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Cervical stenosis and pregnancy rate after ultrasound guided cervical dilation in women undergoing saline infusion sonography

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Abstract

Aim: To assess the effect of ultrasound-guided cervical dilation on clinical pregnancy rates in women with cervical stenosis. **Methods:** A prospective case control study was conducted in women with unexplained infertility. These women underwent saline infusion sonography and were suspected of having cervical stenosis if a 7 French Foley's catheter could not be introduced into the cervical canal. Women with suspected stenosis who agreed to undergo ultrasound guided dilation were included as cases. Those with suspected stenosis who refused dilation were used as controls. Both groups were followed for one year. The primary outcome measure was women who had clinical pregnancy i.e. fetal heart beat present on transvaginal scan during the follow up period. **Results:** During the study period, 1097 women who underwent SIS were included. A total of 117 (10.7%) patients had cervical stenosis. No statistically significant difference was there in both groups in terms of mean age ($p = 0.617$), mean body mass index ($p = 0.598$), duration of infertility ($p = 0.588$) and type of infertility ($p = 0.167$). However, both groups were significantly different in terms of history for risk factors i.e. endometriosis ($p < 0.001$), prior surgery ($p < 0.001$), polyps ($p = 0.004$) and pelvic inflammatory disease ($p = 0.001$). Eighty-nine women agreed to have dilation and were used as cases and 28 women refused and were used as controls. Of the cases, 70.45% conceived as compared to 18.5% of controls. The mean time to conception in months was also significantly lower in cases (8.10 ± 3.43 vs. 11.39 ± 1.97 , $p < 0.001$). **Conclusions:** Our study shows that ultrasound-guided cervical dilation in women with cervical stenosis can lead to improved conception rates.

Introduction

Despite regular sexual intercourse, around 10–15% of couples fail to conceive⁽¹⁾. Cervical factor is implicated in around 5% of these couples⁽²⁾. Cervical factor can also be caused by cervical stenosis, which remains undiagnosed in the usual fertility workup suggested by European Society of Human Reproduction and Embryology (ESHRE) and Royal College of Obstetricians and Gynaecologists (RCOG)⁽³⁾. This happens because the fertility panel run on couples does not involve evaluation of the uterine cavity.

Trans-cervical access to uterine cavity, like sonohystero-gram or hysterosalpingogram, is needed for the investigation of the uterine cavity; therefore, cervical stenosis may go undiagnosed in a woman with insignificant history till intrauterine insemination or embryo transfer in an in vitro fertilization cycle is attempted⁽⁴⁾.

Cervical stenosis can be either congenital or acquired. It may lead to hematometra, pyometra or subfertility⁽⁵⁾. Difficult embryo transfers are a frequently cited cause of decreased clinical pregnancy rates in in vitro fertilization

(IVF) cycles⁽⁶⁾. It has been suggested that trial transfers under ultrasound guidance improve conception rates. Saline infusion sonography involves the use of soft tip Foley's catheter for the introduction of saline used for cavity distension and checking for free spill⁽⁷⁾. Cervical dilation with a Hegar's dilator may be needed prior to introduction of this Foley's catheter in cases of stenosis. Since a stenosis that hinders introduction of a 7 French Foley's may also be relieved after dilation, the couple may conceive after this resistance has been overcome⁽⁸⁾. A closed cervix prevents intrauterine deposition of semen during natural breeding, may delay uterine clearance after insemination, leading to intrauterine fluid accumulation and subsequent infertility.

We undertook this study to assess the effect of cervical dilation in women with cervical stenosis on clinical pregnancy rates.

Methods

Women aged 20 to 39 years with infertility defined as no conception despite 24 months of regular unprotected sexual intercourse were included in the study. Women with history of cervical cancer, congenital abnormality of the cervix, male factor as assessed by World Health Organization (WHO) semen analysis criteria and women with ovulatory disorders were excluded. Also, women who failed to comply with the follow up were excluded. Written informed consent was taken from all women. Those who met the inclusion criteria then underwent saline infusion sonography (SIS) on days 8 and 11 of their menstrual cycle.

