

**Association between Urgency of Cesarean birth and Cesarean Scar Defects:
prospective study**

Short title: Scar niche after emergency cesarean delivery

Mohamed **Elhodiby**¹, Tarek **Tamara**², Eslam **Elkoumy**^{*,1} Radwa **Ali**²

¹ Obstetrics and Gynecology Department, Faculty of Medicine, Misr University for Science & Technology, Cairo, Egypt.

² Obstetrics and Gynecology Department, Faculty of Medicine, Ain shams university, Cairo, Egypt.

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***Corresponding Author: Eslam Elkoumy**, MSc, Assistant lecturer of Obstetrics and Gynecology, Faculty of Medicine, Misr University for Science & Technology, Cairo, Egypt, Egypt. ORCID: 0000-0001-7471-926X, Postal address: 77, Giza, Egypt. First 6th of October, email: elkoumy7@gmail.com

ABSTRACT

Objectives. The aim of this study was to evaluate the association between the urgency of cesarean delivery and uterine wound healing.

Material and Methods. This double center prospective clinical trial was conducted between February 2020 and December 2020 in Ain Shams University Maternity Hospital and Misr University for Science and Technology hospital, Egypt, involving 67 eligible pregnant women undergoing primary CS who were further subdivided into 2 groups according to the urgency of cesarean delivery (CD). The primary outcome was the incidence of cesarean scar defect (CSD) 3 months after CD as assessed by saline contrast sonohysterography (SCSH).

Results. All women underwent emergency CD had CSD on SCHG assessment three months following CS compared to 74.4% of women underwent elective CD, (p value =0.011). Moreover, the healing ratio was significantly higher in women underwent elective CD.

Conclusions. Emergency CS was associated with higher incidence of CS scar defects and had poorer healing process 3 months after primary CS as assessed by SCSH as compared to elective cesarean deliveries.

Key words:

Cesarean section; hysterotomy; ultrasound.

Introduction:

Cesarean delivery is an indispensable tool in obstetric practice, it could be a lifesaving procedure for both the fetus and the mother [1]. The number of caesarean delivery (CD) is growing worldwide being the most common surgical procedures worldwide,[2] with an estimated prevalence of 25% of the UK deliveries, while in Egypt, the reported rate of CD may exceed 55% [3]

CD is associated with short and long-term complications that lead to increased maternal and fetal morbidity and mortality. Moreover, it is associated with increased risk in the future pregnancies, such as uterine rupture and abnormal placentation [4,5]. The observed increase in the long-term gynecological complications and the complications occurring in subsequent pregnancies are both related to the presence of cesarean scar defect (CSD) [6,7]. Yet, the debate whether residual myometrial thickness alone could be considered as the main risk factor for those adverse events is still open [8].

Several clinical and non-clinical interventions have been proposed by WHO aiming to reduce unnecessary CD [9] and hence, the complications attributed to CSD. This aim could be achieved by maintaining the uterine integrity through optimal cesarean wound healing [10].

The National Institute for Health and Clinical Excellence (NICE) classified the urgency of cesarean deliveries into four categories to standardize practice, improve team communication and thereby improve obstetric and anesthetic outcomes [11]. Decision-to-birth interval for unplanned and emergency caesarean birth should be within 30 minutes and 75 minutes of making the decision in both category 1 and 2 cesarean births respectively, where rapid birth can be harmful in certain circumstances [12].

Complications rates increase according to the degree of emergency of the cesarean section. Therefore, it is important to respect different codes that optimize the handling of labor emergencies, and optimize the duration between the decisions to operate thus preventing hyper-acute cesarean section [13].

CSD is one of the considerable and debatable complications of urgent CD, it is associated with long term obstetric and gynecologic morbidities with controversial findings in literature [14-16].

Objectives:

The aim of our study was to evaluate the occurrence of CSD among women with term singleton pregnancy delivered with either elective or emergency primary CD.

