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Timing of cesarean delivery for women with four or more previous cesarean sections

Nergis Kender Erturk [1], Nermin Kilicarslan [2]

[1] University of Health Sciences, Yuksek Ihtisas Educational and Research Hospital, Department of Obstetrics and Gynecology, Bursa, Turkey
[2] University of Health Sciences, Yuksek Ihtisas Educational and Research Hospital, Department of Anesthesiology and Reanimation, Bursa, Turkey

ORCID ID of the author(s)
NKE: 0000-0002-2902-9670
NK: 0000-0002-5855-9099

Corresponding Author
Nergis Kender Erturk
University of Health Sciences, Yuksek Ihtisas Educational and Research Hospital, Department of Obstetrics and Gynecology, Erikli mah, Mimar Sinan cad 16000 Yildirim, Bursa, Turkey
E-mail: nergiskender@gmail.com

Ethics Committee Approval
Ethics Committee approval was taken from the Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee, 2011-KAEK-25/ 2021/12-06.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: The number of recurrent cesareans is increasing worldwide, but the optimal timing for delivery in women who have had previous cesareans is controversial. The aim of this study is to determine the optimal timing of elective cesarean delivery in women with a history of four or more cesarean sections (CSs).
Methods: This retrospective cohort study was conducted in a tertiary hospital; 195 patients with a history of four or more CSs were grouped according to their gestation weeks on operation day and analyzed in terms of demographic features and clinical data as well as maternal and neonatal outcomes. Gestation weeks were grouped as 37-38 weeks and 39 weeks. Logistic regression analysis was used to determine the effect of independent variables on maternal and fetal outcomes.
Results: Of the 195 patients, 118 had CS between 37-38 weeks and 77 at 39 weeks. Clinical and demographic characteristics were similar among groups. The overall maternal complication did not differ between the groups (16.1% vs 16.9%, $P = 0.885$). The 1st and 5th minute APGAR scores were significantly lower in the $37\text{-}38^{6}$ weeks group ($P = 0.013$ and $P = 0.04$, respectively). Logistic regression analysis found that neonatal 5th minute APGAR score was associated with a model including maternal age, number of previous CS, anesthesia type, gestational week at delivery, and neonatal birth weight.
Conclusion: Timing CS at 39 weeks in patients with a history of four or more CSs was found not to worsen maternal outcomes. Additionally, planning at 39 weeks could improve newborn outcomes.

Keywords: Cesarean section, Timing, Maternal outcome, Neonatal outcome

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Introduction

Cesarean section (CS) is a common procedure worldwide, and its rate has increased [1]. Previous CS appears to be the most common medical indication for cesarean delivery [2]. In this case, it could be stated that the number of recurrent CSs is gradually increasing. In developing countries, four or more repeated CSs could be encountered. However, the optimal timing for delivery in women who have had multiple previous CSs is controversial. Both neonatal and maternal risks should be considered together when deciding on the appropriate timing. While early intervention may increase neonatal morbidity, maternal risks may arise in case of delay [3, 4]. In addition to these risks, patient and physician convenience could be regarded as influencing factors for timing, albeit less important.

In general, it is recommended that elective CS not be performed before 39 weeks of pregnancy due to the risk of neonatal respiratory morbidity [5]. On the other hand, planning of CS at 39 weeks is also reported to increase the probability of onset of labor and the possibility of emergency delivery [6]. In addition, elective repeat CS planned at 39 weeks has also been shown to lead to adverse maternal outcomes versus scheduled delivery at 38 weeks [7]. Women with multiple prior low uterine transverse incisions show a particular trend towards an increased risk of rupture versus a single previous CS [8]. Some clinicians may prefer the timing of elective CS earlier than 39 weeks in women with a high number of previous CS to avoid maternal risks such as the onset of uterine contractions, the development of uterine rupture, and the necessity of emergency delivery. However, some have advocated that planned repeat CS should be performed in 39 weeks in patients who have had multiple previous CSs [9]. Thus, there is no consensus on best practice. These contradictory data makes it difficult to plan the timing of four or more repetitive CSs.

Therefore, this study aimed to compare the outcomes of CSs performed before and after 39 weeks in women who had 4 or more previous CS. and to determine the optimal timing of CSs in patients.

