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Original Research Article

Study and analysis of maternal serum alpha-fetoprotein levels as a biomarker of placental adherence in low lying placenta

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ABSTRACT

Background: The objective was to study and analyze maternal serum alpha-fetoprotein levels as a biomarker of placental adherence in low lying placenta.
Methods: This was a prospective observational study analysing the conditions and the data of 80 cases with low lying placenta in a tertiary care hospital. The analysis was done for the association of MSAFP with MRI, perinatal and maternal outcome.
Results: The level of MSAFP was found higher in 12 out of 13 cases (93.3%) of placenta previa with placental adherence. There was significant surgical intervention (80%) and increased maternal morbidity (68.8%) in the study group with placental adherence and raised MSAFP respectively.
Conclusions: MSAFP is an important biomarker for prognostication of placental adherence in low lying placenta.

Keywords: Low lying placenta, MSAFP, Placental adherence

INTRODUCTION

Antepartum hemorrhage forms one of the most dangerous and devastating group of disorders in obstetrics. Placenta previa occurs in approximately 1 in 300 deliveries.[1] At least 5% of such pregnancies have associated placental invasion (placenta accreta), which can necessitate hysterectomy. [2]

The independent risk factor for placenta praevia is a previous caesarean section. The risk increases with the number of caesarean sections performed. The incidence of placenta accreta is 3% in women with placenta previa with one previous cesarean section and the risk increases to 67% with five or more cesarean sections.[3]

Other risk factors include history of myomectomy, vigorous curettage resulting in asherman syndrome, submucous leiomyomas, previous uterine thermal ablation, uterine artery embolization and maternal age greater than 35 years old.[4-6]

MSAFP as a biomarker for complications in women with previa might help obstetricians to recognize placenta previa early and transport them to the major referral hospital, thereby decreasing the maternal and fetal morbidity and mortality.

Furthermore, an increased risk for abnormal placental adherence (i.e. placenta accreta/increta/percreta) also has been demonstrated in women with an elevated maternal

serum AFP level, especially in the presence of a placenta previa.[7,8]

In view of these findings, this study was undertaken to evaluate the abnormal levels of maternal serum alfa feto protein (MSAFP) as biomarker of abnormal placentation and placental adherence in the second and third trimester of pregnancy.

METHODS

This was a prospective observational study done on 80 patients. It was conducted in the department of Obstetrics and Gynaecology, Bebe Nanki Mother and Child Care Centre, Government Medical College, Amritsar, with permission of Institutional Ethics Committee. The study was done from March, 2021 to August 2022 for the pregnant women with low lying placenta and placenta previa at 15-20 weeks of gestation.

Statistical tool

The data was entered into computer and statistical analysis of the results was obtained by using windows-based computer software devised with Statistical Packages for Social Sciences (SPSS-22) (SPSSS Inc, Chicago, IL, USA).

Inclusion criteria includes all pregnant women with singleton pregnancy with USG diagnosis of placenta previa or low lying placenta with structurally normal fetus. Exclusion criteria includes all pregnant women with placenta in upper segment. All pregnant women with other causes of bleeding diagnosed as abortion, abruptio placentae, ectopic pregnancy, hydatiform, mole, local causes of vaginal bleeding, polyp, or foreign body etc.

The venous blood sample was withdrawn and the level of MSAFP was determined by ELISA method and result of MSAFP level was co-related with clinical findings, USG and MRI.

RESULTS

In the present study Majority of women 32.50% were in age group of 26-30 years. 67.50% patient were residing in rural area and 32.50% patients were residing in urban area. 72.50% patients were multigravida and 27.50% were primigravida. 22.50% had history of placenta previa in previous pregnancy and 77.50% patients had no history of placenta previa. 25% patient had previous one CS, 16.25% and 3.75% patients had previous two and previous three CS respectively. On calculating MSAFP levels at 15-20 weeks of gestation of patients with low lying placenta, 32.5% had MSAFP levels >2.5 MOM and 67.5% patients had MSAFP levels <2.5MOM (Table 1). Out of 80 cases, 62 had persistent placenta previa on follow up USG in third trimester. MRI was done only in suspected cases of placental adherence in 34 (54.84%) cases out of 62 cases of placenta previa following which 13 (38.24%) cases out of 34 had placental adherence 'p'<0.001(Significant) (Table 2).

Table 1: Patients demographic.

Characteristics		
Age (in years)	26-30	32.50%
	<30	40%
Area	Rural	67.50%
	Urban	32.50%
Obstetric formula	Primigravida	27.50%
	Multigravida	72.50%
History of placenta previa in previous pregnancy	Yes	22.50%
	No	77.50%
Previous caesarean section	One	25%
	Two	16.25%
	Three	3.75%

Table 2: MRI finings.