Material and Methods:**Study design and participants:**

The current study was a prospective clinical trial, performed between February 2020 and December 2020 at Ain Shams University Maternity Hospital and Misr University for

Science and Technology hospital. The study included 67 pregnant women between 18 and 35 years with term singleton pregnancy that underwent uncomplicated primary prelabor lower segment cesarean section. We excluded women with medical conditions that can affect the uterine healing process as diabetes mellitus, anemia, chronic renal or hepatic disease, coagulopathy and those with platelet disorders. Women receiving medications that can affect wound healing as corticosteroids or anticoagulants. Women who intended to use intrauterine device as a contraceptive method during the study duration and women with any structural uterine abnormality as cervical stenosis or fibroid uterus or with pelvic infection at the time of saline contrast sonohysterography (SCSH) were also excluded.

Ethical considerations:

Before study entry, the study purpose and procedures were explained to potentially eligible women (either hospital admitted women or during the last outpatient antenatal visit) by the principal investigator and a written informed consent was obtained from each participant. The study was approved by the Ethical and Research Committee of the Council of Obstetrics and Gynecology Department, Faculty of Medicine Ain Shams University Ethical Research Committee (FMASU MS 79/2020) on 26/1/2020 and Ethical Committee of the Council of Obstetrics and Gynecology Department; Misr University for Science and Technology. The study was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki and was conducted and reported in accordance with STROBE guidelines for reporting observational trials.

Procedures:

All participants were subjected to a detailed clinical assessment and all data was documented in their medical records. The elective CD is defined as a CD carried out as a planned procedure before the onset of labor or following the onset of labor, when the decision was made before labor. An emergent CD is defined as a CD required because of an emergency situation and CD had not been considered necessary previously [17].

As per both hospitals protocol uniformly a 1-g intravenous cefazolin dose for all women (less than 80 kg) undergoing cesarean delivery prior to skin incision, primary cesarean delivery is performed by the intermediate registrar of a 3 years training program (6 registrars in both hospitals), and uterine incision is closed in all participants using a unified continuous unlocked double-layer closure technique using absorbable polyglactin (910) 1 suture (Vicryl® Ethicon).

After the procedure all participants were observed in the hospital for 48 hours for any complications, received analgesics and intravenous antibiotics and then they were discharged on oral antibiotics as per hospitals protocol.

Three months after CS, the participants were reassessed regarding history and examination. SCSH was performed using Mindray DC-N2 vaginal probe by single sonographer (M.E); Contrast sonography has added value in evaluation of CSD, however the apparent prevalence of any defects increases with SCSH and the increased uterine pressure associated with this procedure may exaggerate the size of any scar present. Premedication with ibuprofen tablets approximately 1 hour before the scheduled SCSH was received, then the participants were assessed while in the lithotomy position with an empty bladder, a sterile vaginal speculum was inserted and the cervix was cleaned with an antiseptic solution. A thin Foley's catheter (size CH 8) was placed into the cervical os and the balloon was inflated with 2-5 ml of sterile saline for stabilization and occlusion of the internal cervical os. The speculum had been carefully removed and the transvaginal ultrasound probe was then inserted into the posterior fornix of the vagina; a 20-mL syringe was attached to the catheter. Five mL of saline was usually required to distend the cavity then the balloon was deflated. The incision site was viewed longitudinally and in the transverse plane for evaluation of uterine wound healing at the site of previous CS scar.

The primary outcome was the presence of CSD (anechoic defect communicating with the endometrial cavity at the anterior wall of lower uterine segment at the site of cesarean scar) indicating inadequate uterine wound healing; any indentation or other defect in the scar was classified as a scar defect [18]. While the secondary outcomes **(as shown in figure 1)** included the measurements of the anterior myometrial thickness (AMT) immediately adjacent to the scar, the thickness of the myometrium bordering the scar i.e. residual myometrial thickness (RMT) (measured from the serosal surface of the uterus to the apex of the niche), the depth (distance between apex of the niche and the estimated middle of the niche base) and width (perpendicular to the line between middle of the niche base and apex) of CSD and the healing ratio (the thickness of residual myometrium covering the defect divided by the sum of the thickness of residual myometrium cover the defect and the height of wedge shaped defect), the degree of deficiency (deficiency ratio) was expressed as the ratio RMT/AMT [19].

