# Effects of Half-Dose and Full-Dose GnRH Antagonists on IVF-ET Outcomes: A Retrospective Study

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# Abstract

Background

Gonadotropin-releasing hormone antagonist(GnRH-ant) has been shown to have a negative effect on endometrial receptivity. Therefore, the use of GnRH-ant dose as small as possible during controlled ovarian stimulation(COS) may has an impact on improving endometrial receptivity and pregnancy rate. However, the GnRH-ant dose is relatively flexible and there is no fixed requirement for guidance. In this retrospective study, we tried to study the effects of half-dose or full-dose GnRH-ant on IVF-ET outcomes.

Methods

Of the 316 cycles for 314 patients analyzed in this study, 149 received half-dose GnRH-ant(Group1) and 167 received full-dose GnRH-ant(Group2). According to age and BMI, the two groups were divided into four subgroups. Age subgroups, they were divided into age≤35(subgroupA)and age>35(subgroupB): 180 cycles in subgroup A(107 cycles in subgroupA1,73 cycles in subgroupA2), 136 cycles in subgroup B(42 cycles in subgroup B1,94 cycles in subgroupB2). BMI subgroups, they were divided into BMI<25 (subgroupC)and BMI≥25 (subgroupD):208 cycles in subgroupC(94 cycles in subgroup C1,114 cycles in subgroupC2), 108 cycles in subgroupD (55 cycles in subgroupD1,53 cycles in subgroupD2).

Results

Neither fertilized oocytes and the number of superior-quality embryos nor clinical pregnancy rate and live production rate significantly differed between the two groups. However, the number of retrieved oocytes and available embryos were significantly larger in Group 1 than in Group 2 (8.17±4.10vs.7.07±4.05,2.96±2.03vs.2.52±1.62, respectively,p□0.05). Indicators in each age subgroups showed no statistical significance.However, in BMI subgroups, neither fertilized oocytes, available embryos and the number of superior-quality embryos nor live production rate significantly differed between the four subgroups. The number of retrieved oocytes was higher in subgroupC1 than in subgroupC2 (8.24±4.04vs.6.83±3.92,p < 0.05), In addition the clinical pregnancy rate was slightly higher in subgroupD1 than in subgroupD2(45.45vs.24.53%,P< 0.05).

Conclusions

The results showed that half-dose GnRH-ant was as effective as full-dose GnRH-ant for most patients. And patients with BMI≥25 may be more suitable for half-dose GnRH-ant. This retrospective analysis and the small sample size are the main limitations of this study, and a large sample RCT will be carried out in the future.

Trial registration

Retrospectively registered

# Background

In recent years, the gonadotropin-releasing hormone antagonist (GnRH-ant) protocol has gained more and more clinical recognition due to its lack of early pituitary inhibition, low dosage, short days of administration, no flare up in the initial stage of administration, more in line with the physiological process, and reducing the risk of ovarian hyperstimulation syndrome (OHSS)[1].However, many studies have shown that the antagonist program will have a certain impact on the endometrium and interfere with the embryo implantation window[2]. In general, conventional dose is the daily GnRH-ant dose to 0.25mg[3]. But some people also use the daily GnRH-ant dose to 0.125mg.The dosage is relatively flexible.Therefore, we compared the pregnancy rate and live birth rate of ovulation induction patients with different dosage of antagonists, and explored the effect of the dosage of antagonists on the outcome of IVF-ET.

# Methods

### Patients

In this retrospective study, we obtained data of patients who

received the GnRH-ant protocol for IVF-ET/ ICSI from January 2015 to

December 2020 at the Reproductive Medical Center of Hospital of Shandong University of traditional Chinese medicine. Approval from the institutional review board was obtained for the analysis of this series. **Inclusion/Exclusion Criteria**

The inclusion criteria were as follows: (a) both husband and wife have IVF / ICSI treatment indications, (b) signed informed consents,[4](c) basal serum FSH < 15 IU/L.The exclusion criteria were as follows: (a) chromosomal aberration in either the mother or father,(b) thyroid disease, endometriosis or immune disease.

### Groups According to Different GnRH-Ant Protocols

Patients were divided into two groups according to the usage of Cetrorelix:Group 1 (n = 149) initially received 0.125 mg of Cetrorelix per day. The patientsin Group 1 were further divided into four subgroups depending on age (subgroup A,age≤35;subgroup B,age35) and BMI (subgroup C,BMI25;subgroup D,BMI≥25) for these patients. Group 2 (n = 167) initially received 0.25 mg of Cetrorelix per day. The four subgroups are the same as above.Nothing else was changed during COS

between the two groups except for the Cetrorelix usage.

