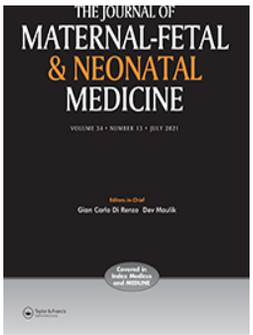

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ORIGINAL ARTICLE

Cervical length should be measured for women with placenta previa: cohort study

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ABSTRACT

Objectives: To study the relevance between cervical length (CL) and different maternal/neonatal outcomes in pregnancies complicated with placenta previa/accreta.

Methods: Three hundred twenty-eight women, who had medically free singleton live pregnancies with the diagnosis of placenta previa and/or accreta, were included and divided regarding their CL into two groups. Threatened preterm labor, maternal tocolysis, multiple gestations, polyhydramnios, ruptured fetal membranes, fetal complications, history of cervical conization, and the presence of cervical cerclage were the exclusion criteria. Demographic data, obstetric history, as well as, the courses of the complicated pregnancies were collected and statistically analyzed.

Results: The short CL group had significantly less distance between the placenta and the internal cervical os (p-value $<$ .001) Also, they showed more ultrasound parameters of complete placenta previa with anterior location (p-value $<$ .001 and .003 respectively) and placental adherence (21.8 versus 41.1%). Women with short cervix had significantly higher rates of preterm birth, antepartum hemorrhage, emergency cesarean sections, intraoperative estimated blood loss, massive bleeding, prevalence of placental adherence and cesarean hysterectomy (p-value $<$ .001 for the entire outcomes). Multivariable binary logistic regression showed that CL ($<$30 mm) was a significant independent risk factor in prediction of severe hemorrhage, PTB, emergency CS, placental adherence, cesarean hysterectomy (p-value $<$ .001 for adverse maternal outcomes) and low cord Ph (p-value = .016).

Conclusions: Assessment of the cervical length could be a crucial step in the work-up and decision making for pregnancies complicated with abnormally situated and/or adherent placenta as it is strongly associated with a wide range of maternal and neonatal morbidities.

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Antepartum hemorrhage; cesarean hysterectomy; cervical length; placenta accreta; placenta previa

Introduction

The prevalent use of routine obstetrical ultrasound (US) with the high cesarean section (CS) rates raised the placenta previa estimated prevalence from between 0.2 and 0.3% of term pregnancies to almost 0.5% [1,2]. Although it can affect one in 300–400 pregnancies, placenta previa and/or accreta remains a leading reason for maternal morbidity and mortality. Also, prematurity, as a result of emergency preterm CS, increases neonatal complications by threefold [2–4].

Antepartum hemorrhage (APH), mostly in the third trimester, starts due to the split of placental attachments during the development of lower uterine segment and cervical dilatation. These changes result in bleeding from the placental vessels, which is often poorly controlled by the poorly developed lower segment myometrium. Also, this mechanism is evidently integrated with cervical effacement and shortening with subsequent preterm birth (PTB) [5–7].

Different US markers had been used to predict the outcomes of women with placenta previa/accreta such as; its type, location, lacunae, marginal sinuses, velamentous cord and cervical length (CL). They were studied and compared against the occurrence of APH episodes, massive bleeding, need of blood transfusion, emergency CS, prevalence of cesarean hysterectomy and PTB [7–20].

However, anticipating the possibility of maternal bleeding and preterm delivery, especially in asymptomatic women, is not simple. Also, emergency CS

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due to uncontrollable bleeding is performed in about 37% of patients with placenta previa, before the selected date of the elective one [11]. Thus, the prediction of the risk of bleeding during pregnancy should help to ensure better both maternal and neonatal outcomes in women with placenta previa. Therefore, we studied a cohort of women whom their CL was evaluated and compared against adverse pregnancy outcomes after being diagnosed with placenta previa.

Materials and methods

This retrospective cohort study was carried out at the obstetrics and gynecology department, Armed Forces Hospitals Southern Region, Khamis Mushayt, Saudi Arabia after being approved by the legitimate local research ethics committee. 955 Medical records of women who were diagnosed to have placenta previa/accreta before 34 weeks of gestation, between January 2010 and December 2017, were reviewed carefully.

