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Management and reproductive outcomes following cesarean scar pregnancy: experiences of two tertiary centers in a cohort of 60 women

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ABSTRACT

Aims: This study aims to analyze the treatment approaches and reproductive outcomes of women diagnosed with cesarean scar pregnancy (CSP).

Methods: A retrospective analysis was conducted on sixty patients diagnosed with CSP between January 2020 and December 2023 at two tertiary centers with a combined total of 49,733 births during the study period. Demographic, clinical, and laboratory characteristics, complications, treatment methods, and reproductive outcomes were examined. Patients were categorized into two groups based on their treatment approach: isolated treatment (n=45, 75%) and combined treatment (n=15, 25%), and the outcomes of the two groups were compared.

Results: The mean age of all patients was 34 years (±5.5) (range: 21-46). The mean gestational age at admission was 6.86 weeks (±1.82), with 35% showing positive fetal heartbeats. Complications occurred in 28.3% of cases, with hematomas being the most common (26.7%). The combined treatment group had higher rates of blood transfusions and complications, including hematomas and bladder injuries (p=0.005 and p<0.001, respectively). Of the 16 patients (26.7%) who desired future pregnancy, 14 successfully conceived. Among these pregnancies, 7 resulted in early pregnancy loss, while 7 resulted in live births, all of which were delivered after 35 weeks of gestation.

Conclusion: Early diagnosis and evidence-based treatment of CSP are essential for preventing life-threatening obstetric complications. Larger, prospective studies are required to establish optimal diagnostic and treatment strategies.

Keywords: Cesarean scar pregnancy, treatment, treatment approaches, reproductive outcome

INTRODUCTION

Cesarean scar pregnancy (CSP) is defined as the implantation of a gestational sac within the scar of a previous cesarean delivery.[1] The prevalence of CSP has been increasing in recent years, with reported frequencies ranging from 1 in 1800 to 1 in 2000 pregnancies.[2] CSP poses a high risk of both short-term and long-term adverse outcomes, including severe hemorrhage, uterine rupture, hysterectomy, placenta accreta spectrum (PAS) disorders, compromised reproductive outcomes, and maternal death.[3,4] Early prenatal diagnosis of CSP is critical for informing prenatal counseling and treatment decisions.

The development of CSP is strongly associated with the presence of a cesarean scar defect, which may disrupt normal decidualization and increase the risk of abnormal implantation of the gestational sac.[5] Although the precise etiopathogenesis of CSP remains unclear, research suggests that scar defects create a vulnerability for improper placental attachment.[6,7] As first demonstrated by Timor-Tritsch et al.,[8] CSP shares histological features with pregnancies affected by PAS disorders, further indicating a possible link between cesarean scar abnormalities and abnormal placentation.

Ultrasound imaging plays a pivotal role in diagnosing cesarean scar pregnancies. Various classification systems have been developed to better categorize CSP. One of the most well-known systems is that studied by Kagen et al.,[9] which distinguishes between two types of CSP: Type 1, where the pregnancy is located "on the scar" (well-healed tissue), and Type 2, where the pregnancy is "in the niche" (imperfectly healed scar). Additionally, measurement of residual myometrial thickness between the bladder and the

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gestational sac in scar pregnancies is one of the important ultrasonographic measurements that provide information about prognosis.[10]

Despite the growing number of case series in the literature, optimal treatment strategies and prognosis for subsequent pregnancies after CSP remain uncertain. Management options vary widely, ranging from expectant management, uterine suction curettage, local excision via laparotomy or laparoscopy, hysteroscopy, uterine artery embolization (UAE), methotrexate (MTX) therapy, to hysterectomy.[11] However, no standardized diagnostic or management guidelines currently exist. Therefore, every case of CSP that is managed and documented provides valuable insights and contributes to the broader understanding of this condition. Moreover, the long-term reproductive outcomes for women who wish to conceive following CSP have been the subject of longitudinal studies.[12,13] This study aims to investigate the etiology, risk factors, clinical presentation, efficacy of various treatment modalities, and reproductive outcomes in women diagnosed with cesarean scar pregnancies.

METHODS

This retrospective cohort study analyzed the data of 60 patients treated for CSP and subsequently followed over the long term at Ankara Etlik City Hospital and Etlik Zubeyde Hanım Women's Health Training and Research Hospital, between 2020 and 2023. These well-known reference centers reported a total of 49,733 births over the four-year study period in Turkey. The study was started with the approval of Ankara Etlik City Hospital Ethics Committee (Decision No: 2023-683). Since the study was designed retrospectively, written informed consent from patients was waived.

