Research Article

Hysteroscopic Repair of Caesarean-Scar Isthmocele to restore fertility

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Abstract

Background: Isthmocele is a pouch defect, which acts as a reservoir, often located on the anterior wall of the uterine isthmus at the site of a previous cesarean section scar. More evidence have been accumulated on the association between the presence of isthmocele and secondary infertility. ~~The aim~~Aim: to determine the possibility of restoring fertility in women with secondary infertility using hysteroscpoic repair of caesarean-induced isthmocele. **Patients and Methods:** This prospective study was done on forty infertile women aged 22-40 years with isthmocele suspected by two-dimensional ultrasound. Physical examination and conventional two-dimensional transvaginal Ultra-sonography were done. Moreover, a laboratory assessment of infertile woman was done ~~and~~ as well as Hystosalpingiography in some cases. **Results:** In the 40 women, we found a statistically significant difference regarding the patients who conceived after correction of caesarean-induced isthmocele by hysteroscopy and patients who did not conceive (n= 25 (60.98%) vs. n = 15S (39.02%)) with 95% CI for difference (44.25% to 60.98%) and p-value <0.0001. **Conclusions:** Significant improvement of infertility after hysteroscopic repair of caesarean-induced isthmocele was achieved in more than half of the cases, Furthermore improvement in post-menstrual bleeding and supra-pubic pelvic pain in all cases was recorded..

Keywords: Hysteroscope, caesarean section, infertility.

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Introduction

In fertile women, caesarean section is considered as the most common surgical procedure involving the uterus.[1] Nevertheless, the most ischemic procedure and slowest re-absorbable suture would be the worst combination, and thus most likely to result in a cesarean scar defect or diverticulum. In 2006, Yazicioglu[2] in a randomized prospective study included 78 patients and analyzed two different techniques: (1) full-thickness, including the endometrial layer, and (2) split-thickness, without the endometrial layer. He found that by picking a full-thickness suturing procedure it may significantly reduce the incidence of incomplete healing of the uterine incision after Cesarean section (CS.). This defective scar in the uterus may occur based on multiple factors, including the degree of cervical dilatation, the contractile effort of the uterine musculature, the occurrence of chronic inflammation or, the particular arrangement of myometrial fibers in the site of uterine occlusion, could contribute to make a discrepancy at level of the incision.[3]

The defect in the anterior wall of the uterine isthmus at the site of previous CS scars is called isthmocele.[3] The prevalence of isthmocele was reported to be more than 52% after CS.[4] However, its presence is considered as an under recognized cause of abnormal uterine bleeding[3] which may contribute in many functional disorders of the menstrual cycle or intrauterine abnormalities including polyps and endometrial hyperplasia.[5]

Moreover, blood retention in the uterine cavity and the scar may introduce a toxic environment for embryo implantation and leads to infertility.[6] Therefore, the awareness of CS scar may help in the diagnosis of abnormal uterine bleeding among fertile patients.

More evidences have accounted for the clear relation between the presence of isthmocele and secondary infertility; and the role of surgical intervention for cesarean-induced isthmocele in restoring fertility plus reliving the symptoms.[7] There are other techniques to correct the defect using vaginal approach through Hysteroscopy and abdominal approach by using Laparoscopy if the patient has isthmocele with thin residual myometrium thickness.[8]

Hysteroscopy means the examination of the uterine cavity by endoscopy which allows physicians to diagnosis of intrauterine pathology by inspection and it acts as a method for surgical intervention. A hysteroscope is an endoscope that drives optical and light channels or fibers. It is introduced in a sheath that provides an inflow and outflow channel for insufflation of the uterine cavity. Moreover, an operative duct may exist to insert scissors, graspers or biopsy tools.[9]

Regarding the time of diagnosis of isthmocele, it is often done when the patients have some clinical symptoms such as dyspareunia, dysmenorrhea, postmenstrual spotting, chronic pelvic pain or even infertility as the physicians evaluate the integrity of the anterior uterine wall using different imaging modalities including hysterography and ultrasonographic evaluation. However, hysterography and hysteroscopy are not particularly useful they allow well visualization of the width and depth of the dehiscence[10] so, the main diagnostic tool for isthmocele is ultrasound. Transvaginal sonography with high-resolution transducers and introduction of sonohysterography has been found to be useful tools in the study of intrauterine lesions.[4] The diagnosis of this defect by transvaginal sonography had 100% correlation with hysteroscopy, with the same positive and negative predictive values for both methods.[11]

