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## Prevalence of Cesarean Section Scar Endometriosis: Ten-Year Experience of a Tertiary Center and Retrospective Evaluation of 40 Cases

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### ABSTRACT

**Objective:** Cesarean scar endometriosis (CSE) is the presence of ectopic endometrial tissue at the site of the previous cesarean section (CS) scar. The prevalence varies between 0.04 and 0.53. We aimed to evaluate the women with CSE in the past 10 years in Niğde.

**Materials and Methods:** The medical records of Ömer Halisdemir University Training and Research Hospital and the single private hospital were retrospectively analyzed through electronic databases between January 2010 and January 2020. Pathological reports with the diagnosis of abdominal wall endometriosis were distinguished. The ones excised from a CS scar were included into the study. For each patient clinical, obstetric and surgical characteristics were recorded.

**Results:** Forty women were included into the study with an average age of  $31.6 \pm 5.9$  years. The diameter of the CSE lesion was positively correlated in medium strength with body mass index (BMI) at the time of CS ( $r=0.448$ ,  $p=0.019$ ). Similarly, the diameter of the lesion and weight gain during pregnancy was correlated in medium strength ( $r=0.423$ ,  $p=0.014$ ). The onset of symptoms was correlated in medium strength with lactation period ( $r=0.539$ ,  $p=0.001$ ). The rate of correct initial diagnosis was significantly higher in years 2015–2019 than in years 2010–2014 ( $p=0.004$ ). The CSE prevalence was 0.15 in the present study.

**Conclusion:** High BMI values at the time of CS and weight gain during pregnancy might be contributors of CSE development. Furthermore, lactation might have protective effects against CSE.

**Keywords:** Abdominal wall endometriosis, cesarean scar endometriosis, cutaneous endometriosis

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### INTRODUCTION

Caesarean scar endometriosis (CSE) is the presence of ectopic endometrial tissue between the muscles and cutaneous tissue of the abdominal wall at the site of the previous caesarean section (CS) scar. Despite the fact that CS is, globally, the most frequently performed abdominal surgery, there are only limited number of case series and case reports about the subject in the literature (1, 2). The main reason is the late onset and rarity of the condition. In the literature, the prevalence for CSE obtained from retrospective case series varies between 0.04 and 0.53 (3).

The mainstay of the pathophysiological mechanism of CSE is implantation theory, first experimentally described by Ridley and Edwards in 1958 (4). According to the implantation theory, viable endometrial tissue is carried during the procedure and directly inoculated into the surgical wound (4). Following the implantation hormonal stimulus and/or immunologic factors lead to the proliferation of endometrial glandular cells and development of metaplasia in the surrounding tissue (5, 6) On the other hand, there are certainly other factors contributing to the growth of ectopic endometrial tissue since only very few of the women undergoing CS suffer the condition (2). Although some demographic factors, menstrual characteristics and environmental factors were investigated, information from these reports is inconsistent and varies widely (7, 8).

Women with CSE typically present with (cyclic/continue) pain accompanying with a (painful/pain free) swelling at the site of the previous CS. Most of the time these patients are referred to general surgeons with initial diagnosis of subcutaneous mass or incisional hernia.

Ömer Halisdemir University Research and Training Hospital is the only public hospital and tertiary reference center addressing a population of 350.000. In addition, there is only one private hospital in the same region. By combining the data obtained from both hospitals, we aimed to evaluate and publish 10-year experience with CSE and calculate the prevalence of CSE in Niğde.

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## MATERIALS and METHODS

The study was carried out at Ömer Halisdemir University Training and Research Hospital and Private Hayat Hospital. The bed capacity of both hospitals is 540 and 80, respectively. The CS numbers of our city for the same date range were obtained from local health authorities.

All the procedures in this study were in compliance with the institutional and national research committee ethical standards and the 1964 Helsinki Declaration and its later amendments. Approval for the study was granted by the Ömer Halisdemir University Non-Invasive Clinical Research Ethics Committee (27.08.2020; 2020/46).

The electronic medical records of Ömer Halisdemir University Training and Research Hospital and Private Hayat Hospital were retrospectively analyzed using both hospitals' computer based database systems between January 2010 and January 2020. Pathological reports with the diagnosis of abdominal wall endometriosis were distinguished (n=46). Among these specimens, the ones excised from a CS scar, confirmed by the surgical operation report, were included into the study. Women with missing data were excluded from the study. All women had Pfannenstiel incision and it is important to emphasize that the characteristics of CS noted for each patient is the CS operation giving rise to CSE.

