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A Case Control Study of Repeated Multiple Cesarean Sections of Four and More as Compared to Two or Three Previous Cesareans

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Abstract. To test the concept that increasing the number of repeated cesarean deliveries increases the maternal and neonatal risks, a case control study comparing patients delivered by repeat cesarean sections following more than 3 previous cesareans (Group A) with those following 2 or 3 previous cesareans (Group B) was conducted at King Abdulaziz University Hospital. The maternal characteristics, associated complications, and the neonatal outcome were compared between the two groups. Statistical analyses were done with Statistical Package for the Social Sciences for Windows 10 (SPSS Inc., Chicago, IL), and logistic regression for clinical variables by means of SAS. 98 patients (Group A) were compared with 101 patients (Group B). Whereas, more patients of Group A required blood transfusions than patients in Group B ($P < 0.01$), all other post-operative maternal morbidity, major operative complications, and neonatal outcome were not statistically different between the two groups ($P > 0.05$ in all variables). Although there was a clinical trend towards increasing the risk to mother or fetus by increasing the number of cesareans, this was not statistically significant.

Keywords: Multiple cesarean sections, Cesarean hysterectomy, Repeated cesareans.

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Introduction

The cesarean delivery rate in the United States increased from 5% to 20.8% between 1970 and 1995[1]. For the year 2000, the rate increased to 22.9% of all live births[2]. The total cesarean delivery rate jumped again from 2000 to 2001 to 24.4% of all births, the highest level reported since these became available on birth certificates (1989)[3]. Recently, the rate increased to reach an all-time high of 26.1% in 2002. The elective repeat cesarean section accounts for one-third of all deliveries. Some reported that a history of previous uterine scarring accounts for over 40% of all cesareans[4].

Rageth *et al.*[5] evaluated 29,046 deliveries after previous cesarean as registered in a cesarean pooled database of 457,825 deliveries used to assess quality control in Switzerland. He concluded that a history of cesarean deliveries significantly elevates the risks for mother and child in future deliveries, for a variety of perinatal complications such as an increased frequency of extra-uterine pregnancy, the necessity for hysterectomy and febrile and thromboembolic complications. Reports have also described increased placental implantation disturbances related to cesarean delivery. Rageth *et al*., also reported that in patients with a history of multiple cesareans, the risk for the uterine rupture is even higher and has been associated with fetal death and serious neonatal disorders[5].

Elective repeat cesareans when compared with a trial of labor showed a higher incidence of postpartum-fever, transfusion and longer hospital stay[6].

In Saudi society, the general trend has always been towards large family size and women have higher parity even if the route of delivery has been by multiple cesareans. This could expose these women, according to the available data, to a higher rate of complications related to repeated operations. This study was conducted to test the hypothesis that increasing the number of repeated cesarean deliveries increases the maternal and neonatal risks of complications.

Materials and Methods

A retrospective chart review was conducted over a six year period (Jan 1994 to May 31, 2000) comparing patients delivered by repeat cesarean sections following more than 3 previous cesareans with those following 2 or 3 previous cesareans. The demographic data of the mothers reviewed included age, parity, a history of vaginal deliveries prior to the index cesarean, the number, indication of previous cesareans, the type of previous scar and the occurrence of pre-delivery scar pain or tenderness. The indications of the first cesarean included: cephalopelvic disproportion, failure to progress, fetal distress, ante-partum hemorrhage, malpresentation and others. The placental implantation site was determined by antenatal ultrasound and confirmed intra-operatively. Complications

related to the repeated multiple cesareans were also noted. These included minor complications, *e.g*., post operative fever, wound infection, urinary tract infections and prolonged hospital stay as well as major complications including wound separation (wound dehiscence and uterine rupture), intra-operative injuries, cesarean hysterectomy and maternal death. Wound dehiscence was defined as a uterine wall defect not requiring emergency laparotomy and with no evidence of fetal compromise or excessive bleeding, and uterine rupture with or without expulsion of the fetus endangering the life of the mother or fetus[8].

The neonatal outcome was also compared focusing at birth weight, APGAR score at 1, 5, 10 min, the need for ventilator assistance, admission to Neonatal Intensive Care Unit (NICU), injuries at cesareans, number of stillbirths (SB) and early or late neonatal deaths (ENND or LNND).

