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GENERAL GYNECOLOGY

Caesarean scar pregnancy: is there a light in the end of the tunnel?

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Abstract

Purpose To summarize and present a single tertiary center's 25 years of experience managing patients with caesarean scar pregnancies and their long-term reproductive and obstetric outcomes.

Methods A 25-year retrospective study included women diagnosed with CSP from 1996 to 2020 in one tertiary center. Data were retrieved from the medical records and through a telephone interview. Diagnosis was made by sonography and color Doppler. Treatments included methotrexate, suction curettage, hysteroscopy, embolization and wedge resection by laparoscopy or laparotomy as a function of the clinical manifestations, the physicians' decisions, patient counseling, and parental requests.

Results Analysis of the records recovered 60 cases of CSP (two of whom were recurrent). All patients had complete resolution with no indication for hysterectomy. Thirty-five patients had a long-term follow-up, of whom 24 (68.6%) attempted to conceive again and 22 (91.6%) succeeded. There were 17/22 (77.3%) patients with at least one live birth, 3/22 (13.6%) spontaneous miscarriages and 2/22 (9%) recurrent CSP. The obstetric complications included abnormal placentation 5/19 (26.3%), premature rupture of membranes 2/19 (10.5%), preterm delivery 4/19 (21%) and abnormality of the uterine scar 2/19 (10.5%). There was one case of neonatal death due to complications of prematurity 1/19 (5.2%).

Conclusion CSP treatment focusing on reducing morbidity and preserving fertility has encouraging long-term reproductive and obstetric outcomes. In subsequent pregnancies, we recommend performing an early first trimester vaginal scan to map the location of the new pregnancy, followed by close monitoring given the obstetric complications mentioned above.

Keywords Caesarean scar pregnancy treatment · Methotrexate · Embolization · Hysteroscopy · Reproductive and obstetric outcomes

What does this study add to the clinical work

This study contributes encouraging data regarding treatment outcomes of cesarean scar pregnancy, with an emphasis on early diagnosis and fertility preservation. Nevertheless, early and close follow-up in subsequent pregnancies is critical given the possible complications.

Introduction

Cesarean scar pregnancy (CSP) is an iatrogenic complication that constitutes a life-threatening condition [1, 2]. The incidence reported in recent studies ranges from 1:1800 to 1:2500 of all cesarean deliveries performed [3–6]. The incidence of CSP appears to be on the rise. This trend can be explained by the increase in the rate of cesarean deliveries, but also by the increase of the use of transvaginal sonography (TVS) and clinical awareness [7, 8]. Although CSP is considered to be a form of ectopic pregnancy it shares its etiology with early placenta accreta [9, 10]. There are two forms of CSP: Type 1 (on the scar) where the pregnancy develops toward the uterine cavity, and Type 2 (in the scar) where the pregnancy develops toward the urine bladder [11].

Four main treatment options are described in the literature [12–15]:

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Medical treatment—the most common treatment is methotrexate (MTX), given locally, systemically or in combination.

Invasive radiology—uterine artery embolization.

Sonographic treatment—high intensity focused ultrasound.

Surgical procedures—ultrasound guided or laparoscopy-monitored dilation and suction curettage (D&C), hysteroscopy, colpotomy, laparotomy or laparoscopic resection.

To date, there is no consensus as to the optimal treatment. Hence, treatment is tailored according to the clinical manifestations, and the experience and abilities of the medical institution.

Expectant management of viable CSP may be life-threatening to both the mother and the fetus, and other complications can arise, such as early uterine rupture, invasive placentation, severe blood loss, preterm delivery and future infertility mainly due to hysterectomy [6, 12, 16–18]. Nevertheless, in recent years there have been a growing number of reports of expectant management of viable CSP some of which resulted in a live birth, even in late preterm or term.

The reproductive outcomes reported in the literature after treatment for CSP are encouraging but are limited given the rarity of this condition. The majority of patients who were managed without a hysterectomy were able to conceive again, though had an increased risk for recurrent CSP, placenta accreta and preterm delivery [2, 19–24].

The goal of the current study was to present our extensive (> 25 years) experience managing patients with CSP and their long-term follow-ups in terms of their reproductive and obstetric outcomes.

