Studying risk factors, maternal and neonatal outcomes in singleton pregnancies complicated by placenta previa

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Abstract

Objective: To quantify risk factors and feto-maternal outcomes in women with singleton pregnancies complicated by placenta previa (PP).

Methods: Acase-control study comparing 157 women with singleton pregnancies complicated by PP to a similar group without PP. The study was conducted from January 2013 through March 2015 at Mansoura University Hospitals, Egypt. Multiple logistic regression models were used to control for confounders.

Results: Multivariate analysis indicated risk factors associated with PP were: maternal age ≥ 30 years (OR=3.183, P= 0.004), parity ≥ 3 (OR=2.6, P=0.016), prior caesarean deliveries ≥ 2 (OR=10.2, P=<0.001), previous PP (OR=5.069, P=0.029) and previous uterine evacuation (OR=2.843, p=0.023). Women with PP had increased risk of massive obstetrics hemorrhage, emergency hysterectomy, admission to ICUand maternal deaths. There was also increased risk to antepartum, intra-partum, and postpartum blood transfusion, maternal sepsis, longer hospital stay. Also infants of cases showed higher rates of perinatal mortality (4.5 vs. 0.6%; P< 0.001), prematurity (23.4 vs. 1%, p<0.001) and admission to NICU (14 vs. 1.9%, p=0.001).

Conclusions: Increasing maternal age, high parity, previous PP, previous evacuation and prior caesarean delivery were independent risk factors for PP. Adverse maternal and perinatal outcomes were also increased significantly.

Keywords: placenta previa, risk factors, maternal, neonatal outcomes.

Introduction

Antepartum hemorrhage (APH) remains one of the major causes of maternal and perinatal mortality worldwide [1] in both developed and developing countries [2]. It complicates 2-5% of pregnancies [3]. Placenta previa is considered as one of its essential etiologies being reported in 0.5–1.0% of the total number of pregnancies [4].The exact etiology of PP is uncertain, but studies have shown its linkto many risk factors including advanced maternal age, infertility treatment, multiparity, multiple gestation, short inter-pregnancy interval, previous uterine surgery or injury, cesarean delivery, recurrent abortions, previous placenta previa, nonwhite ethnicity, low socioeconomic status and those who smoke or cocaine users [5, 6].

Placenta previa has been well documented to be associated with adverse maternal and neonatal outcomes [7]. There is a higher incidence of maternal hemorrhage and higher rates of blood transfusion, placental abruption and increased incidence of postpartum endometritis [8, 9]. Also, there is a significant increase in the risk of postpartum hemorrhage and the need for emergency hysterectomy [10]. Women with PP were more likely to deliver preterm babies with low Apgar score and higher rate of admission to the neonatal intensive care units, stillbirths and neonatal deaths [11, 12]. This study was aimed at determining the prevalence, risk factors, maternal and

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neonatal outcomes in women with singleton pregnancy complicated by placenta previa in an area with low-resource setting. Findings will help in establishing a management and preventive programs for this growing health problem.

Patients and methods

Thisprospective case-control study was conducted at the department of Obstetrics and Gynecology, Mansoura University Hospitals, Egypt from January 2013to March 2015. The study was approved by the University Ethics Committee and the Institutional Research Ethical Committee of the concerned hospitals. A written consent was taken from all participants before being involved and after receiving detailed written and verbal information about the research idea

The study included all patients coming to the emergency or antenatal care units by antepartum hemorrhage, diagnosed clinically and proved by trans-abdominal ultrasound to have PP according to The American College of Radiology (ACR) which described the relationship between the placenta and internal cervical os to determine the degree of PP [13]. Doppler US study was used to exclude or prove placenta accrete in suspicious cases as described by Eliza and Alfred 2013[14].

A total of 157 patients were included in the study. Each patient was matched to the subsequent one who was delivered at the same time with no PP. All patients coming to the hospital or admitted due to antepartum hemorrhage other than PP were excluded together with those diagnosedto have twins or multiple pregnancies for their evident of known risk for PP.

