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"MATERNAL SERUM ALPHA-FETOPROTEIN AS A BIOMARKER OF PLACENTAL ADHERENCE IN PLACENTA PREVIA"

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Abstract :
Aims & Objectives: To study the association between maternal serum alpha feto-protein and morbidly adherent placenta.
Methods: This prospective observational study was carried out in a tertiary care hospital to analyse the condition of 110 cases of third trimester placenta previa. In few strongly suspect cases analysis was done to associate MSAFP with MRI.
Results: The levels of MSAFP was found to be significantly raised i.e more than 2.5MoM in 12 out of 14 cases (85.71%) of adherent placenta previa, having sensitivity of 85.17%, specificity of 94.79%, positive predictive value of 70.59% and negative predictive value of 97.85%. The patients having significantly raised MSAFP levels underwent major surgical intervention.
Conclusions: MSAFP is considered as an important biomarker in detection of adherent placenta in placenta previa cases.

Index Terms: MSAFP (Maternal serum alpha feto-protein), adherent placenta, placenta previa.

I. INTRODUCTION

Morbidly adherent placenta previa represents one of the most dreaded and devastating group of complication in obstetrics. It is one of the major causes of maternal morbidity and mortality worldwide. "Placenta previa is defined as placenta lying partially or completely in the lower uterine segment"[1]. But the term "Morbidly adherent placenta describes abnormal placentation characterized by abnormally implanted, invasive or adherent placenta"[2]. It accounts for 4 per 10,000 deliveries[3] to as high as 90 per 10,000 deliveries[4]. The antepartum diagnosis of placenta accreta/ increta/ percreta is usually accomplished through ultrasound[5] or Magnetic Resonance Imaging[6].

Factors associated with higher incidence of placenta accreta include previous history of caesarean section, prior uterine surgeries (Myomectomy), vigorous curettage[7]. In 2003, Tuzovic L and others in a study[8], stated that the presence of previous uterine scar prevents the migration of the placenta to the uterine fundus leading to placenta previa, which are the combined risk factors for morbidly adherent placenta[9,10,11,12].

Berkley[13] described that in pregnancy associated with morbidly adherent placenta where there is disruption of Nitabuch's membranes i.e feto-maternal interface disruption causes leakage or seepage of AFP into maternal circulation thus causing elevated of MSAFP.

Diagnosing morbidly adherent placenta is usually done by ultrasonography and MRI, but these facilities are not easily available in every FRU (first referral unit) or peripheral centres. Strategy can be implemented for early recognition or suspicion of placenta accreta spectrum in all placenta previa cases by screening them with MSAFP.

II. METHODS

A prospective observational study was carried out among the hospitalized patients for one year from 1st June 2019 to 31st May 2020 analysing the data of 110 placenta previa cases in Department of Obstertrics and Gynaecology in Gauhati Medical College Hospital, Guwahati, Assam after obtaining ethical clearance from Institute of Ethics Committee Gauhati Medical College Hospital, Guwahati, Assam on 10th April 2019.

Inclusion criteria

All hospitalized pregnant women with clinical and ultrasonographic diagnosis of placenta previa in 3rd trimester.

Exclusion criteria

1.All the pregnant women with placenta in upper segment.
2.All the pregnant women with other causes of 1st, 2nd, 3rd trimester bleeding diagnosed as abortion, abruptio placentae, ectopic pregnancy, hyadatidiform mole, local causes of vaginal bleeding, polyp or foreign body, ovarian tumour(endodermal sinus tumour).
3.Open neural defects in fetus (spina bifida, anencephaly), gross structural abnormalities and abdominal wall defect of fetus (omphalocele, gastroschisis),

