Original Research Article

Trans Vaginal versus Trans Abdominal Ultrasound Guided Embryo Transfer in in vitro Fertilization and Intra Cytoplasmic Sperm Injection (IVF–ICSI)

Abstract

Background: Embryo transfer (ET) refers to a step in the process of assisted reproduction in which one or several embryos are placed into the uterus of a female with the intent to establish a pregnancy. This technique, which is often used in connection with in vitro fertilization (IVF), has widely been used in animals or human. The aim of this study was to compare Trans abdominal ultrasound (TAUS) with Trans vaginal ultrasound (TVUS) methods for guidance of (ET) regarding clinical pregnancy rate and patient appreciation of pain during embryo transfer.

Methods: This prospective, randomized, controlled study was conducted on 100 patients undergoing cryopreserved or fresh morula or blastocyte who were randomized (computer generated program) into 2 groups. Group I (the study group): 50 patients were subjected to embryo transfer under trans abdominal ultrasound guidance and Group II (controlled group): 50 patients were subjected to (ET) under (TAUS).

Results: There were no statistically significant differences regarding fresh and cryopreserved. TVUS group demonstrated significant reduction of duration compared to TAUS ones. Minimal pain was observed in TVUS cases compared to TAUS ones. Higher success rate and lower failure rate were demonstrated in TVUS group compared to TAUS group.

Conclusions: TVUS seems to have higher success rate with less pain sensation as well as shorter duration of the procedure in comparison with TAUS.

Keywords: Trans vaginal, Trans abdominal, embryo transfer, intra cytoplasmic sperm injection, in vitro fertilization.

Introduction:

An in vitro fertilization (IVF) cycle includes three stages: controlled ovarian stimulation, oocyte retrieval, and IVF and finally embryo transfer (ET) to the uterus. Most of the research performed in recent years has focused on oocyte and embryo quality [1] and on endometrial receptivity. [2] Embryo transfer techniques are, however, less studied.

Improvement in the ET procedure may increase the success rate of fertility treatments [3] by increasing implantation rates, which are presently less than 50%. [4]

As a rule, ET should be a painless procedure. Pain could originate from passing the catheter through the uterine cervix. If the uterine fundus or walls are touched by the tip of catheter, the patients experience immediate discomfort followed by supra pubic pain. This is most likely associated with the initiation of uterine contractility. [5] It has also been demonstrated that uterine contractions at the time of the ET are correlated with lower clinical pregnancy rates. [6]

It is presently undisputed that ET be performed under ultrasound (US) guidance. Two meta-analyses [7, 8] and a Cochrane review [9] examined over 20 randomized controlled trials that compared ET with and without Trans abdominal ultrasound (TAUS) guidance.

The aim of this study was to compare Trans abdominal ultrasound (TAUS) with Trans vaginal ultrasound (TVUS) methods for guidance of (ET) regarding clinical pregnancy rate and patient appreciation of pain during (ET).

Patients and Methods:

This prospective, randomized, controlled study was conducted on 100 patients undergoing cryopreserved or fresh morula or blastocyte in the fertility unit of Tanta university hospitals and other private centers in the period from August 2019 till October 2020. After approval by the ethical standards of Tanta University's ethical committee and its later amendments or comparable ethical standards. Informed consents were obtained from all individual

participants included in the study. There will be privacy for participants and confidentiality of the data.

Two good qualities cryopreserved or fresh morula or blastocyte in patients aged between 18 and 40 years were included.

Morbid obesity with body mass index (BMI) >35. Preimplantation genetic diagnosis (PGD) cases. Cryopreserved or fresh embryos rather than morula or blastocyst were excluded from the study.