Saline infusion sonography was carried out in the outpatient department. For the procedure, a sterile Cusco's speculum was inserted into the vagina and a cervical Foley's catheter of 6 French was inserted through the cervical os in an aseptic manner. In the case of resistance, the cervical canal was dilated using a Hegar's dilator. Before dilation, a cervical block was applied under local anaesthesia. The insertion was attempted again. The bulb of the Foley's was distended with 1–2 mL of saline, and then the endometrial cavity was distended by instilling normal saline through the cervical Foley's catheter. Detailed method was previously described in the article⁽⁷⁾. In cases where cervical dilation failed under local anaesthesia, the procedure was carried out under general anaesthesia and the catheter was retained for 5 days. Antibiotic cover was given in all cases of dilation. All women received clarithromycin (Klaricid) 500 milligrams in the form of tablets: one tablet twelve hourly for 5 days. Foley's was left in cervixes that were difficult to dilate and had instrumentation done more than once. To ensure no infection takes place, clarithromycin was given for 5 days according to the microbial resistance patterns seen in the local setup. The duration of treatment was also assessed according to local practice.

A Mindray's DP-2200 scanner with a 5 to 7.5 MHz frequency endovaginal transducer was used for all procedures. All scans were performed by the lead author who is a specialist in ultrasound and fertility and has 10 years of experience⁽⁷⁾.

To calculate an adequate sample size we searched the literature for pregnancy rates after cervical dilation. Literature reports that cervical stenosis is seen in 5% of women with subfertility. It has also been reported that dilation for cervical stenosis increased the odds of clinical pregnancy (80% vs. 28%, respectively). Assuming that the patients are not conceiving due to cervical stenosis, with a power of 80% (1- β) and a one-sided 0.05 risk of type I error (α), we needed 11 patients with cervical stenosis in each group to demonstrate a similar rise in pregnancy rate after dilation in this group of patients. We included 117 women with cervical stenosis in the analysis and divided them into groups based on dilation.

Cases and controls

Women who received cervical dilation under local or general anaesthesia were included as group A (cases). Cases where cervix was stenosed but dilation was also unsuccessful with Foley's were not included in the final analysis. Women who did not consent to dilation functioned as group B (controls). They were followed for the study duration but not offered dilation after the initial enrolment, till the completion of study. Those who requested dilation later on during the study period were also excluded to avoid protocol deviation.

Sexual contact was encouraged and the women were asked to report back if they became pregnant. Transvaginal scan was done to confirm fetal heart beat.

All women were followed for a period of twelve months. The follow up was maintained via telephone calls and repeat transvaginal scans at 3, 6, 9 and 12 months. Those who did not comply with the follow up were not included in the final statistical analysis. The primary outcome measure was women who had clinical pregnancy i.e. fetal heartbeat present on transvaginal scan after they were serum beta hCG positive during the follow up period.

All participants provided informed consent. In lieu of formal ethics committee or formal institutional review board approval, Helsinki's declaration was followed. No subjects were harmed, confidentiality was maintained, and no subject was enrolled in the study without formal informed consent.

The Shapiro-Wilk test was used to assess normality of data distribution. The Quantitative variables, such as age, duration of infertility and duration from treatment to conception were presented by means and standard deviation. The t-test for two independent samples was used to compare means for both groups; those requesting dilation and those who did not. Frequency and percentages were computed for qualitative variables: type of infertility and conception. Chi square test was used to compare the groups.

Survival analysis was performed to evaluate the probability of conceiving in both groups. Curves were compared by means of Mantel-Haenszel log-rank test for categorical variables, which in this case was pregnancy. Analyses were performed using SPSS version 15.0 statistical package (SPSS, Inc.) with statistical significance denoted by a *p*-value of less than 0.05.

Tab. 1. Characteristics of study population

	Mean +/- Standard deviation or n (%)
Age in years	28.99 ± 5.40
BMI	27.57 ± 4.39
Duration of infertility in years	3.94 ± 1.59
Type of infertility	
Primary	637 (58.1%)
Secondary	460 (41.9%)
Stenosis	
Yes	117 (10.7%)
No	980 (89.3%)
Dilation	
Yes	89 (8.1%)
No	1008 (91.9%)

Results

During the study period, 1109 women undergoing saline infusion sonography were assessed for eligibility. Seven women refused to consent and were excluded. Of these 1102 women, 5 women got saline sonography under general anaesthesia and were excluded. A total of 1097 women were therefore included. Of these 1097 women, 117 had cervical stenosis. Eighty nine women agreed to have dilation and 28 women refused. Of these eighty nine women, two were lost to follow up, 1 from each group. These women were excluded from the analysis for conception. Figure 1 shows the study profile.