Those parameters of CSD are quantitative measurements that would be useful for longitudinal follow up of uterine healing, they allow for objective measurement of CSD size in women in both groups. Deficiency ratio ranges were 1.0–0.76, 0.75–0.51, 0.5–0.26, and 0.25–0.01 the defects were severe if involving $\geq 50\%$ of the myometrium [20].

Here insert figure 1

Statistical methods:

Data were collected, tabulated and analyzed using SPSS© Statistics version 22 (IBM© Corp., Armonk, NY, USA) and MedCalc Statistical Software version 18.9.1 (MedCalc Software bvba, Ostend, Belgium; 2018). Categorical variables were presented as numbers and percentages and continuous numerical variables were presented as mean

and SD. Two-group comparisons for numerical data were done using the Student's t test for parametric data and categorical data were compared using Chi-square test.

Results:

Between February 2020 and December 2020, 67 women underwent primary CD were included. Three women were lost to follow up and only 64 women were evaluated for presence of CSD by SCSH, of those women 21(32.8%) woman had emergency CD and 43(67.2%) had elective CD.

The baseline demographic and clinical characteristics of the participants are shown in **(Table 1)**.

Here insert table 1

There was no significant difference between both groups regarding Robson classification that divide deliveries into one of ten groups on the basis of five parameters: obstetric history (parity and previous caesarean section), gestational age, onset of labor (spontaneous, induced, or caesarean section before onset of labor), number of fetuses, and fetal presenting part or lie.

Here insert table 2

Three months after CS all women in the emergency CD group had CSD on SCHG assessment. The healing ratio was significantly higher in women had elective CD. **(Table 3)**

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Adverse Events:

No complications e.g. postpartum hemorrhage, fever, or wound complications were observed during the 1st 48 hours or 1 week postoperative in both groups. Regarding SCHG, only one woman reported increased pain needed extradoses of analgesia.

Discussion:

The obstetricians' concerns regarding the alarming increase in CD rates are related to its known short- and long-term risks and consequences. Therefore, different guidelines were released recommending reducing the non-medical indications of CD. Many studies were performed to evaluate risk factors, etiologies, and different methods to treat CSD. The therapeutic interventions targeting CSD increases the medical consultations and related costs, thus; it seems more efficient to prevent CSD development in the first place, thus identification of the related risk factors is of paramount importance [10, 21,22, 23].

The main finding of this double center clinical trial was that emergency CD resulted in higher incidence of CSD. 100% of women delivered by emergency CD had SCD at 3 months follow up compared to 74.4% of women underwent elective CD ($p= 0.011$).

Many studies evaluated the risk factors for CSD development with conflicting results regarding the effect of the urgency of CD.

In their meta-analysis, Yang and Sun suggested that the morbidity of elective CD is quite lower than that of emergent CD regarding the incidence of infection, fever, and wound dehiscence. Moreover, the reoperation rate was higher in emergent CD [24].

Another study reported that cesarean scars following scheduled CD were thicker than those following emergency cesarean sections with less incidence of CSDs among scheduled sections [25].

According to Antila-Långsjö et al., [16] there was no significant difference in the presence of CSD between those underwent elective and emergency CD ($P = 0.898$).

In a systematic review evaluating the potential risk factors for development and symptoms related to the presence of uterine niches, emergency CS was not a risk factor for the niche presence [26]. Moreover, according to Chen et al., [24] more CSDs were linked to elective cesarean deliveries compared to emergency ones.