These 100 patients were randomized (computer generated program) into 2 groups. **Group I** (the study group): 50 patients were subjected to embryo transfer under trans abdominal ultrasound guidance they were instructed to empty their bladder as the trans vaginal ultrasound methods did not require a full bladder. Saline lubricated vaginal speculum was inserted, and the cervix was cleaned with saline medium. The 6.5µH trans vaginal probe was put in the posterior fornix and angulated for visualization of the endometrium to the level of the fundus. **Group II** (controlled group): 50 patients were subjected to (ET) under (TAUS) These patients were instructed to fill their urinary bladder or even the physician might fill their urinary bladder by saline through insertion of foley catheter. As transabdominal ultrasound methods require a full bladder to give good visualization of the uterus. Saline lubricated vaginal speculum was inserted, and the cervix was cleaned with saline medium. The assistant doctor held the 3.5µH trans abdominal probe in the suprapubic region for visualization of the endometrium to the level of the fundus.

The embryos quality was determined by cell number, symmetry, and fragmentation ,and will be graded A, B, or C according to the Society for Assisted Reproductive Technology (SART) grading.

Measurements

- **Primary outcome:** measure of the study was clinical pregnancy rate.

- **Secondary outcomes:**

1. The patient appreciation of pain during embryo transfer. The visual analogue scale (VAS) was used to compare between pain experienced during embryo transfer under guidance of trans vaginal and trans abdominal ultrasound. VAS is continuous scale composed of horizontal or vertical line usually 10 centimeter (100mm) in length anchored by 2 verbal descriptors, one for symptom extreme instruction, time of period reporting and verbal descriptor have varied widely in literature depending on intended use of the scale. The patients were asked to place a line perpendicular to the VAS line at the point that represent their pain intensity using a ruler, the score was determined by measuring the distance (mm) on the 10 cm line between no pain anchor and the patient`s mark provide range of score from (0-100) where 0 is no pain and 100 is the worst possible pain. Postoperative pain was assessed by the visual analogue scale (VAS; 0 no pain while 100 is the maximum pain) and recorded at (Just before femoral block, 2, 4, 6, 8, 12, 16 and 24 hours).
2. Measuring the duration of the procedure from the start to hand off.

Statistical analysis

IBM's SPSS statistics (Statistical Package for the Social Sciences) for windows (version 25, 2017) was used for statistical analysis of the collected data. Shapiro-Wilk test was used to check the normality of the data distribution. All tests were conducted with 95% confidence interval. P (probability) value < 0.05 was considered statistically significant. Quantitative variables were expressed as mean and standard deviation while categorical variables were expressed as frequency and percentage. Independent sample T and Mann Whitney tests were used for inter-group (between subjects) comparison of parametric and non-parametric continuous data, respectively. Fisher exact and Chi square tests were used for inter-group comparison of nominal data using the crosstab function.

Results:

In this study, 112 patients were assessed for eligibility, 9 patients did not meet the criteria and 3 patients refused to participate in the study. The remaining 100 patients were randomly allocated into two groups (50 patients in each). All patients (100) were followed-up and analyzed statistically. **[Figure 1]**

