Impact of high-order repeat cesarean deliveries on early maternal complications among major placenta previa patients in Southern Saudi Arabia

Ayman H. Shaamash, MD, MSc, *Mehad H. AlQasem,* SBOG, MBBCH, *Ahmed A. Mahfouz,* MSc, PhD, *Deama S. Al Ghamdi,* SBOG, MBBCH, *Norah I. Almanie,* SBOG, MBBCH, *Mamdoh A. Eskandar,* FRCSC, MD.

ABSTRACT

الأهداف: دراسة معدلات ونسب احتمالية (ORs) حدوث مضاعفات الأمهات المبكرة بين مريضات المشيمة المنزاحة من الدرجة المتقدمة وخضعن للولادات القيصرية عالية التكرار (الرابعة إلى السابعة) بالمقارنة مع الاتي خضعن الى ولادات قيصرية منخفضة التكرار (الثانية والثالثة).

المنهجية: أجرينا دراسة أترابية مرجعية في مستشفى أبها للأمومة والأطفال لجميع مريضات المشيمة المنزاحة من الدرجة المتقدمة آلائي ولدن قيصرياً من خلال الولادات القيصرية المتكررة الثانية و اللاحقة - في الفترة من يناير 2012م إلى ديسمبر 2021م. تضمنت الدراسة ما مجموعه 184 مريضة وتم تصنيفهن لمجموعتين مجموعة تضم المريضات الاتي خضعن الى ولادات قيصرية متكررة منخفضة التكرار (الثانية والثالثة) (العدد = 100)، ومجموعة خضعن للولادات القيصرية عالية التكرار (الرابعة إلى السابعة) (العدد = 84).

النتائج: بالمقارنة مع الولادات القيصرية منخفضة التكرار، أظهرت مجموعة الولادات القيصرية عالية التكرار مع المشيمة المنزاحة من الدرجة المتقدمة - معدلات أعلى بكثير ونسب احتمالية (ORs) لمضاعفات الأمهات المبكرة بما في ذلك المشيمة المنزاحة الملتصقة (المشخصة بالرنين المغناطيسي)، وعمليات نقل خلايا الدم الحمراء المفصولة، والحالات المتوسطة إلى الشديدة من النزيف الجراحي، واستئصال الرحم الطارئ ، وإصابات المسالك البولية وكذلك مدة الإقامة في المستشفى بعد الولادات القيصرية. بشكل عام كانت الزيادات في معدلات ونسب احتمالية (ORs) حدوث مضاعفات الأمهات المبكرة متناسبة بشكل مباشر مطرد مع عدد الولادات القيصرية المتكررة .على وجه الخصوص أظهرت المجموعة الفرعية التي خضعن للولادة القيصرية السابعة والسادسة أعلى المعدلات ونسب احتمالية للمشيمة المنزاحة والملتصقة واستئصال الرحم الطارئ،كالأتي 84.6% (OR=3.98) و 28.6% (OR=4.04)، على التوالي.

الخلاصة: في مريضات المشيمة المنزاحة من الدرجة المتقدمة فالخضوع لأكثر من "ثلاثة" ولادات قيصرية متكررة يرتبط بزيادة ملحوظة في كل من معدلات ونسب احتمالية (ORs) حدوث مضاعفات الأمهات المبكرة المختلفة. يتوافق هذا الاتجاه في زيادة العديد من المضاعفات بشكل مباشر بالعدد المتزايد للولادات القيصرية عالية التكرار. تشير هذه النتائج ان المريضات آلائي لديهن تاريخ من الولادات القيصرية عالية التكرار قد يستفدن من المستوى الثالث وأعلى للرعاية في سياق وجود المشيمة المنزاحة من الدرجة المتقدمة والملتصقة.

Objectives: To investigate the rates and odds ratios (ORs) of early maternal complications among patients with major placenta previa (PP) who have undergone high-order repeat cesarean deliveries (HOR-CDs) in comparison to those with low-order repeat cesarean deliveries (LOR-CDs).