We excluded women with threatened preterm labor, multiple gestations, rupture of the fetal membranes, polyhydramnios, fetal growth restriction, fetal anomalies, history of cervical operations, presence of cervical cerclage, use of tocolysis and medical disorders that necessitated termination of the pregnancy. Also, women whose CL measurements indicated different types of intervention, according to their gestational ages, were excluded. Data of 328 women were recruited and analyzed for this study.

As a part of our unit protocol, during routine antenatal follow-up, CL for each woman should be recorded at least once per pregnancy between 20–34 weeks of gestation as well as any woman once diagnosed as a case of placenta previa (revealed by transvaginal US when lower placental edge $\leq$20 mm from the internal cervical os). Induction of lung maturity between 24 and 34 weeks' gestation was introduced to all enrolled women. If they were scheduled for elective CS, they received an additional rescue course of corticosteroids.

All measurements were obtained by an experienced and certified obstetrical sonographer (practicing for more than 20 years) using multifrequency transvaginal probe of the same ultrasound machine (Voluson® 730Expert/Pro V. 4.0.x, GEMS Kretz Ultrasound®, Zipf/Austria) and the standard technique described by the National Institute of Child Health and Human Development, Maternal-Fetal Medicine Unit Network [21].

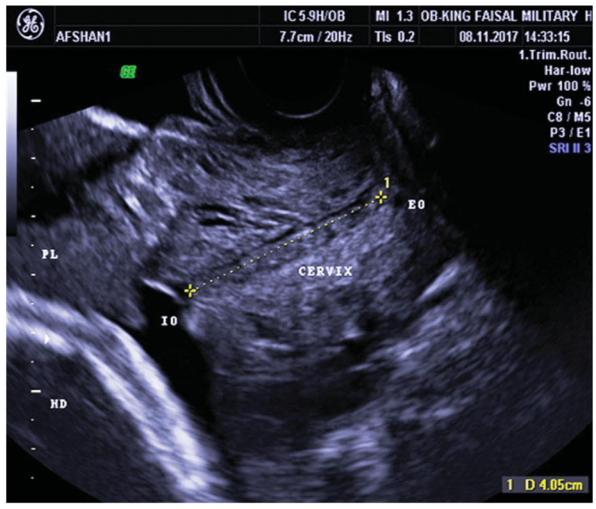

Figure 1. Ultrasound image shows cervical length measurement of a woman with low lying placenta (few millimeters away from the edge of internal os). HD: head; PL: placenta; IO: internal os; EO: external os; line 1 (interrupted) represents cervical length.

Before the US examination, women were asked to empty their bladder. After covering the vaginal probe with a sterile glove, it was used to visualize the full functional CL (the distance between closed internal os to the external os) in sagittal view for three times and the shortest measurement was recorded. If there was a funnel, sonographer excluded the funnel and measurement was obtained from the funnel tip to the external os [22].

Other US findings were obtained to identify the type of placenta previa [low lying if lower placental edge was $<$20 mm and not reaching internal os (Figure 1), incomplete if lower placental edge covered partially the internal os or reached its margin (Figure 2) and complete if the internal os was completely covered by the placenta (Figure 3)], the distance from placental edge to internal os, the degree of placental adherence (markers of placenta accreta) and placental location (anterior or posterior) [23,24].

Data from electronic records of enrolled women were collected including age, full obstetric history, mode of deliveries, history of cervical incompetence, gestational age at time of APH, rate of PTB, gestational age at the time of delivery and its operative details. Also, US reports of these women were also checked for complete records of placental findings as well as CL. Data interpreter was blinded for the CL measurements.