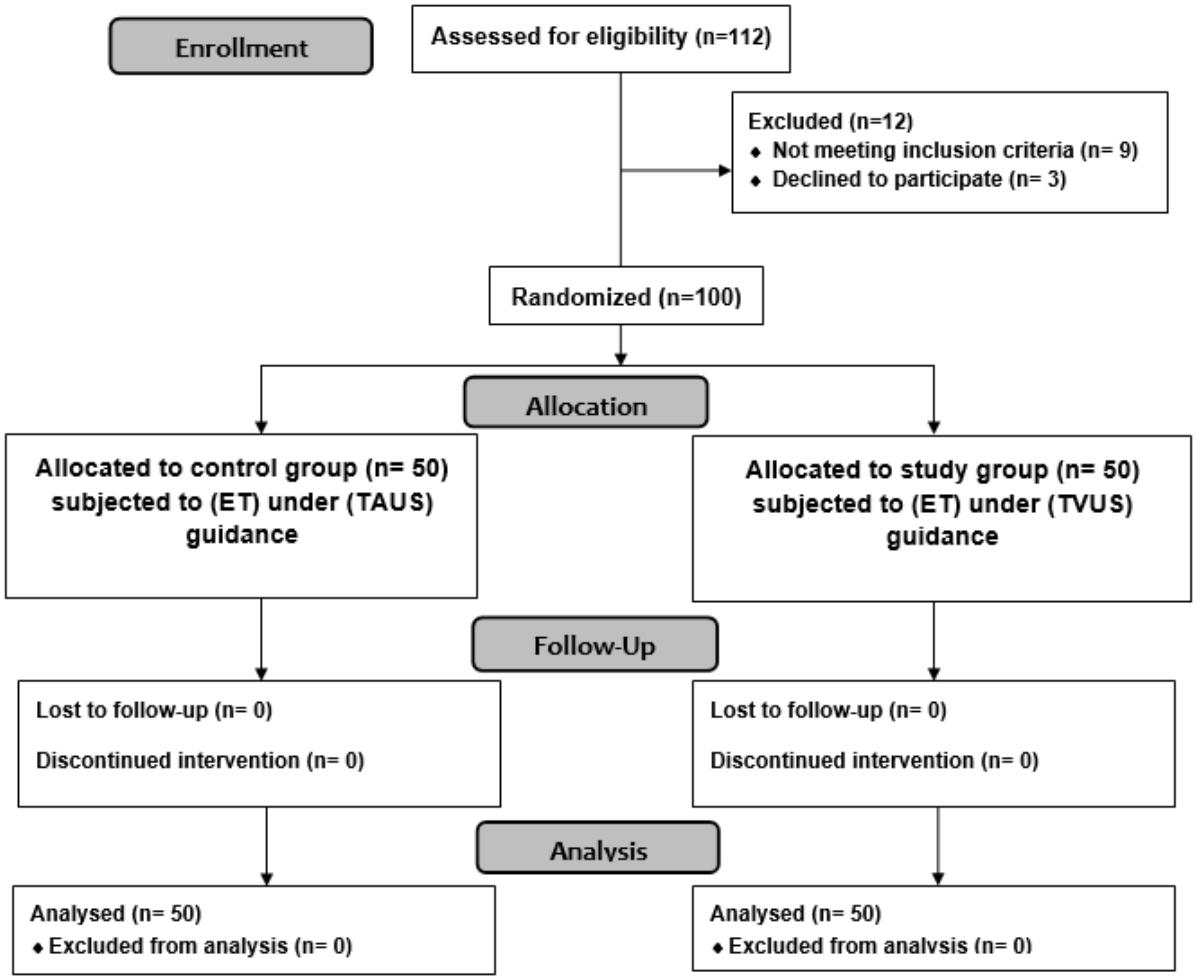

Figure 1: The randomized trial flow diagram, including enrollment, intervention allocation, and analysis.

Demographic characteristics of both studied groups demonstrated insignificant differences concerning age, BMI, occupation, and residency **[**

Table 1**]**

Table 1: Demographic characteristics of the studied groups

		TVUS group (n= 50)	TAUS group (n= 50)	95% CI	P
Age (years)		26.70 ± 4.599	25.34 ± 5.017	- 0.55, 3.27	0.161
BMI (kg/m^2)		30.08 ± 2.045	30.00 ± 2.092	-0.74, 0.90	0.846
Occupation	**Housewife**	64.0% (32)	58.0% (29)	-0.25, 0.13	0.539
	Worker	36.0% (18)	42.0% (21)		
Residency	**Urban**	30.0% (15)	28.0% (14)	-0.2, 0.16	0.826
	Rural	70.0% (35)	72.0% (36)		

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups

There were no statistically significant differences among both studied groups in terms of history of DM, history of HTN, history of hypothyroidism and history of abdominal surgery. **[Table 2]**

Table 2: Medical and surgical history of the studied groups

	TVUS group (n= 50)	TAUS group (n= 50)	95% CI	P
History of DM	24.0% (12)	18.0% (9)	-0.22, 0.1	0.461
History of HTN	0.0% (0)	4.0% (2)	-0.01, 0.09	0.558
History of Hypothyroidism	16.0% (8)	10.0% (5)	-0.19, 0.07	0.372
History of Abdominal surgery	20.0% (10)	18.0% (9)	-0.17, 0.13	0.799

Data is expressed as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups.

