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Transrectal versus transabdominal ultrasound-guided embryo transfer in obese poor responders

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Background/aim

Ultrasound guidance affects the success rate of the embryo transfer (ET), which is considered the most crucial step in the intracytoplasmic sperm injection cycle. In our study, we tried to evaluate the role of transrectal ultrasound during ET in obese poor responder women.

Patients and methods

This pilot study was carried out on 70 women having intracytoplasmic sperm injection cycles. They were divided into two groups: group 1, women who had a transrectal ultrasound during ET (n=31), and group 2, women who had a transabdominal ultrasound during ET (n=39). Our primary outcome was proper visualization of the endometrium and catheter tip during ultrasound-guided ET, whereas the secondary outcomes were chemical and clinical pregnancies.

Results

The endometrial thickness was clearly visualized in 30 (96.77%) women of group 1 and in 17 (43.59%) women of group 2, whereas the catheter tip was clearly visualized in 25 (80.64%) women of group 1 and in seven (17.95%) women of group 2, with P values less than 0.001. In addition, the implantation, chemical pregnancy, and clinical pregnancy rates in group 1 were almost double those in group 2.

Conclusion

ET under transrectal ultrasound guidance may emphasize a better-quality image, resulting in improved pregnancy and implantation rates.

Keywords:

embryo transfer, obese, poor responders, transabdominal, transrectal, ultrasound

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Introduction

The most crucial step in the sequential events that encompass the intracytoplasmic sperm injection (ICSI) cycle is arguably embryo transfer (ET). The success rate of a transfer process depends on several variables, including the type of catheter, atraumatic technique, and the use of ultrasound-guided ET [1].

Ultrasound guidance, which appears to be a critical adjunct toward this goal, is important to optimize clinical outcomes. Ultrasound has several advantages in the context of ET, including reducing the risk of difficult transfers, confirming catheter placement in the correct position of the fundal cavity, minimizing blood and mucus contamination of the catheter tip, and reducing the risk of touching the fundus that may initiate uterine contractions. Several studies, including meta-analyses, have found that ultrasonographic guidance improves clinical pregnancy rates significantly compared to 'clinical touch' [2].

Pelvic ultrasonography is a safe and easy-to-use imaging technology; however, obesity obscures the

imaging process. In terms of pregnancy outcomes, both transabdominal ultrasound (TAUS) transvaginal ultrasound (TVUS) appear to be equally helpful [3]. Image quality may be improved by combining transvaginal or transrectal ultrasonography method with tuning of ultrasound settings [4]. Previously, transrectal ultrasonography examination was utilized to diagnose gynecological problems. In virgin patients, it was just as successful as traditional TVUS in detecting polycystic ovarian syndrome [5]. In the diagnosis of deep infiltrating endometriosis, transrectal ultrasonography yielded a higher diagnostic accuracy [6].

High BMI is associated with reduced implantation, chemical pregnancy, and clinical pregnancies rates [7]. Optimal body weight is considered an important factor affecting fertility power in women. Although the effect of obesity on fertility is known, still there are multiple

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theories such as hyperandrogenemia causing granulosa cell death, peripheral conversion of androgens to estrogen in adipose tissue decreases gonadotrophin production, or may be owing to pulsatile gonadotropin-releasing hormone secretion [8]. Increased BMI resulted in an increase in the number of days of induction and doses of gonadotrophins used, which will increase the effective cost with a significant decrease in the ovarian response. Normalization of BMI before any attempt of induction of ovulation is recommended [9].

Poor responders are commonly encountered during controlled ovarian hyperstimulation in ICSI cycles. These women are diagnosed when the long-agonist protocol fails or the cycle is canceled, and they make up 5–35% of infertile women who undergo controlled ovarian hyperstimulation. After in-vitro fertilization, a poor ovarian response (POR) leads to low pregnancy, implantation, and live birth rates [10]. Obese women had a poorer response to gonadotropin stimulation, fewer retrieved oocytes, poor embryo quality, and reduced implantation, pregnancy, and live birth rates [11].

The present work aimed to evaluate the role of transrectal ultrasound guidance during ET in obese poor responder women whenever the transabdominal approach is not successful.

Patients and methods Patients

criteria.