Materials and methods

This retrospective study included women who were diagnosed with CSP in Shamir (formerly Assaf-Harofeh) medical center in Israel. The data were retrieved from the hospital medical records. Diagnosis of CSP was based on abdominal and transvaginal ultrasound. The sonographic criteria for diagnosis were [1, 5, 8, 25–28] as follows:

1. An empty uterus.
2. An empty cervical canal.
3. Location of the gestational sac in the anterior part of the isthmic portion of the uterus with a diminished myometrial layer between the bladder and the sac.
4. Evidence of a discontinuity in the anterior wall of the uterus on the sagittal view of the uterus when the direction of the ultrasound beam runs through the amniotic sac.
5. Doppler demonstration of a rich vasculature in the area of the cesarean scar.

Treatment

The MTX dosage for intramuscular injection was 50 mg/m^2 (based on calculated body surface area). In case of viable pregnancy (with cardiac activity) an additional fixed dose of 25 mg of MTX was used for local injection to the gestational sac. Repeated doses of systemic MTX were given according to bHCG levels and sonographic findings during the follow-up. In all cases of hemodynamic instability, a laparotomy was performed. In patients who preferred surgical treatment as the first line, a wedge resection under laparotomy or laparoscopy was performed.

The long-term follow-up analysis was based on a review of the hospital's medical records and telephone interviews. Collected data included the patients' family planning, reproductive and obstetric outcomes in subsequent pregnancies.

This study was approved by the Institutional Review Board (0281-16-ASF).

Results

Sixty cases of CSP in 58 women were diagnosed in our department from 1996 to 2020 with an average age of 35.5 years (range 25–44 years). The median number of previous pregnancies was 5 (range 2–18), the median number of previous deliveries was 2 (range 1–7) and the median number of previous cesarean sections was 2 (range 1–4). Two patients had previous CSP. The management and treatment flowchart is presented in Fig. 1. For purposes of the current study the patients were divided into 2 groups according to the conceptus viability (i.e., cardiac activity) of the pregnancy: Group A was composed of 29 cases with cardiac activity (viable) and Group B was composed of 31 cases without cardiac activity (non-viable).

Group A (viable pregnancy) management

Twenty-three out of the 29 patients (79.3%) were treated with MTX (both intramuscular and locally injected to the gestational sac), of whom 19 (82.6%) had complete resolution (Fig. 2). Two patients (8.7%) needed an intervention with suction curettage due to suspected retained products of conception. In two other patients (8.7%) the CSP did not resolve after repeated doses of systemic MTX. These patients had further treatment with selective embolization. One of them needed hysteroscopic removal of the retained products of conception.