Data were collected from all interviewed patients by the senior registrar on duty including patients' demographic data; age, gravidity, parity, residence, occupation, educational levels, height, weight, body mass index (BMI), gestational age on admission and at delivery. Risk factors suspecting increased occurrence of PP were evaluated mainly, past history of PP, previous uterine scar whether due to caesarean section, hysterectomy, history of dilatation and evacuation (D&E) or manual vacuum aspiration (MVA). Our main outcome measures were, antepartum hospital stay in days, amount of antepartum, intra-partum and postpartum hemorrhage, need for intra-partum blood transfusion in units, outcome of pregnancy, fetal weight at delivery, maternal or neonatal admission to intensive care units, postpartum maternal hemoglobin level, and post-partum hospital stay in days. Ante and post-partum blood loss was estimated by using visual aid methodspreviously described and published by Zuckerwise et al [15]. Intraoperative blood loss during caesarean section was estimated by using negative electronic suction methodwhich permits reasonable accurate measurement where the weight of 1 ml blood is taken as 1 gram [16]. The blood measured in the suction bottle is then added to the estimated blood by any of the previous method.

Collected data were analyzed by using the Statistical Package for Social Sciences for Windows (Version 17.0). Means and proportions were compared among women who had placenta previa and women with no placenta previa by student t-test and x^2 respectively. Paired tests and Fishers exact tests were used where necessary. In univariate analysis, predictors of placenta previa were entered separately while in multivariate analysis all predictors were entered simultaneously into the model. Adjusted odds ratios (OR) and the corresponding 95% confidence interval (CI) were estimated. A p-value <0.05 was considered significant.

Results

The total number of deliveries performed during the study period was 13152 deliveries, of them, 157 were women with PP. Thus, the prevalence of PP in the current study was nearly 1.2%. Of women with PP, 37.6 % had complete PP, 8.3% had incomplete, 29.3% had marginal and 24.8% had a low-lying placenta. Compared to controls, women with PP were elder, of high parity, had higher frequencies of caesarean deliveries, history of PPand history of dilation and evacuation (30.6±4.5 vs. 27.8±٥,٥٥, p<0.001), (2.4±0.98 vs.1.57±1.41, p<0.001), (88.5%vs.19.7%, p=0.001), (11.5% vs. 0, p<0.001) and (28.7% vs16.2%, p=0.016) respectively. No significant differences were observed between cases and controls as regard maternal weight, BMI, residence, educational level, occupation and (p>0.05)as shown in Table [1].

In logistic regression; maternal age ≥ 30 years (OR=3.183, 95% CI= 1.460-6.937, P= 0.004), parity ≥ 3 (OR=2.6, 95% CI=1.195-5.658, P=0.016), a prior caesarean deliveries ≥ 2 (OR=10.2, 95% CI=4.152-25.272, P=<0.001), previous placenta previa (OR=5.069, 95% CI=1.180-21.768, P=0.029) and previous uterine surgery(OR=2.843, 95%CI=1.156-6.989,p=0.023) were significantly associated with increased risk of placenta previa. There was no association between residence, occupation, maternal weight, BMI, inter-pregnancy interval and the risk of developing placenta previaas explained in table [2].

During the antenatal admission, women with PP had several episodes of vaginal bleeding compared to controls. They had a significant lower hemoglobin level

compared to controls (9.6±1.1 vs. 11.1±0. 84 gm/dl, p<0.001). Blood transfusion was instituted antenatal in 47.1% of cases. The majority of cases of PP (85.4%) developed intra-partum hemorrhage with an average blood loss of 1759.9±1.4ml. Of these 86.6% required blood transfusion during surgical intervention. In the postpartum period, 36.9% of mothers with PPwere transfused for massive hemorrhage. Paired t-test showed that antepartum-postpartum hemoglobin concentration was significantly raised (9.58±١,٠8 vs. 10.44 ± 0.66, p=<0.001) with no significant differences from controls (10.4±0.6 vs. 11.1±0.9, p=0.285). The rate of caesarean delivery, emergency hysterectomiesand admission to ICU were significantly higher in women with PP compared to controls (87.9% vs.32.8%, p=0.001), (3.8% vs. 0.0%, p=0.003, (15.3% vs. 0.0%p=0.001) respectively. No significant difference between the two groups in postpartum wound infection (4.5% vs. 1.3%, p=0.075). There were three maternal deaths as a result of massive obstetrics hemorrhagegiving to a case fatality rate of 1.9%. Babies born to women with PP had a significantly higher rate of prematurity (23.6% vs.1%, p= <0.001) and higher admitted to NICU and higher rate of neonatal death (14% vs.1.9%, p=0.001) and (4.5% vs.0%, p=<0.001) as recorded in Table [3].

