Predictive Value of Complete Blood Countparameters in Placenta Accreta

Original Article

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ABSTRACT

Background: The CBC is easy tool for pregnant women predicting placental invasion anomalies, Numerous studies proposed that cancer cell invasion has several common features with the trophoblast invasion^[1]. The neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios are recent popular markers for inflammatory response and have been applied as predictive markers and prognostic factors in various gynecological cancers^[2]. We found in placenta accreta increasing Mean platelet Volume(MPV), Neutrophil / lymphocyte (N/L) ratio, decreasing Red cell Distribution Width (RDW), Platelet's count.

Aim of the Work: Aim of our study is to assess the relationship between complete blood count parameters and placental invasion anomalies.

Materials and Methods: Our study is Prospective cohort study done in Labour ward of Ain Shams University Maternity Hospital. From January 2019 to December 2019. On Pregnant women attended Ain Shams University Maternity Hospital with a placenta previa. This study was done after approval of the ethical committee of the department of obstetrics and gynecology, Faculty of Medicine, Ain Shams University. Informed consent was taken from all participants before recruitment in the study, and after explaining the purpose and procedures of the study. The investigator obtained the written, signed informed consent of each subject prior to performing any study specific procedures on the subject. The investigator retained the original signed informed consent form. All laboratory specimens, evaluation forms, reports, video recordings and other records that left the site did not include unique personal to maintain subject confidentiality. The study was based on the investigator self-funding. The main object was presence of significant differences between groups with and without placental invasion anomaly in terms of age, platelet count, mean platelet volume, red cell distribution width and neutrophil to lymphocyte ratio P < 0.05.

Conclusion: There are changes in CBC parameters which can predict placental invasion anomalies such as increase in Mean platelet Volume(MPV), Neutrophil / lymphocyte (N/L) ratio and decrease in Red cell Distribution Width (RDW), Platelet's count. The cut point's in predicting placenta accreta by complete blood count are. Mean platelet Volume(MPV) \geq 8,1fl had the highest diagnostic characteristics. Neutrophil / lymphocyte (N/L) ratio \geq 4.1. Red cell Distribution Width (RDW) \leq 16.6%. Platelet's count \leq 264.0(x103/mL).

Recommendations: In suspected cases of placenta accrete by ultrasound, We recommend to evaluate every change in CBC parameters which can predict placental invasion anomalies eg. Mean platelet Volume(MPV), Neutrophil / lymphocyte (N/L) ratio and Red cell Distribution Width (RDW), Platelet's count.

Key Words: DA: Diagnostic accuracy, **LR:** Diagnostic odd ratio, **LR+:** Positive likelihood ratio, **LR-:** Negative likelihood ratio, **NPV:** Negative Predictive value, **PAS:** Placenta accreta spectrum; **PRBC:** packed red blood cells; **PPV:** Positive Predictive value.

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INTRODUCTION

Implantation requires decidualization and vascular remodeling to provide essential nutrients and substrates to embryo. Some pregnancy complications such as early pregnancy loss, ischemic placental diseases, preeclampsia, intrauterine fetal growth restriction and premature delivery result from disturbed vascular growth in the placenta.^[3] Invasive nature of trophoblasts requires a strict control for healthy placentation.^[4] Highly invasive nature of trophoblastic tissue may result in abnormal attachments to the uterine wall and therefore trophoblastsmay invade into the myometrium.^[5]

The development of PAS is a complex multifactorial process. Normal placenta do not proceed beyond the inner third of the myometrium through tight spatial and temporal

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regulation; however, an invasive placenta proliferates and invades local structures in a similar fashion to a malignant tumour. The underlying molecular mechanisms of invasive placentation are poorly understood; proposed hypotheses include a combination of primary absence of the decidua or basal plate, abnormal maternal vascular remodelling, and excessive extravillous trophoblastic invasion.^[6]

Improved understanding of the molecular basis of other placental disorders such as preeclampsia suggests the inflammation and placental invasion may be closely related. A number of comparisons can be drawn between the microenvironment of PAS and tumour behaviour. Both conditions require an ability of cells to overcome the local immunological systems, activate invasion, and induce angiogenesis. In 2012, Hanahan and Weinberg outlined eight hallmark capabilities of tumours which allow them to invade and metastasise. Herein, we use these eight hallmarks of cancer to highlight some of the molecular similarities between PAS and tumour development.^[7] Including: Inducing Angiogenesis^[8] Sustained Proliferative Signalling^[9] Resisting Cell Death^[10] Evading Immune Destruction^[11] Activating Invasion^[12] Enabling Replicative Immortality/Evasion of Growth Suppression^[13] & Reprogramming of Energy Metabolism.^[14]