Methods: We carried out a retrospective review of all major PP patients (n=184) who delivered through second or subsequent repeat CDs, from January 2012 to December 2021 (Abha Maternity and Children's Hospital, Abha, Saudi Arabia). The patients were categorized into 2 groups: the LOR-CDs group (n=100), comprising individuals with their second and third CDs (CD2-CD3) and the HOR-CDs group (n=84), consisting of those undergoing their fourth to seventh CDs (CD4-CD7).

Results: In comparison to the LOR-CDs, the HOR-CDs group with major PP exhibited significantly higher rates and ORs of early maternal complications, including MRI-diagnosed placenta accreta spectrum (PAS, OR=2.67), transfusions of packed red blood cells (OR=2.71), moderate to severe intra-operative bleeding (OR=1.80), emergency hysterectomy (OR=2.96), urological injuries (OR=3.17), and length of post-operative hospital stay (OR=3.91). The major PP subgroup undergoing CD6-CD7 showed the highest rates and ORs for PAS diagnosis at 84.6% (OR=3.98) and emergency hysterectomy at 28.6% (OR=4.04).

Conclusion: Among patients with major PP, undergoing more than 3 CDs is associated with a notable increase in both the rates and ORs of various early maternal complications. This trend of increasing many complications correlates directly with an ascending number of CDs.

Keywords: repeat cesarean delivery, major placenta previa, maternal complications

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From the Department of Obstetrics and Gynecology (Shaamash, AlQasem, Al Ghamdi, Almanie, Eskandar); from the Department of Family and Community Medicine (Mahfouz), College of Medicine, King Khalid University, and from the Department of Obstetrics and Gynecology (Shaamash, AlQasem, Al Ghamdi, Almanie, Eskandar), Abha Maternity and Children's Hospital, Abha, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Prof. Ayman H. Shaamash, Department of Obstetrics and Gynecology, College of Medicine, King Khalid University, Abha, Kingdom of Saudi Arabia. E-mail: ashaamash@kku.edu.sa
ORCID ID: https://orcid.org/0000-0001-7854-2123

Globally and across various regions, the rates of cesarean deliveries (CDs) has markedly increased over the past 3 decades, exhibiting significant variations between higher and lower resource environments.[1] The average worldwide CD rate has increased from approximately 7% in 1990 to 21% today, with expectations of further increases throughout this decade. According to research findings, should this trend persist, by 2030, the highest rates are projected to be in Eastern Asia (63%) and Western Asia (50%). In fact, during 2021, in 5 countries (Dominican Republic, Brazil, Cyprus, Egypt, and Turkey), CDs have surpassed vaginal deliveries in frequency, as reported by the World Health Organization (WHO).[2]

Saudi Arabia is not an exception; over the last 30 years, local studies have documented a tripling in CD rates at numerous tertiary maternity hospitals, influenced by delivery practices, hospital policies, and regional differences. For instance, King Khalid University Hospital, Riyadh, Saudi Arbia, reported an overall CD rate of 10.3% in 1993 which increased to 32.6% among pregnant women attending the outpatient clinics in 2018.[3,4] Similarly, King Abdulaziz Medical City, Jeddah, Saudi Arabia, observed an increase in the overall CD rate from 8% in 1993 to 27% by 2016.[5] By the end of 2021, Abha Maternity and Children's Hospital (AMCH), Abha, Saudi Arabia, reported an average CD rate of nearly 40% over the preceding decade.[6] These institutional rates align with reports from the WHO and the Saudi Ministry of Health, which noted an overall CD rate of 30.2% in Saudi Arabia (namely, a CD occurs in one out of every 3 Saudi women).[7,8]

Although the WHO does not advocate for a specific CD rate within hospitals, and such rates can vary considerably among healthcare facilities depending on the populations they serve, evidence indicates that higher-order repeat (HOR)-CDs are associated with significantly increased maternal morbidity compared to fewer CDs.[9-13] Additionally, CDs necessitated by abnormal placentation, such as placenta previa (PP) and placenta accreta spectrum (PAS), are linked with heightened risks of severe maternal morbidities, including massive bleeding with repeated blood transfusions, damage to adjacent urinary organs, and emergency cesarean hysterectomy.[14-18] Recent international guidelines reinforce that PP/PAS is correlated with the most significant rates of perinatal maternal complications.[19,20]

