

# The effect on conception rates of bladder fullness during intrauterine insemination: A retrospective cohort study

## İntrauterin inseminasyon esnasında mesane doluluğunun gebelik oranlarına etkisi: Retrospektif kohort çalışma

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### Abstract

**Aim:** Embryo transfer in in-vitro fertilization (IVF) cycles is performed with a full bladder, being careful to avoid surgical instrumentation to the cervix as much as possible, so that uterine contractions are not stimulated. The aim of this study was to investigate whether a full bladder during the application of intrauterine insemination increased pregnancy rates by correcting the cervico-uterine axis, thereby enabling easier access of sperm to the uterine cavity.

**Methods:** This study included 61 patients undergoing IUI procedures, which were performed on patients with infertility since at least one year and those with at least one open oviduct as seen on hysterosalpingography (HSG). Patients' demographic data, folliculometry measurements, spermogram parameters, bladder fullness status on abdominal ultrasonography during the application, and beta hGC levels on the 14<sup>th</sup> day following the application were recorded from the patient files.

**Results:** No statistically significant differences were determined between the two groups in terms of demographic data and folliculometry measurements. The conception rate was 20% in the full bladder group, and 12% in the empty bladder group. Tenaculum application was at a statistically significantly higher rate in the empty bladder group than in the full bladder group ( $P<0.001$ ). The conception rate was insignificantly higher in the full bladder group ( $P=0.342$ ).

**Conclusion:** A full bladder facilitates sperm access to the uterine cavity and may increase conception rates. There is a need for further prospective randomized studies with a larger series to obtain better results.

**Keywords:** Bladder fullness, Conception rate, Intrauterine insemination

### Öz

**Amaç:** In vitro fertilizasyon (IVF) sikluslarında embriyo transferleri uterus kontraksiyonlarını uyarmamak için mümkün mertebe serviks cerrahi alet enstrümantasyonundan kaçınmaya dikkat edilerek ve dolu mesane ile yapılır. Çalışmamızda da intrauterin inseminasyon uygulaması esnasında da mesane doluluğunun serviko-uterin aksı düzeltip spermlerin uterin kaviteye erişimini kolaylaştırarak gebelik oranlarını artırıp artırmadığını araştırmayı amaçladık.

**Yöntemler:** Bu çalışmaya histerosalpingografisinde en az bir tüpünün açık olduğu tespit edilip en az bir yıllık infertilitesi olan ve intrauterin inseminasyon tedavisi yapılan 61 hasta dahil edilmiştir. Hastaların demografik özellikleri, folikülometri ölçümleri, spermogram parametreleri, uygulama esnasındaki abdominal ultrasonografide mesane doluluk durumu ve uygulama sonrası 14. günde beta hGC kaydedildi.

**Bulgular:** İki grup arasında demografik özellikler, folikülometri ölçümleri açısından istatistiksel olarak anlamlı fark yoktu. Gebelik oranı mesane grubunda %20, boş mesane grubunda %12 olarak bulundu. Tenakulum uygulama oranı boş mesane grubunda dolu mesane grubundan anlamlı düzeyde yüksek bulundu ( $P<0.001$ ). Gebelik oranı dolu mesane grubunda daha yüksek olmasına rağmen, fark anlamlı bir seviyeye ulaşmadı ( $P=0,342$ ).

**Sonuç:** Dolu mesane, spermlerin uterin boşluğuna erişimini kolaylaştırıp gebe kalma oranını artırabilir. Daha iyi sonuçlar elde etmek için daha geniş serilerle yapılacak prospektif randomize çalışmaların gerekli olduğuna inanıyoruz.

