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Association between Serum Alfa Fetoprotein and Placenta Previa-Benghazi Medical Center

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Placenta Previa occurs when the placenta is wholly or partially implanted in the lower uterine segment. The exact cause of Placenta Previa is not known, but there is association with various risk factors. The study included 103 placenta Previa cases and 96 control cases. Case control design was used and duration of the study was during August 2020 to January 2021.The most common risk factors associated with study was placenta Previa were, advanced maternal age, history of previous antepartum hemorrhage, previous cesarean section and preterm deliveries and history of present antepartum hemorrhage & postpartum hemorrhage and cesarean section deliveries with preterm deliveries. There was a statistically significant difference between mean of maternal serum alfa fetoprotein of placenta Previa cases which was obviously higher as compared to control group. All cesarean hysterectomy cases had high level of SAFP. This difference was statistically significant. From the present study, it is recommended that there is a need for comprehensive obstetrics care to appropriately treat Placenta Previa and its complications. This calls for proper screening for level of maternal serum alfa fetoprotein, examination and health education during the antenatal care.

Keywords: Placenta Previa; maternal age; abortion; cesarean section.

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1. INTRODUCTION

Placenta Previa occurs when the placenta is wholly or partially implanted in the lower uterine segment. The exact cause of Placenta Previa is not known, but its association with various risk factors such as advanced maternal age, multiparity, previous miscarriages, previous caesarean section, and cigarette smoking is well documented. Traditionally, Placenta Previa is classified as ''complete '' When the placenta completely covers the internal cervical os, ''partial '' when the placenta partially covers the os, ''marginal '' when the lower edge of the placenta just reaches the os , and ''low – lying'' when the placenta is in the lower segment but does not reach the internal os. Complete and partial Placenta Previa are considered ''major placenta Previa', while marginal Placenta Previa and low lying placenta are considered ''minor placenta Previa ''. In recent years, ultrasound scanning has led to more accurate localization of the placenta. Nonetheless, the relationship between the different types of Placenta Previa, associated risk factors, and pregnancy outcome is poorly characterized. Although the clinical course of placental Previa is highly suggestive, the etiology of this condition still retrains obscure. The strongest connection was found between previous history of cesarean section, high parity, and advanced maternal age, but the strength of the connection varies from study to study [1]. Antepartum hemorrhage forms one of the most dangerous and devastating group of disorders in obstetrics. Placenta Previa occurs in approximately 1 in 300 deliveries. At least 5% of such pregnancies have associated placental invasion (placenta accreta), which can necessitate hysterectomy. The independent risk factor for placenta Previa 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 and one previous cesarean section. The risk continues to increase with each additional cesarean section up to 67% in women with a placenta Previa and five or more cesarean sections [2].

Associations' Fetal Abnormality: The Fate of fetal abnormality is approximately doubled in women with placenta Previa. Intra uterine growth restriction: Is common in women with multiple bleeds from a placenta Previa. The overall rate is 15%. Maternal serum alpha - fetoprotein are of great association with Placenta Previa specifically in Women With unexplained elevated its screening level. Ten percent of women with a bleeding Placenta Previa will have a co-existent abruption [1].

Diagnosis: The possibility of placenta Previa should not be dismissed until sonographic evaluation has clearly proved its absence. The simplest, safest, and most accurate method of placental localization is provided by trans abdominal sonography.

Alpha-fetoprotein (AFP) is a serum glycoprotein that was discovered early in human fetal serum by Bergstrand and Czar in 1956n. It is the chief mammalian tumor associated fetal protein found in adult's blood (by a small amount of 10-20 ng/ml).

Maternal serum alpha fetoprotein is elevated in some pregnancy complications such as spontaneous abortion, pre-eclampsia, gestational hypertension, preterm delivery and premature rupture of membranes (PROM). Also, poor maternal and fetal outcome is strongly related to the elevation of maternal AFP (probably as a result of placental injury). In addition, a significant association was found between increasing maternal AFP and the greater likelihood of persistent placenta Previa. Furthermore, the risk for abnormal placental adherence was increased in women with an elevated maternal serum AFP level, especially in the presence of a placenta previa [3].