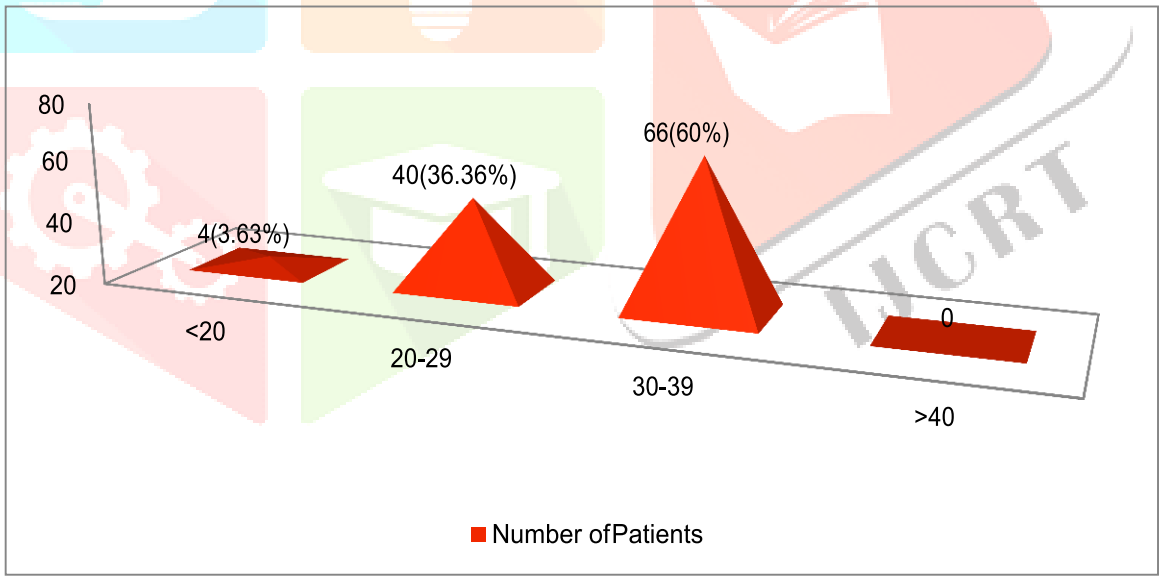
After taking proper history and informed consent, counselling was done regarding the condition and the need of early diagnosis and proper management of such cases. Along with routine blood investigations 4ml of venous blood sample for MSAFP also sent and estimated by ELISA method, and result of MSAFP level were expressed in Multiples of Median and were co-related with USG/MRI findings. All the variables were entered into spreadsheet program i.e MS-Excel 2019®.Data analysis was done using SPSS (IBM corporation® version 21), chi-square test used, p value<0.05 was considered significant.

III. RESULTS

In the present study, we observed that out of 110 cases, 14 cases (12.7%) had Type I placenta previa, 36 cases(32.7%) had Type II placenta previa, 21 cases(19.09%) had Type III placenta previa, 39 cases(35.45%) had Type IV placenta previa. We observed that 70.9% of cases had anterior placenta and 29.09% had posterior placenta previa.
In the present study, out of 110 placenta previa cases, there were 8(7.27%) placenta accreta cases, 3(2.72%) placenta increta cases, 3(2.72%) placenta percreta cases, placental adherence was absent in 96(87.27%) cases of placenta previa.

In the present study, we observed, the highest number that is 6.349%(4 out of 63 cases) of placenta previa was found in previous one caesarean delivery , 41.1%(7 out of 17) of placenta previa found in previous two caesarean delivery cases. 50% (1 out of 2) of placenta previa found in previous three caesarean section cases.

Bar Graph 1. Distribution of cases according to age



Bar Graph 2. Association between parity and MSAFP. n=110, Adherent Placenta = 14.

