

Materno-fetal Outcomes in Patients with Abnormally Invasive Placenta: A 14 Year Experience

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Abstract

Objectives: To establish the incidence of abnormally invasive placenta (AIP); determine trends in the diagnosis and management; and assess maternal and neonatal morbidity associated with AIP.

Methods: Women were identified from a tertiary care referral hospital perinatal database (2000-2013) and crosschecked with confirmed histopathology. Verification of undetected cases using perinatal ultrasound database was performed. Risk factors, antenatal suspicion, hospital course, intrapartum management, maternal and neonatal outcomes were obtained from medical records.

Results: Thirty eight women had AIP confirmed providing an incidence of 1 per 1420 deliveries. The incidence rose by 55% (95% Confidence interval (CI) 37% - 279%) over the 14 year period (Poisson regression). An antenatal diagnosis of AIP was made in 63% (95% CI 46% - 78%). Excluding women with placenta percreta, there was a significantly higher blood loss in women in whom an attempt was made at placental removal compared to women in whom there was no attempt (median 3.5 liters versus 1.5 L, $p=0.002$).

Conclusion: AIP was associated with significant maternal and neonatal morbidity. A significantly higher blood loss ensued in women with AIP in whom an attempt was made at placental separation. A dedicated multidisciplinary team and a standardized pathway can potentially reduce morbidity.

Keywords: Placenta accreta; Increta; Percreta; Caesarean section; Hysterectomy; Postpartum hemorrhage

Introduction

Abnormally invasive placenta (AIP) comprises types of abnormal placentation in which there is abnormal adherence to the myometrium surface and in which chorionic villi attach directly to or invade the myometrium [1]. An increase in the incidence of AIP has been reported. Wu et al. reported a rise in incidence from 1:2510 in 1994 to 1:533 in 2005 [2,3]. A rate of 1:1660 was reported during a period of 7 years (2000-2006) in our hospital [4].

The rates of caesarean delivery have substantially increased worldwide over the past few decades and the risk of AIP rises significantly with increasing number of caesarean deliveries [5]. Infact Solheim et al. thought that rise in complications including AIP will lag behind the rise in caesareans by approximately six years [6].

The purpose of this study was to determine the current incidence and evaluate changing trends in antenatal diagnosis, intrapartum management and materno-fetal outcomes in patients with AIP. The role of various methods of intervention was evaluated as there was uncertainty regarding usefulness of any particular intervention. We examined whether incidence, management and morbidity of patients with AIP had undergone change over the study period.

Materials and Methods

Cases of AIP (including placenta accreta, increta and percreta) who delivered in second and third trimesters of pregnancy between 1st January 2000 and 31st December 2013 at Wellington Hospital (a tertiary referral centre in New Zealand) were identified from the computerized perinatal database. To identify missed cases, the data was crosschecked by obtaining the cases with confirmed histopathology. The pathology reports of all women needing peripartum hysterectomy during the period were reviewed. In addition, undetected cases were verified using the perinatal ultrasound database.

Retrospective analysis of electronic and case files of mothers and

neonates was carried out. Missing data (including number of units of blood transfusion, duration of ICU admission) was obtained by contacting the relevant departments.

Maternal data included age and gestation (in completed weeks) at delivery, risk factors for AIP (previous caesarean section/s, placenta previa, previous AIP and diagnosed Asherman's syndrome), whether antenatally suspected/confirmed AIP, and intraoperative management. Maternal morbidity was assessed using the following indicators: complications, estimated blood loss, need for blood transfusion and other blood products, length of postnatal hospital stay, need for and duration of admission to Intensive Care Unit (ICU).

Neonatal morbidity was assessed by identifying neonatal outcomes such as duration of admission, requirement for blood transfusion and neonatal cooling.

The confidence interval (CI) for incidence was calculated based on the binomial distribution. The time trend in incidence was analysed using Poisson regression with yearly data and a term for year. The time trends in antenatal suspicion and attempts at placental removal were analysed using logistic regression. Proportions were compared with logistic regressions and Fisher's exact tests and continuous variables with linear regressions.