Discussion

Our study results confirmed that the prevalence of PP in the current study was 1.2% which is consistent with 1.1% rate from Cameroon [17] despite some previous studies showed the incidence varies from 0.4% to 3% [9]. Thisrising trends in prevalence of PP can be explained by changing pattern of risk factors of PP mainly increasing maternal age and the number of caesarean deliveries that are documented by many authors as independent risk factors.

After controlling for confounders, our data indicated that previous history of PP; increasing maternal age, high parity, prior caesarean deliveriesand previous evacuation were found to be independent risk factor for PP. These findings strengthen the clinical evidence generated from some clinical and meta-analysis studies [12, 18]. Additional risk factors have been reported in some other studies such as smoking and male fetuses [19]. This heterogeneity in risk factors between various studies can be explained by the degree of certainty in the diagnosis of PP, type of the study, the sample size used and adjustment for confounders.

Moreovermultifactorial theories cannot be excludedin the pathogenesis and consequently the prevalence of PP. The prospective nature of this study and the relatively reasonable number of patients with PP allowed us to study some variables in details e.g. blood loss different stages of pregnancy, blood transfusion and changes in hemoglobin level because the morbidity for mother and fetus is almost always related to massive hemorrhage.

Studies have found that pregnancies complicated with PP and antenatal bleeding at higher risk for adversematernal and perinatal outcomes and also increased liability for obstetrics hysterectomies [12]. In our study, 56% of patients had antenatal bleeding of a variable degree of severity; blood transfusion was performed for 47% Antenatal anemia was very common among our patients compared to control (9.6±1.1 vs.11.1±0.84, p=<0.001)but we are not sure whether this is due to recurrent episodes of bleeding or pre-existing anemia as not all patients were booked from start of pregnancy in our institute for follow up.

Caesareandelivery was the main route used to terminate pregnancy in almost our cases being recorded in 87.9% of them. This rate is comparable to other studiesand actually many authors believed that caesarean section is necessary for nearly all women with placenta previa [20]. Furthermore, it was noted that 66.7% were emergency caesarean deliveries carried primarily for uncontrollable hemorrhage, this come in accordance with some results obtained by others [21].

Our study added and evidence that a main morbidity associated with placenta previa includes emergency hysterectomy particularly with placenta accrete, a fact published by other authors [22]. We reported this in 3.8% of patients. This comes comparable to 5.3% rate reported by Crane et al [10]but much lower than a 13.3% rate reported in another regional study [23]. Variation in the rate of hysterectomies may be due to the number of placenta accreta within each study. Inthis study; 17.8% of our cases were complicated by placenta accreta.

We reported a high rate of maternal sepsis (4.5%) compared to 0.4% rate from other studies [12]and lower than some others in the same region [23]. Puerperal sepsis remains a major contributing cause of morbidity and mortality in developing world and the risk increases especially following caesarean delivery [24]. Management of Sepsis continues to depend on the real implementation of established protocol and routine antibiotic prophylaxis during the operation.In the present studyadverse neonatal outcome occurred significantly in mothers `with PP. these included,prematurity, low birth weight fetuses, admission to NICU and neonatal death despite improvement in gestational age from admission to delivery interval (36.77±2.68 vs.38±1.5,p=<0.001). Previous studies have shown that women with PP

have significantly increased perinatal mortality up to 4-8% without prematurity and the rate may increase to 50% with prematurity [11,13].In the current study, we reported a perinatal death of 4.5% that correlates well with the previous study[25] without adding the effect of prematurity. In the present studyadmission to NICU was significantly high among fetuses of patients compared to those of controls (14 vs. 1.9%, p=0.032) which is consistent with previous studies [23].