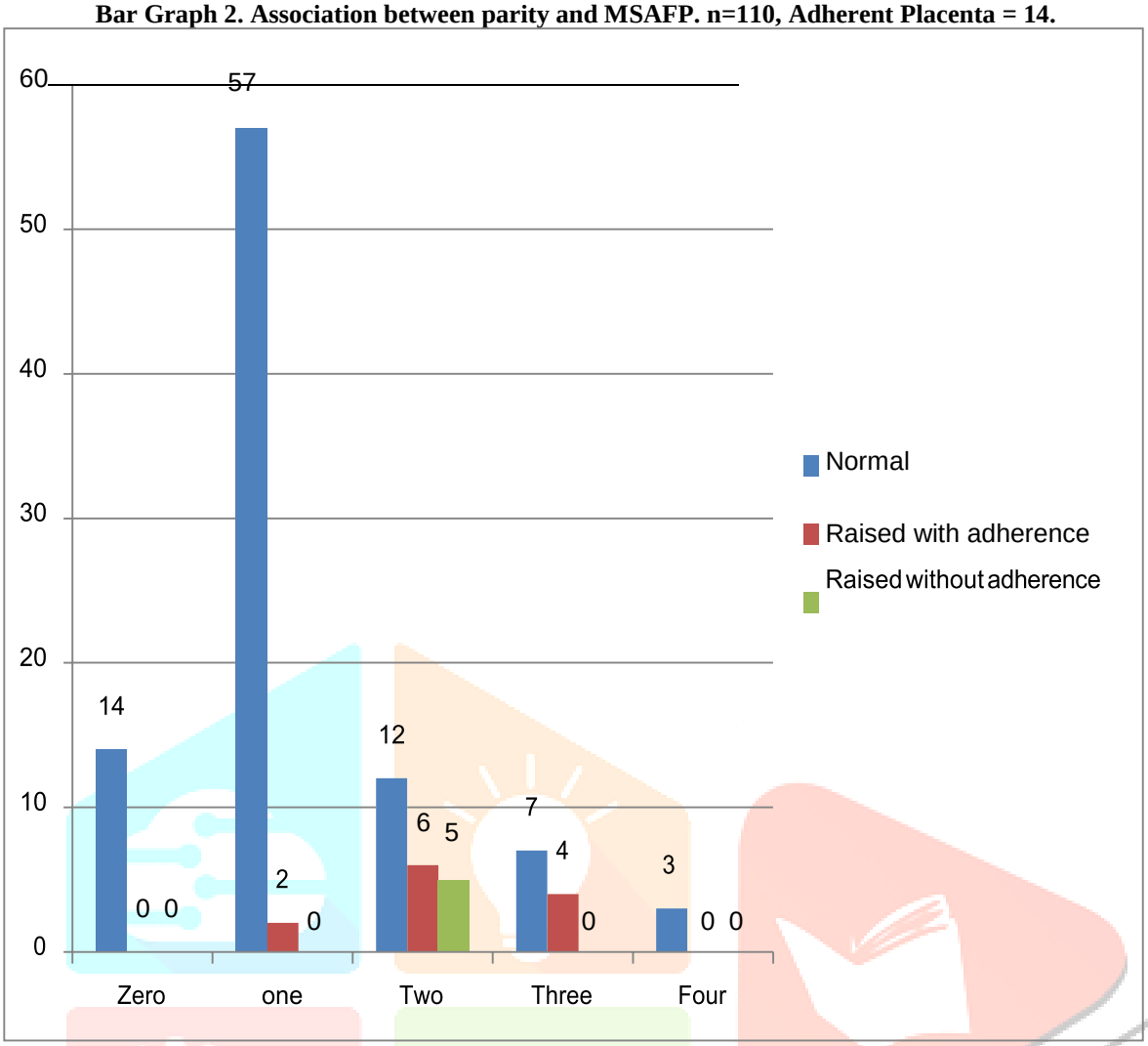


Table 1. Association between number of previous caesarean section and MSAFP in adherent placenta previa.

		MSAFP				
		Normal	Raised with adherence	Raised without adherence	Total	P value
No.of LSCS	0	28	0	0	28	<0.0001
	1	57	4	2	63	
	2	7	7	3	17	
	3	1	1	0	2	
Total		93	12	5	110	

Table 2. Association between MSAFP and MRI

MSAFP	MRI n%				P value
	Normal	Abnormal	Not Done	Total	
Normal	1(1.1%)	0(0%)	92(98.92%)	93 (100%)	<0.0001
Raised	2(11.76%)	6(35.29%)	9(52.94%)	17 (100%)	
Total	3(2.72%)	6 (5.45%)	101(91.81%)	110(100%)	

In our study, table 2 shows out of 110 placenta previa cases, MRI was done in 9 cases, out of them 6(66.66%) cases showed evidence of placental adherence, 3(33.33%) cases had no evidence of placental adherence. Maternal S.AFP was also raised significantly(>2.5 MoM) in those same 6 cases which showed placental adherence. MSAFP was also raised in 2 cases without evidence of placental adherence. (P<0.0001). Thus results showed the relation between MSAFP and placental adherence was significant.