Aims of the Study: To evaluate the relationship between maternal serum alpha-fetoprotein and the risk of persistent placenta Previa and outcome.

2. REVIEW OF LITERATURE

Study in India by Pooja Verma et al, they found that the level of Maternal Serum Alfa Fetoprotein (MSAFP) was higher in 14 out of 15 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. They concluded that the MSAFP is an important biomarker for prognostication of placental adherence in low lying placenta [2].

Study by E L Koster et al included 275 women with Previa at 15-20 weeks' gestation, 33 (12%) had Previa at delivery. Trend analysis revealed a greater likelihood of

persistent Previa with increasing MSAFP values (p=0.01). Mid- trimester MSAFP <1 multiple of the median was associated with a decreased incidence of persistence of 4%, significantly less than the risk at > or =1 multiple of the median (16%; p=0.01). They concluded that there is an association between increasing MSAFP values and greater likelihood of persistent placenta Previa. An MSAFP value <1 multiple of the median is associated with a reduction in the risk of persistence of Previa to delivery [4].

Study by Hümeyra Öztürk et al was found a significant relationship between adverse pregnancy outcomes and abnormal elevation of Human Chorionic Gonadotropin (HCG) and AFP levels in the second trimester. In cases of isolated elevation of HCG, preeclampsia and preterm labor/spontaneous preterm birth rate were slightly higher than in the control group (p=0.043, p=0.015), while Intra Uterine Growth Retardation (IUGR), Premature rupture of Membrane (PPROM), placental abruption, and intrauterine fetal death rates were all similar (p=0.063, p=0.318, p=1.00, p=0.556). In case having an elevation in both markers, increased rate of obstetric complications has been observed. A significant relationship was found between the high levels of maternal serum AFP and HCG multiple of the median and poor pregnancy outcomes like preeclampsia, IUGR, PPROM, intrauterine fetal death (p=0.003, p=0.001, p=0.040, p=0.006). They concluded that no definitive follow-up and treatment protocols have been established for patients at increased risk. In light of these findings, it is recommended to inform and educate patients about the most likely signs and symptoms of complications, to make more often antenatal visits, to perform more frequent ultrasound examination (fetal growth, AFI, etc.), NST, arterial/venous doppler, biophysical profile, and cervical length measurements in high-risk group [5].

Study by E L Butler included 107 women with placenta Previa delivered during the study. Fourteen (13%, 95% CI 7%, 21%) had MSAFP at least 2.0 multiple of the median. They were significantly more likely than those with lower MSAFP levels to have one or more of the following outcomes: hospitalization for antepartum bleeding before 30 weeks' gestation (50% versus 15%), delivery before 30 weeks' gestation (29% versus 5%), or preterm delivery for pregnancy-associated hypertension before 34 weeks' gestation (14% versus none). The MSAFP cut-off of 2.0 multiple of the median provided the best combination of sensitivity and specificity for those outcomes, using receiver operating characteristic curves. They concluded that women with placenta Previa who also have high MSAFP levels are at increased risk of bleeding in the early third trimester and preterm birth [6].

Risk factors of placenta Previa: mostly described are; Prior cesarean delivery, prior pregnancy terminations, history of intrauterine surgery, tobacco use, multiple gestation, multiparity, increased maternal age [7].

The classic clinical presentation of placenta Previa is painless bleeding in the late second trimester or early third trimester. However, some patients with placenta Previa will experience painful bleeding, possibly the consequence of uterine contractions or placental separation, some other cases could experience no bleeding at all before labour. There is a possibility that placenta Previa may lead to an unstable lie or mal presentation in late pregnancy [8].