Maternal morbidity and mortality in PP are secondary to massive obstetrics hemorrhage. We reported three maternal deathsgiving to 19.1/1000 case-fatality rate. The three cases had placenta accreta and developed intra-partum hemorrhage, one case died of associated eclamptic fit complicated with adult respiratory distress syndrome while two cases developed hepato-renal shutdown. Studies have shown maternal mortality rate associated with placenta previa is less than 1% in developed countries but remains high in developing countries where pre-existing anemiaand lack of medical resources are common [7]. This indicates a need for improvement of maternity health services.

Conclusions

increasing maternal age, high parity, previous PP, previous uterine surgeryand prior caesarean delivery were independent risk factors for placenta previa. Adverse maternal and perinatal outcomes increased significantly in pregnancies complicated by PP. The anticipation of placenta previa in mothers with these risk factors, management of the associated complications, improvement of fetal and maternity services mainly blood services may improve fetal and maternal outcomes.

Conflicts of interest: All the authors declare no conflict of interest.

References:

1. Calleja-Agius J, Custo R, Brincat MP, Calleja N. Placental abruption and placenta praevia. EurClinObstetGynaecol 2006; (2):121–7.
2. Brace V, Kernaghan D, Penney G. Learning from adverse clinical outcomes: major obstetric haemorrhage in Scotland, 2003–05. BJOG 2007;114:1388–1396
3. Thorogood C, Donaldson C. Challenges in pregnancy. Midwifery preparation for practice. 2nd ed. Sydney: Churchill Livingstone; 2010. p. 754-817.
4. Matsuda Y., Hayashi K., Shiozaki A., Kawamichi Y., Satoh S., Saito S. Comparison of risk factors for placental abruption and placenta previa: case-cohort study. Journal of Obstetrics and Gynaecology Research. 2011; 37(6):538–546. doi: 10.1111/j.1447-0756.2010.01408.x.
5. Marshall NE, Fu R, Guise JM. Impact of multiple cesarean deliveries on maternal morbidity: a systematic review. Am J Obstet Gynecol. Sep 2011; 205(3):262.e1-8.
6. Milosevic J, Lilic V, Tasic M, Radovic-Janosevic D, Stefanovic M, Antic V. [Placental complications after a previous cesarean section]. Med Pregl. May-Jun 2009; 62(5-6):212-6.
7. Olive E. C., Roberts C. L., Algert C. S., Morris J. M. Placenta praevia: maternal morbidity and place of birth. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2005;45(6):499–504. doi: 10.1111/j.1479-828X.2005.00485.x.
8. Tuzovic L. Complete versus incomplete placenta previa and obstetric outcome. International Journal of Gynecology and Obstetrics. 2006;93(2):110–117. doi: 10.1016/j.ijgo.2006.02.006.
9. Onwere C., Gurol-Urganci I., Cromwell D. A., Mahmood T. A., Templeton A., van der Meulen J. H. Maternal morbidity associated with placenta praevia among women who had elective caesarean section. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2011;159(1):62–66. doi: 10.1016/j.ejogrb.2011.07.008.
10. Crane J. M. G., van den Hof M. C., Dodds L., Armson B. A., Liston R. Maternal complications with placenta previa. The American Journal of Perinatology. 2000;17(2):101–105. doi: 10.1055/s-2000-9269.
11. Schneiderman M., Balayla J. A comparative study of neonatal outcomes in placenta previa versus cesarean for other indication at term. Journal of Maternal-Fetal and Neonatal Medicine. 2013;26(11):1121–1127. doi: 10.3109/14767058.2013.770465.
12. Rosenberg T., Pariente G., Sergienko R., Wiznitzer A., Sheiner E. Critical analysis of risk factors and outcome of placenta previa. Archives of Gynecology and Obstetrics. 2011; 284(1):47–51. doi: 10.1007/s00404-010-1598-7.
13. Peker N, Turan V, Ergenoglu M, Yeniel O, Sever A, Kazandi M, et al. Assessment of total placenta previa by magnetic resonance imaging and ultrasonography to detect placenta accreta and its variants. Ginekol Pol. Mar 2013;84(3):186-92.
14. Eliza M. Berkle and Alfred Z. Abuhamad Prenatal Diagnosis of Placenta Accreta Is Sonography All We Need? 2013 by the American Institute of Ultrasound in Medicine | J Ultrasound Med 2013; 32:1345–1350 | 0278-4297 | www.aium.org
15. Zuckerwise, Lisa C. MD; Pettker, Christian M. MD; Illuzzi, Jessica MD; Raab, Cheryl R.; Lipkind, Heather S. MD. Use of a Novel Visual