We constituted a follow-up form for each patient. We recorded clinical characteristics (age, height, weight at the beginning of pregnancy, and weight at the time of CS), obstetric history (parity, previous deliveries, CS number, gestational week at the time of CS, cervical dilatation recorded before CS decision, and lactation period), and the history of symptoms (the time of the appearance of symptoms, time until excision, and the characteristics of pain and the lesion). Furthermore, the pathological report and the surgical operation report (initial diagnosis, size, and location of the lesion) were incorporated into the patient follow-up form.

### Statistical Analysis

Demographic characteristics were expressed by descriptive analysis. Body mass index (BMI) was calculated according to formula  $BMI = \text{weight (kg)} / \text{height(m)}^2$ . The categorical variables were compared with Pearson  $\chi^2$  test or Fisher exact test where appropriate. In addition, bivariate correlation test with Pearson coefficient was used to determine the correlation between qualitative variables. For all statistical analysis,  $p < 0.05$  with a 95% CI was considered to be significant and SPSS Statistical Package version 22.0 (SPSS Inc., Chicago, IL) was used.

## RESULTS

There were 40 women included into the study. The clinical characteristics of the patients are presented in Table 1. The average age of the patients was  $31.6 \pm 5.9$  years. The mean BMI of the patients at the onset of pregnancy was  $26.8 \pm 5.2$  and the mean BMI at the time of CS was  $33.1 \pm 6.3$ . The weight gain of the patients during pregnancy was  $15.9 \pm 6.5$  kg. The diameter of the CSE lesion and BMI at the beginning of the pregnancy was in weak correlation ( $r = 0.384$ ,  $p = 0.048$ ). The diameter of the lesion and BMI at the

**Table 1.** Clinical characteristics of the patients

	Mean $\pm$ SD
Age (years)	31.6 $\pm$ 5.9
Age at CS (years)	26.8 $\pm$ 5.1
(kg/m <sup>2</sup> )	26.8 $\pm$ 5.2
BMI 2 (kg/m <sup>2</sup> )	33.1 $\pm$ 6.3
Weight gain (kg)	15.9 $\pm$ 6.5
Parity (n)	1.5 $\pm$ 0.6
Gestational week (week)	39.3 $\pm$ 0.9
Lactation period (months)	10.6 $\pm$ 7.4

SD: Standard deviation; BMI: Body mass index; BMI 1: BMI at the beginning of pregnancy; BMI 2: BMI at the time of CS

**Table 2.** Correlation coefficient, r (strength of correlation), and p values of the correlation analysis

Diameter of the endometriotic lesion	r	p
BMI 1	r=0.384 (weak)	p=0.048
BMI 2	r=0.448 (medium)	p=0.019
Weight gain	r=0.423 (medium)	p=0.014
Previous CS	r=0.196	p=0.259
Onset of symptoms		
Lactation	r=0.539 (medium)	p=0.001

SD: Standard deviation; BMI: Body mass index; BMI 1: BMI at the beginning of pregnancy; BMI 2: BMI at the time of CS; CS: Cesarean section

time of CS correlated in medium strength ( $r = 0.448$ ,  $p = 0.019$ ). Similarly, a medium strength positive correlation was significantly detected between the diameter of the lesion and weight gain during pregnancy ( $r = 0.423$ ,  $p = 0.014$ ). The correlation coefficient and P values are summarized in Table 2.

Obstetrical characteristics of the patients and the parameters of the CS are listed in Table 3. Eleven women had at least one previous normal vaginal delivery (NVD). The CS operation giving rise to CSE was first CS in 21 (52.5%) of patients, second in 15 (37.5%) and third in 4 (10%) of the patients. There was no significant correlation between the previous number of CS operations and the diameter of the lesion ( $r = 0.196$ ,  $p = 0.259$ ). In our study, gestational week at the time of CS was  $39.3 \pm 0.9$  weeks and no second trimester hysterotomy was performed. Only 8 (20%) women underwent CS after the spontaneous onset of labor. The average cervical dilatation of those patients was  $4.1 \pm 2.1$  cm. In the remaining 32 (80%), CS was undertaken before the spontaneous onset of labor with various indications. The indications are listed in Table 3. The average lactation period of the study group was  $10.6 \pm 7.4$  months. The onset of symptoms after the CS operation was significantly correlated in medium strength with lactation period ( $r = 0.539$ ,  $p = 0.001$ ). The time elapsed from CS until the appearance of the symptoms was  $20.2 \pm 14.8$  months. The time interval between the two operations, the CS, and the CSE operations was 1–11 years, with a mean of 4.1 years. The average diameter of the lesion excised was  $4.5 \pm 1.7$  cm.