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This study was exempt from ethical approval as per "Ethical guidelines for observational study", published by National Ethics Advisory Committee of New Zealand in December 2006. The audit was prospectively approved by hospitals "Audit and Research Committee".

Results

We identified 44 cases of AIP. Four patients had not delivered at our institution and in 2 patients the diagnosis was not confirmed on histology, these were excluded giving a total of 38 patients. Over the study period there were 53,942 births-an incidence of 1 per 1420 deliveries (95% CI 1 in 1034-1 in 2006). There was an increasing incidence of 1.03 times per year (95% CI 0.97-1.10); but was not statistically significant ($p=0.34$). There were 28 cases of placenta accreta, 5 cases of increta and 5 cases of percreta.

Table 1 illustrates the maternal demographics, gestation at delivery and number of previous caesarean sections. Not all women had an identifiable risk factor for AIP. Two women were nulliparous. The first woman had a caesarean section for failed induction of labor, and had a hysterectomy for persistent bleeding. The second woman had an emergency classical caesarean section at 26 weeks gestation for fetal distress, preterm rupture of membrane and a transverse lie; she did not require a hysterectomy. The surgeon did not recognize abnormal placentation at the time of surgery, rather it was a retrospective diagnosis based on placental histology.

An antenatal diagnosis or high suspicion of AIP was made by an ultrasound scan and/or magnetic resonance imaging in 63% of women

(24 out of 38); though, in 80% of women (8 out of 10) who had a placenta increta or percreta, an antenatal diagnosis was made. Hence, in 37% (95% CI 22% - 54%) of women there was no prior suspicion of AIP. The trend in prior suspicion was not significant (odds ratio 1.01 per year; 95% CI 0.84-1.21; $p=0.94$).

Two women with suspected AIP underwent termination of pregnancy (ToP); one had a surgical ToP at 13 weeks gestation for an undesired pregnancy and required a hysterectomy intraoperative for massive hemorrhage. The other had a medical ToP for fetal abnormalities, who then had a retained placenta with life-threatening hemorrhage necessitating a hysterectomy.

Four patients did not need a hysterectomy; none of whom had prior suspicion of placenta accrete, see in Table 2 and for all an attempt at placental removal was made.

Attempts at placental removal were made in 22 women. Out of 24 women in whom AIP was suspected, 10 (42%) had an attempt at removal of the placenta (this included the 2 ToPs). There was a non-significant decrease in attempts (odds ratio 0.90 per year; 95% CI 0.71-1.15; $p=0.39$). Out of 14 women with unanticipated AIP, 12 (86%) had an attempt at placental removal. In 2 women with an unsuspected AIP, placental removal was not attempted; as one had a uterine rupture, and the other had a clinically evident percreta later confirmed on histology.

Of 5 women with placenta increta, 3 had an attempt at placental separation and 1 had surgical ToP at 13 weeks. Considering the severity of the condition and attendant morbidity, none of the 5 women with

Variables	Median (range)	
Maternal age at delivery	32.5 (24-44)	
Gravidity	4 (1-11)	
Parity (Before delivery)	2 (0-5)	
Gestational age at delivery, in completed weeks	34 (13-41)	
Number of previous Caesarean sections-n (%)	0	9 (24%)
	1	13 (34%)
	2	7 (18%)
	3 or more	9 (24%)

Table 1: Patient demographics of study population diagnosed with AIP.