### IVF-ET Procedure

The stimulation was initiated on menstrual day 2-3, and all the patients were administered recombinant FSH (Gonal-F , Merck- Serono SA, Switzerland). The initial gonadotropin dose was experientially determined by doctors according to age, antral follicle count (AFC), basal FSH, E2levels, and body mass index (BMI), and typically ranged from 150 to 300 U per day. This dose was adjusted every 2–3 days of stimulation

depending on the ovarian response evidenced by the E2levels,LHlevels and follicular growth detected under ultrasound examination. Then when the diameter of follicle is≥14 mm , or the dominant follicle diameter was more than 12mm and serum E2 > 300pg/ml, the patients received the GnRH-ant Cetrorelix acetate(Cetrotide, Merck-Serono SA, Switzerland) 0.125 mg/d or 0.25mg/d.Finally, 10000 IU of human chorionic gonadotropin (hCG; Lizhu, Zhuhai, China) or 250 IU of recombinant human choriogonadotropinalfa solution (OVIDREL;Merck-Serono SA, Switzerland)was administered when two follicles reached a mean diameter of 17 mm or one follicles reached a mean diameter of 18 mm. Oocyte retrieval was performed 35–36 h after hCG or OVIDREL injection by transvaginal ultrasound-guided single-lumen needle aspiration. Intracytoplasmic sperm injection (ICSI) was performed only in case of severe male factor infertility.Oocyte culture, insemination, embryo transfer, and cryopreservation were done as previously described.[5]Embryo transfer was conducted on day 3 after oocyte retrieval. All the patients received embryo transfer on day 3, except in the following cases: (a) serum estrogen >5,007 pg/mL on the trigger day, (b) more than 15 oocytes were retrieved, (d) the presence of uterine or endometrial abnormalities such as endometriosis, uterine myoma, endometrial polyps, or intrauterine adhesion, (e) an initial increase of progesterone over 1.5 ng/mL before the trigger day [6], or (f) the patient refused fresh embryo transfer. A maximum of two embryos were transferred. During luteal phase, 20 mg progesterone injection was injected twice a day from the first day after oocyte retrieval.Clinical pregnancy was determined by visualizing a gestational sac on ultrasound at 6 weeks of gestation. Live birth was defined as having at least one live baby born after 28 weeks of gestation. Live birth rate refered to the percentage of women who gave birth live in a fresh transplant cycle.[7]

### Statistical Analysis

Data were analyzed using SPSS version 18.0 (IBM). Frequency for qualitative variables, and the means and standard deviation for quantitative variables were calculated.The chi-square test and Fisher’s exact test and the Student’st-test for independent samples were used. Statistical significance was defined as $p < 0.05$.

# Results

**Table 1** presents the demographic characteristics of both groups. There were no significant differences in the baseline characteristics, including age; BMI; Years of infertility; and basal FSH and LH between the two groups.

**Table 2-3** presents the demographic characteristics of four subgroups. There were no significant differences in the baseline characteristics, including age; BMI; Years of infertility; and basal FSH and LH between the four subgroups.

As shown in **Table 4**,Gonadotropin consumption was significantly lower (2200.34±915.54 IU vs. 2571.68±905.58 IU, $p < 0.001$) and the

stimulation duration, the number of retrieved oocytes and available embryos were significantly larger(9.59±2.12 vs. 9.01±2.67, $p = 0.036$;8.17±4.10 vs. 7.07±4.05, $p = 0.017$;2.96±2.03 vs. 2.52±1.62, $p = 0.036$) in Group 1 than in Group 2, while the usage days of Cetrorelix did not significantly differ between the groups. Meanwhile, fertilized oocytes and the number of superior-quality embryos did not significantly differ between the two groups.

As shown in **Table 5,**Gonadotropin consumption was significantly lower (2201.40±896.53 IU vs. 2498.29±811.80 IU,2197.62±973.51 IU vs. 2628.67±972.67 IU, $p < 0.05$) in subgroup A1/B1 than in subgroup A2/B2.Furthermore,the number of retrieved oocytes, fertilized oocytes, available embryos and the number of uperior-quality embryos did not significantly differ between the two same subgroups.