In women with a history of prior cesarean delivery(CD), scar defects are found to range between 20-65% of the myometrium after delivery on transvaginal ultrasound. Women with a residual myometrial thickness of <50% of the adjacent myometrium are more likely to develop chronic complications such as intermenstrual spotting.^[15] The myometrial fibers around a scar often show hyalinization or degenerative changes, with a local increase in fibrous tissue and infiltration by inflammatory cells. The comparison of ultrasound features of uterine cesarean scar with histological findings has shown that large and deep myometrial defects are often associated with absence of reepithelialization of the scar area.^[16]

Leukocytes recruitment to the endometrium during the secretory phase may also be affected by the presence of a CD scar. A recent study of the uterine circulation in women with a previous CD has shown that the uterine vascular resistance is increased, while the volume blood flow is decreased, compared to women with a previous vaginal birth.^[17]

These data suggest that the blood circulation around the scar is impaired. Poor vascularization of the scar area may lead or contribute to permanent focal myometrial degeneration, as well as reduced or absent reepithelialization of the scar area.

Numerous studies proposed that cancer cell invasion has several common features with the trophoblast invasion.^[1]

The neutrophil-to-lymphocyte and platelet-tolymphocyte ratios are recent popular markers for inflammatory response and have been successfully applied as predictive markers and prognostic factors in variousgynecological cancers.^[2]

AIM OF THE WORK

Our study is to assess the relationship between complete blood count parameters and placental invasion anomalies.

PATIENTS AND METHODS

Our study is Prospective cohort study done in Labour ward of Ain Shams University Maternity Hospital. From January 2019 to December 2019. On Pregnant women attended Ain Shams University Maternity Hospital with a placenta previa. The inclusion criteria were: Pregnant women with confirmed diagnosis of variable degrees of placenta previa, Gestational age between 37 and 42 weeks, Singleton pregnancy, Living fetus & Elective CS With the possibility of cesarean hysterectomy during delivery. and The exclusion Pregnant women with vaginal bleeding related to other causes, Multiple gestation, Any systemic including cardiovascular, endocrinological, disease metabolic, inflammatory and autoimmune disorders, Prepregnancy obesity (BMI 30 kg/m2), Smoke or on any drug other than iron medication, Fever. Chorioamnionitis.Any septic focus & Any infectious diseases interfering with leukocytic counts and functions.

Study Procedures:

Totally 160 pregnant women with placenta previa who were suspected for placental invasion anomalies underwent complete blood count screening before cesarean section

The localization of the placental implantation and the depth of myometrial invasion were identified on admission with transabdominal and transvaginal 2D gray scale and Doppler sonography by Sonoace Samsung R5 machine (2-8 MHZ, made in korea).

We considered the ultra-sonographic findings of irregularity or loss of the retro-placental echo-lucent area between the uterus and the placenta, thinning of the myometrium to less than 1 mm at the site of placental bed, protrusion of the placenta into the bladder, increased vascularity of the uterine serosa and the bladder wall interface, irregular intra-placental vascularization and the presence of turbulent placental lacunae with high velocity flow, diagnostic of placental invasion anomaly.

The depth and extent of the hyper-vascularized areas were also assessed. The intraoperative diagnosis of the placental abnormality was confirmed at the time of cesarean section and also in histopathological evaluation whatever the patient underwent hysterectomy or not done by consultant obstetricians. All blood samples were retrieved by venipuncture at the time of admission prior to delivery, venipuncture is the most common way to collect blood from adult patient especially the antecubital area of the arm, collection of blood sample take place from the superficial vein in the upper limp generally the median cubital vein this vein is close to the skin and doesn't have many large nerve this reduce pain & discomfort for the patient, and in all cases parameters of complete blood count including lymphocyte, platelet count and red cell distribution width (RDW), neutrophil/lymphocyte ratio and mean platelet volume (MPV) were analyzed to predict cases with real placental invasion anomaly, samples were drawn into vacuum tubes containing edetatetripotassium. total leucocytes & platelets were counted with an automated cell counter (Hemalog).