This study had been carried out on 70 women having ICSI cycles over a period of 30 months, from March 2019 till September 2021. All women who participated in the study had a BMI between 30 and 35 kg/m², primary or secondary infertility, no hormonal treatment in the past 3 months preceding the ICSI trial, and previously diagnosed to be poor responders by having any two of the following according to Bologna Criteria 2018: advanced maternal age (≥40 years), a previous POR (cycles canceled or ≤3 oocytes with a conventional protocol), and an abnormal ovarian reserve test result (antral follicle count <5-7 follicles < 0.5-1.1 ng/ml). anti-Mullerian hormone However, two previous episodes of POR after maximal stimulation were sufficient to classify the women as POR apart from the absence of the other

Women with any of the following criteria have been excluded from the study: any pelvic pathology that may distort the pelvic anatomy (endometriosis, known pelvic pathology such as uterine fibroids or ovarian masses, uterine anomalies such as uterine septum or polyp, and previous pelvic surgery), known autoimmune disease, diabetics, history of previous chemotherapy or radiotherapy that may affect ovarian function, history of difficult ET, women with any anal or rectal pathology (piles and anal fissures), and recent history of coronavirus disease 2019 (COVID-19) infection (unknown effect on ovarian functions).

Ethical approval

This study had been approved by the ethical committee of the National Research Centre and El-Zohour Fertility Centre with approval number 4/19. All participants were informed about the nature of the study. The maneuver had been explained, and written consents were taken from each of them before starting the study. Women included in the study were recruited from private infertility outpatient clinics.

Study design

This pilot study was carried out on 70 women having ICSI cycles. They were divided into two groups: group 1, women who had a transrectal ultrasound during ET (n=31), and group 2, women who had a TAUS during ET (n=39). We started our study with 74 women; however, four of them had difficult ET and thus had been excluded from the final analysis.

Methods

All patients in our study were subjected to the following: BMI calculation, proper history taking, and general, abdominal, and pelvic examinations. Between the days 2 and 4 in the cycle preceding the ICSI cycle, basal follicle-stimulating hormone, luteinizing hormone, E2, and anti-Mullerian hormone were measured for all women. Moreover, TVUS was performed for all patients during the early follicular phase to exclude any pelvic pathology and measure the antral follicle count.

According to the protocol we adopted for poor responders, all women received antagonist fixed stimulation protocol during their ICSI cycles. Controlled ovarian stimulation had been done using recombinant follicle stimulation intramuscular or subcutaneous injections starting dose between 300 and 450 IU/day (Gonapure, Minapharm, Egypt) starting on day 2, and the dose was adjusted according to age, weight, response. Cetrorelix 0.25 mg/day ovarian subcutaneous (Cetrotide, Merck Serono, Germany) was started on day 6 of ovarian stimulation. Women were followed using TVUS and serial E2 measures. The number of mature follicles more than 15 mm and E2 levels at the day of trigger were documented. Human chorionic gonadotropin 10 000 IU trigger shot was given intramuscularly when at least two dominant follicles had reached 18-20 mm. Ovum pickup under TVUS guidance was done 34-36 h following the trigger shot. The couple was counseled about cycle cancellation when there were less than three follicles with diameter of less than 14 mm after 8-9 days of gonadotropin therapy or after 4-5 additional treatment days without attaining the criteria for human chorionic gonadotropin administration.

A mock ET was performed after ovum pickup to assess the difficulty of ET. After 12-24 h from oocytes retrieval, oocytes were checked for fertilization. Oocytes and the embryo grading were recorded according to the published criteria by Veeck [12]; embryos with grades 1 or 2 were considered good quality and therefore suitable for transfer. All ETs were done on day 3.

Before ET, all women were offered transrectal ultrasound after explaining the procedure to them. At the time of ET, all women were placed in lithotomy position and divided into two groups. Group 1 had the ET done guided by transrectal ultrasound using the TVUS probe with a frequency between 5 and 7.5 MHz, whereas in group 2, the ET was guided by the conventional TAUS probe with a frequency between 3 and 5 MHz using GE Logic V2 (Chicago, Illinois, USA). All ETs were performed in the same fashion. After the patient was placed in the lithotomy position, a Cusco's speculum was used to expose the cervix. The cervical mucous was removed using a 1-ml syringe to minimize the risk of retained embryos in the transfer catheter [13], and the cervix was cleansed using a gauze moistened with a small amount of embryo culture medium. For women in the transrectal group, all women were asked to empty their bladders before the procedure, and a digital rectal examination was performed before the insertion of the probe. Any palpable contour abnormalities were documented and excluded from the study.