A database was set up with Microsoft Excel for Windows (Redmond, WA) to facilitate data entry and retrieval. Statistical analysis was performed with Statistical Package for the Social Sciences (SPSS) for Windows 10 (SPSS Inc, Chicago, IL). Results are expressed as mean and standard error of the mean. Bivariate comparisons were made by means of two sample *t* tests for continuous variables and the differences were considered statistically significant at $P < 0.05$.

Categorical variables were assessed by x^2 test for independence or fisher's exact test in cases of small cell frequencies 2×2 contingency tables. $P < 0.05$ was considered statistically significant.

By means of logistic regression, we developed multivariable models in which complications (major and/or minor) were either present or absent, and which was analyzed as dependent variable (each separately) with independent variables age, gravidity, parity, history of (h/o) previous vaginal birth, mode of delivery, intra-operative incision and the indications for the primary cesarean.

Results

There were 98 patients who had been delivered by more than 3 previous cesareans (Group A) and these were compared with 101 patients who had only 2 or 3 previous cesareans (Group B). The cases consisted of 64 patients with previous 4 cesareans, 26 with previous 5 cesareans and 8 patients with previous 6 cesareans. The control group consisted of 87 patient with previous 2 cesareans and 14 patients with previous 3 cesareans. The demographic data of the patients in the two groups are shown in Table 1.

The patients of Group A were older, of higher gravidity and parity and had h/o less previous vaginal births. This was statistically significant ($P < 0.0001$, < 0.001 and < 0.03, respectively). The indications for the primary cesarean

were significantly different between cases and controls P = 0.008. The other characteristics related to the type of previous scars, presence of pre-delivery scar tenderness, the mode of delivery and the type of intra-operative incision, were not different between the two groups (Table 1).

Table 1. A comparison of maternal characteristics between cases (Group A) and Controls (Group B).

Maternal characteristics	Group A (N=98)	Group B (N=101)	P Value
Age (mean)	33.6	30.9	< 0.0001*
Gravidity (mean)	4.9	6.8	< 0.0001*
Parity (mean)	3.3	5.1	< 0.0001*
Weight (kg)	78.6	78.6	0.97
Booking status	95	94	1
Indication of first C.S.:			
CPD	48	27	–
FTP	11	15	–
FD	3	12	–
Breech	3	9	–
APH	5	4	–
Elective	6	1	–
Others	20	25	–
Total cases with known indication	91	93	0.008*
Previous scar	8	63	0.5
Classical	2	0	–
Lower segment	76	63	–
H/O vaginal birth before C. S.	25	40	0.03*
Mode of delivery	98	101	0.6
Elective	71	70	–
Emergency	27	31	–
Scar tenderness	5	6	0.8
Intra-operative incision other than L. S.	11	5	0.12
Placental localization low lying and previa	9	5	0.2
Predelivery Hb (mean)	10.6	11.2	< 0.017*
Post-delivery Hb (mean)	10.4	9.9	0.29

* = significant

Post-operative maternal morbidity (fever, wound infection, urinary tract infection, the need for blood transfusion and the length of hospital stay) and major complications included wound dehiscence, uterine rupture, bladder or bowel injury, neonatal injury and the necessity of cesarean hysterectomy or second laparotomy were also compared. No cases of maternal death occurred in either group.

Serious complications occurred more frequently among cases than controls. Three cases of wound dehiscence plus one uterine rupture occurred among Group A while only two wound dehiscence occurred among controls (Group B). Although this might be clinically relevant, it did not show statistical significance (P = 0.6 and 0.49, respectively). The uterine rupture occurred in the anterior wall in a patient who had previous six cesareans along with placenta previa. This necessitated a cesarean hysterectomy for massive bleeding. Both mother and baby did well post-operatively.

Another two patients of Group A required cesarean hysterectomies for massive intra-operative bleeding. This was due to implantation site bleeding caused by placenta previa in one case and uterine atony in the other. Both mothers required intensive care (ICU) admission and management of massive blood transfusion. They both recovered successfully and were discharged home with their babies in a good condition. Although in Group B, no patient required cesarean hysterectomy or ICU admission, statistically no significant difference was observed (P = 0.12), See Table 2.

