Original Article

Can the Laboratory Results Contribute in the Predıct of Postpartum Haemorrhage

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Abstract

Objective: To determine whether laboratory tests can contribute to the definition of postpartum hemorrhage.
Methodology: The study included 49 patients with postpartum haemorrhage above normal limits due to postpartum uterine atony and 57 healthy women without postpartum haemorrhage (bleeding within normal limits after delivery) in Obstetrics and Pediatrics Hospital in the Adana hospital in the 11month period between January and November 2019.
Results: The rate of the haemoglobin level below 8 g/dl was significantly higher in the group with postpartum atony ($p<0.001$). The mean PDW(Platelet Distribution Width) ($p<0.001$) and neutrophil / lymphocyte ratio (NLR) ($p<0.001$) were significantly higher in the patient group with atony compared to the control group. In the ROCanalyses performed, the threshold value for PDW, which was 18.85, was found to have a sensitivity of 86.3% and a specificity of 98.2% for the development of postpartum atony (AUC: 0.912; $p<0.001$; LB: 0.847; UB: 0.977; CI 95%).
Conclusion: Our study data showed that among the laboratory findings, especially PDW, haemoglobin and NLR levels are important information providers in predicting postpartum uterine atony and excessive bleeding afterward. Also, it was seen that the threshold value determined as 18.15 for PDW can be used as a reliable marker with high sensitivity (86.3%) and specificity (98.2%) in predicting excessive postpartum haemorrhage.

Keywords: Uterine atony, postpartum haemorrhage, PDW,NLR.

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Introduction

Early diagnosis and early intervention of postpartum haemorrhages are of great importance in terms of preventing serious complications. Postpartum bleeding is defined as bleeding that exceeds 500 ml in the first 24 hours after normal spontaneous delivery and 1000 ml after caesarean delivery. Primary or early PPH (Postpartum haemorrhage) is defined as bleeding that develops within the first 24 hours after birth while bleeding between 24 hours and 12 weeks after birth is defined as secondary or late postpartum haemorrhage.[1,2] Traditionally, PPH was defined as 500 ml after vaginal delivery and 1000 ml after cesarean delivery, while the current, mild bleeding by the clinician and invisible bleeding also makes this definition difficult to use in the clinic.[3,4]

Another definition is a 10% reduction in hematocrit. In these studies, however, it is not suitable for the clinical management of massive bleeding. It is widely used in this definition because of the serious differences in clinical practice for bleeding that causes PPH to need

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transfusion.[5]

Although there is no accepted clear definition of postpartum haemorrhage, any amount of bleeding that may threaten the patient's hemodynamic balance should warn the clinician. Postpartum hemorrhages are among the most common causes of maternal deaths. According to multiple sources the most common causes of postpartum hemorrhage are uterine atony, birth tract trauma and placental tissue retention. It has been shown that the risk of postpartum bleeding is higher in women with a history of atony in previous pregnancies, twin pregnancies, or large babies.[6,9]

Uterine atony is a condition in which the contraction and relaxation of the myometrium is impaired after birth. Contractions in the myometrium are the most important factors that stop postpartum bleeding. After the deterioration of these contractions, bleeding in the genital canal and softening due to loosening in the uterus occur. The amount of bleeding that occurs is an important cause of morbidity and mortality.[6,7,10,11] Multiple sources show that the most common factors causing uterine atony are multiple pregnancy, faetal macrosomia, polyhydramnios, labour induction, prolonged labour, history of postpartum haemorrhage in previous pregnancies, obesity, pregnancy status over 35 years of age and various medications.[6,8,11,12]

According to reports physiological hypovolaemia and anaemia level during pregnancy is also effective in prognosis as well as the amount of bleeding in postpartum bleeding. Early recognition and early intervention of postpartum hemorrhages are of great importance in terms of preventing possible serious complications such as hysterectomy or death. For these reasons, hematological parameters and laboratory findings provide important information in the follow-up of pregnant women and in the management of bleeding due to postpartum uterine atonia.[13-16]

PDW is a parameter that gives a measure of the distribution of the size of platelets in the blood. The size and size of the platelets are checked according to the value in the PDW test. Reference values for PDW results were 13.28 with 8 fL in females; It has been calculated between 9 fl and 16.56 fL for males. The reasons for the height of the PDW are as follows: Infectious diseases, Birth control pill, Cancer types, Anemia, Inflammatory disorders, Having the spleen removed, Tuberculosis.