The participants had a mean age of 28.99 ± 5.40 years, a mean BMI of 27.57 ± 4.39 kg/m² and a mean duration of infertility of 3.94 ± 1.59 years. Most couples had primary infertility. Of those included, 3.5% had history of endometriosis, 7.7% had previous episode of pelvic inflammatory

disease, 5.4% had prior surgery and 6.6% had history of intrauterine polyps. Of those assessed at sis, 117 (10.7%) had stenosis and were offered dilation. Table 1 shows characteristics and risk factors in the study population.

When stratified according to groups, both groups, those with stenosis and those without, were similar in mean age ($p = 0.617$), mean BMI ($p = 0.598$), duration of infertility ($p = 0.588$) and type of infertility ($p = 0.167$). However, both groups were significantly different in terms of history for risk factors. Table 2 summarizes the comparison between the two groups.

Of the women who received dilation, 70.45% conceived as compared to 18.5% of those who had stenosis but refused dilation. The mean time to conception (in months) was also significantly lower in women who received dilation (8.10 ± 3.43 vs. 11.39 ± 1.97, $p < 0.001$) (Tab. 3).

Survival analysis also showed that the conception rate was significantly higher in those who opted to undergo dilation. (Log rank, $p < 0.001$) (Fig. 2).

Discussion

Main findings

Our study showed that cervical stenosis existed in 10.7% of women with unexplained subfertility. History of endometriosis, pelvic inflammatory disease, prior surgery and polyps is significantly associated with cervical stenosis.

Cervical dilation in these women leads to better conception rates.

Tab. 2. Comparison of both groups in terms of history parameters

Characteristics	Stenosis		p-value
	Yes	No	
	Mean ± SD or count n (%)	Mean ± SD or count n (%)	
Age in years	28.75 ± 5.08	29.02 ± 5.44	0.617
BMI	27.36 ± 4.48	27.59 ± 4.38	0.598
Duration of infertility in years	4.03 ± 1.68	3.93 ± 1.58	0.588
Type of infertility	70 (59.8%)	567 (57.9%)	0.167
Primary	47 (40.2%)	413 (42.1%)	
Secondary			
History of endometriosis			<0.001
Yes	17 (1.7%)	19 (16.2%)	
No	963 (98.3%)	98 (83.7%)	
History of pelvic inflammatory disease			0.001
Yes	64 (6.5%)	21 (17.9%)	
No	916 (93.5%)	96 (82.1%)	
History of surgery			<0.001
Yes	39 (4.0%)	20 (17.1%)	
No	941 (96.0%)	97 (82.9%)	
History of polyps			0.004
Yes	49 (5.0%)	23 (19.7%)	
No	931 (95.0%)	94 (80.3%)	

Tab. 3. Conception and time to pregnancy in women with cervical stenosis who received dilation vs those with no dilation

	Stenosis		p-value
	Yes		
	Dilation		
	Yes	No	
	Mean ± SD or count n (%)	Mean ± SD or count n (%)	
Pregnancy			
Yes	62 (70.45%)	5 (18.5%)	<0.001*
No	26 (29.54%)	22 (81.48%)	
Time to pregnancy	8.10 ± 3.43	11.39 ± 1.97	<0.001*

Strengths and limitations

Our study shows the importance of a full assessment of a couple before labelling them as having unexplained subfertility. Around 10.7% women had cervical stenosis and dilation led to conception in 70.54% of them. Another major strength is its case control design and extended follow up.

The major limitation of the study is the fact the single centre design; therefore generalizability of results in other populations needs to be verified with further larger multicentre trials.

Interpretation

Cervical stenosis is typically considered as a factor that may lead to infertility in women who have had surgery for cervical intraepithelial neoplasia (CIN)⁽⁹⁾. However, it can also be a culprit in cases where no such history is present.