Table 2. A comparison of clinical outcome and complications between cases (Group A) and controls (Group B).

Clinical outcome	Group A (N = 98)	Group B (N = 101)	P Value
Maternal complications:			
Major:			
Wound dehiscence	3	2	0.67
Ruptured uterus	1	0	0.49
Cesarean hysterectomy	3	0	0.12
Bladder injuries	3	0	0.12
Maternal death	0	0	
Minor:			
Blood loss ml†	735.9/ 1117/114	603/ 138/ 14	0.24
Blood transfusion	10	2	0.01*
Wound infection	10	6	0.43
Post-operative fever	16	9	0.10

Table 2. Cond.

Clinical outcome	Group A (N = 98)	Group B (N = 101)	P Value
Urinary tract infection	13	12	0.79
Post-delivery hospital days†	5.8/ 2.6/ 0.27	4.9/ 1.98/ 0.198	0.011*
Intrapartum bleeding >1 L	7	2	0.09
Tubal ligation (elective)	11	3	0.02*
Neonatal outcome:			
Birth weight gm†	2961/ 512/ 52.6	3103/ 520/ 52.3	0.057
Five minutes apgar score < 7	8	9	0.60
Injuries at C. S	0	2	–
Still births (SB)	1	6	0.12
Early neonatal death (ENND)	0	1	1.00
Late neonatal death (LNND)	0	3	0.25
Neonatal ventilator assistance	1	2	0.75
Admission to neonatal intensive care	1	4	0.36

* = significant, † = (mean/ SD/ SEM)

Intra-operative complications in this series included bladder injuries which occurred in three patients in Group A, but none in Group B, not significantly different (P = 0.116). All injuries were repaired successfully intra-operatively with no delayed complications. One case in Group A had infundibulo-pelvic ligament injury which was successfully managed by unilateral salpingo-oophorectomy.

Post operative fever, wound- and urinary tract- infections were more common among cases than controls, but did not show a statistically significant difference (P = 0.11).

The number of patients requiring blood transfusion were significantly higher among cases than among controls P < 0.01, (Odds Ratio (OR) = 5.53, 95%; confidence interval (CI) {1.25-24.5}). The post-operative hemoglobin level and the mean amount of blood loss was not significantly different between the 2 groups (P = 0.29 and 0.24, respectively). That could be explained by the higher pre-operative mean hemoglobin of patients in Group B than that of patients in Group A, P = 0.010.

Elective tubal ligation was done more frequently among cases than among controls (P < 0.02, odds ratio 3.78, 95% C.I. {1.09-13.14}).

The neonatal outcomes of both groups are shown in Table 2. There was no difference in birth weight, APGAR score < 7 at 5 min and the number of newborns requiring neonatal ventilator assistance or ICU admissions between the two groups (P = 0.057, 0.67, 0.75, 0.36, respectively). The numbers of perinatal deaths (including SB, ENND and LNND) were more common among patients in Group B than among Group A but this was not statistically significant (P = 0.119, 1.00, 0.246, respectively).

By using logistic regression, risk factors were identified that were significantly associated with the development of complications (major and minor maternal complications or fetal complications). Major complications included wound dehiscence, uterine rupture, cesarean hysterectomy and bladder injury. Minor complications included post-operative fever and wound infection. Neonatal complications included perinatal-, early neonatal-, late neonatal-deaths and still-births.

Increased number of previous cesarean sections was associated with increased number of minor complications (including post operative fever and wound infection (OR: 2.11, 95% C.I. {1.02, 4.36} P = 0.044) Table 3. In addition, there was a trend towards increased major complications but this did not reach statistical significance (OR: 3.26, 95% C.I. {0.64, 16.6} with a P = 0.15). Interestingly, if the patient was delivered by emergency cesarean, she was at increased risk of major complications compared to patients delivered electively (OR = 19.08, 95%; CI {2.3, 158.9} with a P = 0.006). See Table 4.

Table 3. Logistic regression of maternal risk factors in relation to minor complications (post-operative fever and wound infection).