Table 3. Association between MSAFP and Placental Adherence, n=110,

MSAF P	Placental Adherence n %					P value
	No.Not adhered	No.Placenta Accreta	No.Placenta Increta	No.Placenta Percreta	Total	
Normal	91(97.8%)	2(2.2%)	0(0%)	0(0%)	93(100%)	<0.0001
Raised	5(29.4%)	6(35.3%)	3(17.6%)	3(17.6%)	17(100%)	
Total	96(87.3%)	8(7.3%)	3(2.7%)	3(2.7%)	110(100%)	

We observed that, table 3, in our hospital incidence of morbidly adherent placenta previa found to be 12.7 % (14 out of 110cases). Incidence of placenta accreta, increta and percreta cases were found to be 7.27 % (8 out of 110), 2.72 % (3 out of 110) and 2.72 % (3 out of 110) respectively. MSAFP was significantly raised i.e >2.5MoM(Multiple of median) in 6(75%) out of 8 cases of placenta accreta, 3(100%) cases of placenta increta and in 3(100%) cases of placenta percreta. 96 out of 110 cases(87.3%) had no placental adherence. we got (p <0.0001). Thus results showed the relation between MSAFP and adherent placenta was significant.

Table 4. Distribution of cases according to maternal mode of delivery along with additional intervention required. n=110, (considering preterm delivery as an independent outcome)

Maternal Outcome	Frequency	%
Normal Delivery	11	10
Preterm Delivery	25	22.72
Caesarean Delivery(CS)	74	67.27
CS with uterine artery ligation	19	17.27
Caesarean Hysterectomy with bilateral uterine artery and bilateral internal iliac artery ligation	6	5.45
Total	110	100

Table 5. Association between MSAFP and delivery outcome.

n=110(considering preterm delivery as an independent outcome), Adherent Placenta=14, Raised MSAFP=17 cases

MSAFP	Delivery outcome					P value
	Normal Delivery	Caesarean Section- No intervention	Caesarean section– only Bilateral uterine artery Ligation	Preterm Delivery	Caesarean hysterectomy with Bilateral Uterine artery and Internal iliac artery ligation	
Normal	11	71	11	21	0	<0.0001
Raised	0	3	8	4	6	
Total	11	74	19	25	6	

Table:6. Sensitivity and specificity of MSAFP test

MSAFP in adherent placenta previa	**True positive**	**False negative**	**True Negative**	**False positive**
MSAFP > 2.5 MoM	12	2	91	5

In table 6 ,out of 14 adherent placenta previa cases 12 could be predicted. Out of 110 placenta previa cases 91 cases could be ruled out of having adherence. Hence MSAFP level has a sensitivity (95% CI) of 85.17%(57.19% to 98.22%) and a specificity (95% CI) of 94.79%(88.26% to 98.29%). Positive predictive value(95% CI) = 70.59%(49.89% to 85.26%) and negative predictive value of 97.85 %(92.65% to 99.40%).

IV. DISCUSION

The risk of placenta previa increases with increasing age. However, in the present study as shown above , maximum number of placenta previa was found in the age group of 26-30years i.e 52.72% of cases followed by 41.81% of cases in the age group of >30years. 3.63% of cases in the age group of <20years, 1.81% cases in the age group of 21-25years. The mean age group in our study is 30.1years, which was similar to the mean age group of in the study done by Dr.Itedal[14] Abdelraheem in 2017 i.e 28.03year. Study done by Lea Tuzovic and others 2003[8] also had showed similar results i.e 31year of mean age. Even in the study done by Mathuriya G[15] and Parikh PM[16] and others showed the maximum number of cases i.e 67.6% and 58.22% respectively, they were of 26-30years age group, which were similar to the present study.

In our present study, the above bar graph 2 showed that out of 110 cases, 14(12.72%) cases were nulliparous, 59(53.63%) cases were para one, 23(20.90%) cases were para two, 11(10%) cases were para three, 3(2.72%) cases were para four or more. 85.71% (12 out of 14) adherent placenta previa cases with raised(>2.5MoM) MSAFP level were multigravida(1-3 para), 29.41%(2 out of 14) Adherent placenta previa had MSAFP(<2.5MoM)levels were para one, thus results showed association between parity and MSAFP, p <0.0001, was significant.