Neutrophil lymphocyte ratio (NLR); The role of cellular immune response, lymphocytes, neutrophils and monocytes in tumorigenesis and carcinogenesis is increasingly recognized. In general, lymphopenia reflects the weakness of cellular immunity, while neutrophilia is a parameter that indicates the response to systemic inflammation. The ratio of these two values to each other can be interpreted as the magnitude of systemic inflammation indicating the adequacy of the cellular immune response against this situation.

In some studies, differences were found in Nlr levels in cardiovascular diseases, thromboembolic conditions, neurovascular diseases, ureter stones, malignancy, and gastrointestinal diseases compared with the normal population.

This study aimed to compare the laboratory findings of patients with excessive postpartum bleeding due to postpartum uterine atony and patients with postpartum hemorrhage within normal limits.

Methodology

This cross-sectional study was approved by the local ethics committee and was planned prospectively.All procedures performed in this study involving human participants were following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

The study included 49 patients who had postpartum haemorrhage above normal limits due to postpartum atony after delivery in the Obstetrics and Gynaecology Department of Obstetrics and Pediatrics Hospital in the Adana hospital in the eleven months between January and November 2019, as well 57 healthy women with postpartum haemorrhage within normal limits after delivery. Blood samples of both patient groups were drawn at the postpartum second hour and their laboratory results were compared. The blood was collected by venepuncture in EDTA vacutainers, gel tube as well as PT tubes containing anticoagulant sodium citrate and processed immediately.

The patient group was evaluated by dividing them into two groups, under 35 years old and 35 years and over.[17]Those with rest placenta, deep laceration, uterine inversion, placentation anomalies, and uterine rupture were excluded from the study. Those with chronic diseases or bleeding or coagulation disorders were excluded from the study. Laboratory findings of all participants at the time of admission to the hospital

were taken from the hospital automation system records and analysed.

The study had a power of 0.899 with 106 participants, calculated using Gpower 3.1.9.7 software (Franz Faul, Universität zu Kiel, Germany).All statistical analyses in the study were performed using SPSS 25.0 software. Descriptive data were given as numbers and percentages. Comparisons between groups in terms of categorical variables were made using Pearson's Chi-Square test. Whether continuous variables were suitable for normal distribution was confirmed by the Kolmogorov-Smirnov Test. Differences between groups in terms of continuous variables were analyzed using Student's t Test. The risk coefficient of categorical variables was evaluated by logistic regression analysis and given as “odds ratio”. Platelet distribution width (PDW) capacity to predict the development of atony in patients was analysed using receiver operating characteristic (ROC) curve analysis. P<0.05 values were considered significant.

Results

The rate of haemoglobin level below 8 g/dl was significantly higher in the group with postpartum atony (p<0.001). The risk of haemoglobin below 8 g / dl in the group with atony was calculated as 2.5 times higher than in the other groups (Odds ratio: (-1.954_3.198-) (Table I).

Table I: Distribution of delivery types and risk analysis by groups.

	Atony (n=49)	Control (n=57)	Total (n=106)	p	OR
Haemoglobin level				<0.001	-
<8 g/dl	13 (100%)	0 (0%)	13		2.5 (1.954-3.198)*
8-10 g/dl	12 (34.3%)	23 (65.7%)	35		
10-12 g/dl	18 (38.3%)	29 (61.7%)	47		
≥12 g/dl	8 (61.5%)	5 (38.5%)	13		

Risk coefficient of the group with <8 g / dl compared to the other groups. OR: Odds ratio.

The mean age of those with atony was 28.4 ± 7.8 years, the mean age of the control group was 27.0 ± 5.1 years. There was no significant difference in mean age between the two groups (p = 0.258). In the patient group with atony, mean leukocyte (p<0.001), neutrophil (p<0.001), PDW (p<0.001), neutrophil percentage (p = 0.003), neutrophil / lymphocyte ratio (p<0.001), serum glucose (p<0.001) and aPTT (p<0.001) were significantly higher than in the control group. In the atony group, mean erythrocyte number(p = 0.017), hematocrit (p = 0.012), lymphocyte percentage (p = 0.003), monocyte (p<0.001), calcium (p = 0.002) and fibrinogen (p<0.001) levels were controlled. It was significantly lower than the other group (Table II).

Table II: Comparison between postpartum atony and control groups in terms of average laboratory values.