Moreover, Transvaginal sonography is a simple, non-invasive, low coast examination so it should be considered as the first choice for screening.[12]
Further research is needed to investigate the impact of repairing Cesarean-scar isthmocele on secondary infertility treatment. So the aim of this study was to restore fertility in women after CS by Hysteroscopic repair of Cesarean-Induced Isthmocele.

Patients and Methods

Study ~~Sample~~ Patients

This was a prospective study on forty infertile women aged 22-40 years (with isthmocele suspected by two dimensional ultrasound) were recruited for the present study from February 2015 to April 2016 after obtaining informed consent, attending fertility clinic in Suez Canal University and Suez health insurance Hospital. Inclusion criteria were more than one year of Secondary infertility with isthmocele. Patients presenting with secondary infertility for any other cause (male factor- Tubal factor-ovarian factor – abnormal hormonal profile) were excluded. Personal History, Special habits, Menstrual history obstetric history, contra-ceptive history, sexual history, surgical and medical history and history of male partner were also obtained.

Ethical approval

We obtained informed consent from subjects prior to their enrollment. Moreover, all the steps of the study including; the aims, the potential benefits and dangers were explained to the parents before the enrollment too. This study was conducted according to the ethical guidelines of Suez Canal university faculty of medicine, and approved by the Medical Research Ethics Committee.

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Patient assessment

All patients had signed an informed consent form to participate in this study. Then a full history was taken for the couple. Physical examination and conventional two-dimensional transvaginal Ultra-sonography was done to all women. Moreover, a laboratory assessment of infertile woman was done and Hystosalpingio-graphy if needed.

Surgical procedures

We placed the patient in dorsal lithotomy then a speculum is inserted into the vagina to visualize the entire cervix and access the os. easily. The cervix and the vagina are then thoroughly scrubbed with antiseptic solution (Betadine solution will be used). Office hysteroscopy was done with vaginoscopic approach by Image 1 S H3-Z Full HD Camera Head (Karl Storz), fibro-optic light Cable and hopkins telescope 30° size 2.9mm with irrigation connector used with continuous –flow examination sheath (Karl Storz, Germany). If vaginoscope approach was difficult or unclear application of a speculum to visualize the cervix and a singletooth tenaculum to fixate the cervix. Straighten the cervico-uterine angle, provide counter-traction and insertion of hopkins telescope. Surgery was not performed if the distance between the bladder and the edge of the isthmocele was less than 2.5 mm to avoid bladder injury or no abnormal uterine bleedin as shown at ultrasound. Confirmation of isthmocele diagnosis and exclude any intrauterine abnormalities.

Operative hysteroscopy was performed under anasethia. Large Neutral electrode, positioned as close as possible to the operating area. Speculum is inserted into the vagina and positioned such that the entire cervix was visualized and the OS is easily accessible. Monopolar was Set-up for cutting at 40-50 w and 20-30 w for co- agulation. Unipolar Resectoscopic Sheath diameter 7mm, including connecting tube for in and outflow, continuous irrigation and suction and rotatable inner sheath with ceramic insulation with Hopkins telescope 30° size 2.9mm. The uterine cavity was inflated by a solution of 1.5% glycine. We used a passive gravity outflow technique for uterine irrigation. The Lower edge of the defect was resected using a cutting loop and pure cutting current and Co-agulation was done by roller ball. Modulating the technique in order to remove the anterior scar tissue completely and align the surface to the cervix.

Follow-up

The patients were maintained in the recovery room for approximately two hours for observation of any vaginal bleeding. Some spotting or vaginal bleeding was expected for three-to-five days and may last three-to-four weeks after operative hysteroscopy. Tampons or douching had been restricted and only pads until the discharge stops. Moreover, Sexual intercourse had been restricted for 2 weeks after surgery. Broad Spectrum Antibiotic had been used for 3 days postoperative. Regarding follow-up visits, there was a Follow-up visit after two-to-four weeks and Trans-vaginal ultrasound for evaluation; and monthly visit for the consecutive six months to determine pregnancy rate and were administered folic acid.