According to the CL, our study population were divided into two groups; the first group was for women who had CL more than 30 mm, while the second group included women with short cervix (CL

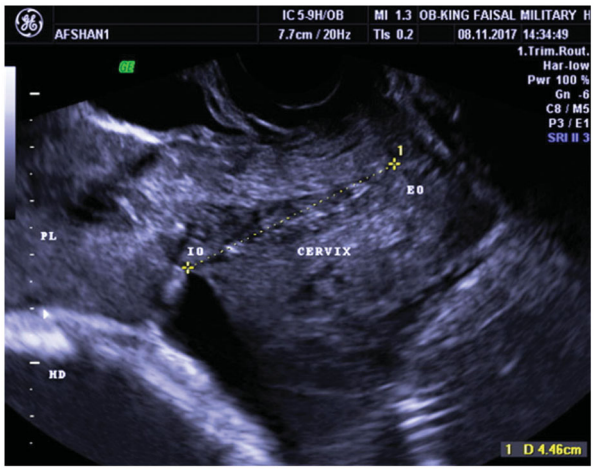

Figure 2. Ultrasound image shows cervical length measurement of a woman with incomplete placenta previa (just reaching the edge of internal os). HD: head; PL: placenta; IO: internal os; EO: external os; line 1 (interrupted) represent cervical length.

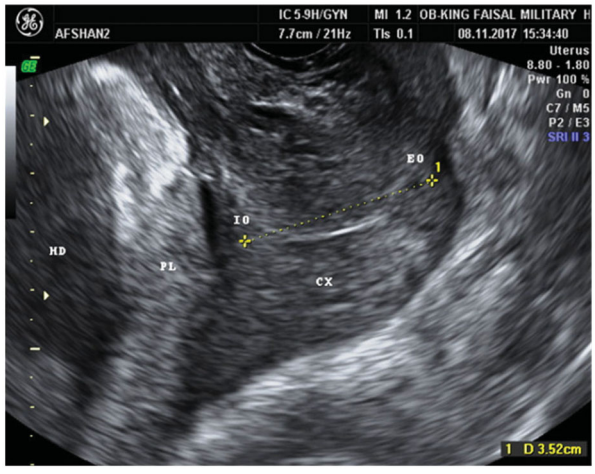

Figure 3. Ultrasound image shows cervical length measurement of a woman with complete placenta previa. HD: head; PL: placenta; IO: internal os; EO: external os; CX: cervix; line 1 (interrupted) represents cervical length.

≤30 mm). Thirty millimeters or less CL was the optimum cut-off value for better prediction of morbid outcomes in women with placenta previa [9,10]. the primary outcome measured was the prevalence of adverse maternal outcomes defined as the occurrence of one or more of the following events; APH (defined as bleeding after 24 weeks' gestation and before the onset of true labor pains), massive hemorrhage (defined as bleeding more than 2000 ml), PTB (giving birth before completed 37 weeks' gestation), emergent CS, bleeding at CS (visually estimated), perioperative hemoglobin levels, need of blood transfusion (in units), caesarean hysterectomy and retained placenta. Moreover, secondary outcomes were the neonatal adverse outcomes as low birth weight, low Apgar score, and low umbilical cord pH.

Data were analyzed using IBM© SPSS© Statistics version 23 (IBM© Corp, Armonk, NY, USA) and MedCalc© version 15.8 (MedCalc© Software, Ostend, Belgium). Shapiro–Wilk test was used to examine the normality of numerical data distribution. Abnormally distributed numerical data were presented as median and interquartile, while Mann–Whitney test was used to compare intergroup differences.

Categorical data were presented as number and percentage and their differences were compared for nominal data (using Fisher's exact test) or for ordinal data (using chi-squared test). Time to event analysis was done using the Kaplan–Meier method. The log-rank test was used to compare Kaplan–Meier curves. Multivariable binary logistic regression analysis was used to identify independent predictors of relevant maternal or fetal adverse outcomes. p-values $< .05$ were considered statistically significant.

Results

Data retrieved from electronic files of the enrolled 328 women were analyzed and compared regarding adverse maternal and neonatal outcomes on the basis of their CL measurements. All participants had abnormally implanted placentae with or without adherence confirmed upon surgery as all were delivered by CS either elective or emergency.

The demographic characteristics of included women and their past obstetric performance are shown in (Table 1). Although the history of documented cervical incompetence was comparable between the groups, women with short CL experienced significantly more miscarriages especially second-trimester ones. Also, they had higher rate and number of CS as well as past history of APH in their previous pregnancies. Kaplan–Meier curve showed that the time between enrollments in the study to delivery was significantly shorter in women with short cervix (Figure 4).

