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# The Role of Saline Sonohysterography Prior to IVF/ICSI and its Impact on Assisted Reproduction Program Outcome in Egyptian Community

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## Abstract

**Aim:** To assess the incidence of undiagnosed intrauterine pathology based on saline sonohysterography in women with normal transvaginal ultrasound and their impact on the success rate of Intracytoplasmic sperm injection in Egyptian community.

**Patients and methods:** Two hundred qualified patients scheduled for first time Intracytoplasmic sperm injection treatment were divided into 2 groups each containing 100 patients. Group 1 did saline sonohysterography and cases with intrauterine lesions were treated by hysteroscopy prior to undergoing Intracytoplasmic sperm injection, while group 2 did Intracytoplasmic sperm injection without prior saline sonohysterography. The main outcome measures were undiagnosed intrauterine abnormalities as uterine anomalies and polyps, in addition to, pregnancy, miscarriage and on-going pregnancy rates.

**Results:** Uterine lesions were found in 35% of cases undergoing sonohysterography, and 27 out of the 35 cases were treated by hysteroscopy. A significant difference in pregnancy rate and on-going pregnancy rate in favour of the sonohysterography group ( $P=0.04$ ) and ( $P=0.031$ ) respectively.

**Conclusion:** Saline sonohysterography is a non-invasive method for the diagnosis of uterine abnormalities improving the outcome of IVF/ICSI cycles.

problems [1]. Hysteroscopy prior to *in vitro* fertilization (IVF) diagnosed unsuspected intrauterine abnormalities in 11-45% of cases [2].

Despite advances in assisted reproductive technology (ART) there is a huge gap between a successful embryo transfer and pregnancy rate, which causes both mental and physical burdens to the patients with each IVF cycle, in addition to, the costs associated with the treatment itself [3].

Saline infusion sonohysterography (SIS) is useful in the diagnosis of intrauterine abnormalities and has the advantages of being inexpensive, very accurate and non-invasive test [4]. In spite of this the Royal College of Obstetricians and Gynaecologists (RCOG) neither recommends SIS nor hysteroscopy as an initial investigation prior to IVF [5], however, other more recent studies as those done by [6,7] reported a significant increase in pregnancy rate after the treatment of unsuspected uterine abnormalities, especially the former study which was done in patients with previous 2 failed IVF attempts. Another important difference between UK and Egypt is that the National health services in UK sponsors up to 3 cycles of IVF/ICSI contrary to Egypt where all the cycle costs are covered by the patients, which causes a lot of financial burden especially that most of those patients can barely finance one treatment cycle.

The aim of our study was to assess the incidence of undiagnosed intrauterine pathology based on saline sonohysterography in women with normal transvaginal ultrasound and their impact on the success rate of ICSI in Egyptian community.

**Keywords** Saline sonohysterography; ICSI outcome; Egyptian community

## Introduction

The uterus has an important role in reproduction. Between 3 and 10% of infertile women have uterine factor of infertility, which may disturb sperm ascend and implantation of the fertilized ovum leading to pregnancy loss and other obstetric

## Patients and Methods

The study was a prospective trial conducted in the International Islamic center for population study and researches in Al-Azhar University in Cairo. The study was approved by the ethical committee of Al-Azhar University. Two hundred patients with either primary or secondary infertility scheduled for first time *in-vitro* fertilization (IVF) and intra-cytoplasmic sperm injection (ICSI) treatment and fulfilling the inclusion criteria, which are age between 25 and 30 years, and having no visible

intra-cavitary pathology by transvaginal ultrasound done in the late follicular phase signed an informed consent to participate in the study, while patients with abnormal transvaginal ultrasound, presence of endometrioma or ovarian cyst, history of recurrent consecutive miscarriage before 20 weeks gestation, prior hysteroscopy treatment, inter-menstrual blood loss, age below 25 or above 30 years were excluded from the study.

The patients were divided into 2 groups each containing 100 patients. Group 1 did saline sonohysterography prior to undergoing ICSI, while group 2 did ICSI without prior saline sonohysterography.