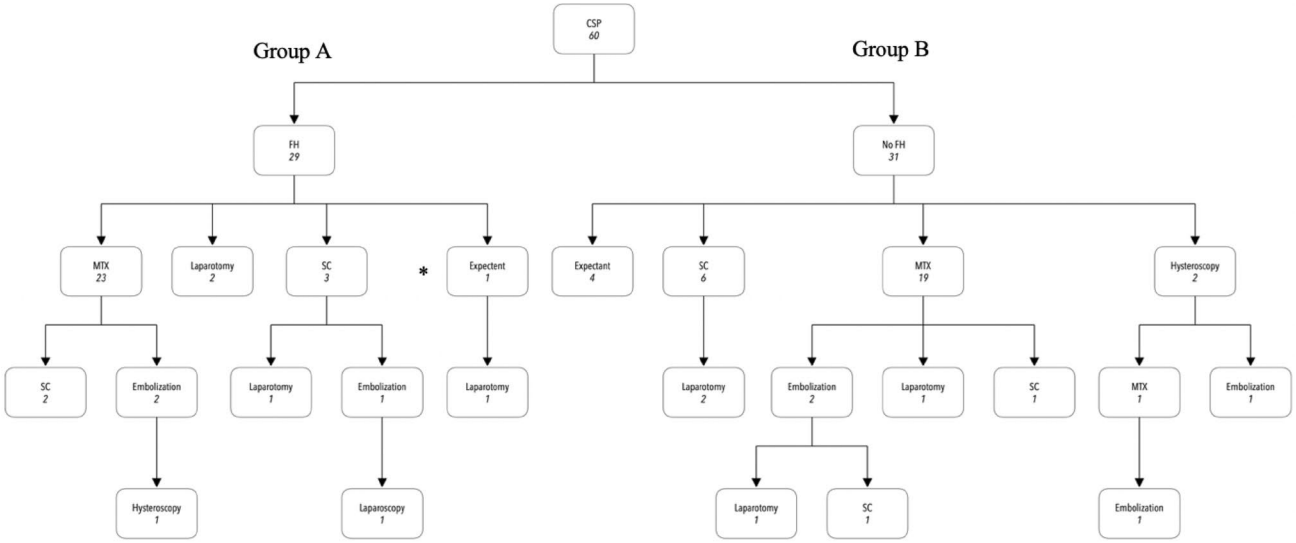


Fig. 1 Flowchart of CSP patient management and treatment

Two patients out of 29 (6.9%) had a laparotomy since both preferred surgical intervention over MTX, and underwent wedge resection.

Three patients out of 29 (10.3%) underwent primary suction and curettage. Two patients were misdiagnosed as having an intra uterine pregnancy implantation before the procedure. One patient needed embolization due to suspected AVM and later on underwent laparoscopic wedge resection. The second patient underwent emergency laparotomy with uneventful wedge resection.

One patient was offered treatment with MTX, but opted for expectant management. She was lost to follow until 24 weeks of gestation, when she presented to the E.R. in a state of hypovolemic shock. She had an emergent laparotomy in which uterine rupture was diagnosed. The fetus did not survive, but the uterus was preserved.

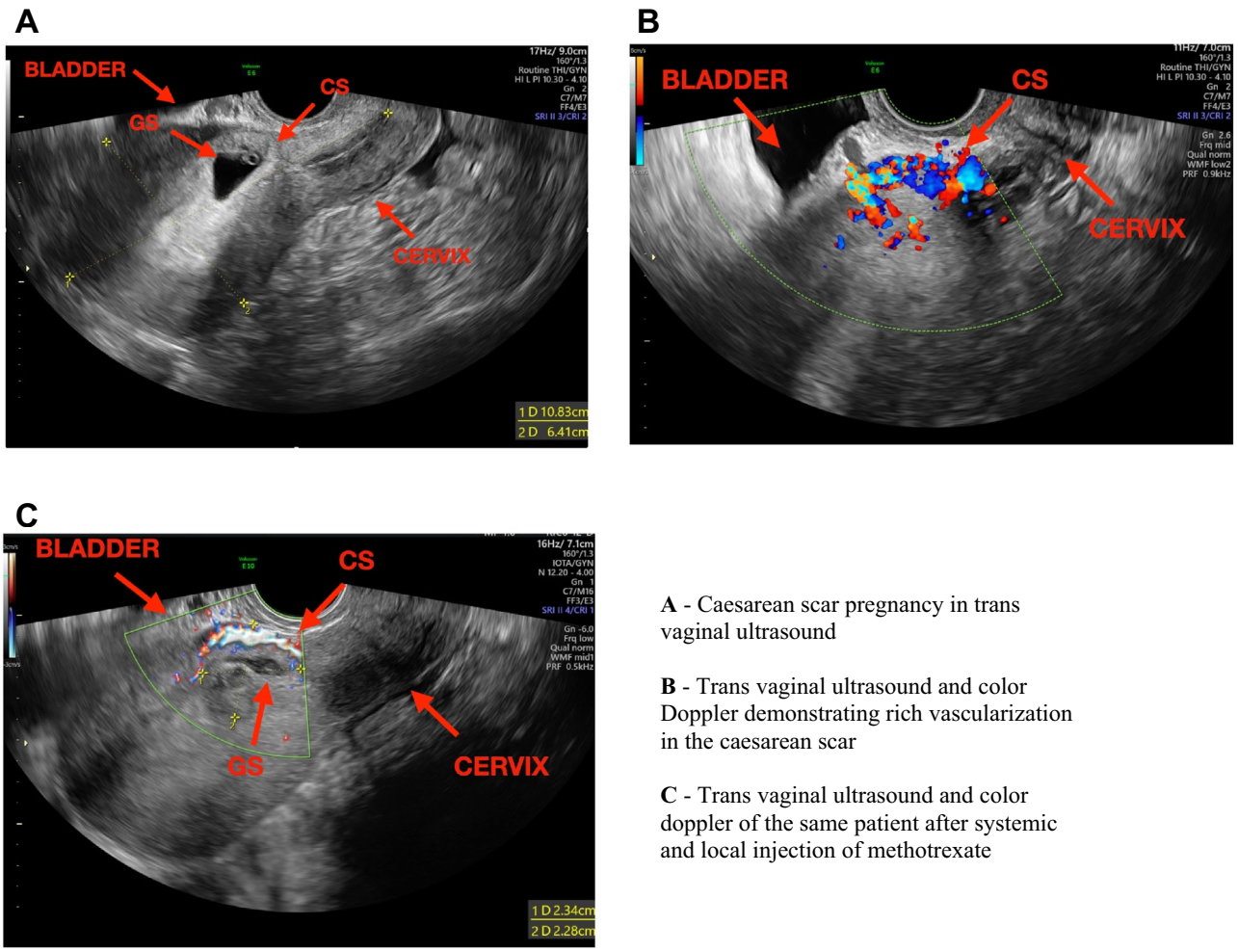
Group B (non-viable pregnancy) management

