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Original article

Endometrial Scratching by an Office Hysteroscopy for Unexplained Infertility: Predictors of Success and Pregnancy Rate

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ABSTRACT

One-half of the infertile couples have unexplained infertility. The endometrial scratch (es) is believed to cause favorable endometrial inflammation, making it more receptive to an implanted embryo. We aimed to assess the success rate of es in enhancing pregnancy and to identify potential predictors for the successful outcome in couples with unexplained infertility. A case-series study included 268 couples with unexplained infertility attending the university teaching hospital in Baghdad for one year after es by an office hysteroscopy. Patients' socio-demographic factors, fertility history, and history of curettage were studied—the success of getting spontaneous pregnancy after es was studied as the dependent variable. SPSS statistical software was used, and the confidence level was employed to verify reliable predictors. The success rate following es was 44 (16.4%), confirmed by clinical pregnancy. There was a 5% decrease in the success rate of the es for every one-year increase in the female age; risk ratio (rr): 0.95; 95% ci 0.907- 0.995). The previous history of curettage increased the rate of the intervention's success by more than two times (rr: 2.412; 95% ci: 1.181 - 4.926). Endometrial scratching improved the odds of pregnancy for couples with unexplained infertility. Potential predictors of the success were younger aged females and previous history of curettage.

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INTRODUCTION

About one-half of infertile couples have infertility with the absence of a gross abnormality [1–3]. It has been supposed that immunological factors, different expressions of the adhesive molecule, and defective endometrial receptivity could be the significant factors contributing to unexplained infertility [4–8]. Implantation stays the rate-restricting step for all infertility treatments. It is believed to be a complex process that includes multiple factors. Observations have suggested that the mechanical injury of the lining endometria may improve uterine receptivity as it triggers the immunity system to generate an inflammatory reaction. In line with this, dendritic cells, a principal component of innate immunity, were recently found to have an essential role in successful implantation in a mouse mode [8,9].

Endometrial scratching (ES) in the luteal phase preceding ovarian stimulation has been suggested to enhance clinical pregnancy in women with repeated implantation failure significantly [10].

The scratch has usually been performed as a biopsy from the endometrium, which is thought to induce a favorable inflammation (injury) within the endometrium lining of the uterine cavity. That way, it will be more receptive to an implanted embryo. It has been postulated that the success of complicated uterine surgery could be attributed to the scratch more than to the surgery itself [11].

Barash et al. 2003 were the first to reveal that doing an endometrial injury with a biopsy catheter in guinea pigs yielded approximately two-fold higher rates of implantation, clinical pregnancy, and live birth [12]. Relji et al. 2017, found that hysteroscopy with endometrial injury before ovarian stimulation could improve rates of implantation and pregnancy in women with repeated implantation failure [13].

Several scholars suggested that endometrial scratching (ES) promotes living birth rates, particularly in females with frequent failure of embryo transfers during in-vitro fertilization (IVF) [14]. A survey in 2016 found that 83% of IVF clinics in New Zealand, Australia, and the United Kingdom were recommending an add-on ES to patients in preparation for IVF treatment [15]. However, a trial carried out at 16 UK centers from 2016 to 2019, including more than 1000 women during IVF cycles, showed no differences between the scratch vs. no-scratch groups with pregnancy rates (42.6% vs. 40.6%) respectively [16].

Similar to the effects in IVF cycles, the ES in natural cycles was supposed to improve pregnancy rates in women with unexplained infertility significantly [17]. Endometrial scratching could be a safe, inexpensive, and well-tolerated intervention to induce subsequent pregnancy in infertile women [17,18]. However, the supporting evidence of endometrial scratching is still disputable, and its impact on pregnancy outcomes remains uncertain [19]. Here, we aimed to verify the success rate of ES to enhance pregnancy in women with unexplained infertility and to highlight potential predictors for successful pregnancy following ES in couples with unexplained infertility attending our clinic.

METHODS

Study design

This is a case series that includes the follow-up of (268) couples with unexplained infertility (who have failed to achieve pregnancy after 12 months of unprotected sex and after the standard fertility test were negative for both partners) after the females had undergone an endometrial scratch procedure using office hysteroscopy. The study started in January 2017 and ended in January 2022.