Statistical analysis

We analyzed the data using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY, USA) and MedCalc© version 15.8 (MedCalc© Software bvba, Ostend, Belgium). The D'Agostino-Pearson test was used to check the normality of numerical data distribution. Regarding the continuous numerical data, it was presented as mean ± SD and range, while categorical data were presented as number and percentage. The unpaired t-test was used to compare intergroup differences as regards numerical variables. Categorical variables were compared using Fisher's exact test (for nominal data) or the chi-squared test for trend (for ordinal data). Paired categorical data were compared using the McNemar test. Time to conception was analyzed using the Kaplan-Meier method. P-value < 0.05 was considered Statistically significant.

Results

Patient characteristics

Patients recruited in our study had a mean age of 31±5 (21-40) years and duration of infertility 2.9 (1-7) years. Number of previous caesarean section was previous one caesarean section in 22 patients (53.7%), previous 2 caesarean sections in 12 patients (29.3%), while only four patients with previous three caesarean sections and previous 4 caesarean sections was 3 (7.3%).

Main findings

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Statistically significant difference regarding the patients who conceived after correction of caesarean-induced isthmocele by hysteroscopy and patients who did not conceive (n= 25 (60.98%) vs. n = 15S (39.02%)) with 95% CI for difference (44.25 % to 60.98 %) and p-value <0.0001.

Using the Kaplan-Meier curve for the two variables probability of conception ad time after operation , we found that the mean time to conception was 3.8 months 95% CI (5.8 to 8.3 months), while the median time to conception was 5 months 95% CI (3-6 months).

There was no statistically significant difference detected between the women who conceived and those didn't conceive regarding the mean age (32 years ±4vs. 30 years ±5), also regarding the duration of infertility there was no statistically significant difference (2.9 years ±1.3vs. 2.8 years ±1.7).

Hysteroscopic repair operation time recorded no statistically significant difference between the women who conceived and those didn't conceive (16 minutes ± 5vs. 18 minutes ±7)

There was no statistically significant difference detected between the women who conceived and those didn't conceive regarding the number of previous cesarean section, previous one cesarean section 11(44%) vs. 11(68.8%), previous two cesarean section n=10 (40.0%) vs. 2(12.5%) , previous 3 cesarean section (3.12%) vs. 1 (6.3%) and previous four cesarean section 1(4%) vs. 2(12.5%).

There was no statistically significant difference detected between the women who conceived and those didn't conceive regarding uterus position, site of isthmocele or the grade of isthmocele.

Site of isthmocele was superior third of cervix in 12 conceived (48.8%) vs. 8 didn't conceive (50%), middle third of cervix isthmocele was found in (8 conceived (32%) vs. 6 didn't conceive (37.5%)) , and isthmocele was in the inferior third of cervix in (5 conceived (20%) vs. 2 didn't conceive (12.5%))

Uterine position was AVF (19 conceived (76 %) vs. 9 didn't conceive (56.3%), while it was RVF uterus (6 conceived (24%)vs. 7 didn't conceive (43.8%).

Grade of isthmocele was Grade I in (12 conceived (48%) vs.6 didn't conceive 37.5%), Grade II in (11 conceived (44%) vs. 5 didn't conceive (31.3%), Grade III (2 conceived (8%) vs. 5 didn't conceive (31.3 %)).

Tables and figures

Table (1): Patients' characteristics

Variable	Mean ± SD (range) / Number (%)
Age (years)	31 ± 5 (21 – 40)
Duration of infertility	2.9 ± 1.5 (1 – 7)
Number of previous CS	
1 CS	22 (53.7%)
2 CS	12 (29.3%)
3 CS	4 (9.8%)
4 CS	3 (7.3%)
Body mass Index (20-24.9)	15(37.5 %)
Body mass Index (> or = 27)	25 (62.5 %)

Please explain any abbreviation used in the table, in a footnote under the table

Table (2): Associated symptoms (use more informative title)

Variable	Number (%)
Suprapubic pain	12 (29.3%)
Postmenstrual bleeding	35 (85.4%)

Table (3): Ultrasound findings

Variable	Number (%)
Uterine position	
AVF	28 (68.3%)
RVF	13 (31.7%)
Site of isthmocele	
Superior	20 (48.8%)
Middle	14 (34.1%)
Inferior	7 (17.1%)
Grade of isthmocele	
Grade I	18 (43.9%)
Grade II	16 (39.0%)
Grade III	7 (17.1%)

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Site Of isthmocele :

Figure (~~8~~1): Site of isthmocele in upper third of cervical canal.

