



Correlation between Blood Glucose Levels on Niche Incidence after Cesarean Section

A. F. S. Desy Handayani¹, Makmur Sitepu, Iman Helmi Effendi, Edwin Martin Asroel, Binarwan Halim, Riza Rivany, Edy Ardiansyah

Department of Obstetric and Gynecology, Faculty of Medicine, Universitas Sumatera Utara, RSUP H. Adam Malik, Medan, Indonesia

Abstract

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***Correspondence:** A. F. S. Desy Handayani, Department of Obstetric and Gynecology, Faculty of Medicine, Universitas Sumatera Utara, RSUP H. Adam Malik, Medan, Indonesia. **E-mail:** desyhafs@gmail.com
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BACKGROUND: Long-term sequelae of cesarean section (CS) is formation of niche in CS surgical scar. Blood glucose involved in wound healing process after CS.

AIM: This study was to find correlation of blood glucose level with niche in CS patients.

METHODS: This research was an observational and analytic study with case series design conducted at Department of Obstetrics and Gynecology, Universitas Sumatera Utara, RSUP H Adam Malik Medan, and Sundari Hospital Medan Starting from July to August 2022. To assess correlation between variables, eta test was used to assess the correlation of blood glucose with incidence of niche. The analysis results were said to be significant if $p < 0.05$, with 95% CI.

RESULTS: Mean of patients were in 21–29 years (70%), multiparity with 12 patients (40%), term gestational age with 30 patients (100%), 16 patients (53.3%) with antelexion uterus, previous CS 2 times were the majority with 9 patients (30%), and 17 patients (56.7%) were elective CS. Incidence of niche was 63.3%. Triangular were the most found niche with 11 patients (36.7%). Mean of total myometrial thickness, depth of niche, and residual myometrial thickness were 5.23 ± 11.2 mm, 2.44 ± 2.75 mm, and 5.23 ± 11.22 mm, respectively. Mean blood sugar level was 103.3 ± 17.4 mg/dl. From eta analysis, there was no correlation between blood glucose levels post-CS patients using eta test with $p = 0.872$.

CONCLUSION: There was no significant correlation between blood glucose levels on niche incidence in post-CS patients.

Introduction

Cesarean section (CS) is most common surgical procedure performed in many countries. Frequency of CS has increased in the past 30 years with proportion 10–15% of births [1], [2], [3], [4]. As on 2015, CS rate reached 21.1% worldwide, which has doubled since 2000 [5]. The main reason for frequency CS increasement is still multifactorial, including clinical and non-clinical indications. Changes in women risk profile as well as non-medical indications such as social, cultural, and economic also increase CS frequency [6], [7].

A long-term sequelae is emergence of niche in CS surgical scar. Niche is an indentation of former CS area with depth at least 2 mm seen from ultrasonography (USG). Niche is present in 56–84% of women with one or more CS Scar. The presence of a niche is associated with several symptoms such as abnormal uterine bleeding, dysmenorrhea, and chronic pelvic pain [8].

Niche occurs due to poor wound healing after CS procedure. Several risk factors for niche

development may be patient or surgery related [9], [10]. Factors related to surgery include cervical dilatation >5 cm, uterine closure techniques, either single layer or double layer, and uterus retroflexion [9], [10], [11]. Patient-related factors include genetics associated with impaired healing, hemostasis, inflammation, or adhesion. Gestational diabetes (OR = 1.73), previous history of CS (OR = 3.14), and high body mass index (BMI) (OR = 1.06) were independent factors [12], [13]. Poor wound healing among diabetic women may be related to high glucose levels which decrease immune response to fight organisms and tissue hypoxia [14].

Increased oxygen demand is required for normal tissue repair, which is insufficient under hypoxic conditions, and wound healing may be slower due to suppression of important oxygen-dependent processes such as fibroblast and myofibroblast activity, angiogenesis, and collagen synthesis [15]. Post-operative hemoglobin <11 g/dl (AUC = 5.28, 95% CI: 1.97, 14.18) was significantly associated with surgical site infection. This may be due to wound hypoperfusion due to anemia and reduced post-operative ambulation [16].