Materials and methods

This retrospective study was performed in a tertiary education and research hospital. After obtaining local ethics committee approval (Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee, 2011-KAEK-25/ 2021/12-06), patients who had a history of four or more previous CSs and who delivered by CS in our hospital between January 2019 and December 2021 were examined from the medical records. Demographic data, medical history, laboratory tests, anesthesia data, as well as maternal and neonatal findings of the patients were recorded. The gestational week at which the patients had CS was calculated according to the crown-lump length (CRL). Subjects aged between 20-45 years, those with a history of four or more CSs, singleton pregnancies, and those whose medical records were fully obtainable were included. Multiple pregnancies, CSs before 37 weeks, those with a history of CS with classical uterine incision, those with a history of uterine rupture, those who have a history of COVID-19 infection during pregnancy, major fetal anomalies, and premature rupture of membranes were excluded.

Cesarean delivery timing is planned on week 38 or 39 of gestation at our hospital. Our hospital is a tertiary referral center, and thus it was not always be possible to perform CSs on these planned days. The timing might change 2-3 days before or after the target date. Thus, the patients were divided into two groups according to their CS dates: 37^0-38^6 weeks and $\geq 39^0$ weeks. The maternal and neonatal data were compared between these groups. Primary outcome was composite maternal outcome, and secondary outcome was adverse neonatal outcome. Those who had CS with fetal distress and active labor indications were defined as emergency CS, and those who had scheduled CS were defined as elective CS. Uterine dehiscence was defined as separation of the lower uterine segment up to the serosa. Uterine rupture was defined as full-thickness separation of uterine wall including the serosa. Gestational diabetes was diagnosed with at least two abnormal results in the 75 g/100 g glucose tolerance tests. Those who were given antihypertensive treatment or those with preeclampsia after the 20^{th} gestational week were defined as gestational hypertension disease.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA). The normality of the data was determined via the Shapiro Wilk test. Categorical data were calculated with the Chi-square test, and non-parametric data were calculated with the Mann Whitney U test. The results were presented as frequency and percentages for qualitative variables and mean (SD) or median (min-max) for quantitative variables. Multivariate logistic regression analysis was performed to detect the independent effects of variables on outcomes. $P < 0.05$ was considered statistically significant.

Results

There were 23,392 women who gave birth of which 8,695 were via CS (37.1%). After considering the inclusion/exclusion criteria, 195 patients were enrolled. Of the 195 patients, 118 had CS between 37-38^6 week and 77 at $\geq 39^0$ weeks. There was no patient in the $\geq 39^0$-week group with a delivery date at 40 weeks or more. The median gestational week was 39^3 in that group and ranged between 39^0- 39^6. The clinical characteristics of the groups are given in Table 1. There were no differences between the groups in terms of age, number of previous CSs, and comorbid diseases (Table 1).

Table 1: Demographic and clinical characteristics of the groups

	37^0-38^6weeks (n = 118)	$39^{0/6}$ weeks (n = 77)	*P*-value
Maternal age (years)*	34 (23-44)	33 (24-42)	0.148
Parity*	4 (4-6)	4 (4-7)	0.992
Cesarean Type			
Elective (n=167)	101 (85.6)	66 (85.7)	
Emergency (n=28)	17 (14.4)	11 (14.3)	0.981
Pregestational diabetes	2 (1.7)	3 (3.9)	0.342
Gestational diabetes	5 (4.2)	3 (3.9)	0.907
Hypertension in pregnancy	6 (5.1)	3(3.9)	0.699

Values are given n (%) and Chi square test was performed unless otherwise specified. *Values are given as median (min-max), Mann Whitney U test was performed.

When the groups were analyzed in terms of maternal outcomes, the overall complication did not differ between the groups (Table 2). There were no differences in terms of bladder injury, uterine atony, abruptio placenta, and infectious morbidity.

However, the rate of uterine dehiscence was significantly high in the 39-week group (10.4% vs 3.4%, P = 0.04) (Table 2). There was no uterine rupture diagnosed in either of the groups. The groups were similar in terms of blood loss or blood transfusion. The time to discharge did not differ between the groups. In addition, none of the patients had intestinal laceration or post-operative ileus.