Similar to other regions in Saudi Arabia, both historical and recent studies from AMCH, Abha, Saudi Arabia, have documented a consistent pattern of high prevalence of grand multiparity, which may be attributed to the prevailing cultural norms within the country.[6,21,22] Consequently, it is common for Saudi women to undergo 3 or more CDs.[3-6,21,22]

This ancillary study was designed to evaluate the rates and associated risk factors, through the calculation of odds ratios (ORs), of early maternal complications in patients with major PP undergoing HOR-CDs compared to those undergoing low-order repeat (LOR)-CDs.

Methods. A retrospective cohort study was carried out at AMCH, Abha, Saudi Arabia. This ancillary study encompassed all admitted patients with major PP who underwent repeated CDs from January 2012 to December 2021. As the largest tertiary referral hospital under Saudi Ministry of Health, AMCH boasts a capacity of 240 beds and averages 5,000 deliveries annually. This is a secondary analysis of data from our patients with major PP. The hospital records of major PP patients undergoing their "second or more CDs" were reviewed (n=184) and subsequently categorized into 2 distinct groups: the LOR-CDs group, comprising patients with their second and third CDs (CD2-CD3, n=100), and the HOR-CDs group, encompassing patients undergoing their fourth to seventh CDs (CD4-CD7, n=84). All patients underwent either planned or emergency repeat CDs, with cesarean hysterectomy carried out as indicated.

The study exclusively included major PP patients with comprehensive medical records who had undergone their second or subsequent CDs (CD2-CD7).

This is an ancillary study, involving a secondary analysis of data from the "major placenta previa study", which received approval from the research ethics committee at King Khalid University, Abha, Saudi Arbia (approval number: 2023-607).

According to the AMCH protocols, a major degree of PP is defined as the placenta reaching or covering the internal cervical os, either partially or entirely.[6] The diagnosis of this condition was established in both symptomatic and asymptomatic patients (regardless of the presence of antepartum hemorrhage) after 24 weeks of gestation, initially using 2D ultrasonography (US), and later confirmed after 32 weeks of gestation. The preliminary antenatal diagnosis of PAS was established through US/color Doppler imaging, considering

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patients positive for PAS if they met 2 or more diagnostic criteria. For cases with equivocal findings or when deep myometrial or extra-uterine extension was suspected on US/color Doppler examination, adjunctive magnetic resonance imaging (MRI) was employed.

The standard approach for managing all major PP patients at AMCH involves inpatient care commencing at a gestational age of 24 weeks. Antenatal steroids were administered intramuscularly between 24-34 weeks of gestation. For those with uncomplicated cases, CDs were scheduled between 37-38 weeks of gestation. Given the diagnosis of major PP, all patients underwent either planned or emergency CDs in alignment with prevailing guidelines.[23] Emergency cesarean hysterectomy was necessitated in cases of associated PAS or when conservative medical and surgical measures were insufficient to manage severe, life-threatening hemorrhage. Intra-operative blood loss was estimated visually. Comprehensive details on the diagnostic and management protocols for major PP (with or without PAS) at AMCH have been extensively documented in our prior publications.[6,24,25]

The study involved retrieving files of major PP patients who underwent their CD2 or more (CD3-CD7) and were admitted during the designated study period. The collected data encompassed the following: I) antenatal maternal characteristics including age, symptomatic status, number of repeat CDs, placental location (anterior or posterior), PAS diagnosis based on antenatal imaging (US/color Doppler ± MRI), MRI grading of PAS (accreta, increta, or percreta), and any history of previous uterine surgery (such as dilatation and curettage or evacuation); II) obstetrical history covering gravidity, parity, miscarriages, current in vitro fertilization (IVF) pregnancy, timing of CD (planned or emergency), admission and termination gestational ages; and III) early maternal complications including pre- and post-operative hemoglobin levels, transfusions of packed red blood cells (RBCs) or fresh frozen plasma, preterm birth <37 weeks, extent of intra-operative bleeding (classified as no excessive bleeding, mild, moderate, or heavy bleeding), emergency cesarean hysterectomy, intra-operative urinary tract injuries (affecting the bladder or ureter), and post-operative hospital stay duration (in days). This data was meticulously recorded and coded within an Excel spreadsheet.