About 10.7% of women in our study had cervical stenosis, which is almost twice the figure reported in literature⁽²⁾.

Cervical stenosis is defined as a narrowing of the cervical canal, but no standardized diagnostic method is mentioned in literature. A recent study labelled women with stenosis if there was difficulty in passing a 3.5 mm sheath hysteroscope into the internal cervical os. We included women when it was difficult to pass a 7 French Foley’s catheter⁽¹⁰⁾. Foley’s catheter has a smaller softer tip that would theoretically include more women as having stenosis than when using a hysteroscope. We also argue that a hysteroscope is not accessible to all clinicians in outpatient departments and an opportunity would be missed in all such cases if the above criterion is used. A Foley’s catheter is readily available and diagnosis is pretty straightforward with introduction into cervical canal.

A historical study showed that retrograde menstruation occurs when the external os is less than 4.5 mm, which may lead to endometriosis and subfertility⁽¹¹⁾. We would still argue that such a constriction may be notable to the woman and the clinician due to symptoms. If women were assessed for unexplained infertility any such history of retrograde menstruation would be conflicting. Furthermore, a 7 French Foley’s has an outer diameter of 2.33 mm, which is less than both the 3.5 mm hysteroscope and the external os diameter of 4.5 mm. This cut-off needs to be assessed in further studies.

Because cervical stenosis is difficult to suspect and diagnose, many cases may go unnoticed until and unless the cervix is evaluated. This evaluation becomes more pressing in cases with certain risk factors. In their analysis,

