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TO STUDY THE ROLE OF PRO-BNP, VEGF AND TROPONIN-I IN PREDICTION OF PLACENTA ACCRETA SPECTRUM AND ITS CORRELATION WITH FETOMATERNAL OUTCOME

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ABSTRACT

Introduction: Placenta accreta spectrum (PAS) is a dreadful complication of pregnancy especially when unsuspected at the time of delivery and is associated with high maternal as well as fetal morbidity and mortality. **Aims & Objectives:** To evaluate maternal serum level of Pro-BNP, Troponin-I and VEGF in prediction of PAS and placenta previa. **Materials & Methods:** This prospective case control study was conducted in the Department of Obstetrics and Gynaecology of a tertiary care institute of Northern India. A total of 180 females having singleton pregnancy and a gestation age of ≥ 28 weeks were enrolled of which 90 patients were in the study group and among these 21 patients were of PAS and rest 69 were placenta previa. The control group comprised of 90 healthy, uncomplicated women with normal placentation. All patients were subjected to history, examination, obstetrical ultrasound and estimation of maternal serum Pro-BNP, Troponin-I and VEGF done. Demographic characteristics, fetomaternal outcomes were noted and biomarkers levels were compared among study groups. **Results:** Patients with PAS had higher serum Pro-BNP levels, higher Troponin-I levels and lower VEGF levels. On ROC analysis Pro-BNP was found to be most sensitive and specific marker for diagnosis of PAS. **Conclusion :** The significantly raised levels of Pro-BNP and Troponin-I and lower levels of VEGF can be helpful in the prompt diagnosis of PAS.

KEYWORDS :

INTRODUCTION

Placenta accreta spectrum is a life threatening complication of pregnancy especially when undiagnosed at the time of delivery with attempt to remove the placenta which can lead to tearing of large vessels due to lack of a detachment layer to the myometrium which is associated with massive intrapartum hemorrhage and high maternal morbidity and mortality. Antenatal diagnosis of PASD (placenta accreta spectrum disorders), preoperative planning, and multidisciplinary approach is necessary to reduce the maternal and perinatal outcomes associated with it. In addition to ultrasound, suitable maternal serum biomarkers might aid in early diagnosis that would help in planning appropriate management of placenta previa and placenta accrete spectrum disorders thereby lessening the sequelae.In LMICs like India where operative and blood transfusion facilities are not available especially in rural areas adverse outcomes associated with PAS and Placenta previa can be notably reduced of diagnosed early and this will ensure timely referral to a well equipped tertiary care centre.

Moreover in tertiary centres also early diagnosis could buy time for making necessary arrangements eg. blood arrangements, ensuring availability of urosurgeon, intervention radiologist, anaesthetist, neonatologist, ICU etc. and subsequently improving maternal and neonatal outcome. So, this study was planned to determine the role of PRO-BNP, Troponin-I and VEGF in prediction of Placenta accreta spectrum disorders.

AIMS AND OBJECTIVES

To study the role of Pro-BNP, Troponin-I and VEGF in prediction and diagnosis of Placenta accreta spectrum.

METHODOLOGY

This prospective case control study was conducted in the department of Obstetrics & Gynecology, in collaboration with the department of Pathology, Nehru hospital, BRD Medical College, Gorakhpur over a period of one year (i.e. from August 2021 to July 2022).Study population comprised of all pregnant women admitted to the indoor of tertiary hospital with singleton pregnancy and gestational age more than 28 weeks of gestation who consented for participation. The inclusion criteria for cases were-All singleton pregnant women with diagnosis of PAS and Placenta Previa by ultrasound and patients coming to emergency with bleeding per vaginum and later diagnosed as PAS or Placenta previa. Exclusion criteria included: -Antepartum hemorrhage because of causes other than Placenta Previa and PAS; -Antenatal patients having Multiple pregnancy /Premature preterm rupture of membranes/ Active Labor/ Thyroid disease/ Hypertension and related disorder /Epilepsy/ Gestational Diabetes MellitusType 1 or 2 Diabetes Mellitus / Heart disease/ Renal disease/ Intrauterine growth restriction/ Drugs which affect cardiovascular system i.e. alcohol cocaine, beta blocker or any other cardiovascular drug/ Liver disease/ Abruptio placentae/ Cancer; -Patients not giving consent. Uncomplicated pregnant women with normal placental location matched with the cases for age, BMI and other baseline characteristics and those giving consent for participation were taken as controls.