Statistical analysis. The Statistical Package for the Social Sciences, version 19.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the extracted data. Descriptive statistics, including rates (numbers and percentages), means ± standard deviations (SDs), and medians with minimum-maximum ranges were employed for the initial analysis. Comparative assessments of antenatal maternal characteristics, obstetrical history, and early maternal complications between the 2 groups (LOR-CDs and HOR-CDs) were carried out using the 2-sided t-test, Mann-Whitney test and Chi-square test (χ^2), depending on the type of data (numerical or categorical) and its distribution (normal or abnormal). The Univariate logistic regression analysis was applied to ascertain the crude odds ratios (cORs) and 95% confidence intervals (CIs) for HOR-CDs as a potential risk factor for increased ORs of early maternal complications. A 2-sided *p*-value of <0.05 was considered significant.

Results. Data from 184 patients with major PP who underwent repeat CDs were analyzed, delineating 2 distinct groups: the LOR-CDs group (n=100, 54.3%), encompassing CD2-CD3 and the HOR-CDs group (n=84, 45.7%), comprising CD4-CD7. Within the LOR-CDs cohort, the majority or 28.8% (n=53) experienced CD3, whereas in the HOR-CDs cohort, 20.7% (n=38) had CD4 and 17.4% (n=32) had CD5 (Table 1).

Table 2 presents a comparison of antenatal maternal characteristics between the study groups (HOR-CDs and LOR-CDs). Significant differences were observed in the means of maternal ages (*p*=0.033), medians of gravidity (*p*=0.001) and parity (*p*=0.001), mean numbers of repeat CDs (*p*=0.001), and the rates of PAS diagnosis through antenatal MRI (*p*=0.005) between the 2 groups. Other characteristics did not show statistically significant differences.

Regarding the rates of early maternal complications, Table 3 illustrates that patients in the HOR-CDs group exhibited significantly higher differences in the medians of RBCs transfusions (*p*=0.003), extended post-operative hospital stays (*p*=0.001), and higher rates of moderate to heavy intra-operative bleeding (*p*=0.048), emergency cesarean hysterectomies (*p*=0.01), and intra-operative

Table 1 - Pattern of repeat cesarean deliveries among our major placenta previa patients (N=184).

Variables	n (%)
Low-order repeat CDs, n=100 (54.3)	
CD2	47 (25.5)
CD3	53 (28.8)
High-order repeat CDs, n=84 (45.7)	
CD4	38 (20.7)
CD5	32 (17.4)
CD6	11 (5.9)
CD7	3 (1.7)

Values are presented as numbers and percentages (%).
CDs: cesarean deliveries

Table 2 - Antenatal maternal characteristics of patients with repeat cesarean deliveries and major placenta previa.

Variables	Values	Test of significance	*P*-values
Maternal age (years), mean±SD			
LOR-CDs (CD2 and CD3)	32.84±5.74	t=2.123*	0.033
HOR-CDs (CD4 - CD7)	34.93±5.33		
Gravidity, median (range)			
LOR-CDs (CD2 and CD3)	4.0 (2-16)	Z=4.388†	0.001
HOR-CDs (CD4 - CD7)	6.0 (4-11)		
Parity, median (range)			
LOR-CDs (CD2 and CD3)	2.0 (2-9)	Z=4.377†	0.001
HOR-CDs (CD4 - CD 7)	4.0 (4-7)		
Number of CDs, mean±SD			
LOR-CDs (CD2 and CD3)	2.53±0.50	t=22.532*	0.001
HOR-CDs (CD4 - CD7)	4.75±0.82		
PAS on MRI (n=150)§			
No PAS	75 (50.0)		
PAS	75 (50.0)		
LOR-CDs (CD2 and CD3), n=80			
No PAS	49 (61.3)		
PAS	31 (38.8)		
HOR-CDs (CD4 - CD7), n=70		8.679‡	0.005
No PAS	26 (37.1)		
PAS	44 (62.9)		