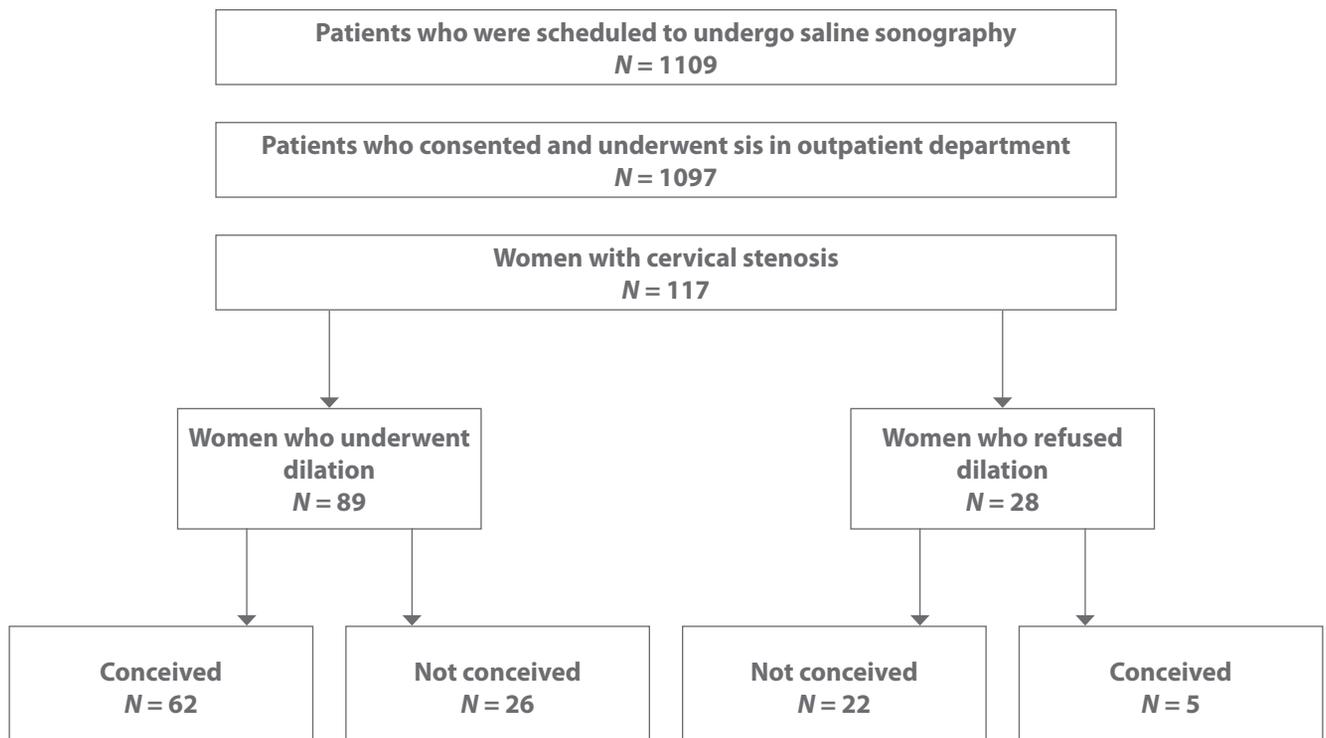


Fig. 1. Profile of the study

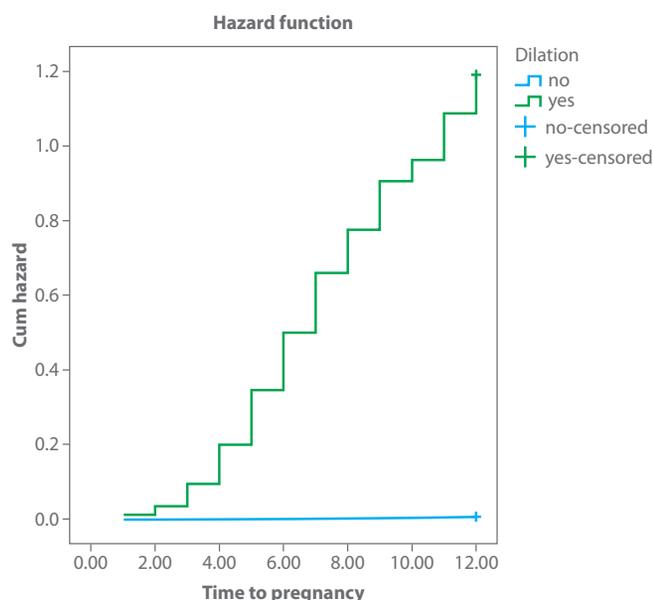


Fig. 2. Conception rate in both groups

Moramazi *et al.* showed a significant correlation with endometriosis, polyps and myomas⁽¹⁰⁾. In our study, prior history of endometriosis, reproductive tract surgery, polyps and pelvic inflammatory disease were significantly associated with cervical stenosis. These findings are in agreement with previous reports^(12,13).

It is important to diagnose and treat cervical stenosis. It hinders sperm deposition in both natural breeding and intrauterine transfers. False passages created during such iatrogenic intervention can be minimized by performing this intervention under ultrasound guidance⁽¹⁴⁾. We performed all dilations under ultrasound guidance. No false passages were created during the study.

Conception can increase after the cervical hindrance to sperm is removed. This has been the essence for adoption of intrauterine insemination in women with cervical factor subfertility⁽¹⁵⁾. Lin *et al.* demonstrated that cervical resection with hysteroscope in cases of stenosis improved conception at subsequent embryo transfer or intrauterine

insemination⁽¹⁶⁾. In our analysis, women conceived spontaneously after dilation, and no intrauterine insemination or IVF was needed. This further cements the observation that cervical stenosis is a clinical entity that can be easily treated and women can conceive without further treatment.

The treatment modalities for unexplained subfertility are currently under scrutiny. Intrauterine insemination, ovulation induction and IVF have all been assessed in trials and currently no consensus exists^(17,18). In our study, a cervical cause was identified and the patients subsequently conceived after receiving dilation. It can be argued that this was not the cause of subfertility in these patients and a stringent protocol may have aided in ascertaining the actual cause. In response we would counter-argue that it may be the case that these women did not have unexplained infertility to begin with. Estimates for natural conception reported from a recent analysis show that women with unexplained subfertility have a 25% chance of conception even without treatment⁽¹⁹⁾. In our study, 70% of women who received dilation conceived compared to only 18% of the controls (who had stenosis defined as per criterion but refused dilation). This observation shows that such dilation is in fact curative and cervical stenosis does lead to subfertility. Natural conception rate of 18% in the control group also shows that in the absence of investigation for cervical factor these women would still have been classified as unexplained group and their conception rate was similar to that reported previously in larger trials⁽¹⁹⁾.

Conclusions

Our study shows that ultrasound-guided cervical dilation in women with cervical stenosis can lead to improved conception rates.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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