**Table 3.** Obstetrical characteristics and parameters of CS

	n	%
Previous NVD		
Yes	11	27.5
No	29	72.7
Previous CS		
1	21	52.5
2	15	37.5
3	4	10.0
CS indication		
Absolute	15	37.5
Relative	25	62.5

Absolute indications: Fetal distress, Cephalopelvic disproportion, Placenta previa, Relative indications: Repeated CS, Breech presentation, Multiple gestation, Failure to progress, IVF pregnancy. CS: Cesarean section; NVD: Normal vaginal delivery

**Table 4.** Characteristics of the symptoms

	n	%
Pain		
Continue pain	13	32.5
Cyclic pain	25	62.5
No pain	2	5
Mass		
Painful mass	29	72.5
Pain free mass	5	12.5
No mass	6	15.0
Localization		
Right	14	35.0
Left	25	62.5
Middle	1	2.5
Initial referral to		
General surgery	37	92.5
Obstetrics and gynaecology	3	7.5

The characteristics of the symptoms are listed in Table 4 and were as follows; 13 (32.5%) patients stated continuous pain, 25 (62.5%) stated cyclic pain, and two women had no pain at presentation. When questioned for the presence of a mass, 29 (72.5%) declared the presence of a painful mass, 5 (12.5%) had pain free mass, and 6 (15%) complained of no mass. The localization of the CSE lesion was right corner of the Pfannenstiel incision in 14 (35%) patients, left corner in 25 (62.5%) patients, and in the middle of the previous scar in one patient (2.5%).

Initial diagnosis was correct in 21 (52.5%) of the women and vast majority (n=37; 92.5%) attended or referred to general surgery clinic instead of gynecology. In the 1<sup>st</sup> 5 years of the study, clinicians were able to make the correct initial diagnosis in only 25% of the patients, whereas in the second half of the study the initial diagnosis was correct in 71% of cases (Table 5). The rate of cor-

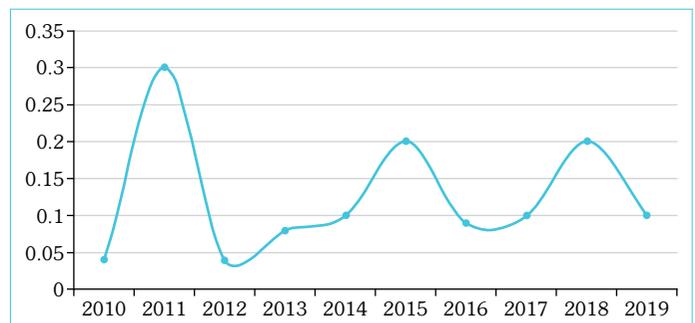
**Table 5.** The rates of correct initial diagnosis in the first half and in the second half of the study

Initial diagnosis	2010–2015		2015–2020		p
	n	%	n	%	
Correct	4	19	17	81	0.04
Incorrect	12	63.2	7	36.8	

**Table 6.** Numbers of NVD, CS, and CSE occurred in city of Niğde

Year	NVD (n)	CS (n)	CSE (n)	CSE prevalence (%)
2010	3648	2259	1	0.04
2011	3573	2080	7	0.3
2012	3405	2393	1	0.04
2013	3264	2343	2	0.08
2014	3242	2825	5	0.1
2015	3124	2843	6	0.2
2016	3447	3088	3	0.09
2017	3203	3018	3	0.1
2018	2957	3075	9	0.2
2019	2921	2793	3	0.1
Total	32784	26717	40	0.15

NVD: Normal vaginal delivery; CS: Cesarean section; CSE: Cesarean scar endometriosis

**Figure 1.** Year-based frequency rates in city of Niğde between 2010 and 2019

rect diagnosis was significantly higher in years 2015–2019 than in years 2010–2014 (p=0.004).

The yearly based CS and CSE numbers are listed in Table 6. In the past 10 years, 26.717 CS occurred and the CSE prevalence was 0.15 in the present city. The graph of subsequent CSE occurrence according to years is shown in Figure 1.

## DISCUSSION

The present study evaluated clinical characteristics of women diagnosed with CSE to determine potential risk factors. The highlights of the present study are the demonstration of; (1) the medium strength correlation between diameters of the lesion with BMI of the women at the time of CS and, (2) the medium strength corre-

lation between the lactation period and the onset of symptoms for the 1<sup>st</sup> time in literature to our knowledge.

