

**Evaluation of effect of endometrial scratching in previously failed intrauterine insemination cases – A case control study**

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**Abstract**

**Background:** Infertility is recognized as a reproductive system disorder defined by the inability to obtain a clinical pregnancy after more than a year of consistent sexual intercourse. The World health organization (WHO) reported that around 17.5% of adult population, roughly 1 in 6 worldwide experiences infertility.

Intrauterine insemination (IUI) is a procedure for assisting conception that includes the placement of a prepared sperm sample in the upper uterus cavity, bypassing natural obstacles to sperm ascension in the female reproductive canal. Endometrial scratching (ES) improves pregnancy outcomes through a variety of reasons, including local stimulating of the endometrium,

which induces decidualization, which enhances the chance of implantation.

**Methods:** This study was done at Obstetrics & Gynaecology department of National Institute of Medical Sciences which are a tertiary care teaching institute in Rajasthan. 268 patients were enrolled for the study out of which 134 were cases which undergone endometrial scratching and 134 were control in which endometrial scratching was not done.

**Results:** It was seen that the endometrial scratching group had a 28.36% pregnancy rate compared to 11.94% pregnancy rate in non-endometrial scratching group.

**Conclusion:** The study was able to conclude that the endometrial scratching had a positive impact on the

pregnancy related outcomes in patients with a prior failed IUI.

**Keywords:** IUI, Endometrial Scratching, Pregnancy.

### Introduction

Infertility is recognized by the WHO as a reproductive system disorder defined by the inability to obtain a clinical pregnancy after more than a year of consistent sexual intercourse. Primary infertility occurs when a couple has never had a child. Failure to conceive after a prior pregnancy is referred to as secondary infertility<sup>1</sup>.

In 2023, the WHO reported that around 17.5% of adult population, roughly 1 in 6 worldwide experiences infertility. The WHO assessed the overall incidence of infertility in the nation to be between 3.9% and 16.8%. As per the WHO data, the estimated prevalence of primary infertility among reproductive age group women in India is 11.8% [1].

In female reproductive system, infertility may be caused by tubal disorders such as blocked fallopian tubes, uterine disorders which can be inflammatory, congenital or benign in nature, and ovarian disorder. Male factors have a crucial role in infertility. Some of the primary male reasons of infertility include blockage of the reproductive system, which causes dysfunctionalities in sperm ejection, hormonal problems, testicular inability to produce sperm, and aberrant sperm function & quality.

IUI is a procedure for assisting conception that includes the placement of a prepared sperm sample in the upper uterus cavity, bypassing natural obstacles to sperm ascension in the female reproductive canal. It is an economical, non-invasive first-line treatment for selected individuals with functionally normal tubes and infertility caused by a cervical factor, moderate male factor, unresolved factors, immunological factor, as well as

ejaculatory disorders, with clinical pregnancy rates ranging from 10 to 20% per cycle<sup>2</sup>.

The important prognostic indicators of IUI success include patient age, length of infertility, stimulation protocol, infertility cause, number of cycles, when to perform insemination, the amount of preovulatory follicles on a given day of human chorionic gonadotropin (hCG), processed total motile sperm over 10 million, and insemination count  $> 1 \times 10^6$  with  $> 4\%$  normal spermatozoa. Alternative insemination procedures, such as Fallopian tube sperm perfusion, intracervical insemination, as well as intratubal insemination, have also been shown to give no significant advantage over IUI<sup>2</sup>.

IUI failure is a significant complication of the assisted reproductive procedure. The phrase “implantation failure” has been used to characterize individuals who have never demonstrated quantitative indicators of implantation, such as higher levels of hCG, as well as those who have increased hCG production but no subsequent ultrasound confirmation of a gestational sac<sup>3</sup>. It has been discovered that scratching the endometrium before ET is one means of increasing the chances of implantation. During the luteal stage of the cycle before IVF, the endometrium is often “scratched”, with a tiny 3 mm wide catheter known as the Pipelle®. The catheter is usually inserted forward through the cervix to the fundus and then withdrawn in circular motions to stimulate the uterine wall<sup>4</sup>.