We examined demographic, clinical, and laboratory characteristics, complications, treatment methods, and reproductive outcomes of the patients. Variables analyzed included maternal age, body mass index (BMI), smoking status, gravidity, parity, history of —abortions, ectopic pregnancies, scar pregnancies, curettage, cesarean sections (CSs)- number of previous curettages and CSs, history of uterine surgery, and the interval between the last pregnancy and the current pregnancy. Presenting symptoms were categorized as asymptomatic, symptomatic (including abnormal vaginal bleeding, abdominal pain, or both). Ultrasonographic and laboratory data were collected, including gestational age, presence of fetal heartbeat, duration of hospitalization, β-human Chorionic Gonadotropin (β-hCG) levels at admission, β-hCG half-life, and hemoglobin levels at admission and discharge.

Transabdominal and transvaginal ultrasound examinations were conducted using Voluson (GE Healthcare, Milwaukee, Wisconsin) E6 and E8 machines. The diagnosis of CSP was based on the following criteria: (1) absence of a gestational sac in the uterine cavity or cervical canal; (2) gestational sac located in the anterior isthmus of the uterus, with or without fetal heart activity; (3) a defect or thinning of the myometrium between the bladder and the gestational sac; (4) presence of increased vascularity around the gestational sac by Doppler examination.[14–16] (Figure 1). Three-dimensional ultrasound was used infrequently but could aid in diagnosis when available.[17]

Although no algorithm was used to determine treatment modalities, treatment selection was largely based on patient-based assessments and clinical experience. In particular, factors such as the presence of a fetal heartbeat, β-hCG levels, and the clinical condition of the patient were important factors affecting the treatment decision. A range of treatment modalities was identified, including isolated treatments (e.g., dilation and curettage with or without a Foley catheter, methotrexate, wedge resection) and combined treatments (e.g., dilation and curettage with or without a Foley catheter+methotrexate, methotrexate+laparotomic wedge resection, and dilation and curettage+methotrexate+laparotomic wedge resection). Patients were categorized into two groups based on their treatment approach: isolated treatment (using a single method) and combined treatment (using multiple methods). These groups were then compared in terms of clinical outcomes.

Reproductive outcomes for women seeking future pregnancies after CSP treatment were documented through digital records and telephone interviews. Outcomes included early pregnancy loss (defined as loss before 13 weeks of gestation) and live birth.

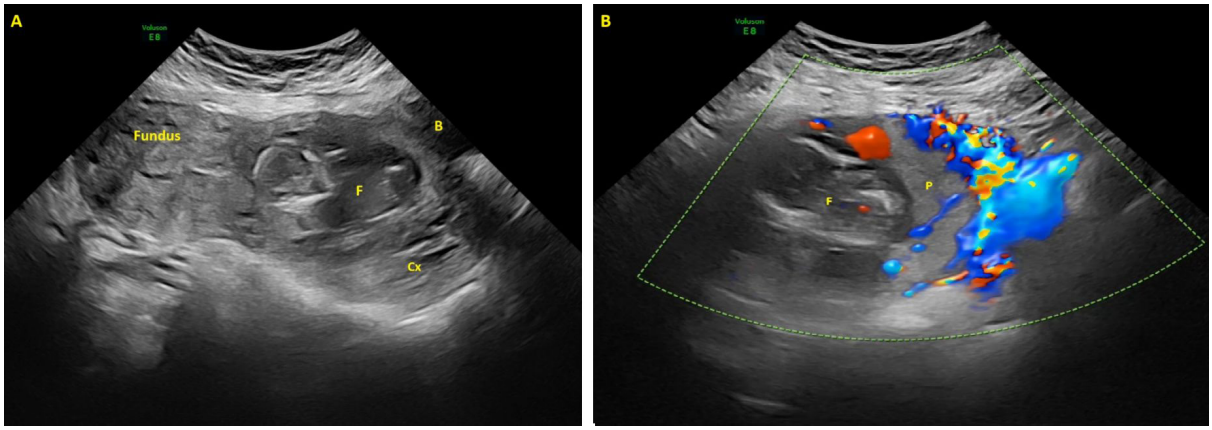

Figure 1. A) 12 weeks and 2 days cesarean scar pregnancy on grayscale imaging (F=Fetus, B=Bladder, Cx=Cervix) **B)** Color Doppler image showing increased vascularity surrounding the placental region (F=Fetus, P=Placenta)