Sample Size Justification:Using PASS program; setting alpha error at 5% and confidence interval width 0.15. Result from previous study^[18] showed that the prevalence of placentaaccreta among placenta previa was 31.5%. Based on this with taking in consideration 10% drop out rate the needed sample size is 160 cases.

Statistical analysis:

The analysis was carried out using PASS version 11. Continuous variables were compared between groups by Student-t test. ROC analyses was used to analyze the predictive value of some variables. Sensitivity test, specificity test, positive predictive value and negative predictive value were calculated. Multi-variate regression analyses was used to show adjusted associations. P < 0.05 was accepted to be statistically significant.

RESULTS

Cł	naracteristics	Mean±SD	Range
I	Age (years)	28.7±4.0	22.0-37.0
В	MI (kg/m^2)	26.4±1.7	21.7-31.2
(GA (weeks)	37.4±0.6	37.0-39.0
		Ν	%
Parity	Multiparous	160	100.0%
	Total	16	50

Table 1: Demographic characteristics of the studied cases.

Table 1: Shows that: Demographic characteristics among the studied cases.

Table 2: Laboratory findings among the studied cases.

Findings	Mean±SD	Range
Hb (gm/dL)	11.0±1.0	8.3-12.9
HCT (%)	31.0±2.9	22.9-37.2
RDW (%)	16.5±1.8	11.3-21.8
Platelets (x10 ³ /mL)	244.4±57.9	99.3-384.2
MPV (fL)	7.9±0.9	6.0-10.2
WBC (x10 ³ /mL)	10.9±1.8	6.5-15.4
Lymphocyte($x10^{3}/mL$)	2.4±0.5	1.1–3.4
Neutrophils(x10 ³ /mL)	11.0±3.6	4.0-23.5
N/L ratio	4.6±1.2	1.5-7.6
P/L ratio	105.4±33.8	36.8-211.1
Total	160	

Table 2: shows that: Laboratory findings among the studied cases.

CBC parameters in Placenta Accreta

Placenta accreta		Ν	%
Introperative diagnosis	Accreta	76	47.5
(Total=160)	No accreta	84	52.5
Intervention	Conservative	48	63.2
(Total=76)	Hysterectomy	28	36.8
Conservative Biopsy	Accreta	37	77.1
(Total=48)	No accreta	11	22.9
Hysterectomy Biopsy	Accreta	24	85.7
(Total=28)	No accreta	4	14.3

Table 3: Intraoperative and histopathology diagnoses among the studied cases.

Table 3: Shows that: Intraoperative and histopathology diagnoses among the studied cases.

Table 4: Placenta accreta among the studied cases.

Place	nta accreta	Ν	0⁄0
Present		61	38.1
Absent		99	61.9
Total			160

Table 4: Shows that: Placenta accretewas in more than one third of the studied cases.

Table 5: Comparison according to placenta accreta

Variables	Accreta (N=61)	No accreta (N=99)	P	
Hb (gm/dL)	10.9±0.1	11.1±0.1	0.424	
HCT (%)	30.8±0.4	31.2±0.3	0.436	
Age (years)	28.8±3.4	28.5±4.3	0.662	
BMI (kg/m ²)	26.6±1.8	26.3±1.7	0.236	
GA (weeks)	37.1±0.3	37.5±0.7	<0.001*	
RDW (%)	15.8±1.7	17.0±1.8	<0.001*	
Platelets (x10 ³ /mL)	228.8±47.1	254.0±61.9	0.004*	
MPV (fL)	8.5±0.8	7.5±0.8	<0.001*	
WBC (x10 ³ /mL)	11.2±0.2	10.7±0.2	0.103	
Lymphocyte(x10 ³ /mL)	2.4±0.5	2.5±0.5	0.355	
Neutrophils(x10 ³ /mL)	11.5±0.5	10.6±0.4	0.113	
N/L ratio	5.1±1.2	4.3±1.1	<0.001*	
P/L ratio	101.0±4.0	108.0±3.5	0.206	

^Independent t-test.*Significant

Table 5 show that: MPV and N/L ratio were significantly higher in cases with placenta accrete. RDW and platelets countwere significantly lower in cases with placenta accrete.

