

Multiple repeat cesarean delivery is associated with increased maternal morbidity irrespective of placenta accreta

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Abstract. – OBJECTIVE: The present study aimed to investigate the perinatal morbidity associated with multiple repeat cesarean deliveries (CD) and, thus, to achieve a body of evidence for the current practice of discouraging pregnancy after undergoing three CDs.

PATIENTS AND METHODS: This study prospectively reviewed a total of 500 women who consecutively underwent CD between January 1, 2009 and April 1, 2009. The patients were allocated into four groups based on the number of CDs they had undergone (Group 1: first CD, Group 2: second CD, Group 3: third CD, Group 4: fourth CD). Data related with their demographic and clinical characteristics were recorded as well as their perioperative characteristics and clinical characteristics of the neonates born to them. Cochran-Armitage test for trends and Spearman rank correlation analysis test was used to evaluate the trend of perioperative complications and neonatal outcome with the increasing number of CDs.

RESULTS: The mean age, gravidity and parity were significantly higher in groups 2-4 than those of the women who had their first CD (Group 1). The average operation time and mean delivery time as well as severe adhesions, bowel injury increased significantly with the number of CD. Neonatal characteristics were similar among groups except for a trend towards a decrease in the rate of meconium stained and a trend towards increase in the rate of neonatal sepsis with the increasing number of CD.

CONCLUSIONS: We have found positive correlation between the maternal morbidity and the number of CDs. The occurrence of adhesions emerges as the most significant indicator of maternal morbidity, eventually leading to the neighboring organ injury and prolonged operation time.

Key Words:

Cesarean delivery, Neonatal morbidity, Maternal morbidity.

Introduction

There has been an ongoing debate about that the number of cesarean deliveries (CDs) that a woman may safely have. This debate is more important in current practice because rate of the CDs has a marked rise in all over the world¹⁻⁵.

The number of women who require multiple CDs is increasing. In addition, the indications for CD have become widespread to the point where a woman's self-request is sufficient²⁻⁴. The problem gets even more complicated in regions where the availability of effective contraception is limited, or social attitudes do not favor contraceptive methods. Conventional obstetric practice discourages pregnancy after two or three CDs. It is well established that repeat cesarean delivery is associated with increased maternal mortality and morbidity⁶⁻¹². But most of this increase can be attributed to placenta previa and concomitant placenta accreta in patients with three or more previous CDs¹⁰⁻¹³. However, aside from placenta accreta there is no solid scientific evidence for the validation of this recommendation^{1,2,10,12}. The present study aimed to investigate the maternal and neonatal morbidity associated with multiple repeat CDs and, thus, to achieve a body of evidence for the current practice of discouraging pregnancy after undergoing three cesarean deliveries.

Patients and Methods

This study prospectively reviewed a total of 500 women with singleton pregnancy that consecutively underwent CD between January 1, 2009 and April 1, 2009. The women with placenta previa, previous dehiscence of CD scar, or a previous classical scar were excluded from the study. The

reviewed women were grouped according to the number of CDs performed so that four patient groups named as first CD, second CD, third CDs and fourth CD were formed. Data related with demographic and clinical features of the study population were recorded on standardized query sheets which had been prepared before the recruitment of the subjects. Moreover, preoperative characteristics of the study population and the clinical characteristics of the neonates born to the reviewed women (including indicators of fetal and maternal morbidity) were recorded on these sheets. Operation time was measured from induction of anesthesia to skin closure. Severe adhesion was defined as dense adhesions or adhesions that caused fusion of the uterine surface to the anterior abdominal wall or urinary bladder. A blood transfusion was given if preoperative hemoglobin (Hb) was < 10 g/dl, or when the estimated blood loss exceeded 20% of total blood volume or postoperative Hb was < 8.5 g/dl. Postoperative pyrexia was defined as elevated body temperature greater than 38 °C for at least 48 hours. Wound infection is described as the invasion of the surgical incision site by pathogenic microorganisms. Hospitalization time indicated the postoperative period between the completion of CD and the discharge time. Delivery time was measured from beginning of the skin incision to the completion of delivery of the neonate. Meconium aspiration syndrome is a medical condition which occurs when meconium is present in the lungs of the newborn during or before delivery. Neonatal sepsis was defined presence of bacteremia along with systemic signs and symptoms of infection in the first 4 weeks of life. Hypoglycemia in the first few days after birth was defined as neonatal hypoglycemia whereas neonatal hyperbilirubinemia was described as the elevation of the bilirubin level in the blood of the newborn.