Bad process of wound repair can predispose to uterine rupture. Therefore, imaging is needed to control wound healing process. There are parameters such as glucose and hemoglobin levels that involved in wound healing process of CS scar. This parameter can assess recovery process of CS surgery scar. Therefore, this study aims to evaluate correlation between blood glucose and hemoglobin levels with niche incidences.

Materials and Methods

This research is an observational and analytic study with case series design conducted at Department of Obstetrics and Gynecology, Haji Adam Malik Medan General Hospital, and Sundari Hospital starting from July to August 2022.

The sample was collected by non-probability sampling, namely, consecutive sampling technique. The research sample was all post CS patients who gave birth by CS since 6 weeks before data collection that met inclusion criteria, namely, women who gave birth by CS, women with singleton pregnancies, willing to participate in this research, and signed informed consent; which also not included in exclusion criteria, namely, presence of adenomyosis or uterine myoma during surgery, history of CS with incision other than low cervical CS, anatomical uterus abnormalities, and damaged blood samples.

Data characteristics were collected on research subjects (name, address, age, parity, gestational age, previous medical history, blood glucose level, and preoperative hemoglobin). Then, a transvaginal ultrasound examination was performed to assess uterine wound healing 6 weeks after CS using USG Voluson S8.

Statistic analysis

Data were analyzed descriptively to determine frequency distribution of research subjects based on research sample characteristics. To assess the correlation of blood glucose and hemoglobin, eta test was used. The analysis results are said to be significant if $p < 0.05$, with 95% confidence level.

Results

From Table 1, based on age, there were 21 patients (70%) aged 21–29 years and 9 patients (30%) aged 30–39 years. Based on parity, 12 patients (40%) were multiparous, 9 patients (30%) were primiparous and secundiparous, respectively. All the

Table 1: Frequency distribution of patients characteristics

| Variable | (n) | Percentage |
|--------------------|-----|------------|
| Age | | |
| <20 | 0 | 0 |
| 21–29 | 21 | 70 |
| 30–39 | 9 | 30 |
| >40 | 0 | 0 |
| Parity | | |
| Primiparous | 9 | 30 |
| Secundiparous | 9 | 30 |
| Multiparous | 12 | 40 |
| Grandemultiparous | 0 | 0 |
| Gestational age | | |
| <37 weeks | 0 | 0 |
| 37–40 weeks | 30 | 100 |
| Surgery indication | | |
| Preeclampsia | 4 | 13.3 |
| Failed induction | 3 | 10.0 |
| Malpresentation | 2 | 6.7 |
| Macrosomia | 1 | 3.3 |
| Contracted pelvic | 7 | 23.3 |
| Previous CS 2x | 9 | 30 |
| Fetal distress | 3 | 10 |
| CPD | 1 | 3.3 |
| Uterine position | | |
| Anteflexion | 16 | 53.3 |
| Retroflexion | 14 | 46.7 |
| Timing | | |
| Elective | 17 | 56.7 |
| Emergency | 13 | 43.3 |

CPD: Cephalopelvic disproportion.

subjects were on 37–40 weeks gestational age (100%). On uterine position examination, 16 patients (53.5%) had anteflexed uterus, and 14 patients (46.7%) had retroflexed uterus. According to surgery indication, 9 patients (30%) had history of twice CS, 7 patients (23.3%) had contracted pelvic, 4 patients (13.3%) had preeclampsia, 3 patients (10%) had fetal distress, 3 patients (10.0%) had failed induction, 2 patients (6.7%) with malpresentation, and 1 patient (3.3%) with macrosomia and cephalopelvic disproportion (CPD), respectively.

From Table 2, based on wound healing process after CS, 19 patients (63.3%) did not recover completely and 11 patients (36.7%) recovered completely. Based on wound shape of niche after CS, 11 patients (36.7%) were found with triangular type, 5 patients (16.7%) with semicircular type, and 3 patients (15.8%) with circular type.