Lab	AUC	SE	Р	95% CI	Cut off
Hb	0.479	0.049	0.662	0.384-0.575	
НСТ	0.483	0.048	0.723	0.388-0.578	
RDW	0.668	0.043	<0.001*	0.583-0.752	≤16.6
Platelets	0.635	0.044	0.004*	0.549-0.721	≤264.0
MPV	0.780	0.036	<0.001*	0.709-0.850	≥8.1
WBC	0.587	0.046	0.066	0.497-0.676	
Lymphocyte	0.535	0.048	0.462	0.441-0.628	
Neutrophils	0.586	0.047	0.065	0.495-0.679	
N/L ratio	0.696	0.043	<0.001*	0.611-0.780	≥4.1
P/L ratio	0.437	0.046	0.184	0.347-0.527	

Table 6: Diagnostic performance of laboratory findings in diagnosing placenta accrete.

AUC: Area under curve, SE: Standard error, CI: Confidence interval, *significant

Table (6) and Figure (1):Only RDW, platelets count, MPV and N/L ratiohad significant diagnostic performance in diagnosing placenta accrete.MPV had highest diagnostic performance.

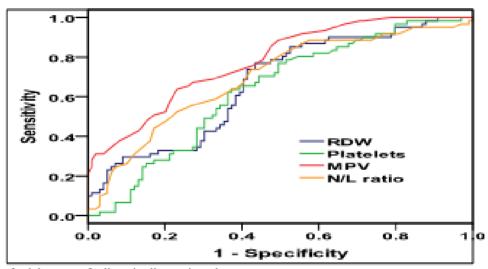


Fig. 1: ROC curve for laboratory findings in diagnosing placenta accrete.

Table 7: Diagnostic charactersitcis of suggested cutoff points in diagnosing placenta accrete.

Characteristics	Value	95% CI	Value	95% CI
	RD	W≤16.6 (%)	Platelets ≤2	64.0 (x10 ³ /mL)
Sensitivity	77.0%	64.5%-86.8%	77.0%	64.5%-86.8%
Specificity	54.5%	44.2%-64.6%	50.5%	40.3%-60.7%
DA	63.1%	55.1%-70.6%	60.6%	52.6%-68.2%
Youden's index	31.6%	17.2%-46.0%	27.6%	13.1%-42.0%
PPV	51.1%	40.4%-61.7%	49.0%	38.6%-59.4%
NPV	79.4%	67.9%-88.3%	78.1%	66.0%-87.5%
LR+	1.70	1.31-2.19	1.56	1.22-1.98
LR-	0.42	0.26-0.69	0.45	0.28-0.75
LR	4.03	1.97-8.24	3.43	1.68-7.00
	MP	PV≥8.1 (fL)	N/L	ratio≥4.1
Sensitivity	67.2%	54.0%-78.7%	88.5%	77.8%-95.3%
Specificity	72.7%	62.9%-81.2%	42.4%	32.5%-52.8%
DA	70.6%	62.9%-77.6%	60.0%	52.0%-67.7%
Youden's index	39.9%	25.3%-54.6%	30.9%	18.3%-43.5%

CBC parameters in Placenta Accreta

PPV	60.3%	47.7%-72.0%	48.6%	39.0%-58.3%
NPV	78.3%	68.4%-86.2%	85.7%	72.8%-94.1%
LR+	2.46	1.71-3.55	1.54	1.27-1.86
LR-	0.45	0.31-0.66	0.27	0.13-0.56
LR	5.47	2.73-10.94	5.68	2.35-13.74

CI: Confidence interval, DA: Diagnostic accuracy, PPV: Positive Predictive value, NPV: Negative Predictive value, LR+: Positive likelihood ratio, LR: Negative likelihood ratio, LR: Diagnostic odd ratio.

Table 7 show that: MPV \ge 8.1 (fL)had highest diagnostic characteristics in diagnosing placenta accreta.MPV \ge 8.1 (fL) had moderate diagnostic characteristics in diagnosing placenta accrete.

DISCUSSION

Implantation requires decidualization and vascular remodeling to provide essential nutrients and substrates to embryo. Some pregnancy complications such as early pregnancy loss, ischemic placental diseases, preeclampsia, intrauterine fetal growth restriction and premature delivery result from disturbed vascular growth in the placenta.^[3]

Placenta previa refers to the presence of placental tissue that extends over the internal cervical os. Sequelae include the potential for severe bleeding and preterm birth, as well as the need for cesarean delivery.^[19]

The pathogenesis of placenta previa is unknown. One hypothesis is that the presence of areas of suboptimally vascularized decidua in the upper uterine cavity due to previous surgery or multiple pregnancies promotes implantation of trophoblast in, or unidirectional growth of, trophoblast toward the lower uterine cavity. Another hypothesis is that a particularly large placental surface area, as in multiple gestation, increases the probability that the placenta will encroach upon/cover the cervical os.^[20]

The most important risk factor for development of a PAS is placenta previa after a prior cesarean delivery. In a prospective study including 723 women with placenta previa undergoing cesarean delivery, the frequency of PAS increased with an increasing number of cesarean deliveries as follows.^[21] First (primary) cesarean birth, 3 percent. Second cesarean birth, 11 percent. Third cesarean births, 40 percent.Fourth cesarean births, 61 percent. Fifth or greater cesarean birth, 67 percent.