Statistical Analysis

Stastical analysis was performed using IBM's Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corporation, Armonk, New York, US). Results are presented as mean±SD, median (min-max), and n (%). To check the normality of data distribution, the Shapiro-Wilk test was utilized. Group differences were evaluated using the Independent Samples T-test if normally distributed, and the Mann-Whitney U test if non-normally distributed, and the relationships between categorical variables were evaluated using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

During the four-year study period, the incidence of CSP was approximately 1.2 per 1000 (60/49,733) pregnancies. Demographic, clinical, and laboratory characteristics of patients are shown in Table 1. The mean age of the patients was 34 years (±5.5), ranging from 21 to 46 years. No adolescent pregnancies (≤19 years) were identified, although 46.7% of the cohort were advanced maternal age pregnancies (≥35 years). The average BMI was 26.1 (±4.3), with a range of 17.7 to 37.4. Smoking was reported by 13.3% of patients. The mean gravidity was 4.15 (±1.93). A history of ectopic pregnancy was present in 1.6% of patients, and 3.3% had experienced a prior scar pregnancy. Curettage had been performed in 45% of cases, with 36.7% undergoing it once. All patients had a history of cesarean section, with varying numbers of previous procedures, and 5% had undergone other types of uterine surgery. The interval between the last pregnancy and the current CSP averaged 4.57 years (±3.79). At the time of admission, the mean gestational age was 6.86 weeks (±1.82), and 35% of cases had a positive fetal heartbeat. The average length of hospital stay was 5.46 days (±4.16). The mean serum β-hCG level at admission was 13,009.9 IU/L (±18,582.1), with 36.7% of patients presenting with levels ≥10,000 IU/L. The β-hCG half-life ranged from 12 to 240 hours, with a mean of 62.7 hours (±68.7). The mean hemoglobin level during hospitalization was 12.2 g/dL (±1.7), and the mean discharge hemoglobin was 11.4 g/dL (±1.7). Blood transfusions were required in 16.7% of cases. Underlying health conditions were present in 20% of patients, while 80% had no comorbidities. Hypertension, diabetes, hypothyroidism, hyperthyroidism, and epilepsy were observed in 6.6%, 5%, 3.4%, 3.4%, and 1.7% of patients, respectively. Complications occurred in 28.3% of cases, with hematomas being the most common (26.7%). Bladder injury occurred in 1.7% of cases. Complications occurred in 28.3% of cases, with hematomas being the most common (26.7%). Bladder injury occurred in 1.7% of cases. Treatment modalities included isolated approaches (75%) and combined methods (25%). The most frequent isolated treatment was dilation and curettage (40%), either with (28.3%) or without (40%) the use of a Foley catheter. The most

Table 1. Demographic, clinical, and laboratory characteristics of patients with scar pregnancy

	Mean±SD	Median (min-max)	Number (n), Percent (%)
Maternal age (year)	34±5.5	33.5 (21-46)	-
Adolescent pregnancy ≤ 19 year	-	-	0
Advanced maternal age ≥ 35 year	-	-	28 (46.7%)
BMI (kg/m²)	26.1±4.3	25.9 (17.7-37.4)	-
Smoking	-	-	8 (13.3%)
Gravidity	4.15±1.93	4 (2-10)	-
Parity			
Nulliparous	-	-	0
Multiparous	-	-	60 (100%)
Living children	2.28±1.35	2 (1-8)	-
Abortus	0.78±1.12	0 (0-4)	-
History of ectopic pregnancy	-	-	1 (1.6%)
History of scar pregnancy	-	-	2 (3.3%)
History of curettage	-	-	27 (45%)
Previous curettage number			
0	-	-	33 (55%)
1	-	-	22 (36.7%)
2	-	-	3 (5%)
3	-	-	1 (1.7%)
≥4	-	-	1 (1.7%)
History cesarean section	-	-	60 (%100)
Previous cesarean section number			
1	-	-	21 (35%)
2	-	-	20 (33.3%)

Continued

Table 1. Demographic, clinical, and laboratory characteristics of patients with scar pregnancy