Endometrial scratching improves pregnancy outcomes through a variety of reasons, including local stimulation of the endometrium, which induces decidualization, which enhances the chance of implantation of the transplanted embryo, an increase in macrophages, dendritic cells, as well as proinflammatory cytokines such as tumor necrosis factor-alpha (TNF- $\alpha$ ), growth-

regulated oncogenes as well as macrophage-inflammatory protein-1B (MIP-1B), all of which promote implantation as well as producing greater amounts of oestrogen, which induces an early rise in progesterone levels<sup>5,6</sup>.

Therefore, to further understand the utility of endometrial scratching in patients undergoing repeat intrauterine insemination with previously failed cases, we performed this study.

### **Aim**

To analyse the effect of endometrial scratching in failed intrauterine insemination cycles cases.

### **Objectives**

To evaluate the effect of endometrial scratching on pregnancy rates after intrauterine insemination.

### **Materials and methods**

**Study type:** Prospective Case Control Observational study

**Site of study:** Department of Gynaecology, National Institute of Medical Sciences and Research, Jaipur, Rajasthan, India after obtaining the clearance from the Institutional ethics committee.

**Study duration:** 18 months, 268 patients enrolled for study.

### **Inclusion criteria**

- All previous failed intrauterine insemination cases.
- All females who are willing to give written informed consent.

### **Exclusion criteria**

- Acute inflammatory condition in both partners
- Age > 5 years
- > 3 failed IUI cycles
- Women with an ovulation in stimulated cycles
- Women not willing to give consent.

### **Study flow**

- This study was a hospital based observational case control study with the prime objective of comparing the endometrial scratching related pregnancy outcomes to the control group outcomes.
- Patients were screened on the basis of the inclusion and exclusion criteria. Informed consent was taken from patients prior to enrolment in this study.
- Detailed history and clinical examination were carried out and each patient was investigated as per designed proforma.
- Patient of case group underwent endometrial scratching on day 20-22 of previous cycle (in women with 28-30 days cycle) or postovulatory day 6-8 (in patient with prolonged cycles) in which ovulation was confirmed by ultrasonography.
- IUI was performed in all patients after controlled ovarian stimulation as per standard protocol.
- Data was compiled in an excel and analysed as per the statistical analysis plan laid out in the following section.

### **Discussion**

Endometrial scratching is a technique that is being increasingly used for infertility management. This technique involves scratching the endometrium lining using a sterile plastic tube and in turn, triggers a repair process which involves release of multiple chemicals and hormones.

### **Demographic parameters**

Age and BMI - The average age of the patients in the endometrial scratching group was  $29.07 \pm 2.65$  years and the average BMI was  $24.44 \pm 4.11$ . These were not significantly different from the findings in the control groups.

Adamson et al (2011) [7] showed that the mean age of the women with infertility was 25.9 years (range: 16-30 years).

Table 1: Demographic parameters

Age (in years)	End Scratching +	No End Scratching	P Value
Mean +/- SD	29.07±2.65	28.61±2.12	0.1178
Min – Max	23-35	20-32	

BMI (in kg/m2)	End Scratching +	No End Scratching	P Value
Mean +/- SD	24.44±4.11	24.23±3.85	0.6663
Min – Max	18-34	18-32	

Residence and Socio-economic status – majority patients belonged to the urban areas and were mostly from middle and upper socioeconomic status strata of the society.

Ganguly et al 2010<sup>8</sup> showed similar findings highlighting that infertility rate was high among women in urban areas. This may be due to lifestyle or a later age at first marriage.

Literacy and marriage duration – majority patients in the study were literate with average duration of marriage around 6 years.

Similar observations were made by Noori et al 2022<sup>9</sup> who also showed that no significant differences were seen between the two groups in terms of age and BMI.