Nineteen patients out of 31 (61.3%) were treated with intramuscular MTX. Fifteen patients (78.9%) had resolution with no further treatment. One patient (5.3%) needed suction and curettage after she was diagnosed with incomplete abortion. Another patient (5.3%) who was treated with MTX had a rise in bHCG a week later. In the follow-up ultrasound, a gap was revealed in the myometrium above the pregnancy sac. A wedge resection was performed during laparotomy. Two patients (10.5%) who were treated with MTX later underwent embolization. One needed further wedge resection by laparotomy. The other patient underwent suction curettage after sonography identified a remaining gestational sac.

Six patients out of 31 (19.3%) were treated primarily with suction and curettage. Three needed no further treatment. The other three patients were misdiagnosed as intra uterine missed abortion. All had massive vaginal bleeding during the elective procedure. In two patients we converted to emergent laparotomy. CSP was diagnosed and resected while preserving the uterus. The third patient was managed conservatively by systemic and local uterotonics and tranexamic acid.

Two patients out of 31 (6.4%) underwent primary hysteroscopy. They were suspected of having retained products of conception after missed abortion. In hysteroscopy the tissue was shown to be embedded in the niche of the cesarean scar. One was treated with methotrexate. Later on, they both underwent embolization due to AVM. Subsequently they underwent another hysteroscopy in which the removal of the retained tissue was performed successfully.

Four patients out of 31 (12.9%) who had spontaneous decrease in bHCG levels were managed expectantly with no complications.



A - Caesarean scar pregnancy in trans vaginal ultrasound

B - Trans vaginal ultrasound and color Doppler demonstrating rich vascularization in the caesarean scar

C - Trans vaginal ultrasound and color doppler of the same patient after systemic and local injection of methotrexate

Fig. 2 Caesarean scar pregnancy ultrasound

Long-term follow-up

The long-term follow-up flowchart is presented in Fig. 3. Thirty-three patients with 35 cases of CSP were followed up. Eighteen out of 60 were lost to follow-up, one patient had tubal sterilization and 6 were recent cases. The median follow-up period was 3.8 years (range 0.5–22 years).

Reproductive outcomes (Fig. 3)

Twenty-four patients hoped to conceive again, of whom 22 (91.6%) were successful. Of these, 19 (86.4%) women conceived spontaneously. Three patients conceived more than once. Three patients had a spontaneous early abortion (13.6%), and two patients (9%) had recurrent CSP. Seventeen patients (77.3%) had a live birth. There was one case of neonatal death due to prematurity complications. Two patients had two live births. The mean gestational age at the time of delivery was 36.5 weeks (range 25–41). There were 4 (21%) preterm deliveries. Sixteen (84.2%) patients delivered by repeat cesarean section. Ten (62.5%) were planned and 6 (37.5%) were emergent. Two (11.7%) patients had a vaginal birth.