### Technique of saline sonohysterography

The procedure was done between day 4 and day 11 of the menstrual cycle when no menses were present. A speculum was inserted vaginally and up to 10 ml of sterile saline solution were infused into the uterine cavity through number 8 pediatric Foley’s catheter to distend the endometrial cavity and the catheter was fixed with 2 ml of normal saline to become fixed inside the uterus and prevent leakage of saline. A transvaginal transducer (Medisonx6) was used to scan the uterine cavity. The findings were recorded in the patients’ files. This procedure costs 200 L.E. (equivalent to 20\$). Cases with lesions found in the uterine cavity were treated by hysteroscopy the following day, which costs 800 L.E. (equivalent to 80\$), before starting ICSI treatment in the following cycle.

All patients performed ICSI using the standard long protocol with short acting GnRH agonist (lucrine 10 unites) injected subcutaneously daily from day 21 of the previous menstrual cycle. Human menopausal gonadotropins(HMG) (Merional 75 units) was given in an adjusted dose for each patient daily intramuscular starting at day 2 of the menstrual cycle. Final oocyte maturation was achieved by administering human chorionic gonadotropins (HCG) when 3 or more follicles of more than 18 mm. were present. Oocyte retrieval was carried out 34-36 hours after HCG administration. The average cost of ICSI cycle was 12000 L.E. (equivalent to 1200 \$).

The main outcome measures were undiagnosed intrauterine abnormalities as uterine anomalies and polyps, in addition to, pregnancy, miscarriage and ongoing pregnancy rates.

## Results

The demographic data: age, weight and body mass index are shown in Table 1. As regards the type of infertility there were 71 cases with primary infertility (71%) and 29 cases with secondary infertility (29%) in group 1 as compared to 70 cases with primary infertility (70%) and 30 cases with secondary infertility (30%) in group 2 (P-value= >0.05). The duration of infertility ranged between 1 and 6 years in both groups with a mean of 3.16 and a standard deviation of +/- 2.03 in group 1, and a mean of 3.22 and a standard deviation of +/- 1.9 in group 2 (P-value=0.850).

The baseline characteristics: anti-Mullerian hormone (AMH) level, basal follicle stimulating hormone (FSH) level, number of HMG ampoules required per cycle, endometrial thickness at the day of ovum pick-up or number of follicles 18 mm. or more are

shown in Table 2. There were no recorded cases of complications or procedure failure in this study. The distribution of intrauterine lesions found in the saline sonohysterography group is shown in Table 3. Saline sonohysterography had a sensitivity of 91.11%, specificity of 88.1%, and positive predictive value of 89.3%, negative predictive value of 90.7% and a diagnostic accuracy of 91% (Confidence Interval 95% for all these values). Positive likelihood ratio was 8.65 and negative likelihood ratio was 0.04. Pregnancy rate, miscarriage rate and on-going pregnancy rate in both groups are shown in Table 4.

**Table 1:** Showing the demographic data in both groups, SD= Standard deviation. n=number of cases. Kg=Kilograms. BMI=Body mass index.

	Group 1 (n=100)	Group 1 Mean +/- SD	Group 2 (n=100)	Group 2 Mean +/- SD	T	P-value
	Range		Range			
Age (years)	25-30	26.8 +/- 3.54	25-30	27.11 +/- 3.16	0.7 15	0.6732
BMI (kg/m <sup>2</sup> )	18-39.4	29.39 +/- 5.68	17.9-41 .1	28.8 +/- 5.47	0.7 482	0.4552

**Table 2:** Showing the baseline clinical characteristics of both groups; AMH=Anti-Mullerian hormone. FSH=Follicle stimulating hormone. HMG=Human menopausal gonadotrophin.

Parameters	Group 1 (Mean +/- SD)	Group 2 (Mean +/- SD)	P-value
AMH (pmol/liter)	4.43 +/- 0.12	4.41 +/- 0.14	0.2794
Basal FSH (mIU/ml)	4.7 +/- 0.9	4.6 +/- 1.1	0.4825
HMG ampoules per cycle	4.9 +/- 1.3	4.7 +/- 2.1	0.4190
Endometrial thickness	7.9 +/- 1.3	8.1 +/- 1.2	0.2596
Number of follicles 18 mm. or more	3.8 +/- 1.1	3.5 +/- 1.6	0.1239

**Table 3:** Showing the diagnosis of the lesions detected in group 1 which performed saline sonohysterography.

Diagnosis	Saline sonohysterography diagnosis (number of patients)	Hysteroscopy
Normal uterus	65	Not done
Submucus fibroid	5	4 (80%)
Endometrial polyp	10	10 (100%)
Adenomyosis	6	Not done
Uterine malformations	6	6 (100%)
Adhesions	8	7 (87.5%)
Total	100	27

P-value	<0.001
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**Table 4:** Showing the pregnancy, miscarriage and on-going pregnancy rate in both groups.