In the present study in table, the incidence of adherent placenta previa was found to be increasing with increase in number of caesarean section i.e in once, twice, thrice previous caesarean delivery were 7.93%(5 out of 63), 47%(8 out of 17 cases) and 50% of cases(1 out of 2) respectively. Results were comparable to other studies. No significant association was seen with dilatation and curettage or any other scar of uterus as of myomectomy. 85.71%(12 out of 14) of adherent placenta previa cases with previous caesarean cases had raised MSAFP. Another study done by Dr.Pooja Verma[17] and others showed 93.3% of adherent placenta previa with raised MSAFP cases had history of previous caesarean section , these results were comparable. According to ACOG(2018)[18] with the presence of placenta previa, the risk of placenta accreta was 3%,11%, 40%,61%, and 67% for the first, second, third, fourth, and fifth or greater repeat caesarean deliveries respectively.

In patients with previous caesarean delivery most of them had anterior placenta and on ultrasonography, few patients had thin anterior myometrial segment (<5mm), loss of sub placental lucent zone, in few cases even blood vessels were found in the bladder. Those cases who had marked rise in MSAFP which were suspected having adherent placenta, in those cases MRI was advised to rule out adherent placenta , later in such 6 patients caesarean hysterectomy was done.

In the present study table 5 showed, out of 110 cases, all 6(100%) cases who underwent caesarean hysterectomy with bilateral uterine artery ligation with internal iliac artery ligation had significantly elevated(>2.5MoM) MSAFP level. 42.10%(8 Out of 19) cases who underwent caesarean delivery with bilateral uterine artery ligation had significantly elevated(>2.5MoM) MSAFP level, all 11cases who had spontaneous delivery their MSAFP level were not raised(<2.5MoM) significantly. Out of 74, 3(2.72%) cases who underwent only caesarean delivery showed elevated MSAFP level. In total p value =<0.0001, thus results were significant.Out of 14 adherent placenta previa cases 12 could be predicted. Out of 110 placenta previa cases 91 cases could be ruled out of having adherence. Hence MSAFP level has a sensitivity of 85.17% and a specificity of 94.79%. Positive predictive value= 70.59% and negative predictive value of 97.85 %.

Incidence of placenta accreta, increta and percreta cases were found to be 7.27%(8 out of 110), 2.72%(3 out of 110) and 2.72%(3 out of 110) respectively in our present study.In our study, MSAFP >2.5MoM (Multiples of the median) in 75%(6 out of 8) cases of placenta accreta , 3(100%) cases of placenta increta , 3(100%) cases of placenta percreta . It has been observed in studies that if there is deficiency of Nitabuch's membrane that will allow the leakage of fetal alpha feto-protein into maternal circulation, upto 45% of women with placenta accreta had elevated Maternal Serum Alpha Feto-Protein (MSAFP) levels in the absence of an obvious cause[13]. In our study 85.71%(12 out 14) adherent placenta had significantly raised MSAFP. Another study done by Dr.Pooja Verma in 2016[17] similar results were shown, i.e MSAFP >2.5MoM (Multiple of the meadian) in 11 out of 12 cases of placenta accreta (91.6%), 2 cases of placenta increta (100%), 1 case of placenta percreta (100%). Study done by Emad ahmed fyala[20] showed , MSAFP levels increases with increase in invasion i.e placenta accreta, increta and percreta with increase in mean=SD(standard deviation) 153.2+38.1, 178.3+25.2 and 263.3+36.1 respectively.

In the present study it was found that 88.18% cases with cephalic presentation, 6.36% with breech presentation, 5.45% with transverse presentation. These results were quite similar to those of other studies like in Rajeshwari RR et al[19] (2016) they were 94%,3%, 3% respectively and in study done by Rangaswamy79(2016) they found 59.6%,24.1% and 9.6% respectively.

V. CONCLUSION

Morbidly adherent placenta previa is a serious situation in obstetrics and should be managed by senior obstetricians with good surgical skills, along with availability of blood and with ICU backup in tertiary care hospital. Majority of the health care facilities in the peripheral hospitals lack proper infrastructure and man power with adequate skills to deal with such serious situation. Diagnosing morbidly adherent placenta is usually done by ultrasonography and MRI, but these facilities are not easily available in every FRU (first referral unit) or peripheral centres. By our study we have found that MSAFP levels can predict adherent placenta previa. Strategy should be implemented for early recognition or suspicion of placenta accreta spectrum in all placenta previa cases by screening them with MSAFP. The elevated levels of MSAFP can be used as a biomarker to predict the occurrence of morbidly adherent placenta previa. The present study showed that there is a significant association between placenta accreta/ increta/ percreta and MSAFP level.