**Anahtar kelimeler:** İntrauterin inseminasyon, Mesane doluluğu, Gebelik oranı

## Introduction

Intrauterine insemination (IUI) is used in infertility treatment in many cases when there is open tubal access. The most common indications are cervical factor-associated infertility, sexual dysfunction, mild male infertility, and unexplained infertility. Sperms prepared in a laboratory environment are administered via a catheter to the uterine cavity of the patient in lithotomy position at the appropriate time in a natural or stimulated cycle [1]. There are many studies in the literature which have investigated the factors that can affect IUI success, which include sperm parameters (number, motility, morphology), the duration of infertility, methods used for ovulation induction and their monitorization, the number of cycles in which they were applied and the application technique [2].

Of the factors affecting pregnancy success in in-vitro fertilization (IVF) cycles, studies related to embryo transfer have focused on triggering uterine contractility in particular [3]. Increasing uterine contractions with intrauterine manipulation and instrument application to the cervix was found to decrease the pregnancy rate in IVF cycles [4]. Similarly, flattening the uterus by filling the bladder during embryo transfer in IVF cycles was found to increase pregnancy rates [5]. However, there are insufficient studies which have investigated the effects of the methods of tenaculum application or increasing the cervico-uterine angle on pregnancy success. The aim of this study was to retrospectively investigate whether there was an increase in pregnancy rates by facilitating sperm access to the uterine cavity during the IUI procedure with fullness of the bladder, which is effective in correcting the cervico-uterine axis.

## Materials and methods

Approval for the study was granted by the Clinical Research Ethics Committee of Kahramanmaraş Sütçü İmam University (decision no: 14, session: 2019/11). The study was conducted in accordance with the principles of Helsinki Declaration. We included all 61 patients with accessible hospital records from January 2016 to June 2018, who had at least one tube open on hysterosalpingography (HSG), were followed with at least one year of infertility and treated in our clinic with IUI. During investigation of the infertility etiology, transvaginal ultrasonography was performed on the 2<sup>nd</sup> or 3<sup>rd</sup> day of the cycle and FSH, LH and E2 levels were measured. IUI was not performed on patients with spermogram results of <10 million/cc mobile sperm. Ovulation induction was applied to patients with unexplained infertility and polycystic ovary syndrome-related infertility with the routinely used Clomiphene Citrate (Klomen, Koçak Farma İlaç ve Kimya Sanayi A.Ş., Üsküdar, Istanbul), or recombinant FSH (Gonal-F, Merck Serono SA, Geneva, Switzerland).

When the dominant follicle size reached 18-20 mm in those who received clomiphene citrate and 17-18mm in those who received recombinant FSH, 6500 units of human chorionic gonadotropin (Ovitrelle, Merck Serono SA, Geneva, Switzerland) was administered. The standard Swim Up method was used in the sperm preparation. IUI was performed to all patients after 36 hours by the same doctor (ZB). Using an

insemination catheter (Gynemed Medical GmbH, Lensahn, Germany), 0.3-0.5 ml of the prepared insemination material was administered slowly to the uterine cavity. During the IUI procedure, whether there was any dominant follicle rupture and the amount of fullness of the bladder were recorded with transabdominal ultrasonography. For calculation of the bladder volume, the longest oblique diameter on sagittal slices, the sagittal anterior-posterior diameter, and the width on the transverse slice were multiplied by 0.7 [6].

Patients with >200cc urine in the bladder were included in the full bladder group. During the procedure, difficulty in tenaculum application to the cervix for correction of the cervico-uterine axis was recorded. At 2 weeks after IUI,  $\beta$ -HCG levels were measured and noted. The patients were separated into 2 groups according to the fullness of the bladder, as the full bladder group and the empty bladder group. The results were analyzed and compared between these two groups.

### Statistical analysis

Data obtained in the study were statistically analyzed using IBM SPSS for Windows v. 22.0 software (IBM Corporation, Armonk, NY, USA). Results were stated as mean (standard deviation (SD)). In the variance analysis for repeated measures, the Repeated Measures ANOVA with Bonferroni correction test was utilized. Tukey HSD was used for the comparison of paired groups. *P*-value <0.05 was considered statistically significant.