	Mean±SD	Median (min-max)	Number (n), Percent (%)
3	-	-	12 (20%)
≥ 4	-	-	7 (11.6%)
Previous uterine surgery	-	-	3 (5%)
Time from last pregnancy to this pregnancy (year)	4.57±3.79	3 (1-17)	-
Pregnancy week (day)	6.86±1.82	6.3 (4-12)	-
Fetal heartbeat			
Positive	-	-	21 (35%)
None	-	-	39 (65%)
Hospitalization duration (day)	5.46±4.16	3 (2-17)	-
β-hCG at admission (IU/L)	13,009.9±18,582.1	5862 (429-85,297)	-
β-hCG ≥10,000 (IU/L)	-	-	22 (36.7%)
Half-life of β-hCG (hour)	62.7±68.7	24 (12-240)	-
Hemoglobin at admission (g/dL)	12.2±1.7	12.6 (6.2-16)	-
Hemoglobin at discharge (g/dL)	11.4±1.7	11.6 (7.6-14.5)	-
Blood transfusion	-	-	10 (16.7%)
Comorbidity			
None	-	-	48 (80%)
Yes			12 (20%)
Hypertension	-	-	4 (6.6%)
Diabetes	-	-	3 (5%)
Hypothyroidism	-	-	2 (3.4%)
Hyperthyroidism	-	-	2 (3.4%)
Epilepsy	-	-	1 (1.7%)
Complication			
None	-	-	43 (71.7%)
Yes			
Hematoma	-	-	16 (26.7%)
Bladder injury	-	-	1 (1.7%)
Treatment method			
Isolated	-	-	45 (75%)
Dilation curettage	-	-	41 (40%)
With Foley	-	-	17 (28.3%)
Without Foley	-	-	24 (40%)
Methotrexate	-	-	2 (3.3%)
Wedge resection	-	-	2 (3.3%)
Combined	-	-	15 (25%)
Dilation curettage+Methotrexate	-	-	6 (10%)
Dilation curettage+Foley+Methotrexate	-	-	6 (10%)
Methotrexate+Wedge resection	-	-	2 (3.3%)
Dilation curettage+ Methotrexate+Wedge resection	-	-	1 (1.7%)

Abbreviations: BMI: Body mass index, SD: Standart deviation, Min-Max: Minimum-Maksimum

common combined treatments were dilation and curettage + methotrexate (10%) and dilation and curettage + a Foley catheter + methotrexate (10%) (Table 1).

Patient symptoms are listed in Table 2. In the cohort, 56.7% were symptomatic, while 43.3% were asymptomatic. The most common symptom was abnormal vaginal bleeding (35%), followed by abdominal pain (18.3%), and a small percentage (3.3%) experienced both (Table 2).

Table 2. Presenting symptoms of patients

	n (%)
Symptoms	
Asymptomatic	26 (43.3%)
Symptomatic	34 (56.7%)
Abnormal vaginal bleeding	21 (35%)
Abdominal pain	11 (18.3%)
Abdominal pain+ Abnormal vaginal bleeding	2 (3.3%)