Pregnancy and obstetric outcomes (Table 1)

Five out of 19 (26.3%) pregnancies were complicated with abnormal placentation, 3 pregnancies with placenta accreta, one placenta previa and one patient had retained products of conception complicated with endometritis. One patient (5.3%) was delivered at 33 weeks of gestation by emergent cesarean section due to placental abruption. Two out of 19 (10.5%) pregnancies were complicated with preterm premature rupture of membranes (PPROM), one of whom had partial placenta previa and was delivered by emergent cesarean section at 25 weeks of gestation due to fetal distress. Unfortunately, this ended with neonatal death in the neonatal intensive care unit (NICU). Two out

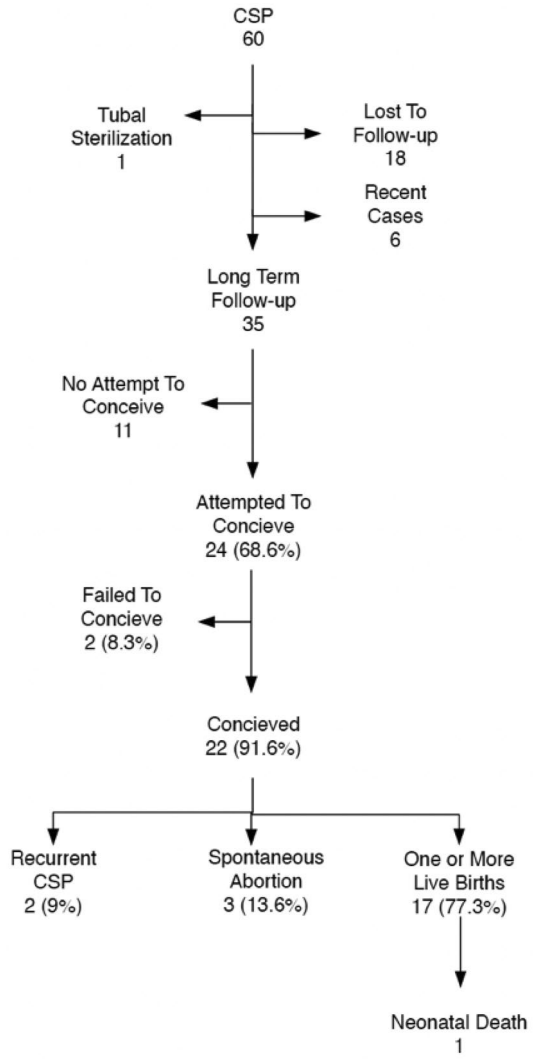


Fig. 3 Long-term follow-up flowchart

of 19 (10.5%) pregnancies were complicated with cesarean scar abnormalities. One was delivered at 37 weeks of gestation by planned cesarean section in which a small uterine rupture was diagnosed. The second patient was delivered at 32 weeks of gestation by emergent cesarean section due to painful cesarean scar. Dehiscence was observed.

In terms of the risk for CSP based on the previous number of cesarean sections (CSs), our data for 2017–2020 indicate 6 cases of CSPs after one CSs, and 12 cases of CSs after 2 or more CSs. During the same period, we had 2744 deliveries after one CSs, and 1135 deliveries after 2 or more CSs. These led to OR = 4.84 (95% CI 1.81–12.91) for CSP post one CS versus CSP post 2 or more CSs.

Discussion

This retrospective 25-year study revealed a rising trend in the rate of CSPs. A 2011 study conducted in our medical center on CSPs from 2000 to 2009 reported a prevalence of 1:3000 for the general obstetric population, and 1:531 among women who had undergone at least one cesarean delivery [2]. In the current study the calculated prevalence for 2010–2020 was 1: 2132 for the general obstetric population, and 1:414 among women who had experienced at least one cesarean delivery. These findings also strengthen the assumption that the risk of CSP is related to the number of previous CSs, which here was OR = 4.84.