Sample size of cases as well as controls were 90 each making a total sample size of 180 which was calculated by **Kelsey et al**[1], Methods in Observational Epidemiology, Second Edition, Table 12-15. The study group comprised of 90 women with either sonological diagnosis of placenta previa or Placenta

accreta spectrum disorders. Out of these 90 patients, twenty one (21) were diagnosed as placenta accreta spectrum disorders either prenatally by grey scale ultrasonography and/ or intraoperatively which were later histologically diagnosed as placenta accreta spectrum disorders (accreta, increta or percreta).

A written informed consent was obtained from all the study participants. Ethical approval was taken from the Institutional Ethics Committee (2/CRC/ 2021 dated 26/08/2021).

All the enrolled women cases as well as controls were subjected to detailed history, including family history, personal history and obstetric history and examination including general physical examination, systemic examination and obstetric examination. All the enrolled women (study group and control group) were subjected to routine antenatal investigations (if earlier not done), obstetrical ultrasonography (by a senior ultrasonologist) and estimation of serum PROBNP, TROPONIN-I and VEGF.

10 ml of venous blood sample was collected from each participant preoperatively in cases of planned cesarean deliveries or at admission to the hospital in cases of attempted vaginal birth and was processed within 1 hour after withdrawal to avoid surgery or birth- associated affection of the biomarker levels by centrifugation at 3000 revolutions/minute for 10 minutes and was analyzed at that time. Plasma levels of PRO-BNP and TROPONIN-I was measured by Heidelco Immunofluorescence Quantitative Analyser using test cards. Serum VEGF was measured by sandwich ELISA method using commercial reagents (Human VEGFA ELISA kit 96T, make ELK Biotechnology). Cut of value of PRO-BNP, TROPONIN-I and VEGF were 432 pg/ml, 0.049 ng/ml and 287 pg/ml respectively. All participants with elevated levels of cardiac markers were further evaluated with electrocardiography (ECG) to exclude any cardiac disorder. Abnormal placentation was confirmed with per operative findings and by histopathological examination.Information on age, parity, abortions, prior uterine surgeries (caesarean section, myomectomy, currettage with or without hysteroscopy), number of cesarean section, any episode of bleeding/ postpartum hemorrhage were analyzed. Maternal outcome assessed were abnormal adherent placentation (placenta increta, accreta, percreta), estimation of blood loss, complications, need for blood transfusion, admission to intensive care unit (ICU) and length of hospital stay.Fetal parameters were gestational age at delivery, fetal malpresentation, birth weight, IUD, APGAR score at 5 minutes, NICU admission, duration of NICU stay, neonatal mortality and complications such as pre maturity, respiratory distress, sepsis etc.

Statistical Analysis:

Analysis was done by data sorting method, classified by tabulation and presentation by pie chart, and histograms.Data was presented as mean (standard deviation), number and percentage (%). The Chi-square test was used to compare the categorical variables and independent t test was used to compare discrete variables between groups.The Sensitivity, Specificity, PPV, NPV and ROC curve were used to assess the overall diagnostic value of serum biomarkers studied. Regression analysis was used for the estimation of relationships between a dependent variable and one or more independent variables. The p value < 0.05 was considered significant.