	Atony		Control		p
	Mean	**SD**	**Mean**	**SD**	
Age (years)	28.4	7.8	27.0	5.1	0.258
WBC (103/mL)	17.9	6.8	12.5	3.1	<0.001
RBC (106/mL)	3.4	0.7	3.7	0.4	0.017
Haemoglobin	9.9	2.3	10.5	1.3	0.115
Haematocrit (%)	29.7	6.6	32.3	3.5	0.012
Platelets (103/mL)	202.2	87.2	188.6	49.5	0.314
MCV (mm3)	85.4	12.3	87.7	7.9	0.236
MPV (fL)	9.2	1.4	9.4	1.1	0.535
PDW (fL)	42.1	17.7	17.8	0.7	<0.001
Neutrophil (109/L)	4.7	1.2	3.4	1.1	<0.001
Lymphocyte (%)	10.6	12.1	16.1	5.9	0.003
Neutrophil (%)	83.3	16.3	76.1	7.2	0.003
NLR	12.3	8.8	5.8	3.5	<0.001
LMR	3.2	2.9	2.9	3.1	0.655
Monocyte (109/L)	3.7	1.7	6.6	2.1	<0.001
Eosinophil (109/L)	1.2	4.1	0.7	0.9	0.395
Glucose (mg/dL)	160.4	67.6	91.3	19.6	<0.001
PT (Sec)	12.6	2.1	13.5	11.3	0.576
aPTT (Sec)	30.9	9.0	25.6	2.7	<0.001
Fibrinogen (mg/dL)	267.4	105.2	354.2	65.7	<0.001

RBC: red blood cells, MCV: mean corpuscular volume, MCH: mean corpuscular haemoglobin, MCHC: mean corpuscular haemoglobin concentration, WBC: white blood cells, MPV: Mean platelet volume, MCV: NLR: Neutrophil / lymphocyte ratio, LMR: Lymphocyte / monocyte ratio, M: Average, SD: Standard deviation.

In the postpartum atony group, all the average laboratory values were found similar between the

groups under 35 and over 35 years old (p>0.05 for each) (Table III).

Table III. Comparison of the postpartum atonia group between the age groups under 35 and over 35 in terms of average laboratory values.

	<35		≥35		p
	Mean	**SD**	**Mean**	**SD**	
WBC (103/mL)	18.1	7.1	17.1	5.9	0.671
RBC (106/mL)	3.5	0.8	3.3	0.6	0.574
Haemoglobin	10.0	2.4	9.5	1.8	0.522
Haematocrit (%)	30.0	7.0	28.4	5.4	0.472
Platelets (103/mL)	208.6	93.6	179.3	55.7	0.329
MCV (mm3)	85.4	13.2	85.4	8.7	0.993
MPV (fL)	9.2	1.3	9.2	1.8	0.981
PDW (fL)	43.3	18.1	37.6	16.1	0.349
Neutrophil (109/L)	4.6	1.3	4.7	1.1	0.677
Lymphocyte (%)	11.2	13.5	8.4	4.7	0.495
Neutrophil (%)	82.4	18.5	86.2	5.6	0.507
NLR	12.1	9.2	13.1	7.5	0.742
LMR	3.5	3.3	2.2	1.3	0.210
Monocyte (109/L)	3.6	1.7	4.3	1.7	0.266
Eosinophil (109/L)	1.4	4.7	0.4	0.5	0.511
Glucose (mg/dL)	2.1	5.7	11.7	28.0	0.165
PT (Sec)	106.0	3.7	107.6	4.0	0.222
aPTT (Sec)	1.4	1.6	1.1	0.2	0.628
Fibrinogen (mg/dL)	31.0	9.0	30.4	9.2	0.839

RBC: red blood cells, MCV: mean corpuscular volume, MCH: mean corpuscular haemoglobin, MCHC: mean corpuscular haemoglobin concentration, WBC: white blood cells, MPV: Mean platelet volume, MCV: NLR: Neutrophil / lymphocyte ratio, LMR: Lymphocyte / monocyte ratio, M: Average, SD: Standard deviation.

In the ROC analyses performed, the threshold value for PDW, which was 18.85 fL, was found to have a sensitivity of 86.3% and a specificity of 98.2% for the development of postpartum atony (AUC: 0.912; p <0.001; LB: 0.847; UB: 0.977; CI 95%) (Figure 1).