Aid to Improve Estimation of Obstetric Blood Loss. Obstetrics &Gynecology: May 2014 - Volume 123 – Issue (5) - p 982–986doi: 10.1097/AOG.0000000000000233
16. A Chaudhary, P Jindal, G Chopra, G Khurana, ASaxena. Clinical Evaluation Of Blood Loss With Or Without Deliberate Hypotensive Anaesthesia In Spinal Surgery. The Internet Journal of Anesthesiology. 2008 Volume (22) Number 1.
17. Tebeu PM, Fosso GK, Mbu RE, Nsangou I, Kouam L, FomuluJN.Placentaprevia at University Hospital, Yaoundé, Cameroon.Int J Gynaecol Obstet. 2013 Mar;120(3):286-8.
18. Yang Q, Wu Wen S, Caughey S, et al. Placenta previa: its relationship with race and the country of origin among Asian women. ActaObstetGynecolScand 2008; 87:612.
19. Kancherla V1, Räisänen S, Gissler M, Kramer MR, Heinonen S. Placenta previa and risk of major congenital malformations among singleton births in Finland.Birth Defects Res AClinMolTeratol. 2015 Mar 24.
20. Heidari Z, Sakhavar N, Mahmoudzadeh-Sagheb H, Ezazi-BojnourdiT.Stereological analysis of human placenta in cases of placenta previa in comparison with normally implanted controls. J ReprodInfertil. 2015 Apr-Jun;16(2):90-5.
21. Hasegawa J, Nakamura M, Hamada S, Matsuoka R, Ichizuka K, Sekizawa A, OkaiT.Prediction of hemorrhage in placenta previa.Taiwan J Obstet Gynecol. 2012 Mar;51(1):3-6.
22. Kastner ES, Figueroa R, Garry D, Maulik D. Emergency peripartum hysterectomy: experience at a community teaching hospital. ObstetGynecol 2002; (99):971e5.
23. Ayaz A, Farooq MU. Risk of adverse maternal and peri-natal outcome in subjects with placenta previa with previous cesareansection.Kurume Med J. 2012; 59(1-2):1-4.
24. Caesarean section, NICE Clinical Guideline (November 2011).
25. Zlatnik MG, Cheng YW, Norton ME, Thiet M-P, Caughey AB. Placenta previa and the risk of preterm delivery. J MaternFetalNeonatal Med 2007; (20):719–23.

Table [1]: Comparison of socio demographic characteristics between women with PP and controls.

Variable	Cases157	Controls 157	P value
Age in years ± SD	30.6± 4.5	27.8±5.55	<0.001
Gravidity ± SD	3.9±1.3	2.9±1.7	<0.001
Parity ± SD	2.4±0.98	1.57±1.41	<0.001
Maternal weight (kg)	85±9.1	82.95±14.51	0.107
Maternal height (cm)	162.1±3.1	160.91±3.78	<0.001
Number of previous CS scars	1.9±1.02	0.24±0.55	<0.001
Duration from last pregnancy (years)	3.54±1.94	3.59±1.94	0.814
BMI ±SD	32.33±3.39	31.99±5.26	0.471
Residence			0.633
Rural	102(65)	106 (67.5)	
Urban	55 (35)	51 (32.5)	
Education level			
primary school	62 (39.5)	62 (39.5)	1.000
prep school	63 (40.1)	63 (40.1)	0.965
secondary school	32 (20.4)	32 (20.4)	0.947
Occupation			
house wife	119 (75.8)	112 (71.3)	0.631
working mother	38 (24.2)	45 (28.7)	0.351
Previous CD	138 (88.5)	62 (19.7)	0.001
Previous placenta previa	18 (11.5)	-	<0.001
Dilation and evacuation	45 (28.7)	26 (16.6)	0.016