The present study was approved by the local Ethical Committee and Institutional Review Board where the study was conducted. Written informed consent was obtained from the women who were included in this study.

Statistical Analysis

Data entry and analysis was performed using Statistical Package for Social Sciences version 22.0 (SPSS, IBM, Chicago, IL, USA) on computerized media. Distributions of continuous variables were tested by Kolmogorov-Smirnov test. Continuous variables were expressed as mean \pm standard deviation or median (minimum-maximum)

while categorical data were shown as numbers or percentages where appropriate. One way ANOVA was used to compare the parametric variables of the four study groups that have a normal distribution whereas Kruskal-Wallis test was utilized to compare parametric variables of these groups which did not distribute normally. Bonferroni adjustment test was utilized to specify statistical significances indicated by variance analysis. Cochran-Armitage test for trends and Spearman rank correlation analysis test was used to evaluate the trend of perioperative complications and neonatal outcome with the number of CDs where appropriate. *p* values less than 0.05 were considered as statistically significant.

Results

Table I shows the demographic and clinical characteristics of the study population in relation with the CD number. Patients in group 2-4 had a significantly higher mean age at delivery, gravidity, parity than patients in group 1. Other perinatal characteristics were similar between groups except for a higher rate of preeclampsia in group 1. Table II demonstrates the perioperative characteristics of the reviewed women. There was a significant trend towards a longer operative time as the number of CD increased. Similarly presence of severe adhesions and the prevalence of bowel injury had a trend towards increase as the number of CD increased. Other perioperative characteristics including prevalence of bladder injury were similar between groups. Table III shows the clinical characteristics of their newborns in association with CD number. The mean delivery time increased significantly with the increasing order of CD. Other neonatal characteristics were similar among groups except for a trend towards a decrease in the rate of meconium stained and a trend towards increase in the rate of neonatal sepsis with the increasing number of CD. No maternal and neonatal deaths occurred during the study period.

Discussion

The present study sought the evidence for the current practice of accepting three CDs as a threshold by investigating the maternal and fetal morbidity associated with multiple repeat cesarean deliveries. Our hospital is a tertiary referral

Repeat cesarean associated morbidity

Table I. Demographic and clinical characteristics of the study population.

	1 st CD (n=242)	2 nd CD (n=110)	3 rd CD (n=95)	4 th CD (n=53)	p*
Age (years)	27.1 ± 6.0	28.3 ± 5.4	29.6 ± 4.7	29.7 ± 4.9	<0.01
Body mass index (kg/m ²)	29.4 ± 5.6	29.2 ± 4.1	30.2 ± 4.5	30.1 ± 4.5	0.48
Gravidity	2.0 (1-4)	2.5 (2-5)	3.4 (3-5)	4.5 (4-7)	<0.01
Parity	0.6 (0-3)	1.1 (1-4)	2.0 (2-4)	2.7 (3-6)	<0.01
Gestational age (weeks)	38.4 ± 3.0	37.9 ± 1.9	38.6 ± 1.5	38.4 ± 1.4	0.22
Preeclampsia	20 (8.3%)	1 (0.9%)	7 (7.4%)	1 (1.9%)	0.02
Delivery < 37 weeks	12 (4.9%)	6 (5.5%)	4 (4.2%)	2 (3.8%)	0.96
Gestational diabetes	11 (4.5%)	1 (0.9%)	4 (4.2%)	0 (0.0%)	0.15
Thyroid disorders	21 (8.7%)	6 (5.5%)	4 (4.2%)	2 (3.8%)	0.32
Previous surgery	23 (9.5%)	3 (2.7%)	9 (9.5%)	6 (11.3%)	0.12

Data expressed as number (%), mean ± SD, mean (minimum-maximum) *p < 0.05 is accepted to be statistically significant. CD: cesarean delivery.

center in Turkey with approximately 20000 deliveries annually. As reported by Simsek et al¹³, there has been an alarming rise in the rate of CD at our institution. Currently, 45% of all deliveries via cesarean and this rate remained steady in recent years. For these reasons it took only 4 months to recruit 500 patients for the present study. In addition, patients with three and 4 CD are generally referred to our hospital and therefore 29.6% of patients in the present cohort had 3 or more CDs. In the present study, the risk of morbidity at the fourth CD was compared with respect to the first, second and third CDs.