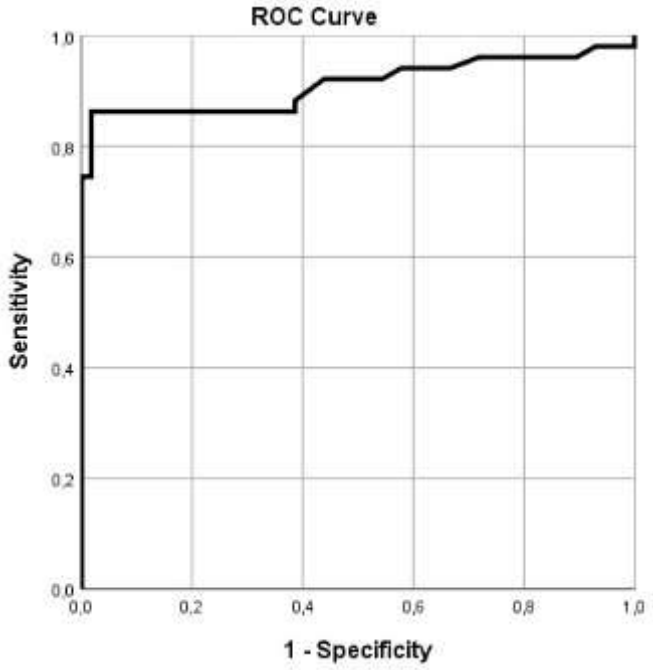

Figure 1. The threshold value for PDW, which was 18.85 fL, was found to have a sensitivity of 86.3% and a specificity of 98.2% (AUC: 0.912; p <0.001; LB: 0.847; UB: 0.977; CI 95%).

In the risk analysis performed, the risk of atonia was found to be 2.86 times higher (OR: 9.137-551.048) in those aged 35 and over compared to those under 35 (Odds ratio: 0.92-8.93).

Discussion

Postpartum uterine atony is a medical emergency because it causes a life-threatening condition by causing excessive bleeding after birth. Prediction of postpartum atony, early diagnosis and early intervention can prevent complications and save live.[1-4] In our study, demographic data and laboratory findings of those with postpartum atony were compared with those with postpartum haemorrhage within the normal range, and some haematological parameters such as PDW, haemoglobin and NLR were found to provide important information.

Reportedly postpartum uterine atony and bleeding can be seen more frequently in women over the age of 35.[1-3,12,13] Driessen et al. [18] calculated that the risk of postpartum hemorrhage in those over the age of 35

was 0.83 times higher than those younger than 35. Lao et al.[12] found that the rate of having postpartum haemorrhage in women over 35 years of age was significantly higher than those below the age of 35, and they calculated that the risk of postpartum hemorrhage increased by 1.23 times in women over 35 years of age. However, these researchers could not find a significant difference between age groups in terms of the uterine atony development rate. Montufar-Rueda et al. [9] reported in their multicente study that there was no significant difference in mean age between those who died and survivors among women who had postpartum bleeding. In the risk analysis performed in our study, the risk of atonia was found to be 2.86 times higher (OR: 9.137-551.048) in those aged 35 and over compared to those under 35 (Odds ratio: 0.92-8.93). These data indicate that the risk of postpartum atony in pregnant women over the age of 35 may be higher than in younger women and thus,these pregnant women should be followed up closely.

According to research, anaemia level increases the risk of postpartum haemorrhage and may negatively affect the level and prognosis of postpartum bleeding.[7-9,17,20] Lao et al.[12] determined that 48% of those with severe anaemia had a severe postpartum haemorrhage. Wetta et al. [20] calculated that the risk of developing atony increased 1.9 times in those with haemoglobin below 9 g / dl. Although there was no significant difference in the mean haemoglobin level between the atony and control groups in our study, the rate of haemoglobin level below 8 g / dl was significantly higher in the group with postpartum atony (p <0.001). The risk of hemoglobin below 8 g / dl in the group with atony was calculated as 2.5 times higher than the other groups (Odds ratio: (1.954-3.198).