(Table 2) shows the significant differences among both groups regarding multiple placental measurements. The short CL group had a significant short distance between lower placental edge to the internal os of the cervix and more ultrasonographic findings that favor presence of placental adherence. Moreover, they had higher prevalence of anterior placental location and complete placenta previa.

The short cervix group experienced massive APH at earlier gestational age. Thus, they had significantly

Table 1. Characteristics of women with normal or short cervix and its significance.

Variable	Normal CL, USA ($n = 170$)	Short CL ($n = 158$)	p-Value
Age (years)	33 (18–44)	33 (20–44)	.536[a]
Parity	3 (0–12)	3 (0–12)	.999[a]
Previous miscarriage	0 (0–5)	0 (0–5)	.029[a]
Past 2nd trimester miscarriage	0 (0–3)	0 (0–3)	.011[a]
Previous PTB	0 (0–4)	0 (0–4)	.862[a]
Number of CS	1 (0–5)	1 (0–6)	.006[a]
Previous CS	90 (52.9%)	110 (69.6%)	.002[b]
Past history of APH	1 (0.6%)	17 (10.8%)	<.001[b]
Cervical incompetence	3 (1.8%)	3 (1.9%)	1.000[b]
Previous surgery			
Appendectomy	6 (3.5%)	2 (1.3%)	.645[b]
Cholecystectomy	2 (1.2%)	2 (1.3%)	
Hernia repair	2 (1.2%)	2 (1.3%)	

Data are expressed as median (range) or number (%). CL: cervical length; PTB: preterm birth; CS: caesarean section; APH: ante-partum hemorrhage. [a]Mann–Whitney test. [b]Fisher's exact test.

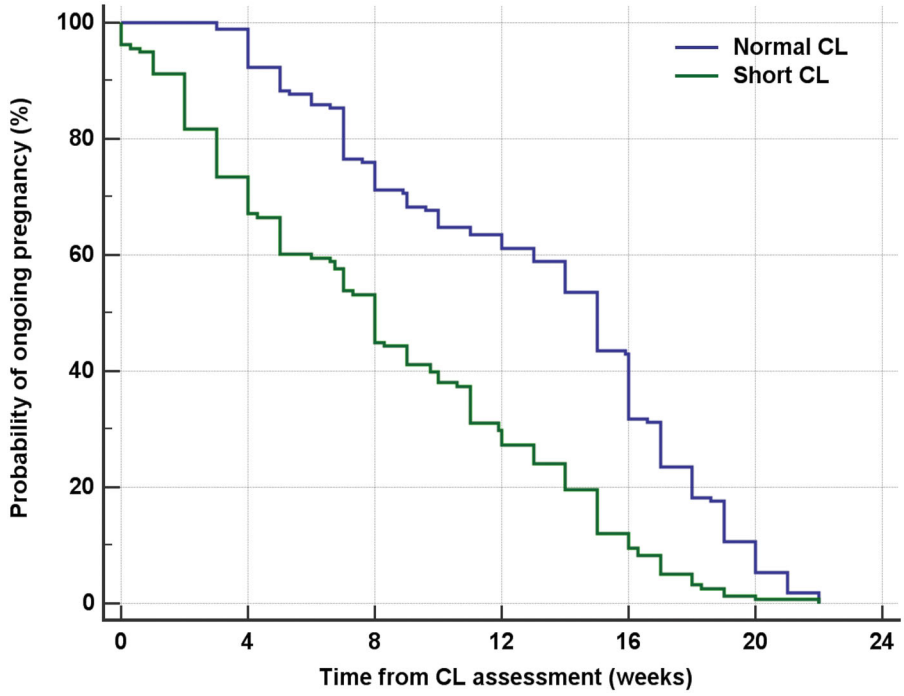

Figure 4. Kaplan–Meier curves for the time to delivery in patients with short or long CL. The difference between the two curves is statistically significant (hazard ratio = 2.06, 95% CI = 1.63–2.60, p-value < .0001).

Table 2. Ultrasonographic findings in both groups and its statistical significance.