MRI	No. of cases (n=80)	Percentage
Not done	46	57.50
Done	34	42.50
	No. of cases of persistent placenta previa (n=62)	%
Placenta adherent	13/34	38.24
Accreta	9/13	69.23
percreta	3/13	23.08
Increta	1/13	7.69
Placenta not adherent	21/34	61.76

Maternal serum alphafetoprotein was raised (>2.5 MoM) in 12/13 cases of placental adherence as compared to 10/21 cases in which placenta was not adherent on MRI (p value < 0.001) (Table 3). Out of 80 cases, 18 cases had placenta moved to upper segment of which 10 cases had normal vaginal delivery, out of which 9 (90%) had normal MSAFP levels, while 1 (10%) had raised MSAFP levels. 41 cases had undergone cesarean section without any intervention, of which 37 (90.24%) cases had normal MSAFP levels and 4 (9.76%) had MSAFP levels more than 2.5 multiple of median.

13 cases had undergone cesarean section with bilateral uterine artery ligation of which 6 (46.15%) cases had raised MSAFP levels whereas all the 3 (100%) cases of cesarean section with internal iliac artery ligation had raised MSAFP levels and 12 out of 13 (92.31%) cases of cesarean hysterectomy had raised MSAFP Levels. (p value 0.001) (Table 4). MSAFP was raised to >2.5MoM in 8 out of 9 (88.89%) of morbidly adherent placenta accreta, 1 (100%) case of placenta increta and all 3 (100%)

cases of placenta percreta. In addition, in 1 patient where MSAFP was <2.5MoM but MRI showed placenta accreta (p value <0.001) (Table 5). MSAFP was raised in 13 out of 20 (65%) cases associated with increased maternal morbidity in form of prolonged hospital stay, ICU stay and increased need of blood transfusion. 76.92% (10 out of 13) cases associated with perinatal morbidity and 6.38% (3 out of 47) who had no increased maternal and perinatal morbidity (p value <0.001) (Table 6).

Table 3: Association between MSAFP and MRI

MSAFP	MRI n (%)				P value
	Normal	Abnormal	Not done	Total	
Normal (<2.5mom)	11 (52.38%)	1 (7.69%)	42 (91.30%)	54 (67.50%)	p<0.001
Raised (>2.5mom)	10 (47.62%)	12 (92.31%)	4 (8.69%)	26 (32.50%)	p<0.001
Total	21 (100.00%)	13 (100.00%)	46 (100.00%)	80 (100.0%)	

Table 4: Association between MSAFP and maternal delivery outcome.

MSAFP		Total number of cases	MSAFP<2.5MOM		MSAFP>2.5MOM	
			No. of cases	%	No. of cases	%
Normal delivery		10	9	90.00	1	10.00
Caesarean section - no intervention		41	37	90.24	4	9.76
Caesarean section with intervention (n=29)	**Caesarean section- bilateral uterine artery ligation**	13	7	53.85	6	46.15
	Caesarean section- internal iliac artery ligation	3	0	0.00	3	100.00
	Caesarean hysterectomy	13	1	7.69	12	92.31
Total		80	54	67.50	26	32.50

Table 5: Association between MSAFP and extent of placenta adherence.

MSAFP	Total number of cases	Normal <2.5MOM		Raised>2.5MOM	
		No. of cases	%	No. of cases	%
Not adhered	67	53	79.10	14	20.90
Placenta accreta	9	1	11.11	8	88.89
Placenta increta	1	0	0.00	1	100.00
Placenta percreta	3	0	0.00	3	100.00
Total	80	54	100.00	26	100.00

Table 6: Association between MSAFP and maternal and perinatal morbidity.

Morbidity	Total	MSAFP			
		Normal (<2.5MoM)		Raised (>2.5MoM)	
		No. of cases	%	No. of cases	%
Mother	20	7	35.00	13	65.00
Perinatal	13	3	23.08	10	76.92
None	47	44	93.62	3	6.38
Total	80	54	67.50	26	32.50

Table 7: Association between maternal morbidity and placental adherence.

Placental adherence		Maternal morbidity (%)				p value
		Increased	%	Absent	%	
Not Adhered	67	9	13.43%	58	86.57%	<0.001
Adhered (n=13)	13	11	84.62%	2	15.38%	
Total	80	20	100.00%	60	100.00%	

Table 8: Maternal morbidity.

Adhered (n=13)	Maternal morbidity (%)			
	Increased	%	Absent	%
Placenta accreta	7	53.85	2	15.38
Placenta increta	1	7.69	0	0.00
Placenta percreta	3	23.08	0	0.00

MSAFP was raised in 13 out of 20 (65%) cases associated with increased maternal morbidity in form of prolonged hospital stay, ICU stay and increased need of blood transfusion. 76.92% (10 out of 13) cases associated with perinatal morbidity and 6.38% (3 out of 47) who had no increased maternal and perinatal morbidity (p value <0.001) (Table 6).