The prevalence of CSE was calculated as 0.15 in the present study. Singh et al. (9) reported a prevalence value of 0.2% derived from their retrospective study involving 10 years similar to the present study. One of the most important points in studies for public health issues, like incidence or prevalence calculations, is to study closed circuit populations as far as possible. As an example, in the study conducted by Andolf et al. (10), the Swedish Patient Register and the Swedish Medical Birth Registry were investigated, revealing a CSE incidence of 0.1. Similarly, we constituted a considerably closed circuit population due to the fact that our university research and training hospital is the only public hospital and there is only one private hospital providing medical care in our city. The calculated prevalence value is in accordance with the value calculated by Andolf et al. (10).

Furthermore, a yearly based analysis of CSE occurrence was performed and a wavy movement in the graph was detected. In the literature, there is no information regarding the incline or decline of CSE occurrence. On the other hand, both movements are possibly expected. The most important preventive measure of CSE is taking necessary precautions to minimize contamination of the wound with live endometrial cells (1). Therefore, a decline in the CSE occurrence over time can be expected because the operational conditions are improving every single year in all around the world. On the contrary, one can expect an incline in the CSE occurrence as well. Number of CS operations demonstrated a mild increase over time in our study. Moreover, recognition of CSE by clinicians is increasing globally. In the present study, the initial diagnosis was correct only in 25% in the first 5 years of the study but was correct in 71% in the second half of the study. This statistically significant difference demonstrates that the rate of correct initial diagnosis significantly rises over time. This might be attributed to deliberately use of additional diagnostic tools such as USG, MRI, FNAB, as well as recognition of the condition by clinicians (6, 11). To sum up, the wavy course of yearly frequency graphic is probably the result of multiple factors. The number of the patients and the follow-up time of the present study might not suffice for concluding an upward or a downwards tendency in occurrence over time.

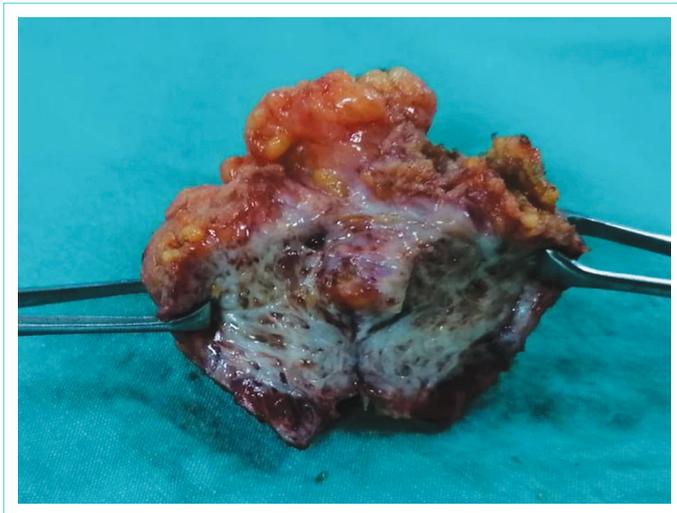
The widely accepted pathophysiological mechanism of CSE involves mainly three steps; transportation, implantation-survival, and finally proliferation of ectopic endometrial cells in the scar of previous CS (1, 4, 5). During CS operation live endometrial cells are inevitably transported to the cutaneous wound through sponges used to swab uterine cavity, aspirator, instruments, and even gloves (12). Especially corners of the Pfannenstiel incision are vulnerable for contamination and accumulation of endometrial cells (8). In the present study, predominantly left corner of the Pfannenstiel incision was involved (62.5%). This predominance might be explained by considering the fact that removing the dirty sponges, changing instruments and using the aspirator is handled by the assistant who occupies the left side of the patient most of the time. In addition, obesity increases and facilitates the contamination of endometrial tissues in the subcutaneous layers (13). In our study, the average BMI at the beginning of the pregnancy was in the overweight group and the average

BMI at the time of CS was in the obese group. Furthermore, in the present study, the diameter of the lesion was significantly correlated in medium strength with the patient's BMI at the time of CS, as well as weight gain during pregnancy. Although in medium strength, these correlations might be possibly the result of inevitable accumulation of live endometrial cells in the stratified adipose and subcutaneous tissues of obese women during CS. In the literature, there are few reports regarding BMI scores of CSE patients (7, 13–18). However, in all of them, the BMI recorded was the BMI at the time of CSE operation. On the other hand, our results demonstrated for the first time in the literature that high BMI at the time of CS might be a potential risk factor for CSE development. Case controlled studies are needed to further investigate this issue.