Data collection

The overall number of infertile couples that registered during the first four years of the study was 417; only 287 (68.3%) of them were eligible for follow-up for one year after the procedure scheduled, as illustrated in the flowchart below. As shown in Figure 1

At the outpatient clinic, participants were informed through direct interviews about the positive value of the procedure and its side effects prior to their enrollment. Participants' demographic criteria were recorded, including age, occupation, and previous medical and obstetrical history. Other recorded parameters included Gravida, parity, primary infertility or secondary infertility and the years of infertility and the number of attempts of endometrial scratch. The intervention: The endometrial scratch procedure was completely done in the outpatient clinic of the Obstetrics and Gynecology clinic in Baghdad using an office hysteroscope. The procedure was carried out in the luteal phase from day 18–to 22 of the menstrual cycle in some patients and in the follicular phase, the rest from day 3 to 25 of the menstrual cycle. The women were lying in a lithotomy position during the procedure. The endometrial lining of the uterine fundus in the included women was scratched using forceps under direct hysteroscopy vision. After the procedure had been done, the included couple was informed to have regular intercourse for a spontaneous pregnancy trial, and they asked to continue their ovulation induction treatment as indicated. The researchers followed up with the eligible couples for one year after the procedure. Dependent variable: the variable under hypothesis testing was the success of getting spontaneous pregnancy after endometrial scratching.

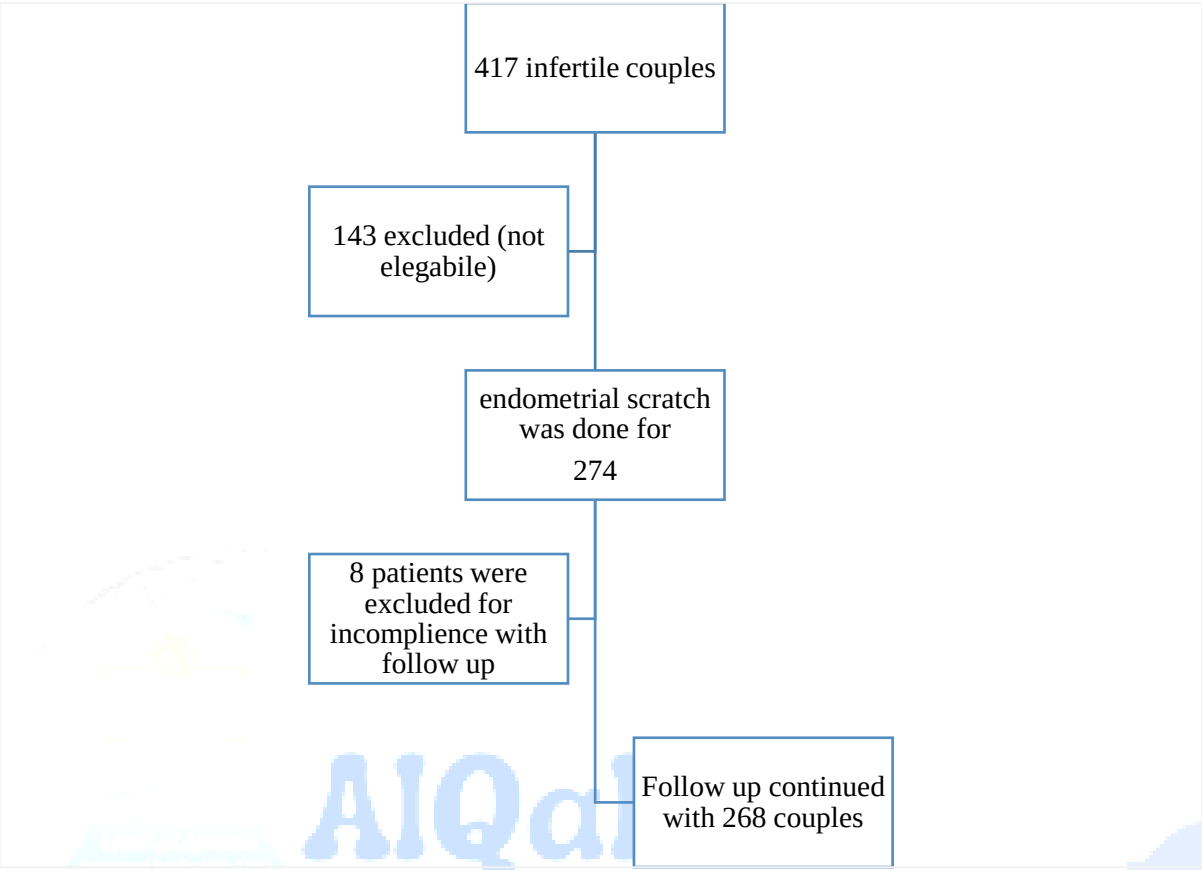

Figure 1. Sample frame of the study.

Inclusion criteria and exclusion criteria

Women who had a history of primary or secondary infertility (infertility refers to the history of at least one year of regular and unprotected sex without having conception), women with a history of previous implantation failure (defined as having experienced at least 1 failed in vitro fertilization cycle [2]), Women have no clear hormonal, pathological, or male factor causes and women having a body mass index (BMI) less than 30, with an age range less than 40 at the time of the procedure.