Cusco's speculum was inserted upright with its handle directed upward to allow free movement of the transvaginal probe introduced transrectally. The outer sheath of the ET catheter was introduced through the external OS. The physician inserts the TVUS probe covered with a sterile condom into the rectum. Pain is minimized by covering the condom over the transrectal probe using 10 ml of 1% lidocaine.

The operator held the TVUS probe with the left hand and manipulated it till obtaining a sagittal view of the uterine cavity and cervix. The nurse fixes the outer sheath till the physician introduces the soft inner catheter loaded with the embryos into the outer sheath. The soft inner catheter was introduced through the internal OS into the uterine cavity under ultrasonographic guidance.

Women in the transabdominal group were instructed to have a full bladder, which would provide an acoustic window for visualization of the uterus. Th nurse held the probe in the suprapubic location showing the uterine sagittal axis with the full urinary bladder. The rest of the procedure was done in the same fashion as described before.

The ET was done without anesthesia or sedation using a soft Wallace catheter. The catheter was loaded with 30 μ l of culture medium between air bubbles (~2 μ l). Then the catheter containing the embryos was inserted and advanced under ultrasound guidance till the tip of the catheter was placed within the mid-uterine cavity with caution not to touch the fundus. The embryos were then injected over 15 s, allowing observation of the movement of the air bubbles into the uterine cavity. Finally, the catheter was checked microscopically by an embryologist to check for retained embryos.

The operators had been asked if they performed the procedure under a complete vision, and they were given a form categorizing visualization. The criteria for ET visualization under ultrasound guidance were as follows:

- (1) Both the endometrium and the tip of the catheter were seen clearly.
- (2) Endometrium is seen but the tip of the catheter is
- (3) Could not detect neither endometrium nor the tip of the catheter.

Luteal support was given using intramuscular progesterone 100 mg once daily starting from the day of ovum pickup. Women were asked to do a blood pregnancy test 14 days after ET, and if positive, they had an ultrasound 2 weeks later to check viability and number of fetuses.

Outcomes: our primary outcome was the proper visualization of the endometrium and catheter tip during ultrasound-guided ET, whereas the secondary outcomes were the implantation, chemical, and clinical pregnancy rates.

Sample size: while performing our study, the COVID-19 pandemic has been declared by the WHO. Hereby, we faced a major limitation in getting a larger sample size. The marked decrease in cases having ICSI urged us to design our work as a pilot study till we can extend into a larger sample size.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences 'SPSS' v 25 (SPSS version 25, SPSS, Inc., IL, USA). Quantitative parameters were expressed as mean±SD for normally distributed variables and as median and range for non-normally distributed variables, whereas qualitative parameters were expressed as numbers and percentages. To compare both groups, we used the independent samples? t test and Mann–Whitney test for quantitative parameters, whereas differences in frequencies were analyzed using the χ^2 test. P value less than 0.05 was considered to be statistically significant.

Results

All women enrolled in this study were offered a transrectal ultrasound instead of TAUS during ET for better visualization. Only 31 women agreed to have the ET guided with transrectal ultrasound (group 1), whereas the other 39 women had the conventional TAUS during ET (group 2). Regarding the demographic data such as age, BMI, and the number of previous failed IVF trials, no significant differences were observed between both groups (P=0.319, 0.161, and 0.639, respectively), as shown in Table 1.

Table 2 demonstrates the distribution of women in both groups according to the degree of ultrasound visualization in both approaches. The endometrial thickness was clearly visualized in 30 (96.77%) women of group 1 (transrectal approach) and in 17 (43.59%) women of group 2 (transabdominal approach), whereas the catheter tip was clearly

visualized in 25 (80.64%) women of group 1 and in seven (17.95%) women of group 2.

In addition, the number of transferred embryos and the embryo grades in both groups were nearly equal, as shown in Table 3. The implantation, chemical pregnancy, and clinical pregnancy rates in group 1 were more than those in group 2. However, there was no statistically significant difference between both groups (Table 3).