Variable	Normal CL, USA ($n = 170$)	Short CL ($n = 158$)	p-Value
Distance between lower placental edge to internal OS (cm)	0 (0–2.8)	0 (0–1.8)	<.001[a]
Placental invasion by US	37 (21.8%)	65 (41.1%)	<.001[b]
Placental location			
Anterior	64 (37.6%)	86 (54.4%)	.003[b]
Posterior	106 (62.4%)	72 (45.6%)	
Type of placenta previa by US			
Low lying	39 (22.9%)	16 (10.1%)	<.001[b]
Incomplete	94 (55.3%)	81 (51.3%)	
Complete	37 (21.8%)	61 (38.6%)	

Data are expressed as median (range) or number (%). [a]Mann–Whitney test. [b]Fisher's exact test.

higher rates of PTB and emergency CS. Also, the presence of placental adherence during CS was higher which precipitating a significant rise of the visually estimated intraoperative blood loss, more need for blood transfusion and higher incidence of cesarean hysterectomies. The preoperative hemoglobin level and subsequent postoperative hemoglobin drop showed no statistically significant difference between the two groups as shown in (Table 3).

Regarding the adverse neonatal outcomes, live births of women with short CL had significantly lower birth weight, Apgar scores and umbilical cord pH as

Table 3. Comparison between maternal outcomes of women with normal or short cervix.

Variable	Normal CL, USA ($n = 170$)	Short CL ($n = 158$)	p-Value
APH	75 (44.1%)	117 (74.1%)	<.001[a]
Gestational age at initial bleeding	32 (3–37.6)	28 (3–37)	<.001[a]
PTB	6 (3.5%)	118 (74.7%)	<.001[a]
Emergency CS	67 (39.4%)	129 (81.6%)	<.001[a]
Gestational age at delivery	37 (29.3–40)	33 (17–38)	<.001[b]
Preoperative hemoglobin level (%)	11.0 (−28.2–74.0)	10.6 (−14.7–40.7)	.879[b]
Drop in hemoglobin (g/dl)	1.2 (−2.9–5.7)	1.1 (−1.4–3.5)	.988[b]
EBL during CS (ml)	700 (400–10,000)	1500 (400–10,000)	<.001[b]
Massive hemorrhage (> 2000 ml)	30 (17.6%)	98 (62.0%)	<.001[a]
Perioperative blood transfusion (units)	0 (0–17)	2 (0–17)	<.001[a]
Placental adherence	33 (19.4%)	77 (48.7%)	<.001[a]
Cesarean hysterectomy	12 (7.1%)	42 (26.6%)	<.001[a]

Data are expressed as median (range) or number (%). CL: cervical length; APH: ante-partum hemorrhage; PTB: preterm birth; CS: caesarean section; EBL: estimated blood loss. [a]Mann–Whitney test. [b]Fisher's exact test.

Table 4. Neonatal outcomes in patients with normal or short cervix.

Variable	Normal CL, USA ($n = 170$)	Short CL ($n = 158$)	p-Value
Birth weight (kg)	2.7 (1.2–3.7)	2.1 (0–3.7)	<.001[a]
Apgar score at 1 min	8 (2–9)	7 (0–9)	.002[a]
Apgar score (<7) at 1 min	0 (0.0%)	0 (0.0%)	NA
Apgar score at 5 min	9 (7–9)	9 (0–9)	.010[a]
Apgar score (<7) at 5 min	0 (0.0%)	4 (2.5%)	.053[b]
Umbilical cord pH	7.2 (6.9–7.4)	7.2 (0–7.3)	.001[a]
Low umbilical cord pH(<7.1)	42 (24.7%)	60 (38.0%)	.012[b]

Data are expressed as median (range) or number (%). [a]Mann–Whitney test. [b]Fisher's exact test.

presented in (Table 4). Although these newborns had lower Apgar scores, the frequency of having a score (<7) was comparable between both groups at 1 and 5-min intervals. Also, having cord pH (<7.1) was significantly prevalent among them. Only one stillbirth in the short cervix group was reported.

Throughout the statistically significant factors that could contribute to the adverse maternal outcomes, we ran multivariable binary logistic regression analysis for prediction of APH, PTB, emergency CS, intraoperative placental adherence, massive hemorrhage, cesarean hysterectomy and low umbilical cord Ph in (Table 5). Short CL can be identified as a statistically significant independent risk factor for the studied adverse maternal as well as neonatal outcomes. History of CS was associated with the risk of having more adherent placentae and more severe bleeding, while anterior placental location and complete placenta previa carried the same risks as well as more frequent cesarean hysterectomies. However, complete placenta previa was also a risk factor for PTB.