Those who were disqualified: Cases who had hormonal or pathological abnormalities or other causes of infertility like male factors and a history of azoospermia, structural uterine abnormalities include congenital as bicornuate, unicornuate or acquired disorders such as myomas or polyps, women with uncontrolled medical illnesses and cases that were lost and were not followed up also have been eliminated.

Ethical issues

The study protocol and clinical plan were thoroughly discussed and reviewed by the Ethical and Consulting Review Committee of the medical college, Mustansiryah University, and ethical approval was obtained accordingly. The participants voluntarily signed an informed consent form before they took part in the study. The anonymous identity of the included women was guaranteed as they were assigned an identification number in data entry software.

Statistical analysis

We used the “Statistical Package of Social Sciences (SPSS)” version 26 (16). Frequencies and percentages were used to present the nominal data, and their association with the dependent variable was tested using Pearson's chi-square test of independence. The continuous data were presented using the average and the

standard deviation, and the differences were tested using the student's t-test. A multivariate regression model was used to roll out any confounding factors (including factors that were significant in bivariate analysis), and the rate ratio (RR) of the conception success predictors with a 95% confidence interval was reported. A p-value of less than 0.05 was set as significant for all tests.

RESULTS

We followed included cases up to one year after the women underwent ES using office endoscopy. The success rate (women having positive clinical pregnancy) was 16.4%, as only 44 women got conceived. The age range was from (19 to 44) years, with an average of 30.5±6.6 years. The bivariate analysis showed that the women who got pregnant were meaningfully younger than those who failed [(28.6 ± 7.1) vs. (30.9 ± 6.5) years; p= 0.047]. Women who had a positive history of abortion show a significantly higher success rate than others (23.7% vs.13.5%; p= 0.043). In addition, the success rate among women with a positive history of curettage was 38.1%, which was significantly higher p= 0.005, among those with a negative history 14.6%. The average years of infertility were also significantly less in those who succeeded in conceiving spontaneously after endometrial scratch [(4 ± 2.9) vs. (5 ± 3.6) years; p= 0.04]. Other factors, husbands' age, women's occupation, gravida, parity, history of cesarean section, types of infertility, cervical examination results as well as endometrial scratch attempts, and the day of the cycle when the procedure was carried out did not show any impact on the final outcome (Table 1).

Multivariate analysis showed that the success rate ratio of endometrial scratch declines by 5% for each year increase in women's age (RR: 0.95; 95% CI: 0.907 – 0.995). Moreover, women with a positive history of curettage have a higher rate of success, twice that of those with no such history (RR: 2.412; 95% CI: 1.181 – 4.926). On the other hand, the history of abortion and the years of infertility were found to be confounders (Table 2). The procedure has hypothesized a trigger to the woman's body to release chemicals and stimulate hormones that might enhance spontaneous implantation of the fertilized ovum and, hence, the pregnancy.

Table 1. Univariate analysis for the possible determinants of endometrial scratch results

Parameters		Result of endometrial scratch				Overall (n=268)		p value
		Succeeded (n=44)		Failed (n=224)				
		No.	Row%	No.	Row%	No.	Col. %	
Women age (Years), Mean & Standard deviation		28.6	7.1	30.9	6.5	30.5	6.6	0.047*[t]
Husband age (Years), Mean & Standard deviation		30.2	6.6	31.1	6.9	30.9	6.7	0.531 [t]
Occupation	House wife	33	15.1%	186	84.9%	219	81.7%	0.207
	Employee	11	22.4%	38	77.6%	49	18.3%	
Parity	Nulliparous	23	14.4%	137	85.6%	160	59.7%	0.272
	Primiparous/ multiparous	21	19.4%	87	80.6%	108	40.3%	
Gravida	Nulli/ primigravida	24	13.6%	153	86.4%	177	66.0%	0.078
	Multigravida	20	22.0%	71	78.0%	91	34.0%	
History of abortion	Positive	18	23.7%	58	76.3%	76	28.4%	0.043*
	Negative	26	13.5%	166	86.5%	192	71.6%	
Cesarean section	Yes	5	20.8%	19	79.2%	24	9.0%	0.541
	No	39	16.0%	205	84.0%	244	91.0%	
History of dilatation and curettage	Positive	8	38.1%	13	61.9%	21	7.8%	0.005**
	Negative	36	14.6%	211	85.4%	247	92.2%	
Type of infertility	Primary infertility	17	13.3%	111	86.7%	128	47.8%	0.185
	Secondary infertility	27	19.3%	113	80.7%	140	52.2%	
Years of infertility, Mean & Standard deviation		4.0	2.9	5.0	3.6	4.9	3.5	0.04* [t]
Cervical examination	Normal	34	16.2%	176	83.8%	210	78.4%	0.848
	Abnormal	10	17.2%	48	82.8%	58	21.6%	
Day of the cycle scratch was done, Mean & Standard deviation		9.3	3.0	9.2	2.9	9.2	2.9	0.956 [t]
> one attempt	Yes	3	16.7%	15	83.3%	18	6.7%	0.976
	No	41	16.4%	209	83.6%	250	93.3%	