In the absence of placenta previa, the frequency of a PAS in women undergoing cesarean delivery was much lower.^[21] First (primary) cesarean birth, 0.03 percent. Second cesarean birth, 0.2 percent. Third cesarean birth, 0.1 percent. Fourth or fifth cesarean birth, 0.8 percent. Sixth or greater cesarean birth, 4.7 percent.

Placenta accreta spectrum (PAS) is a general term used to describe abnormal trophoblast invasion into the myometrium of the uterine wall. It results from placental implantation at an area of defective decidualization typically caused by preexisting damage to the endometrialmyometrial interface. Clinically, the placenta does not spontaneously separate at delivery and attempts at manual removal result in hemorrhage, which can be lifethreatening.^[22]

Improved understanding of the molecular basis of other placental disorders such as preeclampsia suggests the inflammation and placental invasion may be closely related. A number of comparisons can be drawn between the microenvironment of PAS and tumourbehaviour. Both conditions require an ability of cells to overcome the local immunological systems, activate invasion, and induce angiogenesis. In 2012, Hanahan and Weinberg outlined eight hallmark capabilities of tumours which allow them to invade and metastasise. Herein, we use these eight hallmarks of cancer to highlight some of the molecular similarities between PAS and tumour development Hanahan and Weinberg.^[23] As previously mentioned in introduction.

US study reported an overall incidence of 1 in 272 delivery-related discharges. The incidence of placenta accreta in Canada was 1 in 695 deliveries in 2009 to 2010.^[24]

The marked increase in PAS, which has occurred worldwide, has been attributed to the increasing prevalence of cesarean delivery in recent decades.^[25]

Ferretti *et al.*^[26] showed similar features shared by trophoblast and cancer cells that includes the activation of the phosphatidylinositol 3'-kinase (PI3K)/AKT axis which provides proliferative, migratory and invasive properties.

Due to the observations that suggested tumors to be originated at sites of chronic inflammation, Balkwill and Mantovani^[27] stated that some inflammatory markers including neutrophil/lymphocyte and platelet/lymphocyte ratios have been proposed to be used as predictors for malignancy.

A recently published meta-analyses, Templeton *et al*.^[28] revealed that, these markers may be used as predictors for solid tumors originating from several tissues.

Wei *et al*.^[29] and Marchioni *et al*.^[30] also confirmed this association for both diagnostic and prognostic values.

As a result, Li *et al.*^[31] reported favorable results for this screening tool, and introduce this tool as inexpensive and readily available.

A linkage between platelet activation and pathophysiology of diseases prone to thrombosis and inflammation was proposed. Therefore, Gasparvan et al.^[32] investigated a couple of platelet markers, including mean platelet volume to figure out this linkage between platelet activation and both thrombosis and inflammation. Consequently, high mean platelet volume was found to be associated with a variety of systemic disorders including cardio- and cerebrovascular disorders, and low-grade inflammatory conditions prone to arterial and venous thromboses. It was also reported that high-grade inflammation may present with low levels of mean platelet volume which reverse in the course of anti-inflammatory therapy.

Due to the similarity with the cancer cell invasion and evidence for the predictive value of complete blood count parameters for several cancer types. So, in this study we try to assess the relationship between some parameters of complete blood count and placental invasion anomalies.

The main object was presence of significant differences between groups with and without placental invasion anomaly in terms of age, neutrophil, platelet count, mean platelet volume, red cell distribution width and neutrophil to lymphocyte ratio.

Ourprospective cohort study was done on women attending Ain Shams University Maternity Hospital with a confirmed diagnosis of variable degrees of placenta previa with the possibility of cesarean hysterectomy during elective cesarean section with singleton living fetus and gestational age between 37 and 42 weeks.

