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Management of placenta accreta: evaluate the relationship between cervical length and obstetrical outcome in women with placenta accreta.

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ABSTRACT:
__Objective.__ Prior studies have associated short cervix in the setting of placenta previa with adverse obstetric outcomes including maternal hemorrhage, preterm birth, emergency cesarean and abnormally adherent placenta. However, the association between cervical length and placenta accreta has not been evaluated. The aim of this study was to demonstrate the relationship between cervical length and preterm delivery in patients with placenta accreta with the goal of identifying additional prognostic factors to improve our ability to treat women with placenta accreta.
__Methods.__ This retrospective study included all patients with pathologically proven placenta accreta diagnosed at a single institution between 2003 and 2015. Valid cervical length measurements obtained between weeks 12 and 33 were included in our study. The primary outcome was defined as incidence of preterm delivery prior to 32 weeks gestation in women with cervical lengths less than 25 mm .
__Results.__ Seventy-three patients were included. The mean ± SD gestational age at diagnosis of placenta accreta was 24.1 ± 6.5 weeks and the cervical length was 31.7 ± 0.9 mm. Cesarean delivery was performed in 92 cases, at a mean gestational age of 33.2 ± 3.9 weeks. Thirty-six (60%) of the women experienced antepartum hemorrhage. Of those cases, 11 (30.6%) women had cervical lengths <25 mm compared to 25 (69.4%) women with a cervical length >25 mm. Antepartum hemorrhage was not associated with short cervix (P = .09). Twenty-seven (37%) women required an urgent cesarean-hysterectomy either because placenta accreta was not diagnosed prior to delivery or emergent delivery was required prior to the scheduled delivery date. Of those cases, 8 (29.6%) women had short cervix compared to 10 (70.4%) women with normal cervical length measurements. Short cervix was not associated with urgent cesarean hysterectomy (P = .24). Thirteen (17.8%) women delivered prior to 32 weeks gestational age. Frequency of preterm delivery was greater among patients with short cervix compared to patients with cervical length measurements <25 mm (6 of 17 vs. 7 of 56; P = .04).
__Conclusions.__ Sonographic cervical length measurements <25 mm were associated with a high risk of delivery prior to 32 weeks gestation in women with placenta accreta.

INTRODUCTION:
Placenta accreta refers to an abnormal implantation of the placenta in which the placental villi invade the myometrial uterine layer. Though previously a rare entity, with the proliferating rate of cesarean delivery, the incidence of placenta accreta occurs in greater than 1 in 2500 deliveries. The consequence of this condition is often an inability to control hemorrhage from the underlying vessels following delivery of the fetus. The resulting hemorrhage frequently requires emergency hysterectomy. Placenta accreta is the second most common indication for this procedure behind uterine atony. Risk factors, such as the presence of a placenta previa and/or prior uterine surgery, can raise suspicion of such pathology, however final diagnosis is only made clinically at the time of placental separation, and on gross examination of the placenta. As such, women often go undiagnosed until the time of delivery, when massive hemorrhage may occur.

Over the last decade, several diagnostic and therapeutic modalities have developed which have improved our ability to treat women with placenta accreta. The value of making

the diagnosis of placenta accreta prior to delivery is that it enables interdisciplinary planning to reduce adverse maternal and neonatal outcomes. As ultrasound has improved, the diagnosis is being made earlier in pregnancies, even into the first trimester. However, ultrasound, the gold standard, is still not entirely helpful in identifying those at risk of antenatal complications from a diagnosis of placenta accreta.

Various studies have investigated the relationship between a shortened cervical length and increased risk of preterm birth, hemorrhage, and emergent cesarean delivery in pregnancies with placenta previa, a known risk factor for placenta accreta. The purpose of this study was to evaluate the relationship between cervical length and maternal risks in pregnancies with pathologically confirmed placenta accreta. The association between placenta accreta and cervical length has not been reported previously and may improve our ability to anticipate complications and enhance obstetric management in these instances. Our hypothesis is that shortened cervical length is associated with a higher frequency of preterm birth, antepartum hemorrhage, emergent cesarean delivery, and emergent hysterectomy.

PATIENTS AND METHODS:
This was a retrospective study of patients with placenta accreta who delivered at University of California, San Diego Health System between 2003 and 2015. Data for this study was obtained from the UCSD placenta accreta database, which is a prospectively maintained database.

