

## Effect of Ultrasound Guided Embryo Transfer on Pregnancy Rates

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**Abstract: Objective:** to assess the effect of transabdominal ultrasound guidance during embryo transfer (ET) on the per transfer pregnancy rate. **Design:** A prospective randomized double blind study. **Setting:** University based IVF practice. **Patients and methods:** a total of 90 patients undergoing treatment with ICSI were divided into two groups: **Group I:** had ultrasound guided ET, **Group II:** Underwent ET using the clinical touch technique. **Main outcomes measure:** Clinical pregnancy rate, the ongoing pregnancy rate and the abortion rate were evaluated. **Results:** There was an increase in the clinical pregnancy rate and the ongoing pregnancy rate but with no statistical significant difference. **Conclusion:** Ultrasound guided ET is simple and improves the outcomes though with no statistical significance yet it may be used to offer the patients the maximum possibility of pregnancy.

[Ahmed Rushdi Ammar, Khaled Said Mousa, Noha Hamed Rabei and Amira Galal. **Effect of Ultrasound Guided Embryo Transfer on Pregnancy Rates.** *N Y Sci J* 2013;6(12):79-83]. (ISSN: 1554-0200). <http://www.sciencepub.net/newyork>. 13

**Key words:** Embryo transfer, Transabdominal ultrasound, *in vitro* fertilization. ClinicalTrials.gov identifier:

### 1.Introduction

Since the first pregnancy using IVF was achieved nearly 30 years ago many aspects of this procedure have undergone significant progress. In contrast, the technique of ET has remained relatively unchanged. A simple yet critical element in the final step of IVF, ET has received little attention until recently. Because poor implantation rates have increasingly hindered the growing success of IVF, the procedure of ET is now under greater scrutiny. Although poor embryo quality or suboptimal uterine receptivity may be responsible for implantation failure, the transfer technique itself is now also recognized as an important determinant of IVF success. The goal of a successful ET is to deliver the embryos a traumatically to a location in the uterus where implantation is maximized<sup>(1)</sup>.

Ultrasound guidance is used to facilitate atraumatic insertion of the catheter, as well as ensure correct location in the uterine cavity. Touching the fundus can easily be avoided with ultrasound and one can be certain that the catheter is beyond the internal os in cases of an elongated cervical canal. Ultrasound can be especially helpful in uteri distorted by fibroids or those with previous cesarean section scar defects in which the catheter can get hung up or misdirected. Direct visualization of the catheter at the cervicouterine angle can facilitate its insertion, allowing the physician to place an appropriate curve on the catheter, which can be particularly helpful in severely flexed uteri. The full bladder required for abdominal ultrasound also helps to straighten the cervicouterine angle and facilitate entry of the

catheter, particularly for the strongly anteverted uterus<sup>(2,3,4)</sup>.

Most programmes, have relied on "feel" by the clinician placing the transfer catheter and embryos within the uterine cavity at a point "near" the fundus<sup>(5)</sup>.

The aim of the work is to assess the effect of transabdominal ultrasound guidance during embryo transfer on the per transfer pregnancy rate.

### 2.Patients and Methods

This randomized study was carried out in Ain Shams Maternity hospital, in the period between September 2009 and August 2011. A total of 90 infertile patients undergoing treatment with ICSI attending assisted reproductive unit in Ain Shams Maternity Hospital were included in the study. They were divided into 2 groups: **Group I:** Ultrasound guided ET, and **group II:** Clinical touch technique.

An informed written consent was obtained from patients prior to participation in the study.

#### Inclusion criteria

- 1- Age between 20 and 39 years old.
- 2- Male factor infertility.
- 3- Ovarian factor and unexplained infertility.

#### Exclusion criteria

1. Tubal factor infertility.
2. Endometriosis
3. FSH concentration > 16 iu/ml on cycle day 3.
4. Less than two embryos grade A

5. Difficult embryo transfer which needs cervical dilatation, tenaculum or anaesthesia.

Fresh embryos were transferred in all the patients. They were randomized prospectively by computer-generated random table on the day of embryo transfer into two groups:

- 1- Transabdominal ultrasound-guided embryo transfer
- 2- Clinical touch embryo transfer.

The randomization table was made and kept by a nurse who was not involved in the recruitment of subjects. Skilled gynecologist was responsible for conducting embryo transfer in the two groups.