Table 3. Comparison of patient data based on isolated vs. combined treatment			
	Isolated treatment n=45	**Combined treatment n=15**	**p**
Maternal age (year) (mean±SD)	35±6	32±5	0.069
Adolescent pregnancy ≤ 19 year (n,%)	0	0	N/A
Advanced maternal age ≥ 35 year (n,%)	24 (53.3%)	4 (26.7%)	0.073
BMI (kg/m²) (mean±SD)	26.6±4.3	24.6±4.1	0.109
Smoking (n,%)	6 (13.3%)	2 (13.3%)	N/A
Gravidity median (min-max)	4 (2-10)	4 (2-8)	0.480
Parity (n,%)			N/A
Nulliparous	0	0	
Multiparous	45 (100%)	15 (100%)	
Living children median (min-max)	2 (1-8)	1 (1-5)	0.438
Abortus median (min-max)	0 (0-4)	1 (0-4)	0.140
History of ectopic pregnancy (n,%)	1 (2.2%)	0	0.560
History of scar pregnancy (n,%)	0	2 (13.3%)	0.012
History of curettage (n,%)	18 (40%)	9 (60%)	0.177
History cesarean section (n,%)	45 (100%)	15 (100%)	N/A
Previous uterin surgery (n,%)	2 (4.4%)	1 (6.6%)	0.732
Time from last pregnancy to this pregnancy (year) (mean±SD)	4.2±3.2	5.6±5.1	0.600
Pregnancy week (day) (mean±SD)	6.7±1.8	7.3±2	0.254
Fetal heartbeat (n,%)			0.019
Positive	12 (26.7%)	9 (60%)	
None	33 (73.3%)	6 (40%)	
Hospitalization duration (day)	3.6±2.1	10.9±4.1	<0.001
β-hCG at admission (IU/L) (mean±SD)	7798±8388	28645±29745	0.001
β-hCG ≥10,000 (IU/L)	13 (28.9%)	9 (60%)	0.030
Half-life of β-hCG (hour) (mean±SD)	30.8±27.8	158.4±66.5	<0.001
Hemoglobin at admission (g/dL) (mean±SD)	12.3±1.8	30.8±27.8	0.203
Hemoglobin at discharge (g/dL) (mean±SD)	11.6±1.7	10.8±1.8	0.147
Blood transfusion (n,%)	4 (8.9%)	6 (40%)	0.005
Comorbidity (n,%)			0.136
None	34 (75.5%)	14 (93.3%)	
Yes	11 (24.5%)	1 (6.3%)	
Diabetes	3 (6.6%)	0	
Hypertension	4 (8.8%)	0	
Hypothyroidism	1 (2.2%)	1 (6.6%)	
Hyperthyroidism	2 (4.4%)	0	
Epilepsy	1 (2.2%)	0	
Complication (n,%)			<0.001
None	40 (88.9%)	3 (20%)	
Yes	5 (11.1%)	12 (80%)	
Hematoma	5 (11.1%)	11 (73.3%)	
Bladder injury	0	1 (6.7%)	
Symptoms (n,%)			0.763
Asymptomatic	19 (42.2%)	7 (46.7%)	
Symptomatic	26 (57.8%)	8 (53.3%)	
Abnormal vaginal bleeding	16 (35.6%)	5 (33.3%)	
Abdominal pain	8 (17.8%)	3 (20%)	
Abdominal pain+Abnormal vaginal bleeding	2 (4.4%)	0	

Abbreviations: BMI: body mass index, SD: Standart Deviation, Min-Max: Minimum-Maksimum

Table 3 presents a detailed comparison between patients treated with isolated and combined approaches. Both groups had similar mean and advanced maternal ages, BMIs, and obstetric histories, with no statistically significant differences. Notably, a history of scar pregnancy was found in 2 patients (13.3%) in the combined treatment group but in none of the isolated treatment group (p=0.012). The time between the last pregnancy and the current one, as well as the gestational age at admission, were similar between groups. However, the presence of a fetal heartbeat was significantly more frequent in the combined treatment group (60%) compared to the isolated group (26.7%) (p=0.019). The combined treatment group also had significantly longer hospital stays, higher β-hCG levels at admission, more cases with β-hCG ≥10,000 IU/L, and longer β-hCG half-lives (p<0.001, p=0.001, p=0.030, and p<0.001, respectively). Hemoglobin levels at admission and discharge did not differ significantly between the groups. Comorbidities were comparable between groups, though patients in the combined treatment group had a significantly higher rate of blood transfusions and complications, including hematomas and bladder injuries (p=0.005 and p<0.001, respectively). Symptom analysis revealed no statistically significant differences, with a substantial proportion of patients in both groups being asymptomatic (42.2% vs. 46.7%). (Table 3)

Pregnancy desires and pregnancy characteristics of the patients after scar pregnancy were examined in Figure 2. 16 (26.7%) patients desired pregnancy in the next period, 14 of them were able to become pregnant. Among these pregnancies, 7 resulted in early pregnancy loss, while 7 resulted in live births, all of which were delivered after 35 weeks of gestation (Figure 2).