Maternal risk factors	Odds ratio (OR)	Confidence interval {CI}	P Value
Number of previous cesarean sections	2.11	{1.02, 4.36}	0.044*
Age	1.06	{0.99, 1.13}	0.120
Gravidity	1.04	{0.88, 1.20}	0.670
Parity	1. 11	{0.92, 1.34}	0.300
VBPC	1.37	{0.66, 2.80}	0.400
Mode of delivery	1.07	{0.50, 2.30}	0.860
Intra-operative incision	1.01	{0.27, 3.79}	0.980
Indication of P.C.S.	1.01	{0.85, 1.20}	0.940

* = significant

Table 4. Logistic regression of maternal risk factors in relation to major complications.

Maternal risk factors	Odds ratio (OR)	Confidence interval {CI}	P Value
Number of previous cesarean sections	3.270	{0.64, 16.6}	0.150
Age	1.030	{0.89, 1.2}	0.680
Gravidity	1.160	{0.89, 1.5}	0.270
Parity	1.150	{0.85, 1.57}	0.400
VBPC	0.280	{0.03, 2.31}	0.230
Mode of delivery	19.078	{2.30, 158.9}	0.006*
Intra-operative incision	4.096	{0.76, 22.2}	0.100
Indication of P.C. S.	0.940	{0.66, 1.34}	0.700

* = significant

Logistic regression was performed for risk factors and the development of fetal complications (including SB, ENND and LNND). The odd ratio of having SB, ENND or LNND was lower when the number of previous cesareans was higher than when it was 3 or less (OR = 0.154, 95%; CI {0.03, 0.7}) Table 5. This was difficult to explain but most likely it was co-incidental and related to obstetric complications rather than to the cesareans. The stillbirth was a result of uncontrolled insulin-dependent diabetes. One case of early neonatal death was due to severe intra-uterine growth retardation (birth weight: 663 g at 28 wks) and prematurity. The other two cases were due to extreme prematurity and multiple congenital malformations, respectively.

Table 5. Logistic regression of maternal risk factors in relation to fetal outcome perinatal deaths (SB, ENND, LNND).

Maternal risk factors	Odds ratio (OR)	Confidence interval {CI}	P Value
Number of previous cesarean sections	0.15	{0.034, 0.71}	0.016*
Age	1.07	{0.96, 1.2}	0.230
Gravidity	1.08	{0.86, 1.35}	0.500
Parity	1.12	{0.94, 1.5}	0.140
VBPC	4.05	{1.30, 12.6}	0.020*
Mode of delivery	1.89	{0.63, 5.7}	0.260
Intra-operative incision	0.99	{0.12, 8.16}	0.990
Indication of P.C.S.	1.14	{0.86, 1.5}	0.350

* = significant

Discussion

A history of cesarean delivery significantly elevates the risks for mother and child in future deliveries. The maternal mortality rate was 2.4 per 10,000 for women undergoing an elective repeat cesarean in the Meta analysis of Mortimer that included 31 studies[8]. This was much higher than the maternal mortality rate within the United States which was 9.2 per 100,000 live births for 1980; whereas for 1997 the ratio was 8.4[2]. In that study, Harper *et al.* reported that the adjusted odds ratio of pregnancy related deaths associated with cesarean delivery when compared with vaginal delivery was 3.9 (95% C.I. {2.5, 6.1}). They also referred to the study of the National Institute of Child Health and Human Development analyzing 3.5 million births, which showed that the maternal mortality rate was lowest in the group with elective repeat cesarean delivery[9]. However, that was probably neither less than two nor more than four times more hazardous than vaginal delivery.

The likelihood of placenta previa increases as both parity and number of cesarean deliveries increased. The adjusted odds ratio for primiparae with one cesarean delivery was 1.28 (95% C.I. {0.82, 1, 99}). For a woman who has parity greater than four and four or more cesareans that ratio was 8.76 (95% C.I. {1.58-48.53})[10].

Among 164 women with placenta previa reviewed by Hendricks *et al.*, women with 1, 2 and 3 previous cesarean sections had 2.2 (95% C.I. {1.4, 3.4}), 4.1 (95% C.I. {1.9, 8.8}) and 22.4 (95% C.I.{ 6.4, 78.3}) times increased risk of developing placenta previa, respectively[11].