Maternal morbidity (in the form of bladder injury, increase number of days of ICU stay or blood transfusion) was present in 11/13 (84.61%) cases of placental previa with adherence as compared to 9 (13.43%) out of 67 cases of placenta previa without adherence (Table 7).

DISCUSSION

In the present study, maximum number of patients i.e 32.5% belonged to age group of 26-30 years, followed by 27.5% for age group 20-25 years, 22.5% and 17.5%for 31-35 years and >35 years respectively.

In the present study 27.5% patients were primigravida, 72.5% are multigravida. Among the multigravida, 44.83% were gravida two and 43.1% were gravida three. The remaining 12.07% of the cases were gravida four. Babinszki et al reported that incidence increased significantly~ 2.2% in women with para five or greater as compared with women with lower parity.[9]

In the present study, advancing maternal age (40% ≥30 years) and increasing parity (55.17% para three and more) were independent risk factors for placenta previa. However, since women with higher parity are likely to be older, it is possible that advanced maternal age and increased parity may not be independent risk factors. This combined effect of age and gravidity on the risk of placenta previa was demonstrated in a large population-based, cohort study of singleton births from the USA done by Ananth CV et al in 2003.[10] This study showed that the risk of placenta previa was not independent of maternal age and parity, but rather that both factors exerted a joint influence on placenta previa risk.

In the present study, among multigravida 45.0% had no history of previous caesarean section, 25% had history of one previous caesarean section, 16.25% and 3.75% had history of previous two and three caesarean section respectively. None of the patient in study group had history of any curettage or myomectomy. In a study done by Lala ABH et al[11] the incidence of placenta previa is 2% after one previous caesarean section, 4.1% after two and 22% after three previous caesarean sections.

In the present study, out of 80 cases of low-lying placenta, on follow up USG in the third trimester 62(77.5%) had persistent placenta previa. Out of 62, 49(61.25%) cases had placenta previa without adherence and 13 (16.25%) had placenta previa with adherence.

MSAFP was elevated (>2.5 MoM) in 12 out of 13 (92.3%) cases of placenta previa with adherence. Among 13 cases of placental adherence MSAFP levels were elevated in 8 out of 9 (88.8%) cases of placenta accreta, 1 (100%) case of placenta increta and 3 out 3 (100%) cases of placenta percreta. P value was less than 0.001, making result statistically significant. Similar to our findings, Verma P et al in 2016 showed results, that MSAFP >2.5MoM (Multiple of the median) in 11 out of 12 cases of placenta accreta (91.6%), 2 cases of placenta increta (100%), 1 case of placenta percreta (100%).Zelop C et al[7] performed a study in which 45% cases of caesarean hysterectomy due to placenta accreta/increta/percreta had elevated MSAFP levels.[12]

Significant association was seen between raised MSAFP and maternal morbidity with P value <0.001. Butler EL et al performed the study on 107 antenatal patients with placenta previa, out of which 14 had elevated levels of MSAFP and these were the patients who required prolonged hospitalization, ICU monitoring, multiple blood transfusions and even had preterm deliveries. Thus, concluded that raised MSAFP is associated with increased maternal and fetal morbidity.[13] In another study by Verma P et al (2016), MSAFP level was higher in 93.3% of cases with placenta previa with placental adherence.[12] Also, they found a significant surgical intervention (80%) and increased maternal morbidity (68.8%) in cases of placenta previa with adherence. In the present study, out of 13 adherent placenta previa cases 12(true positive) could be predicted by MSAFP levels (>2.5MOM), rest out of 67, 53 cases could be ruled out of having adherence (True negative). Hence MSAFP has a sensitivity of 92.31%, specificity of 79.10% with PPV of 46.15% and NPV of 98.15%.

Limitations

Out of 80 patients of low-lying placenta at 15-20 weeks of gestation, 13 cases had placental adherence among 62 persistent placenta previa cases and MSAFP levels were evaluated for prognostication among them. As the numbers of patients with placental adherence were less in the study, so more studies are needed to evaluate the role of MSAFP as a biomarker for placental adherence in low lying placenta.

CONCLUSION

It was observed that with increase in parity and number of caesarean sections, the risk of placenta previa with adherence keep on increasing. Surgical intervention and maternal morbidity were increased in cases of placenta previa with adherence, in whom MSAFP levels were >2.5 MOM. Hence By our study we have found that elevated levels of MSAFP may be used as a biomarker for prognostication of morbidly adherent placenta previa so that early recognition and timely intervention can be done. However more studies are needed to confirm.

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