RESULTS

The mean age distribution in study group was 26.9 ±4.34 years and in the control group was 24.3 ±3.08 years. The mean gravidity distribution in study group as well as in control group was 2.67±1.32 and 1.37±0.71 respectively. (Table 1)

Table 1 : Maternal Characteristics Among Study Groups

Demographic And Obstetric Characteristics		Study Group		Controls		t	P-value
		Mean	±SD	Mean	±SD		
Age		26.8556	4.34356	24.2778	3.09050	4.59	<0.001
BMI		21.8911	2.21094	21.9311	2.18563	0.12	0.903
Gravidity		2.67	1.32	1.37	0.71		<0.001
Parity		1.39	1.1	1.27	0.59		<0.001
Gestation age at presentation		34.46	3.21	37.98	2.66		<0.001
		n	%	n	%	Chi sq.	p-Value
Residence	Rural	85	94.44	79	87.78	1. 72	0.190
	Urban	5	5.56	11	12.22		
Religion	Hindu	81	90.00	77	85.56	2.57	0.129
	Muslim	9	10.00	13	14.44		
Education	Illiterate	17	18.89	35	38.89	4.4	0.354
	Primary	43	47.78	13	14.44		
	High School	22	24.44	28	31.11		
	Intermediate	7	7.8	10	11.11		
	Graduate	1	1.11	4	4.44		
Socioeconomic Status	Lower	12	13.33	19	21.11	1.93	0.381
	Lower middle	72	80.00	66	73.33		
	Upper middle	6	6.67	5	5.56		
	Upper	0	0	0	0		

The median gestation age at presentation among cases was 34wk 5d and controls was 38wk 3d.

73.6% cases and 2.22% controls had previous cesarean section. Previous LSCS was found to be an important risk factor for development of Placenta previa and PAS ($p<0.006$).

Out of 90 patients 21 patients were of Placenta accreta spectrum among which 76.19% had Placenta accreta, 9.5% had Placenta increta and 14.3% had Placenta percreta.

The mean maternal serum PRO-BNP levels were found to be raised in the PAS group (702.29± 318.38pg/ml) as compared to Placenta previa group (416.25± 285.52pg/ml). In our study the mean value of PROBNP in Placenta accreta was 416.2±285.5 pg/ml, in Placenta increta was 738.8± 336.6 pg/ml and that in percreta was 689.3±280.7pg/ml.

The mean maternal serum TROPONIN-I levels were also found to be raised in the PAS group which was 0.051± 0.017ng/ml when compared to Placenta previa group which was 0.045± 0.024 ng/ml. In this study the mean value of troponin -I in Placenta accreta, increta and percreta was found to be 0.056±0.008 ng/ml, 0.031±0.030 ng/ml and 0.034 ±0.028 ng/ml respectively.

The mean maternal serum VEGF levels were decreased in PAS group (262.67± 32.03pg/ml) when compared to Placenta previa group (325.06±73.65pg/ml). The mean value of VEGF obtained in this study for the respective Placenta accreta, increta and percreta were 261.93±29.87 pg/ml, 268±25.45 pg/ml and 263±56.66 pg/ml.

Emergency lower segment cesarean section was the most common mode of delivery among study group, 66.7% in PAS patients and 91.30% in Placenta previa group. In PAS cases 4.76% had vaginal delivery, 23.81% had elective lower segment cesarean section and 4.76% had exploratory laparotomy.

The median post partum stay in PAS cases was 10 days and in Placenta previa group was 8 days.The mean blood loss in PAS patients was 1104.76±162.71 ml while in placenta previa was 868.11±187.46ml and while in controls was 305.56±194.22ml. 76.19% patients had post partum hemorrhage among the PAS group as compared to control group(2.2%). 76.19% patients in the PAS group underwent hysterectomy. 71.43% patients had ICU admission. Other complications were sepsis(9.52%) and bladder injury in 4.76% of the patients.

90.48% patients of the PAS group and 98.55% patients of the placenta previa group were discharge well whereas 4.76% PAS cases left against medical advice and 4.76% had mortality and 1.45% of the placenta previa patients absconded.

The median gestation age at birth was 34 wk 5 days for the PAS group and 35 wk 4 days for the placenta previa group.

61.90% neonates of the PAS group had low birth weight ranging between 1.5-2.5kg on the other hand 65.22% neonates in the placenta previa group had birth weight between 1.5-2.5kg.