Discussion

Placenta previa with or without variable degrees of accreta obviously remains one of the worst obstetric catastrophes that can lead even to maternal mortality. In this study, we focused on addressing the short cervical length (<30 mm) as a simple indicator that can help to anticipate various maternal and neonatal morbidities. Our results showed that 158 women with short cervix and placenta previa/accreta experienced higher rates of PTB, bleeding, emergent CS and hysterectomies.

To our knowledge, this is the largest sample size of all the published articles as well as conferences' abstracts. In 2009 Chi et al. were the first to arouse the attention to the hypothesis that CL could predict prepartum bleeding and preterm cesarean section in third-trimester women with complete placenta previa [8]. Since that, the authors studied this relationship in different designs, protocols, timings, and outcomes. [7–19].

The early three prospective studies that evaluated CL measurements, when the diagnosis of placenta previa was confirmed, concluded that short cervix could predict severe hemorrhage resulting in preterm CS with high accuracy [8–10]. Moreover, two authors determined a 30 mm or less CL as the proper cut-off value for better prediction of these outcomes [9,10]. In fact, we used these finding as a reference upon dividing our sample into two groups as many of the following reports confirmed the same cut-off value of CL [12,14,16]. Other authors used a different cut-off of 35 or 25 mm [7,17,19], while Garcia–Espinosa et al. adjusted the CL measurements according to gestational age based on a previous publication to produce Z-scores that they used for analysis [13].

We used a single CL recording during our data collection and analysis. This was performed by most

Table 5. Multivariable binary logistic regression analysis for predictors of adverse maternal and neonatal outcomes.

Outcome	Predictor	OR	Lower	Upper	*p*-Value
APH	Previous CS	0.849	0.507	1.423	.534
	Short CL	3.862	2.373	6.285	<.001
	Anteriorly located placenta	0.813	0.500	1.321	.403
	Complete placenta previa	1.008	0.573	1.772	.979
PTB	Previous CS	0.361	0.137	0.954	.040
	Short CL	206.485	67.706	629.725	<.001
	Anteriorly located placenta	0.542	0.258	1.135	.104
	Complete placenta previa	0.362	0.165	0.796	.011
Emergency CS	Previous CS	1.436	0.832	2.477	.194
	Short CL	7.516	4.400	12.840	<.001
	Anteriorly located placenta	0.723	0.428	1.220	.224
	Complete placenta previa	0.658	0.356	1.216	.181
Placental adherence	Previous CS	2.124	1.129	3.997	.020
	Short CL	3.146	1.807	5.476	<.001
	Anteriorly located placenta	2.379	1.375	4.114	.002
	Complete placenta previa	4.741	2.623	8.571	<.001
Massive hemorrhage	Previous CS	2.284	1.236	4.221	.008
	Short CL	6.932	3.958	12.141	<.001
	Anteriorly located placenta	2.174	1.256	3.765	.006
	Complete placenta previa	3.527	1.895	6.563	<.001
Cesarean hysterectomy	Previous CS	2.012	0.736	5.501	.173
	Short CL	3.693	1.722	7.917	.001
	Anteriorly located placenta	2.176	1.052	4.498	.036
	Complete placenta previa	8.838	4.058	19.251	<.001
Umbilical cord pH	Previous CS	0.654	0.381	1.124	.124
	Short CL	1.831	1.120	2.993	.016
	Anteriorly located placenta	1.220	0.746	1.995	.429
	Complete placenta previa	1.471	0.834	2.596	.183

researchers before. On the other hand, Sekiguchi et al. And Shin et al. Tested multiple CL measurements that were serially obtained every 2 weeks from 24 weeks' gestation till delivery by the former and four times between 19 and 34 weeks' gestation for the later [7,15].

Even with the use of different cut-off values at the time of examination and frequency of CL measurements, short cervix was verified to predict strongly the occurrence of massive APH with subsequent preterm emergency CS except for only two reports that showed no significance for determining CL in cases of placenta previa [11,18]. This could be related to that both studies had few cases with short cervix (8 women in one report and 27 in the other).