Although there are a number of trials that assess morbidity in women undergoing multiple repeat

CDs, most of them are limited by small sample size⁶⁻¹¹. Seidman et al⁶, Kirkinen et al⁷, Soltan et al⁸, Tamale-Sali et al⁹, and Lynch et al¹⁰ respectively studied cohorts of 154, 64, 395, 59 and 250 women. These investigators did not show any increase in maternal morbidity attributable to multiple repeat CDs. In contrast, Silver et al¹¹, Makoha et al¹², Qublan et al¹⁴ and Ma et al¹⁵ compared consecutive CD groups and their findings revealed that multiple repeat CD was a significant indicator of maternal morbidity. Previously published studies showed that intraperitoneal adhesions became denser as CD number increased. The existence of adhesions may prolong operating time which in turn leads to higher hemoglobin deficit and infec-

Table II. Perioperative characteristics associated with the number of cesarean deliveries.

	1 st CD (n=242)	2 nd CD (n=110)	3 rd CD (n=95)	4 th CD (n=53)	p*
Operation time (minutes)	34.8 ± 11.3	37.5 ± 10.6	40.3 ± 13.8	44.7 ± 17.2	<0.01 ^a
Tubal ligation	14 (5.8%)	8 (7.3%)	24 (25.3%)	15 (28.3%)	<0.01
Severe adhesions	2 (0.8%)	8 (7.3%)	19 (20.0%)	20 (37.7%)	<0.01 ^b
Bladder injury	1 (0.4%)	0	4 (4.2%)	0	0.14 ^b
Bowel injury	2 (0.8%)	2 (1.8%)	3 (3.2%)	10 (18.9%)	<0.01 ^b
Preoperative hemoglobin (g/dl)	12.4 ± 1.4	12.0 ± 1.4	12.3 ± 1.3	12.0 ± 1.1	0.07
Postoperative hemoglobin (g/dl)	11.0 ± 1.4	11.0 ± 1.3	11.2 ± 1.2	10.9 ± 1.4	0.46
Need for blood transfusion	11 (4.5%)	3 (2.7%)	1 (1.1%)	2 (3.8%)	0.43 ^b
Postoperative pyrexia	3 (1.2%)	1 (0.9%)	0	0	0.20 ^b
Postoperative urinary tract infection	2 (0.8%)	0	0	0	0.54 ^b
Postoperative deep vein thrombosis	1 (0.4%)	0	0	0	0.78 ^b
Wound infection	2 (0.8%)	0	1 (1.1%)	2 (3.8%)	0.14 ^b
Hospitalization time (hours)	49.5 ± 23.8	45.4 ± 12.2	46.1 ± 20.0	50.7 ± 24.4	0.22 ^a

Data expressed as number (%), mean ± SD, *p < 0.05 is accepted to be statistically significant, ap value for spearman rank correlation, bp value for Cochran-Armitage test. CD: cesarean delivery.

Table III. Clinical characteristics of the neonates born to the study population.

	1 st CD (n=242)	2 nd CD (n=110)	3 rd CD (n=95)	4 th CD (n=53)	<i>p</i> [*]
Delivery time (minutes)	3.7 ± 1.0	2.5 ± 0.2	5.9 ± 3.6	7.0 ± 3.3	< 0.01 ^a
Birth weight (grams)	3054.0 ± 786.2	3118.8 ± 480.2	3162.2 ± 468.5	3090.5 ± 522.1	0.55 ^a
First minute Apgar score < 7	10 (4.1 %)	7 (6.4 %)	3 (3.2 %)	2 (3.8 %)	0.80 ^b
Fifth minute Apgar score < 9	6 (2.5 %)	6 (5.5 %)	2 (2.1 %)	1 (1.9 %)	0.85 ^b
Admission to NICU	14 (5.8%)	7 (6.4%)	6 (6.3%)	2 (3.8%)	0.66 ^b
Meconium stained chorioamnion	19 (7.9%)	2 (1.8%)	1 (1.1%)	0 (0.0%)	0.04 ^b
Meconium aspiration syndrome	3 (1.2%)	1 (0.9%)	1 (1.1%)	0 (0.0%)	0.49 ^b
Neonatal sepsis	0	0	0	2 (3.8%)	0.05 ^b
Neonatal hypoglycemia	2 (0.8%)	2 (1.8%)	0	0	0.42 ^b
Neonatal hyperbilirubinemia	2 (0.8%)	0 (0.0%)	0	0	0.21 ^b