The diagnosis of CSP can be challenging, especially in early pregnancy. Misdiagnosis as an intrauterine pregnancy can lead to severe morbidity and mortality if curettage is performed or in cases of viable pregnancies. In this study, five patients were misdiagnosed with intrauterine pregnancy and underwent suction and curettage. All of them had excessive bleeding that led to further interventions including embolization, laparoscopy and laparotomy. AVM and excessive bleeding are a known complication of curettage in the presence of CSP [13, 29, 30].

There is no consensus as to the optimal treatment for CSP in the literature. Our policy involves offering medical treatment (MTX), and surgical treatment including laparoscopy, laparotomy and hysteroscopy, and invasive radiology (embolization) as primary or adjuvant therapy. Our treatment of choice is systemic MTX or combined systemic and local injection of MTX, depending on the clinical, sonographic and laboratory findings. In pregnancies with cardiac activity, we prefer to use the combined MTX treatment. In the cases of non-viable CSPs and spontaneous decrease in bHCG levels, we preferred expectant management.

It seems that the most important aspect of patient management in the case of CSP is making the correct diagnosis, while the treatment can vary as mentioned before.

Studies of reproductive outcomes present the encouraging results in patients with CSPs. Most women were able to conceive again after treatment [2, 19–24]. Our experience further supports these findings.

The reported risk for recurrent CSP varies in different reports. In meta-analysis by Wu et al. and Morlando et al. recurrent CSP rate was reported 15.3–21% [23]. In this study recurrence rate was 9%.

The obstetric complications observed during the following pregnancies which resulted in live births included abnormal placentation (26.3%), preterm deliveries (21%) and one case of extreme prematurity and early neonatal death (5.2%) (see Table 1). These complications were described in other reports as well. Morlando et al. reports

Table 1 Pregnancy and obstetric outcomes following CSP

Patient #	Mode of conception	Pregnancy outcome	Mode of delivery	Gestational age at the time of delivery	Pregnancy complications
3	Spontaneous	Live birth	Planned CS	36	
4	Spontaneous	Live birth	Planned CS	37	Placenta accreta
7	Spontaneous	CSP			
8	Spontaneous	Miscarriage			
10	Spontaneous	CSP			
11	Ovulation induction	Live birth	Vaginal	40	Placenta accreta, endometritis
	IUI	Live birth	Planned CS	38	
13	Spontaneous	Miscarriage			
14	Spontaneous	Live birth	Planned CS	38	
15	IVF	Live birth	Urgent CS	25	Placenta previa, PPROM, spontaneous preterm delivery, neonatal death
16	Spontaneous	Live birth	Planned CS	38	
17	Spontaneous	Live birth	Urgent CS	33	Placenta accreta, placental abruption
26	Spontaneous	Live birth	Urgent CS	37	
27	Spontaneous	Live birth	Planned CS	37	
28	Spontaneous	Live birth	Planned CS	38	
31	Spontaneous	Live birth	Planned CS	38	
	Spontaneous	Live birth	Planned CS	38	
32	Spontaneous	Live birth	Planned CS	37	Uterine rupture
35	Spontaneous	Live birth	Vaginal	41	
37	Spontaneous	Live birth	Urgent CS	32	Cervical insufficiency, PPROM
38	Spontaneous	Live birth	Urgent CS	32	Scar dehiscence
39	Spontaneous	Live birth	Urgent CS	38	Placenta accreta, PROM
41	Spontaneous	Miscarriage			
51	Spontaneous	Live birth	Planned CS	39	

IUI intra uterine insemination, *IVF* in vitro fertilization, *CS* caesarean section, *PROM* premature rupture of membranes, *PPROM* preterm premature rupture of membranes

in meta-analysis 19% preterm deliveries, 10% miscarriages and 4% abnormal placentation [23]

There are recent reports of expectant management of CSPs with cardiac activity. Trich et al. [8] reported ten patients with viable CSP managed expectantly. Four (40%) had a live birth by scheduled cesarean section at 32–36 weeks of gestation. Three of these patients (75%) underwent planned hysterectomies due to placenta previa percreta. Five out of 10 (50%) patients had adverse outcomes and lost their pregnancies between 15 and 20 weeks of gestation, and all needed a hysterectomy (3 because of uterine rupture). Overall 8/10 patients had a hysterectomy. In a meta-analysis by Cali et al. in 2018 [16], 52 CSPs with cardiac activity were managed expectantly, and only 40/52 (76.9%) progressed to the third trimester, with nearly 40% severe bleeding, 10% uterine rupture and more than 60% of the patients needed a hysterectomy during cesarean surgery. About 75% had an abnormal invasive placenta. No data were provided on neonatal outcomes.