**Significant at 0.05; **Significant at 0.01; [t] Student's t-test*

Table 2 Multivariate analysis for the determinants of endometrial scratch success

Parameters		Coefficient	p value	RR	95% C.I. for RR	
					Lower	Upper
(Intercept)		-0.244	0.719	0.784	0.208	2.949
Age (years)		-0.051	0.03*	0.95	0.907	0.995
History of abortion	Positive	0.347	0.265	1.415	0.769	2.606
	Negative			1		
History of Dilatation & curettage	Positive	0.88	0.016*	2.412	1.181	4.926
	Negative			1		
Years of infertility		-0.065	0.251	0.937	0.838	1.047

**Significant at 0.05; C.I.: Confidence interval; RR: relative risk*

DISCUSSION

According to the study results, the success rate of endometrial scratch intervention was 16.4%. Previous research on the topic found that endometrial scratching effectively stimulated subsequent conception, whether in assisted reproduction or while awaiting normal pregnancy [12–14,17].

In Iran, a randomized controlled trial has revealed that the success rate of hysteroscopy and endometrial scratching was 41.5% [20]. A Turkish study has found that after performing endometrial scratching, there was an increase in the rates of both pregnancy and clinical pregnancy [21].

The success rate among couples who achieved pregnancy through Intrauterine Insemination (IUI) and those who achieved spontaneous pregnancy after a previous pregnancy through assisted reproductive technique was 5%. For IUI, the pregnancy rate among couples who achieved pregnancy through ART was 17% [22]. According to the research data, the factors that determined the success of intervention were age of patients and history of previous curettage.

Concerning the sequel of age, it was found that there was a decrease in success rate for each one-year increase in women age which could be fertility and fecundity decline with age [23,24]. It was found that history of curettage increases the success rate by about two a half time this could be related to the fact that curettage increase the injury process to the endometrium which add synergistic effect with endometrial scratch intervention leading to more augmentation of the endometrium and improving the likelihood of uterine implantation [25].

Regarding the limitations of this study absence of control group make it hard to address a conclusion adding to that many unidentified confounders affecting the procedure outcome despite using multivariate analysis

CONCLUSION

The success rate of the endometrial scratch procedure was 16.4%. history of previous curettage and female young age were possible predictor of success. more studies needed with control group, larger sample size to rise the supporting level of evidence.

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Conflict of interest. None to be mentioned.

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خربشـــة الرحم بالناظور الرحمي لحالات العقم الغير معروف الســـبب مؤشرات النجاح ونسبة الحمل

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الخلاصة

نصـف الأزواج المصـابين بالعقم لديهم عقم غير مبرر. يعتقد أن خدش بطانة الرحم (ES) يسـبب التهاب بطانة الرحم المواتية، مما يجعله أكثر تقبلا للحمل. نهدف إلى تقييم معدل نجاح خدش بطانة الرحم في تعزيز الحمل وتحديد التنبؤات المحتملة بالنتيجة الناجحة لدى الأزواج الذين يعانون من العقم غير المبرر .شـملت الدراسـة سـلسـلة حالات لعدد من الازواج (268) زوجا يعانون من العقم غير المبرر الذين يحضرـون مسـتشـفى الجامعة التعليمي في بغداد لمدة عام واحد بعد خدش بطانة الرحم عن طريق تنظير الرحم. تمت دراســـة العوامل الاجتماعية والديموغرافية للمرضى والتاريخ المرضي للخصـــوبة ولإجراء الكحت الرحمي أدى الى نجاح الحصـــول على الحمل التلقائي بعد دراســـة خدش بطانة الرحم كمتغير تابع. تم اســـتخدام برنامج SPSS الإحصـــائي، وتم اســـتخدام مســـتوى الثقة للتحقق من التنبؤات الموثوقة. كان معدل النجاح بعد خدش بطانة الرحم (16.4٪). أكده الحمل السـريري .كان هناك انخفاض بنسـبة 5٪ في معدل نجاح خدش بطانة الرحم لكل زيادة لمدة عام واحد في عمر الإناث؛ نسـبة المخاطر CI ٪95 :0.95 :(RR) .(0.995 -0.907زاد التاريخ السابق للكشط من معدل نجاح التدخل بأكثر من مرتين(RR: 2.412 ؛ 95٪ CI: 1.181 .(4.926 -أدى خدش بطانة الرحم إلى تحســـين احتمالات الحمل للأزواج الذين يعانون من العقم غير المبرر. كان المتنبئون المحتملون بالنجاح هم الإناث الأصغر سنا والتاريخ السابق للكحت.

الكلمات الدالة: العقم. تنظير الرحم. بطانة الرحم، خدش.