## Results

The full bladder group included 30 patients and the empty bladder group, 31 patients. No statistically significant differences were determined between the two groups with respect to patient age, BMI, FSH, LH, and E2 levels on the 3<sup>rd</sup> day of the cycle, duration of infertility, the total drug dose in those using recombinant FSH, endometrium thickness on Hcg day, dominant follicle number and size, and the total number of mobile sperm inseminated. Pregnancy rate was 20% in the full bladder group and 12.9% in the empty bladder group.

There was a significantly lower need for tenaculum application for correction of the cervico-uterine axis in the full bladder group (n=1, 3.33%) compared to the empty bladder group (n=12, 38.7%) (*P*<0.001). The pregnancy rate was insignificantly higher in the full bladder group (*P*=0.342) (Table 1).

Table 1: Patient demographic data, laboratory values, cycle findings and pregnancy outcomes

	Full bladder (n=30)	Empty bladder (n=31)	<i>P</i> -value
Age (years)	26.83 (3.51)	26.54 (3.51)	0.753
Duration of infertility(years)	3.43 (1.56)	3.32 (1.57)	0.784
BMI (kg/m <sup>2</sup> )	25.56 (2.56)	25.90 (2.53)	0.608
HCG day endometrium thickness (mm)	7.96 (1.95)	7.93 (1.89)	0.950
D3 FSH	5.36 (1.95)	5.12 (1.96)	0.645
D3 LH	11.66 (5.14)	11.51 (5.20)	0.910
D3 E2	43.86 (14.05)	44.80 (14.84)	0.801
Dominant follicle count	1.22 (0.51)	1.18 (0.16)	0.886
Dominant follicle size (mm)	19.1 (0.96)	18.84 (1.02)	0.842
Total number of inseminated mobile sperm (million)	33.2 (5.67)	35.91 (4.47)	0.718
Requirement for tenaculum use (n)	1 (3.33 %)	12 (38.7 %)	<0.001
Pregnancy			0.342
Yes	6 (20%)	4 (12.9%)	
No	24 (80%)	27 (87.1%)	

Values are presented as Mean (SD), LH: luteinizing hormone, FSH: follicle-stimulating hormone, E2: Estradiol

Sub-group analysis of the pregnancy rates of the two groups according to the use of clomiphene citrate and recombinant FSH revealed that pregnancy rates reached with IUI performed with a full bladder were insignificantly higher in both drug groups compared to those with an empty bladder (21.4% vs. 13.3%, and 18.75% vs. 12.5%) (Table 2).

Table 2: Subgroup analysis of the agents used in ovulation induction

	Full bladder		Empty bladder		P-value
	Gonadotropin (n = 14)	Clomiphene (n = 16)	Gonadotropin (n = 15)	Clomiphene (n = 16)	
Age (years)	26.71 (3.87)	26.93 (3.29)	26.26 (3.30)	26.06 (3.64)	0.903
Duration of infertility (years)	3.57 (1.69)	3.50 (1.50)	3.23 (1.53)	3.37 (1.62)	0.972
BMI (kg/m <sup>2</sup> )	25.14 (2.47)	25.93 (2.67)	25.64 (2.73)	25.93 (2.40)	0.819
HCG day	8.92 (1.73)	7.12 (1.78)	8.35 (1.65)	7.50 (1.96)	0.031
endometrium thickness (mm)					
D3 FSH	5.78 (1.88)	5.00 (2.16)	5.70 (1.79)	4.75 (2.17)	0.391
D3 LH	12.85 (5.08)	10.62 (5.13)	13.23 (5.39)	10.50 (5.40)	0.317
D3 E2	45.92 (15.86)	42.06 (12.51)	42.70 (15.56)	45.37 (14.50)	0.850
Pregnancy	3 (21.4%)	3 (18.75%)	2 (13.3%)	2 (12.5%)	0.896
Yes					
No	11 (78.6%)	13 (81.25%)	13 (86.7%)	14 (87.5%)	