On the contrary Liu et al., [15] found that women undergoing elective CS tended to have 4.5 times increased risk of CSD formation than those who had a trial of labor but ended up to CS.

The oxidative stress hypothesis may explain the increased SCD in emergency CD. Oxidative stress has been identified as an important feature in the pathogenesis of chronic, non-healing wounds in general [27]. A study evaluated the oxidative stress in amniotic fluid and umbilical cord plasma by determining malondialdehyde concentration and glutathione peroxidase activity found that malondialdehyde concentration was higher in amniotic fluid and umbilical cord plasma in women delivering by emergent cesarean compared to those delivering by elective cesarean [28].

Another possible hypothesis linking emergency CD to higher SCD is the adhesion formation. Dawood et al., evaluated the characteristics of CD and the development of subsequent pelvic adhesions. They reported that emergency CS was an independent risk factor for adhesion formation [OR: 7.74 (1.61–37.19); $p=0.01$] [29]. Adhesions can impair cesarean scar healing due to the retraction of the scar tissue, which pulls on the uterine scar towards the abdominal wall in the opposite direction of the retracting myometrium layers that is required for an optimal approximation and healing [30].

Modification of surgical technique to reduce trauma and tissue ischemia with less invasive techniques and gentle handling of tissue is beneficial in reducing postoperative adhesions however; this usually not thought in emergency CD where the whole goal is to deliver the baby as quickly as possible [31].

CSD leads to many hazardous obstetrical sequelae such as preterm delivery, uterine rupture, caesarean scar pregnancy or abnormal placenta implantation [16]. Therefore,

proper identification of CSD related risk factor along with proper treatment may help reduce these sequelae.

Szkodziak et al., reported two cases where surgical correction of the CSD was not performed and the pregnancies were complicated by caesarean scar dehiscence and caesarean scar pregnancy while the case with corrected CSD prior to pregnancy achieved uncomplicated pregnancy [32].

Another study reported successful trial of labor after cesarean section (TOLAC) can be achieved in women with mild and moderate CSDs [33].

The higher prevalence of CSD in our study (82.2% of women in both groups) came in agreement with previous studies that reported prevalence up to 88% with the use of SCSH [10,18, 26,34,35]. This high prevalence may be due to the use of SCSH and not the un-enhanced ultrasound during the assessment or may be due to performing CS in all participants by intermediate registrars or using of braided sutures (they were the only type of sutures available in both hospitals) for uterine closure. Moreover, any indentation or defect in the scar were considered as a scar defect in contrast to other studies that defined CSD when the defect depth ≥ 2 mm.

Moreover, the studies that reported lower rates of CSD included only the women with symptoms related to CSD.

Conclusion:

Emergency primary CS associated with higher incidence of CS scar defects with less healing process after 3 months as assessed by saline contrast sonohysterography when compared to elective cesarean deliveries.

Strengths and limitations:

The prospective nature of this clinical trial allowed accurate determination of the degree of cesarean urgency, exclusion of women with cervical dilatation as the one of most proposed risk factors for CSD formation in emergency CD. A single sonographer performed SCSH to all participants to avoid interobserver variability; however, we lack a confirmatory evaluation by another sonographer. On the other hand, our study has several limitations; importantly it was performed on a small sample size. Future studies on a bigger sample size are required to allow using the findings in clinical practice. Moreover, long-term follow up is strongly recommended to assess uterine scar thickness and scar related complications during future pregnancies with an assessment of intra-abdominal adhesions.

Declarations:

Authors' contributions:

M.E contributed in Conceptualization, Data curation, Formal Analysis, , Supervision, Writing – review & editing.; **T.T** contributed in Conceptualization, Formal Analysis, Methodology, , Writing – review & editing.; **E. E** was responsible for Data curation, Formal Analysis, Investigation, Writing – review & editing ; and **R.A** contributed in Conceptualization, , Methodology, Resources, , Supervision, Validation, Visualization, Writing – original draft.