Pregnant women with vaginal bleeding related to other causes, multiple gestation, any systemic disease including (cardiovascular, endocrinological, metabolic, inflammatory, autoimmune disorders), pre-pregnancy obesity (BMI 30 kg/m2), fever, chorioamnionitis, any septic focus, any infectious diseases interfering with leukocytic counts and functions, smoking or on any drug other than iron medication and/or were managed conservatively during cesarean section were excluded from our study.

This ourstudy was conducted on (160) women with a confirmed diagnosis of placenta previa or who were suspected for placental invasion anomalies. All of them underwent complete blood count screening before cesarean section. The localization of the placental implantation and the depth of myometrial invasion were identified on admission with transabdominal and transvaginal 2D grav scale ultrasound and Doppler sonography by Sonoace Samsung R5 machine (2-8 MHZ, made in Korea). The ultra-sonographic findings of irregularity or loss of the retro-placental echo-lucent area between the uterus and the placenta, thinning of the myometrium to less than 1 mm at the site of placental bed, protrusion of the placenta into the bladder, increased vascularity of the uterine serosa and the bladder wall interface, irregular intraplacental vascularization and the presence of turbulent placental lacunae with high velocity flow were considered diagnostic of placental invasion anomaly. The depth and extent of the hyper-vascularized areas were also assessed. The intraoperative diagnosis of the placental abnormality was confirmed at the time of cesarean section and also in histopathological evaluation whatever the patient did hysterectomy or not. All blood samples were retrieved by venipuncture at the time of admission prior to delivery and in all cases parameters of complete blood count including lymphocyte, platelet count and red cell distribution width (RDW), neutrophil/lymphocyte ratio and mean platelet volume (MPV) were analyzed to predict cases with real placental invasion anomaly.

Our results found that mean platelet volume (MPV) and neutrophil/ lymphocyte (N/L) ratio were significantly higher in cases with placenta accrete. Gestational age (GA), red blood cell distribution width (RDW) and platelets count were significantly lower in cases with placenta accreta.

Only red blood cell distribution width (RDW), platelets count (P=0,004), mean platelet volume (MPV) and neutrophil/ lymphocyte (N/L) ratiohad significant diagnostic performance in diagnosing placenta accrete and mean platelet volume MPV ≥ 8.1 (fL) had highest diagnostic characteristics in predictingplacentaaccreta. Platelet (PLT) counts were significantly lower.

MPV and large platelet cell ratio (P-LCR) values were significantly higher. Diminution of platelet counts and simultaneous enhancement of their volume and distribution width over the third trimester might be caused by their destruction, regarding microangiopathic reasons, even in a normal pregnancy. It has been well-established in a study by Fay *et al.*^[33].

Yayla *et al.*^[18] study was in line with our results and stated that in addition to the sonographic findings, simple blood count parameters may be utilized to confirm cases with suspected for placental invasion anomalies. Totally 146 pregnant women who were suspected for placental invasion anomalies underwent complete blood count screening before cesarean section. In all subjects white blood cell, lymphocyte, neutrophil and platelet counts with red cell distribution width, mean platelet volume, hemoglobin and hematocrit levels were analysed. All complete blood count parameters were analyzed to predict placental invasion anomalies. There were significant differences between groups with and without placental invasion anomaly in terms of age, neutrophil, platelet count, mean platelet volume, red cell distribution width and neutrophil to lymphocyte ratio. Age, neutrophil to lymphocyte ratio and mean platelet volume were significant predictors for the cases with placental invasion anomaly. In multivariate analyses age, mean platelet volume, red cell distribution width and neutrophil to lymphocyte ratio were significantly associated with the placental invasion anomaly.

Ersoy *et al.*^[34] study agreed with us and stated that platelet and leukocyte indices in the third trimester of pregnancy may be valuable predictors of placenta previa and placenta percreta. Ninety-three pregnant patients diagnosed with PP and 247 controls were recruited for this retrospective study. Platelet and leukocyte indices were compared between the two groups. Total leukocyte count, neutrophil count, and neutrophil-to-lymphocyte ratio were significantly higher in the PP group.

However Ersoy *et al.*^[34] study disagreed with us regarding mean platelet volume (MPV) and large platelet cell ratio (P-LCR) values which were significantly lower in the PP group as compared to controls, with regard to third trimester values. Also, patients who were diagnosed postnatally with placenta percreta had lower MPV and P-LCR values than other patients with PP.