Values are presented as Mean (SD), LH: luteinizing hormone, FSH: follicle-stimulating hormone, E2: Estradiol

## Discussion

The main hypothesis of this study was that just as in embryo transfer in IVF cycles, the IUI procedure would be easier with passive uterine flattening, in other words, with a full bladder. As it would be easier to advance the catheter from the cervical canal, there would be less requirement for cervico-uterine flattening with tenaculum application to the cervix, which would not trigger uterine contractions, consequently resulting in increased pregnancy success. Consistent with this hypothesis, a full bladder was found to reduce the need for tenaculum application to flatten the uterus. However, although the rate of tenaculum application in the full bladder group was low, as was expected, and the pregnancy rate was higher than in the empty bladder group (20% vs. 12.9%), the difference was not statistically significant.

Passive uterine flattening in this study, and the comfortable and easy placement of the catheter in the uterus is related more to IVF studies in the literature than IUI. Two well-designed studies published in Human Reproduction in 1998 [4] and 1999 [3] showed that pregnancy success reduces by increased uterine contractions due to manipulation of the cervix with surgical instruments during embryo transfer in IVF cycles. Supporting the findings of those studies, a 2002 study by Thomas C et al. [7] compared the pregnancy rates of 3 groups of embryo transfer classified as easy, moderate, and difficult. The pregnancy rates were reported as 21.2% in the difficult group and 30.3% in the easy and moderate group, revealing the importance of the degree of ease of embryo transfer as a factor affecting IVF success independent of other factors, and it was therefore recommended to avoid difficult transfers as much as possible. In another study, Dorn et al. [8] determined that uterine contractions stimulated by tenaculum application caused an increase in serum oxytocin levels. Lesny et al. [9] also reported that contact of the catheter with the uterine fundus during embryo transfer in IVF cycles triggered uterine contractions.

Studies related to uterine flattening methods in IUI cycles and the effect of these on pregnancy outcomes were published in the literature approximately 10 years after IVF studies. In a study by Park et al. [10], 233 IUI cycles of 143 couples diagnosed with unexplained infertility were

retrospectively examined. It was reported that tenaculum application to the cervix for correction of the cervico-uterine axis did not change pregnancy outcomes and a pregnancy rate of 14.6% was obtained. This was an acceptable rate when compared with the success rate of 12.6% in the ESHRE study, which examined 120,613 IUI cycles [11]. In a prospective randomized study of 468 IUI cases by Balci et al. [12], the effects of tenaculum application to the cervix on uterine contractions were examined with transabdominal ultrasound. It was determined that tenaculum application increased uterine contractions and this increase both decreased and increased pregnancy outcomes. This was reportedly because the uterine contractions could have increased the sperm transport to the uterine tube.

Another study in literature by Ayas et al. [13], which was similar in design to the current study, is the only prospective, randomized study to have investigated the effect of passive uterine flattening with a full bladder on pregnancy outcomes. Although it was stated that a full bladder increased pregnancy rates by facilitating the IUI procedure, there were several biases in that study related to patient selection and randomization.

Despite the retrospective design and small number of cases in the current study, it can be considered of value as there are few well-designed studies on this subject in literature. That the increased pregnancy rate in the full bladder group did not reach a statistically significant level could be attributed to the number of cases in the study and it can be considered that with a sufficient number of cases this increase would reach a level of statistical significance.

## Limitations

Limitations of this study were primarily the retrospective design and the relatively low number of cases. However, when the legal difficulties of conducting prospective human studies using drugs are considered in Turkey, the findings of this study can be considered to make a valuable contribution to the literature on this subject.

## Conclusion

A full bladder during IUI can affect pregnancy outcomes by reducing the need for cervical manipulation. To objectively demonstrate the effects of uterus flattening methods on uterine contractions, there is a need for electrophysiological studies and prospective, randomized, well-designed studies with a sufficient number of patients.

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