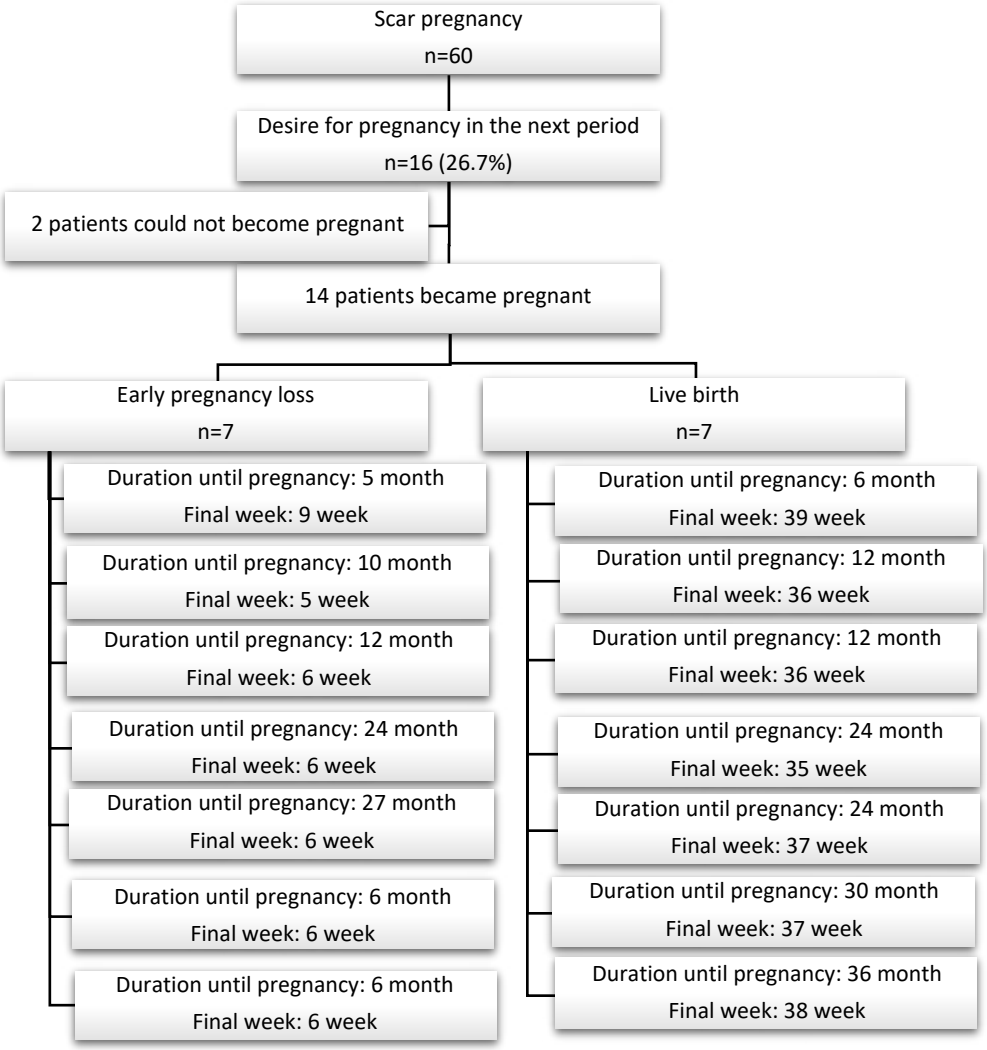

Figure 2. Pregnancy desires and pregnancy characteristics of the patients after scar pregnancy

DISCUSSION

This study provides an analysis of the demographic profiles, clinical characteristics, treatment approaches, and long-term reproductive outcomes in 60 patients diagnosed with CSP. All participants had undergone at least one cesarean section, with 35% having had only one, highlighting that CSP can occur even after minimal surgical birth history. A majority of patients (56.7%) were symptomatic upon admission, with abnormal vaginal bleeding being the most common symptom (35%). The clinical burden of CSP is evident in the significant hospitalization need, with an average stay of 5.46 days (±4.16), and a maximum stay of 17 days. The half-life of β-hCG averaged 62.7 hours (±68.7) and peaking at 240 hours. Hematomas were the most frequent complication, affecting 26.7% of patients. While 75% of cases were successfully managed with isolated treatment approaches, 25% required combination treatments. Notably, significant differences emerged between the isolated and combined treatment groups in key areas, including scar pregnancy history, fetal heartbeat presence, hospitalization duration, β-hCG levels at admission, half-life of β-hCG, blood transfusions, and complications.