As shown in **Table 6,**Gonadotropin consumption was significantly lower (2073.14±934.23 IU vs. 2452.26±896.32 IU,2417.73±847.28 IU vs. 2828.54±879.56 IU, $p < 0.05$) in subgroup C1/D1 than in subgroup C2/D2.However, the number of retrieved oocytes was significantly larger(8.24±4.04 vs. 6.83±3.92, $p = 0.012$) in subgroup C1 than in subgroup C2.

As shown in **Table 7**, there was a total of 316 fresh embryo transfer cycles: 149 in Group 1 and 167 in Group 2. The clinical pregnancy rate (36.2 vs. 37.1%) and live production rate(30.20 vs. 31.74%)were slightly higher in Group 2 than in Group 1, but the differences were not significant. The incidence of OHSS was not analyzed because some of the patients did not received fresh embryos in order to avoid OHSS.

As shown in **Table 8**, in four subgroups grouped by age, the clinical pregnancy rate (44.86 vs. 38.36%) was slightly higher in subgroup A1 than in subgroup A2, but the difference was not significant. On the contrary, live production rate(35.51 vs. 35.62%)were slightly lower in subgroup A1 than in subgroup A2, but the difference was also not significant. However, for the elderly group older than 35, the clinical pregnancy rate (21.43 vs. 37.23%) and live production rate(16.67 vs. 28.72%)were slightly higher in subgroup B2 than in subgroup B1, but the differences were not significant.

As shown in **Table 9**, there was a total of 208 fresh embryo transfer cycles in the BMI below 25 group: 94 in subgroup C1 and 114 in subgroup C2. the clinical pregnancy rate (34.04 vs. 43.86%) and live production rate(27.66 vs. 35.96%)were slightly lower in subgroup C1 than in subgroup C2, but the differences were not significant. However, in the group with BMI greater than or equal to 25, the results were just the opposite. The clinical pregnancy rate (45.45 vs. 24.53%, P=0.023) and live production rate(34.55 vs. 22.64%)were slightly higher in subgroup D1 than in subgroup D2.At the same time, the difference of clinical pregnancy rate was significant.

# Discussion

GnRH antagonist does not need pituitary down regulation before ovulation induction. Compared with GnRH agonist regimen, GnRH antagonist regimen has many advantages, such as milder stimulation and shorter time.[8] In recent years, more and more antagonists have been used in IVF / ICSI ovulation induction therapy. Although it is still controversial, the pregnancy rate achieved with GnRH-ant protocol has been considered to be lower than that achieved with GnRH-agonist protocol, and the impaired endometrial receptivity has been thought of the main cause for this difference. Many articles have also pointed out that the factors influencing the outcome of IVF-ET with antagonist regimen are the patient's age and BMI.[9,21] Doctors in reproductive health services have attempted to achieve satisfactory pregnancy outcomes by reducing the GnRH-ant dose. However, there is no clear requirement for the dosage of antagonists. Currently, 0.25mg of Cetrorelix per day from day 6 of stimulation is considered the standard GnRH-ant protocol, and the LH level can be maintained within the safe range with this protocol. Some other studies have reported that reducing the GnRH-ant dose to 0.125–0.2 mg per day is also effective.[10,22] Therefore, we compared IVF-ET outcomes in patients with 0.125mg and 0.25mg daily in an attempt to find a more appropriate dose.

First, we found there were no differences in terms of fertilized oocytes and superior-quality embryos between the two groups. However, there were significant differences in the number of retrieved oocytes and available embryos between the two groups. The dosage of 0.125 mg per day group was better than that of 0.25 mg per day group.

In addition, compared with group 2, the stimulation time of GnRH-Ant in group 1 was significantly shorter. Many studies have reported that GnRH-Ant has adverse effects on endometrial receptivity, [11,12] and some previous studies also found that antagonists led to an increase in uterine natural killer (UNK) cells and inflammatory factors such as perforin and tumor necrosis factor α (TNFα) with increasing doses. [13,14] Furthermore, prolonged ovarian stimulation was associated with a decreased rate of superior-quality embryos and live birth rates.[15-17]In this present study, the clinical pregnancy rate and live production rate were all lower in Group 1 than in Group 2, although this difference was not statistically significant. This is a little different from previous studies.[18] But the difference between the two data is not big. We assumed that this may be because the number of cases of this retrospective study is insufficient. A multicenter randomized controlled study will be performed in the next step.