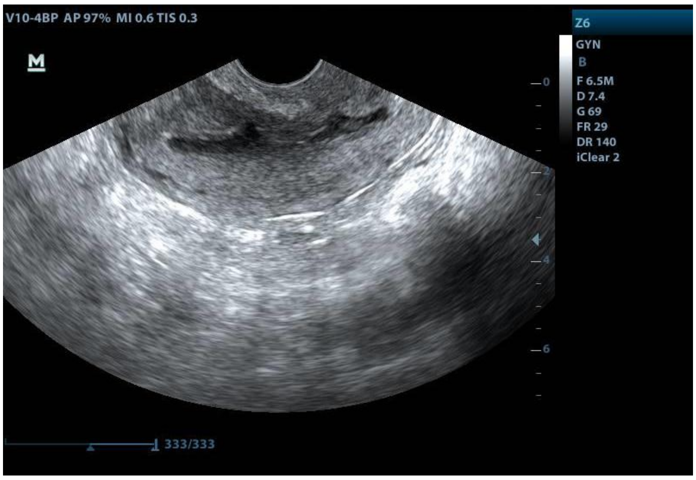

Figure (2):~~9~~ Site of isthmocele in the middle third of cervical canal

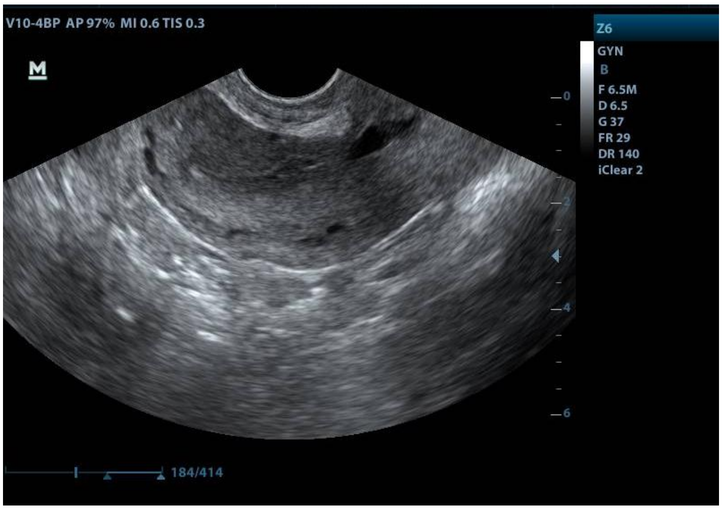

Figure (3): Site of isthmocele in Lower third of cervical canal .