3. SUBJECTS AND METHODS

3.1 Study Design

Type of study: A prospective study included women with singleton pregnancies diagnosed by sonographic have evidence of placenta previa, admitted to Maternity department (Benghazi Medical Center (BMC) during 1st Sep 2021 to 28th Feb. 2021 (six months) and followed till delivery.

Participants: All mothers admitted to Maternity department with singleton pregnancies beyond 24 weeks gestation will be selected in this study and proofed with ultra sound had placenta previa (the most recent ultrasound result will be dependable if the patients had more than one ultra Sound).

Exclusion Criteria: Multiple pregnancy.

Procedure: Full medical and obstetric history will be taken from all patients, general and obstetric examination will be done, MSAFP will be measured. Mothers will be follow till delivery.

Data collection: All needed date will be collected in proforma in Appendix I.

Data Analysis: Data analyzed using (SPSS) statistical package of social science program version 23.

The statistical Analysis Included:

1. Descriptive Statistics: Including (Mean value, Standard deviation, Number and Percentage.
2. Inferential Statistics: will be used when needed as t- test and Chi-square, P-value will be considered significant when ≤ 0.05.

Data will be presented in form of tables and figures, were the figures will be done by Microsoft Excel 2010.

Time Table: This study will done during period from August 2020 to January 2021explained in following time.

4. RESULTS

The study included 103 placenta Previa cases and 96 control cases.

Table 1. Placenta previa cases & their control group

Group	No	%
Placenta Previa cases	103	51.8
Control	96	48.2
Total	199	100.0

The mean age ± standard deviation of cases was 34.89 ± 5.817 years as compared to their control 31.98 ± 6.476 years. This difference was statistically significant, P= 0.001 as shown in Table 2.

The mean number of gravidity ± standard deviation of cases was nearly similar to their controls (5.17 ± 2.43 & 5.17 ± 2.74 years respectively). This difference was not statistically significant, P= 0.996. Regarding parity, the mean number of parity ± standard deviation of cases was 3.39 ± 1.94 as compared to 3.60 ± 2.33 of controls. The difference was not statistically significant, P= 0.478. The mean number of abortions ± standard deviation of cases was 0.91±1.23 as compared to 0.57 ± 0.98, this difference was statistically significant.

The most common blood group among both cases & controls was group O positive, 59.0% were controls as compared to 41.0% were cases, followed by blood group A positive, 51.9% were controls as compared to 48.1% were cases and the least common blood group was AB negative, only one case had this blood group. These differences were not statistically significant, P= 0.06 Table 4.

Regarding history of preterm labor of both cases & controls, all preterm labor cases were recorded among placenta Previa cases and none of the control cases had history of preterm labor. This difference was statistically significant, P= 0.002, as shown by Table 5.

Regarding history of complications in the past deliveries of both cases & controls, all complications were recorded among placenta Previa cases and none of the control cases had history of past pregnancy complications. The complications included; postpartum hemorrhage, blood transfusion, urinary tract infection, adhesions, pre-eclamptic toxemia, perineal tear, abruptio placenta & adhesions, and wound infection. These differences were statistically highly significant, P= 0.001, as shown by Table 6.

Regarding history of bleeding in early pregnancy of both cases & controls, all cases with a history of bleeding in the early present pregnancy cases were recorded among placenta Previa cases and none of the control cases had history of preterm labor. This difference was statistically highly significant, P= 0.000, as shown by Table 7.

Regarding history of bleeding in the second &third trimester of both cases & controls, all cases with a history of bleeding in the second &third trimester of the present pregnancy were recorded among placenta Previa cases and none of the control cases had history of preterm labor. This difference was statistically highly significant, P= 0.000, as shown by Table 8.