Second, there was no difference the number of retrieved oocytes, fertilized oocytes, available embryos, the number of superior-quality embryos, the clinical pregnancy rate and live production rate among the four subgroups of age group, suggesting that the age might not be an important impact factor for the selection of the GnRH-ant dose.

Third, different from the age group, in the four subgroups of BMI group, in the comparison of the two subgroups with BMI less than 25(subgroup C), it was found that the number of oocytes retrieved in the 0.125 mg group(subgroup C1) was much higher than that in the 0.25 mg group(subgroup C2). At the

same time, the difference between the two subgroups was significant. In addition, the clinical pregnancy rate of 0.125 mg subgroup(subgroup D1) was higher than that of 0.25 subgroup(subgroup D2) in the group of BMI than or equal to 25(subgroup D). And the difference between the two subgroups was significant. So we guess that the BMI might be an important impact factor for the selection of the GnRH-ant dose.Although, Engel et al. showed that body weight did not affect the plasma concentration of Cetrorelix, and they suggested that there was no need to modify the dose for individuals of different body weights during COS[19], a few studies have suggested that it is appropriate to reduce the GnRH-ant dose for slim patients[20].

# Conclusion

In conclusion, the results of this present study revealed that GnRH-ant 0.125 mg per day was an advantageous antagonist for patients with BMI greater than or equal to 25. For other patients, the outcomes of GnRH-ant, 0.125mg per day and 0.25mg per day, were not different in this study. In consideration of the impact on endometrium and economic aspects, 0.125 mg daily dose of antagonist is recommended. The retrospective analysis and the small sample size are the main limitations of this study, and a large sample size RCT will be conducted in the next step.

# Declarations

### Ethics approval and consent to participate

This retrospective analysis was approved by the Institutional Review Board and the Institutional Ethics Committee of the Reproductive Medical Center of Hospital of Shandong University of traditional Chinese medicine (Research Ethics Committee reference number: 2021-16).All methods were carried out in accordance with relevant guidelines and regulations, and we consent to participate. Informed consent was obtained from all the participants involved in the study.

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.

### Consent for publication

Not applicable

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### Authors' contributions

YZ conducted the analysis and wrote the manuscript.YQ conducted the analysis and wrote the manuscript.YY statistically analyzed the data.CP and FL were involved in patient recruitment and treatment.SX supervised the study concept and reviewed the manuscript. FL was involved in the patient's treatment, conceived the analysis, and reviewed the manuscript.All authors read and approved the final manuscript.

### Acknowledgements

Not applicable

### Study participants

Consent to participate

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# Tables

**Table 1 presents the demographic characteristics of both groups. There were no significant differences in the baseline characteristics, including age; BMI; Years of infertility; and basal FSH and LH between the two groups**

| **Groups** | Group1 (n = 149) | Group2 (n = 167) | P |
|---|---|---|---|
| Age (years) | 32.56±3.54 | 33.22±3.55 | 0.104 |
| Years of infertility | 3.31±2.46 | 3.54±3.53 | 0.498 |
| Body mass index | 24.16±4.38 | 23.94±4.37 | 0.658 |
| bFSH/bLH | 1.80±1.14 | 2.03±1.76 | 0.195 |

*Data expressed as mean ± SD, or number (percentage).

**Table 2 presents the demographic characteristics of four subgroups. There were no significant differences in the baseline characteristics, including age; BMI; Years of infertility; and basal FSH and LH between the four subgroups.**

| **Subgroup** | Subgroup A1(n = 107) | Subgroup A2(n = 73) | Subgroup B1(n = 42) | Subgroup B2(n = 94) | P |
|---|---|---|---|---|---|
| Years of infertility | 2.96±1.82 | 3.29±1.97 | 4.14±3.48 | 3.79±4.39 | 0.05 |
| Body mass index | 23.77±4.79 | 22.75±5.48 | 24.10±3.24 | 23.85±5.81 | 0.05 |
| bFSH/bLH | 1.83±1.14 | 2.06±2.01 | 1.80±1.14 | 1.93±1.53 | 0.05 |

*Subgroup A1Subgroup A2 basic data p values were0.2570.1870.319

*Subgroup B1Subgroup B2 basic data p values were0.6440.7930.618

*Data expressed as mean ± SD, or number (percentage).