Table 2: Maternal and neonatal outcomes of the groups according to cesarean timing

	37^0-38^6weeks (n = 118)	$39^{0/6}$ weeks (n = 77)	P-value
Anesthesia			
General (n=77)	29 (24.6)	15 (19.5)	0.405
Regional (n=118)	89 (75.4)	62 (80.5)	
Maternal overall complications	19 (16.1)	13 (16.9)	0.885
Uterine Dehiscence	4 (3.4)	8 (10.4)	0.047
Bladder injury	3 (2.5)	1 (1.3)	0.549
Uterine atony	2 (1.7)	5 (6.5)	0.078
Postpartum Hysterectomy	9 (7.6)	0 (0)	0.013
Abruptio placenta	3 (2.5)	2 (2.6)	0.981
Surgical site infection	8 (6.8)	3 (3.9)	0.394
Blood transfusion	13 (11)	9 (11.7)	0.885
Preoperative Hb *(mg/dL)	11.23 (1.20)	11.45 (1.45)	0.408
Postoperative Hb *(mg/dL)	10.58 (1.38)	10.59 (1.40)	0.764
Postoperative HTC (%)*	32.05 (3.93)	32.14 (3.77)	0.858
Duration of hospitalization* (days)	2.57 (1.08)	2.49 (0.77)	0.765
Birth weight (gr)*	2944.06 (487.20)	3205.84 (401.69)	<0.001
APGAR score (1 min)	9 (0-9)	9 (4-9)	0.013
APGAR score (5 min)	10 (5-10)	10 (7-10)	0.040
NICU admission, n(%)	7 (5.9)	3 (3.9)	0.529
Perinatal mortality, n(%)	0 (0)	0 (0)	N/A

Hb: Hemoglobin, HTC: hematocrit, NICU: neonatal intensive care unit, N/A: not applicable. Values are given n (%) and median (min-max), Chi square test was performed unless otherwise specified. * Values are given mean (SD), Mann Whitney U test was performed.

Regional anesthesia rather than general anesthesia was used in most patients (60.5% vs 39.4%). There was no difference between the groups in terms of anesthesia type (Table 2). No anesthesia-related complications were encountered in any of the patients.

There were nine patients who underwent postpartum hysterectomy. All nine patients were between 37^0-38^6 weeks. Five of them were diagnosed with placenta accreata spectrum (PAS) and were scheduled for hysterectomy. Of the other four patients, three were referred to our hospital for delivery with the diagnosis of PAS. The remaining one patient underwent hysterectomy as a result of unsuccessful intrauterine balloon tamponade due to atony. Apart from this, there were six other patients diagnosed with atony across the whole study group. The intrauterine balloon tamponade system was used in five of the patients, and compression sutures were performed in one of them. These were treated successfully.

The results specific to newborns are shown in Table 2. As expected, birth weights were different between groups according to their weeks. The birth weight of the 37-38^6-week group was lower than that of the 39-week group. Additionally, the 1^{st}- 5^{th}-minute APGAR scores were also significantly lower in that group. However, there was no difference between the groups in terms of neonatal intensive care unit (NICU) admission and no perinatal mortality (Table 2).

Logistic regression analysis was used to define the association between the timing of repeat CSs and neonatal 5th min APGAR score. Maternal age (< 35 years or ≥ 35 years), number of previous CSs (4 or > 4), gestational week at delivery, anesthesia type (general or regional), and neonatal birth weight were included as covariates. This model was found to be associated with neonatal 5^{th}-minute APGAR scores (P = 0.001, R^2 = 0.542).

Discussion

We compared the outcomes of CSs performed before and after 39 weeks to detect the most appropriate timing for women who had four or more previous cesarean deliveries. The maternal overall outcomes showed no significant advantage to planning the CS before 39 weeks in these patients. However, uterine dehiscence was significantly more common when CS was performed beyond 39 weeks. The presence of dehiscence was not associated with emergency CS in the 39-week group; only 18.2% (2/11) of emergency CS cases had dehiscence. In this case, the timing of CS before 39 weeks of gestation would likely not have an additional benefit in terms of maternal outcomes.