Table 2: Incidence and form of niche in post-cesarean section patients

| Variables | n | Percentage |
|----------------|----|------------|
| Niche | | |
| Yes | 19 | 63.3 |
| No | 11 | 36.7 |
| Wound type | | |
| Triangle | 11 | 36.7 |
| Semicircular | 5 | 16.7 |
| Square | 0 | 0 |
| Circular | 3 | 15.8 |
| Droplet | 0 | 0 |
| Inclusion cyst | 0 | 0 |

From Table 3, mean of total myometrial thickness was 6.13 ± 5.13 , median was 7.7, minimum-maximum value was 0–14.6, from depth of niche, the mean value was 2.44 ± 2.75 , median value was 2.5,

Table 3: Mean of total myometrial thickness, depth of niche, and residual myoemtrium thickness

| Parameter | Mean \pm SD | Median | Min-max |
|-------------------------------|------------------|--------|---------|
| Total myometrial thickness | 6.13 ± 5.13 | 7.7 | 0–14.6 |
| Depth of niche | 2.44 ± 2.75 | 2.5 | 0–11.4 |
| Residual myometrial thickness | 5.23 ± 11.22 | 2.9 | 0–62.0 |

minimum-maximum value was 0–11.4, mean of residual myometrial thickness was 5.23 ± 11.22 , median value was 2.9, and minimum-maximum value was 0–62.0.

From Table 4, mean blood sugar level research subjects was 103.3 ± 17.4 mg/dl.

Table 4: Mean value of research subjects blood glucose and hemoglobin

| Variable | Mean \pm SD |
|---------------|------------------|
| Blood glucose | 103.3 ± 17.4 |

From Table 5, with eta test, the $p = 0.872$ ($p > 0.05$).

Table 5: Correlation of blood glucose and hemoglobin levels on niche incidences of post-CS patients

| Variables | p-value* |
|---------------|----------|
| Blood glucose | 0.872 |

*Eta test.

Discussion

Transvaginal ultrasound is an early and noninvasive diagnostic method used to evaluate uterine wall integrity. C-section Scar can be isolated niches, niches with fibrosis or isolated fibrosis [17]. Niche is defined as an indentation at uterine cesarean scar site with depth at least 2 mm on USG examination [18], this condition is found in 56–84% of women after one or more CSs [19]. Durations from complaint after CS until diagnosis are quite long as most women are discharged because reported complaints are considered part of normal recovery after CS [20].

In Voet *et al.* study on 2018, dimensional parameters differences in cesarean scar niche were seen among patients, where niche was first examined 6–12 weeks after CS, compared with examinations results performed 1 year after surgery, but niche incidence was not changes [21]. Approximately 30% of women with niche experience spotting 6–12 months after CS. Other symptoms reported in women with niches are dysmenorrhea, chronic pelvic pain, and dyspareunia [10].

From research by Abdelfattah *et al.* results on 2021, patients aged ranged from 18 to 40 with mean 29.32 ± 5.862 years (95% CI for mean 28.65–29.98 years). Based on parity, 194 (64.67%) patients had parity 1–2, 102 (34.00%) patients had parity 3–4, and 4 (1.33%) patients had parity >5. For history of CS, 115 (38.33%) patients had only one history of previous CS, 116 (38.67%) patients had history of two previous CS, 67 (23.33%) patients had history of three previous CS, and 2 (0.67%) patients had history of four previous CS [22].

Stegwee *et al.*, 2020, found mean patients age who experienced niche after CS was 38 years with history of 1.8 times CS. The duration of CS until niche

diagnosis was found <2 years in 31% patients; 2–4 years in 31% patients and >4 years in 38% patients [10]. Mean age of women with niche after CS who experienced postmenstrual spotting was 32 ± 5.75 years old (ranging from 25 to 45-years-old) while mean age of women without postmenstrual bleeding was 32.12 ± 5.34 years (ranging from 25 to 43-years-old) [23]. Alalfy *et al.*, 2020, showed that among 110 women recruited, median age was 28.2 years [24].

Uterine niches occur in up to 70% women with a previous history of CS of which 30% are symptomatic [25], [26]. Reported prevalence varies: 24–70% with transvaginal USG and 56–84% with gel/saline instillation sonohysterography (SHG). A prevalence of 45.6% was reported in prospective observational study ($n = 371$) in which SHG was performed 6 months after CS surgery [11], [26], [27].

CS performed in late labor after cervical effacement and also creation of uterovesical fold in peritoneum which affects uterine incision degree. Incision of lower uterus toward cervix results in poor healing, because mucus secreted by cervical glands interferes myometrial approximation. The slime gradually increases size of the niche. Cervical dilatation >5 cm, duration of labor >5 h, and late fetal station predispose to large niche because of thinner or smaller myometrial vasculature resulting in inadequate healing. The effect of gravity on uterine corpus also increases counteracting forces. Niches are mostly found in retroflexed uterus [10], [11], [19].