The rising cesarean section rates globally have contributed to the increasing prevalence of CSP, which poses substantial risks for maternal morbidity and mortality. Due to limited demographic studies, the reported incidence of CSP varies across regions. In our study, the incidence was 1.2 per 1000 cesarean deliveries, consistent with prior research. Several risk factors for CSP have been proposed, although the exact mechanisms remain unclear. Known risk factors include second-stage cesarean sections, a retroflexed uterus, gestational diabetes, higher maternal BMI, perioperative infections, and previous myomectomy.[6,18,19] Our study found that 6.6% of CSP patients had hypertension, 5% had diabetes, and 6.8% had thyroid dysfunction. Research suggests that thyroid-stimulating hormone (TSH) and thyroid antibodies, such as those against thyroglobulin (TgAb), play a role in placental development by promoting extravillous trophoblast invasion and angiogenesis.[20,21] A recent study found that TSH and TgAb levels were significantly reduced in patients with PAS disorders, a condition closely related to CSP.[22] Given the similarities between CSP and PAS, maternal TSH levels may contribute to CSP development.

Early diagnosis of CSP is essential to prevent complications associated with terminating these pregnancies.[23] Previous studies have reported a mean gestational age at diagnosis of 7.5±2.5 weeks.[14] In our study, the mean gestational age at diagnosis was slightly earlier, at 6.86±1.82 weeks, likely due to our centers' experience and advanced equipment. However, while ultrasonography can identify markers for CSP, current prenatal imaging techniques cannot reliably predict the short- and long-term outcomes of CSP.[9,15,24,25] Since our study was retrospective and all patients requested abortion, we were unable to identify these ultrasonographic markers and determine their association with pregnancy outcomes.

A comprehensive study found that over 90% of CSP patients had only one cesarean section.[26] Some studies have linked the number of CSs to CSP risk. In our cohort, 35% of patients had only one previous cesarean section, while 64.9% had two or more, aligning with prior research linking multiple cesarean deliveries to increased CSP risk.

Symptomatology at diagnosis can distinguish CSP from early miscarriages. In a retrospective study, it was found that 86% of CSP patients had only vaginal bleeding, 9% had both and abdominal pain, and 4.5% had only abdominal pain.[27] In another study of diagnosis complaints, all patients had vaginal bleeding and half of them had abdominal pain.[4] In our study, 43.3% of patients were diagnosed during routine pregnancy follow-up without symptoms. Among symptomatic patients, 35% presented with vaginal bleeding, while 18.3% reported abdominal pain. This finding underscores the importance of early transvaginal ultrasonography for diagnosing asymptomatic patients.

Fetal heartbeat presence and elevated β-hCG levels at admission were more common in the combined treatment group, potentially indicating a poorer prognosis for these patients. The optimal treatment for cesarean scar pregnancies remains uncertain, as various treatment methods have been explored in the literature, each with varying results. In our study, patients underwent different treatment approaches, including dilation and curettage (with or without a Foley catheter), systemic or local methotrexate (administered via the transcervical route), and wedge resection.

Limitations

There is limited data regarding the impact of CSP management on future reproductive outcomes. A recent systematic review and meta-analysis found that 17.6% of CSP cases recurred, while 82.6% of patients achieved intrauterine pregnancy, and 70.6% had successful pregnancies.[12] In our study, 26.7% of patients expressed a desire for future pregnancy, and of those, 50% achieved live births after 35 weeks of gestation, while the remaining 50% experienced early pregnancy loss. Although we observed no recurrent CSP cases in our cohort, the risk of recurrence remains a concern, as reflected in the 17.6% recurrence rate noted in the meta-analysis of 3,598 patients.[12]

One of the strengths of this study is the inclusion of data from two large tertiary referral centers with extensive experience in diagnosing and managing CSP. Additionally, our study comprehensively examines a wide range of demographic, clinical, laboratory, and reproductive outcome data. However, the study is limited by its retrospective design. Furthermore, we could not classify CSP cases based on ultrasonographic markers such as "on the scar", "in the niche", "cross-over sign", and "residual myometrial thickness" due to the lack of prospective follow-up for patients who opted to continue their pregnancies. Future studies should address these limitations through prospective designs and larger sample sizes.

CONCLUSION

Prenatal diagnosis of CSP is critical and requires a detailed assessment of the relationship between the gestational sac and the cesarean scar during the first trimester. Delaying the decision to terminate CSP increases the likelihood of complications. Due to the limited scientific data available, counseling patients who choose to continue their pregnancy is challenging. Our study

provides insights into predicting which patients may require combined treatment approaches, which can guide follow-up and treatment planning. The reproductive outcomes observed in our cohort may also aid in counseling patients about future fertility. Further research with larger sample sizes is needed to reach more definitive conclusions.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was started with the approval of Ankara Etlik City Hospital Ethics Committee (Decision No: 2023-683).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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