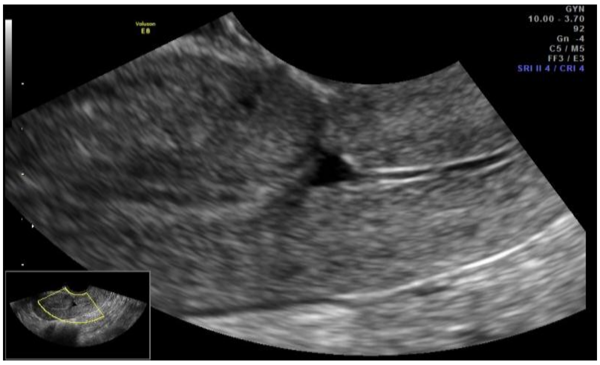

Figure (4): Grade I isthmocele

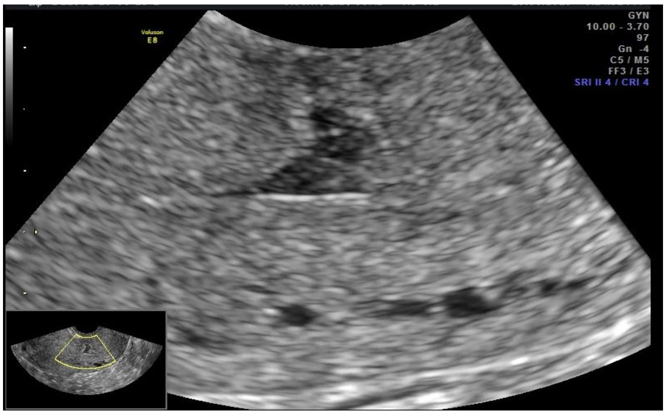

Figure (5): Grade II isthmocele

Figure (6): Grade III isthmocele

Table (4) Operative time of hysteroscopic Repair of isthmocele

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Variable	Mean ± SD (range)
Operative time (min)	16 ± 6 (10 – 35)

Table (5): Conception rate (use more informative title)

Variable	Number (%)
Conception	
Did not conceive	15 (39%)
Conceived	25 (61%)

Table (6): Hypothesis testing for the observed rate of conception

This Table shows that there is a statistically significant difference regarding the patients who conceived after correction of caesarean-induced isthmocele by hysteroscopy and patients who did not conceive (n= 25 60.98% vs. n = 16 39.02%) with 95% CI for difference (44.25 % to 60.98 %) and p-value <0.0001.

Parameter	Value
Observed rate	60.98%
Difference from pre-treatment rate	60.98%
95% CI for difference	44.25% to 60.98%
p-value (H0: difference = 0)¶	**<0.0001**

¶McNemar test.

Table (7): Kaplan-Meier analysis for time to conception

Table 7 discusses the number of cases conceived which was 25 and didn't conceive which was 15 cases within the 6 months and it represents that the average time to conception was 3.8 months .

Summary statistics			
Number of events (conceived)		**Number censored (not conceived)**	
N	**%**	**N**	**%**
25	60.98	15	39.02
Mean and median time to conception (months)			
Mean	**95% CI for mean**	**Median**	**95% CI for median**
5.1	3.8 to 6.0	3	4.0 to 5.0
Kaplan-Meier table			
Time after operation (months)	**Proportion without conception**	**SE for proportion**	
2	0.878	0.051	
3	0.756	0.067	
4	0.61	0.076	
5	0.488	0.078	
6	0.415	0.077	

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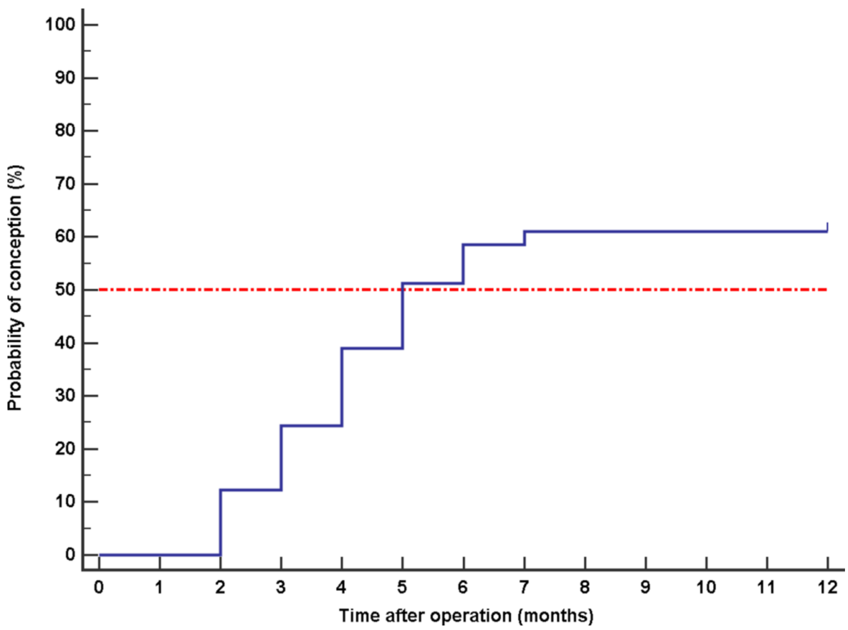

Figure (7):. Kaplan-Meier curve for time to conception. Dotted line intersects curve

at median time to conception.