The charts of 95 women diagnosed with pathologically proven placenta accreta were reviewed. Twenty-two women without electronic cervical length measurements were excluded. This left 73 women in the study of cervical length.

Precise ultrasound examinations were performed using both a transabdominal and transvaginal transducer. Of note, there is controversy regarding the need for routine transvaginal assessment in all pregnant women, including those with a low risk for preterm delivery. In some instances, mean cervical lengths on transabdominal sonography are shorter than those on transvaginal sonography. Thus, transabdominal cervical measurements may be used initially as a cervical length screening tool. In our study, if TAS was close to the critical value of 25 mm, patients were offered TVS for better assessment of cervical length. For study purposes, the shortest cervical length measurement was used for analysis and a cervical length of 25 mm or less was termed short. Our primary outcome of interest was incidence of delivery <32 weeks gestational age in pregnancies with short cervical length (<25 mm). Secondary outcomes included incidence of antepartum hemorrhage, emergent cesarean delivery, urgent hysterectomy, perinatal admission to the neonatal intensive care unit and subsequent length of stay in the NICU. SPSS Version 20 was used to enter and analyze the data. Statistical analyses included t-test, Mann-Whitney U test and chi-square test. Statistical significance was defined as a p value of less than 0.05. The Institutional Review Board at the University of California, San Diego, approved the study.

RESULTS:
Seventy-three women met inclusion criteria. A summary of the patient population and pregnancy outcomes is provided in **Table 1**. The mean $\pm$ SD maternal age was 33.9 $\pm$ 5.8 years. Fifty-nine cases (81.8%) were diagnosed with accreta prior to delivery with a mean $\pm$ SD of 23.6 $\pm$ 5.4 weeks. There were no differences in gestational age at diagnosis of placenta accreta between those with a shortened cervix and those with a normal cervical length (P = .58). The mean $\pm$ SD cervical length for the entire population was 31.7 $\pm$ 0.9 mm and obtained at a mean $\pm$ SD gestational age of 26.1 $\pm$ 6.2 weeks.

The median estimated blood loss in women with placenta accreta was 2 L, with reported ranges between 125 ml and 18 L. Blood transfusion was required in 67 (70.5%) of the 95 women with placenta accreta, with a reported median of 3 units (range from 0 to 34) of packed red blood cells. Twenty-one (22.1%) women required platelet transfusion, with a median of 2 units (ranging from 0 to 5). Thirty-nine (41.1%) of the 95 patients required transfusion with fresh frozen plasma with a calculated median of 0 units, (range was 0 to 18 units).

Of the 73 women with documented cervical length measurements, 17 (23.3%) had a shortened cervix. Pregnancy outcomes associated with cervical length are presented in **Table 2**. Thirty-six women presented with antepartum hemorrhage. Eleven (30.6%) of those cases had short cervix, compared to 25 (69.4%) with normal cervical length (P = .09). Incidence of urgent cesarean-hysterectomy did not differ significantly between those with short cervix and those with normal cervix (47.1% vs. 33.9%; P = .24). There were no differences in median EBL between those with short and normal cervices (median blood loss of 2 L; P = .33). No significant differences were evident in perinatal outcomes such as admission to the neonatal intensive care unit and length of stay in the NICU, between the short and normal cervical length groups. Of note however, there was a higher incidence of preterm delivery among patients with short cervical lengths compared to groups with cervical lengths greater than 25 mm (35.3% vs. 12.5%; P = .04). Six of the 17 women with short cervix delivered prior to 32 weeks. Premature delivery was secondary to bleeding in 3 out of the 6 cases. Non-reassuring fetal status was identified in 1 of the 6 cases. Spontaneous onset of labor resulted in preterm delivery in 1 patient. The mean $\pm$ SD gestational age at delivery among patients with short cervix was 31.8 $\pm$ 4.4 weeks, compared to 33.1 $\pm$ 3.4 weeks in women with normal cervix (P = .25).

A sub analysis comparing women with short cervix identified at or less than 24 weeks was performed given that short cervix prior to or at 24 weeks has been associated with an increased risk of preterm delivery in the obstetric population. This analysis included a very small subset of patients as only 26 (35%) of the original cohort of 73 had a cervical length measurement at or below 24 weeks. Seven out of 26 had a short cervix identified at or below 24 weeks. There were no significant differences in antepartum hemorrhage, urgent cesarean hysterectomy, delivery prior to 32 weeks when short cervix was identified at or <24 weeks.