Values are presented as mean ± standard deviation (SD), median (range), or numbers and percentages (%). Maternal characteristics did not show significant differences included: miscarriages; current IVF pregnancy; previous uterine surgery (curettage-evacuation-hysteroscopic surgery); placental location (anterior or posterior); timing of CD (emergency or planned); admission gestational age (weeks); termination gestational age (weeks); antepartum hemorrhage (present or absent); and degree of PAS on antenatal MRI (accreta or increta/percreta). *2-sided t-test, †Mann-Whitney test, ‡Pearson Chi-square (X^2), §only 150/184 had MRI. LOR: low-order repeat, CDs: cesarean deliveries, HOR: high-order repeat, PAS: placenta accreta spectrum, MRI: magnetic resonance imaging

urological injuries (p=0.03). However, no significant differences were observed in other complications.

Table 4 presents the findings from the univariate logistic regression analysis carried out to investigate the association between HOR-CDs and the risk of early maternal complications in patients with major PP, expressed as ORs. Patients with major PP undergoing HOR-CDs (>CD3) demonstrated elevated ORs for the following maternal complications: antenatal PAS diagnosis (OR=2.67, p=0.001), need for repeated transfusion of 3 or more units of packed RBCs (OR=2.71, p=0.002), moderate to heavy intra-operative bleeding (OR=1.80, p=0.045), emergency hysterectomy (OR=2.96, p=0.013), intra-operative lower urinary tract injuries (OR=3.17, p=0.020), and post-operative hospital stays exceeding 3 days (OR=3.91, p=0.001). Nevertheless, the likelihood of other complications remained unchanged.

A further sub-analysis focusing on the rates and ORs of serious maternal complications including both the antenatal PAS diagnosis and emergency hysterectomy, relative to the stratified number of repeat CDs, revealed a "progressive" increase in these complications with the ascending number of CDs (CD6-CD7 > CD4-CD5 > CD2-CD3). Specifically, in the sub-group of major PP and HOR-CDs (CD6-CD7), the rate and OR of antenatal PAS diagnosis was 84.6% (OR=3.98, p=0.003) and the rate and OR of emergency hysterectomy was 28.6% (OR=4.04, p=0.003, Table 5).

Discussion. Recent reports from AMCH, showed that the average rate of CDs has been doubled within the last 15 years, it increased from approximately 21% in 2006 to approximately 40% in 2021.[6,21] This significant rise parallels trends observed in numerous national Saudi studies.[3-6,21,22]

In general, the current study demonstrates that among major PP the rates of early maternal complications significantly rise with an increasing number of CDs (>CD3) (namely, in patients with HOR-CDs). Collectively, our major PP patients with HOR-CDs (CD4-CD7) exhibited significantly greater occurrences of associated PAS, RBC transfusions, moderate to severe intra-operative bleeding, emergency

Table 3 - Early maternal complications among patients with repeat cesarean deliveries and major placenta previa.