Table 8. Comparison of patients who conceived and those who did not: Numerical variables

Table 8 shows that there was no statistically significant difference detected between the women who conceived and those didn't conceive regarding the mean age , also regarding the duration of infertility there was no statistically significant difference , Hysteroscopic repair operation time alsorecorded no statistically significant difference between the women who conceived and those didn't conceive

	Did not conceive (n=15)		Conceived (n=25)				
Variable	**Mean**	**SD**	**Mean**	**SD**	**t**	**df**	**p-value¶**
Age (years)	30	4	32	5	-1.577	39	0.123
Duration of infertility (years)	2.8	1.7	2.9	1.3	-0.034	39	0.973
Hysteroscopy repair Operative time (min)	18	7	16	5	0.894	39	0.377

t, t statistic; *df*, degree of freedom.

¶Unpaired t test.

Table 9. Comparison of patients who conceived and those who did not: Categorical variables

Table 9 Shows a comparison between cases who got conceived and cases didn't conceive

We compare (Number of previous cesarean section – associated symptoms like postmenstrual bleeding and suprapubic pain –uterine position either AVF or RVF- Site of isthmocele (superior – middle-inferior) – grade of isthmocele and Body mass Index)

	Did not conceive (n=15)		Conceived (n=25)		χ^2	df	p-value
Variable	**N**	**%**	**N**	**%**			
Previous CS					0.206	1	0.650¶
1 CS	11	68.8%	11	44.0%			
2 CS	2	12.5%	10	40.0%			
3 CS	1	6.3%	3	12.0%			
4 CS	2	12.5%	1	4.0%			
Suprapubic pain	6	37.5%	6	24.0%			0.485§
Postmenstrual bleeding	13	81.3%	22	88.0%			0.662§
Uterine position							0.302§
AVF	9	56.3%	19	76.0%			
RVF	7	43.8%	6	24.0%			
Site of isthmocele							0.835§
Superior	8	50.0%	12	48.0%			
Middle	6	37.5%	8	32.0%			
Inferior	2	12.5%	5	20.0%			
Grade of isthmocele					2.016	1	0.156¶
Grade I	6	37.5%	12	48.0%			
Grade II	5	31.3%	11	44.0%			
Grade III	5	31.3%	2	8.0%			
Body mass Index (20-24.9)	4	26.6%	11	44%			
Body mass Index (>or = 27)	14	93.3%	11	44%			

χ^2, chi-squared statistic; df, degree of freedom.

¶Chi-squared test for trend.

§Fisher's exact test.

Discussion

This Prospective Study was conducted at Suez Canal University Faculty of medicine and Suez Health Insurance Hospital on 40 patients presented with secondary infertility with previous caesarean section and after exclusion of male factor, tubal factor, ovarian factor, and other endocrine factors of infertility and diagnosed by ultrasound as isthmocele with or without post menstrual bleeding and suprapubic pelvic pain. In our study, there was a statistically significant difference regarding the patients who conceived after correction of caesarean-induced isthmocele by hysteroscopy and patients who did not conceive (n= 25 (60.98%) vs. n = 15S (39.02%)) with 95% CI for difference (44.25% to 60.98 %) and p-value <0.0001. on the other hand, there were 35 patients presented with postmenstrual bleeding (85.4%) and only 12 presented with suprapubic pelvic pain (29.3%). In all patients, isthmo-plasty was accompanied by resolution of postmenstrual bleeding and suprapubic pelvic pain.

A study by Wang et al.,[4] was conducted on 207 women with history of CS that were diagnosed with an isthmocele using trans-vaginal ultrasound, however our study included 40 women who had undergone caesarean deliveries and were all diagnosed using transvaginal ultrasound for having an isthmocele which was further confirmed using office hysteroscope. Postmenstrual bleeding was present among 63.8% of women in the study by Wang et al.,[4] while in our study it was 85.4%.