Table 2: Baseline demographic parameters

Parameter	Endometrial Scratching +	No Endometrial Scratching	P Value
Residence			
Urban	104 (77.61%)	100 (74.62%)	0.5667
Rural	30 (22.39%)	34 (25.38%)	
Socio Economic status			
Upper	50 (37.31%)	47 (35.07%)	0.7033
Middle	47 (35.08%)	44 (32.83%)	0.6979
Lower	37 (27.61%)	43 (32.08%)	0.4248

Literacy			
Literate	130 (97.02%)	134 (100%)	0.1445
Illiterate	4 (2.98%)	0	
Married duration (in years)			
Mean +/- SD	6.76±3.46	6.23±3.76	0.2309
Min – Max	2-13	2-11	

**Infertility related parameters**

The infertility subtype across both the groups was secondary with 97% secondary infertility rate in endometrial scratching group and 100% in control group. 4 patients were seen to have primary infertility in the study and they were allocated to the endometrial scratching group. The duration of infertility was 5.96±2.07 years in endometrial scratching group which was comparable to the 5.82±1.81 years in the control group. The high duration of infertility was primarily seen due to failures of the prior IUIs.

Carson et al 2022<sup>[10]</sup> showed similarly that 85% of infertile couples have secondary infertility which infertility with an identifiable cause.

Deshpande et al 2019<sup>[11]</sup> showed a slightly different observation when they highlighted that the primary infertility (57.5%) was more prevalent than secondary infertility (42.5%).

Most of the patients had 2 failed attempts of IUI across both the groups (122, 91.04% in both the groups). There were 5.97% patients in scratching group and 7.46% patients in the control group who had 3 failed IUI attempts.

It was crucial to note that the husband semen analysis was normal for all the patients. The HSG and DHL findings were also deemed normal with no major differences.

The first cycle endometrial thickness was comparable for the two groups (7.02±0.48 mm vs 7.08±0.53 mm)

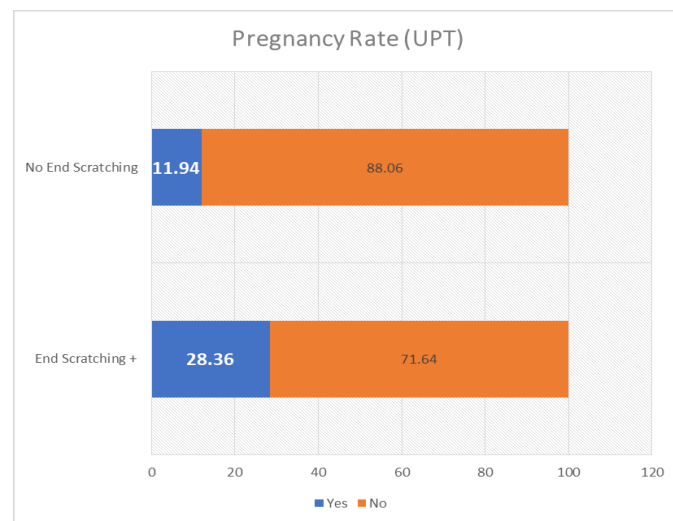
with a P value of 0.3323. The first cycle endometrial vascularity-based distribution was also comparable with no significant difference. ES group had a higher proportion with Z2 vascularity levels while control group had a higher proportion of patients with Z1 vascularity levels but the difference was not significant statistically. The second cycle endometrial thickness was comparable for the two groups (7.17±0.57 mm vs 7.06±0.51 mm) with a P value of 0.0971. The second cycle endometrial vascularity-based distribution was also comparable with no significant difference. ES group had a higher proportion with Z2 vascularity levels while control group had a higher proportion of patients with Z1 vascularity levels but the difference was not significant statistically. A higher proportion of patients across both the groups had 1 follicle.

Mean +/-	7.17±0.57	7.06±0.51	0.0971
SD			
Min – Max	6-8.6	6-8	
2nd cycle Endometrial vascularity (Ovulatory phase) (in mm)			
Z1	55 (41.04%)	59 (44.02%)	0.6224
Z2	60 (44.77%)	54 (40.29%)	0.4591
Z3	12 (8.95%)	17 (12.60%)	0.3362
Z4	7 (5.22%)	4 (2.9%)	0.3369
No. of follicles			
1 follicle	72 (53.73%)	83 (61.95%)	0.1738
2 follicles	62 (46.27%)	51 (38.05%)	

**Pregnancy rate**

It was seen that the endometrial scratching group had a 28.36% pregnancy rate compared to 11.94% pregnancy rate in non-endometrial scratching group. This difference in the pregnancy rates was significantly different with a P value of 0.0012.