Contrary to our results, Helwick et al. [10] recommended that those with more than two previous CSs should be planned at 37 weeks of gestation because it improves maternal outcomes. That study had fewer patients than ours, and the exact maternal outcomes were not clearly stated. Unlike Helwick et al., Tita et al. [11] reported that composite maternal outcomes were increased in recurrent CSs in the early term period and recommended planning repetitive CSs at the 39^{th} gestational week. However, four or more previous CSs were not evaluated separately in Tita et al.

Similar to our data, a recent review about more than two previous CSs stated that early term delivery (delivery at 37-38 weeks) for recurrent CS does not induce maternal benefit [12]. In addition, Mohammed et al. [13] found that repetitive CSs performed at ≥ 39 weeks had a higher risk of emergency CS than those at < 39 weeks (16.6% vs 10.6%, respectively, P < 0.05). While our rate of emergency CS in all patients are higher than Mohammed et al. (14.3% vs 12.3%), we did not detect a difference among our study groups in terms of emergency CS rate. Mohammed et al. [13] also added that uterine rupture was more common in emergency CSs than elective CSs (3.8% vs 0.8% respectively, P < 0.05), which contradicts our data. However, they did not declare a difference between groups of CS at < 39 weeks and ≥ 39 weeks in terms of uterine rupture. They had two complete ruptures and two uterine dehiscence cases. We observed no complete uterine rupture.

Neonatal outcomes were also evaluated. Although NICU hospitalization was similar between groups, the birth weight and APGAR scores were higher in the ≥ 39^0-week group. We concluded that performing repetitive CS at 39 weeks induces neonatal benefits. In agreement with the present study, Hamadneh et al. [14] mentioned that CSs performed at 37 weeks had a higher risk of neonatal respiratory morbidity versus those at 38 weeks. The risk of stillbirth in later gestational weeks is an important factor in deciding the appropriate timing for an elective CS at term. Prior studies reported no increase in stillbirths after 39 weeks of gestation [15, 16]. We had no stillbirth regardless of the timing of CS.

A retrospective study in which 9.4% (83/886) of the patients had four or more cesarean sections reported no significant differences in terms of maternal outcomes between CSs performed at 37 and 38 weeks [14];

A retrospective study, in which 9.4% (83/886) of the patients had four or more cesarean sections, reported that there was no difference in terms of maternal outcomes between CSs performed at 37 and 38 weeks [14]; however, there was a

difference between the groups in terms of anesthesia type when maternal complications were reviewed. General anesthesia rates were higher in CSs at 37 weeks compared to those at 38 weeks (43.4% vs 34.1%, P = 0.005) [14]. The authors mentioned that this may be related to the high rate of emergency CS at 37 weeks. We found no difference between the groups in terms of CS type and anesthesia type. Furthermore, 78.6% (22/28) of emergency CSs were given regional anesthesia.

Still another study compared repeat cesarean deliveries at 38 and 39 weeks; they found that neonatal respiratory morbidity decreased at 39 weeks versus 38 weeks, and there was no change in maternal complications between these groups [17]. Although the rate of unscheduled CS at 39 weeks was higher than that at 38 weeks, the authors recommended elective timing at 39 weeks regardless of the number of previous cesarean sections due to neonatal benefits. Our results were similar, but the number of patients with four or more previous CSs was not explicitly stated in that prior work. The same study added that the number of previous CSs was not associated with adverse neonatal outcomes [17].

To our knowledge, this is the first study to investigate maternal fetal outcomes in women with a history of four or more CSs to define the optimal timing for elective CS. The strengths of the study are that the study included only four or more cesarean section results and the relatively high number of patients enrolled relative to the existing literature. The groups were also quite similar in terms of demographic features and comorbid diseases. The fact that the majority of the patients (60.5%) received regional anesthesia—thus minimizing the effect of anesthesia on maternal and neonatal outcomes—increases the power of the study. On the other hand, some possible limitations to the study are as follows: a) all cases came from a single center and b) elective and emergency CSs were evaluated along with patients with PAS.

Conclusion

In conclusion, the timing of CS at 39 weeks does not appear to worsen maternal outcomes in patients with a history of four or more CSs. In fact, planning at 39 weeks instead of 37-38^{6} weeks could improve neonatal outcomes in this subset of patients. Prospective studies with a larger number of patients are needed to support this interpretation.

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