There were no statistically significant differences regarding Parity, type, and duration of infertility among both studied groups. **[Table 3]**

Table 3: Parity, type, and duration of infertility of the studied groups

		TVUS group (n= 50)	TAUS group (n= 50)	95% CI	P
Parity		0.12 ± 0.385	0.16 ± 0.510	-0.22, 0.14	0.659
Type of infertility	**Primary**	90.0% (45)	76.0% (38)	-0.29, 0.01	0.062
	Secondary	10.0% (5)	24.0% (12)		
Duration of infertility (months)		17.12 ± 4.119	16.76 ± 3.342	- 1.13, 1.85	0.632

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

There were no statistically significant differences regarding FSH, LH and TSH among both studied groups. **[Table 4]**

Table 4: Hormonal assay of the studied groups

	TVUS group (n= 50)	**TAUS group (n= 50)**	**95% CI**	**P**
FSH	4.33 ± 0.278	4.31 ± 0.463	-0.13, 0.17	0.816
LH	10.32 ± 0.456	10.35 ± 0.854	-0.30, 0.24	0.836
TSH	3.06 ± 1.605	3.43 ± 1.861	-1.06, 0.32	0.289

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

There were no statistically significant differences regarding fresh and Cryopreserved. **[Table 5]**

Table 5: Type of embryo transferred in the studied groups

	TVUS group (n= 50)	**TAUS group (n= 50)**	**95% CI**	**P**
Fresh	80.0% (40)	78.0% (39)	-0.18, 0.14	0.806
Cryopreserved	20.0% (10)	22.0% (11)		

Data is expressed as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups.

TVUS group demonstrated significant shortening of duration compared to TAUS ones. In addition, TVUS cases were associated with significant lowering in pain sensation compared to TAUS ones. **[Table 6]**

Table 6: Duration of procedure and VAS score during procedure of the studied groups

	TVUS group (n= 50)	**TAUS group (n= 50)**	**95% CI**	**P**
Duration of procedure (minutes)	7.90 ± 2.225	12.92 ± 3.331	-6.14: - 3.90	**< 0.001***
VAS score during procedure	27.00 ± 9.476	55.70 ± 7.627	-32.11: - 25.29	**< 0.001***

Data is expressed as mean and standard deviation or as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. *: significant as P value < 0.05.

TVUS group was associated with a significant higher in success rate (clinical Pregnancy) with less failure rate compared to TAUS group. **[Table 7]**

Table 7: Outcome in the studied groups

	TVUS group (n= 50)	**TAUS group (n= 50)**	**95% CI**	**P**
Success	56.0% (28)	36.0% (18)	-0.39, - 0.01	**0.045***
Failure	44.0% (22)	64.0% (32)		

Data is expressed as percentage and frequency. 95% CI: 95% confidence interval of the mean difference between both groups. *: significant as P value < 0.05**.**

Discussion

Transvaginal ultrasound (TVS) guidance was first described in the 1990's by Hurly et al., who showed the role of TVS in improving the ET technique over the clinical touch method. [10] Of note, a significant improvement in pregnancy rate was achieved by the use of transabdominal US (TAS) guidance Embryo Transfer (ET) in comparison to clinical touch. The Transvaginal ultrasound (TVS) guided ET was tried but the evidence till now can't prove the superiority of TVS over TAS guided ET. [11] Thus, the aim of the current study was to compare Trans abdominal ultrasound (TAUS) with Trans vaginal ultrasound (TVUS) methods for guidance of embryo transfer (ET) regarding clinical pregnancy rate and patient appreciation of pain during embryo transfer (ET) and measuring the duration of the procedure from the start to hand off.

With regard to, hormonal assay of the studied groups, there were no statistically significant differences regarding FSH, LH and TSH. Such result indicated that both groups were comparable regarding hormonal assessment and such hormones were not interfering with the net result of the study. Similarly, **Samy et al. (104)** compared the hormonal levels among the two studied groups (TVUS versus TAUS) to be sure that both groups had comparable levels prior their participation in the study (P>0.05).