Figure 1: Pregnancy rate



Nienke E et al (2023) [12] in one of the first large scale meta-analysis on 4000+ IPD patients who underwent endometrial scratching, showed that endometrial scratching may improve LB rates in women undergoing IVF/ICSI. The timing of endometrial scratching was postulated to play a role in the overall effectiveness.

Table 3: Infertility related parameters

Parameters	Endometrial Scratching +	No Endometrial Scratching	P Value
1st cycle endometrial thickness (Ovulatory phase) (in mm)			
Mean +/-	7.02±0.48	7.08±0.53	0.3323
SD			
Min – Max	6-7.90	5.6-8	
1st cycle Endometrial vascularity (Ovulatory phase) (in mm)			
Z1	46 (34.32%)	68 (50.74%)	0.6067
Z2	56 (41.79%)	48 (35.82%)	0.3169
Z3	24 (17.91%)	12 (8.95%)	0.0318
Z4	8 (5.97%)	6 (4.47%)	0.5817
Ovulation Induction			
CC	134 (100%)	134 (100%)	NA
2nd cycle endometrial thickness (Ovulatory phase) (in mm)			

Subgroup analysis for age, number of previous failed embryo transfers, treatment type, and infertility cause could not identify subgroups in which endometrial scratching performed better or worse.

Similar conclusions were drawn by **Lakovidou et al (2023)** <sup>[13]</sup> which showed that endometrial scratching during the menstrual cycle prior to an embryo transfer cycle led to a higher probability of live birth in patients with previous IVF failures. The study showed that when endometrial scratching was performed during the menstrual cycle prior to the embryo transfer cycle a significantly higher probability of live birth was present. On the contrary, no effect on the probability of live birth was present when endometrial injury was performed during the embryo transfer cycle.

Another meta-analysis by **Ahmed Maged et al** <sup>[14]</sup> showed that ESI increases the clinical pregnancy, ongoing pregnancy, live birth, multiple pregnancy, and implantation rates in women undergoing IVF cycles. The odds ratio (OR) for the clinical pregnancy rate had an effect estimate of 1.34 with a 95% confidence interval (CI) of 1.14 to 1.58. The live birth rate was reported in 32 studies with 8129 participants. The OR for the live birth rate had an effect estimate of 1.30 with a 95% CI of 1.06 to 1.60. The multiple pregnancy rate was reported in 21 studies with 5736 participants. The OR for the multiple pregnancy rate had an effect estimate of 1.35 with a 95% CI of 1.07 to 1.71. These findings were similar to the findings in our study.

**Kang et al (2022)** <sup>[15]</sup> made a similar observation when they showed that Endometrial scratching could enhance the reproductive outcomes of embryo implantation. This was in line with what was observed in our study. They reported that overall, the clinical pregnancy rate (CPR), Implantation rate (IR) and live birth rate (LBR) were

significantly higher in the intervention group than in the control group.

### Limitations of the study

Some of the major limitations of the study were –

1. The study was a single centre study.
2. The study included a small number of patients which would have led to selection bias in the study.
3. A subgroup analysis on the independent predictors that can influence the pregnancy rate was not done.

### Conclusion

The study was able to conclude that the endometrial scratching had a positive impact on the pregnancy related outcomes in patients with a prior failed IUI. These patients mostly had a secondary infertility and were young females in the late twenties. These patients belonged to the urban areas and were highly literate with long durations of marriage as well as infertility.

The study showed that ES was beneficial in terms of higher odds of conceiving and should be evaluated further. The study however, also concluded that there is marked heterogeneity between the literature as far as ES utility is concerned. Many metanalysis in the domain also supported the finding but contravening literature is also abundant with sufficient strength. It is imperative that the findings of this study should be validated by a larger set of randomised study population across multiple centres to provide heterogenous study population perspective.

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