Data expressed as number (%), mean ± SD, **p* < 0.05 is accepted to be statistically significant, *a* *p* value for Spearman rank correlation, *b* *p* value for Cochran-Armitage test. NICU: neonatal intensive care unit. CD: cesarean delivery.

tion rate. In addition, severe adhesions may lead to increased rates of urinary bladder, bowel injury as well as cesarean hysterectomy^{11,12,14,15,18-20}. The risk of hysterectomy has been shown is increased 15 fold in women undergoing their 5th CD according to a recent meta-analysis²¹. However, up to two thirds of cesarean hysterectomy was performed for placenta accreta.

In the present cohort, 4th CD had a significantly higher rate of operative morbidity. Patients who have undergone their 4th CD had a significantly higher rate of severe adhesions as well as bowel injury. Our results are consistent with these findings, indicating that intraperitoneal adhesions, organ injury and prolonged surgery are responsible for the majority of the maternal morbidity. The rate of bladder injury, however, did not show a trend toward increase with increased number of CD according to our data. In addition, postoperative hemoglobin levels and rate of wound infection were similar in our study population. This disagrees to previous data which consistently reported higher rates of hemorrhage as well as wound infection. We assume these variances can be explained by several factors such as differences in surgical technique, previous emergent CD as well previous infectious morbidity.

As for neonatal morbidity, Qublan et al¹⁴ reported that the rates of satisfying APGAR scores, admission to NICU, premature delivery and perinatal death were similar in the women who underwent one, two and three cesarean deliveries. Ma et al¹⁵ also found that neonatal morbidity was similar in the first, second and third CD groups. However, it has been suggested that abnormal placentation may contribute to neonatal morbidity²².

Our results agree to what has been already suggested. Despite prolongation of delivery time with increasing number of CDs, neonatal outcomes are not negatively influenced by it. There was a higher rate of neonatal sepsis in group 4, but we assume this is not directly related to increased number of CDs as there is no plausible explanation for this association

Our findings are biased by the relatively small size of the sample size and the variance within the experience and skill of the clinicians who performed the CDs. However, the prospective design of the present study may have allowed the required data to be recorded more accurately on standardized query sheets.

Conclusions

We provide some evidence that maternal morbidity increases with the number of successive CDs performed on a woman. However, the third CD does not represent an absolute threshold since morbidity rises from the first through the third CD. It is prudent to assume that a fourth CD does not pose an increased risk to the mother as the third CD with respect to adhesions, neighboring organ injury and prolonged operation time, but worse morbidity can be anticipated with the fifth and ongoing cesarean deliveries. The occurrence of adhesions emerges as the most significant indicator of maternal morbidity, eventually leading to the neighboring organ injury and prolonged operation time. Therefore, secondary preventive measures should be implemented on minimizing complications related with intraperi-

toneal adhesions. Prospective and long-term studies are required to evaluate the effects of multiple repeat cesarean deliveries maternal and neonatal morbidity.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