Platelets are one of the main elements in the process of stopping bleeding. Platelet count in the blood is a very important parameter related to bleeding. Also, the platelet distribution volume,PDW, is a value that provides information about the size of the circulating platelets. If the platelets are of larger volume, this means they have been newly produced. The fact that the platelets are newly produced usually indicates acute bleeding in the body. An increase in the PDW value can be expected with the large amount of bleeding.[21-25] Artunç-Ülkümen et al.[23] reported that the increased PDW value in pregnant women provides meaningful information about the risk of preterm labour, and that the threshold value of 16.15 fL has a medium high sensitivity and specificity value. Arlier et al. [24] calculated in their ROC analysis that the threshold value of 18.5 fL for PDW had 100% sensitivity and 71.6% specificity in predicting placental abruption. Senel etal.[25]found that the mean PDW value increased significantly in patients hospitalized due to gastrointestinal bleeding compared to the control group, and that increased PDW increased the risk of long-term hospitalization 9.66 times. In their ROC analysis, they also calculated that the threshold value of 13.95 fL for PDW had a sensitivity of 99.2% and a specificity of 98.6% in predicting bleeding in the patient. In our study, PDW value was found above the limit value (>13 fL) in all women. This is because women have just given birth and all of them have postpartum bleeding. However, in our study, the mean PDW (p <0.001) in the patient group with atony and excessive bleeding was found to be significantly higher than the control group. This finding means that PDW increases excessively in those with postpartum excessive bleeding. In the ROC analysis, the threshold value for PDW, which was 18.85 fL, was found to have a sensitivity of 86.3% and a specificity of 98.2% for the development of postpartum atony (AUC: 0.912; p <0.001; LB: 0.847; UB: 0.977; CI 95%). This finding shows that the fact that the PDW value measured after birth exceeds 18.85 fL is likely to indicate excessive postpartum bleeding in the patient. Accordingly, in patients with postpartum haemorrhage, PDW value can be used as an auxiliary haematological parameter that provides reliable information to distinguish patients with and without excessive bleeding.

In acute inflammation, it has been reported that the neutrophil count and the calculated neutrophil/lymphocyte ratio, namely the NLR value, increase significantly in bleeding situations as well as in many clinical disorders.[26-28] Lattanzi et al.[27] and Liu et al.[28] reported that NLR increased significantly in patients with cerebral hemorrhage. In Fibrinogen>4 g/litrehad a negative predictive value of 79% for severe haemorrhage, whereas fibrinogen≤2 g/litrehad a positive predictive value of 100%. The data corroborated large retrospective studies reporting fibrinogen levels on admission to the labour ward as the factor most significantly correlated with the incidence of PPH.our study, the mean NLR value in the patient group who developed atony and excessive bleeding afterward was found to be significantly higher than the control group (p <0.001).

It is known that there are acute increases in some laboratory values in patients with acute

bleeding.[20,21,26,27] In our study, the mean leukocyte (p <0.001), leukocyte (p <0.001), serum glucose (p <0.001) and aPTT (p <0.001) were found to be significantly higher in the patient group who developed atony and excessive bleeding after delivery. These data indicate that changes in haematological parameters should be closely monitored after birth.

Both PT and aPTT appear to have value during monitoring for hemostasis during PPH. A recent review of 18,501 deliveries in the UK identified 456 cases complicated by blood loss of more than 1500 ml. 12 PT did not correlate with bleeding volume and aPTT was poorly correlated. The results have been demonstrated by previous research concluding that PT and aPTT have a useful response in predicting PPH progression.[29-30]

In a prospective study of 128 patients, plasma fibrinogen reduction during early PPH was the only variable independently associated with progression to severe PPH.[29]

Fibrinogen had a negative predictive value of 79% for severe bleeding> 4 g / liter, while fibrinogen had a positive predictive value of 2 g / liter of 100%. He confirmed the large retrospective study that reported fibrinogen levels at admission to the maternity ward as the factor most significantly associated with the incidence of PPH.[30]

Conclusion

In our study, in the postpartum atony group, all the average laboratory values were found similar between the groups under 35 years old and those aged 35 years and over (p> 0.05 for each). This finding indicates that the changes in haematological parameters in the case of postpartum atony and excessive bleeding afterward are independent of age.

There were some limitations to the study. Since the study was planned cross-sectionally, the patients were not followed up in the long term and could not be evaluated in terms of complications. In addition, since the number of multiple pregnancies was extremely low in our study, risk analyses regarding multiple pregnancies could not be performed.

In the patient group with atony, mean leukocyte (p <0.001), neutrophil (p <0.001), PDW (p <0.001), neutrophil percentage (p = 0.003), neutrophil / lymphocyte ratio (p <0.001), serum glucose (p <0.001) and aPTT (p <0.001) were significantly higher than in the control group.

In the atony group, monocyte (p <0.001), fibrinogen (p <0.001) levels were controlled. It was significantly lower than the group.

Our study data showed that among the laboratory findings, especially PDW, hemoglobin and NLR levels are important information providers in predicting postpartum uterine atony and excessive bleeding afterward. Besides, it was seen that the threshold value determined as 18.15 for PDW can be used as a reliable marker with high sensitivity (86.3%) and specificity (98.2%) in predicting excessive postpartum haemorrhage.

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