52.4% neonates of PAS group had poor APGAR score and 42.9% had NICU admission on the other hand 59.4% neonates of Placenta previa group had poor APGAR score at 5 minutes and 49.3% newborns required NICU admission.

66.67% neonates of PAS group were healthy and bedside baby on discharge and 33.33% neonates expired while in Placenta previa group 63.77% neonates were healthy at discharge while 23.19% neonates expired after birth and 13.04% were stillborn.

The sensitivity, specificity, NPV, PPV, likelihood ratio (LR+, and LR-) and ROC curves were used to analyse the diagnostic value of PROBNP, Troponin I and VEGF for PAS in study group (Table 2 and Figure 2). The PROBNP, Troponin I and VEGF for PAS in study group has showed significantly large area under the curve (AUC= 00.754, 0.684 and 0.759 respectively) on the ROC curve analysis. The cut-off points of PROBNP, Troponin I and VEGF were 432, 0.049 and 287, respectively for the diagnosis of PAS in cases. Moreover, the PROBNP had more Sensitivity (91.1%) and Specificity (60.8%) with PPV (59.4%) and NPV (81.0%) for PAS in cases. The LR+ and LR- was 2.32 and 0.15 for PAS in cases. (Table 2)

Table 2: Sensitivity, Specificity, Ppv, Npv, Lr+ And Lr- With Receiver Operating Characteristic (ROC) Analysis Of Probnp, Troponin I And Vegf For Pas In Cases

	Cut-off	Sensitivity	Specificity	PPV	NPV	LR	LR	Area under curve	95% CI		P-value
									Lower	Upper	
PROBNP	432	91.1%	60.8%	59.4%	81.0%	2.32	0.15	0.754	0.63	0.88	<0.001*
Troponin I	0.049	62.2%	40.9%	40.6%	19.0%	1.05	0.92	0.684	0.51	0.78	0.041*
VEGF	287	89.1%	56.4%	59.4%	36.4%	1.95	0.19	0.759	0.14	0.34	0.001*

In linear analysis, PREV C.S, PROBNP and VEGF were significantly associated with the risk of PAS in cases. The multiple logistic regression was used for analysis the independent risk factor for PAS in cases. In multiple logistics regression PREV C.S. was significant independent risk factor for PAS in cases. (Table 3)

Table 3 : Linear And Multivariate Logistic Regression (FORWARD-WALD) Analysis Performed In Each Patient Group To Determine The Risk Factors For Pas In Cases

	LINEAR LOGISTICS REGRESSION				MULTIPLE LOGISTICS REGRESSION			
	OR	95.0% C.I. for B		p-Value	OR	95.0% C.I. for EXP(B)		p-Value
		Lower	Upper			Lower	Upper	
AGE	0.02	-0.02	0.02	0.846	1.02	0.87	1.200	0.820
PREV C.S	0.51	0.18	0.37	<0.001*	12.67	3.42	46.995	<0.001*
D&E	0.08	-0.12	0.30	0.396	3.58	0.42	30.723	0.245
PROBNP	0.23	0.00	0.00	0.035*	1.00	1.00	1.005	0.223
TROPONIN I	-0.11	-5.76	1.40	0.228	0.00	0.00	1.387E8	0.304
VEGF	-0.22	0.00	0.00	0.039*	0.97	0.99	1.007	0.118

*Significant (p<0.05)

Table 4: Maternal Outcome Characteristics In Different Studies

	Dwivedi et al[10]	Dua et al[13]	Rani et al[9]	Akhtar et al[14]	Singh et al[12]	Present study
Year	2010-2014	2014-2016	2017-2020	2018-2021	2019-2020	2021-2022
Study type	Prospective	Retrospective	Retrospective	Prospective	Prospective	Prospective
Sample size	37	32	86	305	50	21
Post partum hemorrhage	86%	100%	67.44%	77%	10%	85.71%
Hysterectomy	78%	87.5%	76.74%	69.8%	52%	76.19%
Bladder injury	16%	18.7%	2.33%	21%*	22%	4.76
Sepsis	13%	6.25%	9.5%	-	8%	9.52%
ICU admission	21%	71.8%	69.76%	75.4%	-	71.43%
Mortality	18%	15.6%	2.33%	3.6%	26%	4.76%