The meta-analysis of Ananth *et al*., showed a dose response pattern for the risk of previa on the basis of the number of prior cesarean deliveries. The relative risks were 4.5 (95% C.I. {3.6-5.5}) for one; 7.4 (95% C.I. {7.1-7.7}) for two; 6.5 (95% C.I. {3.6-11.6}) for three; and 44.9 (95% C.I. {13.5-149.5}) for four or more prior cesarean deliveries[12].

Tuzovic *et al*.[13] reported that the risk of placenta previa was significantly increases after two previous cesarean sections (OR, 7.32, 95% C.I. {2.1-2.5}). The risk of placenta accreta ranged from 2% in women < 35-years-old with no previous cesarean deliveries to almost 39% in women with two or more previous cesareans and an anterior or central placenta previa[14]. Similarly, Zaki *et al.* reported that the risk of placenta accreta in cases of placenta previa increased linearly from 4.1% in patients with no cesarean section to 60% in patients who had three or more cesareans[15].

The risk of uterine rupture increases as the number of cesarean deliveries increases. Miller *et al.* reported that uterine rupture was three times more

common with two or more previous cesareans[16]. Excluding cases of asymptomatic scar dehiscence, Gardeil *et al.* reported an overall incidence of uterine rupture to be 1:4,366 deliveries but this increased to 1:304 in multigravidas with a previous cesarean section scar[17]. In the large study of Shipp *et al*.[18] involving more than hundred uterine ruptures, the incidence of uterine rupture with two or three cesareans is between 2-3%. In a 10-year population-based study of uterine rupture; Kieser and Baskett found that in 92% of cases uterine rupture was associated with previous cesarean delivery[19]. In the study of Diaz *et al*.[20], uterine rupture dehiscence (URD) was independently associated with previous cesarean delivery. After one or two cesarean deliveries the risk of URD increased tenfold, OR 9.9 (95% C.I. {2.6-3.8}) and after three or more cesarean deliveries the risk increased 30 fold, OR 30 (95% C.I. {1.9-1600}).

Although Asakura and Myers[4] found no significant difference in the risk of uterine rupture or dehiscence between those with more than one cesarean and the other group of only previous one cesarean (OR 1.58, 95% C.I. {0.69-3.62}) five hysterectomies were done in the first group versus only one in the second group ($P < 0.05$). This was primarily due to placenta accreta in those undergoing elective repeat cesarean.

Cesarean delivery was associated with a 13 fold increased risk of emergent hysterectomy in the case control study by Kacmar *et al.*, comparing fifty cases of emergent cesarean hysterectomy with 100 controls[21].

In a Nigerian tertiary centre, Okogbenin *et al.* reported an incidence of 0.226% obstetric hysterectomies for a variety of indications (including uterine rupture, atonic post partum hemorrhage, and placenta previa) and of these 30% had previous cesarean sections[22].

The incidence of peripartum hysterectomy in the study of Bai *et al.* from South Korea was reported to be 0.09% of vaginal deliveries as compared to 0.45% of cesarean sections[23]. Lau *et al. from* Hong Kong reported an incidence of obstetric hysterectomy to be 0.32% of cesarean sections and 0.02% of vaginal deliveries[24]. The incidence of emergency peripartum hysterectomy in a tertiary center in North Jordan was 0.5 per thousand deliveries, 85% of these cases had previous cesarean sections[25]. In the retrospective review of Chew and Biswas from Singapore, cesarean hysterectomy was performed in 0.17% of cesarean sections and a hysterectomy was done in 0.02% of cases following vaginal deliveries[26].

Other than the common complications reported above, a rare case of cesarean scar pregnancy with a normal intra uterine pregnancy had been reported[27]. A similar case of cesarean scar pregnancy was reported by Lam and Lo but it was not associated with intra-uterine pregnancy[28]. Another rare complication was been reported by Mathelier in a patient with previous two cesarean sections who

was found to have uterine synechiae and ventral fixation of the uterus to the anterior abdominal wall[29].

Besides maternal complications, Hook *et al.* reported that infants delivered by elective repeat cesarean sections (ERCS) had an increased rate of developing any respiratory problem with adjusted odds ratio being 2.3 (95% C.I. {1.4-3.8}) when compared with routine vaginal deliveries[30]. Levine *et al.*, in their review found that the incidence of persistent pulmonary hypertension among 1,889 elective cesarean section was 0.37%, almost five times higher than those delivered vaginally (21,017) 0.08% with an OR of 4.6 and $P < 0.001$[31].