Finally, Karapinar et al.[35] disagreed with our results and stated that 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. 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. 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. 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).

Strengths of the study are: Every effort was made to ascertain that all data were correct, and only complete information was included in data analysis. The examination was done by the same sonographer for all the patients. The operation was performed by the same seniorobstetric team. Sample size of this study was large enough and the Limitations of the study are: To compare other measures of efficacy and safety would have required considerably more study predictive techniques rather than complete blood parameters. In addition to the sonographicfindings, simple blood count parameters may be utilized to predict cases with suspected for placental invasion anomalies. Among all the parameters mean platelet volume seems to be most powerful predictor.

CONCLUSION

There are changes in CBC parameters which can predict placental invasion anomalies such as increase in Mean platelet Volume(MPV), Neutrophil / lymphocyte (N/L) ratio and decrease in Red cell Distribution Width (RDW), Platelet's count.

The cut point's in predicting placenta accreta by complete blood count are .Mean platelet Volume(MPV) \geq 8,1fl had the highest diagnostic characteristics, Neutrophil/ lymphocyte (N/L) ratio \geq 4.1.Red cell Distribution Width (RDW) \leq 16.6% & Platelet's count \leq 264.0(x10³/mL).

RECOMMENDATIONS

In suspected cases of placenta accrete by ultrasound, We recommend to evaluate every change in CBC parameters which can predict placental invasion anomalies eg. Mean platelet Volume(MPV), Neutrophil / lymphocyte (N/L) ratio and Red cell Distribution Width (RDW), Platelet's count.

CONFLICT OF INTEREST

There are no conflicts of interests.

REFERENCES

- 1. Knöfler M, and Pollheimer J (2013): Human placental trophoblast invasion and differentiation: a particular focus on Wnt signaling. Front and 4:190.
- 2. Feng Z, Wen H, Bi R, Ju X, Chen X, *et al.* (2016): Preoperative neutrophil-to-lymphocyte ratio as a predictive and prognostic factor for high-grade serous ovarian cancer. PLoS One and 11:e0156101.
- Zygmunt M, Herr F and Munstedt K (2013): Angiogenesis and vasculogenesis in pregnancy. Eur J ObstetGynecolReprodBiol and 110:S10–18.
- 4. Ahmed A, Dunk C, Ahmad S and Khaliq A (2010): Regulation of placental vascular endothelial growth factor (VEGF) and placenta growth factor (PIGF) and soluble Flt-1 by oxygen-a review. Placenta and 21:S16–24.

- 5. Scand, Chantraine F and Langhoff-Roos J (2013): Abnormally invasive placenta-AIP. Awareness and pro-active management is necessary. Acta Obstet Gynecol and 92:369–71.
- Tantbirojn P, Crum CP and M MParast (2008): "Pathophysiology of placenta creta: the role of decidua and extravilloustrophoblast," Placenta, 29 (7): 639–645.
- 7. Hanahan D and Weinberg RA (2011): "Hallmarks of cancer: the next generation," Cell, 144(5): 646–674.
- Shainker SA, Dannheim K and Gerson KD (2017): "Down-regulation of soluble fms-like tyrosine kinase 1 expression in invasive placentation," Archives of Gynecology and Obstetrics, 296 (2):257–262.
- 9. Stanek J and Drummond Z. (2007): "Occult placenta accreta: the missing link in the diagnosis of abnormal placentation, "Pediatric and Developmental Pathology, 10 (4): 266–273.
- Gu Y, Bian Y and Xu X (2016): "Downregulation of miR-29a/b/c in placenta accreta inhibits apoptosis of implantation site intermediate trophoblast cells by targeting MCL1," Placenta, 48: 13–19.
- 11. Ernst LM R L, Linn L, Minturn and E S Miller (2017): "Placental pathologic associations with morbidly adherent placenta potential insights into pathogenesis," Paediatric pathology society, 20:5.
- Chen Y, Zhang H and F Han (2018): "The depletion of MARVELD1 leads to murine placenta accreta via integrin β4- dependent trophoblast cell invasion," Journal of Cellular Physiology, 233: 2257–2269.
- 13. Geffen T, Gal H and Vainer I (2017): "Senescence and telomere homeostasis might be involved in placenta percreta-preliminary investigation," Reproductive Sciences.
- Kilcoyne A, Shenoy-Bhangle AS, Roberts DJ, Sisodia RC Gervais DA *et al.*, (2017): "MRI of placenta accreta, placenta increta, and Placenta Percreta: Pearls and Pitfalls," American Journal of Roentgenology, vol. 208, no. 1, pp. 214–221.
- 15. Voet LF, Bij de Vaate AM, Veersema S, Brölmann HA and Huirne JA (2014): Long term complications of cesarean section. The niche in the scar: a prospective cohort study on niche prevalence and its relation to abnormal uterine bleeding. BJOG and 121:236-44.
- 16. Ben-Nagi J, Walker A and Jurkovic D (2009): Effect of cesarean delivery on the endometrium.Int J GynaecolObstet and 106:30.