### Ovarian stimulation protocol

The patients were all treated with a long protocol for ovarian stimulation. In the long protocol, pituitary down-regulation was achieved by administering Triptolin<sup>®</sup> (0.1 mg S.C.) per day starting from day 21 of menstrual cycle and the dose was decreased to 0.05 mg per day with the onset of menstruation. Human menopausal gonadotrophin (HMG) (Menogon<sup>®</sup>, Ferring, Germany) was started from the second day of the menstrual cycle with a dose of 150-300 IU per day according to the patient's age, body mass index (BMI), antral follicular count and FSH basal level.

Just prior to ovarian stimulation a mock transfer was performed. In the mock transfer the following data was recorded: uterine position, special characteristics of cervical canal, length of cervix and any difficulty that has occurred. The information of mock transfer was recorded and used when performing the embryo transfer. For embryo transfer as well as mock transfer the Lapotect catheter was used.

Monitoring was carried out by transvaginal ultrasound on day 7 of HMG stimulation. When 3 follicles or more larger than 18 mm in diameter were observed, 10000 IU of human chorionic gonadotrophin (hCG) (Choiomon<sup>®</sup> 5000) was administered intramuscularly, and 36 hours later, oocytes were retrieved under general anesthesia by transvaginal ultrasound-guided aspiration. Mature oocytes were retrieved from follicular fluid and placed in G-1 TM version 3 (Vitrolife, Goteborg, Sweden) All embryo transfers were performed 48 hrs after oocyte retrieval. Before the transfer, the embryos were evaluated microscopically and the best-quality embryos were selected for the transfer. A maximum of three embryos were transferred. The luteal phase was supported with progesterone in oil, intramuscularly, per day administered by starting on day of ovum retrieval. Embryo transfer was carried out on the fifth day after fertilization.

### Technique of embryo transfer

Patients were admitted on the morning of embryo transfer and were randomized into two groups: embryo transfer under transabdominal ultrasound-guidance and clinical touch method. Those patients randomized to the ultrasound-guided group were asked to keep a full bladder before the transfer to assist visualization during the procedure. The patients in the clinical touch were allowed to pass urine according to their need. The patient was placed in the dorsolithotomy position and a sterile speculum was inserted into the vagina. When the speculum was adequately positioned to visualize the cervix, the cervix was washed with a sponge soaked with transfer media.

Embryos were prepared in the laboratory by lab technician prior to the transfer. When ultrasound was used, the position of the uterus and cervix was ascertained before placement of the transfer catheter, labotect catheter was used in all patients of both groups.

In case group where ultrasound guidance was used, the catheter was advanced so that the tip was approximately 1.5 cm from the uterine fundus and the 2 embryos were slowly released. In control group where the clinical touch method was used, the catheter was inserted through the cervical canal and the embryos were released according to the clinician's feeling as to the position of the catheter. In both groups, the catheter was carefully removed after a period of 10s. Then it was checked under a stereomicroscope to ensure that all embryos had been transferred. After embryo transfer, the patient was transferred to the recovery room and allowed to rest in the supine position with her legs slightly elevated for 30 min following the procedure.  $\beta$ HCG was measured 2 weeks after transfer while ultrasound was done 4 weeks after ET.

Clinical pregnancy was defined as the presence of at least one gestational sac by ultrasound examination. An ongoing pregnancy was defined as the presence of at least one fetus with positive heart pulsations seen with ultrasound examination beyond the first trimester of pregnancy. Also the incidence of miscarriage was included.

### 3. Results

Both groups were comparable as regards the main demographic characteristics as well as the main cycle parameter as shown in table (1).

Clinical pregnancy rate was 22.2% in the ultrasound-guided group and 15.5% in the clinical touch group ( $p$  value =0.3). The difference was not statistically significant. The ongoing pregnancy rate was 20% in the ultrasound and 11.2% in the clinical group and again the difference was not statistically

significant. In addition, all of the embryos were singleton and no significant differences were

observed between two groups as shown in table 2.

**Table (1):** Main characteristics of ultrasound-guided transfer and clinical touch transfer populations.

	Ultrasound guided 45 patients		Clinical touch 45 patient		P value
Mean age (years)	29±5		30±5		NS
No of embryo transfer	2.11±0.6		2.2±0.6		NS
<b>Type of infertility</b>	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	
Primary	43	96	40	90	NS
Secondary	2	31	5	11	NS
<b>Etiology of infertility</b>					
Male factor	30	67	27	63	NS
Ovarian factor	9	19	5	21	NS
Unexplained factor	6	12	13	16	NS

There was no significant differences in the age, duration and etiology of infertility and the number of embryos transferred between the ultrasound guided and the clinical touch groups.