VI. REFERENCE

1. Ian Donald's Practical Obstetric Problem 7edition 2014 Editor Mishra R.
2. Williams Obstetrics 25th edition 2018 Copyright© 2018 by McGraw-Hill education.
3. Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. United Kingdom Obstetric Surveillance system Steering Committee. Caesarean delivery and peripartum hysterectomy. Obstet Gynecol. 2008; 111(1):97-105.
4. Miller DA, Chollet JA, Goodwin TM. Clinical risk factors for placenta previa- placenta accreta. Am J Obstet Gynecol. 1997; 177(1):210-14.
5. SHIH J C., PALACIOS JARAQUEMADA J.M., SU Y.N., et al.: Role of three- dimensional power Doppler in antenatal diagnosis of placenta accrete: Comparison with grey-scale and Doppler techniques. Ultrasound Obstet. Gynecol., 33 (2): 193-203, 2009.
6. LAM G., KULLER J. and McMAHON M.: Use of Magnetic resonance imaging and ultrasound in antenatal diagnosis of placenta accreta. J. Soc. Gynecol. Investig., 9 (1): 37-40, 2002.
7. Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty-year analysis. Am J Obstet Gynecol 2005;192: 1458-61.
8. Lea Tuzović, Josil Djelmiš, Marcela Ilijić. Obstetric Risk Factors Associated with Placenta Previa Development: Case – Control Study.Croatia. 2003; 44(6):728-733.
9. Tuzovic L, Djelmis J, Ilijic M. Obstetric risk factors associated with placenta previa development: case control study. Croat Med J. 2003; 44(6):728-33.
10. Abu-Heija AT, El-Jallad F, Ziadeh S. Placenta previa: effect of age, gravidity, parity and previous caesarean section. Gynecol Obstet Invest. 1999; 47(1):6-8.
11. Rao KP, Belogolovkin V, Yankowitz J, Spinnato JA 2nd. Abnormal placentation: evidence-based diagnosis and management of placenta previa, placenta accreta, and vasa previa. Obstet Gynecol Surv. 2012; 67(8):503-19.
12. Sheiner E, Shoham-Vardi I, Hallak M, Hershkowitz R, Katz M, Mazor M. Placenta previa: obstetric risk factors and pregnancy outcome. J Matern Fetal Med. 2001; 10(6):414-9
13. Berkeley AS, Killackey MA, Cedarqvist LL. Elevated maternal serum alpha- fetoprotein levels associated with breakdown in fetal-maternal-placental barrier. Am J Obstet Gynecol.1983;146:85.
14. Dr.Itedal Abdelraheem Mohamed Ahmed. Impact of Maternal Age and Parity in Incidence of placenta previa. IJCR Vol 9, June 2017, 53060-53064.
15. Mathuriya G, Lokhande P. Comparative study of obstetric outcome between scarred and unscarred uterus in placenta previa cases. Indian J Clin Pract 2013; 24(6): 568-71.
16. Parikh PM, Makwana S, Shah S, Vithalani V. Feto - Maternal Outcome in Placenta Previa in Scarred Uterus Vs Non Scarred Uterus. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS).Jan. 2016; 15(1): 69-73.

17. Pooja Verma, Kavita N.Singh, Vineeta Ghanghoriya. To study analyse maternal serum alpha-fetoprotein as a biomarker of placental adherence in low lying placeta. IJRC, 2016 Jun; 5(6):1959-1963.
18. Placenta Accreta Spectrum, Obstetric Care Consensus Number 7 December 2018 (Replaces Committee Opinion No.%29,July)
19. Rajeshwari RR, Rubini M. Maternal and perinatal outcome in placenta previa - one year study intertiary care center in Tamil Nadu, India. Int J Reprod Contracept Obstet Gynecol. 2016 Aug; 5(8):2819-2822
20. Shaukat A, Zafar F, Asghat S, Nighat, Ayoob A , Nafeesa Ambreen, Rahim A, Zenab Aziz Z. Frequency of Placenta Previa with Previous C-Section. PJMHS 2009; 3(3): 234-237.