DISCUSSION

The incidence of placenta accreta spectrum disorders in our study was found to be 4.84 per 1000 deliveries which is quite high than the Global incidence of 1 in 2500 deliveries[2] and the national incidence of 4.3 per 10000 deliveries[3]. This could be attributed to the rising cesarean section rates, increased diagnosis of PAS due to availability of better resolution ultrasound markers and strengthening of referral systems.

Table 5: Fetal Outcome Characteristics In Different Studies

	Desai et al [15]	Bhati et al [16]	Rani et al[9]	Akhtar et al[14]	Singh et al [12]	Present study
Year	2014-2016	2017-2019	2017-2020	2018-2021	2019-2020	2021-2022
Study type	Retrospective &Prospective	Retrospective &prospective	Retrospective	Prospective	Prospective	Prospective
Sample size	10	21	86	305	50	21
Mean Gestation age	32.1 weeks	35.76 weeks	--	35.55 weeks	--	34.38 weeks
Low birth weight	50%	38.09%	44.19%	30.8%	57.1%	76.19%

Poor APGAR score	--	--	--	14.4%	28.6%	52.4%
NICU admission	60%	61.9%	41.86%	80%	64.3%	42.9%
Perinatal mortality	10%	9.52%	4.65%	15.1%	14%	33.33%

The baseline demographic and obstetric characteristics were comparable among the study groups.

The mean maternal serum PROBNP levels in patients with placenta accreta spectrum disorder was 702.29± 318.38 pg/ml and that in placenta previa patients was 416.25±285.52 pg/ml. These values were much higher when compared with controls (75.41± 43.55pg/ml). It was suggested by **Ersoy et al, 2016**[4] that increased maternal serum ProBNP levels might be an indicator of the increased angiogenesis in placenta accreta patients and hence the levels found in our study. In the current study it was found that the values of serum PROBNP were raised consecutively with the degree of placental invasion with mean values being 430±8.5 pg/ml, 738.8±336.6 pg/ml and 689.3± 280.7 pg/ml in placenta accreta, increta and percreta respectively.

The levels of TROPONIN-I were significantly raised in patients of Placenta accreta spectrum disorders (mean 0.051± 0.017 ng/ml) and placenta previa (mean 0.045± 0.024 ng/ml) in the present study as compared to the control group (0.005± 0.007 ng/ml). The current study showed raised value of TROPONIN-I in Placenta accreta spectrum disorders. This was contrary to the findings of **Ersoy et al, 2016**[4] who found that TROPONIN-I could not be shown as diagnostic marker for Placenta accreta. In present study the levels of VEGF were considerably lower in patients of Placenta accreta spectrum disorders (mean 262.67± 32.03 pg/ml) and placenta previa (mean 325.06± 73.65 pg/ml) as compared to the control group (mean 441.68± 63.94 pg/ml) The main underlying pathophysiological mechanism in Placenta accreta spectrum disorders is the neoangiogenesis induced by oxidative stress. The increased neoangiogenesis augmented oxidative stress might lead to a downregulation of VEGF. As a result when blood was sampled during the third trimester (median Gestation age 35weeks), this hypothesis explained the paradoxically low serum VEGF levels obtained by **Schwickert et al, 2021**[5] in cases of Placenta accreta spectrum disorders. Thus the lower levels obtained in present study could be related to the above mechanism.