Variables	n (%)	Test of significance	*P*-values
RBCs transfusions (units), median (range)			
LOR-CDs (CD2 - CD3), n=100	2 (0-7)	Z=3.011*	0.003
HOR-CDs (CD4 - CD7), n=84	2 (0-13)		
Hospital stay (days), median (range)			
LOR-CDs (CD2 - CD3), n=100	3 (1-14)	Z=3.729*	0.001
HOR-CDs (CD4 - CD7), n=84	3 (1-15)		
Intra operative bleeding			
No to mild bleeding			
LOR-CDs (CD2 - CD3)	61 (61.0)		
HOR-CDs (CD4 - CD7)	39 (46.4)		
Moderate to heavy		3.907†	0.048
LOR-CDs (CD2 - CD3)	39 (39.0)		
HOR-CDs (CD4 - CD7)	45 (53.6)		
Emergency hysterectomy (n=28)			
No			
LOR-CDs (CD2 - CD3)	91 (91.0)		
HOR-CDs (CD4 - CD7)	65 (77.4)		
Yes		6.563†	0.01
LOR-CDs (CD2 - CD3)	9 (9.0)		
HOR-CDs (CD4 - CD7)	19 (22.6)		
Urological injuries (bladder and ureter), n=17			
No			
LOR-CDs (CD2 - CD3)	95 (95.0)		
HOR-CDs (CD4 - CD7)	72 (85.7)		
Yes		4.694†	0.03
LOR-CDs (CD2 - CD3)	5 (5.0)		
HOR-CDs (CD4 - CD7)	12 (14.3)		

Values are presented as numbers and percentages (%) or median and range. Early maternal complications did not show significant differences included: fresh frozen plasma transfusions; pre-operative hemoglobin; post-operative hemoglobin; premature delivery <37 weeks; and emergency CD. *Mann-Whitney test, †Pearson Chi-square (X^2). RBCs: red blood cell counts, LOR: low-order repeat, CDs: cesarean deliveries, HOR: high-order repeat

hysterectomy, intra-operative urological injuries, and extended post-operative hospital stays. A comprehensive comparison with analogous studies is challenging due to variations in the definition of HOR-CDs (≥3), the associated risk factors such as PP±PAS, maternal characteristics, and the surgical proficiency of the operating teams. In practice, previous large studies and systematic reviews assessing the risk of various maternal complications have documented significant increases with a rising number of CDs, especially in the presence of PP. These maternal risks are predominantly linked to the associated PAS with the necessity for massive transfusions and difficult emergency hysterectomy.[10-13] The US National Institutes of Health Consensus Development conference on vaginal birth after CD carried out a previous large systematic review and meta analysis that found that women with PP and repeated CDs, had significantly higher risks of accreta, hysterectomy, and other maternal complications.[11]

In the same way, recent multi-centric studies from China concluded that PP attached to a cesarean scar with an invasive placenta could increase the risk of adverse maternal outcomes such as hemorrhage, blood transfusions, bladder injury, and hysterectomy. These studies examined the effect of prior repeat CDs on the outcomes of various degrees of PP±PAS.[14-18]

Our findings revealed a significant elevation in the rate of PAS diagnosis among the HOR-CDs group compared to the LOR-CDs group (62.9% vs. 38.8%, p=0.005). In our major PP patients undergoing repeat CDs, antenatal MRI identified PAS in 38.8% of patients experiencing CD2-CD3, in 57.9% of those with CD4-CD5, and in 84.6% of patients with CD6-CD7. These figures align with the findings from a comprehensive multi-centric US cohort study, which determined that the risk of PAS escalated with each subsequent CD, 3% for the first CD, 11% for the

Table 4 - Univariate analysis for the high-order repeat cesarean delivery (CD4-CD7) as a risk factor for early maternal complications in major placenta previa patients.

Risk Factors	LOR-CDs (CD2-CD3) n=100	HOR-CDs (CD4-CD7) n=84	cOR (95% CI)	*P*-values
PAS by MRI (n=150)*				
No PAS (n=75)	49 (61.3)	26 (37.1)	2.67 (1.39-5.16)	0.001
With PAS (n=75)	31 (38.7)	44 (62.9)		
RBCs transfusions (units)				
<3 units	83 (83.0)	54 (64.3)	2.71 (1.37-5.37)	0.002
≥3 units	17 (17.0)	30 (35.7)		
Intra operative bleeding				
Normal and mild bleeding	61 (61.0)	39 (46.4)	1.80 (1.01-3.24)	0.045
Moderate and heavy bleeding	39 (39.0)	45 (53.6)		
Emergency hysterectomy, n=28				
No hysterectomy	91 (91.0)	65 (77.4)	2.96 (1.18-6.89)	0.013
Hysterectomy	9 (9.0)	19 (22.6)		
Lower urinary injuries, n=17				
No injuries	95 (95.0)	72 (85.7)	3.17 (1.07-9.34)	0.020
Bladder/ureter injuries	5 (5.0)	12 (14.3)		
Post operative hospital stay (days)				
≤3 days	87 (62.1)	53 (37.9)	3.91 (1.88-8.14)	0.001
>3 days	13 (29.5)	31(70.5)		