Abbreviations: BMI; body mass index, CS; caesarean section, CD; caesarean delivery. P. value <0.05 was set significant

Table [2]: Comparison of the risk factors of PP in both groups with univariate and multivariate analysis.

Variable	Univariate analysis			Multivariate analysis		
	OR	95%CI	P-value	OR	95%CI	P value
Maternal age ≥ 30 years	2.928	1.849-4.636	<0.001	3.183	1.460-6.937	0.004
Parity ≥ 3	3.144	1.921-5.145	<0.001	2.6	1.195-5.658	0.016
Residence	1.121	0.702-1.790	0.633	1.725	0.777-3.831	0.180
Occupation	1.258	1.258-2.081	0.371	1.269	0.567-2.841	0.562
Education level	1.000	0.745-1.343	1.000	0.981	0.614-1.566	0.936
Maternal weight	0.981	0.963-1.000	0.048	1.016	0.984-1.049	0.321
Maternal height	0.912	0.912-0.972	004	0.914	0.824-1.014	0.09
Number of CS>2	0.027	0.012-0.060	<0.001	10.2	4.152- 5.272	<0.001
Inter-pregnancy interval	1.016	0.905-1.141	0.790	1.183	0.946-1.479	0.141
Previous PP	3.937	1.424-10.886	0.008	5.069	1.180-1.768	0.029
Previous uterine surgery	0.494	0.287-0.852	0.011	2.843	1.156-6.989	0.023
Fetal sex	1.000	0.642-1.557	1.000	0.738	0.354-1.536	0.417
Previous CS	0.000	14.5-49.95	<0.001	3.923	1.247-12.337	0.019
BMI	0.969	0.922-1.019	0.225	0.985	0.922-1.053	0.661

Abbreviations: CS; caesarean section, BMI; body mass index, OR; odds ratio, CI, confident interval. P-value <0.05 was set significant.

Table [3]: Comparison of antepartum and intra-partum, fetal and maternal complications in both groups.

Variable	Cases 157	Controls 157	P value
Antepartum bleeding			
One attack	25 (15.9)	-	0.001
Two attacks	72 (45.9)	-	0.001
≥ 3	60 (38.2)	-	0.001
Ante partum blood transfused cases	74 (47.1)	-	0.001
Cases with intra-partum blood loss ≥ 1000 ml	134 (85.4)	-	0.001
Postpartum blood loss (mean ± SD)	1759.9±1.4	350.8±124.5	0.001
Cases needed intra-partum transfusion	116 (91.3)	-	0.001
Cases needed postpartum transfusion	58 (36.9)	-	0.001
Ante partum Hb%	9.6±1.1	11.1±0. 84	<0.001
Postpartum Hb%	10.4±0.6	11.1±0.9	0.285
Rate of caesarean delivery	138 (87.9)	103 (65.6)	0.001
Emergency hysterectomy	6 (3.8)	-	0.003
Maternal admission to ICU	24 (15.3)	-	0.001
Postpartum wound infection	7 (4.5)	2 (1.3)	0.174
Maternal death	3 (1.9)	-	0.038
Gestational age at admission	34.7±1.9	38.89±1.41	<0.001
Gestational age at delivery	37.1±0.9	38.94±1.37	<0.001
Fetal weight at delivery	2888.9±370.2	3055.41±391.83	<0.001
Prematurity	37(23.6)	3 (1.9)	<0.001
NICU	22 (14)	6 (3.8)	0.001
Neonatal death	7 (4.5)	1 (0.06)	0.001

Abbreviations: ICU; intensive care unit, NICU; neonatal intensive care unit. P-value <0.05 was set significant.