Concerning, method of embryo transferred in the studied groups, the current study demonstrated that, there were no statistically significant differences regarding fresh and Cryopreserved. Such result indicated that both groups were comparable regarding method of ET and such methods were not interfering with the net result of the study.

In terms of the duration of procedure, TVUS group demonstrated significant shorter of duration compared to TAUS ones. (7.90 ± 2.225) vs (12.92 ± 3.331) While **Bodri et al.** who demonstrated that, total duration (154±119 versus 85±76 seconds) was statistically significantly higher in the TVUS group in comparison with TAUS ones. [12]

The study by **Bodri et al.** [12, 13] may be criticized for the use of different catheters in the two groups and the performance of the transfer by several operators, whereas the transfer technique requires training.

They explain such increase in time by the fact that, this is easily explained by the extra time needed to insert the vaginal probe and to obtain the correct sagittal plane of the uterus by slightly adjusting the position of the probe. TVUS, due to its higher resolution, frequently permits a high-definition view of the ET procedure which is highly reassuring both for the patient and the operator. [14]

In addition, **Samy et al.** [10] conducted a randomized, prospective trial included 178 infertile couples from Al Shatbi Reproductive Gynecology Unit in Alexandria University Hospital, during the period between June 2016 and May 2018. The patients were divided randomly prior to ET into two equal groups: the first group used TAS guidance for ET and the second group used the TVS guidance for ET. They displayed that; the total duration of ET was statistically significantly longer in the TV arm.

Concerning pain sensation, VAS score was used to assess the degree among the studied cases. TVUS cases were associated with significant lower in pain sensation compared to TAUS ones. (27.00 ± 9.476) vs (55.70 ± 7.627). This came in accordance with, **Karavani et**

al. [15] who demonstrated that, pain sensation assessed by a visual analogue scale (VAS) before, during, and after the procedure was statistically significantly lower in the TVUS group compared with the TAUS group (5.45 vs. 1.48, 5.03 vs. 2.42 and 2.97 vs. 1.52). In addition, they demonstrated that there were marked reduction in discomfort, and anxiety especially during procedure preparation and performance. In the same line, **Samy et al.** [10] demonstrated that, the mean discomfort intensity during ET was significantly higher in TAS-guided ET group (1.81 ± 1.03 vs. 1.50 ± 0.92) (P = 0.040).

A recently published large, retrospective study by **Larue et al.** [16] described opposite results with an advantage for the TVUS technique. This may be related to a more precise embryo deposition in the uterine cavity, with minimal mucosal trauma.

Most of the randomized, controlled trials showed a low risk of bias concerning random sequence generation. In contrast, the risk of bias was considered unclear or high. [10] On the contrary, **Porat et al.** [17] did not find any difference in pain reported by their patients. The discrepancies among results regarding pain assessment may be due to the fact that, **Porat et al.** [17] did not try to differentiate between uterine cramping and discomfort related to bladder distension.

Regarding outcome, the current study demonstrated that TVUS group was associated with significant higher in success rate compared to TAUS group. (56.0% (28) vs (36.0% (18). On the contrary, **Bodri et al.** [12] demonstrated that, Transvaginal ultrasound-guided ET yielded similar success rates compared with the TA ultrasound-guided procedure without requiring the assistance of a sonographer. In addition, **Karavani et al.** [15] demonstrated that, the implantation and live-birth rates did not differ between the two groups (32.9% vs. 23.4%, OR 1.61; 95% CI, 0.85-3.07; 31.6% vs. 25.0%, OR 1.39; 95% CI, 0.63-3.09, respectively).

However, **Karavani et al.** [15] demonstrated that, TVUS guidance to facilitate ET is superior to TAUS in visualization of embryo transfer location. Furthermore, **Wageh et al.** [11]

conducted their study on 550 women underwent fresh ET with US guidance. 276 underwent TVS guided ET (group A) and 274 underwent TAS guided ET (group B). The Chemical pregnancy was 129 (46.7) vs 123 (44.9) p value 0.66 and clinical pregnancy 119 (43.1) vs 108 (39.4) p value 0.38. Thus, the concluded that, there was no significant difference between TVS guided ET and TAS guided ET as regards the chemical or clinical pregnancy rates.