Values are presented as numbers and percentages (%). Variables that did not represent risk factors on univariate regression analysis are not shown in the table including: fresh frozen plasma transfusions (cOR [95% CI]: 1.39 [0.69-2.77]); post-operative hemoglobin (cOR [95% CI]: 1.37 [0.64-2.93]); timing of CD (cOR [95% CI]: 1.31 [070-2.47]); antepartum hemorrhage (cOR [95% CI]: 1.07 [0.51-2.25]); previous uterine surgery (cOR [95% CI]: 1.01 [0.41-2.41]); placental location (anterior or posterior) (cOR [95% CI]: 1.14 [0.49-1.57]); premature delivery <37 weeks (cOR [95% CI]: 1.10 [0.49-1.68]); degree of PAS (accreta or increta/percreta) (cOR [95% CI]: 1.05 [0.42-2.63]). *Only 150/184 had MRI.
cOR: crude odds ratios, PAS: placenta accreta spectrum, MRI: magnetic resonance imaging, LOR: low-order repeat, CDs: cesarean deliveries, HOR: high-order repeat, RBCs: red blood cell count, CI: confidence interval

second, 40% for the third, 61% for the fourth, and 67% for the fifth or additional CDs.[10]

Our analysis further indicates that patients with major PP and HOR-CDs exhibited an increased OR of antenatal PAS diagnosis (OR=2.67). Particularly, in a sub-analysis of patients with CD6-CD7, there was a 4-fold rise in the OR of PAS diagnosis (OR=3.98), aligning with the OR of 3.6 (95% CI: [2.3-5.6]) reported by Zhou et al[17] and 3.02 (95% CI: [1.50-6.08]) reported by De Mucio et al.[26] A prior systematic review and meta-analysis confirmed that the absolute risk of PAS intensifies with an increasing number of previous CDs.[26] Unpredictably, a retrospective analysis from the United Arab Emirates revealed a higher OR of PAS (OR=26.5; 95% CI: [4.2-166.3]) for patients with more than 5 previous CDs.[27]

Concerning Saudi research on repeated CDs and the risk of PP/PAS alongside associated maternal morbidity, several studies corroborate our findings.[24,25,28,29] In contrast, others do not substantiate our observations of increased maternal complications.[21,30] Nonetheless, the exclusive inclusion of patients with major PP in our study could explain the observed heightened risk of PAS and consequent maternal complications.

Among our patients with PP and HOR-CDs, we observed a significant elevation in the rate and OR of heavy intra-operative bleeding (>3000 ml) attributed to repeated attempts to detach invasive placentas (39.0% vs. 53.6%; OR=1.80). Such hemorrhagic morbidity is a major expected complication for PP/PAS with repeat CDs. The combination of repeat CDs and abnormal placentation (PP/PAS) are recognized risk factors for significant bleeding during CDs.[10-17] Earlier and current reports from AMCH on our major PP cohorts with prior CDs persistently corroborate these findings.[22,24,25]

The concurrent presence of major PP and HOR-CDs invariably led to significant bleeding, necessitating transfusions of 3 or more units of RBCs (17% vs. 35.7%; OR=2.71) and, in some cases, emergency life-saving hysterectomy (9% vs. 22.6%; OR=2.96). Recent research on PP and previous CDs has demonstrated comparable trends. Zheng et al[16] reported an OR for repeated blood transfusions of 6.912 (95% CI: [13.239-102.922]), and a Jordanian study documented an OR for emergency hysterectomy

Table 5 - Univariate analysis for the stratified number of repeat cesarean deliveries as a risk factor for placenta accreta spectrum diagnosis and hysterectomy in major placenta previa patients.