**Table 3 presents the demographic characteristics of four subgroups. There were no significant differences in the baseline characteristics, including age; BMI; Years of infertility; and basal FSH and LH between the four subgroups.**

| **Subgroup** | Subgroup C1(n = 94) | Subgroup C2(n = 114) | Subgroup D1(n = 55) | Subgroup D2(n = 53) | P |
|---|---|---|---|---|---|
| Years of infertility | 3.44±2.58 | 3.12±2.19 | 3.05±2.22 | 4.53±5.32 | 0.05 |
| Age (years) | 33.62±4.44 | 34.32±4.05 | 32.95±5.37 | 34.64±4.35 | 0.05 |
| bFSH/bLH | 1.77±1.05 | 2.09±1.90 | 1.91±1.27 | 1.80±1.38 | 0.05 |

*Subgroup C1Subgroup C2 basic data p values were0.3440.2370.140

*Subgroup D1Subgroup D2 basic data p values were0.0660.0750.683

*Data expressed as mean ± SD, or number (percentage).

**Table 4 Gonadotropin consumption was significantly lower (2200.34±915.54 IU vs. 2571.68±905.58 IU, p < 0.001) and the stimulation duration, the number of retrieved oocytes and available embryos were significantly larger(9.59±2.12 vs. 9.01±2.67, p = 0.036;8.17±4.10 vs. 7.07±4.05, p = 0.017;2.96±2.03 vs. 2.52±1.62, p = 0.036) in Group 1 than in Group 2, while the usage days of Cetrorelix did not significantly differ between the groups. Meanwhile, fertilized oocytes and the number of superior-quality embryos did not significantly differ between the two groups.**

| **Groups** | Group1 (n = 149) | Group2 (n = 167) | P |
|---|---|---|---|
| Cetrorelix usage days | 3.44±1.52 | 3.72±1.71 | 0.115 |
| Gn usage days | 9.59±2.12 | 9.01±2.67 | 0.036 |
| Gn total | 2200.34±915.54 | 2571.68±905.58 | 0.000 |
| retrieved oocytes | 8.17±4.10 | 7.07±4.05 | 0.017 |
| fertilized oocytes | 4.89±3.06 | 4.47±3.00 | 0.220 |
| available embryos | 2.96±2.03 | 2.52±1.62 | 0.036 |
| superior-quality embryos | 0.80±1.15 | 0.73±0.97 | 0.568 |

*Data expressed as mean ± SD, or number (percentage).

**Table 5 Gonadotropin consumption was significantly lower (2201.40±896.53 IU vs. 2498.29±811.80 IU,2197.62±973.51 IU vs. 2628.67±972.67 IU, p < 0.05) in subgroup A1/B1 than in subgroup**

**A2/B2.Furthermore,the number of retrieved oocytes, fertilized oocytes, available embryos and the number of uperior-quality embryos did not significantly differ between the two same subgroups.**

| **Subgroup** | Subgroup A1(n = 107) | Subgroup A2(n = 73) | Subgroup B1(n = 42) | Subgroup B2(n = 94) | P |
|---|---|---|---|---|---|
| Cetrorelix usage days | 3.52±1.57 | 3.68±1.68 | 3.21±1.39 | 3.76±1.73 | 0.05 |
| Gn usage days | 9.71±1.81 | 9.52±2.83 | 9.29±2.76 | 8.62±2.51 | 0.05 |
| Gn total | 2201.40±896.53 | 2498.29±811.80 | 2197.62±973.51 | 2628.67±972.67 | 0.05 |
| retrieved oocytes | 8.37±4.21 | 9.07±3.95 | 5.88±3.57 | 6.06±3.63 | 0.05 |
| fertilized oocytes | 5.38±3.12 | 5.16±3.31 | 3.64±2.51 | 3.94±2.64 | 0.05 |
| available embryos | 2.85±1.81 | 3.21±2.24 | 2.33±1.20 | 2.27±1.42 | 0.05 |
| superior-quality embryos | 0.86±1.27 | 0.73±0.93 | 0.64±0.76 | 0.73±1.00 | 0.05 |

*Subgroup A1Subgroup A2 experimental data P values were0.5100.5840.0220.2530.6530.2590.443

*Subgroup B1Subgroup B2 experimental data P values were0.0770.1660.0180.7860.5440.7900.598

*Data expressed as mean ± SD, or number (percentage).