Table 1 Patient characteristics and pregnancy outcome in 73 women with placenta accreta

Characteristic/outcome	n (%) *or mean* $\pm$ SD
Maternal age (years)	33.9 $\pm$ 5.8
Gravity	4.6 $\pm$ 2.3
Parity	2.7 $\pm$ 1.9
Prior Cesarean section	2.0 $\pm$ 1.3
Cervical length (mm)	31.7 $\pm$ .9
Gestational age at cervical length measurement (weeks)	26.1 $\pm$ 6.2

Table 2 Outcome of pregnancy according to cervical length in 73 women with placenta accreta

	Cervical Length 25 mm or Less (n=17, 23.3%)	Cervical Length More Than 25 mm (n=56, 76.7%)	P value
Antepartum hemorrhage	11(30.6%)	25(69.4%)	.09
Urgent cesarean-hysterectomy	8(29.6%)	19(70.4%)	.24
Delivery <32weeks gestation	6(46.1%)	7(53.8%)	.04
NICU admission	16(23.2%)	53(76.8%)	.77

DISCUSSION

Evaluation of the risk for preterm delivery is one of the most important factors in the management of placenta accreta. Early detection of placenta accreta and short cervix is essential to guiding management.

Our retrospective review of cervical length in cases of pathologically proven placenta accreta suggests that short cervix (<25 mm) is associated with a higher risk of earlier delivery, prior to 32 weeks. The higher incidence of delivery <32 weeks in women with placenta accreta and short cervix could be explained by the fact that shortened cervical length is a known risk factor for spontaneous preterm delivery in both low- and high-risk pregnancies. Sub analysis of outcomes of women identified with short cervix prior to or at 24 weeks didn't demonstrate any significant increase in adverse outcomes. However, this analysis was limited by small number of women diagnosed with short cervix during this time period and a type II error cannot be excluded in interpreting this sub analysis.

Sonographic evidence of a short cervix is associated with an earlier onset of labor. A short cervix among women with placenta accreta may therefore also incite premature onset of labor. Our study suggests that in women with placenta accreta, the risk of antepartum hemorrhage, emergent delivery, and urgent cesarean hysterectomy does not seem to vary according to cervical length. We suspect that this is in large part due to greater prenatal surveillance among patients with short cervix and subsequent planned premature delivery via cesarean to avoid adverse maternal and neonatal outcomes.

A number of interventions have been studied in the prevention of spontaneous premature birth in high-risk pregnancies with short cervix, but none of this have been studied in the setting of placenta accreta for either safety or efficacy. No consistent evidence has been shown that bed rest and hydration help to delay delivery. Similarly, there is no reliable data to suggest that tocolytic medications delay delivery for longer than 24 to 48 hours, and therefore, should not be used for long-term maintenance purposes. Data surrounding the utility of cervical cerclage placement is highly contentious, however more recent data suggests that cerclage in women with cervical shortening may be of benefit in women with prior preterm delivery. Cerclage has not been studied in pregnancies complicated by accreta given the concern for bleeding at time of cerclage placement due to increased vascularity in the setting of this placental abnormality. Progesterone supplementation with weekly injections of 17hydroxyprogesterone, has been shown to be an effective intervention to prevent preterm birth in patients with a prior history of spontaneous preterm delivery, however, it has not been investigated in cases of short cervix in the setting of placenta accreta. Alternatively, vaginal progesterone has been shown to prevent preterm birth in the setting of an incidental short cervix. This also has not been

studied in cases of placenta accreta however, it may be an alternative treatment to women with short cervix identified between 16-24 weeks in women with suspected accreta.

The main limitations of our study are two-fold. This study was a retrospective assessment and the small number of women enrolled raises concern for type II error. However, this is the first analysis of the interactions between short cervix and placenta accreta. If our observations are confirmed by a prospective study in a larger series, transvaginal measurement of cervical length could be implemented as part of the routine third-trimester scan in women with placenta accreta in order to predict the risk of preterm delivery.

In conclusion, a shortened cervical length is associated with an increased risk of preterm delivery due to early bleeding, fetal distress and preterm labor. High-risk pregnancies with placenta accreta and cervical lengths $\leq$ 25 mm should be closely monitored and every effort should be made to preserve cervical length, as their risk for preterm delivery seems to be increased. If our findings are confirmed in a larger study, closer clinical monitoring in women with placenta accreta and short cervix may be a beneficial option.

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