Table 2. Age in years of placenta previa cases & their control group

Placenta Previa cases N= 103		Control N=96	
Mean	**Standard deviation**	**Mean**	**Standard deviation**
34.89	5.817	31.98	6.476

P= 0.001

Table 3. Gravidity, parity and number of abortions of Placenta Previa cases & their control group

Variable	Groups	Mean	Standard deviation	P value
Gravida	Placenta Previa cases N= 103	5.17	2.43	P= .996
	Control N=96	5.17	2.74	
Parity	Placenta Previa cases N= 103	3.39	1.94	P= .478
	Control N=96	3.60	2.33	
Number of abortions	Placenta Previa cases N= 103	.91	1.23	P=0.034
	Control N=96	.57	.98	

Table 4. Blood groups of placenta previa cases & their control group

Group	Blood group							
	B positive	B negative	A positive	A negative	AB positive	AB negative	O positive	O negative
Case No	20	0	28	7	15	1	25	7
Case %	(54.1%)	0.0%	51.9%	87.5%	57.7%	100.0%	41.0%	70.0%
Control No	17	2	26	1	11	0	36	3
Case %	45.9%	100.0%	48.1%	12.5%	42.3%	0.0%	59.0%	30.0%
Total No	37	2	54	8	26	1	61	10
Total %	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

P= 0.06

Table 5. History of preterm labor of placenta previa cases & their control group

Group	History of preterm labor	
	Yes	No
Case No	10	93
Case %	100.0%	49.2%
Control No	0	96
Case %	0.0%	50.8%
Total No	10	189
Total %	100.0%	100.0%

P= 0.002

Regarding history of passive smoking of both cases & controls, 54.1% of cases with a history of passive smoking were recorded among placenta Previa cases and 45.9% of the control cases had history of passive smoking. A higher proportion of cases who had no history of passive were control group (78.6%) compared to 21.4% who were placenta Previa cases. These differences were statistically significant, P= 0.025, as shown by Table 9.

Regarding type of placenta of both cases & controls, all cases with low lying placenta, all marginal placenta cases, partial placenta and central placenta were recorded among placenta Previa cases. All cases with anterior & posterior fundal placenta were recorded among control group. These differences were statistically highly significant, P= 0.000, as shown by Table 10.

Regarding history of postpartum hemorrhage of both cases & controls, all cases with a history of postpartum hemorrhage of the present pregnancy were recorded among placenta Previa cases and none of the control cases had history of postpartum hemorrhage of the present pregnancy. These differences were statistically highly significant, P= 0.002, as shown by Table 11.

Table 6. History of complications in the past deliveries of placenta previa cases & their control group

Group	History of any complication in the past delivery							
	Post- partum hemorrhage	**Urinary tract infection**	**Blood transfusion**	**Adhesions**	**Pre-eclamptictoxemia**	**Perineal tear**	**Abruptio placenta & adhesions**	**Wound infection**
Case No	2	1	2	2	1	1	1	1
Case %	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Control No	0	0	0	0	0	0	0	0
Case %	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Total No	2	1	2	2	1	1	1	1
Total %	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

P=0.001

Table 7. History of Bleeding in early pregnancy among Placenta Previa cases & their control group

Group	History of Bleeding in early pregnancy	
	Yes	No
Case No	24	79
Case %	100.0%	45.1%
Control No	0	96
Case %	0.0%	54.9%
Total No	24	175
Total %	100.0%	100.0%

P= 0.000

Table 8. History of Bleeding in in the second & third trimester among Placenta Previa cases & their control group

Group	History of Bleeding in the second & third trimester	
	Yes	No
Case No	99	4
Case %	100.0%	4.0%
Control No	0	96
Case %	0.0%	96.0%
Total No	99	100
Total %	100.0%	100.0%

P= 0.000

Table 9. History of passive smoking among placenta previa cases & their control group

Group	History of passive smoking	
	Yes	No
Case No	100	3
Case %	54.1%	21.4%
Control No	85	11
Case %	45.9%	78.6%
Total No	185	14
Total %	100.0%	100.0%

P= 0.025

Table 10.Type of placenta among placenta previa cases & their control group

Group	Type of placenta					
	Low lying placenta	Marginal placenta	Partial placenta	Central placenta	Anterior fundal placenta	Posterior fundal placenta
Case No	58	2	2	41	0	0
Case %	100.0%	100.0%	100.0%	100.0%	0.0%	0.0%
Control No	0	0	0	0	95	1
Case %	0.0%	0.0%	0.0%	0.0%	100.0%	100.0%
Total No	58	2	2	41	95	1
Total %	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

P=0.000

Regarding preterm delivery of the present pregnancy of both cases & controls, all preterm deliveries were recorded among placenta Previa cases and none of the control cases had preterm delivery. These differences were statistically significant, P= 0.000, as shown by Table 12.

