and Xu.[23] discovered that, in comparison to the control category, the recurrent loss category had a substantially higher PDW.

A small sample size was one of the investigation's limitations. So, we recommended that PLT counts and indices should not be used for predicting cases of unexplained RM. Exploration of the exact role of PLT function and activation in the pathophysiology of RM.

CONCLUSIONS

In women with unexplained RM, PLT count, and indices were shown to be like those in women without RM.

ABBREVIATIONS

RM: Recurrent Miscarriagea, **PLTs:** Platelets, **MPV:** Mean Platelet Volume, **PCT:** Platelet Crit, **PDW:** Platelet Distribution Width, **US:** Ultrasonography, **RPL:** Recurrent Pregnancy Loss, **TSH:** Thyroid Stimulating Hormone, **IgG:** Immunoglobulin G, **IgM:** immunoglobulin M, **Fl:** Femtoliters, **ASRM:** American Society for Reproductive Medicine, **CBC:** Complete Blood Count, **EDETA:** Ethylenediaminetetraacetic Acid

CONFLICT OF INTERESTS

There are no conflicts of interest.

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