Variables	Antenatal suspicion		Antenatal suspicion versus not suspected	
	Yes (n=24) 63%	No (n=14) 37%	Unadjusted	Adjusted for attempted placental separation
			(95% CI)	(95% CI)
Total blood loss (in litres) Mean (SD), mean difference †	2.8 (1.9)*	3.4 (2.5)	-0.5 (-2.0-0.9) P=0.46	0.4 (-1.1-1.9) P=0.56
Blood transfusions - % (n), odd ratio ‡	71% (17)	86% (12)	0.4 (0.1-2.3) p=0.31	0.7 (0.1-4.8) p=0.71
Number of units of blood transfused - Mean (SD), mean difference †	5.0 (4.2)	5.5 (5.0)	-0.5 (-3.6-2.6) p=0.77	0.4 (-3.0-3.8) p=0.82
Other blood products required - % (n), odds ratio ‡	46% (11)	50% (7)	0.8 (0.2-3.2) p=0.80	1.2 (0.3-5.2) p=0.82
Hysterectomy - % (n Primary / n Return to theatre), §	100% (21/3)	71% (6/4)	p=0.014	
Bladder injury - % (n), §	25% (6)	0% (0)	p=0.067	
ICU admission - % (n), odds ratio ‡	38% (9)	21% (3)	2.2 (0.5-10.1) p=0.31	2.0 (0.4-10.6) p=0.41
Duration of postnatal stay in days - Median (interquartile range), ratio of geometric means †	6 (5-10.5)	5 (4-7)	1.5 (1.0-2.1) p=0.029	1.2 (0.9-1.8) p=0.24

*In 1 woman blood loss was not recorded so the median calculated from 23 women; †Linear regression; ‡Logistic regression; §Fisher's exact test, too few events or non-events for logistic regression

Table 2: Maternal outcomes if antenatal suspicion of AIP.

Variables	Attempted placental separation		Attempted placental separation versus not attempted	
	Yes (n=22)	No (n=11)	Unadjusted	Adjusted for antenatal suspicion
			(95% CI)	(95% CI)
Estimated total blood loss in litres*, Mean (SD), mean difference †	3.9 (2.2)	1.7 (1.2)	2.2 (0.8-3.6) p=0.004	2.3 (0.6-4.0) p=0.008
No of units of blood transfused, Mean (SD) , mean difference †	6.0 (4.5)	3.6 (4.3)	2.3 (-1.0-5.6) p=0.16	2.2 (-1.6-5.9) p=0.25
Requirement of other blood products, n (%), odds ratio ‡	12 (55%)	4 (36%)	2.1 (0.5-9.3) p=0.33	2.0 (0.4-10.6) p=0.39
ICU admission, n (%), odds ratio ‡	6 (27%)	4 (36%)	0.7 (0.1-3.1) p=0.59	0.8 (0.1-4.5) p=0.81
Postnatal stay in days , Median (interquartile range), ratio of geometric means †	5 (4-6)	6 (5-18)	0.6 (0.4-0.9) p=0.017	0.7 (0.5-1.0) p=0.081

*In 1 woman blood loss was not recorded so the median calculated from 23 women; †Linear regression; ‡Logistic regression; §Fisher's exact test, too few events or non-events for logistic regression.

Table 3: Maternal outcomes in relation to attempted placental removal at birth (excluding women with placenta percreta).

placenta percreta had attempts at placental removal and hence were not included in the calculations reflected in Table 3.

Nine women had to return to theatre (24%; 95% CI 11% - 40%), two women required an oophorectomy and one woman had to have a ureteric transection and re-implantation for placenta percreta invading the ureter, 1 woman needed reoperation 13 days later for bowel obstruction and adhesiolysis, 1 woman had an interval hysteroscopic resection of placental tissue 6 months post-partum. Four women underwent uterine artery embolization; of which 3 women also had chemotherapy with methotrexate. Two women had preoperative placement of internal iliac balloon occlusion catheters.

None of the neonates required blood transfusion, nor did any of them require cooling. All but one were singleton pregnancies (total 39 babies), one was a set of twins. The median gestational age at delivery was 34 completed weeks. Twenty four neonates including a set of twins required admission to the neonatal unit (NNU). The median duration of NNU admission was 19 days (range 1-57 days). There was one fetal death in utero at 24 weeks associated with intrauterine growth restriction, preterm rupture of membranes and chorioamnionitis.

Discussion

In our analysis there were 38 histologically confirmed cases of AIP in women who delivered at our hospital during the 14 year study period giving an incidence of 1 per 1420 deliveries. The overall modeled incidence rose by 55% over the 14 year period, from 6.39 per 10,000 deliveries in the first half of study period (year 2000-2006) to 7.68 per 10,000 deliveries in the second half of the study period (2007-2013).