For NT-proBNP, the most favorable cut-off level to differentiate between placenta accreta spectrum disorders and normal placentation as determined by ROC curve analysis in this study was 432 pg/ml. In study conducted by **Schwickert et al, 2021**[5] it was 303.5 pg/ml while **Ersoy et al, 2016**[4] proposed a cut-off at 125.85 pg/ml. In present study sensitivity was 91.1%, specificity of 60.8%, PPV of 59.4%, NPV of 81.0%, LR + of 2.32 and LR - of 0.15 for Placenta accreta spectrum disorders (AUC = 0.754, 95% CI 0.63-0.88, p <0.001). In the study by **Schwickert et al, 2021**[5] PROBNP level with a cut-off at 303.5 pg/ml had a negative likelihood ratio (LR−) of 0.6 and a positive likelihood ratio (LR+) of 1.6 for the outcome of abnormal invasive placentation. (AUC = 0.632, 95% CI 0.516–0.747, p = 0.03).

Similarly for TROPONIN-I the most favorable cut-off level to differentiate between placenta accreta spectrum disorders and normal placentation as determined by ROC curve analysis in this study was 0.049 ng/ml. In the study conducted by **Ersoy et al, 2016**[4] it was 0.0045 ng/ml. In present study for the diagnosis of Placenta accreta spectrum disorders sensitivity was 62.2% , specificity of 40.9%, PPV of 40.6%, NPV of 10.0%, LR+ was 1.05 and LR- was 0.92 (AUC = 0.684, 95% CI 0.51-0.78, p= 0.041). This was in corraboration with the findings of **Ersoy et al, 2016**[4] who reported AUC = 0.808, 95% CI 0.690-0.926, p= 0.001.

Likewise for VEGF, the most favorable cut-off level to differentiate between placenta accreta spectrum disorders and normal placentation by ROC curve analysis in this study was determined to be 287 pg/ml.The present study yielded a sensitivity of 89.1%, specificity of 56.4% , PPV of 59.4%, NPV of 36.4%, LR+ of 1.95 and LR- of 0.19 for VEGF in diagnosis of Placenta accreta spectrum disorders (AUC = 0.759, 95% CI 0.14-0.34, p= 0.001). In a previous study conducted by **Schwickert et al, 2021**[5] VEGF levelcut-off at 328.0 pg/ml had a negative likelihood ratio of 0.4 and a positive likelihood ratio of 2.5 for the same (AUC = 0.729, 95% CI 0.622□0.836, p < 0.001).

When regression analysis was done to assess the risk factors, a previous cesarean section, high maternal serum PROBNP levels and low VEGF levels were found to be significant predictor of Placenta accreta spectrum disorders. This was in corraboration with the findings of **Ersoy et al, 2016**[4] who depicted previous cesarean section, TROPONIN-I and PROBNP levels as strong predictors of Placenta accreta spectrum disorders.

The preferred mode of delivery in this study was emergency lower segment cesarean section (66.67%) followed by elective lower segment cesarean section (23.81%) in Placenta accreta spectrum disorder patients as well as placenta previa group when compared to control group. This was consistent with the study conducted by **Kumari et al, 2022**[6] and **Lad et al, 2022**[7] in which 73.77% and 72.98% of the PAS patients respectively required emergency cesarean section and 26.22% and 27.02% respectively had elective lower segment cesarean section.

In the present study 100% patients of Placenta accreta spectrum disorders required blood transfusion which was similar to the study conducted by **Kadhim et al, 2020**[8] who reported that 100% of the patients needed blood transfusion.

In our study 16.67% patients underwent hysterectomy of which all the patient were from the PAS group and none from Placenta previa group. In all 76.19% patients of Placenta accreta spectrum disorders had hysterectomy and among remaining ones placenta was left in situ in one patient (4.76%) who was given methotrexate in the post partum period. The others had either manual separation of placenta or focal resection of the placenta. This was in accordance with the study conducted by **Rani et al, 2020**[9] and **Dwivedi et al, 2016**[10].

There was one (4.76%) maternal mortality because of hemorrhagic shock with acute kidney injury and the patient was critical at the time of admission due to antepartum hemorrhage with severe anemia in shock. This was consistent with the study performed by **Rani et al, 2020**[9] who reported 2 (2.33%) maternal deaths due to hemorrhagic shock with DIC because they were already in critical condition with antepartum hemorrhage and shock at the time of admission.