He *et al.*, 2016, used posterior wall thickness according to same scar center location to represent anterior wall thickness before CS because normal anterior and posterior uterine wall thicknesses are similar to each other in normal women [28]. The relative decrease in anterior wall myometrial thickness in scar area compared to posterior uterine wall was significantly higher in women with post-CS niche who had postmenstrual spotting with mean reduction 79% compared to 57% in women without postmenstrual spotting [23].

Niche frequency distribution and niche form in post CS wound

Niche is observed in 50–60% of women after CS. A prospective and cohort study reported spotting in 30% of women with niche at 6–12 months after CS surgery compared with 15% of women without niche [29]. Approximately half of ($n = 16$) women with post-CS niche who experienced postmenstrual spotting had droplet niche shape and 18 patients (53%) women with postmenstrual spotting had semicircular niche shape ($p = 0.02$) [23]. From Vaate *et al.*, research on 2011, it was found that the most common niche shapes were semicircular (50.4%), triangular (31.6%), droplet shapes (10.3%), and inclusion cysts (6.8%) [27].

Niche formation may result from poor wound repair of CS surgical Scar. Some of risk factors that have potential to cause niche divided to surgery or patient related. Factors related to lower uterine segment such as cervical dilatation above 5 cm and duration of labor more than 5 h are predisposing factors for niche occurrence because myometrium is getting thinner and less vascularized which will lead to inadequate wound repair [10], [11], [27].

Niches often appear after CS, in more than 95% of patient's uterus is closed by single layer, without peritoneal closure [30]. This closing strategy increases niche potential risk. In a recent survey conducted in Netherlands on 2015, among 528 gynecologists and residents, it was confirmed that majority (92.2%) applied a single layer closure using continuous multifilament sutures (96.2%) and unlocking techniques (87.1%). About half of gynecologists use endometrial preservation techniques. The peritoneum was not closed by 86.2% gynecologists. The meta-analysis found that niche relative risk (RR) was 2.38 (95%, CI 0.63–8.96) [10].

Closure techniques have changed over the years and there is no uniform standard for CS or uterine closure procedures. Two meta-analyses reported low to moderate evidence that closure of single- and double-layer uterine incisions was associated with same rate of niche findings on ultrasound examination [31], [32]. Then, the presence of adhesions or adhesions on abdominal wall will pull CS CSar toward abdominal wall causing an opposite pull on CS CSar therefore wound repair is disrupted. Then, patient factors such as presence of predisposing genes that contribute to impaired wound repair, poor hemostasis, inflammation, or adhesion, and post-operative infection. Gestational diabetes mellitus (GDM) (odds ratio = 1.73), former CS (odds ratio = 3.14), and increased BMI (odds ratio = 1.06) were independent risk factors [10], [33].

Correlation of blood glucose on niche incidence of post-CS patients

The longest follow-up studies have shown that up to 50% of women with a history of GDM develop during 20–30 year period or 30% of patients develop DM within 10 years of delivery [36], [37], [38]. Blood glucose cutoff value was determined at 155 mg/dl (area under the curve [AUC] 0.78; sensitivity, 88.6%; specificity, 57.5%), and HbA1c cutoff value was 5.3% (34 mmol/mol). (AUC 0.62, sensitivity, 61.5%; specificity, 91.2%) for determining postpartum glucose intolerance [34].

Gestational diabetes (odds ratio, 1.73), history of previous CS (OR, 3.14), and advanced BMI (OR, 1.06) were independent risk factors. The risk increases by 6% for each additional unit increase in BMI. Longer active labor before emergency CS also increased risk (OR, 1.06). However, there is

no difference between elective and emergency CS [33]. After bivariate analysis, there was no significant relationship between blood glucose and hemoglobin levels on niche incidence in post-CS patients. Several human studies have reported an association between potential niche development and BMI, preeclampsia, or hypertension, but the mechanisms involved remain unclear [35].

Conclusion

There was no significant relationship between blood sugar levels on niche incidence in post-CS patients.

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