Conclusions:

TVUS seems to have higher success rate with less pain sensation as well as shorter duration of the procedure in comparison with TAUS.

Competing interests disclaimer:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References:

1. Blake DA, Farquhar CM, Johnson N, Proctor M. Cleavage stage versus blastocyst stage embryo transfer in assisted conception. Cochrane Database Syst Rev. 2007:CD002118.

2. Achache H, Revel A. Endometrial receptivity markers, the journey to successful embryo implantation. Hum Reprod Update. 2006;12:731-46.

3. Teixeira DM, Dassuncao LA, Vieira CV, Barbosa MA, Coelho Neto MA, Nastri CO, et al. Ultrasound guidance during embryo transfer: a systematic review and meta-analysis of randomized controlled trials. Ultrasound Obstet Gynecol. 2015;45:139-48.

4. Society for Assisted Reproductive T. Final National Summary Report for 2017. Birmingham, AL: Society for Assisted Reproductive Technology (SART). 2017.

5. Mansour RT, Aboulghar MA. Optimizing the embryo transfer technique. Hum Reprod. 2002;17:1149-53.

6. Fanchin R, Righini C, Olivennes F, Taylor S, de Ziegler D, Frydman R. Uterine contractions at the time of embryo transfer alter pregnancy rates after in-vitro fertilization. Human reproduction (Oxford, England). 1998;13:1968-74.

7. Buckett WM. A meta-analysis of ultrasound-guided versus clinical touch embryo transfer. Fertil Steril. 2003;80:1037-41.

8. Sallam HN. Ultrasound guidance during embryo transfer: a systematic review and meta-analysis of randomized controlled trials. Ultrasound Obstet Gynecol. 2015;45:757-8.

9. Abou-Setta AM, Peters LR, D'Angelo A, Sallam HN, Hart RJ, Al-Inany HG. Post-embryo transfer interventions for assisted reproduction technology cycles. Cochrane Database Syst Rev. 2014:CD006567.

10. Samy AA, El-Kassar YS, Gaafar SS, Hamza HA, Menshawi SS. Comparison between transvaginal and transabdominal ultrasound-guided embryo transfer: a randomized, prospective trial. Menoufia Medical Journal. 2020;33:419.

11. Wageh A, Abdelhafez MS, Shams M. Transvaginal sonography (TVS) guided versus transabdominal sonography (TAS) guided embryo transfer: A retrospective analysis. Middle East Fertility Society Journal. 2018;23:431-4.

12. Bodri D, Colodron M, Garcia D, Obradors A, Vernaeve V, Coll O. Transvaginal versus transabdominal ultrasound guidance for embryo transfer in donor oocyte recipients: a randomized clinical trial. Fertil Steril. 2011;95:2263-8, 8 e1.

13. Papathanasiou A, Osmani B, Teoh PJ, Maheshwari A. Morphological assessment of embryo quality during assisted reproduction: a systematic review. Fertility Science and Research. 2014;1:67.

14. Cenksoy PO, Fıcıcıoglu C, Yesiladali M, Akcin OA, Kaspar C. The importance of the length of uterine cavity, the position of the tip of the inner catheter and the distance between the fundal endometrial surface and the air bubbles as determinants of the pregnancy rate in IVF cycles. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2014;172:46-50.

15. Karavani G, Ben-Meir A, Shufaro Y, Hyman JH, Revel A. Transvaginal ultrasound to guide embryo transfer: a randomized controlled trial. Fertil Steril. 2017;107:1159-65.

16. Larue L, Keromnes G, Massari A, Roche C, Moulin J, Gronier H, et al. Transvaginal ultrasound-guided embryo transfer in IVF. J Gynecol Obstet Hum Reprod. 2017;46:411-6.

17. Porat N, Boehnlein LM, Schouweiler CM, Kang J, Lindheim SR. Interim analysis of a randomized clinical trial comparing abdominal versus transvaginal ultrasound-guided embryo transfer. J Obstet Gynaecol Res. 2010;36:384-92.