Our evaluation reaffirms that an abnormally invasive placenta is associated with considerable maternal and neonatal morbidity; with AIP is being a major contributor to emergency peripartum hysterectomy [7,8]. During our study period there were 50 peripartum hysterectomies in whom a total of 34 women (68%) had AIP.

This study illustrates the level of difficulty in diagnosing an AIP antenatally [9]. Despite having a tertiary ultrasound unit and imaging expertise, the suspicion was raised antenatally only in 24 women (63%) and was not anticipated in 14 women (37%). Of the 14 women in whom the diagnosis was not suspected, there was no recognisable risk factor in 10 women.

Our study showed that in women with a histologically confirmed AIP, an antenatal suspicion is associated with reduced level of hemorrhage and lower need for a blood transfusion; however, these

were not statistically significant. Lower blood loss might be because once AIP is suspected it allows clinicians to institute prophylactic measures and possible earlier recourse to a hysterectomy if warranted. Six women in antenatally suspected group had a bladder injury; this may have been related to the fact that women with an antenatal suspicion had a potentially more severe condition. In fact out of 6 women with a bladder injury, 3 had placenta percreta and 1 had placenta increta.

A key highlight is the substantial maternal morbidity related to the condition. Overall median blood loss was 3 L and median units of blood transfusion were 4 units. The chance of returning to theatre was 1 in 4. The median postnatal stay was 5.5 days. These results are consistent with a report by Tan et al. [10].

There is a wide variation in practice and management of women with a morbidly adherent placenta; and the optimal management strategies for AIP is the subject of debate [11].

The use of vaso-occlusive catheter has been described but there is uncertainty regarding its usefulness. Furthermore, balloon placement is associated with a complication rate of up to 15.8% [12]. There were 2 women in our series who had prophylactic internal iliac balloon catheters placed. Both of them had a primary hysterectomy; however, both needed to return to theatre. One had a vault hematoma which required drainage, and the second woman had an interval left oophorectomy due to compromised blood supply causing persistent pelvic pain.

The use of embolization can be helpful but difficult to arrange in emergencies. We had 4 women who underwent embolization. One woman had embolization for persistent bleeding following an emergency hysterectomy for an unsuspected AIP. Two women out of the other three had embolization immediately after their caesarean sections with attempted conservative management. The fourth woman required embolization for sustained bleeding after an emergency hysterectomy; 59 days after her caesarean section following an attempt at conservative management.

The use of Methotrexate has been suggested as an additional modality for conservative management of AIP but there is no convincing data to support its use [13]; nevertheless, in our study it was used in 3 patients all of whom had interval hysterectomies; 2 of them had placenta percreta and 1 had placenta accreta.

In our institution, patients with suspected AIP are managed by a team of 3-4 senior obstetric specialists. Our study draws attention to the fact that despite an antenatal diagnoses, the management of patients

with AIP was inconsistent. Even in patients in whom conservative management of AIP was attempted, embolization was performed immediately after caesarean section in only two out of three women.

The intraoperative management of AIP is contentious as the antenatal diagnosis has limitations; there is desire to preserve fertility, and a possibility of false positives which leads to dilemma; i.e., whether an attempt at removal of the placenta should be made or not [14]. Both the Royal College of Obstetricians and Gynecologists and the American College of Obstetricians and Gynecologists advise a planned caesarean hysterectomy with the placenta left in situ, as removal of placenta is associated with significantly more bleeding [13,15]. Eller et al. also reported a significant increase in early morbidity in women with an antenatal suspected AIP, in whom an attempt at placental removal was made [16]. Our study suggests that, excluding women with placenta percreta, there is a significantly higher blood loss in women with AIP in whom an attempt was made at placental separation as compared to women in whom there was no attempt at removal of the placenta (3.9 ± 2.2 litres and 1.7 ± 1.2 litres, $P=0.002$).