The Glenn et al. [13] review summarized current management strategies for CSPs and found that expectant management in viable CSP entails a high rate of morbidity. In particular, they noted that "more than 50% of patients having complications including hysterectomy, preterm deliveries, uterine rupture, significant hemorrhage and future infertility."

Recent reports distinguish between two types of CSP termed Type 1 (on the scar) and Type 2 (in the scar) CSP [11]. The prognosis for Type 1 CSP is considered favorable for live births in cases which are followed up expectantly. Although Type 2 CSP has a higher risk for uterine rupture, both types of CSP have risks for severe invasive placentation which can also lead to massive blood loss and fertility loss. For these reasons we recommend treatment and termination of pregnancy to all of our patients with viable CSP. In our series, only one patient who had CSP with cardiac activity chose expectant management and declined to follow our recommendations. She presented later to the ER at 24 weeks of

gestation in a state of hemorrhagic shock following uterine rupture, and her fetus did not survive.

In light of our experience and the recent literature we consider that expectant management is reasonable for non-viable CSPs (no cardiac activity and spontaneously decreasing bHCG levels), whereas termination of pregnancy is the best choice for viable CSPs. This approach can improve the long-term chances of fulfilling the patients' desire for live births, while lowering the likelihood of complications in this dangerous scenario. Thus, when providing consultation to women with CSP, they should be made aware of the high rates of successful subsequent pregnancies, yet with the increased risk of recurrence, preterm delivery and abnormal placentation.

Research limitations

This study utilized a retrospective design, and therefore, there could be no control of other associated factors. Records with incomplete data could not be completed. Some of the patients did not deliver in our medical center. In these cases, the data were based on a telephone interview. There was no comparison between patients and different kinds of treatments because there was no standardization of treatment or fixed management protocol. The treatment was tailored to the patient according to the clinical presentation as discussed above. We could not compare expectant management of viable CSP to termination of pregnancy as we strongly recommend against continuation of the CSP.

Research strengths

This study included a relatively large number of patients over a long follow-up period in one tertiary medical center. In Israel there is a high birth rate and we were able to document a large number of repeat pregnancies.

Conclusion

The current findings support studies indicating an increase in the rate of CSPs in recent years. We also found that the risk for CSP is higher after repeat CSs. Health care providers should be aware of this type of ectopic implantation and be familiar with the different treatment options and the benefits and drawbacks of each of them. This study emphasizes the encouraging long-term obstetric and reproductive outcomes of early treatment of CSPs. These can be achieved with treatment focusing on fertility preservation. In subsequent pregnancies a higher risk for abnormal placentation should be expected.

We now follow all our patients who have undergone a cesarean section (including post CSP) in a special clinic that offers them a pre-conceptual scan to assess the appearance of the uterine scar (niche) and a 5–7-week scan after conception to determine pregnancy implantation. Based on the above we advise each of our patients individually and assess their need for close monitoring in high-risk pregnancy units to maximize the obstetric outcomes.

Author contributions YS: manuscript writing; RM: manuscript editing; MG–K: data collection; NK: data collection; MP-Z: data collection; NS: manuscript editing; ZV: manuscript editing.

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Data availability The authors declare that the data supporting the findings of this study are available within the article. Additional data are available by the corresponding author upon a reasonable request and subjected to the ethical standards and patients confidentiality.

Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval This study was approved by the Institutional Review Board (0281-16-ASF).

Informed consent Since this is a retrospective study, no informed consent was needed. Patients who were interviewed by the phone gave their informed consent verbally at the beginning of the survey.

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