Following the seeding of endometrial cells to the wound, the second step of the CSE mechanism takes place. Wicherek et al. (5) concluded that CS performed before spontaneous onset of labor may substantially increase the risk of occurrence of scar endometriomas. Immune tolerance of pregnancy suppresses cellular immunity providing a survival mechanism for the fetus, but consequently might be the pitfall for development of scar endometriosis (19). Alpha- and beta-free globulins secreted by decidual cells during the process of cervical ripening might play a role in protection against invading cells (20). In the present study, CS was undertaken before the spontaneous onset of labor in 80% of the patients with various indications, only which 37.5% was absolute CS indication. Spontaneous onset of uterine contractions following cervical ripening is the result of timely termination of immune tolerance of pregnancy (5). A premature interruption in this mechanism facilitates the survival of transported endometrial cells.

Finally, in women with reproductive capacity cyclic hormonal stimulus proliferates and invades the surrounding tissues in time (19). In general, lactation suppresses hormonal stimulus during puerperium and some proposals were made regarding the protective effects of lactation against CSE but without scientific evidence (21). Statistical analysis in our study demonstrated that lactation period is positively correlated in medium strength with the time between CS and the onset of symptoms. In other words, the women with shorter lactation periods had relatively earlier symptoms. This information might constitute a baseline for further investigations necessary to confer the effects of lactation. In the literature, the time between the surgery and the onset of symptoms of CSE vary widely (8, 11, 22, 23). In some reports, the time between the surgery and the onset of symptoms was reported as 1 month (8, 22). Considering the pathophysiologic mechanism, the formation of a painful mass in 1 month is unexpected. In the present study, the average time elapsed from the CS until the onset of symptoms was  $20.2 \pm 14.8$  months (range 4–60). The average time and minimum time elapsed from the CS in the present study are in accordance with rest of the literature (1, 11, 23).

In the present study, no correlation was detected between the diameter of the lesion and the number of the previous CS operations. In more than half of the patients (52.5%), the CS predating CSE was the first CS operation of the patient. Previously, other researchers investigated whether the number of previous CS operations increases the occurrence of CSE but no significant relation was detected as in the present study (15).



**Figure 2. Treatment is excision of the lesion with safety margins**

The cyclic pattern of the symptoms synchronous with menstrual cycle, occurrence after CS and worsening with time alarms the clinician and differential diagnosis can easily be made without further intervention (18). The typical presentation of cyclic/continuous pain and/or mass in the corners of the previous CS scar referred to 95% of the population in the present study. Further, diagnostic measures are rarely necessary (15). Cases in which physical examination or anamnesis is insufficient (morbid obesity, mentally debilitated, etc.) or in which malignancy is suspected USG, MRI, and even FNAB are indicated after ruling out incisional hernia (1, 12). Once diagnosed the treatment is surgical excision (1). The recommended technique is excision of the lesion with 1 cm safety margins (6) (Fig. 2). Although medical treatment with GnRH-agonist was previously used, no satisfactory result was obtained (12, 24).

The retrospective design of the present study is the main limitation. Information bias encountered in retrospective reviews is result of missing or illegible data and/or errors in data collection. We cannot comment on the risk factors of CSE with this study design. On the other hand, main power of this study is the relatively large number of patients and long observation time. Although the correlations detected are in medium strength, findings of the present study are suggestive that high BMI values at the time of CS and weight gain during pregnancy might contribute to the development of CSE. In addition, the medium strength correlation between the duration of lactation and the time between the CS and the appearance of symptoms might be a starting point for further investigations on whether lactation has any protective affect against CSE. Better recognition of frequency, risk factors, clinical presentation, and characteristics of CSE would certainly guide health-care professionals more precisely while handling this miscellaneous condition in the future.

**Ethics Committee Approval:** The Ömer Halisdemir University Non-Invasive Clinical Research Ethics Committee granted approval for this study (date: 27.08.2020, number: 2020/46).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – AE; Design – AE, PE; Supervision – AE; Resource – AE, PE; Materials – AE, PE; Data Collection and/or Processing – AE, PE; Analysis and/or Interpretation – AE, PE; Literature Search – PE; Writing – AE, PE; Critical Reviews – AE, PE.

**Conflict of Interest:** The authors have no conflict of interest to declare.

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