- 17. Flo K, Widnes C, Vårtun Å and Acharya G (2013): Blood flow to the scarred gravid uterus at 22-24 weeks of gestation. BJOG and 121:210-5.
- 18. Yayla CA, Ozkaya E, Tayyar A, Senol T, Senturk MB *et al.*, (2016): Predictive value of complete blood count parameters for placental invasion anomalies, The Journal of Maternal-Fetal & Neonatal Medicine.
- Cresswell JA, Ronsmans C, Calvert C and Filippi V (2013): Prevalence of placenta praevia by world region: a systematic review and meta-analysis. Trop Med Int Health, 18:712.
- 20. Charles J Lockwood, Karen RS, Deborah L, Vincenzo B and Vanessa A B (2019): Placenta previa: Epidemiology, clinical features, diagnosis, morbidity, mortality and treatment. Up-to-date.
- 21. Silver RM, Landon MB, Rouse DJ (2006). Maternal morbidity associated with multiple repeat cesarean deliveries. ObstetGynecol and 107:1226.
- 22. Resnik R, Robert Ms S, Deborah L, Lynn LS and Vanessa AB (2019): Clinical features, diagnosis and management of placenta accrete spectrum (placenta accreta, increta, and percreta). Up-to-date 2019.
- 23. Hanahan D and Weinberg R A (2011): "Hallmarks of cancer: the next generation," Cell, 144(5): 646–674.
- 24. Mogos MF, Salemi JL, Ashley M (2016): Recent trends in placenta accreta in the United States and its impact on maternal-fetal morbidity and healthcare-associated costs, 1998-2011. J Matern Fetal Neonatal Med and 29:1077.
- 25. Jauniaux E, Collins S and Burton GJ (2018): Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. Am J ObstetGynecol and 218:75.
- 26. Ferretti C, Bruni L, Dangles-Marie V, Pecking AP and Bellet D (2007): Molecular circuits shared by placental and cancer cells, and their implications in the proliferative, invasive and migratory capacities of trophoblasts. Hum Reprod Update and 13(2):121-4.
- 27. Lancet, Balkwill F and Mantovani A (2001): Inflammation and cancer: back to Virchow? and 539–545., 357.
- Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P *et al.*, (2014): Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. May 29 and 106(6).

- 29. Wei B, Yao M, Xing C, Wang W, Yao J *et al.*, (2016): The neutrophil lymphocyte ratio is associated with breast cancer prognosis: an updated systematic review and meta-analysis. Onco Targets Ther, 8 and 9: 5567-75.
- Marchioni M, Primiceri G, Ingrosso M, Filograna R, Castellan P *et al.*, (2016): The Clinical Use of the Neutrophil to Lymphocyte Ratio (NLR) in Urothelial Cancer: A Systematic Review. ClinGenitourin Cancer.
- Li MX, Liu XM, Zhang XF, Zhang JF, Wang WL *et al.*, (2014): Prognostic role of neutrophil-to-lymphocyte ratio in colorectal cancer: a systematic review and meta-analysis. Int J Cancer and 134(10):2403-13.
- 32. Gasparyan AY, Ayvazyan L, Mikhailidis DP and Kitas

GD (2011): Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des and 17(1):47-58.

- Fay RA, Hughes AO and Farron NT (1983): Platelets in pregnancy: hyperdestruction in pregnancy. ObstetGynecol and 238–240., 61:
- Ersoy AO, Ozler S, Oztas E, Ersoy E, Kirbas A *et al.*, (2016): The association between placenta previa and leukocyte and platelet indices a case control study. GinekologiaPolska and 367–371., 87(5):.
- 35. Karapinar OS, Gözükara I, Hakverdi AU and Güngören A (2017): A new marker for the prediction of mean platelet volume, placenta previa and placental invasion anomalies. Perinatal Journal and 25(1): 32–37.