Discussion

Nowadays, there is a growing number of pregnancies that occur as a result of assisted reproductive techniques. As obesity is a worldwide problem, obese infertile poor responding women are not infrequently encountered. In turn, it is essential to alleviate all of the factors that may decrease the pregnancy rate among those cohort of women [14,15]. Several studies found out that obesity decreases the pregnancy rate in ICSI cycles owing to multiple factors, in addition to the effect of BMI on improper ET technique due to poor visualization by the traditional abdominal ultrasound. In our study, we concentrated on optimizing the ET technique in obese women using a transrectal ultrasound for better visualization of the ET technique aiming to increase the pregnancy rate between obese poor responder women [16].

Table 1 Demographic data of both groups

	Group 1 (<i>N</i> =31): transrectal approach	Group 2 (<i>N</i> =39): transabdominal approach	<i>P</i> value
Age (years) ^a	40.35±1.92	39.87±2.05	0.319
BMI ^a	32.93±1.26	32.47±1.38	0.161
Previuos IVF failure [n (%] ^b	26 (83.87)	31 (79.49)	0.639

alndependent samples t test was used. Pearson χ^2 test was used.

Table 2 Distribution of women in both groups according to the degree of visualization using both ultrasound approaches

		- 11	
	Group 1 (<i>N</i> =31): transrectal approach [<i>n</i> (%)]	Group 2 (<i>N</i> =39): transabdominal approach [<i>n</i> (%)]	P value
Both the endometrial thickness and the catheter tip were clearly visualized (A)	25 (80.64)	7 (17.95)	
Only the endometrial thickness was visualized, while the catheter tip could not be determined (B)	5 (16.13)	10 (25.64)	<0.001*
Neither the endometrial thickness nor the catheter tip was clearly visualized (C)	1 (3.23)	22 (56.41)	

^{*}Statistically significant at P value less than or equal to 0.05. Pearson χ^2 test was used.

Table 3 Comparisons between both groups regarding visualization and pregnancy rate

	Group 1 (<i>N</i> =31): transrectal approach	Group 2 (<i>N</i> =39): transabdominal approach	P value
Endometrial thickness (mm) ^a	N=30	N=17	0.353
	10 (8–12)	11 (8–12)	
Distance of catheter tip from fundus (mm) ^a	N=25	N=7	0.889
	13 (10–15)	13 (10–15)	
Number of embryos ^a	1 (1–3)	1 (1–3)	0.672
Embryo grade ^a	2 (1–2)	2 (1–2)	0.890
Implantation rate ^b [n (%)]	6/44 (13.64)	4/53 (7.55)	0.326
Chemical pregnancy rate ^b [n (%)]	6 (19.35)	4 (10.26)	0.280
Clinical pregnancy rate ^b [n (%)]	6 (19.35)	3 (7.69)	0.148

^aMann–Whitney test was used. ^bPearson χ² test was used.

Traditionally, ET has been performed blindly. Any additional measures that may improve the optimal deposition of the transferred embryos should be investigated for validity. Many published data showed that the use of abdominal ultrasound resulted in a better pregnancy rate, especially for clinicians starting their careers [17]. Ultrasound-guided transfer can emphasize the proper positing of the embryo inside the uterine cavity [17,18]. Catheter placement at the time of transfer needs experience and clear visualization of the catheter tip as embryos placed too high in the cavity may increase the risk of endometrial trauma, which in turn may cause uterine contractions, with potentially adverse effects [1].

The ultrasound scan can help not only with access to the cavity in cases of tortuosity of the cervical canal but also in depositing the embryo at the appropriate place at mid-uterine cavity. Where alternative access to the cavity is required, the procedure would not be possible without ultrasound guidance [19]. Embryos placed properly under clear visualization are identified as air bubbles containing the embryos expelled from the catheter recognized as bright echoes on the ultrasound, with attempt not to touch the uterine fundus [20].

A systemic review and a meta-analysis in 2018 based on the results of only three randomized trials stated that the quality of evidence supporting the equivalence of transvaginal versus transabdominal approach in clinical pregnancy and ongoing or live birth rates is not enough and that more studies are needed to explore the superiority of TVUS [21].

In our opinion, using the transvaginal route is technically difficult, as the speculum needs to be removed before the probe introduction to the vagina that could affect the outer sheath previously placed,

which in turn needs further readjustment. This process is time consuming and causes more manipulation within the cervical canal, leading to possible uterine contractions. For those causes, we started to study the transrectal ultrasound approach as an alternative during ET especially in obese women with POR to get a better outcome from the few number of embryos available.