**Table 6 Gonadotropin consumption was significantly lower (2073.14±934.23 IU vs. 2452.26±896.32 IU,2417.73±847.28 IU vs. 2828.54±879.56 IU, p < 0.05) in subgroup C1/D1 than in subgroup C2/D2.However, the number of retrieved oocytes was significantly larger(8.24±4.04 vs. 6.83±3.92, p = 0.012) in subgroup C1 than in subgroup C2.**

| Subgroup | Subgroup C1(n = 94) | Subgroup C2(n = 114) | Subgroup D1(n = 55) | Subgroup D2(n = 53) | P |
|---|---|---|---|---|---|
| Cetrorelix usage days | 3.35±1.50 | 3.63±1.60 | 3.58±1.55 | 3.92±1.91 | 0.05 |
| Gn usage days | 9.28±1.79 | 8.86±2.93 | 10.13±2.52 | 9.34±2.06 | 0.05 |
| Gn total | 2073.14±934.23 | 2452.26±896.32 | 2417.73±847.28 | 2828.54±879.56 | 0.05 |
| retrieved oocytes | 8.24±4.04 | 6.83±3.92 | 8.05±4.22 | 7.58±4.31 | C 0.05<br>D 0.05 |
| fertilized oocytes | 5.00±2.94 | 4.35±2.83 | 4.71±3.26 | 4.74±3.36 | 0.05 |
| available embryos | 3.02±2.04 | 2.61±1.65 | 2.85±2.03 | 2.34±1.56 | 0.05 |
| superior-quality embryos | 0.79±0.98 | 0.70±0.94 | 0.82±1.40 | 0.79±1.03 | 0.05 |

*Subgroup C1Subgroup C2 experimental data P values were0.1980.2290.0030.0120.1070.1060.523

*Subgroup D1Subgroup D2 experimental data P values were0.3070.7880.0150.5680.9670.1430.914

*Data expressed as mean ± SD, or number (percentage).

**Table 7 there was a total of 316 fresh embryo transfer cycles: 149 in Group 1 and 167 in Group 2. The clinical pregnancy rate (36.2 vs. 37.1%) and live production rate(30.20 vs. 31.74%)were slightly higher in Group 2 than in Group 1, but the differences were not significant. The incidence of OHSS was not analyzed because some of the patients did not received fresh embryos in order to avoid OHSS.**

| Groups | Group1 (n = 149) | Group2 (n = 167) | P |
|---|---|---|---|
| clinical pregnancy rate | 36.20% | 37.10% | 0.871 |
| live production rate | 30.20% | 31.74% | 0.768 |

*Data expressed as mean ± SD, or number (percentage).

**Table 8 in four subgroups grouped by age, the clinical pregnancy rate (44.86 vs. 38.36%) was slightly higher in subgroup A1 than in subgroup A2, but the difference was not significant.**

| Subgroup | Subgroup A1(n = 107) | Subgroup A2(n = 73) | Subgroup B1(n = 42) | Subgroup B2(n = 94) | P |
|---|---|---|---|---|---|
| clinical pregnancy rate | 44.86% | 38.36% | 21.43% | 37.23% | 0.05 |
| live production rate | 35.51% | 35.62% | 16.67% | 28.72% | 0.05 |

*Subgroup A1Subgroup A2 pregnancy outcome P values were0.3860.989

*Subgroup B1Subgroup B2 pregnancy outcome P values were0.0690.134

*Data expressed as mean ± SD, or number (percentage).

**Table 9 there was a total of 208 fresh embryo transfer cycles in the BMI below 25 group: 94 in subgroup C1 and 114 in subgroup C2.**

| Subgroup | Subgroup C1(n = 94) | Subgroup C2(n = 114) | Subgroup D1(n = 55) | Subgroup D2(n = 53) | P |
|---|---|---|---|---|---|
| clinical pregnancy rate | 34.04% | 43.86% | 45.45% | 24.53% | C 0.05<br>D 0.05 |
| live production rate | 27.66% | 35.96% | 34.55% | 22.64% | 0.05 |

*Subgroup C1Subgroup C2 pregnancy outcome P values were0.1490.202

*Subgroup D1Subgroup D2 pregnancy outcome P values were0.0230.172

*Data expressed as mean ± SD, or number (percentage).