- 1) LURIE S. The changing motives of cesarean delivery from ancient times to 21st century. *Arch Gynecol Obstet* 2005; 271: 281-285.
- 2) SADAN O, LESHNO M, GOTTFREICH A, GOLAN A, LURIE S. Once a cesarean delivery always a cesarean? A computer-assisted decision analysis. *Arch Gynecol Obstet* 2007; 276: 517-521.
- 3) GONZALEZ-PEREZ GJ, VEGA-LOPEZ M, CABRERA-PIVARAL C, MUNOZ A, VALLE A. Cesarean deliveries in Mexico: are there too many? *Health Policy Plan* 2001; 16: 62-67.
- 4) BURKE G. The rise in caesarean delivery rates. *Ir Med J* 2010; 103: 61-62.
- 5) MANKUTA DD, LESHNO MM, MENASCHE MM, BREZIS MM. Vaginal birth after cesarean delivery: trial of labor or repeat cesarean delivery? A decision analysis. *Am J Obstet Gynecol* 2003; 189: 714-719.
- 6) SEIDMAN DS, PAZ I, NADU A, DOLLBERG S, STEVENSON DK, GALE R, MASHIACH S, BARKAI G. Are multiple cesarean deliveries safe? *Eur J Obstet Gynecol Reprod Biol* 1994; 57: 7-12.
- 7) KIRKINEN P. Multiple caesarean deliveries: outcomes and complications. *Br J Obstet Gynecol* 1988; 95: 778-782.
- 8) SOLTAN MH, AL NUAIM L, KHSHOOGI T, CHOWDHURY N, KANGAVE B, ADELUSI B. Sequelae of repeat cesarean deliveries. *Int J Gynecol Obstet* 1996; 52: 127-132.
- 9) TAMALE-SALI EG, ISKANDAR MN. Is there a risk of lower segment scar rupture in pregnancy after multiple caesarean delivery? *J Obstet Gynecol* 1992; 12: 19-21.
- 10) LYNCH CM, KEARNEY R, TURNER MJ. Maternal morbidity after elective repeat caesarean delivery after two or more previous procedures. *Eur J Obstet Gynaecol Reprod Biol* 2003; 106: 10-13.
- 11) SILVER RM, LANDON MB, ROUSE DJ, LEVENO KJ, SPONG CY, THOM EA, MOAWAD AH, CARITIS SN, HARPER M, WAPNER RJ, SOROKIN Y, MIODOVNIK M, CARPENTER M, PEACEMAN AM, O'SULLIVAN MJ, SIBAI B, LANGER O, THORP JM, RAMIN SM, MERCER BM; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol* 2006; 107: 1226-1232.
- 12) MAKOKHA FW, FELIMBAN HM, FATHUDDIEN MA, ROOMI F, GHABRA T. Multiple cesarean delivery morbidity. *Int J Gynecol Obstet* 2004; 87: 227-232.
- 13) SIMSEK Y, CELEN S, ERTAS E, DANISMAN N, MOLLAMAHMUTOGLU L. Alarming rise of cesarean births: a single center experience. *Eur Rev Med Pharmacol Sci* 2012; 16: 1102-1106.
- 14) QUBLAN HS, TAHAT Y. Multiple cesarean delivery. The impact on maternal and fetal outcome. *Saudi Med J* 2006; 27: 210-214.
- 15) MA LK, LIU N, BIAN XM, TENG LR, QI H, GONG XM, LIU JT, YANG JQ. Pregnancy outcomes of repeat cesarean delivery in Peking Union Medical College Hospital. *Chin Med Sci J* 2009; 24: 147-150.
- 16) KASTNER ES, FIGUEROA R, GARRY D, MAULIK D. Emergency peripartum hysterectomy: experience at a community teaching hospital. *Obstet Gynecol* 2002; 99: 971-975.
- 17) NISENBLAT V, BARAK S, GRINESS OB, DEGANI S, OHEL G, GONEN R. Maternal complications associated with multiple cesarean deliveries. *Obstet Gynecol* 2006; 108: 21-26.
- 18) KARAYALÇIN R, OZCAN S, OZYER S, MOLLAMAHMUTOGLU L, DANISMAN N. Emergency peripartum hysterectomy. *Arch Gynecol Obstet* 2011; 283: 723-727.
- 19) PAREKH N, HUSAINI SW, RUSSELL IF. Cesarean delivery for placenta previa: a retrospective study of anaesthetic management. *Br J Anaesth* 2000; 84: 725-730.
- 20) GIELCHINSKY Y, ROJANSKY N, FASOULIOTIS SJ, EZRA Y. Placenta accreta--summary of 10 years: a survey of 310 cases. *Placenta* 2002; 23: 210-214.
- 21) MARSHALL NE, FU R, GUISE JM. Impact of multiple cesarean deliveries on maternal morbidity: a systematic review. *Am J Obstet Gynecol* 2011; 205: 262.e1-8.
- 22) SMITH GC, PELL JP, CAMERON AD, DOBBIE R. Risk of perinatal death associated with labor after previous cesarean delivery in uncomplicated term pregnancies. *JAMA* 2002; 287: 2684-2690.