**Table (2):** The pregnancy outcomes of the 90 cycles fresh embryo transfer cycles.

Pregnancy	Ultrasound guided N=45		Clinical touch technique N=45		P value
	No.	%	No.	%	
Clinical pregnancy	10	22.2	7	15.5	N S
Miscarriage	1	2.2	2	4.4	NS
On-going pregnancy	9	20	5	11.1	N S

NS: Non significant

There was no significant difference between both groups as regards the clinical pregnancy rate and the ongoing pregnancy rate.

#### 4. Discussion

Since the introduction of ultrasound guided embryo transfer during the mid-1980s, this technique has evolved into a more routine part of assisted reproductive technique (ART) practices around the world<sup>(6)</sup>.

Various facets of embryo transfer may be pivotal in improving implantation and pregnancy clinical success: catheter position in the uterine cavity, choice of transfer catheter, volume of transfer medium, retention of the fluid droplet and endometrial receptivity<sup>(5)</sup>. The use of ultrasound clearly plays a role in embryo transfer. Tactile assessment of embryo transfer has been assessed as unreliable<sup>(7)</sup>.

Woolcott and Stranger noted sub-optimal catheter placement, from subendometrial transfers to tubal transfers and embedding of the transfer catheter within the endometrium or the fundus<sup>(7)</sup>. Although facilitation of proper embryo placement with ultrasound seems intuitive, the use of ultrasound to minimize endometrial trauma and possibly to

decrease myometrial contractions may indeed be helpful in enhancing implantation and clinical pregnancy rates<sup>(8,9)</sup>.

Strong fundus-cervical contractions and random uterine waves were demonstrated<sup>(10)</sup> by touching the uterine fundus twice with the soft end of the catheter. Following the pathway of the catheter by ultrasound guidance should decrease the propensity for the clinician to make catheter contact with the fundus.

The value of ultrasound-guided transfer is in its ability to detect malpositioned catheters and to circumvent transfer of the embryo to an inappropriate site which might decrease the probability of implantation. By one report, suboptimal catheter location is estimated to occur in 24.7% of cases<sup>(7)</sup>. The role of ultrasound, then, is to optimize transfer by directing and confirming catheter placement<sup>(11)</sup>.

The use of ultrasonography may have additional benefits other than visualization of catheter location. Although no difference was seen in pregnancy outcome when using ultrasound guidance, the use of ultrasound has been associated with easier transfer

<sup>(12,13)</sup> decreased use of a tenaculum. And decreased presence of blood in the catheter following retrieval <sup>(12)</sup>, and this may justify its use <sup>(12)</sup>.

In the current study, the clinical pregnancy rate and the ongoing pregnancy rate increased in the US guided group compared to the clinical touch group but with no significant difference.

In a prospective study by Prapas *et al.* (1995), it was found that there was a significant effect of ultrasound on pregnancy outcome <sup>(14)</sup>.

In a study by Coroleu (2000) a higher pregnancy and implantation rates were found in the ultrasound-guided group (50% and 25.3% respectively) compared with the clinical touch group (33.9% and 18.07% respectively). The advantage of the use of ultrasound in guiding the embryo replacement is that it assures the correct positioning of the catheter <sup>(15)</sup>.

In a prospective study using abdominal ultrasound, Al Shawaf *et al.* (1993) found that there was no significant affect of ultrasound on pregnancy outcome <sup>(16)</sup>. More recently, in what was until then the largest prospective study. Kan *et al.* found that there was still no significant improvement seen in either pregnancy or implantation rates <sup>(17)</sup>. A possible key factor in Al Shawaf's and Kan's studies is that the catheter tip was positioned 1 cm from the fundus of the uterine cavity. In Coroleu's study, the tip of the catheter was positioned with the use of ultrasound at 1.5 cm from the fundus of the uterine cavity.

A 2010 Cochrane review of 17 RCTs comparing ultrasound versus clinical touch concluded that ultrasound did increase ongoing clinical PRs over clinical touch (441/1254 vs. 350/1218, odds ratio [OR] 1.38, 95% CI 1.16-1.64,  $P < 0.0003$ ) <sup>(18)</sup>. Three other meta-analyses of RCTs have had similar conclusions <sup>(2,19)</sup>. Due to the simplicity and good outcomes in the previously mentioned studies, ultrasound guidance would appear to be an essential factor in improving the results of embryo transfer and, moreover, is one which offers our patients the maximum possibility of a successful pregnancy <sup>(15)</sup>.

#### Conflict of interest statement

There is no relationship for any author that may influence the objectivity of the paper.

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12/2/2013