Additionally, suprapubic pelvic pain was present among 39.6% of women in Wang's study while 29.3% of women in our study demonstrated suprapubic pelvic pain. Another factor studied is the prevalence of isthmoceles and the position of the uterus. Wang et al.,[4] found that 84% of isthmocele patients had anteflexed uterus while 16% had retroflexed uterus. We found that 68.3% (28 patients) of isthmocele patients had AVF uterus while 31.7% (13 patients) had RVF uterus.

Another study conducted by Fabres et al.,[12] focused on surgical treatment of isthmocele in women who had intermenstrual bleeding. Like our study, they used transvaginal ultrasound for diagnosis. However, Fabres et al., used a 9mm resectoscope while we used a 7mm resecto-scope. Additionally, they used sorbitol-mannitol solution while we used 1.5% glycine solution.

Moreover, the mean age of women in Fabres' study was 36 years while in our study it was 31 years. In both Fabres' study and our study, postmenstrual bleeding resolved in all the patients selected. However, Fabres et al.,[12] reported that 16% of women had recurrence of abnormal bleeding. In Fabres' study, 45% of patients were seeking fertility treatment and 82% of those women conceived successfully. In our study, the conception rate was 61%.

In 2008, Gubbinni et al.[3] conducted a study including 26 patients who underwent one or even more CS then, they was evaluated for postmenstrual bleeding and secondary infertility which was detected in 9 patients all of whom had a niche. Regarding the site of the isthmocele he found that 69% of patients had the isthmocele in the superior third of the cervical canal, 15% presented with an isthmocele in the middle third of the cervical canal and 15% in the inferior third of the cervical canal. In our study, the site of isthmocele was also determined by transvaginal ultrasound to find that 20 patients (48.8%) had isthmocele in the superior third of the cervical canal, while 14 patients (34.1%) had isthmocele in the middle third of the cervical canal and 7 patients (17.1%) had isthmocele in the inferior third of the cervical canal.

Gubbinni et al.,[3] used transvaginal ultrasound 3-6 days after last menstruation using the formula (base X height /2) to classify isthmoceles into 3 grades. Grade 1 is less than 15 mm^2, grade 2 is 16 to 25 mm^2 and grade 3 is greater than 25 mm^2.

In this study using Gubbini's formula, we found that 18 patients (43.9%) presented with Grade 1 isthmocele, while 16 patients (39%) had grade 2 isthmocele, and only 7 patients (17.1%) had grade 3 isthmoce.

In both our study and that of Gubbinni et al.,[3], we used the same technique doing office hysteroscopy using Hopkins telescope 30^o size 2.9mm to confirm diagnosis, and repair of isthmocele using 7mm resectoscope with unipolar electrical current to perform resection of inferior and superior edges of the defect using a cutting loop and complete removal of the scar tissue modulating the technique according to the defect site. The bottom of the pouch was treated using electrocauterization with a roller ball.

In 2011, Gubbinni et al.,[13] conducted another study using the same technique but on a larger sample including 41 patients who presented mainly with secondary infertility and other secondary symptoms like postmenstrual bleeding and suprapubic pain.

This study resulted in 100% conception rate and improvement of symptoms related menstruation. However, in our study 61% of patients conceived. Postmenstrual abnormal uterine bleeding was found to be associated with isthmocele –a condition characterized by spotting for a variable numbers of days after menstruation– because isthmocele slows evacuation of blood from the uterus. All patients with isthmocele presented with postmenstrual bleeding, whereas 46 % of patients presented with suprapubic pelvic pain Gubbini et.al., [13]

Limitations

First of all, the population of the experimental group is small, only forty one women represented with isthmocele. Secondly, the short follow-up period for conception rate for women after repair of isthmocele; result might have been more conclusive if the follow-up was for a longer time

Conclusion

Our results showed improvement of fertility after hysteroscopic repair of caesarean-induced isthmocele as 61 % of cases successfully conceived, as well as it shows improvement in post-menstrual bleeding and supra-pubic pelvic pain in all cases, which supports operative hysteroscopy as the minimally invasive approach to treat cesarean-induced isthmocele.

Recommendations

We recommend a wide Scale Study on all cases of Cesarean section in Suez canal university faculty of medicine is needed to show factors increase the incidence of isthmocele as well as prevalence of infertility in patients with isthmocele.

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