When we compared the two groups regarding the quality of clear visualization, the endometrial thickness was clearly visualized in 30 (96.77%) women of group 1 (transrectal approach) and in 17 (43.59%) women of group 2 (transabdominal approach), whereas the catheter tip was clearly visualized in 25 (80.64%) women of group 1 and in seven (17.95%) women of group 2. The differences statistically significant (P<0.001). implantation, chemical pregnancy, and clinical pregnancy rate in group 1 were almost double those in group 2. However, there was no significant difference between both groups, which may be attributed to the small sample size.

There were concerns that transrectal ultrasound would probably be the cause of trauma to the rectum. However, Ludwig et al. [22] stated that during rectoscopy, the occurrence of rectal lesions is rare. Hence, a transrectal ultrasound performed by introducing the probe through the anal sphincter into the rectal canal does not seem to result in injuries [5]. So, we thought transrectal ultrasound would offer a reasonable alternative. After proper patient selection and counseling, transrectal ultrasound provides images better than TAUS and comparable to those obtained by TVUS [23].

The transrectal route has an advantage that the operator could be able to hold the probe by himself to visualize clearly the catheter tip during ET with better hand-eye coordination. On the contrary, ET

under TAUS guidance needs an extra well-trained person to hold the probe. Moreover, the TVUS is done with an empty urinary bladder, whereas the TAUS is done with a full bladder, which is time consuming and also causes abdominal discomfort and uterine cramps, leading to increased patient anxiety [24]. Theoretically, embryo expulsion could

happen, thus decreasing the implantation and

pregnancy rates [25].

We searched the literature and did not find any studies, except for a very few research works that studied the use of transrectal ultrasound in gynecology and assisted reproductive techniques [5,6]. As transrectal ultrasound is comparable to TVUS, we compared our work to those done using TVUS.

Hassan *et al.* [26] compared 400 obese women who had a TVUS to another 400 obese women who had TAUS-guided ET, and they showed a prominent superior role of TVUS-guided ET over TAUS in obese participants. Sohan *et al.* [27] published a case report on the use of transrectal ultrasound for ET in obese women. They stated that transrectal ultrasound offers an excellent view of the endometrium, comparable to TVUS. They also reported another potential privilege of this route is that a full bladder is not required, as with TAUS, reducing patient anxiety and discomfort. According to their experience, some patients are fearful of emptying their bladders directly after ET as they think that this may cause embryos to be expulsed.

Nakano *et al.* [28] and his coworkers found women who had fresh ET guided by TVUS-guided had significantly better pregnancy rates than those who had the procedure guided by the TAUS in the subgroups of women aged 36–39 years and more than or equal to 40 years. Nevertheless, in women aged less than or equal to 35 years, pregnancy rates did not show a significant difference.

In contrast to our findings, Karavani *et al.* [24] and Samy *et al.* [29] performed a randomized, prospective trial on infertile couples and found no significant difference between TVUS-guided and TAUS-guided ET in terms of the clinical pregnancy rate. Despite taking a longer time, the TVUS-guided ET reduces patient discomfort and better endometrial visualization during ET.

The limitation against our study was the patient selection, especially in the era of COVID-19 as well as patient acceptance to perform the transrectal ultrasound as an alternative to TAUS. The

psychological issue in the patient's unease sensation of the ultrasound probe transrectally misleads us in evaluating whether this procedure is painful or not. That is why we could not get an opinion regarding the pain perception of the patient. We consider this as a point of weakness in our study. However, the strong points in our study are the good visualization of the site of the embryo placement in the uterus which is very reassuring for both the patient and the operator. Another point of strength is that it is one of the first studies that evaluated the possible role of transrectal ultrasound in assisted reproductive techniques. Moreover, we targeted the obese poor responder women who have many challenging factors that need to be studied to optimize their pregnancy rates.

Conclusion

The results of our study showed that performing the ET under transrectal ultrasound guidance may emphasize a better-quality image, resulting in improvement in both pregnancy and implantation rates. Another privilege of the transrectal route is that the clinician could be able to hold the probe by himself to see the tip of the catheter at the time of ET with better hand-eye coordination.

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Author's contribution: All authors have read and approved the final manuscript. Sameh Salama: research idea, study design, manuscript writing, and data collection. Kareem El-Nahhas: manuscript writing and data collection. Mazen A. Rasheed: data analysis, manuscript writing, and data collection. Ehab Salama: study design, data analysis, manuscript writing, and data collection.

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Conflicts of interest

There are no conflicts of interest.

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