Risk factors	No PAS by MRI* (n=75)	PAS by MRI* (n=75)	cOR (95% CI)	*P*-values
CD2-CD3 (n=80)	49 (61.3)	31 (38.8)	Reference	
CD4-CD5 (n=57)	24 (42.1)	33 (57.9)	2.17 (1.03-4.61)	0.037
CD6-CD7 (n=13)	2 (15.4)	11 (84.6)	3.98 (1.4-14.29)	0.003
Risk factors	**No hysterectomy (n=156)**	**Hysterectomy (n=28)**	**cOR (95% CI)**	***P*-values**
CD2-CD3 (n=100)	91 (91.0)	9 (9.0)	Reference	
CD4-CD5 (n=70)	55 (78.6)	15 (21.4)	1.158 (1.01-1.33)	0.020
CD6-CD7 (n=14)	10 (71.4)	4 (28.6)	4.04 (1.09-14.97)	0.003

Values are presented as numbers and percentages (%). *Only 150/184 had MRI. PAS: placenta accreta spectrum, MRI: magnetic resonance imaging, cOR: crude odds ratios, CI: confidence interval

of 16.25 (95% CI: [1.95-135.01]).[31] Additionally, our analysis revealed a significantly elevated risk of lower urinary tract injury (mostly affecting the urinary bladder) in cases of PP and HOR-CDs (5% vs. 14.3%; OR=3.17). This increased risk of urinary injuries may be attributed to the presence of dense surgical adhesions between the uterus and lower urinary organs or the direct invasion by deeply infiltrating PP/PAS with difficult emergency hysterectomy.[10-18] For these reasons, the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine recommend that the PP/PAS patients should receive level-III (subspecialty) or higher care.[20]

Moreover, the presence of higher rates of maternal complications, such as emergency hysterectomy and urinary injuries, in our cohort with major PP and HOR-CDs was expected to extend the post-operative hospital stay beyond 3 days (29.5% vs. 70.5%; OR=3.91). This observation parallels with findings from other studies examining the repeat CDs in PP/PAS patients. For instance, Bahar et al[22] reported an OR of 1.91 (95% CI: [1.21-3.02], p=0.005) for extended hospital stays, while Han et al[18] found that the median post-operative stay was 5 days (interquartile range [IQR]: [4-11] days) for patients undergoing HOR-CDs, compared to 3 days (IQR: [3-5] days) for those with LOR-CDs (p<0.001).

Finally, the observed complication rates and ORs for serious events as associated PAS and emergency hysterectomy were clearly proportional to the sequence of repeat CDs, with the highest rates noted in the CD6-CD7 subgroup, followed by CD4-CD5 and CD2-CD3. Specifically, within the CD6-CD7 subgroup, we documented significantly elevated rates of antenatal PAS diagnosis at 84.6% and 28.6% for emergency hysterectomy. A previous large systematic review and meta-analysis of observational studies on the impact of increasing numbers of CDs on maternal morbidity, women with PP and ≥3 CDs had a statistically significant increased risk of both accreta and emergency hysterectomy up to 50-67%.[11]

Study limitations. This study is constrained by its single-center nature and a modest sample size. The exclusive use of MRI for the PAS diagnosis (without histopathology) is a confounding factor in determining the true percentage of PAS.

The study highlights the importance of carrying out a nationwide multicenter study in Saudi Arabia to assess the rates of CDs across various regions and their potential impact on maternal health.

In conclusion, among patients with major PP, undergoing more than 3 CDs is associated with a notable increase in both the rates and ORs of various early maternal complications. This trend of increasing many complications correlates directly with an ascending number of CDs. Our findings suggest the patients with history of more than 3 CDs may get benefit from level-III or higher care, particularly in the context of PP/PAS.

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