Regarding history of placenta accrete of the present pregnancy of both cases & controls, all of placenta accrete cases were recorded among placenta Previa cases and none of the control cases had preterm delivery. These differences

were statistically significant, P= 0.000, as shown by Table 13.

Regarding Mode of delivery of the present pregnancy of both cases & controls, all of the placenta Previa cases had cesarean section compared to none of the control cases. These differences were statistically significant, P= 0.000, as shown by Table 14.

Table 11.History of Present pregnancy postpartum hemorrhage among placenta previa cases & their control group

Group	History of postpartum hemorrhage	
	Yes	**No**
Case No	10	93
Case %	100.0%	49.2%
Control No	0	96
Case %	0.0%	50.8%
Total No	10	189
Total %	100.0%	100.0%

P= 0.002

Table 12. History of preterm delivery of the present pregnancy of placenta previa cases & their control group

Group	History of preterm delivery of the present pregnancy	
	Yes	**No**
pCase No	27	76
Case %	100.0%	44.2%
Control No	0	96
Case %	0.0%	55.8%
Total No	27	172
Total %	100.0%	100.0%

P= 0.000

Table 13. History of placenta accrete of the present pregnancy of placenta previa cases & their control group

Group	History of Present pregnancy placenta accrete of the present pregnancy	
	Yes	**No**
Case No	14	89
Case %	100.0%	48.1%
Control No	0	96
Case %	0.0%	51.9%
Total No	14	185
Total %	100.0%	100.0%

P= 0.000

Table 14. Mode of delivery of the present pregnancy of placenta previa cases & their control group

Group	Mode of delivery of the present pregnancy	
	Normal delivery	**Cesarean Section**
Case No	9	94
Case %	8.6%	100.0%
Control No	96	0
Case %	91.4%	0.0%
Total No	105	94
Total %	100.0%	100.0%

P= 0.000

Regarding history of cesarean hysterectomy of the present pregnancy of both cases & controls, all of the placenta Previa cases had cesarean hysterectomy compared to none of the control cases. These differences were statistically significant, P= 0.000, as shown by Table 15.

Regarding history of cesarean hysterectomy of the present pregnancy of both cases & controls, all of the placenta Previa cases had cesarean hysterectomy compared to none of the control cases. These differences were statistically significant, P= 0.000, as shown by Table 16.

Regarding history of blood transfusion of the present pregnancy of both cases & controls, 90.3% of the placenta Previa cases had history of blood transfusion compared to 9.7% of the control cases. These differences were statistically significant, P= 0.000, as shown by Table 17.

5. DISCUSSION

Placenta Previa can result in life-threatening maternal complications such as hemorrhage and shock and similarly adverse infant outcomes such as prematurity, stillbirth and neonatal death [9].

Regarding maternal age the present study showed that placenta cases had higher mean age as compared to control cases similarly, ZAHRA et al in her Master degree thesis had advanced maternal age among the studied cases associated with Placenta [10].