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Disclosure of interests:

The authors declare that they have no competing interests.

Ethics approval:

The study was approved by the Ethical and Research Committee of the Council of Obstetrics and Gynecology Department, Faculty of Medicine Ain Shams University Ethical Research Committee (FMASU ERC) (FMASU MS 79/2020) on 26/1/2020 and Ethical Committee of the Council of Obstetrics and Gynecology Department; Misr University for Science and Technology and an informed consent was obtained from all subjects involved in the study.

Informed consent:

Informed consent for data collection for research purposes was obtained from all subjects involved in the study.

Data availability statement:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table (1): Basic demographic and clinical characteristics of the study population

Variables		Emergency CD (N=21)	Elective CD (N=43)	P	95% CI
Age (years)	Mean ± SD	27.2±3.40	28.41± 3.0	^ 0.163	-0.48 to 2.85
BMI(kg/m ²)	Mean ± SD	22.81±1.30	22.08±1.37	^ 0.043	0.022 to 1.43
No. of prior vaginal	No	8(12.5%)	14 (21.9%)	#	

deliveries (N, %)	yes	13 (20.3%)	29 (45.3%)	0.661	-0.22% to 43.85%
No. of prior miscarriage (N, %)		3 (4.7%)	4 (6.3%)	#0.549	-16.7% to 13.64%
Gestational age at delivery (weeks)	Mean ± SD	38.90± 1.13	38.93± 0.82	^ 0.91	-0.47 to 0.52
Postoperative Hemoglobin (gm/dL)	Mean ± SD	11.84± 0.74	11.87± 0.74	^ 0.85	-0.359 to 0.432
Postoperative Hematocrit (%)	Mean ± SD	32.59± 2.71	33.68 ± 2.87	^ 0.152	-0.412 to 2.594
Postoperative White blood cell count (x10³/mL)	Mean ± SD	7.73± 1.39	7.32± 1.29	^ 0.251	-1.117 to 0.297
Postoperative Platelet count (x10³/mL)	Mean ± SD	288.05± 53.76	284.79±48.70	^ 0.80	-30.07 to 23.56

% within total sample

Table 2: Robson classification of cesarean section in both groups:

Robson classification group	Emergency CD (N=21)	Elective CD (N=43)	P
2 (Nulliparous, singleton, cephalic, ≥ 37 weeks' gestation, caesarean section before labor)	8(12.5%)	14(21.9%)	0.357
4 (Multiparous without a previous uterine scar, with singleton, cephalic pregnancy, ≥ 37 weeks' gestation, caesarean section before labor)	13(20.3%)	23(35.9%)	
7 (multiparous with a single breech)	0(0.0%)	4(6.3%)	
9 (women with a single pregnancy in transverse or oblique lie)	0(0.0%)	2(3.1%)	

% within total sample

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Table 3: The CSD related measurements in the two groups

		Emergency CD	Elective CD	P-value	95% CI
Measurements by saline sonography					
CSD	N (%)	21 (100%)	32(74.4%)	0.011	6.82% to 40.25%
Anterior myometrial thickness (mm)	Mean ± SD	14.61± 3.07	13.65 ±2.7	0.204	-2.47 to 0.53
Thickness of residual myometrium (mm)	Mean ± SD	9.28± 2.75	8.88± 2.02	0.512	-1.61 to 0.815
Depth of scar niche (mm)	Mean ± SD	4.52± 1.32	4.25± 1.54	0.508	-1.09 to 0.55
Width of scar niche (mm)	Mean ± SD	4.0 ± 1.140	3.78± 1.38	0.550	-0.94 to 0.51
Healing ratio (%)	Mean ± SD	66.76 ± 9.47	76.77± 15.97	0.010	2.45 to 17.57
Severe defects	N (%)	3(14.3%)	2(4.7%)	0.177	-4.67% to 30.23%

* Statistical significant difference

% within each group

Figure 1: different measurements as assessed by SCSH