On analysis of gestation age at delivery it was found that 76.19% patients of Placenta accreta spectrum disorders and 46.38% cases of placenta previa delivered preterm. This was consistent with the study conducted by **Kumari et al, 2022**[6] who reported 62.30% patients had preterm delivery.

Most of the patients (95.2% PAS and 78.3% placenta previa) were appropriate for gestation age at birth. However, 13% new borns in placenta previa group were small for gestation age. This was comparable to findings reported by **Jauniaux et al, 2019**[11] where 11% patients were small for gestation age.

In this study 33.33% neonates of the PAS group and 23.19% of placenta previa group had neonatal mortality while 13.4% newborns of placenta previa group were stillborn. **Singh et al, 2021**[12] reported 14% neonatal deaths. The high perinatal mortality in the current study could be attributed to the preterm termination of pregnancy and fetal prematurity.

Receiver operator analysis of the various biomarkers revealed a significant association of high maternal serum PROBNP and TROPONIN-I levels and low maternal serum VEGF levels with poor fetal outcome. Regression analysis was done to analyse the predictors of poor fetal outcome in our study. Among the different variables studied birth weight, high maternal serum PROBNP levels and high maternal serum TROPONIN-I levels were found to be significantly associated with poor fetal outcome.

Strength Of The Study

To the best of our knowledge this was the first study in India to identify the relationship between maternal venous PROBNP, TROPONIN-I and VEGF levels in placenta accreta spectrum disorders and placenta previa.

Matched age, BMI values, adjustment of the gestational age at birth values and regression analyses increased the validity of the comparisons among groups.

High internal validity.

No loss to follow up.

Limitations Of The Study

Single center study.

The limited number of patients of Placenta accreta spectrum disorders.

As most of the blood samples were drawn during third trimester, the usefulness of determining these biomarkers earlier in pregnancy which would be the prerequisite for a useful biomarker still must be investigated.

CONCLUSION

The novel maternal serum biomarkers viz. PROBNP, troponin-I and VEGF can be helpful in this condition as this is cost - effective and time saving than MRI and requires less expertise. Therefore the use of these biomarkers in addition to the ultrasonography further confirms the diagnosis of PAS making us doubly sure. The prompt diagnosis can help plan the further management in the form of timely referral from periphery centres and can buy time in making necessary arrangements for planning appropriate multidisciplinary management at higher centres well equipped with blood banks, anaesthesia, ICUs, radiology, urosurgery and neonatal facilities thereby lessing the dreaded sequalae.

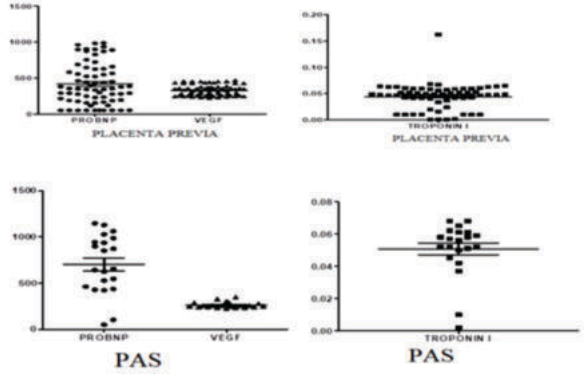

Figure 1: Scatter Plot For The Levels Of PROBNP, TROPONIN-I And VEGF In Patients With Placenta Previa And Placenta Accreta Spectrum Disorders

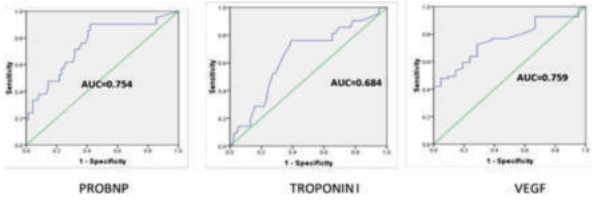

Figure 2: Receiver Operating Characteristic (ROC) Analysis Curve For PRO-BNP, TROPONIN-I And VEGF Of Pas Patients In Cases

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