Parameters	Group 1 (Study group)		Group 2 (Control group)		P-value
	Number	%	Number	%	
Pregnancy rate	48	48%	33	33%	0.044
Miscarriage rate	11	11%	18	18%	0.153
Ongoing pregnancy rate	37	37%	15	15%	0.031

## Discussion

Both the uterine cavity and the fallopian tubes have active roles in several reproductive functions, for example, ovum retrieval and transportation, sperm transportation and capacitation, fertilization, embryo nourishing and transportation, in addition to, implantation [8]. Therefore, it is important to evaluate both the uterine cavity and the fallopian tubes, which represents one third of the costs of management of the infertile couple [9].

Transvaginal ultrasound is a popular method in the initial assessment of infertile couples; however, it has its limitation in detecting small nodular lesions with similar echogenicity to the endometrium [10]. Saline sonohysterography has the advantages of being quick, easy, safe and well tolerated method for assessing both the uterine cavity and the fallopian tubes [11], in addition to, 96% agreement with hysteroscopy in the diagnosis of growing focal lesions in the study done by [12].

The current study had no significant difference between both groups as regards the demographic data of the patients (Table 1), AMH and basal FSH levels, number of HMG ampoules required per cycle, endometrial thickness at the day of ovum pick-up or number of follicles 18 mm. or more (Table 2). The type and duration of infertility didn't differ significantly between both groups, however, we found uterine lesions in 35 cases (35%) of group 1, of which 27 cases (27%) were treated by hysteroscopy, this was highly significant ( $P < 0.001$ ) (Table 3) and resulted in a significant difference in both pregnancy and on-going pregnancy rates (Table 4) the latter results agreed with the results of the study done by [6] who found 9-13% increase in clinical pregnancy rate in the following IVF cycle in patients who had previous 2 failed IVF attempts after treating their intra-uterine lesions. Although the current study recruited patients undergoing ICSI for the first time we think that the financial costs which is totally covered by our patients is an important factor to take into consideration, taking into account that the costs of sonohysterography is 20 \$ and hysteroscopy if needed is 80 \$ are together a lot less than that of a failed ICSI cycle (1200\$). This point should be taken into account when

counselling the patients regarding treatment options, expected cycle fecundity and treatment cost.

The current study showed 91.11% sensitivity, 89.3% positive predictive value and 91% diagnostic accuracy, which is near the values found by [13] who found 93.3% sensitivity, 94.6% positive predictive value and 93.3% diagnostic accuracy in detection of endometrial polyps, and less than the study done by [14] who found 100% sensitivity in detection of the same type of lesion.

Procedural failure of sonohysterography is reported to be between 2.9 and 6% [15] and [16], however, we had no cases of procedural failure a possible explanation for this is that all the patients were premenopausal with cervixes easy to catheterize. Dueholm and co-workers [17], reported 1% infection rate following sonohysterography, however, we had neither infected cases nor other complications in the current study.

Endometrial local injury is another controversial point, while some studies as [18] concluded that local endometrial injury increased the pregnancy rate other studies as that done by [19] concluded the opposite. The current study showed that the pregnancy rate was increased in the group that had local endometrial injury by the sonohysterography procedure.

The current study is not without limitations as certain points were not discussed as the patient's preference, discomfort and the time spent. Studies addressing these points are small and future work is needed to address these areas.

## Conclusion

Saline sonohysterography is a non-invasive method for the diagnosis of uterine abnormalities and tubal patency improving the outcome of ICSI cycles. Saline sonohysterography is a simple, safe and inexpensive procedure avoiding aesthetic complications and has rare adverse effects.

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