Conservative management of AIP is particularly contentious. While successful in many women, there is a continued risk of severe bleeding for many months after delivery [9]. Sentilhes et al. in a study of 167 women suggested that conservative management can successfully preserve the uterus in 78.4% of women with a maternal morbidity rate of 6% [17]. We had 3 patients in whom the placenta was left in situ after a caesarean delivery. All of them had interval hysterectomies; 2 of them developed life threatening haemorrhage. The first one had placenta percreta and was readmitted with massive haemorrhage resulting in an emergency hysterectomy 59 days after delivery, and had an estimated blood loss of 5 L. The second woman also had placenta percreta; she was readmitted with heavy vaginal bleeding, and underwent a hysterectomy 60 days after delivery, and had a blood loss of 4 litres. The third woman had placenta accreta and wanted to preserve her fertility; however post-operatively she changed her mind and had an elective hysterectomy 26 days after delivery; she bled 400 ml. The reason for this decision was not documented clearly in her notes.

With an incidence of 1:1420 deliveries AIP is not an uncommon event, and its incidence is predicted to raise due to rising caesarean section rates worldwide [18]. In view of the significant maternal morbidity associated with AIP, it is vital to have clinical guidelines for management of women with AIP.

We recommend that a woman with risk factors for AIP or a suspected AIP should have an ultrasound scan at a tertiary centre preferably with expertise of a maternal-fetal medicine specialist. As no current diagnostic technique has sufficient negative predictive value; a woman with a placenta previa and one or more previous caesarean deliveries should raise a high suspicion of possible AIP [19]. However, if AIP is suspected then the delivery should be planned at a tertiary level centre with the necessary expertise and precautions to limit maternal and neonatal morbidity [20].

A careful management plan should be put into place involving the woman and a multidisciplinary team i.e., senior obstetricians, gynecology oncologist, anesthetist, intensivist, interventional radiologist, urologist, transfusion medicine specialist and neonatologist. A neonatologist's involvement cannot be overemphasized considering the significant neonatal morbidity as shown by all the studies including ours [21].

Ideally, a dedicated obstetric team (involving 3-4 senior obstetricians) should individualize care in each case after full discussion with the woman.

Although current evidence is lacking regarding the use of embolization [13], we suggest selective use of embolization in women with placenta percreta, which could be then followed by an elective hysterectomy; potentially reducing their risk of suffering a major hemorrhage and requiring an emergency procedure. The hysterectomy can be undertaken 1-2 weeks after the delivery allowing time to plan the resources and reduce pelvic vascularity. In a review by Clausen et al. the majority of patients (58%) with placenta percreta who were managed conservatively required a hysterectomy up to 9 months after delivery, and this was associated with significant maternal morbidity [22]. We had two women with placenta percreta in whom a conservative approach was undertaken; one with prophylactic and the other without prophylactic embolization. Both had massive hemorrhages nearly two months after delivery requiring a hysterectomy accompanied by severe maternal morbidity.

Limitations

Being a retrospective cohort study our study has drawback of any retrospective case series; relying on the accuracy of patient coding systems and on the written or computerized patient records. There might be potential underreporting of cases with partially invasive placentation. As a tertiary referral centre there may be a potential bias for inclusion of more significant cases. Although patients were managed by a team of senior obstetricians with multidisciplinary input, there was a lack of a standardized protocol. In spite of the fact that our study is one of the largest reported series from a single centre with histologically confirmed AIP, the size of our sample resulted in low power for tests and wide confidence intervals. Our data collection is from various sources and we contacted the relevant departments for missing data with the intention to reduce the chance of underreporting. Further, we only included cases with confirmed pathology reducing the changes of including false positive cases.

Conclusion

Our study revealed the importance of an antenatal diagnosis of AIP, which helps clinicians to optimize conditions for delivery by instituting prophylactic measures to minimize adverse outcomes, organize a multidisciplinary approach, and adequately counsel women of possible outcomes. A checklist for risk factors, diagnosis, antenatal, intrapartum and postpartum management of AIP can be helpful [23].

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