They also noted increased respiratory conditions that prompted admission to NICU were almost three fold greater in the elective cesarean group than among vaginally delivered neonates[31]. Flamm[32] reported that a study found that 1.5% of infants delivered by elective repeat cesarean (ERC) were admitted with serious respiratory difficulty. Of even greater concern is the occasional occurrence of severe neonatal respiratory failure after ERC without evidence of iatrogenic prematurity. Eighteen percent of infants referred to two major university NICUs for extracorporeal membrane oxygenation therapy were products of ERCS at term. He concluded although these cases occur very infrequently they can have catastrophic outcomes (80% probability of neonatal death).

The results of this study were not expected but it is encouraging that an increased number of cesarean section is not exposing the mother or the fetus to a significant risk especially with the recent trend towards elective primary cesarean to prevent pelvic floor relaxation and stress incontinence in future life. Nygaard and Cruikshank[33] raised the issue of whether there is a role in modern obstetrics for elective cesarean delivery before labor for prevention of pelvic floor disorders. This was commented on in the paper of Dietz and Bennett[34] who concluded in their study using translabial ultrasound and correlating perinatal changes in mobility of urethra, bladder, cervix and rectal ampulla with labor and delivery data, that all forms of cesarean delivery were associated with relatively less pelvic organ descent. Similarly, Goldberg *et al.* study concluded that cesarean only delivery was associated with a markedly reduced risk of urinary incontinence among women with previous multiple childbirth (OR 0.52, $P = 0.002$) after controlling for age, parity and body mass index by multivariate regression[35].

This is probably not as important in a society where the number of deliveries is limited but is of crucial significance to Saudi society where large family size is common.

Conclusion

As noted above the variety of complications associated with cesarean delivery was expected to increase with increasing numbers and that was thought will be confirmed by this study. This study's findings only confirmed a trend towards increased risk of some of the major complications including wound dehiscence, uterine rupture, cesarean hysterectomy and bladder injuries but this was not statistically significant.

Finally, increased number of cesarean section was associated with significantly increased minor complications and a significant increase in the need for blood transfusion. This should be considered when counseling patients who had multiple cesarean sections before allowing them to get pregnant plus mentioning the trend toward increasing major complications.

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دراسة مقارنة لحالات الولادة بأربع عمليات قيصرية أو أكثر مع حالات الولادة بعمليات قيصرية أكثر من اثنين أو ثلاث قيصريات

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المستخلص. هدف البحث إلى اختبار الفكرة أن تزايد عدد العمليات القيصرية المتكررة يزيد من مخاطر مضاعفات للطفل والأم. تمت دراسة بحثية لمقارنة حالات المريضات اللآتي ولدن بعمليات قيصرية أكثر من ثلاث بهؤلاء اللاتي ولدن بعمليات قيصرية أقل من ثلاث على مدى ٧ سنوات (١٩٩٤-٢٠٠٠م) في المستشفى بجامعة الملك عبد العزيز بجدة، وذلك عن طريق مقارنة المواصفات العامة للأم والمضاعفات المصاحبة، وناتج الطفل حديث الولادة بين المجموعتين (SPSS for windows 10 و SPSS Inc., Chicago, IL)، تم إجراء عمليات الإحصاء بواسطة التحليل للمتغيرات السريرية بواسطة ساس (logistic regression). أظهرت النتائج أن ٩٨ مريضة أجريت لهن أكثر من ثلاث عمليات قيصرية (المجموعة أ)، بينما المجموعة الثانية مكونة من ١٠١ مريضة أجريت لهن ٢-٣ عمليات قيصرية (المجموعة ب)، بينما المجموعة (أ) احتاجت نقل دم أكثر من المجموعة (ب)، كل المضاعفات الأخرى والمضاعفات الجراحية الكبرى لم تختلف إحصائيًا بين المجموعتين . ولم يكن أيضًا هناك اختلاف في نتاج الأطفال حديثي الولادة بين المجموعتين، مما يؤكد أنه بالرغم من أن هنالك اتجاه إكلينيكي نحو زيادة المخاطر للأم والطفل بزيادة عدد العمليات القيصرية إلا أنه لم يصل إلى حد الأهمية.