Table 15. History of cesarean hysterectomy of the present pregnancy of Placenta Previa cases & their control group

Group	Cesarean hysterectomy of the present pregnancy	
	Yes	No
Case No	12	91
Case %	100.0%	48.7%
Control No	0	96
Case %	0.0%	51.3%
Total No	12	187
Total %	100.0%	100.0%

P= 0.000

Table 16. History of cesarean hysterectomy of the present pregnancy of Placenta Previa cases & their control group

Group	Cesarean hysterectomy of the present pregnancy	
	Yes	No
Case No	12	91
Case %	100.0%	48.7%
Control No	0	96
Case %	0.0%	51.3%
Total No	12	187
Total %	100.0%	100.0%

P= 0.000

Table 17. History of blood transfusion of the present pregnancy of placenta previa cases & their control group

Group	Blood transfusion	
	Yes	No
Case No	28	75
Case %	90.3%	44.6%
Control No	3	93
Case %	9.7%	55.4%
Total No	31	168
Total %	100.0%	100.0%

P= 0.000

The present study showed that cases with placenta Previa had a history of prior cesarean section, advanced age, multiparity, and history of passive smoking. Many studies showed that placenta Previa include a history of prior cesarean delivery, uterine injuries, increasing age and multiparity [11-13].

The current study illustrated that advanced maternal age was associated with increased risk of placenta Previa, similarly, Rosenberg et al., showed that advanced maternal age has been associated with a slight increase in the risk of placenta Previa, and also could be due to effect of multiparity. Similarly, Surraya concluded that there's an association between incidence of placenta Previa and increasing parity [14].

A systematic review and meta-analysis of 22 studies including over 2 million deliveries indicated that the incidence of placenta Previa increases from 10 in 1000 deliveries with one previous caesarean delivery to 28 in 1000 with three or more caesarean deliveries [15]

Wright et al., reported that the mean blood loss for PAS disorders cases undergoing cesarean hysterectomy was 3000ml, whereas the mean required packed red blood cell (PRBC) units for transfusion was 5 units. An estimated blood loss of ≥5000 mL was found in about 41.7% of women with a known diagnosis of PAS disorders [16,17]. In the current study there was all of women with a history of abortion in the placenta Previa group than in the control group. Bulk studies concluded that a history of abortion has a contributing role in placenta Previa in the succeeding pregnancy [18-22].

6. CONCLUSION

It is concluded that placenta Previa is associated with advanced maternal age, history of previous abortion, multiparity, history of previous antepartum & postpartum hemorrhage, preterm deliveries and previous history of cesarean section. Similarly, history of present bladder injury, blood transfusion, premature delivery and history of antepartum hemorrhage in the present pregnancy.

6. RECOMMENDATIONS

From the present study, it is recommended that there is a need for comprehensive obstetrics care to appropriately treat Placenta Previa and its complications. This calls for proper examination and education during the antenatal care.

ETHICAL APPROVAL AND CONSENT

As per international standard or university standard written ethical approval Ethical Approval of the study obtained from the manager of the hospital & informed consent obtained from the mothers.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIXES: I

Name----------Age----------Nationality----------Blood group------
Level of education: - Illiterate or primary-----Secondary----------University----------
Occupation----------Address:----------
Past surgical history:----------
Medical history----------Diabetes----------Hypertension----------
Other----------
Obstetric history:
Gravida……para----------Abortion ----------History of Curettage----------
History of previous myomectomy----------History of IUCD----------
History of pre term labour----------
Previous caesarean section----------
History of any complication in past pregnancy----------
History of any complication in past delivery----------
History of previous placenta previa----------
Present pregnancy:
LMP----------EDD----------Booking----------
Bleeding in Early pregnancy---------- Bleeding in 2nd& 3rd trimester----------
History of passive smoking ----------
History of APH----------

Investigation:

HB%----------Calcium level---------- MSAFP level----------
Outcome:
Type of placenta previa:
Low lying ------- Marginal ------- Partial ---------- Central----------
APH----------P.P.H----------
Preterm deliveries---------- PP accrete-------
Normal vaginal delivery----------Caesarean section----------
Caesarean hysterectomy……. Operative complications --------
Urinary tract injury ……..Yes …….. No
Blood transfusion …… Yes ……... No
Neonatal outcome:
Baby body wt.---------- sex---------Alive----------Died----------
ABGAR SCORE …..1min----------2min

Peer-review history:
The peer review history for this paper can be accessed here:
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