Although the definite relationship between PTB and the short cervix is well described [21], it remains unclear if the presence of short cervix is solely responsible for the maternal and neonatal morbidities that might complicate pregnancies with placenta previa/accreta. Other contributing factors included complete placenta previa, uterine contractions, PTB rate and history of previous CS [9,12,25]. Also, the dilemma of what is the initiating factor for the other, contractions or bleeding remains unsolved. Authors explained these queries by hypothesis that bleeding is a result of uterine contractions that affected placenta previa implanted on a changing cervix. Shorter cervixes in women with placenta previa/accreta carried the risk of PTB and possible placental detachment and hemorrhage from its low inelastic insertion as the placenta may not adapt the progressive cervical effacement [1,9,25]. Others proposed different hypotheses such as the wide lower uterine segment and high vascularity over smaller surface area of short cervix [26].

The multivariable binary logistic regression analysis revealed that CL a statistically significant independent predictor for PTB, massive APH, emergency CS, cesarean hysterectomy, intraoperative placental adherence and blood loss. In concordance with our results, Fukushima et al. Proved the relevance of CL to placental adherence, operative blood loss, and cesarean hysterectomy. They reported odds ratios for preterm CS, massive intraoperative hemorrhage, and placental adherence in women with short CL to be 3.29, 6.68, and 7.54, respectively [12]. The incidence of hysterectomy was significantly higher with shorter cervix in previous studies [10,14]. Also, prediction of emergency delivery in women with placenta previa included history of CS, APH and the need for blood transfusion [27].

Furthermore, Polat et al. Specifically studied the impact of the short cervix on the operative difficulties in women underwent cesarean hysterectomy due to placenta accreta. CL cut-off value of 20.5 mm increased blood transfusion needs, operative duration of, hospital stay as well as technical operative difficulties as clamping and ligation of lateral and medial pedicles,

the dissection of the pararectal and paravesical spaces and ureter identification [26]. Peri-operative blood transfusion was significantly higher with short cervix in different reports [10,14,28].

Anterior complete placenta previa is also an independent risk factor for intraoperative placental adherence and increased incidence of severe bleeding requiring a caesarean hysterectomy. This was agreed in previously published data [12,16,28]. Sekiguchi et al. Suggested a reason for such correlation that the mechanical stimulation of the anterior uterine wall during daily life, which can induce uterine contractions due to unknown reactions in the underlying decidua basalis with abundant blood flow, is frequently more direct than of the posterior wall which is hypothetically protected by the pelvis [28]. However, others noticed that the uterine electromyographic activity was independent of placental site when it was measured through the abdominal surface during the mid-trimester [29].

Regarding the neonatal outcomes, women with shorter cervices delivered babies with significantly lower birth weight, Apgar scores, and umbilical cord pH mainly due to prematurity. We did not record any cases of neonatal mortality. Some studies revealed similarly low birth weight [7,10]. On the other hand, some reports found no significant changes among neonatal outcomes [9,12].

Although transvaginal ultrasound was frequently used for predicting the type, persistence, and adhesion of placenta previa, it should be more directed to predict different maternal and neonatal outcomes through obtaining CL measurement. To sum up, short cervix can be used as a single independent factor that is accompanied with significant increase of occurrence of attacks of severe bleeding, emergency CS and cesarean hysterectomy.

Author contributions

AT, ME, EB, and AM shared the protocol writing and design; AT, ME, and AM collected the data for analysis; AT, ME, and EB conducted the data analysis and interpretation; and AT and EB wrote the first manuscript draft. AT and AM carried the follow-up of participants files. All authors contributed equally in the manuscript appraisal, fully agreed to its integrity and accuracy. They approved the final manuscript. Whenever needed, any required data or materials can be provided by the corresponding author.

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Ethical approval

We started after obtaining appropriate approval from the local research ethics committee in Armed Forces Hospitals Southern Region. Confidentiality of all women admitted to our trial was protected. Also, the records were anonymous for the interpreters. Consent for publication was not applicable.

Disclosure statement

There is no conflict of interest reported by any author.

Data availability

Whenever applicable and needed, required data or materials can be provided by the corresponding author.

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